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Aripiprazole versus other atypical antipsychotics for schizophrenia (Review)

Khanna P, Suo T, Komossa K, Ma H, Rummel-Kluge C, El-Sayeh HG, Leucht S, Xia J

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Aripiprazole versus other atypical antipsychotics for schizophrenia

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ABSTRACT

Background

In most western industrialised countries, second generation (atypical) antipsychotics are recommended as first-line drug treatments for people with schizophrenia. In this review, we specifically examine how the efficacy and tolerability of one such agent - aripiprazole - differs from that of other comparable second generation antipsychotics.

Objectives

To review the effects of aripiprazole compared with other atypical antipsychotics for people with schizophrenia and schizophrenia-like psychoses.

Search methods

We searched the Cochrane Schizophrenia Group Trials Register (November 2012), inspected references of all identified studies for further trials and contacted relevant pharmaceutical companies, drug approval agencies and authors of trials for additional information.

Selection criteria

We included all randomised clinical trials (RCTs) comparing aripiprazole (oral) with oral and parenteral forms of amisulpride, clozapine, olanzapine, quetiapine, risperidone, sertindole, ziprasidone or zotepine for people with schizophrenia or schizophrenia-like psychoses.

Data collection and analysis

We extracted data independently. For dichotomous data we calculated risk ratios (RR) and their 95% confidence intervals (CI) on an intention-to-treat basis based on a random-effects model. Where possible, we calculated illustrative comparative risks for primary outcomes. For continuous data, we calculated mean differences (MD), again based on a random-effects model. We assessed risk of bias for each included study and used GRADE approach to rate quality of evidence.

Main results

We now have included 174 trials involving 17,244 participants. Aripiprazole was compared with clozapine, quetiapine, risperidone, ziprasidone and olanzapine. The overall number of participants leaving studies early was 30% to 40%, limiting validity (no differences between groups).

When compared with clozapine, there were no significant differences for global state (no clinically significant response, $n = 2132$, 29 RCTs, *low quality evidence*); mental state (BPRS, $n = 426$, 5 RCTs, *very low quality evidence*); or leaving the study early for any reason ($n = 240$, 3 RCTs, *very low quality evidence*). Quality of life score using the WHO-QOL-100 scale demonstrated significant difference, favouring aripiprazole ($n = 132$, 2 RCTs, RR 2.59 CI 1.43 to 3.74, *very low quality evidence*). General extrapyramidal symptoms (EPS) were no different between groups ($n = 520$, 8 RCTs, *very low quality evidence*). No study reported general functioning or service use.

When compared with quetiapine, there were no significant differences for global state ($n = 991$, 12 RCTs, *low quality evidence*); mental state (PANSS positive symptoms, $n = 583$, 7 RCTs, *very low quality evidence*); leaving the study early for any reason ($n = 168$, 2 RCTs, *very low quality evidence*), or general EPS symptoms ($n = 348$, 4 RCTs, *very low quality evidence*). Results were significantly in favour of aripiprazole for quality of life (WHO-QOL-100 total score, $n = 100$, 1 RCT, MD 2.60 CI 1.31 to 3.89, *very low quality evidence*). No study reported general functioning or service use.

When compared with risperidone, there were no significant differences for global state ($n = 6381$, 80 RCTs, *low quality evidence*); or leaving the study early for any reason ($n = 1239$, 12 RCTs, *very low quality evidence*). Data were significantly in favour of aripiprazole for improvement in mental state using the BPRS ($n = 570$, 5 RCTs, MD 1.33 CI 2.24 to 0.42, *very low quality evidence*); with higher adverse effects seen in participants receiving risperidone of general EPS symptoms ($n = 2605$, 31 RCTs, RR 0.39 CI 0.31 to 0.50, *low quality evidence*). No study reported general functioning, quality of life or service use.

When compared with ziprasidone, there were no significant differences for global state ($n = 442$, 6 RCTs, *very low quality evidence*); mental state using the BPRS ($n = 247$, 1 RCT, *very low quality evidence*); or leaving the study early for any reason ($n = 316$, 2 RCTs, *very low quality evidence*). Weight gain was significantly greater in people receiving aripiprazole ($n = 232$, 3 RCTs, RR 4.01 CI 1.10 to 14.60, *very low quality evidence*). No study reported general functioning, quality of life or service use.

When compared with olanzapine, there were no significant differences for global state ($n = 1739$, 11 RCTs, *very low quality evidence*); mental state using PANSS ($n = 1500$, 11 RCTs, *very low quality evidence*); or quality of life using the GQOLI-74 scale ($n = 68$, 1 RCT, *very low quality of evidence*). Significantly more people receiving aripiprazole left the study early due to any reason ($n = 2331$, 9 RCTs, RR 1.15 CI 1.05 to 1.25, *low quality evidence*) and significantly more people receiving olanzapine gained weight ($n = 1538$, 9 RCTs, RR 0.25 CI 0.15 to 0.43, *very low quality evidence*). None of the included studies provided outcome data for the comparisons of 'service use' or 'general functioning'.

Authors' conclusions

Information on all comparisons is of limited quality, is incomplete and problematic to apply clinically. The quality of the evidence is all low or very low. Aripiprazole is an antipsychotic drug with an important adverse effect profile. Long-term data are sparse and there is considerable scope for another update of this review as new data emerge from ongoing larger, independent pragmatic trials.

PLAIN LANGUAGE SUMMARY

Aripiprazole versus other atypical antipsychotics

In many countries in the industrialised world there has been a huge growth in the prescription of medication for people with mental health problems, taken orally as a tablet or by injection. Atypical and second generation antipsychotic drugs have become ever more popular, because they are thought to help people with mental health problems who do not respond quite so well to initial treatment. These newer drugs hold the promise of both reducing symptoms, such as hearing voices or seeing things, and reducing problematic side effects, such as sleepiness, weight gain, and shaking.

However, there is little research and comparison of the ways in which drugs differ from one another. This review examines the effectiveness of aripiprazole with other new antipsychotics.

Originally the review included 12 research trials. After an update search carried out in November 2012, 162 trials were added. Most of these trials were from China and although new data were added to the review, overall conclusions did not change. The review now has five comparisons with aripiprazole being compared with clozapine, olanzapine, quetiapine, risperidone and ziprasidone.

For people with schizophrenia it may be important to know that aripiprazole may not be as good or effective as olanzapine but that it has less side effects. Aripiprazole is similar in effectiveness to risperidone and somewhat better than ziprasidone. Aripiprazole had less side-effects than olanzapine and risperidone (such as weight gain, sleepiness, heart problems, shaking and increased cholesterol levels). Aripiprazole was not as good as ziprasidone for dealing with restlessness or people's inability to sit still. Comparison with other antipsychotic drugs as a group showed that people preferred taking aripiprazole. However, people with schizophrenia as well as mental health professionals and policy makers should know that the evidence is limited and mostly of low or very low quality. More trials and research is required, including on outcomes such as: quality of life; the views of service users and carers; and patient preference.

This plain language summary has been written by a consumer from Rethink Mental Illness, Benjamin Gray. Email: ben.gray@rethink.org

SUMMARY OF FINDINGS FOR THE MAIN COMPARISON *[Explanation]*

COMPARISON 1. ARIPIPRAZOLE versus CLOZAPINE for schizophrenia						
Patient or population: patients with schizophrenia						
Settings: inpatient and outpatient						
Intervention: COMPARISON 1. ARIPIPRAZOLE versus CLOZAPINE						
Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Control	COMPARISON 1. ARIPIPRAZOLE versus CLOZAPINE				
Global state: No clinically significant response Follow-up: up to 12 weeks	Low ¹		RR 1.05 (0.87 to 1.27)	2132 (29 studies)	⊕⊕○○ low ^{2,3}	
	100 per 1000	105 per 1000 (87 to 127)				
	Moderate ¹					
	150 per 1000	157 per 1000 (131 to 190)				
	High ¹					
	200 per 1000	210 per 1000 (174 to 254)				
Mental state: as measured by BPRS BPRS (high score = poor)		The mean mental state: as measured by BPRS in the intervention groups was 0.22 lower (1.44 lower to 1 higher)		426 (5 studies)	⊕○○○ very low ^{2,3,4,5}	

Leaving the study early - Any reason Follow-up: up to 12 weeks	Low ¹		RR 1.41 (0.46 to 4.29)	240 (3 studies)	⊕○○○ very low ^{2,3}
	0 per 1000	0 per 1000 (0 to 0)			
	Moderate ¹				
	50 per 1000	70 per 1000 (23 to 214)			
	High ¹				
	100 per 1000	141 per 1000 (46 to 429)			
Quality of life: as measured by WHO-QOL-100 WHO-QOL-100 (low score = poor) Follow-up: up to 12 weeks		The mean quality of life: as measured by WHO-QOL-100 in the intervention groups was 2.59 higher (1.43 to 3.74 higher)		132 (2 studies)	⊕○○○ very low ⁶
Adverse effects: extrapyramidal effects Follow-up: up to 12 weeks	Low ¹		RR 1.91 (0.75 to 4.85)	520 (8 studies)	⊕○○○ very low ^{2,3,5}
	0 per 1000	0 per 1000 (0 to 0)			
	Moderate ¹				
	50 per 1000	96 per 1000 (38 to 242)			
	High ¹				
	100 per 1000	191 per 1000 (75 to 485)			

General functioning - not measured	See comment	See comment	Not estimable	-	See comment	No study measured or reported this outcome.
Service use - not measured	See comment	See comment	Not estimable	-	See comment	No study measured or reported this outcome.

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; **RR:** Risk ratio;

GRADE Working Group grades of evidence

High quality: Further research is very unlikely to change our confidence in the estimate of effect.

Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Very low quality: We are very uncertain about the estimate.

¹ Risk: moderate risk approximately equates to that of the control group risk in the study population.

² Risk of bias: rated 'serious' - majority of the included studies had inadequate study design - unclear randomisation, allocation concealment and blinding. Some also had selective reporting concerns.

³ Imprecision: rated 'serious' - most of these included studies are of small samples with small effect size and wide confidence interval. The combined effect was not statistically significant.

⁴ Imprecision: rated 'serious' - we were unable to obtain direct binary measure of mental state, thus used BPRS score as an indicator.

⁵ Publication bias: rated 'strongly suspected' - only a small number of studies favouring intervention group were identified.

⁶ Indirectness: rated 'serious' - we were unable to obtain direct binary measure of quality of life, thus employed WHO-QOL-100 rating score as an indicator.

BACKGROUND

Description of the condition

Schizophrenia is usually a chronic and disabling psychiatric disorder, which afflicts approximately one per cent of the population worldwide, affecting male and female patients in similar proportions. The annual incidence of schizophrenia averages 15 per 100,000 population and the risk of developing the illness over one's lifetime averages 0.7% (Tandon 2008). Its typical manifestations include 'positive' symptoms such as fixed, false beliefs (delusions) and perceptions without cause (hallucinations), 'negative' symptoms such as apathy and lack of drive, disorganisation of behaviour and thought, and catatonic symptoms such as mannerisms and bizarre posturing (Carpenter 1994). The degree of suffering and disability is considerable with 80% to 90% of those affected not working (Marvaha 2004) and up to 10% dying prematurely (Tsuang 1978). In the age group of 15 to 44 years, schizophrenia is among the top 10 leading causes of disease-related disability in the world (WHO 2001). Conventional antipsychotic drugs, such as chlorpromazine and haloperidol, have traditionally been used as first line antipsychotics for people with schizophrenia (Kane 1993). The introduction and subsequent use of clozapine in the United States of America identified that clozapine seemed to be more effective, and was associated with fewer movement disorders than existing agents such as chlorpromazine (Kane 1988). These results boosted the development and marketing of new/second/atypical generation antipsychotics (SGAs).

Description of the intervention

There is no good definition of what constitutes an atypical/second generation antipsychotic, but they were initially said to differ from older generation drugs in that they did not cause movement disorders (catalepsy) in rats at clinically effective doses (Arnt 1998). The terms new or second generation to describe clozapine, a very old drug, are equally poor descriptors. According to treatment guidelines (APA 2004; Gaebele 2006), SGAs include drugs such as amisulpride, aripiprazole, clozapine, olanzapine, quetiapine, risperidone, sertindole, ziprasidone and zotepine. It is unclear whether some old and inexpensive compounds such as sulpiride, perazine or even low-dose chlorpromazine, have similar properties (Möller 2000). High expectations were raised for these SGAs as regards their alleged superiority in a number of areas such as compliance, cognitive functioning, negative symptoms, movement disorders, quality of life and efficacy in treatment-resistant schizophrenia.

How the intervention might work

Aripiprazole is said to be the prototype of a new and third generation of antipsychotics; the so called dopamine-serotonin system stabilisers. It is reported to exert its antipsychotic effects by acting as a partial agonist at D2 dopamine and 5-HT1a serotonin receptors and as an agonist at 5-HT2 serotonin receptors. It has been postulated that through the above receptor site actions, and hence dopamine and serotonin system stabilisation, a partial D2 agonist would be able to act as an antagonist in pathways where an abundance of dopamine was producing psychosis, yet it would stimulate receptors as an agonist at sites in which low dopaminergic tone would produce adverse effects (e.g. areas mediating motor movement and prolactin release (Rivas-Vasquez 2003)). Aripiprazole, however, also has an affinity to other receptors including D3, D4, 5-HT2c, 5HT7, alpha-1 adrenergic and histamine receptors. This may explain adverse effects associated with this compound such as somnolence, headache, gastrointestinal upset and light headedness (FDA 2002). The recommended target dose for aripiprazole is 10-15 mg per day (dose range 10-30 mg/day). Phase III trials were initially conducted in Japan in 1995 and the drug was granted Approved Status by the FDA (USA) on the 15 November 2002 for the treatment of schizophrenia. Aripiprazole has since been licensed in most countries worldwide.

Why it is important to do this review

The debate as to how far the second generation antipsychotic drugs improve these outcomes compared to conventional antipsychotics continues (Duggan 2005) and results from recent studies were sobering (Jones 2006; Lieberman 2005). Nevertheless, in some parts of the world, particularly in western industrialised countries, SGAs have become the mainstay of treatment. Second generation antipsychotics also differ in terms of their costs. Amisulpride and risperidone, for example, are already generic in many countries. Therefore, the question as to whether they differ from each other in their clinical efficacy becomes increasingly important. In this review we aim to summarise evidence from randomised controlled trials comparing aripiprazole with other SGAs. This acts as a continuum to the comparisons previously published by EL-Sayeh 2006, Leucht 2008 and Komossa 2009.

This review was published in early 2013 with a vast number of Chinese studies in awaiting classification, thus we have updated it again in June 2013.

OBJECTIVES

To review the effects of aripiprazole compared with other second generation/atypical antipsychotics for people with schizophrenia.

METHODS

Criteria for considering studies for this review

Types of studies

We included both open and double-blinded, randomised controlled trials. We included open trials as we felt that important data that could potentially have an impact on the results might otherwise be overlooked. Where a trial was described as “double-blind” but it was only implied that the study was randomised, we included these trials in a sensitivity analysis. If there was no substantive difference within primary outcomes (see [Types of outcome measures](#)) when these ‘implied randomisation’ studies were added, then we included these in the final analysis. If there was a substantive difference, we only used clearly randomised trials and described the results of the sensitivity analysis in the text. We excluded quasi-randomised studies, such as those allocating by using alternate days of the week.

Types of participants

We included people with schizophrenia and other types of schizophrenia-like psychosis (e.g. schizophreniform and schizoaffective disorders), irrespective of the diagnostic criteria used. There is no clear evidence that the schizophrenia-like psychoses are caused by fundamentally different disease processes or require different treatment approaches ([Carpenter 1994](#)).

Types of interventions

1. Aripiprazole

Any oral form of application, any dose.

2. Other new/atypical antipsychotic drugs

These include amisulpride, clozapine, olanzapine, quetiapine, risperidone, sertindole, ziprasidone, zotepine: any oral or parenteral form of application, any dose.

Types of outcome measures

We grouped outcomes into the short term (up to 12 weeks), medium term (13-26 weeks) and long term (over 26 weeks).

Primary outcomes

1. Global state

No clinically important response - as defined by the individual studies (e.g. global impression less than much improved or less than 50% reduction on a rating scale) - medium term

2. General functioning

No clinically important change in general functioning - medium term

3. Adverse effects

Clinically important specific adverse effects - medium term

Secondary outcomes

1. Global state

1.1 No clinically important change in global state (as defined by individual studies)

1.2 Relapse (as defined by the individual studies)

2. Mental state

2.1 No clinically important change in general mental state score

2.2 Average endpoint general mental score

2.3 Average change in general mental state score

2.4 No clinically important change in specific symptoms (positive symptoms of schizophrenia, negative symptoms of schizophrenia)

2.5 Average endpoint specific symptom score

2.6 Average change in specific symptom score

3. Leaving the studies early

3.1 Any reason, adverse events, inefficacy of treatment

4. Quality of life/satisfaction with treatment

4.1 No clinically important change in general quality of life

4.2 Average endpoint general quality of life score

4.3 Average change in general quality of life score

5. General functioning

5.1 No clinically important change in general functioning,- short and long term

5.2 Average endpoint general functioning score

5.3 Average change in general functioning score

6. Cognitive functioning

6.1 No clinically important change in overall cognitive functioning

6.2 Average endpoint of overall cognitive functioning score

6.3 Average change of overall cognitive functioning score

7. Service use

7.1 Number of patients hospitalised

8. Adverse effects

8.1 Number of participants with at least one adverse effect

8.2 Clinically important specific adverse effects (cardiac effects, death, movement disorders, prolactin increase and associated effects, weight gain, effects on white blood cell count), short and long term

8.3 Average endpoint in specific adverse effects

8.4 Average change in specific adverse effects

9. 'Summary of findings' table

We used the GRADE approach to interpret findings (Schünemann 2008) and used the GRADE profiler to import data from Review Manager (RevMan) to create 'Summary of findings' tables. These tables provide outcome-specific information concerning the overall quality of evidence from each included study in the comparison, the magnitude of effect of the interventions examined, and the sum of available data on all outcomes we rated as important to patient-care and decision making. We selected the following main outcomes for inclusion in the 'Summary of findings' tables.

1. Global state
2. Mental state
3. Leaving the study early
4. Quality of Life
5. Adverse effects
6. General functioning
7. Service use

Search methods for identification of studies

No language restriction was applied within the limitations of the search tools.

Electronic searches

1. Update search

We searched the Cochrane Schizophrenia Group Trials Register (5 November 2012) using the phrase:

[((aripiprazol* AND (amisulprid* OR clozapin* OR olanzapin* OR quetiapin* OR risperidon* OR sertindol* OR ziprasidon* OR zotepin*)) in title, abstract or index terms of REFERENCE) or ((aripiprazol* AND (amisulprid* OR clozapin* OR olanzapin* OR quetiapin* OR risperidon* OR sertindol* OR ziprasidon* OR zotepin*)) in interventions of STUDY)]

The Cochrane Schizophrenia Group's Trials Register is compiled by systematic searches of major databases, handsearches of journals and conference proceedings (see [Group Module](#)). Incoming trials are assigned to relevant existing or new review titles.

2. Previous electronic search

Please see [Appendix 1](#).

Searching other resources

1. Reference searching

We inspected the reference lists of all studies identified in the search for more trials.

2. Personal contact

Where possible, we contacted the first author of each included study for missing information.

3. Drug companies

We contacted the manufacturers of all atypical antipsychotics included for additional data in the 2011 update.

Data collection and analysis

For previous data collection and analysis methods please see [Appendix 2](#).

Selection of studies

Review author TS inspected the reports for this update. TS resolved any doubts by discussion with other review authors, and where there was still doubt, TS acquired the full article for further inspection. Once the full articles were obtained, TS decided whether the studies met the review criteria. Twenty per cent of the references were randomly checked by HXM for reliability. Any disagreements were resolved by discussion. For any persistent disagreement, TS sought further information from authors of studies and added these trials to the list of those awaiting assessment. (See also [Figure 1](#), [Figure 2](#) and [Figure 3](#) for detailed flow chart of the selection process).

Figure 1. Study flow diagram: original search

Figure 2. Study flow diagram: update 2011

Figure 3. Study flow diagram: update 2012

Data extraction and management

1. Extraction

For this update, TS and HXM extracted data from included studies. If data were presented only in graphs and figures, TS and HXM extracted data whenever possible. When further information was necessary, TS contacted authors of studies in order to obtain missing data or for clarification. If studies were multicentre, where possible, TS extracted data relevant to each component centre separately.

2. Management

2.1 Forms

We extracted data onto standard, simple forms.

2.2 Scale-derived data

We included continuous data from rating scales only if:

- a. the psychometric properties of the measuring instrument have been described in a peer-reviewed journal (Marshall 2000); and
- b. the measuring instrument has not been written or modified by one of the trialists for that particular trial.

Ideally, the measuring instrument should either be i. a self-report or ii. completed by an independent rater or relative (not the therapist). We realise that this is not often reported clearly; we have noted whether or not this is the case in [Description of studies](#).

2.3 Endpoint versus change data

There are advantages of both endpoint and change data. Change data can remove a component of between-person variability from the analysis. On the other hand, calculation of change needs two assessments (baseline and endpoint), which can be difficult in unstable and difficult to measure conditions such as schizophrenia. We decided primarily to use endpoint data, and only use change data if the former were not available. We combined endpoint and change data in the analysis as we used mean differences (MD) rather than standardised mean differences (SMD) throughout (Higgins 2011, Chapter 9.4.5.2).

2.4 Skewed data

Continuous data on clinical and social outcomes are often not normally distributed. To avoid the pitfall of applying parametric tests to non-parametric data, we aimed to apply the following standards to all data before inclusion:

- a) standard deviations (SDs) and means are reported in the paper or obtainable from the authors;
- b) when a scale starts from the finite number zero, the SD, when multiplied by two, is less than the mean (as otherwise the mean is unlikely to be an appropriate measure of the centre of the distribution (Altman 1996));
- c) if a scale started from a positive value (such as the Positive and Negative Syndrome Scale (PANSS, (Kay 1986)), which can have values from 30 to 210), we modified the calculation described above to take the scale starting point into account. In these cases skew is present if $2\text{ SD} > (S - S_{\min})$, where S is the mean score and $S_{\min}$ is the minimum score.

Endpoint scores on scales often have a finite start and end point and these rules can be applied. We entered skewed endpoint data from studies of fewer than 200 participants in as other data within the data and analyses tables rather than into an analysis. Skewed data pose less of a problem when looking at mean if the sample size is large; we entered such endpoint data into syntheses.

When continuous data are presented on a scale that includes a possibility of negative values (such as change data), it is difficult to tell whether data are skewed or not; we entered skewed change data into analyses regardless of the size of study.

2.5 Common measure

To facilitate comparison between trials, we intended to convert variables that can be reported in different metrics, such as days in hospital (mean days per year, per week or per month) to a common metric (e.g. mean days per month).

2.6 Conversion of continuous to binary

Where possible, we made efforts to convert outcome measures to dichotomous data. This can be done by identifying cut-off points on rating scales and dividing participants accordingly into 'clinically improved' or 'not clinically improved'. It is generally assumed that if there is a 50% reduction in a scale-derived score such as the Brief Psychiatric Rating Scale (BPRS, Overall 1962) or the PANSS (Kay 1986), this could be considered as a clinically significant response (Leucht 2005a; Leucht 2005). If data based on these thresholds were not available, we used the primary cut-off presented by the original authors.

2.7 Direction of graphs

Where possible, we entered data in such a way that the area to the left of the line of no effect indicated a favourable outcome for aripiprazole.

Assessment of risk of bias in included studies

For this update, review author TS worked independently by using criteria described in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011) to assess trial quality. This new set of criteria is based on evidence of associations between overestimate of effect and high risk of bias of the article such as sequence generation, allocation concealment, blinding, incomplete outcome data and selective reporting.

Where inadequate details of randomisation and other characteristics of trials were provided we contacted the authors of the studies in order to obtain additional information.

We have noted the level of risk of bias in both the text of the review and in the [Summary of findings for the main comparison](#); [Summary of findings 2](#); [Summary of findings 3](#); [Summary of findings 4](#); [Summary of findings 5](#).

Measures of treatment effect

1. Binary data

For binary outcomes, we calculated a standard estimation of the risk ratio (RR) and its 95% confidence interval (CI). It has been shown that RR is more intuitive (Boissel 1999) than odds ratios and that odds ratios tend to be interpreted as RR by clinicians (Deeks 2000). The Number Needed to Treat/Harm (NNT/H) statistic with its CI is intuitively attractive to clinicians but is problematic both in its accurate calculation in meta-analyses and interpretation (Hutton 2009). For binary data presented in the 'Summary of findings' tables, where possible, we calculated illustrative comparative risks.

2. Continuous data

For continuous outcomes, we estimated the mean difference (MD) between groups. We would prefer not to calculate effect size measures (standardised mean difference (SMD)). However, if scales of very considerable similarity were used, we presumed there was a small difference in measurement, and we calculated effect size and transformed the effect back to the units of one or more of the specific instruments.

Unit of analysis issues

1. Cluster trials

Studies increasingly employ 'cluster randomisation' (such as randomisation by clinician or practice), but analysis and pooling of clustered data poses problems. Authors often fail to account for intra-class correlation in clustered studies, leading to a 'unit of analysis' error (Divine 1992) whereby P values are spuriously low, CIs unduly narrow and statistical significance overestimated. This causes type I errors (Bland 1997; Gulliford 1999).

No cluster-randomised trials were identified in our search; however, if reviews in the future include such trials, where clustering is not accounted for in primary studies, we will present data in a table, with a (*) symbol to indicate the presence of a probable unit of analysis error. In subsequent versions of this review, we will seek to contact first authors of such studies to obtain intra-class correlation coefficients (ICCs) for their clustered data and to adjust for this by using accepted methods (Gulliford 1999). Where clustering is incorporated into the analysis of primary studies, we will present these data as if from a non cluster-randomised study, but adjust for the clustering effect.

We have sought statistical advice and have been advised that the binary data as presented in a report should be divided by a 'design effect'. This is calculated using the mean number of participants per cluster (m) and the ICC [Design effect = $1 + (m-1) \times \text{ICC}$] (Donner 2002). If the ICC was not reported it was assumed to be 0.1 (Ukoumunne 1999).

If, in future updates of this review cluster trials are identified, cluster studies will be appropriately analysed taking into account ICCs and relevant data documented in the report, synthesis with other studies would be possible using the generic inverse variance technique.

2. Cross-over trials

A major concern of cross-over trials is the carry-over effect. It occurs if an effect (e.g. pharmacological, physiological or psychological) of the treatment in the first phase is carried over to the second phase. As a consequence, on entry to the second phase the participants can differ systematically from their initial state despite a wash-out phase. For the same reason cross-over trials are not appropriate if the condition of interest is unstable (Elbourne 2002). As both effects are very likely in severe mental illness, if we encountered such trials, we planned only to use data of the first phase of cross-over studies.

3. Studies with multiple treatment groups

Where a study involves more than two treatment arms, if relevant, we presented the additional treatment arms in comparisons. If data were binary, we simply added these and combined them within the two-by-two table. If data were continuous, we combined data following the formula in section 7.7.3.8 (Combining groups) of the *Cochrane Handbook for Systematic reviews of Interventions* (Higgins 2011). Where the additional treatment arms were not relevant, we did not reproduce these data.

Dealing with missing data

1. Overall loss of credibility

At some degree of loss of follow-up, data must lose credibility (Xia 2009). Although high rates of premature discontinuation are a major problem in this field, we felt that it was unclear which degree of attrition leads to a high degree of bias. We, therefore, did not exclude outcomes on the basis of the percentage of participants completing them. However, we addressed the attrition problem in all parts of the review, including the abstract. For this purpose, we calculated, presented and commented on frequency statistics (overall rates of leaving the studies early in all studies and comparators pooled and their ranges). We assumed that the people who discontinued the studies for any reason did not show any response to the treatment.

2. Binary

We presented data on a 'once-randomised-always-analyse' basis (an intention-to-treat (ITT) analysis). We undertook a sensitivity analysis to test how prone the primary outcomes are to change when data only from people who complete the study to that point are compared with the ITT analysis using the above assumptions.

3. Continuous

3.1 Attrition

In the case of continuous outcomes, we preferred to use ITT results, but if not available we used completer data.

3.2 Standard deviations

If SDs were not reported, we first tried to obtain the missing values from the authors. If not available, where there are missing measures of variance for continuous data, but an exact standard error (SE) and CIs available for group means, and either a P value or T value available for differences in mean, we can calculate them according to the rules described in the *Cochrane Handbook for Systemic reviews of Interventions* (Higgins 2011): When only the SE is reported, SDs are calculated by the formula $SD = SE \times \text{square root } (n)$. Chapters 7.7.3 and 16.1.3 of the *Cochrane Handbook for Systemic reviews of Interventions* (Higgins 2011) present detailed formulae for estimating SDs from P values, T or F values, CIs, ranges or other statistics. If these formulae do not apply, we would have calculated the SDs according to a validated imputation method, which is based on the SDs of the other included studies (Furukawa 2006). Although some of these imputation strategies can introduce error, the alternative would be to exclude a given study's outcome and thus to lose information. We nevertheless would have

examined the validity of the imputations in a sensitivity analysis excluding imputed values, had we imputed any values.

3.3 Last observation carried forward

We anticipated that in many studies the method of last observation carried forward (LOCF) would be employed within the study report. As with all methods of imputation to deal with missing data, LOCF introduces uncertainty about the reliability of the results (Leucht 2007). We nevertheless used LOCF data being aware that many results are the product of LOCF assumptions.

Assessment of heterogeneity

1. Clinical heterogeneity

We considered all included studies initially, without seeing comparison data, to judge clinical heterogeneity. We simply inspected all studies for clearly outlying people or situations which we had not predicted would arise. When such situations or participant groups arose, we discussed these fully.

2. Methodological heterogeneity

We considered all included studies initially, without seeing comparison data, to judge methodological heterogeneity. We simply inspected all studies for clearly outlying methods which we had not predicted would arise. When such methodological outliers arose, we discussed these fully.

3. Statistical heterogeneity

3.1 Visual inspection

We visually inspected graphs to investigate the possibility of statistical heterogeneity.

3.2 Employing the I^2 statistic

We investigated heterogeneity between studies by considering the I^2 method alongside the ChI^2 P value. The I^2 provides an estimate of the percentage of inconsistency thought to be due to chance (Higgins 2003). The importance of the observed value of I^2 depends on i. magnitude and direction of effects and ii. strength of evidence for heterogeneity (e.g. P value from ChI^2 test, or a confidence interval for I^2). An I^2 estimate greater than or equal to around 50% accompanied by a statistically significant ChI^2 statistic was interpreted as evidence of substantial levels of heterogeneity (Higgins 2011). When substantial levels of heterogeneity were found in the primary outcome, we explored reasons for heterogeneity (Subgroup analysis and investigation of heterogeneity).

Assessment of reporting biases

Reporting biases arise when the dissemination of research findings is influenced by the nature and direction of results (Egger 1997). These are described in Section 10 of the *Handbook* (Higgins 2011). We are aware that funnel plots may be useful in investigating reporting biases but are of limited power to detect small-study effects. We did not use funnel plots for outcomes where there were 10 or fewer studies, or where all studies were of similar sizes. In other cases, where funnel plots were possible, we sought statistical advice in their interpretation.

Data synthesis

We understand that there is no closed argument for preference for use of fixed-effect or random-effects models. The random-effects method incorporates an assumption that the different studies are estimating different, yet related, intervention effects. This often seems to be true to us and the random-effects model takes into account differences between studies even if there is no statistically significant heterogeneity. There is, however, a disadvantage to the random-effects model: it puts added weight onto small studies, which often are the most biased ones. Depending on the direction of effect, these studies can either inflate or deflate the effect size. Where possible, for both dichotomous and continuous data we used the random-effects model for data synthesis.

Subgroup analysis and investigation of heterogeneity

1. Subgroup analyses - only primary outcomes

We did not anticipate any subgroup analyses.

2. Investigation of heterogeneity

If inconsistency was high, we reported this. First, we investigated whether data had been entered correctly. Second, if data were correct, we visually inspected the graph and successively removed outlying studies to see if homogeneity was restored. For this review we decided that should this occur with data contributing to the summary finding of no more than around 10% of the total weighting, we would present data. If not, then we did not pool data and discussed relevant issues. We know of no supporting research for this 10% cut-off, but we used prediction intervals as an alternative to this unsatisfactory state.

When unanticipated clinical or methodological heterogeneity was obvious, we simply stated hypotheses regarding these for future reviews or versions of this review. We did not anticipate undertaking analyses relating to these.

Sensitivity analysis

1. Implication of randomisation

We aimed to include trials in a sensitivity analysis if they were described in some way so as to imply randomisation. For the primary outcomes, we included these studies and, if there was no substantive difference when the implied randomised studies were added to those with better description of randomisation, then we entered all data from these studies.

2. Assumptions for lost binary data

Where assumptions had to be made regarding people lost to follow-up (see [Dealing with missing data](#)), we compared the findings of the primary outcomes when we used our assumptions and when we used data only from people who completed the study to that point. If there was a substantial difference, we reported results and discussed them, but continued to employ our assumption.

Where assumptions had to be made regarding missing SDs data (see [Dealing with missing data](#)), we compared the findings of the primary outcomes when we used our assumptions and when we used data only from people who completed the study to that point. A sensitivity analysis was undertaken to test how prone results were to change when completer-only data only were compared to the imputed data using the above assumption. If there was a substantial difference, we reported results and discussed them, but continued to employ our assumption.

3. Risk of bias

We analysed the effects of excluding trials that were judged to be at high risk of bias across one or more of the domains of randomisation (implied as randomised with no further details available): allocation concealment, blinding and outcome reporting for the meta-analysis of the primary outcome. If the exclusion of trials at high risk of bias did not substantially alter the direction of effect or the precision of the effect estimates, then we included data from these trials in the analysis.

4. Imputed values

We planned to undertake a sensitivity analysis to assess the effects of including data from trials where we used imputed values for ICC in calculating the design effect in cluster randomised trials. However, no cluster-randomised trials were identified for this update.

In future updates, if cluster randomised trials are included we will undertake sensitivity analyses. If we note substantial differences in the direction or precision of effect estimates in any of the sensitivity analyses listed above, we will not pool data from the excluded trials with the other trials contributing to the outcome, but present them separately.

5. Skewed data

We planned sensitivity analyses a priori for examining the change in the robustness of the sensitivity to including studies with potentially skewed data.

6. Comparator dose

A recent report showed that some of the comparisons of atypical antipsychotics may have been biased by using inappropriate comparator doses (Heres 2006). We, therefore, also analysed whether the exclusion of studies with inappropriate comparator doses changed the results of the primary outcome and the general mental state.

Comparator doses were considered inappropriate where they exceeded BNF and Martindale recommended maximum doses (BNF 2013; Martindale 2013).

- Aripiprazole: usual maintenance dose of 15 mg daily; range 10 to 15 mg once daily; maximum dose 30 mg daily.
- Clozapine: usual dose 200 to 450 mg daily; maximum dose 900 mg daily.
- Quetiapine: usual range 300 to 450 mg daily in two divided doses; maximum dose 750 mg daily.
- Risperidone: usual dose 4 mg daily; maximum dose 50 mg every two weeks.
- Ziprasidone: (oral) 20 mg twice daily, increased if necessary up to maximum 80 mg twice daily; usual maintenance dose 20 mg twice daily; (intramuscular (IM) for acute agitation) 10 to 20 mg as required; maximum dose 40 mg daily for three consecutive days (to switch to oral therapy as soon as possible).
- Olanzapine: usual range 5 to 20 mg daily; maximum dose 20 mg daily.

RESULTS

Description of studies

For a substantive description of studies please see [Characteristics of included studies](#) and [Characteristics of excluded studies](#) tables.

Results of the search

1. Original search (2005/2007)

The first search yielded 3620 reports of which 28 were closely inspected. After excluding 22 studies, six publications on four trials and two comparisons could be included: aripiprazole versus olanzapine (two) and aripiprazole versus risperidone (two) (Komossa 2009) (Figure 1).

2. Updated search (November 2011)

The search we undertook for the first update of the review (Khanna 2013) identified 618 further results and, after close inspection, we included eight more studies; making a total of 12 studies altogether. We excluded 38 trials, added 216 trials to 'Studies awaiting classification' (due to the need for translation or data extraction) and 16 trials to 'Ongoing studies' category (Khanna 2013) (Figure 2).

3. Updated search (November 2012)

The 2012 updated search for this current version of the review yielded 215 new citations; 209 full-text articles were assessed for eligibility, and ultimately 162 studies (from 167 references) were included. The total amount of included studies in this current review is 174 (Figure 3).

Included studies

The 174 included studies randomised 17,244 participants with the diagnosis of schizophrenia or schizoaffective disorder. All studies were described as randomised. We included both double blind and open label studies. Many were sponsored by pharmaceutical companies with some pecuniary interest in the result.

1. Length of studies

One trial was only five days long. The vast majority were short term with a duration of three to eight weeks. Seven medium-term studies ranged from 20 to 26 weeks, and long-term studies from 28 weeks to two years.

2. Setting

Studies reported inpatient and outpatient settings; the vast majority of studies were undertaken in China, where, it seems, aripiprazole is being heavily marketed.

3. Participants

Participants were diagnosed with varying diagnostic criteria; Diagnostic Statistical Manual version 4 (DSM-IV); clinical diagnosis (or no mention). The vast majority of participants in included studies were diagnosed using the Chinese Classification of Mental Disorders (CCMD-3). Participants were usually relatively chronically ill with mean ages in the late thirties.

4. Study size

The sample size varied from $n = 40$ (Zhang 2008b) to $n = 1599$ (Tandon 2006) people.

5. Interventions

5.1 Aripiprazole

Doses ranged between 2.5 to 30 mg/day.

5.2 Control drugs

Other atypical drugs, namely olanzapine, risperidone, ziprasidone and quetiapine were used as controls. As some studies did not elucidate doses it can only be presumed that therapeutic doses were employed.

6. Outcomes

6.1 Leaving the study early

Thirty-five studies reported on participants leaving the study early due to any reason.

6.2 Rating scales

Details of scales that provided usable data are shown below. Reasons for exclusion of data from other instruments are given under 'Outcomes' in the [Characteristics of included studies](#).

6.2.1 Global state scales

6.2.1.1 Clinical Global Impression Scale - CGI Scale ([Guy 1976](#))
This is used to assess both severity of illness and clinical improvement, by comparing the conditions of the person standardised against other people with the same diagnosis. A seven-point scoring system is used with low scores showing decreased severity and/or overall improvement.

6.2.1.2 Investigator's Assessment Questionnaire - IAQ ([Tandon 2005](#))

The IAQ is a quantifiable clinical tool that can provide detailed information regarding common safety, efficacy and tolerability concerns that patients experience while taking antipsychotics. It has been shown to highly correlate with time to study discontinuation which is a common measure of effectiveness.

6.2.1.3 Arizona Sexual Experience Scale - ASEX ([McGahuey 2000](#))

This is a brief scale for self-rating of sexual function. It has five items and is rated in five steps. Possible scores range from five to 30 with higher scores indicating more sexual dysfunction.

6.2.2 Mental state scales

6.2.2.1 Positive and Negative Syndrome Scale - PANSS ([Kay 1986](#))

This schizophrenia scale has 30 items, each of which can be defined on a seven-point scoring system varying from one - absent to seven - extreme. It can be divided into three sub scales for measuring the severity of general psychopathology, positive symptoms (PANSS-P), and negative symptoms (PANSS-N). A low score indicates lesser severity.

6.2.2.2 Positive and Negative Syndrome Scale-Excited Component - PANSS-EC ([Chaichan 2008](#))

The PANSS-EC scale is derived as a sub scale of PANSS and is a simple scale used to measure the degree of agitation. The scale consists of five items (poor impulse control, tension, hostility, uncooperativeness, excitement), each being ranked from one to seven giving a potential maximum score of 35 points.

6.2.2.3 Brief Psychiatric Rating Scale - BPRS ([Overall 1962](#))

This consists of 18 to 24 items (depending on the version) each rated on a scale from one (absent) to seven (extreme).

6.2.3 Adverse effects scales

6.2.3.1 Abnormal Involuntary Movement Scale - AIMS ([Guy 1976](#))

This scale has been used to assess tardive dyskinesia, a long-term, drug-induced movement disorder and short-term movement disorders such as tremor.

6.2.3.2 Simpson Angus Scale - SAS ([Simpson 1970](#))

This 10-item scale (with a scoring system of zero to four on each item) measures drug-induced parkinsonism, a short-term drug-induced movement disorder. A low score indicates low levels of parkinsonism.

6.2.3.3 Barnes Akathisia Scale - BAS ([Barnes 1989](#))

The scale comprises items rating the observable, restless movements that characterise akathisia, a subjective awareness of restlessness, and any distress associated with the condition. These items are rated from zero (normal) to three (severe). In addition, there is an item for rating global severity (from zero (absent) to five (severe)). A low score indicates low levels of akathisia.

6.2.4 Quality of Life

6.2.4.1 Euro-QoL-5D - EQ-5D ([Jelsma 2001](#))

The EuroQoL-5D is a generic preference based measure of health-related quality of life. It has five domains which are mobility, self-care, usual activities, pain/ discomfort and anxiety/ depression, each having three short questions. The EQ-5D Utility score assesses all five items on a scale of zero to one, where zero represents worst possible health and one represents perfect health. The EQ-5D Health Dimension Scale assesses each item on three possible scores where one is the best and three the worst score.

6.2.4.2 Quality of Life Scale - QLS (Heinrichs 1984)

Quality of Life Scale (QLS), a 21-item scale divided into four domains including Interpersonal relations, Instrumental role, Intrapsychic foundations and common objects/activities scored on a seven-point scale with lowest score indicating severe dysfunction.

6.2.4.3 Impact of Weight on Quality of Life - IwQOL-Lite (Kolotkin 2002)

This is a survey instrument that is used to quantitatively assess an individual's perception of how their weight affects their day-to-day life. This instrument is especially valuable to obesity researchers, clinicians, psychologists, medical device and/or pharmaceutical companies seeking to validate the effectiveness of their treatments for obesity using metrics that go beyond the physical measurements of weight loss.

6.2.4.4 World Health Organisation Quality of Life Scale (WHO-QoL-Bref, O'Carroll 2000)

The WHOQoL-Bref is a 26-item self-report comprising satisfaction with health, psychological functioning, social relationships and environmental opportunities. Each item is scored on a five-point scale from one (poor) to five (worse). The Chinese version of the WHOQoL scale, the generic quality of life inventory (GQOLI-74), was also used in included Chinese studies.

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6.3 Adverse effects

Adverse effects were mainly recorded in open interviews. In addition, continuous data were provided for weight, QTc time and cholesterol levels.

6.4 Missing outcomes

No information was provided on the number of people hospitalised or global functioning. This can be an important and useful measure of the efficacy of medications being used. Also, not one study reported on functional outcomes, such as living skills, ability to live independently or employment. These trials clearly are more

explanatory than pragmatic, focusing on whether in ideal circumstances aripiprazole has an effect rather than whether it would be useful in everyday routine care (Thorpe 2009).

Excluded studies

There are a total of 79 excluded studies in this 2012 update. The most common reason for exclusion was because of lack of randomisation (see [Characteristics of excluded studies](#)).

Awaiting classification

Four studies are awaiting assessment (Wang 2006f; Zhao 2006a; Zheng XR 2008; 陶建青, 2007). Three of these were because of inconsistent reporting of denominators. Since we were unable to get clarification from the authors, we decided to leave these trials in [Studies awaiting classification](#) until further information becomes available. Please refer to [Characteristics of studies awaiting classification](#) for further details.

Ongoing studies

There are 16 studies in this category (see [Characteristics of ongoing studies](#)). There appeared to be much ongoing research activity in 2005 but completed studies have not yet been identified. We have contacted authors for current information but have received no updates.

Risk of bias in included studies

For details please refer to the 'Risk of bias' table for each study and [Figure 4](#) and [Figure 5](#) for the graphic overview.

Figure 4. 'Risk of bias' graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.

Figure 5. 'Risk of bias' summary: review authors' judgements about each risk of bias item for each included study.

Allocation

The vast majority of included studies were rated as an 'unclear' risk of bias. Eighteen trials were rated as a 'low' risk of bias and described randomisation methods in some detail (Figure 5). Three of these used computer-generated voice recognition systems. It remained unclear whether there was a risk of bias. Only one study described the method of allocation concealment - by means of a sealed envelope (Wei 2006).

Blinding

Only 11 included studies were described as double blind (Chen 2007a; Du 2006; Feng 2006; Fleischhacker 2008; Guo 2006; Kane 2009; Kinon 2004; McQuade 2004; Potkin 2003; Xu 2010; Zimbroff 2007). Chan 2007 and Potkin 2003 described using identical capsules for blinding. Zimbroff 2007 used double dummy administration of medication. The other studies did not provide any information on the blinding procedure. No study examined whether blinding was effective. Six studies were open label (Chen 2009; Kern 2006; Kerwin 2007; Tandon 2006; Włodzimirz 2006; Wolf 2007), and two described single-blinding (Zhang 2009a; Zhu 2005). We found that the adverse effect profiles of examined compounds are quite different which may have made blinding difficult. We therefore conclude that the risk of bias for objective outcomes (e.g. death or laboratory values) was low but there was considerable risk of bias for subjective outcomes.

Incomplete outcome data

In two studies the rates of participants leaving the study early were higher than 30% (McQuade 2004; Potkin 2003); in McQuade 2004 it was as high as 72%. Overall attrition was about 35% to

40%. Last observation carried forward (LOCF) method to account for participants leaving the study early was used in studies that made clear attrition numbers, which we now know to be a far from ideal assumption (Leucht 2007). Only McQuade 2004, however, analysed the study completers in a secondary analysis assuming that a participant who left the study prematurely would not have had a change of condition if he/she had stayed in the study. This assumption can also be misleading. The majority of new data from Chinese studies states no incomplete data - therefore, this domain is largely rated across studies as a 'low' risk of bias. Twenty-eight studies did not mention or make explicit any participants lost through attrition, and so were rated as an 'unclear' risk of bias.

Selective reporting

In terms of selective reporting there was a high risk of bias in the majority of included studies. Overall, only 13 studies rated as a 'low' risk of bias, and only one rated as 'unclear', meaning that the remainder of the 174 included studies (160) were rated at a 'high' risk of bias with not all recorded outcomes reported. Six studies reported only adverse events that occurred in at least 5% to 10% of participants (Chan 2007; Fleischhacker 2008; Kane 2009; Potkin 2003; Zimbroff 2007). By this procedure rare, but important adverse events, can be missed. Kinon 2004 reported adverse effects that occurred in at least 1% of patients. McQuade 2004 did not report on the PANSS positive sub score despite having recorded it. See funnel plots for the primary outcome of no clinically significant response (Figure 6; Figure 7; Figure 8; Figure 9), where distribution of studies is relatively symmetrical, except for comparison 5.1 (Figure 9), perhaps owing to less included studies.

Figure 6. Funnel plot of comparison: I COMPARISON I. ARIPIPRAZOLE versus CLOZAPINE, outcome: I.I Global state: I. No clinically significant response (as defined by the original studies).

Figure 7. Funnel plot of comparison: 2 COMPARISON 2. ARIPIPRAZOLE versus QUETIAPINE, outcome: 2.1 Global state: 1.No clinically significant response (as defined by original studies).

Figure 8. Funnel plot of comparison: 3 COMPARISON 3. ARIPIPRAZOLE versus RISPERIDONE, outcome: 3.1 Global state: 1. No clinically significant response (as defined by the original studies).

Figure 9. Funnel plot of comparison: 5 COMPARISON 5. ARIPIPRAZOLE versus OLANZAPINE, outcome: 5.1 Global state: 1.No clinically significant response (as defined by the original studies).

Other potential sources of bias

Many included studies were sponsored by the manufacturer of aripiprazole or the comparator drug. There is evidence that pharmaceutical companies may be selective in reporting the benefits and disadvantages of their own compounds (Heres 2006).

Effects of interventions

See: [Summary of findings for the main comparison COMPARISON 1. ARIPIPRAZOLE versus CLOZAPINE for schizophrenia](#); [Summary of findings 2 COMPARISON 2. ARIPIPRAZOLE versus QUETIAPINE for schizophrenia](#); [Summary of findings 3 COMPARISON 3. ARIPIPRAZOLE versus RISPERIDONE for schizophrenia](#); [Summary of findings 4 COMPARISON 4. ARIPIPRAZOLE versus ZIPRASIDONE for schizophrenia](#); [Summary of findings 5 COMPARISON 5. ARIPIPRAZOLE versus OLANZAPINE for schizophrenia](#)

We used risk ratios (RR) for dichotomous data and mean differences (MD) for continuous data, with their respective 95% confidence intervals (CIs) throughout.

COMPARISON 1: ARIPIPRAZOLE versus CLOZAPINE

1.1 Global state: 1. No clinically significant response (as defined by the original studies)

Data demonstrate there was no difference between groups (29 RCTs, n = 2132, RR 1.05 CI 0.87 to 1.27, [Analysis 1.1](#)).

1.2 Mental state: 1. Specific - binary outcomes

1.2.1 Anxiety and agitation

In the short term, there was significant favour ($P = 0.01$) for clozapine with higher levels of anxiety seen in participants receiving aripiprazole (11 RCTs, n = 732, RR 2.62 CI 1.21 to 5.70), however, with a slight degree of heterogeneity ($\text{Chi}^2 = 13.34$; $\text{df} = 10$; $P = 0.21$; $I^2 = 25\%$). Data demonstrate no difference between

groups at medium term (1 RCT, n = 90). Data for levels of agitation at short term demonstrated no difference between groups (1 RCT, n = 60, [Analysis 1.2](#)).

1.3 Mental state: 2. Average endpoint scores of various scales (short term, up to 12 weeks, high = poor)

Data for all scales demonstrated no significant difference, including the BPRS (5 RCTs, n = 426); PANSS (23 RCTs, n = 1638), however with considerable heterogeneity present ($\text{Chi}^2 = 61.84$; $\text{df} = 22$; $P = 0.0$; $I^2 = 64\%$); and SANS (1 RCT, n = 50, [Analysis 1.3](#)).

1.4 Mental state: 3. Average endpoint scores of various scales (medium term, 12 to 26 weeks, high = poor)

When using PANSS, data from 3 RCTs significantly favoured ($P = 0.0004$) aripiprazole (n = 236, MD -5.41 CI -8.42 to -2.41, [Analysis 1.4](#)).

1.5 Mental state: 4. Average endpoint scores of various scales (skewed)

All data for this outcome are skewed and are best inspected by viewing [Analysis 1.5](#).

1.6 Mental state: 5. Specific - average endpoint positive score (PANSS, high = poor)

Overall, there was no difference between groups at both short and medium term (22 RCTs, n = 1523, [Analysis 1.6](#)), however there was considerable heterogeneity present ($\text{Chi}^2 = 74.67$; $\text{df} = 21$; $P = 0.00001$; $I^2 = 72\%$).

By short term, data indicate no significant difference between groups (19 RCTs, n = 1287), however, considerable heterogeneity was present ($\text{Chi}^2 = 66.47$; $\text{df} = 18$; $P = 0.00001$; $I^2 = 73\%$). Again, by the medium term, data indicate no significant difference between groups (3 RCTs, n = 236), however there was considerable heterogeneity present ($\text{Chi}^2 = 5.87$; $\text{df} = 2$; $P = 0.05$; $I^2 = 66\%$).

1.7 Mental state: 6. Specific - average endpoint negative score (PANSS, high = poor)

Overall, there was no significant difference between aripiprazole between short term and medium term (23 RCTs, n = 1640), however considerable heterogeneity was present ($\text{Chi}^2 = 114.66$; $\text{df} = 22$; $P = 0.0001$; $I^2 = 81\%$).

Short-term data indicate no significant difference between groups (20 RCTs, n = 1404), however there was considerable heterogeneity present ($\text{Chi}^2 = 51.61$; $\text{df} = 19$; $P = 0.0001$; $I^2 = 63\%$). Medium-term data significantly favoured aripiprazole (3 RCTs, n = 236, MD -3.24 CI -5.82 to -0.67, [Analysis 1.7](#)), however with

considerable heterogeneity ($\text{Chi}^2 = 15.99$; $\text{df} = 2$; $P = 0.0003$; $I^2 = 87\%$).

1.8 Mental state: 7. Specific - average endpoint general psychopathological score (PANSS, high = poor)

Overall, data indicate no significant difference between groups (19 RCTs, n = 1330, [Analysis 1.8](#)). Data indicate a significant difference ($P = 0.02$) favouring aripiprazole at medium term (3 RCTs, n = 236 MD -1.89 CI -3.45 to -0.34).

1.9 Mental state: 8. Specific - average total score decreased rate (PANSS, low = poor)

1.9.1 By up to 12 weeks

Data in one small study indicate no significant difference between groups (1 RCT, n = 118, [Analysis 1.9](#)).

1.10 Mental state: 9. Specific - average positive score decreased rate (PANSS, low = poor)

Short-term data in one small study indicate no significant difference between groups (1 RCT, n = 118, [Analysis 1.10](#)).

1.11 Leaving the study early

Data demonstrate no significant difference between groups when leaving the study for any reasons (3 RCTs, n = 240, [Analysis 1.11](#)). This was also the case for adverse events (3 RCTs, n = 212) and due to 'economic issues' (1 RCT, n = 120).

1.12 Quality of life: 1a. Average scores (short term, up to 12 weeks, WHO-QOL-100, low = poor)

Data demonstrate statistical significance ($P = 0.0001$) in favour of aripiprazole in two small RCTs (n = 132, MD 2.59 CI 1.43 to 3.74, [Analysis 1.12](#)). On the physical health component, data demonstrate statistical significance ($P = 0.01$) in favour of aripiprazole in two small RCTs (n = 132, MD 7.73 CI 1.51 to 13.94), however with considerable heterogeneity present ($\text{Chi}^2 = 6.04$; $\text{df} = 1$; $P = 0.014$; $I^2 = 83\%$). Again, mental health component data demonstrate statistical significance ($P = 0.0001$) in favour of aripiprazole in two small RCTs (n = 132, MD 9.21 CI 4.74 to 13.68), however there was considerable heterogeneity present ($\text{Chi}^2 = 2.31$; $\text{df} = 1$; $P = 0.13$; $I^2 = 57\%$). Data from one small RCT demonstrate statistical significance ($P = 0.00001$) in favour of aripiprazole for the spiritual support component (1 RCT, n = 72, MD 6.61 CI 4.25 to 8.97), and for external environment ($P = 0.0001$) (3 RCTs, n = 248, MD 13.82 CI 8.69 to 18.94) again with considerable heterogeneity present ($\text{Chi}^2 = 7.63$; $\text{df} = 2$; $P = 0.02$; $I^2 = 74\%$).

Data demonstrate no statistical significance for social function (2 RCTs, $n = 132$) again with considerable heterogeneity present ($\text{ChI}^2 = 23.23$; $\text{df} = 1$; $P = 0.00001$; $I^2 = 96\%$) or independence (1 RCT, $n = 72$).

1.13 Quality of life: 1b. Average scores (medium term, 12 to 24 weeks, WHO-QOL-100, low = poor)

The endpoint score demonstrated statistical significance ($P = 0.00001$) in favour of aripiprazole (2 RCTs, $n = 176$, MD 2.75 CI 1.98 to 3.53, [Analysis 1.13](#)). Data demonstrate statistical significance in the physical health component ($P = 0.04$) in favour of aripiprazole (3 RCTs, $n = 256$, MD 4.89 CI 0.22 to 9.56), however with considerable heterogeneity present ($\text{ChI}^2 = 33.90$; $\text{df} = 2$; $P = 0.00001$; $I^2 = 94\%$). Mental health data demonstrate statistical significance ($P = 0.00001$) in favour of aripiprazole (3 RCTs, $n = 256$, MD 7.39 CI 5.26 to 9.53), again with considerable heterogeneity present ($\text{ChI}^2 = 2.6$; $\text{df} = 2$; $P = 0.27$; $I^2 = 23\%$). This was also the case for social function with significant favour ($P = 0.0008$) of aripiprazole (3 RCTs, $n = 256$, MD 6.68 CI 2.79 to 10.56), again with considerable heterogeneity present ($\text{ChI}^2 = 13.19$; $\text{df} = 2$; $P = 0.001$; $I^2 = 85\%$). Data in two small studies demonstrate statistical significance ($P = 0.00001$) in favour of aripiprazole for the independence component (2 RCTs, $n = 176$, MD 6.71 CI 4.76 to 8.66). Data demonstrate no significant difference between groups for material life (1 RCT, $n = 80$) and spiritual support (2 RCTs, $n = 176$).

1.14 Quality of life: 2. Average endpoint general quality of life score (GQOLI - 74, low = poor)

Physical health data from one small RCT demonstrate statistical significance ($P = 0.01$) in favour of aripiprazole ($n = 120$, MD 7.70 CI 2.95 to 12.45, [Analysis 1.14](#)). Data for social function from one small RCT demonstrate statistical significance ($P = 0.0002$) in favour of aripiprazole ($n = 120$, MD 6.60 CI 3.15 to 10.05). Data from one small RCT demonstrate statistical significance ($P = 0.0002$) in favour of aripiprazole for environmental area ($n = 90$, MD 11.50 CI 5.55 to 17.45) and independence ($P = 0.0003$) in favour of aripiprazole ($n = 90$, MD 6.16 CI 2.84 to 9.48). No significant difference was found for: total GQOLI score (1 RCT, $n = 114$); mental health data (1 RCT, $n = 120$); and material life (1 RCT, $n = 120$).

1.15 Adverse effects: 1. At least one adverse effect, non-specific

Data demonstrate statistical significance ($P = 0.02$) in favour of aripiprazole, with more people receiving clozapine experiencing at least one adverse effect (7 RCTs, $n = 574$, RR 0.67 CI 0.48 to 0.95, [Analysis 1.15](#)), however with considerable heterogeneity present ($\text{ChI}^2 = 18.17$; $\text{df} = 7$; $P = 0.01$; $I^2 = 61\%$). There was no significant difference between groups in the short term for:

epilepsy (1 RCT, $n = 60$); abnormal liver function (5 RCTs, $n = 364$); stuffy nose (3 RCTs, $n = 258$); sweating (1 RCT, $n = 74$); urinary retention (2 RCTs, $n = 132$); and urinary incontinence (2 RCTs, $n = 120$).

1.16 Adverse effects: 2. Cardiac effects

Overall, less cardiac effects were seen in people receiving aripiprazole compared with clozapine.

Significant results were found in the short term for abnormal ECG ($P = 0.00001$), with less occurrences found in people receiving aripiprazole (12 RCTs, $n = 921$, RR 0.38 CI 0.29 to 0.51, [Analysis 1.16](#)). Data were also significantly in favour of aripiprazole ($P = 0.0003$) for short-term general adverse cardiac events (1 RCT, $n = 62$, RR 0.32 CI 0.17 to 0.60). QTc prolongation was significantly in favour ($P = 0.001$) of aripiprazole in both the short (4 RCTs, $n = 334$, RR 0.16 CI 0.05 to 0.49) and medium ($P = 0.03$) term (1 RCT, $n = 90$, RR 0.05 CI 0.00 to 0.79), as well as tachycardia ($P = 0.00001$) in the short term (15 RCTs, $n = 1104$, RR 0.29 CI 0.22 to 0.38). There was no significant difference between groups for a short-term decrease in blood pressure (3 RCTs, $n = 194$); and medium-term tachycardia (1 RCT, $n = 60$).

1.17 Adverse effects: 3. Central/peripheral nervous system

Data showing a decrease in activity from one small RCT demonstrate statistical significance ($P = 0.0002$) in favour of aripiprazole at short term ($n = 120$, RR 0.21 CI 0.10 to 0.48, [Analysis 1.17](#)). This was also the case for blurred vision ($P = 0.003$) (6 RCTs, $n = 472$, RR 0.29 CI 0.12 to 0.66) with slight heterogeneity present ($\text{ChI}^2 = 9.11$; $\text{df} = 5$; $P = 0.105$; $I^2 = 45\%$). Dizziness was also seen significantly more at short term ($P = 0.05$) in people receiving clozapine (9 RCTs, $n = 698$, RR 0.60 CI 0.36 to 1.00). Data from one small RCT for general vegetative nervous system adverse reaction demonstrate statistical significance ($P = 0.01$) in favour of aripiprazole ($n = 62$, RR 0.48 CI 0.27 to 0.84) by short term. Other short-term CNS adverse effects that were significantly in favour of aripiprazole include: hyper-salivation ($P = 0.00001$) (16 RCTs, $n = 1074$, RR 0.06 CI 0.03 to 0.10); memory decline ($P = 0.04$) (1 RCT $n = 80$, RR 0.13 CI 0.02 to 0.95); sedation ($P = 0.02$) ($n = 80$, RR 0.03 CI 0.00 to 0.52); and somnolence ($P = 0.00001$) (21 RCTs, $n = 1492$, RR 0.15 CI 0.09 to 0.24), with slight heterogeneity present ($\text{ChI}^2 = 35.6$; $\text{df} = 20$; $P = 0.02$; $I^2 = 44\%$).

Data significantly favoured clozapine at medium term for: headache ($P = 0.03$) (16 RCTs, $n = 1102$, RR 2.28 CI 1.07 to 4.86), however with considerable heterogeneity present ($\text{ChI}^2 = 45.69$; $\text{df} = 15$; $P = 0.0001$; $I^2 = 67\%$); and insomnia ($P = 0.00001$) (14 RCTs, $n = 990$, RR 5.62 CI 2.90 to 10.91).

There was no difference between groups in the short term for: increase in activity (1 RCT, $n = 48$); fatigue (4 RCTs, $n = 300$); general CNS adverse reaction (1 RCT, $n = 62$); irritability (2 RCTs,

n = 120); as well as insomnia at medium term (1 RCT, n = 90); and headache at medium term (1 RCT, n = 90).

1.18 Adverse effects: 4. Extrapyramidal effects

No significant difference was found between groups at short term for the following outcomes: general EPS (8 RCTs, n = 520); tardive dyskinesia (1 RCT, n = 72). For medium-term outcomes, the following demonstrated no significant difference: akathisia (1 RCT, n = 80); dystonia (1 RCT, n = 80); spasmodic torticollis (1 RCT, n = 80); and tremor (1 RCT, n = 80, [Analysis 1.18](#)).

The only homogenous data that demonstrate statistical significance ($P = 0.01$) was in favour of clozapine for the outcome of dystonia at short term (5 RCTs, n = 374, RR 3.24 CI 1.29 to 8.12). All other data either presented no significant difference between groups, or no difference with varying degrees of heterogeneity. The latter include short-term data for akathisia, with no significant difference between groups (13 RCTs, n = 916, RR 1.21 CI 0.54 to 2.68) with considerable heterogeneity present ($\text{ChI}^2 = 25.43$; $\text{df} = 12$; $P = 0.01$; $I^2 = 53\%$). Data for tremor at short term demonstrated no significant difference between groups (6 RCTs, n = 460, RR 1.99 CI 0.72 to 5.48) with slight heterogeneity present ($\text{ChI}^2 = 7.17$; $\text{df} = 5$; $P = 0.208$; $I^2 = 30\%$). This was the same for use of antiparkinson medication in the short term (2 RCTs, n = 140, RR 2.84 CI 0.07 to 117.07) with considerable heterogeneity present ($\text{ChI}^2 = 6.94$; $\text{df} = 1$; $P = 0.008$; $I^2 = 86\%$).

1.19 Adverse effects: 5. Gastrointestinal

No significant difference was found in the short term for: general gastrointestinal adverse reaction (2 RCTs, n = 130); and indigestion (1 RCT, n = 60). Data for dry mouth at short term also demonstrated no significant difference between groups (4 RCTs, n = 268, RR 0.64 CI 0.08 to 5.38) with substantial heterogeneity present ($\text{ChI}^2 = 13.3$; $\text{df} = 3$; $P = 0.004$; $I^2 = 77\%$). This was also true for nausea/vomiting (10 RCTs, n = 790, RR 1.55 CI 0.71 to 3.38) again with heterogeneity present ($\text{ChI}^2 = 17.01$; $\text{df} = 9$; $P = 0.05$; $I^2 = 47\%$, [Analysis 1.20](#)).

Data were significantly in favour of clozapine for abdominal discomfort or pain at short term ($P = 0.03$) (2 RCTs, n = 132, RR 10.21 CI 1.32 to 79.12). Short-term data for constipation demonstrate statistical significance ($P = 0.00001$) in favour of aripiprazole (19 RCTs, n = 1390, RR 0.15 CI 0.08 to 0.31) with substantial heterogeneity present ($\text{ChI}^2 = 74.05$; $\text{df} = 18$; $P = 0.0$; $I^2 = 76\%$). Remaining data for medium-term outcomes were in favour of aripiprazole, with significantly less instances of constipation ($P = 0.007$) (1 RCT, n = 90, RR 0.02 CI 0.00 to 0.36) and hypersalivation ($P = 0.005$) (1 RCT, n = 90, RR 0.02 CI 0.00 to 0.29).

1.20 Adverse effects: 6. Haematological

All data for this outcome were homogenous and statistically significant in favour of aripiprazole, including abnormal blood routine in the short term ($P = 0.007$) (5 RCTs, n = 368, RR 0.16 CI 0.04 to 0.60, [Analysis 1.19](#)); and leucopenia in the short term ($P = 0.002$) (10 RCTs, n = 726, RR 0.21 CI 0.08 to 0.56). Abnormal blood routine in the medium term also demonstrates statistical significance ($P = 0.008$) in favour of aripiprazole (2 RCTs, n = 152, RR 0.32 CI 0.14 to 0.75).

1.21 Adverse effects: 7. Hormonal (short term, up to 12 weeks)

Data for lactation or menstrual changes demonstrate statistical significance ($P = 0.003$) in favour of aripiprazole (3 RCTs, n = 214, RR 0.11 CI 0.03 to 0.47, [Analysis 1.21](#)).

1.22 Adverse effects: 8a. Metabolic - binary measures

1.22.1 Blood glucose - increased (short term, up to 12 weeks)

Data demonstrate statistical significance ($P = 0.0002$) in favour of aripiprazole (5 RCTs, n = 410, RR 0.12 CI 0.04 to 0.37, [Analysis 1.22](#)).

1.22.2 C-peptide (short term, up to 12 weeks)

Data from one small RCT demonstrate statistical significance ($P = 0.01$) in favour of aripiprazole (1 RCT, n = 60, RR 0.03 CI 0.00 to 0.45).

1.22.3 Decrease appetite (short term, up to 12 weeks)

Data demonstrate statistical significance ($P = 0.01$) in favour of aripiprazole (2 RCTs, n = 130, RR 0.07 CI 0.01 to 0.54).

1.22.4 Postural hypotension (short term, up to 12 weeks)

Data demonstrate statistical significance ($P = 0.001$) in favour of aripiprazole (5 RCTs, n = 344, RR 0.16 CI 0.07 to 0.39).

1.22.5 PRL- increase (short term, up to 12 weeks)

Data from one small RCT demonstrate statistical significance ($P = 0.04$) in favour of aripiprazole (1 RCT, n = 48, RR 0.05 CI 0.00 to 0.82).

1.22.6 Weight gain (short term, up to 12 weeks)

Data demonstrate statistical significance ($P = 0.00001$) in favour of aripiprazole (18 RCTs, n = 1318, RR 0.13 CI 0.08 to 0.22).

1.22.7 Blood glucose - increased (medium term, 12 to 24 weeks)

Data demonstrate no significant difference between groups (1 RCT, n = 90).

1.22.8 Decreased appetite (medium term, 12 to 24 weeks)

Data from one small RCT demonstrate statistical significance (P = 0.05) in favour of aripiprazole (n = 90, RR 0.06 CI 0.00 to 0.99).

1.22.9 Weight gain (medium term, 12 to 24 weeks)

Data from one small RCT demonstrate statistical significance (P = 0.009) in favour of aripiprazole (n = 90, RR 0.02 CI 0.00 to 0.39, [Analysis 1.22](#)).

1.23 Adverse effects: 8b. Metabolic - continuous measures

1.23.1 Blood glucose - FPG in HbA1c normal group (in mmol/L)

Data demonstrate no significant difference between groups (1 RCT, n = 36).

1.23.2 Blood glucose - FPG in HbA1c abnormal group (in mmol/L)

Data demonstrate no significant difference between groups (1 RCT, n = 19).

1.23.3 Blood glucose - PBG in HbA1c normal group (in mmol/L)

Data demonstrate no significant difference between groups (1 RCT, n = 36).

1.23.4 Blood glucose - PBG in HbA1c abnormal group (in mmol/L)

Data from one small RCT demonstrate statistical significance (P = 0.00001) in favour of aripiprazole (1 RCT, n = 19, MD -1.90 CI -2.63 to -1.17).

1.23.5 Blood glucose - FPG average endpoint (in mmol/L)

Data demonstrate statistical significance (P = 0.0009) in favour of aripiprazole (2 RCTs, n = 134, MD -0.52 CI -0.83 to -0.22).

1.23.6 Blood glucose - C-peptide average endpoint (in mg/dlmmol/L)

Data from one small RCT demonstrate statistical significance (P = 0.05) in favour of aripiprazole (1 RCT, n = 60, MD -0.72 CI -1.45 to 0.01).

1.23.7 Weight gain - average endpoint level (in kg)

Data demonstrate no significant difference between groups (1 RCT, n = 74, [Analysis 1.23](#)).

1.24 Cost-effectiveness analysis (skewed)

All data for this outcome are skewed and are best inspected by viewing [Analysis 1.24](#).

COMPARISON 2: ARIPIPRAZOLE versus QUETIAPINE

2.1 Global state: 1. No clinically significant response (as defined by original studies)

Data demonstrate no significant difference between groups (12 RCTs, n = 991, [Analysis 2.1](#)).

2.2 Global state: 2 a. Average endpoint total score (short term, up to 12 weeks, high = poor)

Data for the CGI demonstrate no significant difference between groups (1 RCT, n = 80, [Analysis 2.2](#)). This was also the case for PANSS (10 RCTs, n = 831), however with considerable heterogeneity present ($ChI^2 = 21.14$; $df = 9$; $P = 0.012$; $I^2 = 57\%$). Data from the BPRS from one small RCT demonstrate statistical significance (P = 0.007) in favour of aripiprazole (1 RCT, n = 80, MD -2.63 CI -4.55 to -0.71).

2.3 Global state: 2b. Average endpoint scale score (medium term, 12 to 24 weeks, high = poor)

Data for PANSS demonstrate no significant difference between groups (1 RCT, n = 100, [Analysis 2.3](#)).

2.4 Global state: 3. Average endpoint SI score (CGI, high = poor)

2.4.1 Up to 12 weeks - short term

Data demonstrate no significant difference between groups (1 RCT, n = 108, [Analysis 2.4](#)).

2.5 Mental state: 2a. Specific - binary outcomes

There was no significant difference between groups in the short term for: agitation (5 RCTs, $n = 423$); anxiety (2 RCTs, $n = 168$); and depression (1 RCT, $n = 108$, [Analysis 2.5](#)). This was also the case for agitation at medium term (1 RCT, $n = 100$).

2.6 Mental state: 3. Specific - average endpoint positive score (PANSS, high = poor)

2.6.1 By up to 12 weeks - short term

Short-term data demonstrate no significant difference between groups (7 RCTs, $n = 583$, [Analysis 2.6](#)) with substantial heterogeneity present ($\text{Chi}^2 = 20.25$; $\text{df} = 6$; $P = 0.002$; $I^2 = 70\%$). Medium term data, again, demonstrate no significant difference between groups (1 RCT, $n = 100$).

2.7 Mental state: 4. Specific - average endpoint negative score (PANSS, high = poor)

2.7.1 Up to 12 weeks - short term

Short-term data demonstrate no significant difference between groups using PANSS negative score (6 RCTs, $n = 443$, [Analysis 2.7](#)); this is also the case for medium-term data (1 RCT, $n = 100$).

2.8 Mental state: 5. Specific - average endpoint general pathological score (PANSS, high = poor)

2.8.1 Up to 12 weeks - short term

Short-term data for PANSS pathological score demonstrate no significant difference between groups (10 RCTs, $n = 831$, [Analysis 2.8](#)) with substantial heterogeneity present ($\text{Chi}^2 = 83.29$; $\text{df} = 9$; $P = 0.00001$; $I^2 = 89\%$). Medium-term data also demonstrate no significant difference between groups (1 RCT, $n = 100$).

2.9 Mental state: 6. Average scores of various scales (skewed)

All data for the various scales are skewed and are best inspected by viewing [Analysis 2.9](#)

2.10 Leaving the study early

All data for leaving the study early showed no significant difference between groups: any reason (2 RCTs, $n = 168$); because of no effect (1 RCT, $n = 108$); early discharge (1 RCT, $n = 60$); early treatment termination (2 RCTs, $n = 168$); violation of test scheme (1 RCT, $n = 108$); and withdrawal of informed consent (1 RCT, $n = 108$, [Analysis 2.10](#)).

2.11 Quality of life: Average score (medium term, 12 to 24 weeks, WHO-QOL-100, low = poor)

The majority of data from a single study are significantly in favour of aripiprazole for a better outcome using this scale, including: total score ($P = 0.0001$) (1 RCT, $n = 100$, MD 2.60 CI 1.31 to 3.89); physical health ($P = 0.00001$) (1 RCT, $n = 100$, MD 6.00 CI 4.38 to 7.62); mental health ($P = 0.00001$) (1 RCT, $n = 100$, MD 9.10 CI 5.92 to 12.28); social function ($P = 0.00001$) (1 RCT, $n = 100$, MD 5.60 CI 3.33 to 7.87); environmental area ($P = 0.0001$) (1 RCT, $n = 100$, MD 11.50 CI 5.86 to 17.14); and independence ($P = 0.0001$) (1 RCT, $n = 100$, MD 6.20 CI 3.05 to 9.35, [Analysis 2.11](#)). Data for spiritual pillar demonstrate no significant difference between groups (1 RCT, $n = 100$).

2.12 Adverse effects: 1. At least one adverse effect

For non-specific adverse effects, data demonstrate no significant difference between groups (3 RCTs, $n = 258$). All other data also demonstrated no significant difference, including: abnormal urinary test results (1 RCT, $n = 108$); abnormal liver function (8 RCTs, $n = 658$); stuffy nose (2 RCTs, $n = 188$); sweating (1 RCT, $n = 70$); urine routine abnormal (1 RCT, $n = 80$, [Analysis 2.12](#)).

2.13 Adverse effects: 2. Cardiac effects (short term, up to 12 weeks)

Data for tachycardia demonstrate statistical significance ($P = 0.003$) in favour of aripiprazole (8 RCTs, $n = 643$, RR 0.35 CI 0.18 to 0.69). All other data demonstrate no significant difference between groups: abnormal ECG (6 RCTs, $n = 528$); decrease in blood pressure (4 RCTs, $n = 348$); and QTc prolongation (3 RCTs, $n = 225$, [Analysis 2.13](#)).

2.14 Adverse effects: 3a. Central nervous system

No significant difference was found between groups in the short term for the following outcomes: blurred vision (6 RCTs, $n = 521$); dizziness (8 RCTs, $n = 671$); headache (5 RCTs, $n = 436$) with substantial heterogeneity present ($\text{Chi}^2 = 13.42$; $\text{df} = 4$; $P = 0.009$; $I^2 = 70\%$); and insomnia (7 RCTs, $n = 591$). There was no difference at medium term for: dizziness (1 RCT, $n = 100$); insomnia (1 RCT, $n = 100$); or somnolence (1 RCT, $n = 100$, [Analysis 2.14](#)).

Data at short term for somnolence demonstrate statistical significance ($P = 0.01$) in favour of aripiprazole (9 RCTs, $n = 731$, RR 0.34 CI 0.15 to 0.77) with heterogeneity present ($\text{Chi}^2 = 18.37$; $\text{df} = 8$; $P = 0.019$; $I^2 = 56\%$). Medium-term data for headache demonstrate statistical significance ($P = 0.03$) in favour of quetiapine (1 RCT, $n = 100$, RR 9.00 CI 1.18 to 48.42).

2.15 Adverse effects: 4. Various extrapyramidal symptoms (short term, up to 12 weeks)

All data demonstrated no significant difference between groups for akathisia (7 RCTs, $n = 571$, [Analysis 2.15](#)); dystonia (2 RCTs, $n = 145$); general EPS (4 RCTs, $n = 348$); and tremor (4 RCTs, $n = 343$).

2.16 Adverse effects: 5. Gastrointestinal

Data were significantly in favour of aripiprazole in the short term from constipation ($P = 0.005$) (7 RCTs, $n = 591$, RR 0.38 CI 0.19 to 0.75, [Analysis 2.16](#)); dry mouth ($P = 0.0007$) (7 RCTs, $n = 611$, RR 0.23 CI 0.10 to 0.53); and in the medium term for dry mouth ($P = 0.009$) (1 RCT, $n = 100$, RR 0.11 CI 0.01 to 0.84). Data were significantly in favour of quetiapine in the short term for: nausea/ vomiting ($P = 0.004$) (7 RCTs, $n = 611$, RR 2.68 CI 1.36 to 5.26). There was no significant difference at medium term for nausea/vomiting (1 RCT, $n = 100$).

2.17 Adverse effects: 6. Haematological

Data demonstrate no significant difference in the short term for abnormal blood routine (1 RCT, $n = 85$, [Analysis 2.17](#)) and leucopenia (2 RCTs, $n = 140$).

2.18 Adverse effects: 7. Hormonal - binary measures

2.18.1 Menstrual disorder (short term, up to 12 weeks)

There was no significant difference between groups for menstrual disorder at both short term (6 RCTs, $n = 518$) and medium term (1 RCT, $n = 100$, [Analysis 2.18](#)).

2.19 Adverse effects: 8a. Metabolic - binary measures

At short term, there was no significant difference between groups for a decrease in appetite (4 RCTs, $n = 328$) and lactation (5 RCTs, $n = 383$). Medium data were also not significant for weight gain (1 RCT, $n = 100$). Data were significantly in favour of aripiprazole in the short term for weight gain ($P = 0.01$) (10 RCTs, $n = 823$, RR 0.45 CI 0.24 to 0.85) and at medium term for decreased appetite ($P = 0.05$) (1 RCT, $n = 100$, RR 0.13 CI 0.02 to 0.96, [Analysis 2.19](#)).

2.20 Adverse effects: 8b. Metabolic - continuous measure

Data from one small RCT demonstrate statistical significance ($P = 0.03$) in favour of aripiprazole for cholesterol TC average endpoint level (in mmol/L) (1 RCT, $n = 180$, MD -0.19 CI -0.36 to -0.02, [Analysis 2.20](#)). However, all other data demonstrated no significant difference between groups.

COMPARISON 3: ARIPIPRAZOLE versus RISPERIDONE

3.1 Global state: 1. No clinically significant response (as defined by the original studies)

Data are equivocal at short term, demonstrating no significant difference between groups (80 RCTs, $n = 6381$, RR 1.08 CI 0.96 to 1.21, [Analysis 3.1](#)).

3.2 Global state: 2. Average endpoint total score (short term, up to 12 weeks, CGI, high = poor)

Data demonstrate statistical significance ($P = 0.006$) in favour of risperidone (2 RCTs, $n = 196$, MD 0.35 CI 0.09 to 0.61, [Analysis 3.2](#)).

3.3 Global state: 3. Average CGI subscale scores (short term, up to 12 weeks, high = poor)

CGI-EI data demonstrate statistical significance ($P = 0.006$) in favour of risperidone (1 RCT, $n = 120$, MD 0.50 CI 0.14 to 0.86, [Analysis 3.3](#)), and CGI-SI data demonstrate statistical significance ($P = 0.006$) in favour of risperidone (1 RCT, $n = 120$, MD 0.40 CI 0.12 to 0.68).

3.4 Global state average endpoint of various scales (skewed)

All data are skewed and are best inspected by viewing [Analysis 3.4](#).

3.5 Mental state: 1. Specific - binary outcomes (short term, up to 12 weeks)

Data for anxiety demonstrate statistical significance ($P = 0.01$) in favour of risperidone (9 RCTs, $n = 744$, RR 1.81 CI 1.12 to 2.94, [Analysis 3.5](#)); however all other data are equivocal, demonstrating no difference between groups, including for agitation/excitement (26 RCTs, $n = 2038$) and irritability (1 RCT, $n = 100$).

3.6 Mental state: 2a. Average endpoint scale score (short term, up to 12 weeks, high = poor)

Data at short term for BPRS demonstrate statistical significance ($P = 0.004$) in favour of aripiprazole (5 RCTs, $n = 570$, MD -1.33 CI -2.24 to -0.42, [Analysis 3.6](#)), as were data for PANSS short term which showed a risk reduction by 0.8 on the PANSS scale favouring aripiprazole group (77 RCTs, $n = 5733$, MD -0.80 95% CI -1.58 to -0.02, [Analysis 3.6](#)). However, all other data show no significant difference between groups: PANSS medium term (1 RCT, $n = 50$) and SANS medium term (1 RCT, $n = 50$).

3.7 Mental state: 3. Specific - average endpoint positive score (PANSS, high = poor)

Data are equivocal at both short and medium term, demonstrating no significant difference between groups (40 RCTs, n = 3205, MD 0.02 CI -0.37 to 0.41, [Analysis 3.7](#)).

3.8 Mental state: 4. Specific - average endpoint negative score (PANSS, high = poor)

Data demonstrate statistical significance ($P = 0.001$) in favour of aripiprazole at short term (37 RCTs, n = 2976, MD -0.64 CI -1.04 to -0.25, [Analysis 3.8](#)).

3.9 Mental state: 5. Specific - average endpoint general psychopathological score (PANSS, high = poor)

Data are equivocal at both short and medium term, demonstrating no significant difference between groups (58 RCTs, n = 4243, MD -0.25 CI -0.71 to 0.20, [Analysis 3.9](#)).

3.10 Mental state: 6. PANSS average score decreased rate (short term, up to 12 weeks, low = poor)

Data for total scale score decreased rate demonstrate statistical significance ($P = 0.03$) in favour of aripiprazole (3 RCTs, n = 219, MD 3.06 CI 0.24 to 5.87, [Analysis 3.10](#)). All other data demonstrate no significant difference between groups.

3.11 Mental state: 7. BPRS total score decreased rate (short term, up to 12 weeks, high = poor)

Data demonstrate no significant difference between groups (2 RCTs, n = 132, MD -2.97 CI -6.61 to 0.67, [Analysis 3.11](#)).

3.12 Mental state: 8. General - average total score (PANSS, high = poor)

Data from two RCTs demonstrate no significant difference between groups at short term (2 RCTs, n = 372, MD 1.50 CI -2.96 to 5.96, [Analysis 3.12](#)).

3.13 Mental state: 9. Average scores of various scale (skewed)

All data for this outcome are skewed, and are best inspected by viewing [Analysis 3.13](#).

3.14 Leaving the study early

All data for leaving the study early demonstrate no significant difference between groups, including leaving for any reason (12 RCTs, n = 1239, [Analysis 3.14](#)); progressive disease (2 RCTs, n = 188); incomplete data (1 RCT, n = 180); adverse effects (9 RCTs, n = 1272); and no effect of study drug (5 RCTs, n = 681).

3.15 Adverse effects: 1. At least one adverse effect, non-specific

With more non-specific adverse effects seen with people receiving risperidone, data demonstrate statistical significance ($P = 0.0002$) in favour of aripiprazole (28 RCTs, n = 2361, RR 0.81 CI 0.73 to 0.91, [Analysis 3.15](#)). Generally, data demonstrated no significant difference between groups, including hyper-salivation (7 RCTs, n = 554), and sweating (4 RCTs, n = 278).

Data demonstrate statistical significance ($P = 0.003$) in favour of aripiprazole for abnormal liver function (29 RCTs, n = 2300, RR 0.63 CI 0.46 to 0.86) and sexual desire change ($P = 0.0001$) (8 RCTs, n = 614, RR 0.11 CI 0.04 to 0.30).

3.16 Adverse effects: 2a. Cardiac effects (short term, up to 12 weeks)

Data for tachycardia demonstrate statistical significance ($P = 0.02$) in favour of aripiprazole (49 RCTs, n = 3835, RR 0.76 CI 0.61 to 0.96, [Analysis 3.16](#)). All other data are equivocal, demonstrating no significant difference between groups.

3.17 Adverse effects: 2b. Cardiac - QTc change from baseline (in ms)

Data demonstrate statistical significance ($P = 0.005$) in favour of aripiprazole (2 RCTs, n = 383, MD -7.19 CI -12.19 to -2.19, [Analysis 3.17](#)).

3.18 Adverse effects: 3. Central nervous system (short term, up to 12 weeks)

The majority of data are equivocal, demonstrating no difference between groups. Data for headache demonstrate statistical significance ($P = 0.01$) in favour of risperidone (20 RCTs, n = 1505, RR 1.91 CI 1.31 to 2.78, [Analysis 3.18](#)). Data from one small RCT demonstrate statistical significance ($P = 0.04$) in favour of aripiprazole for decrease in memory, with higher instances seen in people receiving risperidone (1 RCT, n = 60, RR 0.22 CI 0.05 to 0.94).

3.19 Adverse effects: 3a. Endocrine - Prolactin - average change (ng/mL)

Data demonstrate statistical significance ($P = 0.00001$) in favour of aripiprazole (2 RCTs, $n = 383$, MD -54.71 CI -60.06 to -49.36, [Analysis 3.19](#)).

3.20 Adverse effects: 3b. Endocrine - Prolactin - associated

Data from one small RCT demonstrate statistical significance ($P = 0.00001$) in favour of aripiprazole for abnormally high prolactin value (1 RCT, $n = 301$, RR 0.04 CI 0.02 to 0.08, [Analysis 3.20](#)). Data demonstrate no significant difference between groups for dysmenorrhoea (1 RCT, $n = 91$).

3.21 Adverse effects: 4. Various extrapyramidal symptoms (short term, up to 12 weeks)

3.21.1 Akathisia

Data demonstrate statistical significance of aripiprazole for: akathisia ($P = 0.00001$) (42 RCTs, $n = 3501$, RR 0.60 CI 0.48 to 0.74, [Analysis 3.21](#)); tremor ($P = 0.00001$) (36 RCTs, $n = 2799$, RR 0.35 CI 0.27 to 0.45); dystonia ($P = 0.00001$) (32 RCTs, $n = 2640$, RR 0.35 CI 0.25 to 0.49); and EPS ($P = 0.00001$) (31 RCTs, $n = 2605$, RR 0.39 CI 0.31 to 0.50) with slight heterogeneity present ($\text{Chi}^2 = 53.91$; $df = 30$; $P = 0.005$; $I^2 = 44\%$). All other data demonstrate no difference between groups for parkinsonism (1 RCT, $n = 301$); use of antiparkinson medication (1 RCT, $n = 83$); tremor (2 RCTs, $n = 391$).

3.22 Adverse effects: 4b. Extrapyramidal - average score

3.22.1 Abnormal Involuntary Movement Scale (high = poor)

Data demonstrate no significant difference between groups (2 RCTs, $n = 383$, MD -0.25 CI -1.24 to 0.75, [Analysis 3.22](#)) with considerable heterogeneity present ($\text{Chi}^2 = 3.09$; $df = 1$; $P = 0.079$; $I^2 = 68\%$).

3.22.2 Barnes Akathisia Scale (high = poor)

Data demonstrate no significant difference between groups (2 RCTs, $n = 383$, MD -0.11 CI -0.49 to 0.27) with slight heterogeneity present ($\text{Chi}^2 = 1.98$; $df = 1$; $P = 0.16$; $I^2 = 49\%$).

3.22.3 Simpson-Angus Scale (high = poor)

Data demonstrate no significant difference between groups (2 RCTs, $n = 383$, MD -0.70 CI -2.22 to 0.82) with substantial heterogeneity present ($\text{Chi}^2 = 5.11$; $df = 1$; $P = 0.024$; $I^2 = 80\%$).

3.23 Adverse effects: 5. Gastrointestinal

Data for constipation (27 RCTs, $n = 2067$) and dry mouth (33 RCTs, $n = 2658$) are equivocal, demonstrating no significant difference between groups ([Analysis 3.23](#)). For nausea and vomiting data demonstrate statistical significance ($P = 0.00001$) in favour of risperidone (28 RCTs, $n = 2180$, RR 1.84 CI 1.31 to 2.56).

3.24 Adverse effects: 6. Haematological

All data demonstrate no difference between groups for abnormal blood routine (6 RCTs, $n = 515$, [Analysis 3.24](#)); leucopenia (1 RCT, $n = 60$) and abnormal blood lipids (1 RCT, $n = 80$).

3.25 Adverse effects: 7a. Metabolic - binary measures (short term, up to 12 weeks)

3.25.1 Appetite - decrease

Data demonstrate statistical significance ($P = 0.05$) in favour of aripiprazole (2 RCTs, $n = 204$, RR 0.26 CI 0.07 to 1.03, [Analysis 3.25](#)).

3.25.2 Blood glucose- increase

Data demonstrate statistical significance ($P = 0.02$) in favour of aripiprazole (5 RCTs, $n = 358$, RR 0.28 CI 0.09 to 0.82).

3.25.3 Endocrine disorder

Data demonstrate statistical significance ($P = 0.00001$) in favour of aripiprazole (9 RCTs, $n = 642$, RR 0.07 CI 0.03 to 0.17).

3.25.4 Lactation

Data demonstrate statistical significance ($P = 0.01$) in favour of aripiprazole (3 RCTs, $n = 216$, RR 0.11 CI 0.02 to 0.60).

3.25.5 Menstrual disorder/lactation

Data demonstrate statistical significance ($P = 0.00001$) in favour of aripiprazole (29 RCTs, $n = 2278$, RR 0.10 CI 0.06 to 0.16).

3.25.6 Menstrual disorder or sexual function change

Data demonstrate no significant difference between groups (1 RCT, $n = 68$).

3.25.7 Menstrual disorder

Data demonstrate statistical significance ($P = 0.00001$) in favour of aripiprazole (9 RCTs, $n = 655$, RR 0.13 CI 0.06 to 0.27).

3.25.8 Skin symptoms

Data demonstrate statistical significance ($P = 0.02$) in favour of aripiprazole (9 RCTs, $n = 778$, RR 0.32 CI 0.12 to 0.86).

3.25.9 PRL-increase

Data demonstrate statistical significance ($P = 0.002$) in favour of aripiprazole (3 RCTs, $n = 184$, RR 0.07 CI 0.01 to 0.38).

3.25.10 Obesity

Data demonstrate no significant difference between groups (1 RCT, $n = 72$).

3.25.11 Vaginal bleeding

Data demonstrate no significant difference between groups (1 RCT, $n = 72$).

3.25.12 Weight gain

Data demonstrate statistical significance ($P = 0.00001$) in favour of aripiprazole (58 RCTs, $n = 4623$, RR 0.22 CI 0.17 to 0.29).

3.25.13 Weight loss

Data demonstrate no significant difference between groups (1 RCT, $n = 101$).

3.26 Adverse effects: 7b. Metabolic - continuous measures

3.26.1 Endpoint average weight (in kg)

Data demonstrate statistical significance ($P = 0.02$) in favour of aripiprazole (5 RCTs, $n = 465$, MD -2.30 CI -4.17 to -0.44, [Analysis 3.26](#)), however with substantial heterogeneity present ($\text{Chi}^2 = 37.17$; $\text{df} = 4$; $P = 0.0$; $I^2 = 89\%$).

3.26.2 Weight change from baseline (in kg)

Data from one small RCT demonstrate statistical significance ($P = 0.00001$) in favour of aripiprazole (1 RCT, $n = 100$, MD -1.50 CI -1.84 to -1.16).

3.26.3 Average endpoint BMI of male participants (in kg/m²)

Data from one small RCT demonstrate statistical significance ($P = 0.003$) in favour of aripiprazole (1 RCT, $n = 60$, MD -2.46 CI -4.08 to -0.84).

3.26.4 Average endpoint BMI of female participants (in kg/m²)

Data demonstrate no significant difference between groups (2 RCTs, $n = 124$, MD -1.47 CI -3.55 to 0.60) with substantial heterogeneity between groups ($\text{Chi}^2 = 4.32$; $\text{df} = 1$; $P = 0.038$; $I^2 = 77\%$).

3.26.5 Average endpoint blood glucose of female participants (in mmol/L)

Data demonstrate statistical significance ($P = 0.00001$) in favour of risperidone (1 RCT, $n = 60$).

3.26.6 Average endpoint blood glucose of male participants (in mmol/L)

Data demonstrate no significant difference between groups (1 RCT, $n = 60$).

3.26.7 Average endpoint blood glucose FBG (in mg/dL)

Data demonstrate no significant difference between groups (1 RCT, $n = 60$).

3.26.8 Average endpoint cholesterol - TC of female participants (in mmol/L)

Data from one small RCT demonstrate statistical significance ($P = 0.03$) in favour of aripiprazole (1 RCT, $n = 60$, MD -0.51 CI -0.96 to -0.06).

3.26.9 Average endpoint cholesterol - TC of male participants (in mmol/L)

Data from one small RCT demonstrate statistical significance ($P = 0.05$) in favour of aripiprazole (1 RCT, $n = 60$, MD -0.48 CI -0.96 to 0.00).

3.26.10 Average endpoint cholesterol - TC level (in mmol/L)

Data demonstrate no significant difference between groups (2 RCTs, $n = 240$).

3.26.11 Average endpoint cholesterol - TG level (in mmol/L)

Data demonstrate no significant difference between groups (1 RCT, $n = 60$).

3.26.12 Average endpoint cholesterol - LDL level (in mmol/L)

Data demonstrate no significant difference between groups (2 RCTs, $n = 240$).

3.26.13 Average endpoint waistline (in cm)

Data from one small RCT demonstrate statistical significance ($P = 0.003$) in favour of aripiprazole (1 RCT, $n = 180$, MD -3.30 CI -5.47 to -1.13).

3.27. Adverse effect: 7c. Metabolic - continuous measures

Data from one small RCT demonstrate statistical significance ($P = 0.01$) in favour of aripiprazole for change in cholesterol from baseline (1 RCT, $n = 83$, MD -22.30 CI -39.69 to -4.91, [Analysis 3.27](#)). Remaining data demonstrate no significant difference between groups.

3.28 Adverse effect: 8. required additional drug combination

3.28.1 Benzodiazepines

Data demonstrate no significant difference between groups (2 RCTs, $n = 138$, RR 1.07 CI 0.73 to 1.58, [Analysis 3.28](#)).

3.28.2 Benzhexol

Data from one small RCT demonstrate statistical significance ($P = 0.04$) in favour of aripiprazole (1 RCT, $n = 69$, RR 0.34 CI 0.12 to 0.93).

3.28.3 Benzhexol/propranolol

Data demonstrate no significant difference between groups (1 RCT, $n = 69$, RR 1.11 CI 0.45 to 2.72).

3.29 Adverse effects: 9. TESS score (short term, up to 12 weeks, high = poor)

Data demonstrate statistical significance ($P = 0.006$) in favour of aripiprazole (4 RCTs, $n = 250$, MD -1.34 CI -2.3 to -0.39, [Analysis 3.29](#)), however with substantial heterogeneity present ($\text{Chi}^2 = 48.54$; $df = 3$; $P = 0.00001$; $I^2 = 94\%$).

3.30 Adverse effects: 10. TESS score (skewed)

All data for this outcome are skewed and are best inspected by viewing [Analysis 3.30](#).

3.31 Adverse effects: 11. weight gain (skewed)

All data for this outcome are skewed and are best inspected by viewing [Analysis 3.31](#).

3.32 Cognitive functioning: 1. Specific - average endpoint total score

3.32.1 Short term, up to 12 weeks, WMS, low = poor

Data demonstrate no significant difference between groups for both WMS (1 RCT, $n = 72$, [Analysis 3.32](#)) and WAIS-RC (1 RCT, $n = 72$).

3.33 Cost-effectiveness analysis (skewed)

All data for this outcome are skewed and are best viewed by inspecting [Analysis 3.33](#).

COMPARISON 4: ARIPIPRAZOLE versus ZIPRASIDONE

4.1 Global state: 1. No clinically significant response (as defined by the original studies)

Short term data demonstrate no significant difference between groups (6 RCTs, $n = 442$, RR 0.97 CI 0.62 to 1.52, [Analysis 4.1](#)).

4.2 Global state: 2. Average endpoint CGI-GI score (short term, up to 12 weeks, high = poor)

Data from one small RCT demonstrate statistical significance ($P = 0.001$) in favour of aripiprazole (1 RCT, $n = 86$, MD -3.93 CI -6.32 to -1.54, [Analysis 4.2](#)).

4.3 Global state: 3. Average change score (CGI-S, decline = best)

Data demonstrate no significant difference between groups (1 RCT, $n = 247$, MD -0.03 CI -0.28 to 0.22, [Analysis 4.3](#)).

4.4 Mental state: 1. Average endpoint total score (short term, up to 12 weeks, high = poor)

PANSS data demonstrate no significant difference between groups (7 RCTs, $n = 689$, [Analysis 4.4](#)), neither do BPRS data (1 RCT, $n = 247$). However, SANS data demonstrate statistical significance ($P = 0.02$) in favour of aripiprazole (3 RCTs, $n = 238$, MD -1.39 CI -2.56 to -0.22).

4.5 Mental state: 2. Specific - binary outcomes (up to 12 weeks - short term)

There was no significant difference between groups for anxiety (1 RCT, $n = 86$) or agitation (2 RCTs, $n = 150$, [Analysis 4.5](#)).

4.6 Mental state: 3. Specific - average endpoint PANSS subscale scores (short term, high = poor)

There was no significant difference between groups for positive symptom score (2 RCTs, n = 146); negative symptom scores (4 RCTs, n = 272); and general pathology scores (5 RCTs, n = 382, [Analysis 4.6.](#))

4.7 Mental state: 4. Average endpoint scores of various scales (skewed)

All data for this outcome are skewed and are best inspected by viewing [Analysis 4.7.](#)

4.8 Leaving the study early

All data for leaving study early were equivocal, demonstrating no significant difference between groups ([Analysis 4.8.](#))

4.9 Adverse effects: 1. At least one adverse effect, non-specific

Data demonstrate statistical significance ($P = 0.0001$) in favour of ziprasidone for sexual function change (2 RCTs, n = 172, RR 8.00 CI 2.96 to 21.65, [Analysis 4.9.](#)); all other data for adverse effects were equivocal.

4.10 Adverse effects: 2. Cardiac effects (short term, up to 12 weeks)

All data for cardiac effects are equivocal and demonstrate no difference between groups ([Analysis 4.10.](#))

4.11 Adverse effects: 3. Central/ peripheral nervous system

Data for dizziness demonstrate statistical significance ($P = 0.002$) in favour of ziprasidone (5 RCTs, n = 376, RR 3.24 CI 1.57 to 6.70, [Analysis 4.11.](#)), as well as data for insomnia ($P = 0.02$) (5 RCTs, n = 382, RR 2.93 CI 1.17 to 7.30), however with slight heterogeneity present ($\text{ChI}^2 = 7.38$; $\text{df} = 4$; $P = 0.117$; $I^2 = 46\%$). All other data are equivocal, demonstrating no significant difference between groups, including for headache (2 RCTs, n = 150); blurred vision (1 RCT, n = 84) and somnolence (4 RCTs, n = 296).

4.12 Adverse effects: 4. Various extrapyramidal symptoms (short term, up to 12 weeks)

All data were equivocal, demonstrating no difference between groups ([Analysis 4.12.](#)), including dystonia (1 RCT, n = 84); tremor (2 RCTs, n = 152) and use of anti-Parkinson drugs (2 RCTs, n = 140) with substantial heterogeneity present ($\text{ChI}^2 = 6.94$; $\text{df} = 1$; $P = 0.008$; $I^2 = 86\%$).

4.13 Adverse effects: 5. Gastrointestinal (short term, up to 12 weeks)

Again, all data were equivocal, demonstrating no difference between groups ([Analysis 4.13.](#)), including: constipation (3 RCTs, n = 230); dry mouth (4 RCTs, n = 296); hyper-salivation (1 RCT, n = 86) and nausea/vomiting (6 RCTs, n = 442).

4.14 Adverse effects: 6. Haematological

Data for leucopenia demonstrate no significant difference between groups (2 RCTs, n = 140, [Analysis 4.14.](#))

4.15 Adverse effects: 7. Hormonal

Data for menstrual disorder demonstrate no significant difference between groups (6 RCTs, n = 538, [Analysis 4.15.](#))

4.16 Adverse effects: 8a. Metabolic - binary measures

All data were equivocal, demonstrating no difference between groups, including appetite decrease (2 RCTs, n = 152, [Analysis 4.16.](#)) with substantial heterogeneity present ($\text{ChI}^2 = 4.04$; $\text{df} = 1$; $P = 0.045$; $I^2 = 75\%$); abnormal blood routine (1 RCT, n = 85); lactation (1 RCT, n = 66); and weight gain (3 RCTs, n = 232).

4.17 Adverse effects: 8b. Metabolic - continuous measures

Most data were equivocal, demonstrating no difference between groups; however, data for HDL demonstrate statistical significance ($P = 0.04$) in favour of aripiprazole (1 RCT, n = 180, MD 0.10 CI 0.01 to 0.19) and data for waistline average endpoint level (in cm) demonstrate statistical significance ($P = 0.0004$) in favour of aripiprazole (1 RCT, n = 180, MD -3.40 CI -5.29 to -1.51 [Analysis 4.17.](#))

COMPARISON 5: ARIPIPRAZOLE versus OLANZAPINE

5.1 Global state: 1. No clinically significant response (as defined by the original studies)

Data are equivocal at short term (10 RCTs, n = 1422) and medium term (1 RCT, n = 317), demonstrating no significant difference between groups ([Analysis 5.1.](#))

5.2 Global state: 2. Not responded (decline in PANSS of 30% or more)

5.2.1 By up to 12 weeks (short term)

Data from one small RCT demonstrate statistical significance ($P = 0.04$) in favour of olanzapine at short term (1 RCT, $n = 566$, RR 1.16 CI 1.01 to 1.34, [Analysis 5.2](#)) and long term ($P = 0.05$) (1 RCT, $n = 566$, RR 1.13 CI 1.0 to 1.27).

5.3 Global state: 3. Remission not achieved (as defined in the study)

Data demonstrate no significant difference between groups at short term (1 RCT, $n = 566$, [Analysis 5.3](#)). Data from one small RCT demonstrate statistical significance ($P = 0.00001$) in favour of olanzapine by long term (1 RCT, $n = 566$, RR 1.38 CI 1.23 to 1.56).

5.4 Global state: 4. Average endpoint EI score (CGI, high = poor)

Data demonstrate no significant difference between groups at short term (2 RCTs, $n = 180$, [Analysis 5.4](#)).

5.5 Global state: 5. Average endpoint CGI score decreased rate (short term, low = poor)

Data demonstrate no significant difference between groups (1 RCT, $n = 60$, [Analysis 5.5](#)).

5.6 Global state: 6. Average change score (CGI-S, decline = best)

Data demonstrate no significant difference between groups at long term (1 RCT, $n = 566$, [Analysis 5.6](#)).

5.7 Global state: 7. Improvement (CGI-I, high = poor)

Data demonstrate no significant difference between groups (1 RCT, $n = 566$, [Analysis 5.7](#)).

5.8 Mental state: 1. General - average total score (PANSS, high = poor)

Data are equivocal, demonstrating no significant difference between groups at short term (11 RCTs, $n = 1500$, [Analysis 5.8](#)) and medium term (2 RCTs, $n = 139$). Data from one small RCT demonstrate statistical significance ($P = 0.04$) in favour of olanzapine (1 RCT, $n = 566$, MD 4.20 CI 0.10 to 8.3) in the long term.

5.9 Mental state: 2. Average endpoint scale score (SANS, high = poor)

Data demonstrate no significant difference between groups at short term (1 RCT, $n = 89$, [Analysis 5.9](#)) and long term (1 RCT, $n = 48$).

5.10 Mental state: 3. average endpoint score (PANSS, skewed)

All data for this outcome are skewed and are best inspected by viewing [Analysis 5.10](#).

5.11 Mental state: 4. Specific - average endpoint positive score (PANSS, high = poor)

Overall, data from all time frames demonstrate statistical significance ($P = 0.01$) in favour of olanzapine (7 RCTs, $n = 1043$, MD 0.71 CI 0.17 to 1.26, [Analysis 5.11](#)). Data are equivocal at short term, demonstrating no significant difference between groups (5 RCTs, $n = 429$) with slight heterogeneity between groups ($\text{Chi}^2 = 6.26$; $\text{df} = 4$; $P = 0.181$; $I^2 = 36\%$). Data demonstrate no significant difference at medium term (1 RCT, $n = 48$) or long term (1 RCT, $n = 566$).

5.12 Mental state: 5. Specific - average endpoint negative subscale score (PANSS, high = poor)

At both short and medium term, data demonstrate no significant difference between group (6 RCTs, $n = 967$, [Analysis 5.12](#)).

5.13 Mental state: 6. Specific - average endpoint general pathological score (PANSS, high = poor)

At both short and medium term, data demonstrate no significant difference between groups (8 RCTs, $n = 642$, [Analysis 5.13](#)).

5.14 Mental state: 7. Specific - binary outcomes

5.14.1 Anxiety - labelled as "adverse effect"

Data demonstrate no significant difference between groups for anxiety (2 RCTs, $n = 778$, [Analysis 5.14](#)) or exacerbation of schizophrenia (2 RCTs, $n = 778$). Data from one small RCT demonstrate statistical significance ($P = 0.04$) in favour of aripiprazole for depression (1 RCT, $n = 566$, RR 0.27 CI 0.08 to 0.95).

5.15 Mental state: 8. Average various scale scores decreased rate (skewed)

All data for this outcome are skewed and are best inspected by viewing [Analysis 5.15](#).

5.16 Adverse effects: 1. At least one adverse effect

For non-specific adverse effects, data demonstrate no significant difference between groups (1 RCT, $n = 75$, [Analysis 5.16](#)). For endocrine dyscrasia, data from one small RCT demonstrate statistical significance ($P = 0.01$) in favour of aripiprazole (1 RCT, $n = 80$, RR 0.08 CI 0.01 to 0.61); and for high prolactin level ($P =$

0.001) (1 RCT, n = 317, RR 0.27 CI 0.12 to 0.60). Remaining data are equivocal and demonstrate no difference between groups, including skin reaction (1 RCT, n = 89); and liver function abnormality (5 RCTs, n = 348).

5.17 Adverse effects: 2. Cardiac effects

All data are equivocal and demonstrate no difference between groups for abnormal ECG (2 RCTs, n = 121); decrease in blood pressure (1 RCT, n = 89); QTc prolongation (3 RCTs, n = 618) and tachycardia (5 RCTs, n = 339).

5.18 Adverse effects: 3a. Cardiac - QTc change from baseline (in ms)

Data from one RCT demonstrate no significant difference between groups (1 RCT, n = 317, [Analysis 5.18](#)).

5.19 Adverse effects: 3b. Central/ peripheral nervous system

Data from two RCTs demonstrate statistical significance ($P = 0.0001$) in favour of aripiprazole for levels of sedation (2 RCTs, n = 883, RR 0.37 CI 0.23 to 0.60) and data from one small RCT demonstrate statistical significance ($P = 0.05$) in favour of aripiprazole for headache/dizziness (1 RCT, n = 89, RR 0.29 CI 0.09 to 1.00, [Analysis 3.19](#)). All other data are equivocal and demonstrate no difference between groups, including dizziness (6 RCTs, n = 1057); blurred vision (1 RCT, n = 75); fatigue (3 RCTs, n = 721) and insomnia (7 RCTs, n = 1141), however with considerable heterogeneity present ($\text{Chi}^2 = 13.87$; $\text{df} = 6$; $P = 0.031$; $I^2 = 57\%$).

5.20 Adverse effects: 4. Endocrine - Prolactin - average increase

Data from one small RCT demonstrate statistical significance ($P = 0.0001$) in favour of aripiprazole (1 RCT, n = 566, MD -8.89 CI -12.96 to -4.82, [Analysis 5.20](#)).

5.21 Adverse effects: 5. Extrapyramidal - various

All data are equivocal and demonstrate no difference between groups, including: tremor (1 RCT, n = 61); EPS (4 RCTs, n = 667); and parkinsonism (3 RCTs, n = 618). Data for akathisia are equivocal, demonstrating no significant difference between groups (6 RCTs, n = 1320, [Analysis 5.21](#)), however with considerable heterogeneity present ($\text{Chi}^2 = 19.45$; $\text{df} = 6$; $P = 0.003$; $I^2 = 69\%$).

5.22 Adverse effects: 6. Gastrointestinal

Data from one small RCT demonstrate statistical significance ($P = 0.03$) in favour of aripiprazole for abdominal pain (1 RCT, n = 566, RR 2.96 CI 1.09 to 8.03). All remaining data are equivocal and

demonstrate no significant difference between groups, including: dry mouth (5 RCTs, n = 854); constipation (6 RCTs, n = 443) and nausea/vomiting (6 RCTs, n = 948, [Analysis 5.22](#)).

5.23 Adverse effects: 7. Hormonal

5.23.1 Menstrual changes

Data are equivocal and demonstrate no significant difference between groups (3 RCTs, n = 198, [Analysis 5.23](#)).

5.24 Adverse effects: 8a. Metabolic - binary measures

Data demonstrate statistical significance ($P = 0.001$) in favour of aripiprazole for blood glucose increase (3 RCTs, n = 227, RR 0.12 CI 0.03 to 0.44); for abnormally high cholesterol level ($P = 0.0001$) (1 RCT, n = 223, RR 0.32 CI 0.19 to 0.54, [Analysis 5.24](#)); and weight gain ($P = 0.00001$) (9 RCTs, n = 1538, RR 0.25 CI 0.15 to 0.43). All remaining data demonstrate no significant difference between groups for appetite increase (2 RCTs, n = 655); lactation (1 RCT, n = 60) and PRL increase (1 RCT, n = 89).

5.25 Adverse effects: 8b. Metabolic - continuous measures (high = poor)

5.25.1 Weight - average endpoint level (in kg)

Data demonstrate statistical significance ($P = 0.00001$) in favour of aripiprazole (3 RCTs, n = 242, MD -7.43 CI -9.21 to -5.65, [Analysis 5.25](#)).

5.25.2 Weight gain - change from baseline (in kg)

Data demonstrate no significant difference between groups (2 RCTs, n = 656), however with substantial heterogeneity present ($\text{Chi}^2 = 6.31$; $\text{df} = 1$; $P = 0.012$; $I^2 = 84\%$).

5.25.3 Cholesterol - change from baseline (in mg/dL)

Data demonstrate statistical significance ($P = 0.00001$) in favour of aripiprazole (2 RCTs, n = 789, MD -15.37 CI -21.62 to -9.11).

5.25.4 Cholesterol - TC average endpoint level (in mmol/L)

Data demonstrate statistical significance ($P = 0.00001$) in favour of aripiprazole (2 RCTs, n = 182, MD -1.00 CI -1.44 to -0.56).

5.25.5 Cholesterol - TG average endpoint level (in mmol/L)

Data from one small RCT demonstrate statistical significance ($P = 0.00001$) in favour of aripiprazole (1 RCT, $n = 102$, MD -1.00 CI -1.31 to -0.69).

5.25.6 Blood glucose - PBG average endpoint level (in mg/dL)

Data from one small RCT demonstrate statistical significance ($P = 0.00001$) in favour of aripiprazole (1 RCT, $n = 60$, MD -0.95 CI -1.27 to -0.63).

5.25.7 Glucose - change from baseline (in mg/dL)

Data demonstrate no significant difference between groups (2 RCTs, $n = 883$).

5.26 Adverse effects: average endpoint scale scores (TESS, skewed)

All data for this outcome are skewed and are best inspected by viewing [Analysis 5.26](#).

5.27 Leaving the study early

Data for leaving for any reason from one small RCT demonstrate statistical significance ($P = 0.002$) in favour of olanzapine (9 RCTs, $n = 2331$, RR 1.15 CI 1.05 to 1.25, [Analysis 5.27](#)); statistical significance was also found in inefficacy ($P = 0.003$) in favour of olanzapine (4 RCTs, $n = 1352$, RR 1.81 CI 1.23 to 2.67). Remaining reasons for leaving the study early demonstrated no significant difference between groups, including adverse event (4 RCTs, $n = 1352$); early discharge (1 RCT, $n = 60$); medication non-compliance (1 RCT, $n = 255$); and death (1 RCT, $n = 214$).

5.28 Quality of life: I. Average endpoint general quality of life score (GQOLI-74, low = poor)

All data are equivocal and demonstrate no difference between groups ([Analysis 5.28](#)).

COMPARISON 6: ARIPIRAZOLE versus OLANZAPINE (acutely agitated people - all data by five days)

One study was included in this category.

6.1 Global state

An improvement was defined as reduction in the Brief Psychiatric Rating Scale (BPRS). There was no significant difference in the two groups ($n = 471$, MD -0.18, CI -0.79 to 0.43, [Analysis 6.1](#)).

6.2 Mental state

There was no significant difference reported in participants on aripiprazole and olanzapine in agitation level (defined as at least 40% reduction in PANSS-EC ($n = 604$, RR 0.92, CI 0.76 to 1.12). No significant difference was noted in agitation ($n = 578$, RR 0.25, CI 0.05 to 1.17); anxiety ($n = 604$, RR 0.93, CI 0.40 to 2.17) and exacerbation of schizophrenia ($n = 604$, RR 5.13, CI 0.25 to 106.49, [Analysis 6.2](#)). All such outcomes were labelled as "adverse effects" in the published report.

6.3 Leaving the study early

Both groups were similar in the number of participants leaving the study early due to adverse effects ($n = 604$, RR 0.68 CI 0.12 to 4.07, [Analysis 6.3](#)).

6.4 Adverse effects

6.4.1 Central nervous system

No significant difference was reported between administering aripiprazole or olanzapine in acutely agitated patients with regards to CNS side effects of dizziness ($n = 578$, RR 0.29, CI 0.06 to 1.36); sedation ($n = 578$, RR 0.71, CI 0.23 to 2.22); insomnia ($n = 604$, RR 1.60, CI 0.87 to 2.94) and somnolence ($n = 578$, RR 0.14, CI 0.02 to 1.15). Participants on aripiprazole reported more headaches ($n = 578$, RR 2.43, CI 1.02 to 5.77) and lethargy ($n = 578$, RR 1.33, CI 0.30 to 5.90, [Analysis 6.4](#)).

6.4.2 Endocrine system - increase in average levels of prolactin

People allocated aripiprazole reported significantly lower ($P = 0.00001$) prolactin level increase compared with participants given olanzapine ($n = 604$, MD -15.76, CI -19.18 to -12.34, [Analysis 6.5](#)).

6.4.3 Extrapyramidal side effects

Participants in both groups experienced similar rates of akathisia ($n = 604$, RR 1.43, CI 0.79 to 2.56) and parkinsonian symptoms ($n = 604$, 1 RCT, RR 1.71 CI 0.41 to 7.10, [Analysis 6.6](#)).

6.4.4 Extrapyramidal symptoms

Extrapyramidal symptoms were also reported by using scales where higher score represents a poor outcome. There was no significant difference between groups when assessed using Barnes Akathisia scale ($n = 604$, MD 0.07, CI -0.24 to 0.38) or Simpson Angus scale ($n = 604$, MD -0.05, CI -0.13 to 0.03, [Analysis 6.7](#)).

6.4.5 Gastrointestinal side effects

Both groups reported similar occurrence of dry mouth (n = 578, RR 1.00, CI 0.20 to 4.91) and twice the number of participants on olanzapine reported nausea/dyspepsia (n = 578, RR 0.50, CI 0.09 to 2.71, [Analysis 6.8](#)).

6.4.6 Metabolic side effects- increase in triglyceride levels

These results favoured patients on aripiprazole significantly (P = 0.00001) (n = 604, MD -35.62, CI -49.25 to -21.99, [Analysis 6.9](#)).

COMPARISON 7. ARIPIRAZOLE versus OTHER ANTIPSYCHOTIC DRUGS

We used data from three studies for this comparison. In all three studies aripiprazole was compared with any one of several new generation antipsychotic drugs.

7.1 Global state: 1. No change as defined by the original study (measured by IAQ)

[Kerwin 2007](#) showed an improvement in global state in energy (n = 523, 1 RCT, RR 0.69 CI 0.56 to 0.84); mood (n = 523, 1 RCT, RR 0.77 CI 0.65 to 0.92); negative symptoms (n = 523, 1 RCT, RR 0.82 CI 0.68 to 0.99); somnolence (n = 523, 1 RCT, RR 0.80 CI 0.69 to 0.93) and weight gain (n = 523, 1 RCT, RR 0.84 CI 0.76 to 0.94) when aripiprazole was used but no significant difference was noted in cognition (n = 523, 1 RCT, [Analysis 7.1](#)).

7.2 Global state: 2. Change in sexual dysfunction (measured by ASEX)

No significant difference was seen in the two groups (n = 85, 1 RCT, [Analysis 7.2](#)).

7.3 Mental state: 1. Binary outcomes

No significant difference was noted in anxiety (n = 1361, 2 RCTs); "schizophrenia" (n = 548, 1 RCT) and psychotic disorder (n = 2881, 3 RCTs). Participants on aripiprazole experienced slightly less agitation (n = 548, 1 RCT, RR 2.64 CI 0.96 to 7.23, [Analysis 7.3](#)).

7.4 Medication preference (study medication worse than or equal to previous medication)

People reported aripiprazole being better in the short term (n = 446, 1 RCT, RR 0.67 CI 0.49 to 0.91) and medium term (n = 330, 1 RCT, RR 0.39 CI 0.25 to 0.61). Carers, however, reported no difference in the two groups both in the short (n = 121, 1 RCT) and medium term (n = 80, 1 RCT, [Analysis 7.4](#)).

7.5 Quality of life: 1. Unsatisfactory response (Health dimension scale)

Fewer participants reported an unsatisfactory response on the health dimension scale when using aripiprazole (n = 329, 1 RCT, RR 0.29 CI 0.13 to 0.66, [Analysis 7.5](#)).

7.6 Quality of life: 2. Average change in Quality of Life score (high is better)

The results favoured other antipsychotics (n = 326, 1 RCT, MD 6.20 CI 3.08 to 9.32, [Analysis 7.6](#)).

7.7 Quality of life: 3. Average EQ-5D utility score (high is better)

No significant difference was noted in the two groups (n = 329, 1 RCT, [Analysis 7.7](#)).

7.8 Quality of life: 4a. Weight-related score - no meaningful change (measured by Impact of Weight on Quality of Life (IWQoL-Lite))

No significant difference was noted in the two groups when weight was measured in binary scale (n = 327, 1 RCT, [Analysis 7.8](#)).

7.9 Quality of life: 4b. Weight-related score (measured by Impact of Weight on Quality of Life (IWQoL-Lite))

No significant difference was noted in the two groups for average change in weight in the short term (n = 443, 1 RCT) and medium term (n = 328, 1 RCT, [Analysis 7.9](#)).

7.10 Leaving the study early

No significant difference was noted in the participants who left the study early in the three groups for any reason (n = 2908, 3 RCTs, RR 0.97 CI 0.78 to 1.19); administrative reasons (n = 833, 1 RCT, RR 0.80 CI 0.00 to 1.84); death (n = 555, 1 RCT, RR 0.48 CI 0.04 to 5.23); inefficacy (n = 2908, 3 RCTs, RR 0.94 CI 0.45 to 1.96); lost to follow-up (n = 1388, 2 RCTs, RR 0.85 CI 0.34 to 2.13); no longer meets criteria (n = 1388, 2 RCTs, RR 0.65 CI 0.16 to 2.63); other (n = 1388, 2 RCTs, RR 0.62 CI 0.10 to 3.80); compliance issues (n = 1388, 2 RCTs, RR 1.10 CI 0.53 to 2.32) and pregnancy (n = 555, 1 RCT, RR 0.95 CI 0.14 to 6.73). More participants in the aripiprazole group left due to adverse events (n = 2908, 3 RCTs, RR 1.40 CI 1.11 to 1.76). Fewer participants in the aripiprazole group withdrew from the study (n = 2908, 3 RCTs, RR 0.48 CI 0.36 to 0.66, [Analysis 7.10](#)).

7.11 Adverse effects - 1. At least one side effect

Participants taking other antipsychotics reported this slightly more (n = 2333, 2 RCTs, RR 1.14 CI 1.05 to 1.23, [Analysis 7.11](#)).

7.12 Adverse effects - 2. Central nervous system

No significant difference was noted in sleep disorder (n = 813, 1 RCT, RR 1.79 CI 0.78 to 4.10) and fatigue (n = 548, 1 RCT, RR 0.59 CI 0.27 to 1.28). A larger number of participants on aripiprazole reported insomnia (n = 2881, 3 RCTs, RR 2.09 CI 1.65 to 2.66) and headache (n = 2881, 3 RCTs, RR 1.47 CI 1.09 to 1.99). Fewer participants on aripiprazole reported somnolence (n = 2881, 3 RCTs, RR 0.52 CI 0.39 to 0.71, [Analysis 7.12](#)).

7.13 Adverse effects - 3a. Endocrine system - increase in prolactin level

Significantly fewer participants on aripiprazole reported an increased prolactin level (n = 548, 1 RCT, RR 0.31 CI 0.23 to 0.41, [Analysis 7.13](#)).

7.14 Adverse effects - 3b. Endocrine system - change in prolactin level from baseline

The results favoured aripiprazole (n = 94, 1 RCT, MD -8.60 CI -19.14 to 1.94, [Analysis 7.14](#)).

7.15 Adverse effects - 4. Extrapyramidal symptoms (EPS)

The results did not favour any of the comparison groups with a large confidence interval (n = 2881, 3 RCTs, RR 1.02 CI 0.09 to 11.09, [Analysis 7.15](#)) and prohibitively high heterogeneity (97%). It is unclear why [Tandon 2006](#) causes this and removal of this study results in homogeneity being restored.

7.16 Adverse effects - 5. Gastrointestinal

A significantly larger number of people given aripiprazole reported symptoms of nausea (n = 2881, 3 RCTs, RR 3.13 CI 2.12 to 4.61, [Analysis 7.16](#)).

7.17 Adverse effects - 6a. Metabolic - binary measures

Significantly fewer people allocated aripiprazole reported 7% or more weight gain in the medium term (n = 330, 1 RCT, RR 0.35 CI 0.19 to 0.64); average weight gain (n = 548, 1 RCT, RR 0.11 CI 0.03 to 0.37); total cholesterol increase (n = 269, 1 RCT, RR 0.75 CI 0.62 to 0.91) and low-density lipoprotein (LDL) increase (n = 268, 1 RCT, RR 0.65 CI 0.51 to 0.84). We found no significant difference in either group in high-density lipoprotein (HDL) increase (n = 269, 1 RCT, RR 0.87 CI 0.61 to 1.22); triglyceride increase (n = 267, 1 RCT, RR 0.80 CI 0.64 to 1.00) and increase in fasting glucose (n = 236, 1 RCT, RR 0.95 CI 0.62 to 1.47). A greater number of people given aripiprazole reported 7% or more of weight loss in the medium term (n = 330, 1 RCT, RR 1.75 CI 0.97 to 3.19, [Analysis 7.17](#)).

7.18 Adverse effects - 6b. Metabolic - continuous measures

Aripiprazole was favoured for no risk of weight gain (n = 537, 1 RCT, MD -2.70 CI -3.68 to -1.72); weight change from baseline (n = 441, 1 RCT, MD short term -2.48 CI -3.30 to -1.66; n = 327, 1 RCT, MD medium term -3.74 CI -4.65 to -2.83); and change in fasting cholesterol (n = 262, 1 RCT, MD -9.70 CI -16.07 to -3.33). There was no difference reported in change in fasting glucose (n = 229, 1 RCT, MD -1.90 CI -5.78 to 1.98, [Analysis 7.18](#)).

8. SENSITIVITY ANALYSIS

We planned to undertake a sensitivity analysis for the primary outcomes of interest of (i) no clinically important response (as defined by each study); (ii) general functioning; and (iii) clinically important specific adverse effects. No study, however, reported data for the outcome of general functioning. For sensitivity analysis of 'comparator dose', we tested outcome of (i) no clinically important response (as defined by each study); and (ii) general mental state.

8.1 Implication of randomisation

8.1.1 Aripiprazole versus Clozapine

8.1.1.1 Global state: no clinically significant response (as defined by the individual studies)

There remained no significant differences between groups after removing studies from meta-analysis that only implied randomisation (n = 322, 4 RCTs, RR 1.04 CI 0.76 to 1.44).

8.1.1.2 Adverse effects - clinically important specific adverse effects

Few studies provided data at medium term for any clinically important adverse effects; for EPS effects, only one study ([Li 2007](#)) provided relevant data. This study only implied randomisation, therefore after removing this study from data and analysis, there were no data left to compare. However, at short term, there remained no significant differences between groups after removing studies from meta-analysis that only implied randomisation for the outcome of 'general EPS' (n = 60, 1 RCT, RR 1.50 CI 0.27 to 8.34). When implied randomised studies were removed from the outcome of akathisia, there was significantly greater instances (P = 0.002) in people receiving aripiprazole (n = 180, 2 RCTs, RR 4.99 CI 1.78 to 14.00).

8.1.2 Aripiprazole versus Quetiapine

8.1.2.1 Global state: no clinically significant response (as defined by the individual studies)

There remained no significant differences between groups after removing studies from meta-analysis that only implied randomisation (n = 108, 1 RCT, RR 1.00 CI 0.26 to 3.79).

8.1.2.2 Adverse effects - clinically important specific adverse effects

All adverse data reported are for the short term; there remained no significant differences between groups after removing studies from meta-analysis that only implied randomisation for the outcome of akathisia (n = 108, 1 RCT, RR 2.00 CI 0.19 to 21.41). This was also the case for tremor (n = 108, 1 RCT, RR 0.33 CI 0.01 to 8.01). Remaining studies in other outcomes of dystonia and general EPS were all implied as randomised; therefore, the removal of these studies left us with no data to compare.

8.1.3 Aripiprazole versus Risperidone

8.1.3.1 Global state: no clinically significant response (as defined by the individual studies)

There remained no significant differences between groups after removing studies from meta-analysis that only implied randomisation (n = 703, 7 RCTs, RR 1.29 CI 0.87 to 1.92).

8.1.3.2 Adverse effects - clinically important specific adverse effects

All adverse data reported are for the short term; data were no longer statistically significant in favour of aripiprazole for akathisia after removing studies from the meta-analysis that only implied randomisation (n = 293, 4 RCTs, RR 0.93 CI 0.45 to 1.90), this was also the case for tremor (n = 210, 3 RCTs, RR 0.61 CI 0.30 to 1.23). Data were still statistically significant (P = 0.003, albeit slightly lower in the level of significance) in favour of aripiprazole for the outcome of dystonia after the removal of implied randomised studies from meta-analysis (n = 210, 3 RCTs, RR 0.17 CI 0.05 to 0.56), as well as for general EPS (n = 367, 4 RCTs, RR 0.53 CI 0.35 to 0.80). All data for tremor and parkinsonism were from implied randomised studies, which left no data to compare after removal.

8.1.4 Aripiprazole versus Ziprasidone

8.1.4.1 Global state: no clinically important response (as defined by the individual studies)

All studies reporting this outcome were implied as randomised; therefore, there were no data left to compare once they were removed from the meta-analysis.

8.1.4.2 Adverse effects - clinically important specific adverse effects

All adverse data reported are for the short term; data remained equivocal for akathisia after removing implied randomised studies (n = 253, 1 RCT, RR 1.26 CI 0.48 to 3.27). Data for all other various EPS outcomes, including dystonia, tremor, use of antiparkinson medication and general EPS effects, were reported by implied randomised studies, leaving no data to compare once removed from analysis.

8.1.5 Aripiprazole versus Olanzapine

8.1.5.1 Global state: no clinically significant response (as defined by the individual studies)

There remained no significant differences between groups after removing studies from meta-analysis that only implied randomisation (n = 778, 2 RCTs, RR 1.00 CI 0.82 to 1.23).

8.1.5.2 Adverse effects - clinically important specific adverse effects

Data proved statistically significant (P = 0.05) in favour of olanzapine for akathisia after removing implied randomised studies from meta-analysis (n = 75, 1 RCT, RR 16.68 CI 1.01 to 276.65), while data for remaining extrapyramidal effects (tremor, EPS, parkinsonism) were from implied randomised studies, leaving no data to compare.

8.1.6 Aripiprazole versus Olanzapine (acutely agitated)

The one study included in this comparison only implied randomisation, therefore there were no data left to compare.

8.1.7 Aripiprazole versus Other antipsychotic drugs

8.1.7.1 Global state: no clinically significant response (as defined by the individual studies)

The one study included in this outcome only implied randomisation, therefore there were no data left to compare.

8.1.7.2 Adverse effects - clinically important specific adverse effects

For the outcome of akathisia, after removing the two studies that implied randomisation, only one study (with higher methodological quality) was left to compare (Tandon 2006), which eliminated the heterogeneity present and found statistical significance ($P = 0.00001$) in favour of aripiprazole over other antipsychotic drugs ($n = 1520$, 1 RCT, RR 0.17 CI 0.12 to 0.22).

8.2 Assumptions for lost binary data

8.2.1 Aripiprazole versus Clozapine

Only one study for this comparison did not report all data. Yu 2006 reported the loss of $n = 5$ participants; however it was not clear to which group these participants belonged.

8.2.2 Aripiprazole versus Quetiapine

No included studies reported losses for this comparison.

8.2.3 Aripiprazole versus Risperidone

8.2.3.1 Global state: no clinically significant response (as defined by the individual studies)

There remained no difference in the estimate of effect when completer-only data were pooled at short term (79 RCTs, $n = 6245$, RR 1.12 CI 0.98 to 1.28).

8.2.4 Aripiprazole versus Ziprasidone

No included studies reported losses for this comparison.

8.2.5 Aripiprazole versus Olanzapine

8.2.5.1 Global state: no clinically significant response (as defined by the individual studies)

There remained no difference in the estimate of effect when completer-only data were pooled in the short and medium term combined (11 RCTs, $n = 1558$, RR 1.04 CI 0.93 to 1.16).

8.2.6 Aripiprazole versus Olanzapine (acutely agitated)

The one study included in this comparison did not report losses for this comparison.

8.2.7 Aripiprazole versus Other antipsychotic drugs

No included studies reported losses for this comparison.

8.3 Risk of bias

8.3.1 Aripiprazole versus Clozapine

8.3.1.1 Global state: no clinically significant response (as defined by the individual studies)

There remained no significant differences between groups after removing studies from meta-analysis that rated as a 'high' risk on one or more of the risk of bias domains ($n = 90$, 1 RCT, RR 0.91 CI 0.32 to 2.62).

8.3.1.2 General functioning: no clinically important change in general functioning

No included study reported this outcome.

8.3.1.3 Adverse effects - clinically important specific adverse effects

For extrapyramidal effects, all studies rated as a 'high' risk on one or more of the risk of bias domains, leaving no data to compare for this outcome.

8.3.2 Aripiprazole versus Quetiapine

8.3.2.1 Global state: no clinically significant response (as defined by the individual studies)

All studies rated as a 'high' risk on one or more of the risk of bias domains, leaving no data to compare for this outcome.

8.3.2.2 General functioning: no clinically important change in general functioning

No included study reported this outcome.

8.3.2.3 Adverse effects - clinically important specific adverse effects

All studies rated as a 'high' risk on one or more of the risk of bias domains, leaving no data to compare for this outcome.

8.3.3 Aripiprazole versus Risperidone

8.3.3.1 Global state: no clinically significant response (as defined by the individual studies)

There remained no significant differences between groups after removing studies from meta-analysis that rated as a 'high' risk on one or more of the risk of bias domains ($n = 465$, 6 RCTs, RR 1.27 CI 0.69 to 2.31).

8.3.3.2 General functioning: no clinically important change in general functioning

No included study reported this outcome.

8.3.3.3 Adverse effects - clinically important specific adverse effects

All adverse data reported are for the short term; data were no longer statistically significant in favour of aripiprazole for akathisia after removing studies that rated as a 'high' risk on one or more of the risk of bias domains ($n = 161$, 2 RCTs, RR 0.59 CI 0.14 to 2.55), this was also the case for tremor ($n = 161$, 2 RCTs, RR 0.20 CI 0.04 to 1.14), and dystonia ($n = 161$, 2 RCTs, RR 0.17 CI 0.59 to 4.21). However, data were still statistically significant ($P = 0.0001$) in favour of aripiprazole for general EPS ($n = 284$, 4 RCTs, RR 0.29 CI 0.16 to 0.51). All data for tremor and parkinsonism were

rated as 'high' risk on one or more of the risk of bias domains, which left no data to compare after removal.

8.3.4 Aripiprazole versus Ziprasidone

All studies providing data for all primary outcomes rated as a 'high' risk on one or more of the risk of bias domains, leaving no data to compare for this outcome in a sensitivity analysis.

8.3.5 Aripiprazole versus Olanzapine

All studies providing data for all primary outcomes rated as a 'high' risk on one or more of the risk of bias domains, leaving no data to compare for this outcome in a sensitivity analysis.

8.3.6 Aripiprazole versus Olanzapine (acutely agitated)

The one study included in this comparison rated as a 'high' risk on one or more of the risk of bias domains, therefore there were no data left to compare.

8.3.7 Aripiprazole versus Other antipsychotic drugs

Again, all studies providing data for all primary outcomes rated as a 'high' risk on one or more of the risk of bias domains, leaving no data to compare for this outcome in a sensitivity analysis.

8.4 Imputed values

No values were imputed for intra-class correlation coefficients (ICC), since we included no cluster randomised trials in meta-analysis.

8.5 Skewed data

All skewed data have been presented separately in tables within data and analyses, therefore a sensitivity analysis was not possible via meta-analysis.

8.6 Comparator dose

Not all studies reported mean doses and standard deviations; therefore, this sensitivity analysis has been undertaken with the dose values made available, taking predominantly ranges into account.

8.6.1 Aripiprazole versus Clozapine

8.6.1.1 Global state: no clinically significant response (as defined by the individual studies)

There remained no significant difference between groups when removing two studies (Li 2007; Yu 2007) that compared doses of aripiprazole that exceeded BNF recommendations to lower doses of clozapine (27 RCTs, n = 1978, RR 1.08 CI 0.88 to 1.32).

8.6.1.2 General mental state (BPRS/ PANSS)

At short term, none of the five studies rating mental state using the BPRS (endpoint scores) used inappropriate comparator doses, therefore there were no differences between results. Using the PANSS at short term, after removing the two studies (Li 2007; Yu 2007) that compared doses of aripiprazole that exceeded BNF recommendations to lower doses of clozapine, there was still no significant difference between groups, (23 RCTs, n = 1484, MD 0.55 CI -0.53 to 1.63), however the degree of heterogeneity was reduced from $I^2 = 64\%$ ($P = 0.0001$) to $I^2 = 44\%$ ($P = 0.02$). At medium term, three studies provided data using PANSS used comparisons within the recommended doses.

8.6.2 Aripiprazole versus Quetiapine

8.6.2.1 Global state: no clinically significant response (as defined by the individual studies)

Three studies exceeded recommended doses of clozapine, each employing a maximum dose of 800 mg daily (Chen 2009; Li 2007b; Luo 2008). There was no difference in the estimate of the effect when these studies were excluded from meta-analysis (9 RCTs, n = 801, RR 0.91 CI 0.59 to 1.14)

8.6.2.2 General mental state (BPRS/ PANSS)

No studies provided data for general average endpoint scores using either the BPRS or PANSS.

8.6.3 Aripiprazole versus Risperidone

The majority of studies used a range with a maximum of 6 mg daily risperidone, which exceeds the 4 mg BNF recommendation.

8.6.3.1 Global state: no clinically significant response (as defined by the individual studies)

After excluding 70 studies with a range of 1 to 6 mg risperidone, there remained no difference between groups (9 RCTs, n = 727, RR 1.14 CI 0.76 to 1.71).

8.6.3.2 General mental state (BPRS/ PANSS)

For average endpoint mental state in the short term using BPRS, after excluding four of the five studies providing data, there was no longer significant favour for aripiprazole, instead showing no difference between groups (1 RCT, n = 68, MD 2.30 CI -1.17 to 5.77) and removing all heterogeneity. For PANSS in the short term, after removing 69 studies that used a higher than recommended dose of risperidone, results still demonstrated no difference (8 RCTs, n = 659, MD -0.50 CI -2.09 to 1.09s), however all heterogeneity was removed.

8.6.4 Aripiprazole versus Ziprasidone

None of the included studies for the outcomes of interest used inappropriate comparator doses; therefore, there were no studies to exclude.

8.6.5 Aripiprazole versus Olanzapine

None of the included studies for the outcomes of interest used inappropriate comparator doses; therefore, there were no studies to exclude.

8.6.6 Aripiprazole versus Olanzapine (acutely agitated)

The one study included in this comparison did not use any inappropriate comparator doses, therefore there was no difference in results.

8.6.7 Aripiprazole versus Other antipsychotic drugs

Of the three studies included in this outcome, Kerwin 2007 used higher than recommended doses of risperidone and quetiapine; however, this study did not provide data for the outcomes of interest, therefore there were no difference between results.

ADDITIONAL SUMMARY OF FINDINGS *[Explanation]*

COMPARISON 2. ARIPIPRAZOLE versus QUETIAPINE for schizophrenia					
Patient or population: patients with schizophrenia Settings: inpatient and outpatient Intervention: COMPARISON 2. ARIPIPRAZOLE versus QUETIAPINE					
Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)
	Assumed risk	Corresponding risk			
	Control	COMPARISON 2. ARIPIPRAZOLE versus QUETIAPINE			
Global state: No clinically significant response (as defined by original studies)	Low ¹		RR 0.92 (0.64 to 1.32)	991 (12 studies)	⊕⊕○○ low ^{2,3}
	50 per 1000	46 per 1000 (32 to 66)			
	Moderate ¹				
	100 per 1000	92 per 1000 (64 to 132)			
	High ¹				
	150 per 1000	138 per 1000 (96 to 198)			
Mental state: as assessed by PANSS positive symptom scale score PANSS positive symptom subscale (high		The mean mental state: as assessed by PANSS positive symptom scale score in the intervention groups was 0.97 lower		583 (7 studies)	⊕○○○ very low ^{4,5,6,7}

score = poor) Follow-up: up to 12 weeks		(2.34 lower to 0.41 higher)			
Leaving the study early Follow-up: up to 12 weeks	Low¹		RR 0.8 (0.22 to 2.87)	168 (2 studies)	⊕○○○ very low ^{2,8}
	0 per 1000	0 per 1000 (0 to 0)			
	Moderate¹				
	50 per 1000	40 per 1000 (11 to 143)			
	High¹				
	100 per 1000	80 per 1000 (22 to 287)			
Quality of life: as measured by WHO-QOL-100 Follow-up: up to 12 weeks		The mean quality of life: as measured by WHO-QOL-100 in the intervention groups was 2.6 higher (1.31 to 3.89 higher)		100 (1 study)	⊕○○○ very low ^{8,9,10,11}
Adverse effects: extrapyramidal symptoms Follow-up: up to 12 weeks	Low¹		RR 2.8 (0.64 to 12.31)	348 (4 studies)	⊕○○○ very low ^{2,7,12,13}
	0 per 1000	0 per 1000 (0 to 0)			
	Moderate¹				
	50 per 1000	140 per 1000 (32 to 616)			
	High¹				

	100 per 1000	280 per 1000 (64 to 1000)				
General functioning - not measured	See comment	See comment	Not estimable	-	See comment	No study measured or reported this outcome.
Service use - not measured	See comment	See comment	Not estimable	-	See comment	No study measured or reported this outcome.

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; RR: Risk ratio;

GRADE Working Group grades of evidence

High quality: Further research is very unlikely to change our confidence in the estimate of effect.

Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Very low quality: We are very uncertain about the estimate.

¹ Risk: moderate risk approximately equates to that of the control group risk in the study population.

² Risk of bias: rated 'serious' - majority of the included studies had inadequate study design - unclear randomisation, allocation concealment and blinding. A large proportion of them also had selective reporting concerns.

³ Imprecision: rated 'serious' - most of these included studies are of small samples with small effect size and wide confidence interval. The 95% confidence interval of the combined estimated effect was not statistically significant.

⁴ Imprecision and risk of bias: rated 'serious' - most of the studies included are of small sample size, the overall pooled estimate of effect is not significant.

⁵ Inconsistency: rated 'serious' - unexplained heterogeneity is high (70%).

⁶ Indirectness: rated 'serious' - we were unable to obtain direct binary measure of mental state, thus used the best approximate measure available as an indicator.

⁷ Publication bias: rated 'strongly suspected' - only small number of studies were identified - publication bias likely.

⁸ Imprecision and publication bias: rated 'serious' - only small number of studies with poor methodological design favouring intervention group were identified - publication bias likely

⁹ Risk of bias: rated 'serious' - the only included study has unclear study design (randomisation, allocation concealment, blinding were unclear) and concerns of selective reporting.

¹⁰ Indirectness: rated 'serious' - we are unable to obtain a direct binary measure of quality of life, thus used the best available proximate measure of WHO-QOL-100 as an indicator.

¹¹ Imprecision: rated 'very serious' - only one study is available on this outcome. The sample size is small and the CI of effect estimate is wide.

¹² Inconsistency: rated 'serious' - unexplained heterogeneity is around 53%.

¹³ Imprecision: rated 'serious' - overall event rate is small (<300).

COMPARISON 3. ARIPIPRAZOLE versus RISPERIDONE for schizophrenia						
Patient or population: patients with schizophrenia Settings: inpatient and outpatient Intervention: COMPARISON 3. ARIPIPRAZOLE versus RISPERIDONE						
Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Control	COMPARISON 3. ARIPIPRAZOLE versus RISPERIDONE				
Global state: No clinically significant response (as defined by the original studies)	Low ¹		RR 1.08 (0.96 to 1.21)	6381 (80 studies)	⊕⊕○○ low ^{2,3}	
	50 per 1000	54 per 1000 (48 to 61)				
	Moderate ¹					
	100 per 1000	108 per 1000 (96 to 121)				
	High ¹					
	150 per 1000	162 per 1000 (144 to 182)				
Mental state: as measured by BPRS BPRS (high score = poor) Follow-up: up to 12 weeks		The mean mental state: as measured by BPRS in the intervention groups was 1.33 lower (2.24 to 0.42 lower)		570 (5 studies)	⊕○○○ very low ^{4,5,6}	

Leaving the study early Follow-up: up to 12 weeks	Low ¹		RR 1.02 (0.79 to 1.32)	1239 (12 studies)	⊕○○○ very low ^{6,7}	
	0 per 1000	0 per 1000 (0 to 0)				
	Moderate ¹					
	100 per 1000	102 per 1000 (79 to 132)				
	High ¹					
	150 per 1000	153 per 1000 (119 to 198)				
Quality of life - not measured	See comment	See comment	Not estimable	-	See comment	No study measured or reported this outcome.
Adverse effects: extrapyramidal symptoms Follow-up: up to 12 weeks	Low ¹		RR 0.39 (0.31 to 0.5)	2605 (31 studies)	⊕⊕○○ low ^{2,8}	
	100 per 1000	39 per 1000 (31 to 50)				
	Moderate ¹					
	300 per 1000	117 per 1000 (93 to 150)				
	High ¹					
	400 per 1000	156 per 1000 (124 to 200)				
General functioning - not measured	See comment	See comment	Not estimable	-	See comment	No study measured or reported this outcome.

Service use - not measured	See comment	See comment	Not estimable	-	See comment	No study measured or reported this outcome.
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*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; RR: Risk ratio;

GRADE Working Group grades of evidence

High quality: Further research is very unlikely to change our confidence in the estimate of effect.

Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Very low quality: We are very uncertain about the estimate.

¹ Risk: moderate risk approximately equates to that of the control group risk of the study population.

² Risk of bias: rated 'serious' - majority of the included studies had inadequate study design - unclear randomisation, allocation concealment and blinding. A large proportion of them also had selective reporting concerns.

³ Imprecision: rated 'serious' - 95% CI around the pool estimate of effect was not statistically significant.

⁴ Risk of bias: rated 'serious' - only a small number of publications with poor methodological design favouring intervention group were identified - publication bias likely.

⁵ Indirectness: rated 'serious' - we were unable to find direct binary measure of mental state, thus used the best available data as an indicator.

⁶ Publication bias: rated 'strongly suspected' - overall event number is small (<300) and the pooled effect estimate is not statistically significant.

⁷ Imprecision: rated 'serious' - overall event number is small (<300).

⁸ Publication bias: rated 'strongly suspected' - most of the studies identified were of poor methodological quality favouring intervention group - publication bias likely.

COMPARISON 4. ARIPIPAZOLE versus ZIPRASIDONE for schizophrenia					
Patient or population: patients with schizophrenia Settings: inpatient and outpatient Intervention: COMPARISON 4. ARIPIPAZOLE versus ZIPRASIDONE					
Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)
	Assumed risk	Corresponding risk			
	Control	COMPARISON 4. ARIPIPAZOLE versus ZIPRASIDONE			
Global state: No clinically significant response (as defined by the original studies)	Low ¹		RR 0.97 (0.62 to 1.52)	442 (6 studies)	⊕○○○ very low ^{2,3,4}
	100 per 1000	97 per 1000 (62 to 152)			
	Moderate ¹				
	150 per 1000	146 per 1000 (93 to 228)			
	High ¹				
	200 per 1000	194 per 1000 (124 to 304)			
Mental state: as measured with BPRS BPRS (high score = poor) Follow-up: up to 12 weeks		The mean mental state: as measured with BPRS in the intervention groups was 2.2 lower (4.97 lower to 0.57 higher)		247 (1 study)	⊕○○○ very low ^{5,6,7}

Leaving the study early Follow-up: up to 12 weeks	Low ¹		RR 0.94 (0.66 to 1.34)	316 (2 studies)	⊕○○○ very low ²	
	150 per 1000	141 per 1000 (99 to 201)				
	Moderate ¹					
	250 per 1000	235 per 1000 (165 to 335)				
	High ¹					
	350 per 1000	329 per 1000 (231 to 469)				
Quality of life - not measured	See comment	See comment	Not estimable	-	See comment	No study measured or reported this outcome.
Adverse effects: weight gain Follow-up: up to 12 weeks	Low ¹		RR 4.01 (1.1 to 14.6)	232 (3 studies)	⊕○○○ very low ^{2,3,8}	
	0 per 1000	0 per 1000 (0 to 0)				
	Moderate ¹					
	40 per 1000	160 per 1000 (44 to 584)				
	High ¹					
	100 per 1000	401 per 1000 (110 to 1000)				
General functioning - not measured	See comment	See comment	Not estimable	-	See comment	No study measured or reported this outcome.

Service use - not measured	See comment	See comment	Not estimable	-	See comment	No study measured or reported this outcome.
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*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; **RR:** Risk ratio;

GRADE Working Group grades of evidence

High quality: Further research is very unlikely to change our confidence in the estimate of effect.

Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Very low quality: We are very uncertain about the estimate.

¹ Risk: moderate risk approximately equates to that of the control group risk in the study population.

² Risk of bias: rated 'serious' - majority of the included studies had inadequate study design - unclear randomisation, allocation concealment and blinding. A large proportion of them also had selective reporting concerns.

³ Imprecision: rated 'serious' - the total event number is small (<300) and that the 95% CI of the pooled best estimate of effect is not statistically significant.

⁴ Publication bias: rated 'strongly suspected' - only a small number of trials with small sample size were identified. It is likely that these trials with low methodological quality would have exaggerated intervention effect.

⁵ Risk of bias: rated 'serious' - the only included study has serious concern with selective reporting and unclear allocation concealment and incomplete outcome.

⁶ Indirectness: rated 'serious' - we were unable to find direct binary measure of mental state, thus used BPRS score as an indicator.

⁷ Imprecision: rated 'serious' - only one study is identified, the estimate of effect is not statistically significant.

⁸ Publication bias: rated 'strongly suspected' - only small number of trials with poor methodological quality were identified - publication bias likely.

COMPARISON 5. ARIPIPRAZOLE versus OLANZAPINE for schizophrenia					
Patient or population: patients with schizophrenia Settings: inpatient and outpatient Intervention: COMPARISON 5. ARIPIPRAZOLE versus OLANZAPINE					
Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)
	Assumed risk	Corresponding risk			
	Control	COMPARISON 5. ARIPIPRAZOLE versus OLANZAPINE			
Global state: No clinically significant response Follow-up: up to 12 weeks	Low ¹		RR 1.06 (0.96 to 1.17)	1739 (11 studies)	⊕○○○ very low ^{2,3,4}
	200 per 1000	212 per 1000 (192 to 234)			
	Moderate ¹				
	350 per 1000	371 per 1000 (336 to 409)			
	High ¹				
	500 per 1000	530 per 1000 (480 to 585)			
Mental state: as measured with PANSS PANSS (high score = poor) Follow-up: up to 12 weeks		The mean mental state: as measured with PANSS in the intervention groups was 0.61 higher (0.23 lower to 1.46 higher)		1500 (11 studies)	⊕○○○ very low ^{2,5,6,7}

Leaving the study early Follow-up: up to 12 weeks	Low¹		RR 1.15 (1.05 to 1.25)	2331 (9 studies)	low ^{2,7}
	200 per 1000	230 per 1000 (210 to 250)			
	Moderate¹				
	350 per 1000	402 per 1000 (367 to 438)			
	High¹				
	500 per 1000	575 per 1000 (525 to 625)			
Quality of life: as measured with GQOLI-74 GQOLI-74 (low score = poor)		The mean quality of life: as measured with gqoli-74 in the intervention groups was 1.26 lower (6.37 lower to 3.85 higher)		68 (1 study)	very low ^{7,8,9,10}
Adverse effects: weight gain Follow-up: up to 12 weeks	Low¹		RR 0.25 (0.15 to 0.43)	1538 (9 studies)	very low ^{2,3,7}
	100 per 1000	25 per 1000 (15 to 43)			
	Moderate¹				
	200 per 1000	50 per 1000 (30 to 86)			
	High¹				
	300 per 1000	75 per 1000 (45 to 129)			

General functioning - not measured	See comment	See comment	Not estimable	-	See comment	No study measured or reported this outcome.
Service use - not measured	See comment	See comment	Not estimable	-	See comment	No study measured or reported this outcome.

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; **RR:** Risk ratio;

GRADE Working Group grades of evidence

High quality: Further research is very unlikely to change our confidence in the estimate of effect.

Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Very low quality: We are very uncertain about the estimate.

¹ Risk: moderate risk approximately equates to that of the control group risk of the study population.

² Risk of bias: rated 'serious' - majority of the included studies had inadequate study design - unclear randomisation, allocation concealment and blinding. Some of them also had selective reporting concerns.

³ Imprecision: rated 'serious' - total number of events is small (<300) and that the 95% CI of pooled estimate of effect is not statistically significant.

⁴ Publication bias: rated 'strongly suspected' - only small number of trials with small sample size were identified. It is likely that these small studies with poor methodological quality have negatively affected on the estimate of treatment effect.

⁵ Indirectness: rated 'serious' - we are unable to find direct binary measure of mental state, thus used PANSS score as an indicator.

⁶ Imprecision: rated 'serious' - the overall pooled estimate of effect was not statistically significant and with wide confidence interval.

⁷ Publication bias: rated 'strongly suspected' - only a small number of studies with poor methodological design were identified - publication bias likely.

⁸ Risk of bias: rated 'serious' - unclear randomisation, allocation concealment, blinding and serious concern with selective reporting.

⁹ Indirectness: rated 'serious' - we are unable to find direct binary measure of quality of life, thus used GQOLI-74 score as an indicator.

¹⁰ Imprecision: rated 'very serious' - only one study with serious methodological concerns was identified and the estimate of effect is not significant.

DISCUSSION

Many trials were sponsored by the manufacturers of aripiprazole or the comparator agent manufacturers. In a blinded analysis of abstracts it has been shown that pharmaceutical companies emphasize positive aspects of their compounds (Heres 2006). Every result, without exception, therefore, must be viewed with this in mind.

Summary of main results

1. COMPARISON 1. ARIPIPRAZOLE versus CLOZAPINE

Thirty-nine studies fell into this category, please see [Summary of findings for the main comparison](#). Data are generally of poor quality and we found no data on indices including service use or global functioning. Overall, inclusion of new Chinese studies gave us much more data for this comparison. Quality of life outcomes, more often than not, significantly favoured use of aripiprazole over clozapine. However, there was no difference between the use of either drug for the primary outcome of clinically significant response in global state. Largely, people were at significantly less risk of adverse effects when receiving aripiprazole ([Analysis 1.15](#); [Analysis 1.16](#)), but greater risk of central nervous system (CNS) adverse effects such as headache and insomnia than people receiving clozapine ([Analysis 1.17](#)). Extrapyramidal effects (EPS) were largely equivocal between groups. Data were heterogeneous as regards EPS, which may well be attributable to the differing doses employed between studies - as some used low doses (between 5 to 20 mg aripiprazole versus 5 to 500 mg clozapine) of either drugs, and some used slightly higher (10 to 30 mg aripiprazole versus 50 to 270 mg clozapine). Evidence from 11 studies (n = 732) does suggest that people receiving aripiprazole had a greater risk of experiencing anxiety in the short term ([Analysis 1.2](#)).

2. COMPARISON 2. ARIPIPRAZOLE versus QUETIAPINE

Fifteen studies provided data for this comparison, please see [Summary of findings 2](#); again, the inclusion of new Chinese studies gave us data for this comparison, which was lacking in the previous version of this review. The quality of the data were generally 'low' to 'very low', due to poor outcome reporting and methodological quality. There were, again, no data for service use; only one study reported data using any quality of life scale, which significantly favoured use of aripiprazole in six out of the seven components measured. Further larger scale, high-quality trials are needed in order to reach any confident conclusions for this outcome. The evidence from 12 included studies (n = 991) suggest no significant difference between the two drugs in terms of clinically significant

response. Adverse effect data do suggest a greater risk of tachycardia in people receiving quetiapine ([Analysis 2.13](#)), as well as dry mouth, constipation ([Analysis 2.16](#)) and weight gain ([Analysis 2.19](#)). However, nausea and vomiting was more common in people receiving aripiprazole ([Analysis 2.16](#)).

3. COMPARISON 3. ARIPIPRAZOLE versus RISPERIDONE

Eighty studies (n = 6381) report data for the primary outcome of clinically significant response for this important comparison. Risperidone, now off-licence, is inexpensive and widely accessible; aripiprazole is not. Data are, again, of limited quality (randomisation and concealment methods being unclear, [Summary of findings 3](#)), however, this current update search has provided data that were lacking in the previous version of this review, including global functioning, and economic analyses; however, service use data are still missing. The majority of reported data are short term; adverse effects were selectively reported and studies were often sponsored by pharmaceutical companies.

For global outcomes there were no convincing differences between the two drugs ([Analysis 3.1](#), [Analysis 3.2](#), [Analysis 3.3](#), [Analysis 3.4](#)). Binary mental state data were largely equivocal, with the exception of anxiety, which was significantly higher in people receiving aripiprazole ([Analysis 3.5](#)). Scale data for mental state favoured aripiprazole using the BPRS and PANSS average endpoint negative score ([Analysis 3.6](#); [Analysis 3.8](#)). As regards adverse effects, the only convincing data were for tachycardia ([Analysis 3.16](#)) and abnormal liver function ([Analysis 3.15](#)) in risperidone. Risperidone also carried greater risk of metabolic adverse effects ([Analysis 3.25](#)) including weight gain, menstrual disorder and lactation. General EPS, akathisia, tremor and dystonia were all significantly higher in people receiving risperidone than aripiprazole ([Analysis 3.21](#)). Again, headache ([Analysis 3.18](#)), and nausea and vomiting were significantly more prominent in people receiving aripiprazole ([Analysis 3.23](#)). Both drugs may cause movement disorders and about one third of people allocated aripiprazole used antiparkinsonian drugs ([Analysis 3.21](#)).

4. COMPARISON 4. ARIPIPRAZOLE versus ZIPRASIDONE

The addition of new Chinese studies gave us an additional 15 studies to add to the previous one in this comparison. Ziprasidone is a major competitor of aripiprazole but data are of limited quality ([Summary of findings 4](#)), and there are still no data for service use. Data are all short term (four weeks).

There really does seem to be very little suggestion of differences in global state, attrition (about one third of people left in a matter of a few weeks) and mental state; however, there was greater improvement noted using SANS in people receiving aripiprazole in three RCTs (n = 238).

As regards adverse effects, there were largely no clear differences between groups; however, people receiving aripiprazole were significantly more likely to show signs of dizziness and insomnia ([Analysis 4.11](#)) as well as weight gain ([Analysis 4.16](#)). There is a need for better trials providing clear information for all interested in the care of people with schizophrenia who have access to these drugs.

5. COMPARISON 5. ARIPIPAZOLE versus OLANZAPINE

Nineteen studies reported data for this comparison, see [Summary of findings 5](#). Data are generally of poor quality and we found no data on indices including service use or global functioning. The inclusion of new Chinese studies gave data for quality of life outcomes (one RCT), which were lacking in the previous version of this review. The studies, although randomised and blinded, lack clarity on how both were carried out. Some studies were sponsored by pharmaceutical companies and adverse effects were seemingly selectively reported.

Even with the addition of new studies, global state outcomes show no clear differences between the drugs and the various measures of mental state did not clearly point to an advantage of one drug over another. The only significant findings from PANSS showed greater improvement in positive symptoms over each short, medium and long term combined ([Analysis 5.11](#)). Approaching 50% of people left these studies for any reason ([Analysis 5.27](#)) which may be a reflection of study design.

Regarding adverse effects, extrapyramidal side effects did not appear to be a major problem. Weight gain appears to be olanzapine's major shortcoming when compared with aripiprazole ([Analysis 5.24](#)). This is important as there were significantly smaller mean increase of cholesterol levels from baseline in the aripiprazole group than in people allocated olanzapine ([Analysis 5.25](#)). Few people like gain weight or to be exposed to risks resulting from higher cholesterol levels. Olanzapine seemed to have a higher sedative effect on people in two randomised trials ([Analysis 5.19](#)).

6. COMPARISON 6. ARIPIPAZOLE versus OLANZAPINE (in acutely agitated patients)

These results were based on a single five-day trial but with nearly 500 participants. This comparison was included to comply with the protocol of this review but, in retrospect, we feel would be best in a separate review and are pleased to see that this is underway ([Pagadala 2009](#)). Overall, the results suggest that the two drugs may be of some use in the acute situation but data are few, not of high quality, undertaken by those with a pecuniary interest in the findings, and do not have a comparison group of other more widely used treatments for acute agitation thought due to serious mental illness.

Very few (0.83%) participants left the study early with numbers being similar in both groups. This very low figure may reflect the

coercive nature of the treatment and that people were not free to leave. This is an observation and is not meant as criticism as this too may reflect real-world practice.

7. COMPARISON 7. ARIPIPAZOLE versus OTHER ANTIPSYCHOTIC DRUGS

The studies were randomised but no concealment methods were clarified. We do think the comparison of aripiprazole with any one of several new generation antipsychotic drugs is practical and reflects real-world practice. One of the studies reported quality of life measures, which we feel gives a fresh dimension to the comparison. Although some attempts were made to incorporate clinically important issues, the overall quality of evidence remains low.

Many general measures did improve with aripiprazole although there was not any difference for sexual dysfunction. Several measures of mental state did not improve although evidence of limited quality did show some advantage of aripiprazole for negative symptoms. This latter finding is important and should be replicated in a study independent of industry conflicts of interest.

We are not sure why people with schizophrenia reported aripiprazole being preferred when their carers did not ([Analysis 7.4](#)). This could be a chance finding. Despite this expression of preference, about one third of participants left the trial early. Perhaps this is reflective of a vote of lack of confidence for the trial design rather than the drug itself.

It is good that quality of life is now recorded as a matter of routine in these studies but not good that it is measured by many scales that are problematic to interpret. Partly as a result of this, we are unsure of the effects of aripiprazole on quality of life compared with several of its competitors.

Aripiprazole is not free of adverse effects but there may be slightly less overall than with the other drugs. Nausea may be a problem ([Analysis 7.16](#)) but weight gain less problematic than other drugs.

Overall completeness and applicability of evidence

1. Completeness

Randomised evidence is available for only five out of eight possible comparisons of aripiprazole with other second generation antipsychotic drugs, although three studies compared aripiprazole with other atypical antipsychotics grouped together. Overall, evidence is incomplete. We do not have any good data on the implications of the use of aripiprazole on use of services from trials and we do think that 'admission' is a key outcome for people with schizophrenia. There are also very few economic data, which could be most important in this area.

2. Applicability

In terms of applicability, we highlight that most included studies were 'efficacy' studies. Large and simple, pragmatic, real-world effectiveness studies are not available, greatly limiting external validity (Thorpe 2009).

Quality of the evidence

All studies were randomised and double blind or open label, but details were rarely presented. It is therefore unclear whether randomisation and blinding, where mentioned, were really appropriately done. The high number of participants leaving studies early (between 30% to 40% overall) must call into question the credibility of the findings (Xia 2007) because, once a person is lost to follow-up outcomes become a matter of assumption. Three long-term studies were available but in a chronic, often life-long, disorder such as schizophrenia it is important that many more participants are followed up for longer. Overall, we considered the quality of evidence to be 'medium' at best with a moderate risk of bias.

Potential biases in the review process

It is possible that some important information may have been excluded during the review process due to human error or information not being available. New data from 162 Chinese studies that were previously awaiting assessment did not substantially change the findings of the first review, however they have given us more comparisons and increased precision whilst not clearly effecting overall quality of data.

Agreements and disagreements with other studies or reviews

An earlier Cochrane review compared aripiprazole with any other antipsychotic drugs (EL-Sayeh 2006). In this past review authors combined olanzapine and risperidone as one group of 'atypical antipsychotic' drugs. A subsequent review comparing aripiprazole with other atypical antipsychotics was also published (Komossa 2009) where the authors concluded that aripiprazole was not much different from other second generation antipsychotic drugs. This current update again concludes that aripiprazole was similar to other atypical antipsychotic drugs but we have found some evidence of it being better tolerated than its competitors.

Implications for practice

1. For people with schizophrenia

For people with schizophrenia, it may be important to know that aripiprazole may be slightly less effective than olanzapine, but is less associated with adverse effects such as weight gain, cholesterol and prolactin increase and sedation. Aripiprazole's efficacy seems to be similar to that of risperidone, but certain movement disorders, cholesterol and prolactin increase may occur less frequently when taking aripiprazole. Aripiprazole may also be slightly better than ziprasidone with no clear differences apparent in adverse effects. When compared to other atypical antipsychotics as a group, people allocated to aripiprazole preferred its use. However, effects on quality of life were similar and carers found the two groups to be similar.

2. For clinicians

Clinicians should know that randomised evidence of the effects of aripiprazole compared with other second generation antipsychotic drugs is only available for a few drugs. Aripiprazole does not seem dogged by the problems of weight gain and raised prolactin. As with many antipsychotic drugs, it may, however, cause some extrapyramidal effects. More studies are needed to clarify the role of aripiprazole compared to other second generation antipsychotic drugs.

3. For managers/policy makers

Data that are relevant for policy makers such as service utilisation, functioning in society or costs are not available. We therefore find it difficult to make recommendations for decision makers.

Implications for research

1. General

Outcome reporting remains insufficient in antipsychotic drug trials. Strict adherence to the CONSORT statement (Moher 2001) would make such studies much more informative. Making all data available would set this compound far ahead of its competitors (ALLTRIALS). Increasingly healthcare sub-specialities are gaining universal agreement on core outcomes to be reported within all trials (COMET). This would greatly reduce disaggregation of data and add to the power of reviews such as this.

2. Specific

2.1 Reviews

AUTHORS' CONCLUSIONS

Many interesting and potentially informative trials have had to be excluded as they are not of direct relevance to this review. Suggestions for their use within reviews are given in Table 1.

2.2 Trials

There is much room for further, better, randomised trials comparing aripiprazole with other second generation antipsychotic drugs. Comparisons with amisulpride, sertindole and zotepine are currently missing. We present a suggestion in Table 2 recognising that much goes into design and conduct of such a large study that cannot be captured in a table.

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Khanna P, Komossa K, Rummel-Kluge C, Hunger H, Schwarz S, El-Sayeh HG, et al. Aripiprazole versus other atypical antipsychotics for schizophrenia. *Cochrane Database of Systematic Reviews* 2013, Issue 2. DOI: 10.1002/14651858.CD006569.pub4

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies [ordered by study ID]

An 2008

Methods	Allocation: randomised. No further details. Blindness: unclear. Duration: eight weeks. Design: parallel. Setting: inpatient and outpatient, China.	
Participants	Diagnosis:schizophrenia (CCMD-3). PANSS score of 60 or more. N = 78. Age: not reported. Gender: not reported. History: duration of illness not reported, age at onset not reported	
Interventions	1. Aripiprazole: Dose range: 5-30 mg/day. Mean dose: not reported. N = 41. 2. Clozapine: Dose range: 25-500 mg/day. Mean dose: not reported. N = 37	
Outcomes	Global state:PANSS score decreased rate (recovery: $\geq 80\%$, markedly improved: $\geq 50\%$, improved: $\geq 20\%$, no effect: $< 20\%$) Mental state: PANSS total score, PANSS positive subscale score, PANSS negative subscale score, PANSS general pathological subscale score	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	There was no drop-out.

An 2008 (Continued)

Selective reporting (reporting bias)	High risk	Although TESS was used to assess adverse effects, no data on score were available. Data on use of use of alprazolam, propranolol and anticholinergic medication were missing
Other bias	Low risk	None obvious.

Bai 2007

Methods	Allocation: randomised, no further detail. Blindness: unclear. Duration: twelve weeks. Design: parallel. Setting: inpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 118. Age: 20- 50 years, aripiprazole group, mean = (32 ± 11) years; clozapine group, mean = (32 ± 13) years Gender: aripiprazole group: 34 male, 25 female; clozapine group: 38 male, 21 female. History: aripiprazole group: 1- 36 months, mean = (22 ± 5) months; clozapine group: 1 - 36 months, mean = (20 ± 7) months. Age at onset not reported
Interventions	1. Aripiprazole: Dose range: 5-30 mg/day. Mean = (20 ± 5) mg/day. N = 59. 2. Clozapine: Dose range: 50-650 mg/day. Mean dose: (450 ± 125) mg/day. N = 59
Outcomes	Global state: PANSS score decreased rate (markedly improved: > 60%, improved: 40%-60%, no effect: < 25%) Mental state: PANSS total score, PANSS positive subscale score, PANSS negative subscale score Adverse events. Unable to use: Mental state: PANSS anxiety subscale score - unvalidated subscale Cognitive functioning: PANSS cognitive factor subscale score - unvalidated subscale
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.

Bai 2007 (Continued)

Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Unclear.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.
Selective reporting (reporting bias)	High risk	The outcome did not include missing data. There were no data on other adverse events. This procedure may have missed important data
Other bias	Low risk	None obvious.

Bai 2009

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: eight weeks. Design: parallel. Setting: inpatient, China.	
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 60. Age: aripiprazole group: mean = (32.1 ± 7.1) years; ziprasidone group: mean = (31.8 ± 7.1) years Gender: not reported. History: aripiprazole group: mean= (5.5 ± 2.2) years; ziprasidone group: mean = (5.6 ± 2.3) years. Age at onset not reported	
Interventions	1. Aripiprazole: Dose range: 5-30 mg/day. Mean= (15.8 ± 5.1) mg/day. N = 30. 2. Ziprasidone: Dose range: 20-140 mg/day. Mean= (88.7 ± 12.6) mg/day. N = 30	
Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 75%, markedly improved: 50%-75%, improved: 25%-50%, no effect: < 25%) Mental state: PANSS total score, PANSS positive subscale score, PANSS negative subscale score Adverse effects.	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement

Bai 2009 (Continued)

Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.
Selective reporting (reporting bias)	High risk	Data on liver function, insomnia, somnolence, and sleep disorder were missing or incomplete
Other bias	Low risk	None obvious.

Ban 2008

Methods	Allocation: randomised, no further detail. Blindness: unclear. Duration: eight weeks. Design: parallel. Setting: inpatient and outpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). BPRS of 35 or more. N = 80. Age: aripiprazole group, 16- 45 years. mean= (29 ± 8.8) years; quetiapine group, 18-45 years, mean = (30 ± 2.7) years Gender: aripiprazole group: 17 male, 23 female; quetiapine group: 21 male, 19 female. History: aripiprazole group: mean = (1.2 ± 1.0) months; clozapine group: mean = (0.9 ± 1.1) months. Age at onset not reported
Interventions	1. Aripiprazole: Dose range: 5-30 mg/day. Mean dose: (11.8 ± 3.4) mg/day. N = 40. 2. Quetiapine: Dose range: 50-750 mg/day. Mean dose: (544.8 ± 83.8) mg/day. N = 40
Outcomes	Global state: no clinically significant improvement. Mental state: BPRS total score. Adverse effects. Unable to use - BPRS anxiety-depression subscale score, BPRS thought disorder subscale score, BPRS activation subscale score, BPRS hostile subscale score - subscales are unvalidated

Ban 2008 (Continued)

Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.
Selective reporting (reporting bias)	High risk	Although TESS was used to assess adverse effects, no data on score were available. Data on renal function, EEG, use of benzodiazepines and other medication were missing
Other bias	Low risk	None obvious.

Chan 2007

Methods	Allocation: random, permuted block randomisation stratified by centre. Blindness: double, identical capsules. Duration: four weeks. Design: parallel. Location: multicentre.
Participants	Diagnosis: (DSM-IV) schizophrenia (N = 80) or schizoaffective disorder (N = 3), acute relapse. PANSS total score of 60 or more. N = 83. Age: 18-65 years (mean aripiprazole = 35.2 years, mean risperidone = 35.1 years). Gender: 45 M, 38 F. History: duration of illness not reported, age at onset not reported. Setting: inpatient.
Interventions	1. Aripiprazole: fixed dose: 15 mg/day. N = 49. 2. Risperidone: fixed dose: 6 mg/day. N = 34.

Outcomes	Leaving the study early: any reason, adverse events, inefficacy. Global state: CGI. Mental state: PANSS total score, PANSS positive sub score, PANSS negative sub score. Adverse effects: at least one adverse effect, cardiac effects (QTc), extrapyramidal adverse effects (use of antiparkinson medication, extrapyramidal symptoms, AIMS, BAS, SAS), cholesterol increase, glucose elevation, prolactin increase, weight	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Random, permuted block randomisation stratified by centre.
Allocation concealment (selection bias)	Unclear risk	No further details.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Double, identical capsules. Whether blinding was successful has not been examined, but both compounds differ quite substantially in adverse effects. This can be a problem for blinding
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Objective outcomes such as laboratory measures or death are unlikely to have been much affected by problems of blinding
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Total number of drop-out = 25%. The LOCF method was used to account for people leaving the study early
Selective reporting (reporting bias)	High risk	Only adverse events with an incidence of at least 5% in any treatment group were reported, therefore important side effects may have been missed by this procedure
Other bias	High risk	The study was industry sponsored by the manufacturer of aripiprazole

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: six weeks. Design: parallel. Setting: inpatient, China.	
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 100. Age: aripiprazole group: 18- 48 years. mean= (29.5 ± 11.7) years; risperidone group: 16 ~ 60 years, mean = (29.3 ± 10.6) years Gender: aripiprazole group: 29 male, 21 female; risperidone group: 28 male, 22 female. History: aripiprazole group: 1 month- 10 years, mean = (6.4 ± 1.5) years; risperidone group: 1.5 months- 13 years, mean = (6.3 ± 1.8) years. Age at onset not reported	
Interventions	1. Aripiprazole: Dose range: 5-20 mg/day. Mean dose: not reported. N = 50. 2. Risperidone: Dose range: 1-4 mg/day. Mean dose: not reported. N = 50	
Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 75%, markedly improved: 50%-75%, improved: 25%-50%, no effect: < 25%) Mental state: PANSS total score, PANSS positive subscale score, PANSS negative subscale score, PANSS general pathological subscale score, irritability- labelled as “adverse effect” Adverse effects.	
Notes		
<i>Risk of bias</i>		
Bias	Authors’ judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.
Selective reporting (reporting bias)	High risk	Data on TESS total score, blood glucose, liver function, use of benzodiazepines and other medicines were missing

Chang 2007 (Continued)

Other bias	Low risk	None obvious.
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Chen 2006

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: two weeks wash-out period + eight weeks intervention. Design: parallel. Setting: inpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 101. Age: aripiprazole group: 16- 60 years, mean = (28.6 ± 12.9) years; risperidone group: 17 - 59 years, mean = (25.4 ± 7.7) years Gender: aripiprazole group: 19 male, 32 female; risperidone group: 26 male, 24 female. History: aripiprazole group: 1.4- 240 months, mean = (23.3 ± 43.2) months; risperidone group: 1.7- 108 months, mean = (23.3 ± 37.1) months. Age at onset not reported
Interventions	1. Aripiprazole: Dose range: 5-25 mg/day. Mean = (15.9 ± 4.0) mg/day. N = 51. 2. Risperidone: Dose range: 1-6 mg/day. Mean = (3.3 ± 1.1) mg/day. N = 50
Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 75%, markedly improved: 50%-75%, improved: 25%-50%, no effect: < 25%). CGI-SI score, CGI-EI score Mental state: PANSS total score, PANSS positive subscale score, PANSS negative subscale score, PANSS general pathological subscale score Adverse effects.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.

Chen 2006 (Continued)

Selective reporting (reporting bias)	Low risk	No selective reporting.
Other bias	Low risk	None obvious.

Chen 2007a

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: six months. Design: parallel. Location: inpatient and outpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 100. Age: not reported. Gender: not reported. History: 1- 6 months, mean = (2.8 ± 1.3) years. Age at onset not reported
Interventions	1. Aripiprazole: Dose range: 5-30 mg/day. Mean dose: not reported. N = 50. 2. Quetiapine: Dose range: 100-600 mg/day. Mean dose: not reported. N = 50
Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 80%, markedly improved: 50%-80%, improved: 30%-50%, no effect: < 30%); CGI-SI total score Mental state: PANSS total score. PANSS positive subscale score, PANSS negative subscale score, PANSS general pathological subscale score. agitation-labelled as "adverse effect" Life of quality: WHO-QOL-100. Adverse effects. Unable to use - Adverse effects: TESS total score, blood routine, blood glucose, electrolyte, ECG, liver function (deficient data)
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.

Chen 2007a (Continued)

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.
Selective reporting (reporting bias)	High risk	Although TESS was used to assess adverse effects, no data on score were available. Data on blood routine, blood glucose, electrolyte, ECG, liver function were deficient
Other bias	Low risk	None obvious.

Chen 2008a

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: eight weeks. Design: parallel. Setting: inpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 60. Age: aripiprazole group: mean = (32.5 ± 9.3) years; risperidone group: mean = (33.2 ± 8.0) years Gender: 60 female. History: aripiprazole group: mean = (3.6 ± 1.3) years; risperidone group: mean = (3.9 ± 1.5) years. Age at onset not reported
Interventions	1. Aripiprazole: Dose range: 5-25 mg/day. Mean = (18.6 ± 7.4) mg/day. N = 30. 2. Risperidone: Dose range: 1-6 mg/day. Mean = (4.3 ± 1.3) mg/day. N = 30
Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 75%, markedly improved: 50%-75%, improved: 25%-50%, no effect: < 25%) Mental state: PANSS total score, excitement labelled as "adverse effect" Adverse effects.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.

Chen 2008a (Continued)

Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.
Selective reporting (reporting bias)	High risk	Although TESS was used to assess adverse effects, no data on score were available. Data on blood routine, blood glucose, use of propranolol, benzodiazepines and other medication were missing
Other bias	Low risk	None obvious.

Chen 2009

Methods	Allocation: randomised, no further details. Blindness: open. Duration: eight weeks. Design: parallel. Location: inpatient and outpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 60. Age: aripiprazole group: 18- 58 years; mean = (25.63 ± 7.9) years; quetiapine group: 18 - 55 years; mean = (29.4 ± 9.5) years Gender: aripiprazole group: 18 male, 12 female; quetiapine group: 17 male, 13 female. History: aripiprazole group: 3 months- 5 years, mean = (2.39 ± 1.8) years; quetiapine group: 3 months- 5 years, mean = (3.2 ± 1.6) years. Age at onset not reported
Interventions	1. Aripiprazole: Dose range: 5-30 mg/day. Mean dose: not reported. N = 30. 2. Quetiapine: Dose range: 100-800 mg/day. Mean dose: not reported. N = 30
Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 80%, markedly improved: 50%-80%, improved: 30%-50%, no effect: < 30%) Mental state: PANSS total score, PANSS positive subscale score, PANSS negative subscale score, PANSS general psychogenic pathological subscale score Unable to use - Mental state: SANS subscale score - unvalidated subscale.
Notes	
<i>Risk of bias</i>	

Chen 2009 (Continued)

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open label.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open label.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.
Selective reporting (reporting bias)	High risk	Although TESS was used to assess adverse effects, no data on score were available. Data on EEG, ECG, urine routine, use of benhexol, benzodiazepine and propranolol were also missing
Other bias	Low risk	None obvious.

Chen 2009a

Methods	Allocation: randomised, random number table. Blindness: unclear. Duration: 3- 7 days wash-out period + six weeks intervention. Design: parallel. Setting: inpatient and outpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more, Excited subscales (PEC) of 14 or more. N = 75. Age: aripiprazole group: mean = 38.4 years; olanzapine group: mean = 37.1 years Gender: aripiprazole group: 25 male, 15 female; olanzapine group: 22 male, 13 female. History: not reported. Age at onset not reported.
Interventions	1. Aripiprazole: Dose range: 5-20 mg/day. Mean dose: not reported. N = 40. 2. Olanzapine: Dose range: 5-20 mg/day. Mean dose: not reported. N = 35
Outcomes	Global state: PANSS score decreased rate (recovery: $\geq 75\%$, improved: 50%-75%, no effect: $< 50\%$) Mental state: PANSS total score. Leaving the study early.

Chen 2009a (Continued)

	Adverse effects. Unable to use - Mental state: PANSS PEC subscale score - unvalidated.	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomised, random number table.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	4% patients were lost to follow up (2/40 vs 1/35), and there were no difference between the two groups
Selective reporting (reporting bias)	High risk	Data on TESS total score, blood routine, ECG, EEG, use of benzodiazepines were missing
Other bias	Low risk	None obvious.

Chen 2010

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: eight weeks. Design: parallel. Setting: inpatient and outpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 64. Age: aripiprazole group 18- 50 years, mean = (22.35 ± 7.15) years; risperidone group 18 ~ 49 years, mean = (22.25 ± 9.55) years Gender: aripiprazole group: 14 male, 18 female; risperidone group: 17 male, 15 female. History: aripiprazole group 1 month- 10 years; risperidone group 1 month- 9 years. Age at onset not reported

Interventions	1. Aripiprazole: Dose range: 5-30 mg/day. Mean = (19.4 ± 2.1) mg/day. N = 32. 2. Risperidone: Dose range: 1-6 mg/day. Mean = (2.7 ± 0.7)mg/day. N = 32	
Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 75%, markedly improved: 50%-74%, improved: 25%-49%, no effect: < 25%) Mental state: PANSS total score, PANSS positive subscale score, PANSS negative subscale score, PANSS general pathological subscale score Adverse effects.	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Low riskUnclear riskHigh risk
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Low riskUnclear riskHigh risk
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.
Selective reporting (reporting bias)	High risk	Data on TESS total score, nausea/vomiting, dizziness, blurred vision, insomnia, constipation, excitement, use of benzodiazepines and other medicines was missing
Other bias	Low risk	None obvious.

Chen 2010a

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: six weeks. Design: parallel. Setting: inpatient, China.
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Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 120. Age: 18- 60 years, aripiprazole group mean= (31.8 ±7.9) years; risperidone group mean = (32.5 ± 6.8) years Gender: aripiprazole group: 24 male, 36 female; risperidone group: 26 male, 34 female. History: aripiprazole group: mean = (11.2 ± 6.1) months; risperidone group: mean= (11.8 ± 6.9) months. Age at onset not reported	
Interventions	1. Aripiprazole: Dose range: 5-30 mg/day. Mean dose: not reported. N = 60. 2. Risperidone: Dose range: 1-6 mg/day. Mean dose: not reported. N = 60	
Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 75%, markedly improved: 50%-74%, improved: 25%-49%, no effect: < 25%) Mental state: PANSS total score, PANSS positive subscale score, PANSS negative subscale score, PANSS general pathological subscale score Adverse effects.	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.
Selective reporting (reporting bias)	High risk	Although TESS was used to assess adverse effects, no data on score were available. Data on use of benzodiazepines and other medicines was missing
Other bias	Low risk	None obvious.

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: eight weeks. Design: parallel. Setting: inpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more, SANS of 60 or more. N = 86. Age: aripiprazole group: mean = (29.35 ± 7.6) years; ziprasidone group: mean = (30.28 ± 8.1) years Gender: aripiprazole group: 25 male, 18 female; ziprasidone group: 26 male, 17 female. History: aripiprazole group: mean = (5.23 ± 2.81) years; ziprasidone group: mean = (5.16 ± 2.6) years. Age at onset not reported
Interventions	1. Aripiprazole: Dose range: 5-20 mg/day. Mean = (11.7 ± 1.2) mg/day. N = 43. 2. Ziprasidone: Dose range: 20-120 mg/day. Mean = (86.26 ± 10.2) mg/day. N = 43
Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 75%, markedly improved: 50%-75%, improved: 25%-50%, no effect: < 25%) Mental state: PANSS total score, PANSS positive subscale score, PANSS negative subscale score, PANSS general pathological subscale score. SANS total score score Adverse effects.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.
Selective reporting (reporting bias)	High risk	Data on CGI-GI score, TESS score, blood routine, urine routine, use of benzodiazepines and anticholinergic medication were missing

Cheng 2009 (Continued)

Other bias	Low risk	None obvious.
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CuiMeng 2008

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: eight weeks. Design: parallel. Setting: inpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 120. Age: aripiprazole group: 18- 64 years, mean = (25.2 ± 7.5) years; risperidone group: 18 ~ 65 years, mean = (25 ± 8) years Gender: aripiprazole group: 40 male, 20 female; risperidone group: 36 male, 24 female. History: aripiprazole group 1- 55 months, mean = (22 ± 12) months; risperidone group 1 ~ 55 months, mean = (22 ± 13) months. Age at onset not reported
Interventions	1. Aripiprazole: Dose range: 5-25 mg/day. Mean dose: not reported. N = 60. 2. Risperidone: Dose range: 1-4 mg/day. Mean dose: not reported. N = 60
Outcomes	Mental state: PANSS total score, PANSS positive subscale score, PANSS negative subscale score Adverse effects: TESS score.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.

Selective reporting (reporting bias)	High risk	Although GQL I - 74 was used to assess Quality of life, no data on score were available. Data on anxiety, somnolence, ECG, use of benzodiazepines and other medicines were missing
Other bias	Low risk	None obvious.

Dai 2005

Methods	Allocation: randomised, no further detail. Blindness: unclear. Duration: eight weeks. Design: parallel. Setting: inpatient and outpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more, CGI of 4 or more. N = 80. Age: aripiprazole group: 18- 58 years. mean = (31 ± 8) years; quetiapine group: 19 - 57 years, mean = (32 ± 9) years Gender: aripiprazole group: 20 male, 20 female; quetiapine group: 21 male, 19 female. History: aripiprazole group: 1 month- 10 years, mean = (5.9 ± 3) years; clozapine group: 1 month- 9 years, mean = (5 ± 3) years. Age at onset not reported
Interventions	1. Aripiprazole: Dose range: 5-30 mg/day. Mean dose: (23.3 ± 3.1) mg/day. N = 40. 2. Quetiapine: Dose range: 75-700 mg/day. Mean dose: (565 ± 85) mg/day. N = 40
Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 75%, markedly improved: 50%-75%, improved: 25%-50%, no effect: < 25). CGI average endpoint scale score Mental state: PANSS total score, PANSS positive subscale score, PANSS negative subscale score, PANSS general pathological subscale score Adverse effects.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.

Dai 2005 (Continued)

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.
Selective reporting (reporting bias)	High risk	No selective reporting.
Other bias	Low risk	None obvious.

Dai 2006

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: eight weeks. Design: parallel. Setting: inpatient and outpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 80. Age: aripiprazole group: 24- 58 years, mean = 31 years; risperidone group: not reported Gender: aripiprazole group: 28 male, 12 female; risperidone group: 24 male, 16 female History: aripiprazole group: 1 month- 8 years, mean = 6.4 years; risperidone group: not reported. Age at onset not reported
Interventions	1. Aripiprazole: Dose range: 5-20 mg/day. Mean dose: not reported. N = 40 2. Risperidone: Dose range: 5-20 mg/day. Mean dose: not reported. N = 40
Outcomes	Global state: PANSS score decreased rate (markedly improved: $\geq 70\%$, improved: 40%-70%, no effect: < 40%) Mental state: PANSS total score. Adverse effects
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.

Dai 2006 (Continued)

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.
Selective reporting (reporting bias)	Low risk	No selective reporting.
Other bias	Low risk	None obvious.

Deng 2008

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: one week wash-out period + eight weeks. Design: parallel. Setting: inpatient, China.	
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 50. Age: mean = (63.5 ± 2.3) years; risperidone group: mean = (65.2 ± 2.7) years Gender: aripiprazole group: 17 male, 8 female; risperidone group: 15 male, 10 female. History: aripiprazole group: mean= (3.7 ± 2.4) years; risperidone group: mean=(5.2 ± 1.4) years. Age at onset not reported	
Interventions	1. Aripiprazole: Dose range: 5-20 mg/day. Mean dose: not reported. N = 25. 2. Risperidone: Dose range: 1-4 mg/day. Mean dose: not reported. N = 25	
Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 80%, markedly improved: ≥50%, improved: ≥25%, no effect: < 25%) Mental state: PANSS total score, PANSS positive subscale score, PANSS negative subscale score, PANSS general pathological subscale score Adverse effects.	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.

Deng 2008 (Continued)

Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	There were no incomplete data.
Selective reporting (reporting bias)	High risk	Data on TESS total score, ESRS score, blood and urine routines, liver function, use of benzodiazepine and anticholinergic medicine were missing
Other bias	Low risk	None obvious.

Deng 2008a

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: eight weeks. Design: parallel. Setting: inpatient, China.	
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 90. Age: aripiprazole group: mean= (25 ± 5. 2) years; risperidone group: mean = (29 ± 4. 2) years Gender: aripiprazole group: 25 male, 20 female; risperidone group: 23 male, 22 female. History: aripiprazole group: mean = (1.3 ± 1.1) years; risperidone group: mean = (1.5 ± 1.0) years. Age at onset not reported	
Interventions	1. Aripiprazole: Dose range: 5-30 mg/day. Mean dose: not reported. N = 45. 2. Risperidone: Dose range: 2-6 mg/day. Mean dose: not reported. N = 45	
Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 75%, improved: 50%-74%, improved: 25%-50%, no effect: < 25%) Mental state: PANSS total score, PANSS positive subscale score, PANSS negative subscale score, PANSS general pathological subscale score Adverse effects.	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement

Deng 2008a (Continued)

Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	There were no incomplete data.
Selective reporting (reporting bias)	High risk	Data on TESS total score, use of benzhexol, benzodiazepine and propranolol were missing
Other bias	Low risk	None obvious.

Ding 2007

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: eight weeks. Design: parallel. Setting: inpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). BPRS of 35 or more. N = 60. Age: aripiprazole group: 18- 56 years, mean = (28.6 ± 3.7) years; risperidone group: 19 ~ 55 years, mean = (28.1 ± 5.6) years Gender: aripiprazole group: 13 male, 17 female; risperidone group: 14 male, 16 female. History: aripiprazole group: 1 month- 3 years, mean = (1.4 ± 0.5) years. risperidone group: 1 month- 3 years, mean = (1.3 ± 0.6) years. Age at onset not reported
Interventions	1. Aripiprazole: Dose range: 5-30 mg/day. Mean dose: not reported. N = 30. 2. Risperidone: Dose range: 1-6 mg/day. Mean dose: not reported. N = 30
Outcomes	Global state: BPRS score decreased rate (recovery: ≥ 75%, markedly improved: 50%-74%, improved: 25%-49%, no effect: < 25%) Mental state: anxiety - labelled as "adverse effect". Adverse effects.
Notes	

Ding 2007 (Continued)

<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	No incomplete data.
Selective reporting (reporting bias)	Unclear risk	Data on BPRS score, TESS score, ECG, EEG were missing.
Other bias	Unclear risk	None obvious.

Du 2006

Methods	Allocation: randomised, no further details. Blindness: double. Duration: one week wash-out period + six weeks intervention. Design: parallel. Setting: inpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). N = 65. Age: aripiprazole group: 18- 65 years, mean = (29 ± 9) years; risperidone group: 18 ~ 60 years, mean = (31.1 ± 9.7) years Gender: not reported. History: 1 month ~ 20 years, mean= (6.8 ± 8.4) years; risperidone group: 1 month ~ 23 years, mean= (7.3 ± 8) years. Age at onset not reported
Interventions	1. Aripiprazole: Dose range: 5-30 mg/day. Mean = (21 ± 6.2) mg/day. N = 33. 2. Risperidone: Dose range: 1-6 mg/day. Mean = (4.5 ± 1) mg/day. N = 32
Outcomes	Adverse effects: level of PRL, weight.
Notes	

Du 2006 (Continued)

<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Unclear if there were incomplete data.
Selective reporting (reporting bias)	Low risk	No selective reporting.
Other bias	Low risk	None obvious.

Fan 2005

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: eight weeks. Design: parallel. Setting: inpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 72. Age: aripiprazole group, mean = (32 ± 10.2) years; clozapine group: mean = (31 ± 10.8) years Gender: aripiprazole group: 19 male, 13 female; clozapine group: 20 male, 12 female. History: aripiprazole group: mean = (6.6 ± 3.3) years; clozapine group: mean = (6.4 ± 3.2) years. Age at onset not reported
Interventions	1. Aripiprazole: Dose range: 10-30 mg/day. Mean = (15.68 ± 6.42) mg/day. N = 36. 2. Clozapine: Dose range: 50-500 mg/day. Mean = (211 ± 31.82) mg/day. N = 36
Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 75%, markedly improved: 50%-75%, improved: 25%-50%, no effect: < 25) Mental state: PANSS total score, PANSS positive subscale score, PANSS negative subscale score, PANSS general pathological subscale score Adverse effects: central nervous system (somnolence) extrapyramidal side-effects, weight

Fan 2005 (Continued)

	gain, postural hypotension, tardive dyskinesia, constipation,endocrine (menstrual disorder), ECG abnormal (Q-Tc prolongation), change of blood routine	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.
Selective reporting (reporting bias)	High risk	Although TESS was used to assess adverse effects, no data on score were available. Data on laboratory tests (urine routine, glucose, liver function) and ECG were missing
Other bias	Low risk	None obvious.

Fan 2010

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: one week wash-out period + eight weeks. Design: parallel. Setting: inpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 60. Age: aripiprazole group: 19- 60 years, mean = (33.5 ± 6.9) years; risperidone group: 18 - 60 years, mean = (32.7 ± 8.1) years Gender: aripiprazole group: 17 male, 13 female; risperidone group: 18 male, 12 female. History: aripiprazole group: 1- 146 months, mean = (6.3 ± 5.7) years; risperidone group: 1- 160 months, mean = (6.9 ± 6.4) years. Age at onset not reported

Interventions	1. Aripiprazole: Dose range: 5-30 mg/day. Mean dose: (22.5 ± 6.6)mg/day. N = 30. 2. Risperidone: Dose range: 1-6 mg/day. Mean dose: (4.5 ± 1.4)mg/day. N = 30	
Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 75%, markedly improved: 50%-74%, improved: 25%-49%, no effect: < 25%) Mental state: PANSS total score, PANSS positive subscale score, PANSS negative subscale score, PANSS general pathological subscale score Adverse effects.	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.
Selective reporting (reporting bias)	High risk	Although TESS was used to assess adverse effects, no data on score were available. Data on blood and urine routine, renal function, use of benzodiazepines and other medicines were missing
Other bias	Low risk	None obvious.

Methods	Allocation: randomised, no further details. Blindness: double. Duration: eight weeks. Design: parallel. Setting: inpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 69. Age: 18- 55 years. Gender: not reported. History: < 1 year. Age at onset not reported.
Interventions	1. Aripiprazole: Dose range: 5-30 mg/day. Mean = (22.68 ± 4.91) mg/day. N = 35. 2. Risperidone: Dose range: 1-6 mg/day. Mean = (3.94 ± 1.43) mg/day. N = 34
Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 75%, markedly improved: 50%-74%, improved: 25%-49%, no effect: < 25%). CGI score Mental state: PANSS total score, PANSS positive subscale score, PANSS negative subscale score, PANSS psychopathological subscale score Leaving the study early. Adverse effects.

Notes

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Blinded evaluation.
Incomplete outcome data (attrition bias) All outcomes	Low risk	The total proportion of loss to follow-up was 13.4% (5/35 vs. 4/34), there no no difference between the two groups
Selective reporting (reporting bias)	High risk	Data on TESS total score, blood and urine routine, ECG, liver function and other adverse effects were missing

Other bias	Low risk	None obvious.
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Fleischhacker 2008

Methods	Allocation: random, no further details. Blindness: double, no further details. Duration: 52 weeks (first six weeks observed). Design: parallel. Location: multicentre.
Participants	Diagnosis: (DSM-IV) acute schizophrenia, PANSS of 60 or more. N = 703. Age: 18-65 years. Gender: M, F. History: duration of illness not reported, age at onset not reported. Setting: in- and out-patient.
Interventions	1. Aripiprazole: flexible dose. Allowed dose range: 15-30 mg/day. N = 355. 2. Olanzapine: flexible dose. Allowed dose range: 10-20 mg/day. N = 348
Outcomes	Leaving the study early: any reason. Global state: CGI. Mental state: PANSS total score, MADRS. Quality of life/satisfaction with treatment: Quality of Life Enjoyment and Satisfaction Questionnaire, Medication adherence scale. Adverse effects: open interviews, EPS (SAS, AIMS, BAS), cardiac effects (ECG), weight gain (BMI) Unable to use - Adverse event outcomes (no data, interim report)
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	1:1 randomisation using SARA (System for Automated Randomisation). QTONE an automated touch tone system was used. Statistical blocking factor of four was used and stratified by the study centre
Allocation concealment (selection bias)	Unclear risk	No further details.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Double, no further details. Whether blinding was successful has not been examined, but both compounds differ quite substantially in adverse effects. This can be a prob-

		lem for blinding
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Objective outcomes such as laboratory measures or death are unlikely to have been much affected by problems of blinding
Incomplete outcome data (attrition bias) All outcomes	High risk	Leaving the study early data within the first six weeks were 25% overall, but data on reason for dropout were not available. The LOCF method was used to account for people leaving the study early
Selective reporting (reporting bias)	High risk	Data for the predefined primary outcome are available but secondary outcome measures like 30% PANSS total reduction are missing in the six-week interim report. Treatment emergent adverse events are hardly addressed in the interim report
Other bias	High risk	The study was industry sponsored by the manufacturer of aripiprazole. Baseline data reporting is insufficient in terms of missing data on history of illness

Fu 2009

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: eight weeks. Design: parallel. Setting: inpatient and outpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 69. Age: 12- 18 years, aripiprazole group: mean = (16.9 ± 3.4) years; risperidone group: mean = (15.6 ± 5.7) years Gender: aripiprazole group: 20 male, 13 female; risperidone group: 21 male, 15 female. History: aripiprazole group: mean = (4.7 ± 2.9) years; risperidone group: mean = (5.2 ± 3.5) years. Age at onset not reported
Interventions	1. Aripiprazole: Dose range: 5-20 mg/day. Mean = (16.5 ± 3) mg/day. N = 33. 2. Risperidone: Dose range: 0.5-6 mg/day. Mean = (3.6 ± 1) mg/day. N = 36
Outcomes	Global state: PANSS score decreased rate (recovery: > 75%, markedly improved: 50%-75%, improved: 25%-50%, no effect: < 25%) Mental state: PANSS total score, PANSS total score decreased rate, "agitation" labelled as adverse effect Drug combination.

Fu 2009 (Continued)

	Adverse effects.	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.
Selective reporting (reporting bias)	High risk	Although TESS was used to assess adverse effects, no data on score were available. Data on blood routine, liver function were incomplete
Other bias	Low risk	None obvious.

Ge 2009

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: eight weeks. Design: parallel. Location: inpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 80. Age: 18- 40 years, aripiprazole group: mean = (22.1 ± 5.9) years; quetiapine group: mean = (24.8 ± 7.2) years Gender: Not reported. History: aripiprazole group: mean = (1.1 ± 0.7) years; quetiapine group: mean = (1.3 ± 0.7) years. Age at onset not reported
Interventions	1. Aripiprazole: Initial dose: 5 mg/day. Mean = (25.5 ± 1.8) mg/day. N = 40. 2. Quetiapine: Initial dose: 100mg/day. Mean = (425 ± 27) mg/day. N = 40

Ge 2009 (Continued)

Outcomes	Mental state: PANSS total score. PANSS positive subscale score, PANSS negative subscale score, PANSS general psychogenic pathological subscale score Adverse effects.	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Unclear if there were incomplete data.
Selective reporting (reporting bias)	High risk	Although TESS was used to assess adverse effects, no data on score were available
Other bias	Low risk	None obvious.

Ge 2010

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: eight weeks. Design: parallel. Location: inpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 80. Age: 16- 55 years, aripiprazole group: mean = (30 ± 2.4) years; quetiapine group: mean = (31 ± 3.2) years Gender: 80 female. History: < 3 years, aripiprazole group: not reported; quetiapine group: 3 months- 3 years, mean = (2.05 ± 0.5) years. Age at onset not reported

Interventions	1. Aripiprazole: Dose range: 2.5-30 mg/day. Mean dose: not reported. N = 40. 2. Quetiapine: Dose range: 50-600 mg/day. Mean dose: not reported. N = 40	
Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 75%, markedly improved: 50%-74%, improved: 25%-49%, no effect: < 25%) Mental state: PANSS total score. PANSS positive subscale score, PANSS negative subscale score, PANSS general psychogenic pathological subscale score, anxiety- labelled as “adverse effect” Adverse effects.	
Notes		
<i>Risk of bias</i>		
Bias	Authors’ judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.
Selective reporting (reporting bias)	High risk	Data on TESS total score and use of benzodiazepine were missing. Data on weight-average endpoint level were incomplete
Other bias	Low risk	None obvious.

Guo 2006

Methods	Allocation: randomised, no further details. Blindness: double. Duration: 3-7 days wash-out period + six weeks intervention. Design: parallel. Setting: inpatient, China.
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Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. BPRS of 35 or more. N = 38. Age: aripiprazole group: mean = (28.9 ± 7.3) years; risperidone group: mean= (27.7 ± 8.4) years Gender: aripiprazole group: 11 male, 7 female; risperidone group: 14 male, 6 female. History: not reported. Age at onset not reported.	
Interventions	1. Aripiprazole: Dose range: 10-30 mg/day. Mean dose: not reported. N = 18. 2. Risperidone: Dose range: 2-6 mg/day. Mean dose: not reported. N = 20	
Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 80%, markedly improved: 50%-80%, improved: 30%-50%, no effect: < 30%) Mental state: PANSS total score, PANSS positive subscale score, PANSS negative subscale score, PANSS psychopathological subscale score. BPRS total score Adverse effects.	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Double.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.
Selective reporting (reporting bias)	High risk	Data on TESS total score, blood and urine routine, use of benzodiazepines and anti-cholinergic medicine were missing
Other bias	Low risk	None obvious.

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: eight weeks. Design: parallel. Setting: inpatient, China.	
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 70. Age: 18- 60 years, mean aripiprazole group = (27 ± 6) years; mean clozapine group = (29 ± 8) years Gender: aripiprazole group: 18 male, 17 female; clozapine group: 19 male, 16 female. History: aripiprazole group, mean = (1.5 ± 2) years; clozapine group: mean = (1.7 ± 2) years. Age at onset not reported	
Interventions	1. Aripiprazole: Dose range: 10-30 mg/day. Mean dose: not reported. N = 35. 2. Clozapine: Dose range: 25-450 mg/day. Mean dose: not reported. N = 35	
Outcomes	Global state: PANSS score decreased rate(recovery: ≥ 75%, markedly improved: 50%-75%, improved: 25%-50%, no effect: < 25) Mental state: PANSS total score, PANSS positive subscale score, PANSS negative subscale score, PANSS general pathological subscale score Adverse effects: Central nervous system (dizziness, headache,insomnia, somnolence), extrapyramidal side-effects, gastrointestinal (constipation, salivate), weight gain, blood glucose increase, blood routine abnormal, change of ECG (Q-T abnormal) Unable to use - Adverse effects: TESS score (no data), EEG, laboratory tests (urine routine, hepatorenal function) and use of Benzodiazepines azoles or Artane (no data) Mental state: PANSS anxiety subscale score - unvalidates subscale Cognitive function: PANSS cognitive factor subscale score - subscale unvalidated	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.

Han 2005 (Continued)

Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.
Selective reporting (reporting bias)	High risk	Although TESS was used to assess adverse effects, no data on score were available. Data on laboratory tests (urine routine, hepatorenal function) and EEG were missing
Other bias	Low risk	None obvious.

Han 2007

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: eight weeks intervention. Design: parallel. Setting: inpatient, China.	
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 61. Age: aripiprazole group: mean = (31.0 ± 10.1) years; olanzapine group: mean = (29.9 ± 9.3) years Gender: aripiprazole group: 14 male, 16 female; olanzapine group: 14 male, 17 female. History: aripiprazole group: mean = (5.89 ± 1.1) years; olanzapine group: mean= (6.26 ± 1.2) years. Age at onset not reported	
Interventions	1. Aripiprazole: Dose range: 10-30 mg/day. Mean = (20.8 ± 3.1) mg/day . N = 30. 2. Olanzapine: Dose range: 5-20 mg/day. Mean dose = (13.6 ± 2.7) mg/day. N = 31	
Outcomes	Global state: markedly improved, improved, slight improved, no effect Mental state: PANSS total score, PANSS positive subscale score, PANSS negative subscale score, PANSS psychopathological subscale score Leaving the study early. Adverse effects.	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.

Han 2007 (Continued)

Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	One patient was lost to follow-up in olanzapine.
Selective reporting (reporting bias)	High risk	Data on CGI score, TESS total score, blood and urine routine, use of benzodiazepines anticholinergic medicine were missing
Other bias	Low risk	None obvious.

Han 2007a

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: eight weeks. Design: parallel. Setting: inpatient and outpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 86. Age: aripiprazole group: 16- 61 years, mean = (25.7 ± 7.9) years; risperidone group: 16 ~ 62 years, mean = (26.9 ± 8.4) years Gender: aripiprazole group: 19 male, 24 female; risperidone group: 20 male, 23 female. History: aripiprazole group: 1 month- 10 years, mean = (4.8 ± 2.6) years; risperidone group: 1 month- 9 years, mean = (4.6 ± 2.8) years. Age at onset not reported
Interventions	1. Aripiprazole: Dose range: 5-30 mg/day. Mean dose: (15.3 ± 3.2) mg/day. N = 43. 2. Risperidone: Dose range: 1-6 mg/day. Mean dose: (3.8 ± 1.6) mg/day. N = 43
Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 75%, improved: 50%-75%, no effect: < 50%) Mental state: PANSS total score, PANSS positive subscale score, PANSS negative subscale score, PANSS general pathological subscale score Adverse effects. Unable to use - Mental state: PANSS subscale score decreased rate - unvalidated subscales
Notes	
<i>Risk of bias</i>	

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	There were no incomplete data.
Selective reporting (reporting bias)	High risk	Data of TESS total score, blood routine, blood glucose, electrolyte, ECG, liver function was missing
Other bias	Low risk	None obvious.

Hu 2010

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: eight weeks. Design: parallel. Setting: inpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 50. Age: aripiprazole group 18- 56 years, mean = (28.9 ± 4.6) years; risperidone group 16 ~ 58 years, mean = (30.1 ± 5.2) years Gender: aripiprazole group: 13 male, 12 female; risperidone group: 12 male, 13 female. History: aripiprazole group: 1 month- 5 years, mean = (3.6 ± 2.1) years; risperidone group: 2 months- 5.2 years, mean = (3.8 ± 2.4) years. Age at onset not reported
Interventions	1. Aripiprazole: Dose range: 10-30 mg/day. Mean dose: not reported. N = 25. 2. Risperidone: Dose range: 2-8 mg/day. Mean dose: not reported. N = 25
Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 75%, markedly improved: 50%-75%, improved: 25%-50%, no effect: < 25%) Mental state: PANSS total score, PANSS positive subscale score, PANSS negative subscale score, PANSS general pathological subscale score Adverse effects.

Hu 2010 (Continued)

Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.
Selective reporting (reporting bias)	High risk	Data on TESS total score, blood routine, ECG, liver function, blood glucose, use of benzodiazepines and other medicines were missing
Other bias	Low risk	None obvious.

Huang 2009

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: six weeks. Design: parallel. Setting: inpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS total score = 50. N = 60. Age: 16- 55 years, aripiprazole group mean = (30.90 ± 11.05) years; risperidone group mean = (29.55 ± 12.35) years Gender: aripiprazole group: 12 male, 18 female; risperidone group: 13 male, 17 female. History: aripiprazole group: mean = (4.5 ± 6.9) months; risperidone group mean = (5.7 ± 8.7) months. Age at onset not reported
Interventions	1. Aripiprazole: Dose range: 10-30 mg/day. Mean dose: not reported. N = 30. 2. Risperidone: Dose range: 2-6 mg/day. Mean dose: not reported. N = 30

Huang 2009 (Continued)

Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 75%, markedly improved: 50%-75%, improved: 25%-50%, no effect: < 25%) Leaving the study early. Adverse effects: the average endpoint score of BMI, blood glucose, TCHO, TG, PRL, LEP Unable to use - Mental state: PANSS total score (no data).	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.
Selective reporting (reporting bias)	High risk	Although PANSS was used to assess mental state, no end data on score were available. Data on use of benzodiazepines and other medicines were missing
Other bias	Low risk	None obvious.

Ji 2007

Methods	<p>Allocation: randomised, no further details.</p> <p>Blindness: unclear.</p> <p>Duration: one week wash-out period + eight weeks intervention.</p> <p>Design: parallel.</p> <p>Setting: inpatient and patient, China.</p>	
Participants	<p>Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more.</p> <p>N = 64.</p> <p>Age: aripiprazole group: 18- 58 years, mean = (32.8 ± 6.2) years; risperidone group: 17</p>	

	~ 59 years, mean = (30.6 ± 7.8) years Gender: aripiprazole group: 19 male, 13 female; risperidone group: 18 male, 14 female. History: aripiprazole group: 1 month- 9 years, mean = (4.2 ± 3.9) years; risperidone group: 1 month- 11 years, mean = (5.2 ± 3.4) years. Age at onset not reported	
Interventions	1. Aripiprazole: Dose range: 5-30 mg/day. Mean = (15 ± 5) mg/ day. N = 32. 2. Risperidone: Dose range: 1-6 mg/day. Mean = (3.2 ± 1.8) mg/ day. N = 32	
Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 75%, markedly improved: 50%-74%, improved: 25%-49%, no effect: < 25%) Mental state: PANSS total score, PANSS positive subscale score, PANSS negative subscale score, PANSS psychopathological subscale score, anxiety-labelled as “adverse effect” Adverse effects.	
Notes		
<i>Risk of bias</i>		
Bias	Authors’ judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.
Selective reporting (reporting bias)	High risk	Data on TESS total score, blood and urine routine, use of benzodiazepines and anti-cholinergic medicine were missing
Other bias	Low risk	None obvious.

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: eight weeks. Design: parallel. Location: not reported, China.	
Participants	Diagnosis: schizophrenia (CCMD-3). N = 80. Age: Aripiprazole group: 18- 56 years, mean = (33 ± 6) years; Clozapine group: 18 ~ 57 years, mean = (35 ± 5.7) years. Gender: aripiprazole group: 26 female, 14 male; clozapine group: 27 male, 13 female. History: aripiprazole group: 2- 8 years, mean =(5 ± 3.2) years; clozapine group: 2 ~ 15years, mean =(5.7 ± 4.1) years. Age at onset not reported. Setting: not reported.	
Interventions	1. Aripiprazole: Dose range: 5-30 mg/day. Mean = (23.5 ± 1.4) mg/d. N = 40. 2. Clozapine: Dose range: 25-500 mg/day. Mean = (400 ± 14.2) mg/d. N = 40	
Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 75%, markedly improved: 50%-75%, improved: 25%-50%, no effect: < 25) Mental state: PANSS total score, PANSS positive subscale score, PANSS negative subscale score, PANSS general pathological subscale score Adverse effects.	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.
Selective reporting (reporting bias)	High risk	Although TESS was used to assess adverse effects, no data on score were available. Data on use of use of alprazolam, propa-

		nolol and anticholinergic medication were missing
Other bias	Low risk	None obvious.

Jie 2008

Methods	Allocation: randomised, random number table. Blindness: unclear. Duration: eight weeks. Design: parallel. Setting: inpatient, China.	
Participants	Diagnosis: schizophrenia (CCMD-3), PANSS of 60 or more, SANS of 60 or more. N = 50. Age: aripiprazole group: 18~ 50 years, mean = (25.7 ± 5.8) years; clozapine group: 18 ~ 57 years, mean = (27.85 ± 5.75) years. Gender: aripiprazole group: 16 male, 9 female; clozapine group: 15 male, 10 female. History: aripiprazole group: 1~ 10 years, mean = (4.15 ± 3.14) years; clozapine group: 1 ~ 11years, mean = (4.18 ± 3.15) years. Age at onset not reported	
Interventions	1. Aripiprazole: Dose range: 5-25 mg/day. Mean = (13.5 ± .8) mg/d. N = 25. 2. Clozapine: Dose range: 50-500 mg/day. Mean = (385.5 ± 75.5) mg/d. N = 25	
Outcomes	Global state: PANSS score decreased rate(recovery: ≥ 80%, markedly improved: 50%-75%, improved: 25%-50%, no effect: < 25) Mental state: PANSS total score, PANSS positive subscale score, PANSS negative subscale score, PANSS general pathological subscale score Adverse effects: TESS total score.	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomised, random number table.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.

Jie 2008 (Continued)

Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.
Selective reporting (reporting bias)	High risk	Data on somnolence, weight gain, EGG abnormal, salivation, dry mouth, blurred vision (no data) and use of alprazolam, propranolol, anticholinergic medication were missing
Other bias	Low risk	None obvious.

Kane 2009

Methods	Allocation: random, no further details. Blindness: double, no further details. Duration: 28 weeks. Design: parallel. Location: multicentre.
Participants	Diagnosis: (DSM-IV) schizophrenia catatonic (n = 3), disorganised (n = 29), paranoid (n = 464), undifferentiated (n = 62), residual (n = 6), missing (n = 2), PANSS total score of ≥ 75 , minimum of ≥ 4 PANSS positive items, score of ≥ 4 on CGI-S, score of ≥ 3 on CGI-I. N = 566. Age: 18-65 years. Mean for males 38 years. Gender: 384 M, 182 F. History: duration of illness not reported, mean (SD) previous episodes 7.7 (8.0). Setting: inpatient and outpatient.
Interventions	1. Aripiprazole: 15- 30 mg/day, N = 285. 2. Olanzapine: 10-20 mg/day. N = 281.
Outcomes	Leaving the study early. Global state: CGI. Mental state: PANSS total score. Adverse effects: EPSE (SAS, AIMS, BAS), laboratory results- lipids, glucose, increase in prolactin level, sedation, weight gain and others
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No information available.
Allocation concealment (selection bias)	Unclear risk	No further information.

Kane 2009 (Continued)

Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No details.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Objective outcomes such as death are unlikely to have been much affected by lack of blinding
Incomplete outcome data (attrition bias) All outcomes	Low risk	LOCF.
Selective reporting (reporting bias)	High risk	Only adverse events with an incidence of more than 5% were reported. This procedure may have missed important adverse events
Other bias	High risk	Drug company involvement.

Kern 2006

Methods	Allocation: random, 1:1 ratio. Blindness: open label, no further details. Duration: 26 weeks. Design: parallel. Location: multicentre.	
Participants	Diagnosis: (DSM-IV) schizophrenia or schizo-affective disorder. N = 255. Age: 18-65 years. Gender: 109 M, 60 F. History: duration of illness not reported. Setting: outpatient.	
Interventions	1. Aripiprazole: 15- 30 mg/day, N = 128. 2. Olanzapine: 10-15 mg/day. N = 127.	
Outcomes	Leaving the study early. Unable to use - Cognitive function: CVLT, BVRT-R, WCST, Trail Making A and B, Verbal Fluency, Letter-Number Sequencing, Grooved Pegboard Test, CPT-IP (no usable data). Mental state: PANSS total score (used as co-variate, no usable data)	
Notes	Study compared the neuro-cognitive effects of medications.	
Risk of bias		
Bias	Authors' judgement	Support for judgement

Kern 2006 (Continued)

Random sequence generation (selection bias)	Unclear risk	No information available.
Allocation concealment (selection bias)	High risk	Open label.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open label.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No details.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	LOCF.
Selective reporting (reporting bias)	High risk	Few neuro-cognitive tests were mentioned but usable data was not available from them
Other bias	High risk	Drug company involvement.

Kerwin 2007

Methods	Allocation: random, computer generated 1: 1. Blindness: open label. Duration: 26 weeks. Design: parallel, naturalistic. Location: multicentre.
Participants	Diagnosis: schizophrenia (DSM IV). N = 271. Age: 18-65 years (mean about 38 years). Gender: M and F. History: duration of illness not reported, age at onset not reported. Setting: community or hospital-based outpatient centre. .
Interventions	1. Aripiprazole: 10-30 mg/day (mean-18.7 mg). N = 284. 2. Standard care: olanzapine 5-20 mg/day (mean 12.5 mg); N = 75, risperidone 2-16 mg/day (mean-4.6 mg); N = 81, quetiapine 100-800 mg/day (mean-386.8 mg); N = 110
Outcomes	IAQ, Leaving the study early: any reason, adverse events, inefficacy. Global state: CGI (data not usable) ASEX. Quality of life: QLS, IWQoL-Lite, EQ-5D. Adverse effects: at least one adverse effect, extrapyramidal adverse effects, cholesterol increase, fasting triglycerides abnormalities, glucose elevation, prolactin increase, weight change
Notes	

Kerwin 2007 (Continued)

<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No information available.
Allocation concealment (selection bias)	High risk	Open label.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open label.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No details.
Incomplete outcome data (attrition bias) All outcomes	Low risk	LOCF.
Selective reporting (reporting bias)	High risk	Only adverse events with an incidence of more than 5% were reported. This may have missed important adverse events. Some scales used had no reported usable data
Other bias	High risk	Drug company involvement.

Kinon 2004

Methods	Allocation: random (1: 1), no further details. Blindness: double, no further details. Duration: 5 days. Design: parallel. Location: multicentre.
Participants	Diagnosis: schizophrenia, schizoaffective disorder or schizophreniform disorder N = 604. Age 18-55 years. Gender: male/female. History: duration of illness not reported, acutely ill. Setting: originally inpatient.
Interventions	1. Aripiprazole: 15-30 mg/day, mean 19.26 mg (SD 5.46). N = 298. 2. Olanzapine: 20 mg/day, mean 19.97 mg (SD 0.27). N = 306.

Outcomes	Agitation symptoms: PANSS-EC. Leaving the study early: any reason, adverse events, inefficacy. Global state: CGI. Mental state: PANSS total score, BPRS. Adverse effects: at least one adverse effect, cardiac effects (QTc), extrapyramidal adverse effects (use of antiparkinson medication, extrapyramidal symptom (BAS, SAS-modified) , cholesterol increase, glucose elevation, prolactin increase, weight, Other measures: GANI, DAI-10, ACES.	
Notes	Lorazepam was used as required throughout the study. Data were not made available for other scales used	
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Random 1:1, no further details available.
Allocation concealment (selection bias)	Unclear risk	Not defined.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Double. No further details available.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Objective outcomes such as laboratory measures or death are unlikely to have been much affected by problems of blinding
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	The LOCF method was used to account for people leaving the study early
Selective reporting (reporting bias)	High risk	Adverse effects were reported if $\geq 1\%$ of patients in either treatment group experienced them. Some scales used had no data published
Other bias	High risk	The study was industry sponsored by the manufacturer of olanzapine

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: eight weeks. Design: parallel. Location: inpatient, China.	
Participants	Diagnosis: schizophrenia (CCMD-3), BPRS of 35 or more. N = 120. Age: aripiprazole group: 18- 60 years, mean = (32 ± 9) years, clozapine group: 18- 60 years, mean = (31 ± 10) years. Gender: aripiprazole group: 32 male, 24 female; clozapine group: 32 male, 24 female. History: aripiprazole group: mean = (6 ± 2.1) months; clozapine group: mean = (5 ± 2.3) months. Age at onset not reported	
Interventions	1. Aripiprazole: Dose range: 10-30 mg/day. Mean = (20 ± 5) mg/day. N = 60. 2. Clozapine: Dose range: 75-600 mg/day. Mean = (550 ± 50) mg/day. N = 60	
Outcomes	Global state: BPRS score decreased rate (recovery: ≥ 75%, markedly improved: 50%-74%, improved: 25%-49%, no effect: < 25%) Mental state: BPRS score. Leaving the study early. Quality of life: GQOLI-74 (material life, physical health, mental health, social function) Adverse effects.	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	The total rate of loss to follow-up was 5% (6/120), and there was no difference between the two group. All 6 participants dropped out because of economic issue

Selective reporting (reporting bias)	High risk	Although TESS was used to assess adverse effects, no data on score were available. Data on laboratory tests (blood routine, urine routine, glucose, liver function, etc) were missing
Other bias	Low risk	None obvious.

Li 2006

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: eight weeks. Design: parallel. Setting: inpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 70. Age: aripiprazole group: 22- 43 years, mean = (32.83 ± 9. 42) years; risperidone group: 20 ~ 42 years, mean = (33. 64 ± 7. 26) years Gender: aripiprazole group: 18 male, 17 female; risperidone group: 20 male, 15 female. History: aripiprazole group: 1~ 3 months, mean= (2.14 ± 0.87) months; risperidone group: 1~ 3 months, mean= (2.15 ± 0.97) months. Age at onset not reported
Interventions	1. Aripiprazole: Dose range: 5-30 mg/day. Mean dose: not reported. N = 35. 2. Risperidone: Dose range: 1-4 mg/day. Mean dose: not reported. N = 35
Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 75%, markedly improved: 50%-74%, improved: 25%-49%, no effect: < 25%) Mental state: PANSS total score, PANSS positive subscale score, PANSS negative subscale score, PANSS psychopathological subscale score. agitation-labelled as “adverse effect” Leaving the study early. Adverse effects.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.

Li 2006 (Continued)

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	The total proportion of loss to follow-up was 4.29% (1/35: 2/35), and there was no difference between the two groups. All because of adverse effects
Selective reporting (reporting bias)	High risk	Data on TESS total score, use of benzodiazepines, benzhexol, and propranolol were missing
Other bias	Low risk	None obvious.

Li 2006a

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: eight weeks. Design: parallel. Setting: inpatient and outpatient, China.	
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 76. Age: aripiprazole group: 18- 59 years. mean = (8. 6 ± 8. 7) years; risperidone group: 20 ~ 58 years, mean = (29. 8 ± 9. 3) years Gender: aripiprazole group: 20 male, 18 female; risperidone group: 21 male, 17 female. History: aripiprazole group: 1 month- 13 years, mean = 6.5 years; risperidone group: 2 months- 12 years, mean = 7.2 years. Age at onset not reported	
Interventions	1. Aripiprazole: Dose range: 10-30 mg/day. Mean = (18.3 ± 4.2) mg/day. N=38. 2. Risperidone: Dose range: 1-6 mg/day. Mean = (3.1 ± 1.2) mg/day. N=38	
Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 75%, markedly improved: 50%-75%, improved: 25%-50%, no effect: < 25%). CGI score Mental state: PANSS total score, PANSS positive subscale score, PANSS negative subscale score, PANSS psychopathological subscale score, anxiety- labelled as “adverse effect”, excitement/agitation-labelled as “adverse effect” Leaving the study early. Adverse effects.	
Notes		
<i>Risk of bias</i>		
Bias	Authors’ judgement	Support for judgement

Li 2006a (Continued)

Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	The total proportion of loss to follow-up was 2.63% (1/38: 0/38), all because of adverse effects
Selective reporting (reporting bias)	High risk	Data on TESS total score, blood and urine routine, renal function, use of benzodiazepines and anticholinergic drug were missing
Other bias	Low risk	None obvious.

Li 2007

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: twelve weeks. Design: parallel. Setting: not reported, China.
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 80. Age: aripiprazole group: mean = (28.9 ± 13.1) years; clozapine group: mean = (30.2 ± 12.5) years Gender: aripiprazole group: 22 male, 18 female; clozapine group: 23 male, 17 female. History: aripiprazole group: mean = (7.3 ± 4.1) months; clozapine group: mean = (7.4 ± 4.2) months. Age at onset not reported
Interventions	1. Aripiprazole: Dose range: 10-60 mg/day. Mean = (21.1 ± 6.6) mg/day. N = 40. 2. Clozapine: Dose range: 75-500 mg/day. Mean = (301 ± 115.2) mg/day. N = 40
Outcomes	Global state: PANSS score decreased rate(recovery: ≥ 75%, markedly improved: 50%-75%, improved: 25%-50%, no effect: < 25%) Mental state: PANSS total score, PANSS positive subscale score, PANSS negative subscale score, PANSS general pathological subscale score Adverse effects: extrapyramidal side-effects (akathisia, tremor, dystonia, spasmodic tor-

Li 2007 (Continued)

	ticollis) Quality of life: WHO-QOL-100.	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.
Selective reporting (reporting bias)	High risk	Although ESRS was used to assess adverse effects, no data on score were available. Data on laboratory tests(blood routine, urine routine, glucose, liver function, etc) and ECG were missing
Other bias	Low risk	None obvious.

Li 2007a

Methods	Allocation: random, no further details. Blindness: unclear. Duration: six months. Design: parallel. Location: inpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3), PANSS of 60 or more. N = 60. Age: aripiprazole group: mean = (25.1 ± 6.8) years; clozapine group: mean = (26.4 ± 6.2) years. Gender: aripiprazole group: 13 male, 17 female; clozapine group: 15 male, 15 female. History: 2 years or less. aripiprazole group: mean = (5.7 ± 4.3) months; clozapine group, mean= (6.5 ± 4.8) years. Age at onset not reported

Li 2007a (Continued)

Interventions	1. Aripiprazole: Dose range: 15-30 mg/day. Mean dose: not reported. N = 30. 2. Clozapine: Dose range: 200-350 mg/day. Mean dose: not reported. N = 30	
Outcomes	Mental state: PANSS total score, PANSS positive subscale score, PANSS negative subscale score, PANSS general pathology subscale score, anxiety - labelled as "adverse effect" Quality of life: WHOQOL100. Adverse effects.	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.
Selective reporting (reporting bias)	High risk	Although TESS was used to assess adverse effects, no data on score were available. Data on use of anti-psychotic drugs and benzhexol were missing
Other bias	Low risk	None obvious.

Li 2007b

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: eight weeks. Design: parallel. Setting: inpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 60. Age: aripiprazole group: 18- 50 years. mean = (24.4 ± 13.9) years; quetiapine group: 18-

	48 years, mean = (27.2 ± 8.4) years Gender: aripiprazole group: 17 male, 13 female; quetiapine group: 17 male, 13 female. History: aripiprazole group: 3 months- 5 years, mean= (2.8 ± 2.2) years; quetiapine group: 3 months- 5 years, mean= (2.6 ± 2.3) years. Age at onset not reported	
Interventions	1. Aripiprazole: Dose range: 5-30 mg/day. Mean dose: not reported. N=30. 2. Quetiapine: Dose range: 100-800 mg/day. Mean dose: not reported. N=30	
Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 80%, markedly improved: 50%-80%, improved: 30%-50%, no effect: < 30%) Mental state: PANSS total score, PANSS positive subscale score, PANSS negative subscale score, PANSS general psychogenic pathological subscale score Unable to use - Adverse effects: TESS total score, menstrual disorder, lactation, weight gain, EEG, ECG, blood routine, urine routine, hepatorenal function, use of benzhexol, benzodiazepine and propranolol (no data)	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.
Selective reporting (reporting bias)	High risk	Data on TESS total score, menstrual disorder, lactation, weight gain, EEG, ECG, blood routine, urine routine, hepatorenal function, use of benzhexol, benzodiazepine and propranolol were missing
Other bias	Low risk	None obvious.

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: eight weeks. Design: parallel. Setting: inpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 84. Age: aripiprazole group: 15- 62 years. mean = (29.4 ± 11.2) years; ziprasidone group: 18-60 years, mean = (28.3 ± 10.1) years Gender: aripiprazole group: 18 male, 24 female; ziprasidone group: 20 male, 22 female. History: aripiprazole group: 1 month- 12 years, mean = 5.6 years; ziprasidone group: 2 months- 13 years, mean = 6.1 years. Age at onset not reported
Interventions	1. Aripiprazole: Dose range: 5-30 mg/day. Mean = (25 ± 5) mg/day. N = 42. 2. Ziprasidone: Dose range: 20-160 mg/day. Mean = (120 ± 40) mg/day. N = 42
Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 75%, markedly improved: 50%-75%, improved: 25%-50%, no effect: < 25%) Mental state: PANSS total score, PANSS positive subscale score, PANSS negative subscale score, PANSS general pathological subscale score Leaving the study early: no patient. Adverse effects. Unable to use - Adverse effects: TESS total score, blood routine, EEG, weight, use of alprazolam, propranolol and anticholinergic medication (no data)
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.

Li 2007c (Continued)

Selective reporting (reporting bias)	High risk	Data on TESS score, blood routine, EEG, weight, and use of alprazolam, propranolol and anticholinergic medication were missing
Other bias	Low risk	None obvious.

Li 2007d

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: 1-2 weeks wash-out period + eight weeks intervention. Design: parallel. Setting: inpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 120. Age: aripiprazole group: 16-60 years, mean = (28.4 ± 9.1) years; risperidone group: 17-56 years, mean = (29.6 ± 8.3) years Gender: aripiprazole group: 28 male, 32 female; risperidone group: 46 male, 14 female. History: aripiprazole group: mean = (2.3 ± 1.8) months; risperidone group: mean = (2.4 ± 1.6) months. Age at onset not reported
Interventions	1. Aripiprazole: Dose range: 5-30 mg/day. Mean dose: not reported. N = 60. 2. Risperidone: Dose range: 1-6 mg/day. Mean dose: not reported. N = 60
Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 75%, markedly improved: 50%-75%, improved: 25%-50%, no effect: < 25%). CGI-SI, CGI-GI Mental state: PANSS total score, PANSS positive subscale score, PANSS negative subscale score, PANSS psychopathological subscale score. agitation-labelled as "adverse effect" Adverse effects. Unable to use - Adverse effects: TESS total score, blood routine, renal function, PRL, use of benzodiazepines and anticholinergic medication (no data)
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.

Li 2007d (Continued)

Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.
Selective reporting (reporting bias)	High risk	Data on TESS total score, blood routine, renal function, PRL, use of benzodiazepines and anticholinergic medication were missing
Other bias	Low risk	None obvious.

Li 2009

Methods	Allocation: random, no further details. Blindness: unclear. Duration: eight weeks. Design: parallel. Location: inpatient and outpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). N = 60. Age: aripiprazole group: 15~ 50 years, mean = (26. 9 ± 10. 1) years, clozapine group: 15 ~ 45 years, mean = (25. 5 ± 9. 3) years. Gender: aripiprazole group: 18 male, 12 female; clozapine group: 20 male, 10 female . History: aripiprazole group: 2 months~ 10 years, mean = (7.1 ± 5.12) years; clozapine group: 2 months~ 13 years, mean = (7.8 ± 6.2) years. Age at onset not reported
Interventions	1. Aripiprazole: Dose range: 5-30 mg/day. Mean dose: not reported. N = 30. 2. Clozapine: Dose range: 50-475 mg/day. Mean dose: not reported. N = 30
Outcomes	Global state: PANSS score decreased rate(recovery: ≥ 75%, markedly improved: 50%-75%, improved: 25%-50%, no effect: < 25%) Mental state: PANSS total score, PANSS positive subscale score, PANSS negative subscale score, PANSS general pathological subscale score Adverse effects: TESS total score(no data), central nervous system (somnolence, dizziness, headache, insomnia), extrapyramidal side-effects (akathisia), gastrointestinal (constipation, salivate), weight gain, blood glucose increase, blood routine abnormal, change of ECG, tachycardia, appetite decrease Unable to use - Adverse effects: Laboratory tests (urine routine, hepatorenal function), use of alprazolam, propranolol and anticholinergic medication (no data)

Li 2009 (Continued)

Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.
Selective reporting (reporting bias)	High risk	Data on laboratory tests (urine routine, hepatorenal function), use of alprazolam, propranolol and anticholinergic medication were missing
Other bias	Low risk	None obvious.

Li 2009a

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: six weeks. Design: parallel. Setting: inpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3), BPRS total score of 20 or more. N = 60. Age: aripiprazole group: mean = (28.6 ± 6.49) years; risperidone group: mean = (29.13 ± 8.61) years Gender: aripiprazole group: 16 male, 14 female; risperidone group: 17 male, 13 female. History: aripiprazole group: mean = (2.17 ± 4.82) years; risperidone group: mean = (3.22 ± 6.71) years. Age at onset not reported
Interventions	1. Aripiprazole: Dose range: 5-30 mg/day. Mean dose: not reported. N = 30. 2. Risperidone: Dose range: 1-6 mg/day. Mean dose: not reported. N = 30

Li 2009a (Continued)

Outcomes	Global state: BPRS score decreased rate (recovery: $\geq 75\%$, markedly improved: 50%-74%, improved: 25%-49%, no effect: $< 25\%$) Mental state: BPRS total score. Adverse effects Unable to use - Adverse effects: TESS total score, use of benzodiazepines and other medicines (no data)
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Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.
Selective reporting (reporting bias)	High risk	Data on TESS total score, use of benzodiazepines and other medicines were missing
Other bias	Low risk	None obvious.

Li 2009b

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: one week wash-out period + eight weeks intervention. Design: parallel. Setting: inpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 60. Age: aripiprazole group: 15~ 45 years, mean = (25.3 ± 10.2) years; risperidone group: 17 ~ 50 years, mean = (28.3 ± 1.2) years Gender: aripiprazole group: 14 male, 16 female; risperidone group: 15 male, 15 female. History: aripiprazole group: 1 month~ 2 years, mean = (1.1 ± 0.8) years; risperidone

	group: 2 months- 2 years, mean = (1.2 ± 0.3) years. Age at onset not reported	
Interventions	1. Aripiprazole: Dose range: 5-30 mg/day. Mean = (25.3 ± 5.1) mg/day. N = 30. 2. Risperidone: Dose range: 2-6 mg/day. Mean = (3.9 ± 1.7) mg/day. N = 30	
Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 80%, markedly improved: 50%-80%, improved: 30%-50%, no effect: < 30%) Mental state: PANSS total score, PANSS positive subscale score, PANSS negative subscale score, PANSS general pathological subscale score Adverse effects. Unable to use - Adverse effects: TESS total score, use of benzodiazepines and other medicines (no data)	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.
Selective reporting (reporting bias)	High risk	Data on TESS total score, ECG, EPS, use of benzodiazepines, propranolol, and anti-cholinergic medication were missing
Other bias	Low risk	None obvious.

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: 3~ 7 days wash-out period + eight weeks intervention. Design: parallel. Setting: inpatient, China.	
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 71. Age: aripiprazole group: mean = (38.1 ± 8.6) years; risperidone group: mean = (36.3 ± 10.2) years Gender: aripiprazole group: 25 male, 11 female; risperidone group: 22 male, 13 female. History: aripiprazole group: mean = (6.4 ± 3.9) years; risperidone group: mean = (5.9 ± 4.0) years. Age at onset not reported	
Interventions	1. Aripiprazole: Dose range: 5-30 mg/day. Mean dose: not reported. N = 36. 2. Risperidone: Dose range: 1-6 mg/day. Mean dose: not reported. N = 35	
Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 75%, markedly improved: 50%-74%, improved: 25%-49%, no effect: < 25%) Mental state: PANSS total score, PANSS positive subscale score, PANSS negative subscale score, PANSS general pathological subscale score. agitation-labelled as “adverse effect” Adverse effects. Unable to use - Adverse effects: TESS total score.	
Notes		
<i>Risk of bias</i>		
Bias	Authors’ judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomisation, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.
Selective reporting (reporting bias)	High risk	Data on TESS total score were missing.

Other bias	Low risk	None obvious.
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Lian 2008

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: six weeks. Design: parallel. Setting: inpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 86. Age: aripiprazole group: 21- 53 years, mean = 38.1 years; risperidone group: 23- 56 years, mean = 37.6 years Gender: aripiprazole group: 27 male, 16 female; risperidone group: 30 male, 13 female. History: aripiprazole group: 2 months- 8 years, mean = 4.5 years; risperidone group: 2 months- 10 years, mean = 4.6 years. Age at onset not reported
Interventions	1. Aripiprazole: Dose range: 5-20 mg/day. Mean dose: not reported. N = 43. 2. Risperidone: Dose range: 1-6 mg/day. Mean dose: not reported. N = 43
Outcomes	Global state: PANSS score decreased rate (excellent: $\geq 60\%$, improved: $\geq 40\%$, no effect: $< 40\%$) Mental state: PANSS total score, PANSS positive subscale score, PANSS negative subscale score, PANSS general pathological subscale score Adverse effects. Unable to use - Adverse effects: TESS total score, blood and urine routines, liver function, ECG (no data)
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.

Lian 2008 (Continued)

Incomplete outcome data (attrition bias) All outcomes	Low risk	There were no incomplete data.
Selective reporting (reporting bias)	High risk	Data of TESS total score, blood and urine routines, liver function, ECG were missing (no data)
Other bias	Low risk	None obvious.

Liang 2008

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: twelve weeks. Design: parallel. Setting: not reported, China.	
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 120. Age: aripiprazole group 18- 60 years, mean = (24. 9 ± 10. 7) years; risperidone group 18 - 58 years, mean = (26. 5 ± 9. 2) years Gender: aripiprazole group: 32 male, 28 female; risperidone group: 31 male, 29 female. History: not reported. Age at onset not reported.	
Interventions	1. Aripiprazole: Dose range: 5-30 mg/day. Mean = 18.7 mg/day. N = 60. 2. Risperidone: Dose range: 0.5-6 mg/day. Mean = 4.8 mg/day. N = 60	
Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 80%, markedly improved: 50%-80%, improved: 30%-50%, no effect: < 30%) Mental state: PANSS total score. agitation labelled as “adverse effect” Leaving the study early. Adverse effects. Unable to use - Adverse effects: TESS total score, blood routine, use of benzodiazepines (no data)	
Notes		
<i>Risk of bias</i>		
Bias	Authors’ judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomisation, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.

Liang 2008 (Continued)

Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	High risk	Six patients were lost to follow-up in risperidone group, four because of adverse effect, two due to progressive disease. No patient was lost to follow-up in aripiprazole group
Selective reporting (reporting bias)	High risk	Data on TESS total score, blood routine, use of benzodiazepines were missing
Other bias	Low risk	None obvious.

Liu 2006

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: six weeks. Design: parallel. Setting: inpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS score of 60 or more. N = 60. Age: aripiprazole: 15- 45 years, mean = (25.3 ± 10.2) years; clozapine: 17- 50 years, mean = (28.3 ± 1.2) years. Gender: aripiprazole group: 13 male, 17 female; clozapine group: 14 male, 16 female . History: aripiprazole group: 1 month - 2 years, mean = (1.1 ± 0.8) years; clozapine group: 2 months - 2 years, mean = (1.2 ± 0.3) years. Age at onset not reported
Interventions	1. Aripiprazole: Dose range: 5-30 mg/day. Mean dose: not reported. N = 30. 2. Clozapine: Dose range: 50-500 mg/day. Mean dose: not reported. N = 30
Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 80%, markedly improved: 50%-80%, improved: 30%-50%, no effect: < 30%) Mental state: PANSS total score. Adverse effects. Unable to use - Adverse effects: Laboratory tests (urine routine), use of alprazolam, propranolol and anticholinergic medication (no data)
Notes	Efficacy and side effects of aripiprazole for first-episode schizophrenia

Liu 2006 (Continued)

<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.
Selective reporting (reporting bias)	High risk	Although TESS was used to assess adverse effects, no data on score were available. Data on use of benzodiazepines, benzhexol and propranolol medication were also missing
Other bias	Low risk	None obvious.

Liu 2006a

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: eight weeks. Design: parallel. Setting: inpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 90. Age: aripiprazole group: 18- 56 years, mean = (28 ± 4.6) years, risperidone group: 18 ~ 58 years, mean = (30.1 ± 5) years Gender: aripiprazole group: 26 male, 19 female; risperidone group: 23 male, 22 female. History: aripiprazole group: 1 month- 5 years, mean = (3.6 ± 2.1) years; risperidone group: 1 month- 5.2 years, mean = (3.8 ± 2.4) years. Age at onset not reported
Interventions	1. Aripiprazole: Dose range: 10-30 mg/day. Mean dose: not reported. N = 45. 2. Risperidone: Dose range: 1-6 mg/day. Mean dose: not reported. N = 45

Liu 2006a (Continued)

Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 75%, markedly improved: 50%-75%, improved: 25%-50%, no effect: < 25%) Mental state: PANSS total score. PANSS positive subscale score, PANSS negative subscale score, PANSS general psychogenic pathological subscale score. agitation/excitement labelled as “adverse effect” Adverse effects. Unable to use - Adverse effects: TESS score, blood routine, blood glucose, use of benzodiazepines, benzhexol (no data)	
Notes		
<i>Risk of bias</i>		
Bias	Authors’ judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details..
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.
Selective reporting (reporting bias)	High risk	Data on TESS score,blood routine, blood glucose, use of benzodiazepines, benzhexol were missing
Other bias	Low risk	None obvious.

Liu 2007

Methods	<p>Allocation: randomised, no further details.</p> <p>Blindness: unclear.</p> <p>Duration: eight weeks.</p> <p>Design: parallel.</p> <p>Location: inpatient and outpatient, China.</p>
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Participants	Diagnosis: schizophrenia (CCMD-3). PANSS score of 70 or more. N = 68. Age: aripiprazole group: 25~ 54 years, mean = (35.5 ± 9.8) years; clozapine group: 21 ~ 56 years, mean = (33.6 ± 8.9) years. Gender: aripiprazole group: 19 male, 15 female; clozapine group: 21 male, 13 female . History: aripiprazole group: 5.5~ 21 years; clozapine group: 5.3 ~ 23 years. Age at onset not reported	
Interventions	1. Aripiprazole: Dose range: 5-30 mg/day. Mean = (18 ± 4.2) mg/day. N = 34. 2. Clozapine: Dose range: 50-500 mg/day. Mean = (425 ± 5.5) mg/day. N = 34	
Outcomes	Global state: PANSS score decreased rate(recovery: ≥ 75%, markedly improved: 50%-75%, improved: 25%-50%, no effect: < 25%) Mental state: PANSS total score, PANSS positive subscale score, PANSS negative subscale score,PANSS general pathological subscale score Adverse effects. Unable to use - Adverse effects: TESS total score(no data); use of benzodiazepines, benzhexol, or propranolol medication (no data)	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.
Selective reporting (reporting bias)	High risk	Although TESS was used to assess adverse effects, no data on score were available. Data on use of benzodiazepines, benzhexol and propranolol medication were also missing

Liu 2007 (Continued)

Other bias	Low risk	None obvious.
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Liu 2008

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: eight weeks. Design: parallel. Location: inpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS score of 60 or more. N = 62. Age: aripiprazole group: mean = (26.68 ± 5.69) years; clozapine group: mean = (26.5 ± 5.58) years. Gender: aripiprazole group: 18 male, 13 female; clozapine group: 20 male, 11 female . History: aripiprazole group: 1~ 12 months, mean = (6.35 ± 6.49) months; clozapine group: 1~ 12 months, mean = (6.05 ± 5.76) months. Age at onset not reported
Interventions	1. Aripiprazole: Dose range: 5-30 mg/day. Mean dose: not reported. N = 31. 2. Clozapine: Dose range: 50-500 mg/day. Mean dose: not reported. N = 31
Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 75%, markedly improved: 50%-75%, improved: 25%-50%, no effect: < 25%) Mental state: PANSS total score, PANSS positive subscale score, PANSS negative subscale score, PANSS general pathological subscale score Adverse effects.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.

Liu 2008 (Continued)

Selective reporting (reporting bias)	High risk	Although TESS was used to assess adverse effects, no data on score were available. Data on use of benzodiazepines, benzhexol and propranolol medication were also missing
Other bias	Low risk	None obvious.

Liu 2008a

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: eight weeks. Design: parallel. Setting: inpatient, China.	
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 66. Age: aripiprazole group: 17- 65 years, mean = (32.5 ± 6.8) years; ziprasidone group: 18 ~ 63 years, mean = (30.4 ± 7.7) years Gender: aripiprazole group: 19 male, 14 female; ziprasidone group: 18 male, 15 female. History: aripiprazole group: 1.5- 22 months, mean = (5.1 ± 1.9) months; ziprasidone group: 1~ 20 months, mean = (4.5 ± 2.1) years. Age at onset not reported	
Interventions	1. Aripiprazole: Dose range: 5-30 mg/day. Mean = (13.12 ± 4.27) mg/day. N = 33. 2. Ziprasidone: Dose range: 20-80 mg/day. Mean = (38.71 ± 12.63) mg/day. N = 33	
Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 75%, markedly improved: 50%-75%, improved: 25%-50%, no effect: < 25%) Mental state: PANSS total score, PANSS positive subscale score, PANSS negative subscale score, PANSS general pathological subscale score. SANS total score score Leaving the study early. Adverse effects. Unable to use - Mental state: SANS subscale scores - unvalidated subscale.	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details..
Allocation concealment (selection bias)	Unclear risk	Not reported.

Liu 2008a (Continued)

Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.
Selective reporting (reporting bias)	High risk	Data on TESS score, blood routine, liver function, use of alprazolam, propranolol and anticholinergic medication were missing
Other bias	Low risk	None obvious.

Liu 2008b

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: eight weeks. Design: parallel. Setting: inpatient and outpatient, China.	
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 78. Age: mean = (33 ± 11) years. Gender: 33 male, 45 female. History: 1 month- 20 years, mean = (13 ± 8.4) years. Age at onset not reported	
Interventions	1. Aripiprazole: Dose range: 10-30 mg/day. Mean = (15.4 ± 5.8) mg/day. 2. Risperidone: Dose range: 3-6mg/day. Mean = (3.8 ±1.5) mg/day	
Outcomes	Mental state: PANSS total score, PANSS positive subscale score, PANSS negative subscale score, PANSS general psychogenic pathological subscale score Unable to use - PANSS subscale scores - unvalidated subscales.	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.

Liu 2008b (Continued)

Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Unclear if there were incomplete data.
Selective reporting (reporting bias)	High risk	Data on blood and urine routines, ECG, hepatorenal function, use of benzodiazepines and other medicine were missing
Other bias	Low risk	None obvious.

Liu 2008c

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: eight weeks. Design: parallel. Setting: inpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 63. Age: aripiprazole group: mean = (27.5 ± 9.179) years; risperidone group: mean = (28.29 ± 11.25) years Gender: aripiprazole group: 12 male, 20 female; risperidone group: 14 male, 17 female. History: aripiprazole group: 1- 20 years, mean = (4.31 ± 6.214) years; risperidone group: 1- 29 years, mean = (2.87 ± 2.952) years. Age at onset not reported
Interventions	1. Aripiprazole: Dose range: 5-30 mg/day. Mean = (21.67 ± 1.12) mg/day. N = 37. 2. Risperidone: Dose range: 1-6mg/day. Mean = (4.56 ± 1.24) mg/day. N = 35
Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 80%, markedly improved: 50%-79%, improved: 30%-49%, no effect: < 30%) Mental state: PANSS total score, PANSS positive subscale score, PANSS negative subscale score, PANSS general psychogenic pathological subscale score Adverse effects. Unable to use - Adverse effects: TESS total score, hepatorenal function, use of benzodiazepines, propranolol and other medicine (no data)
Notes	

Liu 2008c (Continued)

<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.
Selective reporting (reporting bias)	High risk	Data on TESS total score, hepatorenal function, use of benzodiazepines, propranolol and other medicine were missing
Other bias	Low risk	None obvious.

Liu 2008d

Methods	Allocation: randomised, lottery. Blindness: unclear. Duration: eight weeks. Design: parallel. Setting: inpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 72. Age: aripiprazole group: 16- 49 years, mean = (33.27 ± 8.21) years; risperidone group: 15 ~ 42 years, mean = (30.94 ± 8.77) years Gender: aripiprazole group: 20 male, 17 female; risperidone group: 19 male, 16 female. History: aripiprazole group: 0.25- 3 years, mean = (1.54 ± 0.74) years; risperidone group: 0.25- 2.5 years, mean = (1.98 ± 0.81) years. Age at onset not reported
Interventions	1. Aripiprazole: Dose range: 5-30 mg/day. Mean= (21.67 ± 1.12) mg/day. N = 37. 2. Risperidone: Dose range: 1-6 mg/day. Mean= (4.56 ± 1.24) mg/day. N = 35
Outcomes	Global state: PANSS score decreased rate (recovery: > 75%, markedly improved: 50%-75%, improved: 25%-50%, no effect: < 25%) Mental state: PANSS total score, PANSS positive subscale score, PANSS negative subscale

Liu 2008d (Continued)

	score, PANSS general pathological subscale score. WAI-RC (Wechsler adult intelligence scale) score. WMS (Wechsler memory scale) score Adverse effects. Unable to use - Cognitive functioning: WMS subscale scores - unvalidated subscale	
Notes		
<i>Risk of bias</i>		
Bias	Authors’ judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomised, lottery.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.
Selective reporting (reporting bias)	High risk	Data on TESS total score were missing.
Other bias	Low risk	None obvious.

Liu 2009

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: eight weeks. Design: parallel. Setting: inpatient and outpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 68. Age: aripiprazole group: mean = (26.1 ± 7.5) years; olanzapine group: mean = (27.4 ± 8.4) years Gender: aripiprazole group: 18 male, 16 female; olanzapine group: 17 male, 17 female. History: aripiprazole group: mean = (6.9 ± 3.4) years; olanzapine group: mean = (6.5 ± 3.6) years. Age at onset not reported

Liu 2009 (Continued)

Interventions	1. Aripiprazole: Dose range: 10-30 mg/day. Mean = (19.7 ± 5.3) mg/day. N = 34. 2. Olanzapine: Dose range: 10-20 mg/day. Mean = (15.4 ± 4.5) mg/day. N = 34
Outcomes	Mental state: PANSS total score, PANSS positive subscale score, PANSS negative subscale score, PANSS psychopathological subscale score Quality of life: GQOLI- 74 total score, GQOLI- 74 material life score, GQOLI- 74 physical health score, GQOLI- 74 mental health score, GQOLI- 74 social function score Adverse effects.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Unclear if there were incomplete data.
Selective reporting (reporting bias)	High risk	Data on TESS total score, use of benzodiazepines and benzhexol were missing
Other bias	Low risk	None obvious.

Liu 2009a

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: eight weeks. Design: parallel. Setting: inpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 60. Age: not reported. Gender: aripiprazole group: 16 male, 14 female; risperidone group: 17 male, 13 female.

Liu 2009a (Continued)

	History: not reported. Age at onset not reported.	
Interventions	1. Aripiprazole: Dose range: 5-30 mg/day. Mean dose: not reported. N = 30. 2. Risperidone: Dose range: 2-6 mg/day. Mean dose: not reported. N = 30	
Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 75%, markedly improved: 50%-75%, improved: 25%-50%, no effect: < 25%) Mental state: PANSS total score, PANSS positive subscale score, PANSS negative subscale score, PANSS general pathological subscale score, PANSS general psychogenic pathological subscale score Adverse effects.	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome were assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.
Selective reporting (reporting bias)	High risk	Data on TESS total score, use of benzodiazepines and other medicines were missing
Other bias	Low risk	None obvious.

Liu 2009b

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: eight weeks. Design: parallel. Setting: inpatient, China.
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Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 120. Age: aripiprazole group:16- 60 years. mean = (28.4 ± 7.9) years; quetiapine group: 18 ~ 63 years, mean = (29 ± 8.5) years Gender: aripiprazole group: 28 male, 32 female; quetiapine group: 30 male, 30 female. History: aripiprazole group: mean = (2.3 ± 1.5) years; quetiapine group: mean = (2.3 ± 1.3) years. Age at onset not reported	
Interventions	1. Aripiprazole: Dose range: 10-30 mg/day. Mean dose: not reported. N = 60. 2. Quetiapine: Dose range: 50-600 mg/day. Mean dose: not reported. N = 60	
Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 75%, markedly improved: 50%-75%, improved: 20%-50%, no effect: < 20%) Mental state: PANSS total score. PANSS positive subscale score, PANSS negative subscale score, PANSS general psychogenic pathological subscale score Adverse effects. Unable to use - Adverse effects: TESS total score, headache, insomnia, somnolence, nausea/vomiting, weight gain, extrapyramidal side-effects, blood routine, urine routine, hepatorenal function, use of benzodiazepines and propranolol (no data)	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.
Selective reporting (reporting bias)	High risk	The data on TESS total score, headache, insomnia, somnolence, nausea/vomiting, weight gain, extrapyramidal side-effects, blood routine, urine routine, hepatorenal function, use of benzodiazepines and propranolol were missing

Other bias	Low risk	None obvious.
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Liu 2010

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: not reported. Design: trial with three arms. Setting: inpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 112. Age: not reported. Gender: not reported. History: not reported. Age at onset not reported.
Interventions	1. Aripiprazole: Dose range: 10-30 mg/day. Mean = (19.83 ± 6.50) mg/day. N = 30. 2. Risperidone: Dose range: 2-6.5 mg/day. Mean = (3.82 ± 0.86) mg/day. N = 54 3. Clozapine: Dose range: 150-500 mg/day. Mean = (265.18 ± 82.59) mg/day. N = 28
Outcomes	Global state: PANSS score decreased rate (recovery: > 75%, markedly improved: 50%-5%, improved: 25%-50%, no effect: < 25%) Adverse effects. Cost-effect analysis. Unable to use - Adverse effects: TESS total score, ECG, blood glucose and serum lipids, use of benzodiazepines and other medicine (no data)
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.

Liu 2010 (Continued)

Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.
Selective reporting (reporting bias)	High risk	Data on TESS total score, ECG, blood glucose and serum lipids, use of benzodiazepines and other medicine were missing
Other bias	Low risk	None obvious.

Lou 2007

Methods	Allocation: randomised, random number table method. Blindness: unclear. Duration: six weeks. Design: parallel. Setting: inpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 45. Age: aripiprazole group: 50~ 67 years, mean = (56.1 ± 5.9) year, risperidone group: 49 ~ 70 years, mean = (54.6 ± 6.1) years Gender: aripiprazole group: 11 male, 10 female; risperidone group: 11 male, 13 female. History: aripiprazole group: 5~ 14 years, mean = (10.3 ± 2.6) years; risperidone group: 3 ~ 12 years, mean = (12.1 ± 2.2) years. Age at onset not reported
Interventions	1. Aripiprazole: Dose range: 5-30 mg/day. Mean dose: not reported. N = 21. 2. Risperidone: Dose range: 0.5-4 mg/day. Mean dose: not reported. N = 24
Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 75%, markedly improved: 50%-74%, improved: 25%-49%, no effect: < 25%) Mental state: PANSS total score, PANSS positive subscale score, PANSS negative subscale score, PANSS general psychogenic pathological subscale score Adverse effects. Unable to use - Adverse effects: TESS score, ECG, use of benzodiazepines (no data)
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, random number table method.
Allocation concealment (selection bias)	Unclear risk	Not reported.

Luo 2007 (Continued)

Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.
Selective reporting (reporting bias)	High risk	Data on TESS total score, ECG, use of benzodiazepines were missing
Other bias	Low risk	None obvious.

Luo 2008

Methods	Allocation: randomised, no further detail. Blindness: unclear. Duration: eight weeks. Design: parallel. Setting: inpatient, China.	
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 70. Age: aripiprazole group: mean = (28. 5 ± 8. 2) years; quetiapine group: mean = (27. 1 ± 7. 6) years Gender: aripiprazole group: 19 male, 16 female; quetiapine group: 18 male, 17 female. History: aripiprazole group: mean =(1.2 ± 0.7) years; quetiapine group: mean =(1.1 ± 0. 8) years. Age at onset not reported	
Interventions	1. Aripiprazole: Dose range: 5-25 mg/day. Mean dose: not reported. N = 35. 2. Quetiapine: Dose range: 200-800 mg/day. Mean dose: not reported. N = 35	
Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 75%, markedly improved: 50%-75%, improved: 25%-50%, no effect: < 25%) Mental state: PANSS total score, PANSS positive subscale score, PANSS negative subscale score, PANSS general psychogenic pathological subscale score Unable to use - Adverse effects: TESS total score (no data).	
Notes		
Risk of bias		
Bias	Authors' judgement	Support for judgement

Luo 2008 (Continued)

Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.
Selective reporting (reporting bias)	High risk	Data on TESS total score were missing.
Other bias	Low risk	None obvious.

Luo 2009

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: eight weeks. Design: parallel. Setting: inpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 80. Age: 18- 56 years, aripiprazole group: mean = (31.6 ± 7.8) years; risperidone group: mean = (32.2 ± 7.4) years Gender: aripiprazole group: 23 male, 17 female; risperidone group: 21 male, 19 female. History: 1 month- 26 years, aripiprazole group: mean = (6.2 ± 5.8) years; risperidone group: mean = (6.5 ± 5.6) years. Age at onset not reported
Interventions	1. Aripiprazole: Dose range: 5-30 mg/day. Mean = (20.4 ± 3.2)mg/d. N = 40. 2. Risperidone: Dose range: 1-6 mg/day. Mean = (4.2 ± 2.3)mg/d. N = 40
Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 75%, markedly improved: 50%-74%, improved: 25%-49%, no effect: < 25%) Mental state: PANSS total score, PANSS positive subscale score, PANSS negative subscale score, PANSS general psychogenic pathological subscale score Adverse effect. Unable to use - Adverse effects: TESS total score, EPS, tachycardia, menstrual changes, etc. and use of benzhexol, benzodiazepine, propranolol (no data)

Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.
Selective reporting (reporting bias)	High risk	Data on TESS total score, EPS, tachycardia, menstrual changes, etc. and use of benzhexol, benzodiazepine, propranolol were missing
Other bias	Low risk	None obvious.

Lv 2007

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: eight weeks. Design: parallel. Setting: inpatient and outpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 80; complete study N = 77. Age: aripiprazole group: 18-46 years, mean = (28.8 ± 7.50) years, risperidone group: 19-45 years, mean = (28.6 ± 16.5) years Gender: aripiprazole group: 21 male, 18 female; risperidone group: 20 male, 18 female. History: not reported. Age at onset not reported.
Interventions	1. Aripiprazole: Dose range: 5-30 mg/day. Mean = (18.6 ± 6.8) mg/day. N = 40. 2. Risperidone: Dose range: 1-6 mg/day. Mean = (4.3 ± 1.8) mg/day. N = 40

Lv 2007 (Continued)

Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 75%, markedly improved: 50%-74%, improved: 25%-49%, no effect: < 25%) Mental state: PANSS total score. PANSS positive subscale score, PANSS negative subscale score, PANSS general psychogenic pathological subscale score. agitation/excitement labelled as “adverse effect” Leaving the study early. Adverse effects. Unable to use - Adverse effects: TESS score, use of benzodiazepines, anticholinergic drug (no data)	
Notes		
<i>Risk of bias</i>		
Bias	Authors’ judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	The total proportion of loss to follow-up was 7.5% (1/40: 2/40), and there was no difference between the two groups
Selective reporting (reporting bias)	High risk	Data on TESS score, use of benzodiazepines, anticholinergic drug were missing
Other bias	Low risk	None obvious.

Ma 2009

Methods	<p>Allocation: randomised, random number table.</p> <p>Blindness: unclear.</p> <p>Duration: 1 week wash-out period + six weeks intervention.</p> <p>Design: parallel.</p> <p>Setting: inpatient and outpatient, China.</p>
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Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more, Excited subscales (PEC) of 14 or more. N = 89. Age: aripiprazole group: mean = (30.93 ± 8.21) years; olanzapine group: mean = (31.29 ± 7.38) years Gender: aripiprazole group: 25 male, 15 female; olanzapine group: 22 male, 13 female. History: aripiprazole group: mean = (4.52 ± 3.81) years; olanzapine group: mean = (4.73 ± 4.71) years. Age at onset not reported	
Interventions	1. Aripiprazole: Dose range: 5-30 mg/day. Mean = (19.54 ± 8.35) mg/day. N = 45. 2. Olanzapine: Dose range: 5-20 mg/day. Mean = (15.36 ± 8.21) mg/day. N = 40	
Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 75%, improved: 50%-75%, no effect: < 50%) Mental state: PANSS total score, PANSS positive subscale score, PANSS negative subscale score,PANSS general psychogenic pathological subscale score. SANS total score. Cognitive function total score Adverse effects. Unable to use - Mental state: SANS subscale score - unvalidated subscale.	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.
Selective reporting (reporting bias)	High risk	Data on TESS total score, blood and urine routine, use of benzodiazepines and anticholinergic medicine were missing
Other bias	Low risk	None obvious.

Ma 2009a

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: eight weeks. Design: parallel. Setting: outpatient, China.	
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 98. Age: 18- 55 years, mean = (32 ± 18.79) years. Gender: 43 male, 55 female. History: not reported. Age at onset not reported.	
Interventions	1. Aripiprazole: Dose range: 5-20 mg/day. Mean dose: not reported. N = 49. 2. Risperidone: Dose range: 1-5 mg/day. Mean dose: not reported. N = 49	
Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 75%, markedly improved: 50%-75%, improved: 25%-50%, no effect: < 25%) Mental state: PANSS total score, PANSS positive subscale score, PANSS negative subscale score, PANSS general psychogenic pathological subscale score Adverse effect. Unable to use - Adverse effects: TESS total score, tremor, dry mouth, dystonia, use of benzhexol, benzo-diazepine and propranolol (no data)	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	There were no incomplete data.
Selective reporting (reporting bias)	High risk	Data of TESS total score, tremor, dry mouth, dystonia, use of benzhexol, benzo-diazepine and propranolol were missing

Ma 2009a (Continued)

Other bias	Low risk	None obvious.
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Mai 2005

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: six weeks. Design: parallel. Setting: inpatient and outpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 72. Age: aripiprazole group: 18- 60 years, mean = (27. 8 ± 8. 9) year, risperidone group: 17 ~ 60 years, mean = (28. 1 ± 8. 5) years Gender: aripiprazole group: 19 male, 17 female; risperidone group: 18 male, 18 female. History: aripiprazole group: 1 month- 9 years, mean = (4.7 ± 2.5) years; risperidone group: 1 month- 10 years, mean = (4.8 ± 2.9) years. Age at onset not reported
Interventions	1. Aripiprazole: Dose range: 5-30 mg/day. Mean = (23.2 ± 3.3) mg/day. N = 36. 2. Risperidone: Dose range: 1-6 mg/day. Mean = (4.1 ± 1.6) mg/day. N = 36
Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 75%, markedly improved: 50%-75%, improved: 25%-50%, no effect: < 25%) Mental state: PANSS total score, PANSS positive subscale score, PANSS negative subscale score, PANSS general psychogenic pathological subscale score Adverse effects. Unable to use - Adverse effects: TESS score, use of benzodiazepines, anticholinergic drug (no data)

Notes	
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Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.

Mai 2005 (Continued)

Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.
Selective reporting (reporting bias)	High risk	Data on TESS score, use of benzodiazepines, anticholinergic drug were missing
Other bias	Low risk	None obvious.

Mao 2010

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: twelve weeks. Design: parallel. Setting: inpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). N = 70. Age: aripiprazole group: mean = (28.7 ± 9.9) years; olanzapine group: mean = (30.2 ± 8.7) years Gender: aripiprazole group: 19 male, 16 female; olanzapine group: 18 male, 17 female. History: aripiprazole group: mean = (6 ± 4.8) years; olanzapine group: mean = (6.3 ± 3.2) years. Age at onset not reported
Interventions	1. Aripiprazole: Dose range: 10-30 mg/day. Mean = (20.5 ± 5.2) mg/day. N = 35. 2. Olanzapine: Dose range: 10-20 mg/day. Mean = (14.5 ± 4.6) mg/day. N = 35
Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 75%, markedly improved: 50%-74%, improved: 25%-49%, no effect: < 25%) Mental state: PANSS total score, PANSS positive subscale score, PANSS negative subscale score, PANSS general psychopathological subscale score Leaving the study early. Adverse effects. Unable to use - Mental state: PANSS cognitive subscale score - unvalidated subscale
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.

Mao 2010 (Continued)

Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.
Selective reporting (reporting bias)	High risk	Data on TESS total score, use of benzodiazepines and anticholinergic medication were missing
Other bias	Low risk	None obvious.

McQuade 2004

Methods	Allocation: random, no further details. Blindness: double, no further details. Duration: 26 weeks. Design: parallel. Location: multicentre.
Participants	Diagnosis: (DSM-IV) schizophrenia disorganised (n = 17), paranoid (n = 271), residual (n = 3) or undifferentiated (n = 26), in acute relapse and hospitalised. PANSS total score of 60 or more. N = 317. Age: > 17 years (mean = 38.4 years). Gender: 229 M, 88 F. History: duration of illness not reported, age at first hospitalisation mean = 24.5 years. Setting: originally inpatient.
Interventions	1. Aripiprazole: flexible dose. Allowed dose range: 15-30 mg/day. Mean dose: 25.1 mg/day. N = 156. 2. Olanzapine: flexible dose. Allowed dose range: 10-20 mg/day. Mean dose: 16.5 mg/day. N = 161
Outcomes	Leaving the study early: any reason, adverse events, inefficacy. Global state: CGI. Mental state: PANSS total score. Adverse effects. Unable to use - Adverse effects: use of antiparkinson medication (no data), metabolic syndrome (> 70% incomplete)
Notes	

<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Random, no further details.
Allocation concealment (selection bias)	Unclear risk	No further details.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Double, no further details. Whether blinding was successful has not been examined, but both compounds differ quite substantially in adverse effects. This can be a problem for blinding
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Objective outcomes such as laboratory measures or death are unlikely to have been much affected by lack of blinding
Incomplete outcome data (attrition bias) All outcomes	High risk	Quote: "Because of the high number of participants who discontinued the study (72%) results of analysis by time point are described on the observed case (OC) basis (except for primary outcome), as the last observation-carried-forward analysis would have included a large amount of data carried forward from patients who discontinued the study." Due to the high number of participants leaving the study early, the validity is definitely limited
Selective reporting (reporting bias)	High risk	Although inclusion criteria required participants in acute relapse, no data on PANSS positive sub score were available. Data on use of antiparkinson medication were missing
Other bias	High risk	The study was industry sponsored by the manufacturer of aripiprazole

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: eight weeks. Design: parallel. Setting: inpatient, China.	
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 100. Age: 25- 45 years. Gender: 100 female. History: not reported. Age at onset not reported.	
Interventions	1. Aripiprazole: Dose range: 5-30 mg/day. Mean = (25.2 ± 3.2) mg/day. N = 50. 2. Risperidone: Dose range: 1-6 mg/day. Mean = (4.8 ± 0.5) mg/day. N = 50	
Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 75%, markedly improved: 50%-74%, improved: 25%-49%, no effect: < 25%) Mental state: PANSS total score, PANSS positive subscale score, PANSS negative subscale score, PANSS general psychopathological subscale score Leaving the study early. Adverse effects. Unable to use - Adverse effects: TESS total score, use of benzodiazepines and anticholinergic medication (no data)	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.
Selective reporting (reporting bias)	High risk	Data on TESS total score, use of benzodiazepines and anticholinergic medication

Mu 2008 (Continued)

		were missing
Other bias	Low risk	None obvious.

Mu 2010

Methods	Allocation: Simple randomisation. Blindness: unclear. Duration: one week wash-out period + eight weeks intervention. Design: parallel. Setting: inpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3), BPRS total score of 35 or more. N = 258, complete study: N=257. Age: aripiprazole group: mean = (38.12 ± 10.34) years; risperidone group: mean = (39.56 ± 10.67) years Gender: aripiprazole group: 58 male, 71 female; risperidone group: 61 male, 66 female. History: aripiprazole group: mean = (6.92 ± 4.18) years; risperidone group: mean = (7.48 ± 4.37) years. Age at onset not reported
Interventions	1. Aripiprazole: Dose range: 5-30 mg/day. Mean = (22.5 ± 3.6) mg/day. N = 129. 2. Risperidone: Dose range: 1-6 mg/day. Mean = (3.7 ± 1.7) mg/day. N = 129
Outcomes	Global state: BPRS score decreased rate (recovery: ≥ 75%, markedly improved: 50%-74%, improved: 25%-49%, no effect: < 25%) Mental state: BPRS total score. Leaving the study early. Adverse effects. Unable to use - BPRS and TESS subscale scores - unvalidated subscales.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Simple randomisation.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.

Mu 2010 (Continued)

Incomplete outcome data (attrition bias) All outcomes	Low risk	Two cases lost in risperidone group because of lactation.
Selective reporting (reporting bias)	High risk	Data on blood and urine routine, ECG, liver function, use of benzodiazepines and other medicines were missing
Other bias	Low risk	None obvious.

Pan 2007

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: two weeks wash-out period and six weeks intervention. Design: parallel. Setting: inpatient and outpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 60. Age: aripiprazole group: 18- 60 years. mean = (26.8 ± 8.7) year, risperidone group: 17 ~ 60 years, mean = (27.1 ± 8.5) years Gender: aripiprazole group: 13 male, 17 female; risperidone group: 12 male, 18 female. History aripiprazole group: 1 month- 7 years, mean = (4.7 ± 3.5) years; risperidone group: 1 month- 8 years, mean = (4.8 ± 3.7) years. Age at onset not reported
Interventions	1. Aripiprazole: Dose range: 5-30 mg/day. Mean = (25.2 ± 3.3) mg/day. N = 30. 2. Risperidone: Dose range: 1-6 mg/day. Mean = (4 ± 1.5) mg/day. N = 30
Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 75%, markedly improved: 50%-75%, improved: 25%-50%, no effect: < 25%) Mental state: PANSS total score. PANSS positive subscale score, PANSS negative subscale score, PANSS general psychogenic pathological subscale score Unable to use - Adverse effects (no data).
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.

Pan 2007 (Continued)

Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.
Selective reporting (reporting bias)	High risk	The data on adverse effects were missing.
Other bias	Low risk	None obvious.

Peng 2007

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: eight weeks. Design: parallel. Setting: inpatient, China.	
Participants	Diagnosis: schizophrenia (CCMD-3). BPRS of 35 or more. N = 85. Age: aripiprazole group: 17~ 56 years. mean = (31. 7 ± 10. 8) years; quetiapine group, 17 ~ 57 years, mean = (29. 5 ± 11. 3) years Gender: aripiprazole group: 24 male, 20 female; quetiapine group: 21 male, 20 female. History: aripiprazole group: mean = (2.7 ± 1.5) months; clozapine group: mean = (2.7 ± 1.9) months. Age at onset not reported	
Interventions	1. Aripiprazole: Dose range: 5-25 mg/day. Mean dose: not reported. N = 44. 2. Quetiapine: Dose range: 100-600 mg/day. Mean dose: not reported. N = 41	
Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 75%, markedly improved: 50%-75%, improved: 25%-50%, no effect: < 25%) Mental state: PANSS total score. PANSS positive subscale score, PANSS negative subscale score, PANSS general psychogenic pathological subscale score Adverse effects. Unable to use - Adverse effects: TESS total score, EEG, liver function, use of benzodiazepines (no data)	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement

Peng 2007 (Continued)

Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	The total rate of lost to follow-up was 3.5% (3/85), and there was no difference between the two groups (2/44: 1/41)
Selective reporting (reporting bias)	High risk	The data on TESS total score, EEG, liver function, use of benzodiazepines were missing
Other bias	Low risk	None obvious.

Peng 2007a

Methods	Allocation: randomised, no further detail. Blindness: unclear. Duration: eight weeks. Design: parallel. Setting: inpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 46. Age: aripiprazole group: 18- 50 years, mean = (22.35 ± 7.15) years; clozapine group: 16 - 49 years, mean = (23.25 ± 9.75) years Gender: aripiprazole group: 23 male, 11 female; clozapine group: 23 male, 11 female. History: aripiprazole group: 1- 36 months, mean = (22.55 ± 12.45) months; clozapine group: 1- 30 months, mean = (22.25 ± 11.25) months. Age at onset not reported
Interventions	1. Aripiprazole: Dose range: 10-30 mg/day. Mean dose: not reported. N = 23. 2. Clozapine: Dose range: 50-400 mg/day. Mean dose: not reported. N = 23
Outcomes	Global state: PANSS score decreased rate (recovery: ≥80%, markedly improved: ≥50%, improved: ≥25%, no effect: < 25%) Mental state: PANSS total score, PANSS positive subscale score, PANSS negative subscale score, PANSS general psychopathological subscale score Adverse events: TESS total score.

Peng 2007a (Continued)

Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.
Selective reporting (reporting bias)	High risk	Data on somnolence, ECG abnormal, mouth dry, constipation blurred vision, use of benzodiazepines were incomplete
Other bias	Low risk	None obvious.

Potkin 2003

Methods	Allocation: random, no further details. Blindness: double, identical capsules. Duration: four weeks. Design: parallel. Location: multicentre.
Participants	Diagnosis: (DSM-IV) schizophrenia (n = 289) or schizoaffective disorder (n = 115), hospitalised due to an acute relapse, response to previous antipsychotic treatment other than clozapine, PANSS of 60 or more. N = 404. Age: 18-65 years (mean = 38.9 years). Gender: 283 M, 121 F. History: duration of illness not reported, age at onset not reported. Setting: inpatient.
Interventions	1. Aripiprazole: fixed dose: 20 mg/day. N = 101. 2. Aripiprazole: fixed dose: 30 mg/day. N = 101. 3. Risperidone: fixed dose: 6 mg/day. N = 99.

Outcomes	Leaving the study early: any reason, adverse events, inefficacy. Global state: CGI. Mental state: PANSS total score, PANSS positive sub score, PANSS negative sub score. Adverse effects.	
Notes	Note: There is a placebo group (n = 103), which is not relevant for this review	
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Random, no further details.
Allocation concealment (selection bias)	Unclear risk	No further details.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Double, identical capsules. Whether blinding was successful has not been examined, but both compounds differ quite substantially in adverse effects. This can be a problem for blinding
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Objective outcomes such as laboratory measures or death are unlikely to have been much affected by lack of blinding
Incomplete outcome data (attrition bias) All outcomes	High risk	The overall drop out rate was 36.9 %. The LOCF method was used to account for people leaving the study early
Selective reporting (reporting bias)	High risk	For efficacy outcomes there was no standard deviation or standard error indicated which had to be back calculated. Only adverse events with an incidence of more than 5% were reported. This procedure may have missed important adverse events
Other bias	High risk	The study was industry sponsored by the manufacturer of aripiprazole. The study used a fixed dose regimen, where it is difficult to say which comparator doses may be appropriate

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: eight weeks. Design: parallel. Setting: inpatient and outpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). N = 60. Age: aripiprazole group: mean = (27.43 ± 7.17) years; risperidone group: mean = (27.06 ± 2.33) years Gender: aripiprazole group: 32 female; risperidone group: 32 female. History: aripiprazole group: total = (2.2 ± 1.5) years; risperidone group: total = (2.12 ± 1.61) years. Age at onset not reported
Interventions	1. Aripiprazole: Dose range: 15-30 mg/day. Mean = (19.50 ± 5.14) mg/day. N = 30. 2. Risperidone: Dose range: 3-6 mg/day. Mean = (4.03 ± 0.87) mg/day. N = 30
Outcomes	Mental state: BPRS total score, PANSS score decreased rate. Change of BMI, PRL.

Notes

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Unclear if there were incomplete data.
Selective reporting (reporting bias)	Low risk	No selective reporting.
Other bias	Low risk	None obvious.

Methods	Allocation: randomised, random number table. Blindness: unclear. Duration: eight weeks. Design: parallel. Setting: inpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS more than 60 years. N = 80. Age: aripiprazole group: 16- 47 years, mean = (25 ± 3.1) years; olanzapine group: 18 - 43 years, mean = (26 ± 2.7) years Gender: 80 female. History: aripiprazole group: mean= (1.2 ± 2.7) years; olanzapine group: mean = (1.3 ± 0.5) years. Age at onset not reported
Interventions	1. Aripiprazole: Dose range: 5-30 mg/day. Mean = (20 ± 5) mg/day . N = 40. 2. Olanzapine: Dose range: 10-20 mg/day. Mean = (20 ± 5) mg/day. N = 40
Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 75%, improved: 50%-75%, no effect: < 50%) Leaving the study early. Adverse effects. Unable to use - Adverse effects: TESS total score, blood routine, liver function, blood pressure change, blood glucose change (no data)
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	One patient was lost to follow-up because of economic issues in aripiprazole group

Selective reporting (reporting bias)	High risk	Data on TESS total score, blood routine, liver function, blood pressure change, blood glucose change were missing
Other bias	Low risk	None obvious.

Qin 2008

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: one week wash-out period and eight weeks intervention. Design: parallel. Setting: inpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 60. Age: aripiprazole group: 21- 45 years, mean = (32.1 ± 7.2) years; risperidone group: 24 - 53 years, mean = (35.2 ± 5.9) years Gender: aripiprazole group: 18 male, 12 female; risperidone group: 17 male, 13 female. History: aripiprazole group: 5- 14 years; risperidone group: 5- 16 years. Age at onset not reported
Interventions	1. Aripiprazole: Dose range: 5-30 mg/day. Mean dose: not reported. N = 30. 2. Risperidone: Dose range: 1-6 mg/day. Mean: not reported. N = 30
Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 75%, markedly improved: 50%-74%, improved: 25%-49%, no effect: < 25%) Mental state: PANSS total score. Adverse effects. Unable to use - Adverse effects: TESS total score, liver function, blood and urine routines, use of benzodiazepines, propranolol, and anticholinergic medication (no data)
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.

Qin 2008 (Continued)

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.
Selective reporting (reporting bias)	High risk	Data on TESS total score, liver function, blood and urine routines, use of benzodiazepines, propranolol, and anticholinergic medication were missing
Other bias	Low risk	None obvious.

Qu 2009

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: eight weeks. Design: parallel. Setting: inpatient, China.	
Participants	Diagnosis: schizophrenia (CCMD-5). PANSS of 60 or more. N = 120. Age: 19- 64 years. aripiprazole group: mean = (31.6 ± 7.8) years; risperidone group: mean = (32.2 ± 7.4) years Gender: aripiprazole group: 40 male, 20 female; risperidone group: 36 male, 24 female. History: not reported. Age at onset not reported.	
Interventions	1. Aripiprazole: Dose range: 5-25 mg/day. Mean dose: not reported. N = 30. 2. Risperidone: Dose range: 1-4 mg/day. Mean dose: not reported. N = 30	
Outcomes	Mental state: PANSS total score. Adverse effects. Unable to use - Quality of life: GQOLI - 74 score (no data). Adverse effects: anxiety, EPS, somnolence, ECG, mouth dry, liver function, use of benzodiazepines (no data)	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.

Qu 2009 (Continued)

Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Unclear if there were incomplete data.
Selective reporting (reporting bias)	High risk	Data on GQOLI - 74 score, anxiety, EPS, somnolence, ECG, anxiety, EPS, somnolence, ECG, mouth dry, liver function, use of benzodiazepines were missing
Other bias	Low risk	None obvious.

Shan 2008

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: eight weeks. Design: parallel. Setting: inpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 60. Age: aripiprazole group: mean = (43.37 ± 8.85) years; risperidone group: 17-59 years, mean = (42.52 ± 9.85) years Gender: aripiprazole group: 16 male, 14 female; risperidone group: 15 male, 15 female. History: aripiprazole group: mean = (10.46 ± 4.65) years; risperidone group: mean = (11.35 ± 3.28) years. Age at onset not reported
Interventions	1. Aripiprazole: Dose range: 5-30 mg/day. Mean dose: not reported. N = 30. 2. Risperidone: Dose range: 1-6 mg/day. Mean dose: not reported. N = 30
Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 80%, markedly improved: ≥ 50%, improved: ≥ 30%, no effect: < 30%). Mental state: PANSS total score, PANSS positive subscale score, PANSS negative subscale score, PANSS general pathological subscale score Adverse effects. Unable to use - Adverse effects: TESS total score, use of benzodiazepines and other medication (no data)
Notes	

Shan 2008 (Continued)

<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.
Selective reporting (reporting bias)	High risk	Data on TESS total score, use of benzodiazepines and other medication were missing
Other bias	Low risk	None obvious.

Shuai 2008

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: eight weeks. Design: parallel. Setting: inpatient and outpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 84. Age: aripiprazole group: 19- 52 years, mean = (30 ± 6) years; risperidone group: 18 ~ 55 years, mean = (32 ± 7) years Gender: aripiprazole group: 19 male, 23 female; risperidone group: 21 male, 21 female. History: aripiprazole group: 1- 9 months, mean = (3.4 ± 2.6) months; risperidone group: 2- 9 months, mean = (4.3 ± 2.9) months. Age at onset not reported
Interventions	1. Aripiprazole: Dose range: 5-30 mg/day. Mean = (15 ± 5) mg/day. N = 42. 2. Risperidone: Dose range: 1-6 mg/day. Mean = (3.2± 1.8) mg/day. N = 42
Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 75%, markedly improved: 50%-74%, improved: 25%-49%, no effect: < 25%) Mental state: agitation.

Shuai 2008 (Continued)

	Adverse effects. Unable to use - Adverse effects: TESS total score, blood routine, use of benzodiazepines and other medication (no data)	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.
Selective reporting (reporting bias)	High risk	Data on TESS total score, blood routine, use of benzodiazepines and other medication were missing
Other bias	Low risk	None obvious.

Song 2008

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: eight weeks. Design: parallel. Location: inpatient and outpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS total score of 60 or more. N = 60. Age: aripiprazole group: 20~ 60 years, mean = (45.5 ± 3.05) years; risperidone group: 19 ~ 60 years, mean = (43.7 ± 3.3) years. Gender: 60 female . History: aripiprazole group: mean = (8.4 ± 1.5) years; risperidone group: mean = (8.5 ± 1.4) years. Age at onset not reported

Song 2008 (Continued)

Interventions	1. Aripiprazole: Dose range: 5-30 mg/day. Mean = (15.2 ± 5.1) mg/day. N = 30. 2. Risperidone: Dose range: 0.5-6 mg/day. Mean = (4.12 ± 1.43) mg/day. N = 30
Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 75%, markedly improved: 50%-75%, improved: 25%-50%, no effect: < 25%) Mental state: PANSS total score, PANSS positive subscale score, PANSS negative subscale score, PANSS general psychogenic pathological subscale score Unable to use - Adverse effects: (no data).
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.
Selective reporting (reporting bias)	High risk	Data on adverse effects were missing.
Other bias	Low risk	None obvious.

Song 2009

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: eight weeks. Design: parallel. Setting: inpatient and outpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 60. Age: aripiprazole group: 17- 62 years; risperidone group: 16- 60 years Gender: aripiprazole group: 10 male, 20 female; risperidone group: 21 male, 9 female.

Song 2009 (Continued)

	History: aripiprazole group: 1 month- 10 years; risperidone group: 1.5 months- 13 years Age at onset not reported.	
Interventions	1. Aripiprazole: Dose range: 5-30 mg/day. Mean dose: not reported. N = 30. 2. Risperidone: Dose range: 1-8 mg/day. Mean dose: not reported. N = 30	
Outcomes	Mental state: PANSS total score. PANSS positive subscale score, PANSS negative subscale score, PANSS general psychogenic pathological subscale score Adverse effects. Unable to use - Adverse effects: TESS total score, use of benzhexol and benzodiazepines	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.
Selective reporting (reporting bias)	High risk	Data on TESS total score and use of benzhexol and benzodiazepines were missing
Other bias	Low risk	None obvious.

Song 2010

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: eight weeks. Design: parallel. Setting: inpatient and outpatient, China.
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Participants	Diagnosis: schizophrenia (CCMD-3). PANSS more than 60. N = 80. Age: aripiprazole group: 19~ 56 years, mean = (27.6 ± 4.3) years; olanzapine group: 18 ~ 58 years, mean = (28.2 ± 3.6) years Gender: aripiprazole group: 20 male, 20 female; olanzapine group: 20 male, 20 female. History: aripiprazole group: 5 months- 4 years, mean = (3.1 ± 1.9) years; olanzapine group: 3 months- 4 years, mean = (3.5 ± 1.1) years. Age at onset not reported	
Interventions	1. Aripiprazole: Dose range: 5-30 mg/day. Mean dose: not reported. N = 40. 2. Olanzapine: Dose range: 5-20 mg/day. Mean dose: not reported. N = 40	
Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 75%, markedly improved: 50%-75%, improved: 25%-50%, no effect: < 25%). CGI - SI Mental state: PANSS total score. Adverse effects. Unable to use - Adverse effects: TESS total score, excitement, insomnia, myotonia, akathisia, tremor, use of benzodiazepines (no data)	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.
Selective reporting (reporting bias)	High risk	Data on TESS total score, excitement, insomnia, myotonia, akathisia, tremor, use of benzodiazepines were missing
Other bias	Low risk	None obvious.

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: one week wash-out period + six weeks intervention. Design: parallel. Setting: inpatient and outpatient , China.	
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 78. Age: aripiprazole group: 18 ~ 60 years, mean = (27. 6 ± 8. 5) years; risperidone group: 15 ~ 65 years, mean = (28. 7 ± 8. 4) years Gender: aripiprazole group: 23 male, 18 female; risperidone group: 25 male, 14 female. History: aripiprazole group: 6 months ~ 6 years; risperidone group: 1 month ~ 10 years. Age at onset not reported	
Interventions	1. Aripiprazole: Dose range: 5-30 mg/day. Mean dose: not reported. N = 39. 2. Risperidone: Dose range: 1-6 mg/day. Mean dose: not reported. N = 39	
Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 75%, markedly improved: 50%-74%, improved: 25%-49%, no effect: < 25%) Mental state: PANSS total score, PANSS positive subscale score, PANSS negative subscale score, PANSS general pathological subscale score Adverse effects.	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomisation, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.
Selective reporting (reporting bias)	High risk	Data on TESS total score, use of benzodiazepines and other medicines were missing
Other bias	Low risk	None obvious.

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: one week washout + eight weeks intervention. Design: parallel. Setting: inpatient, China.	
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS more than 60. N = 100. Age: aripiprazole group: 17~ 55 years, mean = (28.5 ± 3.5) years; olanzapine group: 18 ~ 56 years, mean = (28.2 ± 4.5) years Gender: aripiprazole group: 20 male, 30 female; olanzapine group: 20 male, 30 female. History: aripiprazole group: 7 months- 4 years, mean = (2.5 ± 2.6) years; olanzapine group: 6 months- 5 years, mean = (2.5 ± 1.2) years. Age at onset not reported	
Interventions	1. Aripiprazole: Dose range: 5-30 mg/day. Mean dose: not reported. N = 50. 2. Olanzapine: Dose range: 5-20 mg/day. Mean dose: not reported. N = 50	
Outcomes	Global state: PANSS score decreased rate (recovery: 75≥ %, markedly improved: 50%-74%, improved: 25%-49%, no effect: < 25%). CGI-SI score Mental state: PANSS total score, PANSS positive subscale score, PANSS negative subscale score, PANSS general psychopathological subscale score Adverse effects. Unable to use - Adverse effects: TESS total score, lactation, menstrual disorders, excitement, insomnia, myotonia, akathisia, tremor, use of benzodiazepines (no data)	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.

Su 2008 (Continued)

Selective reporting (reporting bias)	High risk	Data on TESS total score, lactation, menstrual disorders, excitement, insomnia, myotonia, akathisia, tremor, use of benzodiazepines were missing
Other bias	Low risk	None obvious.

Sun 2006

Methods	Allocation: randomised, stratified random. Blindness: unclear. Duration: twelve weeks. Design: parallel. Setting: inpatient and outpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 80. Age: aripiprazole group: 18- 47 years, mean = (27.1 ± 3.4) years; risperidone group: 19 ~ 48 years, mean = (26.3 ± 3.8) years Gender: aripiprazole group: 24 male, 16 female; risperidone group: 23 male, 17 female. History: aripiprazole group: 5- 14 months, mean = (7.4 ± 4.6) months; risperidone group: 2- 16 months, mean = (7.3 ± 4.7) months. Age at onset not reported
Interventions	1. Aripiprazole: Dose range: 5-30 mg/day. Mean dose: not reported. N = 40. 2. Risperidone: Dose range: 1-6 mg/day. Mean dose: not reported. N = 40
Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 75%, markedly improved: 50%-75%, improved: 25%-50%, no effect: < 25%) Mental state: PANSS total score, PANSS positive subscale score, PANSS negative subscale score, PANSS general pathological subscale score Adverse effects. Unable to use- Mental state: PANSS subscale score decreased rate - unvalidated subscales
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomised, stratified randomisation.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.

Sun 2006 (Continued)

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.
Selective reporting (reporting bias)	Low risk	No selective reporting.
Other bias	Low risk	None obvious.

Sun 2009

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: eight weeks. Design: parallel. Setting: inpatient, China.	
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 84. Age: 18- 60 years, aripiprazole group: mean = (27.3 ± 6.68) years; risperidone group: mean = (26.8 ± 7.32) years Gender: aripiprazole group: 23 male, 19 female; risperidone group: 24 male, 18 female. History: < 2 years, aripiprazole group: mean = (1.2 ± 0.77) years; risperidone group: mean = (1.1 ± 0.84) years. Age at onset not reported	
Interventions	1. Aripiprazole: Dose range: 5-30 mg/day. Mean = (19.32 ±6.94) mg/ day. N = 42. 2. Risperidone: Dose range: 1-6 mg/day. Mean = (4.25 ±1.7) mg/ day. N = 42	
Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 75%, markedly improved: 50%-74%, improved: 25%-49%, no effect: < 25%) Mental state: PANSS total score. PANSS positive subscale score, PANSS negative subscale score, PANSS general psychogenic pathological subscale score Adverse effects Unable to use - Adverse effects: TESS total score, use of anticholinergic medicine and benzodiazepines (no data)	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.

Sun 2009 (Continued)

Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.
Selective reporting (reporting bias)	High risk	Data on TESS total score, use of anticholinergic medicine and benzodiazepines were missing
Other bias	Low risk	None obvious.

Sun 2009a

Methods	Allocation: randomised, no further detail. Blindness: unclear. Duration: eight weeks. Design: parallel. Setting: inpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 60. Age: aripiprazole group: 17- 50 years. mean = (27. 5 ± 7. 9) years; quetiapine group: 18 ~ 51 years, mean = (26. 7 ± 8. 4) years Gender: aripiprazole group: 23 male, 21 female; quetiapine group: 22 male, 22 female. History: aripiprazole group: mean = (4. 1 ± 2.7) years; quetiapine group: mean = (4. 5 ± 2. 9) years. Age at onset not reported
Interventions	1. Aripiprazole: Dose range: 5-30 mg/day. Mean= (11. 6±4. 6) mg/day. N=30. 2. Quetiapine: Dose range: 50-600 mg/day. Mean= (407±65) mg/day. N=30
Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 75%, markedly improved: 50%-75%, improved: 25%-50%, no effect: < 25%) Mental state: PANSS total score, PANSS positive subscale score, PANSS negative subscale score, PANSS general psychogenic pathological subscale score Unable to use - Adverse effects: TESS total score and use of benzodiazepine (no data)
Notes	
<i>Risk of bias</i>	

Sun 2009a (Continued)

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.
Selective reporting (reporting bias)	High risk	Data on TESS total score, use of benzodiazepine and other medicines were missing
Other bias	Low risk	None obvious.

Tandon 2006

Methods	Allocation: random. Blindness: open label. Duration: 8 weeks. Design: prospective, parallel group. Location: multicentric in USA.
Participants	Diagnosis: Schizophrenia or schizoaffective disorder (DSM IV), required initiation of antipsychotics, antipsychotic switch clinically appropriate N = 1599. Age: 18-75 years. History: duration of illness not reported, age at onset not reported. Setting: Outpatients.
Interventions	1. Aripiprazole: 10 mg-30 mg/day (mean 19.9 mg/day); N = 1295. 2. Other antipsychotic: recommended dose; N = 304.
Outcomes	Global state: CGI-I. Adverse effects: At least one adverse effect, extrapyramidal adverse effects, gastrointestinal disorders, sleep disturbances. Others: POM.
Notes	Primary goal was evaluating the effectiveness of aripiprazole in general psychiatric out-patient practice setting. The other antipsychotic treatment group was primarily included

Tandon 2006 (Continued)

	for interpreting the safety data and not for direct comparison. Unable to use data from CGI-I and POM	
<i>Risk of bias</i>		
Bias	Authors’ judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	4:1 computer-generated randomised schedule using Interactive Voice Response System
Allocation concealment (selection bias)	High risk	Open label.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open label.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open label.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	LOCF method used to account for people leaving the study early
Selective reporting (reporting bias)	High risk	Adverse events were reported if they were > 5%. Scales if used were not reported
Other bias	High risk	Industry sponsored.

Tang 2006

Methods	Allocation: simple randomisation. Blindness: unclear. Duration: eight weeks. Design: parallel. Setting: inpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 72. Age: aripiprazole group: 18- 61 years, mean = (31.3 ± 6.2) years; risperidone group: 16 ~ 60 years, mean = (30.8 ± 6.1) years Gender: aripiprazole group: 37 female; risperidone group: 35 female. History: aripiprazole group: 1 month- 4.5 years; risperidone group: 1 month- 4.6 years. Age at onset not reported
Interventions	1. Aripiprazole: Dose range: 5-30 mg/day. Mean = (10 ± 5.22) mg/day. N = 37. 2. Risperidone: Dose range: 1-6 mg/day. Mean = (3.5 ± 0.81) mg/day. N = 35

Tang 2006 (Continued)

Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 75%, markedly improved: 50%-74%, improved: 25%-49%, no effect: < 25%) Mental state: PANSS total score, PANSS positive subscale score, PANSS negative subscale score, PANSS psychopathological subscale score Adverse effects. Unable to use - Adverse effects: TESS total score, use of benzodiazepines, propranolol and benzhexol (no data)	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Simple randomisation.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.
Selective reporting (reporting bias)	High risk	Data on TESS score, use of benzodiazepines, propranolol and benzhexol were missing
Other bias	Low risk	None obvious.

Tang 2007

Methods	<p>Allocation: randomised, no further details.</p> <p>Blindness: unclear.</p> <p>Duration: eight weeks.</p> <p>Design: parallel.</p> <p>Setting: inpatient, China.</p>
Participants	<p>Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more.</p> <p>N = 60.</p> <p>Age: aripiprazole group: 18- 63 years, mean = (29.7 $\pm$ 12.5) years; risperidone group: 18</p>

	~ 62 years, mean = (29.5 ± 11.4) years Gender: aripiprazole group: 16 male, 14 female; risperidone group: 18 male, 12 female. History: aripiprazole group: mean = (3 ± 1.7) years; risperidone group: mean = (3 ± 2) years. Age at onset not reported	
Interventions	1. Aripiprazole: Dose range: 5-30 mg/day. Mean = (23. 3 ± 3. 2) mg/day. N = 30. 2. Risperidone: Dose range: 1-6 mg/day. Mean = (4. 6 ± 2. 4) mg/day. N = 30	
Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 75%, markedly improved: 50%-74%, improved: 25%-49%, no effect: < 25%) Mental state: PANSS total score, PANSS positive subscale score, PANSS negative subscale score, PANSS psychopathological subscale score Adverse effects. Unable to use - Adverse effects: TESS total score, EEG, use of benzodiazepines and other medication (no data)	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.
Selective reporting (reporting bias)	High risk	Data on TESS score, EEG, use of benzodiazepines and other medication were missing
Other bias	Low risk	None obvious.

Tang 2010

Methods	Allocation: simple randomisation. Blindness: unclear. Duration: eight weeks. Design: parallel. Setting: inpatient and outpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 78. Age: aripiprazole group: 18- 59 years. mean = (28.3 ± 6.2) years; risperidone group: 18 ~ 58 years, mean = (27.8 ± 6.1) years Gender: aripiprazole group: 18 male, 20 female; risperidone group: 19 male, 21 female. History: aripiprazole group: 1 month- 4.5 years; risperidone group: 1 month- 4.6 years. Age at onset not reported
Interventions	1. Aripiprazole: Dose range: 5-30 mg/day. Mean = (10 ± 5.22) mg/day. N = 38. 2. Risperidone: Dose range: 1-6 mg/day. Mean = (4.3 ± 0.81) mg/day. N = 40
Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 75%, markedly improved: 50%-74%, improved: 25%-49%, no effect: < 25%) Mental state: PANSS total score, PANSS positive subscale score, PANSS negative subscale score, PANSS psychopathological subscale score. agitation-labelled as “adverse effect” Leaving the study early. Adverse effects. Unable to use - Adverse effects: TESS total score, use of benzodiazepines and other medication (no data)
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Simple randomisation.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	One patient lose to follow-up.

Tang 2010 (Continued)

Selective reporting (reporting bias)	High risk	Data on TESS score, use of benzodiazepines and other medication were missing
Other bias	Low risk	None obvious.

Tang 2010a

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: one week wash-out period + eight weeks intervention. Design: parallel. Setting: inpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 70. Age: 18- 65 years, aripiprazole group: mean = (28.5 ± 7.3) years; risperidone group: mean = (30.1 ± 8.9) years Gender: aripiprazole group: 18 male, 17 female; risperidone group: 20 male, 15 female. History: aripiprazole group: mean = (2.9 ± 2.4) years; risperidone group: mean = (3.3 ± 2.9) years. Age at onset not reported
Interventions	1. Aripiprazole: Dose range: 5-30 mg/day. Mean dose: not reported. N = 35. 2. Risperidone: Dose range: 1-6 mg/day. Mean dose: not reported. N = 35
Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 75%, markedly improved: 50%-74%, improved: 25%-49%, no effect: < 25%) Mental state: PANSS total score, PANSS positive subscale score, PANSS negative subscale score, PANSS general psychogenic pathological subscale score Adverse effects Unable to use - Adverse effects: TESS total score, insomnia, anxiety, nausea, endocrine, weight gain, headache, dizziness, use of benzodiazepines and other medicines (no data)
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.

Tang 2010a (Continued)

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.
Selective reporting (reporting bias)	High risk	Data on TESS total score, insomnia, anxiety, nausea, endocrine, weight gain, headache, dizziness, use of benzodiazepines and other medicines were missing
Other bias	Low risk	None obvious.

Tao 2008

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: eight weeks. Design: four arms intervention. Location: inpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 70 or more. N = 360. Age: aripiprazole group: mean = (30. 72 ± 11. 59) years; risperidone group: mean = (32. 51 ± 14. 30) years; quetiapine group: mean = (35. 53 ± 14. 23) years; ziprasidone group: mean = (26. 03 ± 7. 23) years. Gender: aripiprazole group: 22 male, 68 female; risperidone group: 43 male, 47 female; quetiapine group: 4 male, 86 female; ziprasidone group: 65 male, 25 female. History: not reported. Age at onset not reported.
Interventions	1. Aripiprazole: Dose range: 10-30 mg/day. Mean dose: not reported. N = 90. 2. Risperidone: Dose range: 2-5 mg/day. Mean dose: not reported. N = 90 3. Quetiapine: Dose range: 200-600 mg/day. Mean dose: not reported. N = 90 4. Ziprasidone: Dose range: 40-80 mg/day. Mean dose: not reported. N = 90
Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 80%, markedly improved: 50%-80%, improved: 25%-50%, no effect: < 25%) Mental state: PANSS total score, PANSS positive subscale score, PANSS negative subscale score, PANSS general pathological subscale score Leaving the study early. Adverse effects.
Notes	
<i>Risk of bias</i>	

Tao 2008 (Continued)

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	The total rate of loss to follow-up was 4.4%(3/90 vs. 1/90), 1 participant dropped out because of adverse effect, 1 dropped out because of no effect, 2 dropped out because of incomplete data
Selective reporting (reporting bias)	Low risk	No selective reporting.
Other bias	Low risk	None obvious.

Tong 2007

Methods	Allocation: randomised, stratified random. Blindness: unclear. Duration: eight weeks. Design: parallel. Setting: outpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). BPRS of 60 or more. N = 68; complete study: N = 50. Age: aripiprazole group: mean = (41 ± 19) years; risperidone group: mean = (36 ± 20) years Gender: aripiprazole group: 11 male, 14 female; risperidone group: 8 male, 17 female. History: aripiprazole group: mean = (3.4 ± 6.7) months; risperidone group: mean = (2.9 ± 5.7) months. Age at onset not reported
Interventions	1. Aripiprazole: Dose range: 5-20 mg/day. Mean = (17 ± 6) mg/day. N = 36. 2. Risperidone: Dose range: 1-4 mg/day. Mean = (4 ± 1) mg/day. N = 32
Outcomes	Global state: GAS score (recovery: > 80%, markedly improved: > 70%, improved: > 60%, no effect: ≤ 60%) Mental state: BPRS total score, SANS total score Adverse effects.

Tong 2007 (Continued)

	Unable to use - Mental state: BPRS & SANS subscale scores are not reported, as these subscale scores are unvalidated	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	High risk	The total rate of lost to follow-up was 26.5% (18/68, 11/36 vs. 7/32). 8 participants dropped out because of progressive disease, 10 dropped out because the trialists could not insist on follow-up
Selective reporting (reporting bias)	High risk	Data on TESS total score and use of benzodiazepines were missing
Other bias	Low risk	None obvious.

Tu 2009

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: eight weeks. Design: parallel. Setting: inpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 68. Age: aripiprazole group: 18-59 years, mean = (25 ± 11) years; risperidone group: 20-56 years, mean = (28 ± 10) years Gender: aripiprazole group: 27 male, 8 female; risperidone group: 23 male, 10 female. History: aripiprazole group: mean = (2.9 ± 4) years; risperidone group: mean = (2.1 ± 3.6) years. Age at onset not reported

Tu 2009 (Continued)

Interventions	1. Aripiprazole: Dose range: 5-30 mg/day. Mean dose: not reported. N = 35. 2. Risperidone: Dose range: 2-6 mg/day. Mean dose: not reported. N = 33
Outcomes	Global state: CGI scale: markedly improved, improved, slight improved, no effect Mental state: PANSS total score, PANSS positive subscale score, PANSS negative subscale score, PANSS general pathological subscale score
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.
Selective reporting (reporting bias)	High risk	Data on adverse effects were missing.
Other bias	Low risk	None obvious.

Wang 2005

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: six weeks. Design: parallel. Location: outpatient and inpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). N = 60. Age: aripiprazole group: mean = (27 ± 9) years; clozapine group: mean = (28 ± 10) years. Gender: aripiprazole group: 14 male, 17 female; clozapine group: 15 male, 14 female. History: aripiprazole group: 1-11 months, mean = (7.3 ± 4.7) months; clozapine group: 1-12 months, mean = (7.7 ± 4.5) months. Age at onset not reported

Interventions	1. Aripiprazole: Dose range: 10-30 mg/day. Mean dose: not reported. N = 31. 2. Clozapine: Dose range: 50-270.3 mg/day. Mean dose: not reported. N = 29	
Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 75%, markedly improved: 50%-75%, improved: 25%-50%, no effect or deteriorate: < 25%) Mental state: PANSS total score. anxiety and agitation, as binary outcomes Adverse effects. Unable to use - Adverse effects: TESS total score (no data); Laboratory tests (hepatorenal function, glucose, electrolyte) (unclear data), weight and ECG (no data)	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	One patient discontinued therapy due to leucopenia.
Selective reporting (reporting bias)	High risk	Although TESS was used to assess adverse effects, no data on score were available. Data on ECG and weight were missing. Data on laboratory tests (hepatorenal function, glucose, electrolytes) were unclear
Other bias	Low risk	None obvious.

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: eight weeks. Design: parallel. Location: inpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 64. Age: aripiprazole group: 15- 50 years, mean = (24.4 ± 6.8) years; clozapine group: 18 - 40 years, mean = (25.5 ± 9.3) years. Gender: aripiprazole group: 18 male, 14 female; clozapine group: 21 male, 11 female. History: aripiprazole group: 1- 60 months, mean = (24.7 ± 13.9) months; clozapine group: 1- 60 months, mean = (25 ± 14) months. Age at onset not reported
Interventions	1. Aripiprazole: Dose range: 5-30 mg/day. Mean dose: not reported. N=32. 2. Clozapine: Dose range: 50-500 mg/day. Mean dose: not reported. N=32
Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 80%, markedly improved: 50%-80%, improved: 25%-50%, no effect: < 25%) Mental state: PANSS total score. PANSS positive subscale score, PANSS negative subscale score, PANSS general pathological subscale score Adverse effects: TESS total score, central nervous system (somnolence), ECG abnormal, liver function Unable to use - Adverse effects: gastrointestinal (dry mouth, constipation), blurred vision, weight gain and EEG abnormal (unclear data). blood and urine routine, blood pressure (no data)
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.

Wang 2006 (Continued)

Selective reporting (reporting bias)	High risk	Data on gastrointestinal (dry mouth, constipation), blurred vision, weight gain and EEG abnormal were unclear. Data on blood and urine routine, blood pressure were missing
Other bias	Low risk	None obvious.

Wang 2006a

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: eight weeks. Design: parallel. Location: inpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 60. Age: aripiprazole group: mean = (38.7 ± 8.47) years; clozapine group: mean = (35.56 ± 3.78) years. Gender: aripiprazole group: 16 male, 14 female; clozapine group: 14 male, 16 female. History: aripiprazole group: 1 month- 10 years, mean = (12.6 ± 8.38) months; clozapine group: 3 months- 9 years, mean = (12.15 ± 7.22) months. Age at onset not reported
Interventions	1. Aripiprazole: Dose range: 10-30 mg/day. Mean dose: not reported. N = 30. 2. Clozapine: Dose range: 50-400 mg/day. Mean dose: not reported. N = 30
Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 75%, markedly improved: 50%-75%, improved: 25%-50%, no effect: < 25%) Mental state: PANSS total score. PANSS positive subscale score, PANSS negative subscale score, PANSS general psychopathological subscale score. anxiety - labelled as "adverse effect" Adverse effects. Unable to use - Adverse effects: TESS total score, hepatorenal function (no data)
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.

Wang 2006a (Continued)

Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.
Selective reporting (reporting bias)	High risk	Although TESS was used to assess adverse effects, no data on score were available. Data on hepatorenal function were missing
Other bias	Low risk	None obvious.

Wang 2006b

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: eight weeks. Design: parallel. Setting: inpatient, China.	
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 60. Age: aripiprazole group: 18- 60 years. mean = (26.2 ± 7.5) years; risperidone group: 18- 60 years, mean = (27.1 ± 8.5) years Gender: aripiprazole group: 20 male,10 female; risperidone group: 18 male,12 female. History: aripiprazole group: 1- 60 months, mean = (22.4 ± 13.8) months; risperidone group: 1- 60 months, mean = (24.9 ± 14) months. Age at onset not reported	
Interventions	1. Aripiprazole: Dose range: 5-25 mg/day. Mean dose: not reported. N = 30. 2. Risperidone: Dose range: 1-4 mg/day. Mean dose: not reported. N = 30	
Outcomes	Mental state: PANSS total score. Adverse effect: TESS score. Unable to use - Quality of life: GQOLI-74 score (no data). Adverse effects: EPS, ECG, liver function, mouth dry (no data)	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement

Wang 2006b (Continued)

Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Unclear if there was drop-out.
Selective reporting (reporting bias)	High risk	Although GQOLI-74 was used to assess quality of life, no data on score were available. Data on EPS, ECG, liver function, and mouth dry were missing
Other bias	Low risk	None obvious.

Wang 2006c

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: eight weeks. Design: parallel. Setting: inpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 50. Age: aripiprazole group: 25- 39 years. mean = (32.5 ± 6.2) years; risperidone group: 20 - 58 years, mean = (22.5 ± 6.2) years Gender: aripiprazole group: 8 male, 17 female; risperidone group: 10 male, 15 female. History: aripiprazole group: 5- 16 years; risperidone group: 5- 18 years. Age at onset not reported
Interventions	1. Aripiprazole: Dose range: 5-30 mg/day. Mean dose: not reported. N = 25. 2. Risperidone: Dose range: 0.5-5 mg/day. Mean dose: not reported. N = 25
Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 80%, markedly improved: 60%-79%, improved: 30%-59%, no effect: < 30%) Mental state: PANSS total score. Unable to use: Adverse effects - the N numbers reported in these outcomes are greater than that of the people randomised. Since we are unable to reach the authors, we are unable to use these

Wang 2006c (Continued)

	data	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete outcome data.
Selective reporting (reporting bias)	High risk	Data on TESS score were missing.
Other bias	Low risk	None obvious.

Wang 2006d

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: six weeks. Design: parallel. Setting: inpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). BPRS of 35 or more. N = 120. Age: aripiprazole group: 18- 45 years, mean = (28.9± 7.9) years; risperidone group: 16- 50 years, mean = (31.53 ± 9.03) years Gender: aripiprazole group: 32 male, 28female; risperidone group: 46 male, 14 female. History: aripiprazole group: 3 months- 10 years, mean = (3.3 ± 4.5) years; risperidone group: 3 months- 10 years, mean = (5.03 ± 3.3) years. Age at onset not reported
Interventions	1. Aripiprazole: Dose range: 5-30 mg/day. Mean= 20 mg/day. N = 60. 2. Risperidone: Dose range: 1-6 mg/day. Mean= 20 mg/day. N = 60

Wang 2006d (Continued)

Outcomes	Global state: BPRS score decreased rate (recovery: $\geq 75\%$, markedly improved: 50%-75%, improved: 25%-50%, no effect: $< 25\%$) Mental state: BPRS total score. Adverse effects. Unable to use - Adverse effects: TESS total score, blood, urine, and stool routine, use of benzodiazepines and anticholinergic medication (no data)
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.
Selective reporting (reporting bias)	High risk	Data TESS total score, blood, urine, and stool routine, use of benzodiazepines and anticholinergic medication were missing
Other bias	Low risk	None obvious.

Wang 2007

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: eight weeks. Design: parallel. Setting: outpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). BPRS of 35 or more. N = 95. Age: aripiprazole group: 16~ 54 years, mean = (24.4 $\pm$ 13.2) years; risperidone group: 13 ~ 67 years, mean = (25. 4 $\pm$ 14. 6) years

	Gender: aripiprazole group: 22 male, 24 female; risperidone group: 23 male, 26 female. History: not reported. Age at onset not reported.	
Interventions	1. Aripiprazole: Dose range: 5-30 mg/day. Mean dose: not reported. N = 46. 2. Risperidone: Dose range: 1-6 mg/day. Mean dose: not reported. N = 49	
Outcomes	Global state: PANSS score decreased rate (recovery: $\geq 75\%$, markedly improved: 50%-75%, improved: 25%-50%, no effect: $< 25\%$) Mental state: PANSS total score. Leaving the study early. Adverse effects. Unable to use - Adverse effects: TESS total score, blood routine, use of benzodiazepines and anticholinergic medication (no data)	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Total proportion of drop-out was 3.15% and the data of the two groups were balanced (2/46: 1/49). Two because of adverse effect, one due to economic issue
Selective reporting (reporting bias)	High risk	Data on TESS total score, blood routine, use of benzodiazepines and anticholinergic medication were missing
Other bias	Low risk	None obvious.

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: one week wash-out period + eight weeks intervention. Design: parallel. Setting: inpatient, China.	
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 60. Age: aripiprazole group: mean = (37. 5 ± 9. 8) years; risperidone group: mean = (36. 7 ± 10. 5) years Gender: 60 female. History: aripiprazole group: 1 month- 3 years, mean = (2 ± 1.5) years; risperidone group: 3 months- 3 years, mean = (2.3 ± 1.8) years. Age at onset not reported	
Interventions	1. Aripiprazole: Dose range: 10-30 mg/day. Mean dose: not reported. N = 30. 2. Risperidone: Dose range: 2-6 mg/day. Mean dose: not reported. N = 30	
Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 75%, markedly improved: 50%-74%, improved: 25%-49%, no effect: < 25%) Mental state: PANSS total score. PANSS positive subscale score, PANSS negative subscale score, PANSS general psychopathological subscale score Adverse effects. Unable to use - Adverse effects: TESS total score, blood and urine routine, kidney function, electrolyte, use of benzodiazepines and anticholinergic medication (no data)	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.

Wang 2007a (Continued)

Selective reporting (reporting bias)	Low risk	Data on TESS total score, blood and urine routine, kidney function, electrolyte, use of benzodiazepines and anticholinergic medication were missing
Other bias	Low risk	None obvious.

Wang 2007d

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: eight weeks. Design: parallel. Setting: inpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 64. Age: aripiprazole group: 16- 52 years, mean = (29. 1 ± 3. 2) years; risperidone group: 19 ~ 54 years, mean = (28. 3 ± 2. 8) years Gender: aripiprazole group: 19 male, 13 female; risperidone group: 15 male, 17 female. History: aripiprazole group: 8 months- 5 years, mean = (2. 7 ± 1. 1) years; risperidone group: 7 month- 6 years, mean = (2. 6 ± 1. 7) years. Age at onset not reported
Interventions	1. Aripiprazole: Dose range: 10-30 mg/day. Mean= (20. 4 ± 3. 5) mg/day. N=32. 2. Risperidone: Dose range: 1-7 mg/day. Mean= (4. 1 ± 1. 2) mg/day. N=32
Outcomes	Global state: PANSS score decreased rate (markedly improved: ≥ 60%, improved: 40%-60%, no effect: < 40%) Adverse effects. Unable to use - Adverse effects: TESS total score (no data).
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.

Wang 2007d (Continued)

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.
Selective reporting (reporting bias)	High risk	Data on TESS total score were missing. Data on extrapyramidal symptoms were incomplete
Other bias	Low risk	None obvious.

Wang 2007e

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: one week wash-out period and six weeks intervention. Design: parallel. Setting: inpatient and outpatient, China.	
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 60. Age: aripiprazole group: 18- 54 years, mean = (29. 4 ± 3. 1) years; risperidone group: 19 ~ 53 years, mean = (27. 4 ± 2. 9) years Gender: aripiprazole group: 17 male, 13 female; risperidone group: 16 male, 14 female. History: aripiprazole group: 1 month- 16 years, mean = (2. 7 ± 3. 2) years; risperidone group: 1 month- 18 years, mean = (3.1 ± 3.2) years. Age at onset not reported	
Interventions	1. Aripiprazole: Dose range: 5-30 mg/day. Mean = (3.1 ± 3.2) mg/day. N = 30. 2. Risperidone: Dose range: 0.5-6 mg/day. Mean = (4.0 ± 1.5) mg/day. N = 30	
Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 75%, markedly improved: 50%-74%, improved: 25%-49%, no effect: < 25%) Mental state: PANSS total score, PANSS positive subscale score, PANSS negative subscale score, PANSS general psychopathological subscale score Adverse effects. Unable to use - Adverse effects: TESS total score, ECG, EPS, use of benzodiazepines, propranolol, and anticholinergic medication (no data)	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement

Wang 2007c (Continued)

Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.
Selective reporting (reporting bias)	High risk	Data on TESS total score, ECG, EPS, use of benzodiazepines, propranolol, and anticholinergic medication were missing
Other bias	Low risk	None obvious.

Wang 2008

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: two weeks wash-out period + eight weeks intervention. Design: parallel. Setting: inpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 60. Age: aripiprazole group: 16- 61 years, mean = (30.1 ± 12.5) years; risperidone group: 18 - 65 years, mean = (32.7 ± 11.3) years Gender: aripiprazole group: 17 male, 13 female; risperidone group: 16 male, 14 female. History: aripiprazole group: 1 month- 410 months, mean = (91.7 ± 115.5) months; risperidone group: 1 month- 379 months, mean = (85.7 ± 98.4) months. Age at onset not reported
Interventions	1. Aripiprazole: Dose range: 5-30 mg/day. Mean = (21.60 ± 6.89) mg/day. N = 30. 2. Risperidone: Dose range: 1-6 mg/day. Mean = (5.25 ± 1.03) mg/day. N = 30
Outcomes	Mental state: PANSS total score. Adverse effects. Unable to use- Global state: PANSS score decreased rate (recovery: ≥ 75%, markedly improved: 51%-74%, improved: 26%-50%, no effect: ≤25%) - no data reported

Wang 2008 (Continued)

Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.
Selective reporting (reporting bias)	High risk	Although PANSS score decreased rate was used to assess effect, no data were available
Other bias	Low risk	None obvious.

Wang 2008c

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: one week washout period + eight weeks intervention. Design: parallel. Setting: inpatient and outpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. SANA of 60 or more. N = 86. Age: aripiprazole group: mean = (29.4 ± 7.6) years; ziprasidone group: mean = (30.3 ± 8.1) years Gender: not reported. History: aripiprazole group: mean = (5.5 ± 2.8) years; ziprasidone group: mean = (5.2 ± 2.7) years. Age at onset not reported
Interventions	1. Aripiprazole: Dose range: 10-30 mg/day, mean = (16.7 ± 1.4) mg/day. N = 43. 2. Ziprasidone: Dose range: 20-80 mg/day, mean = (46.3 ± 10.3) mg/day. N = 43

Wang 2008c (Continued)

Outcomes	Global state: PANSS score decreased rate (recovery: $\geq 75\%$, markedly improved: 50%-75%, improved: 25%-50%, no effect: $< 25\%$). CGI-GI total score Mental state: PANSS total score, PANSS positive subscale score, PANSS negative subscale score. SANS total score score Adverse effects. Unable to use - Mental state: SANS subscale score - unvalidated subscale.	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.
Selective reporting (reporting bias)	High risk	Data on TESS score, blood and urine routine, ECG. were missing
Other bias	Low risk	None obvious.

Wang 2009

Methods	<p>Allocation: randomised, stratified random.</p> <p>Blindness: unclear.</p> <p>Duration: eight weeks.</p> <p>Design: parallel.</p> <p>Setting: inpatients, China.</p>
Participants	<p>Diagnosis: schizophrenia (CCMD-3), PANSS total score of 60 or more.</p> <p>N = 60.</p> <p>Age: mean = (35.2 $\pm$ 9.7) years.</p> <p>Gender: 36 male, 24 female.</p> <p>History: duration of illness not reported. Age at onset not reported</p>

Wang 2009 (Continued)

Interventions	1. Aripiprazole: Dose range: 20-30 mg/day. mean dose: not reported. N = 30. 2. Clozapine: Dose range: 400-600 mg/day. Mean dose: not reported. N = 30	
Outcomes	Leaving the study early. Adverse events: Fasting plasma glucose (FPG), glucose tolerance test (OGTT) 2h post-prandial blood glucose (PBG) value	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Stratified random.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Total proportion of drop-out was 8.3% and the data of the two groups were balanced. The proportion of missing outcomes was not enough to have a clinically relevant impact on the intervention effect estimate
Selective reporting (reporting bias)	High risk	No data on efficacy were available. Data on other adverse effects were also missing
Other bias	Low risk	None obvious.

Wei 2006

Methods	Allocation: randomised, random number table. Blindness: unclear. Duration: eight weeks. Design: parallel. Setting: inpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more, CGI of 4 or more. N = 108; complete study: N = 101. Age: aripiprazole group: 19- 58 years. mean = (32.2 ± 8.8) years; quetiapine group: 18

	~ 57 years, mean = (32.1 ± 7.1) years Gender: 104 female. History: aripiprazole group: 1 month- 5 years, mean = (2.8 ± 2.6) years; quetiapine group: 1 month- 6 years, mean = (2.7 ± 2.8) years. Age at onset not reported	
Interventions	1. Aripiprazole: Initial dose: 5- 10 mg/day. Mean dose: not reported. N = 54. 2. Quetiapine: Initial dose: 75- 100 mg/day. Mean dose: not reported. N = 54	
Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 75%, improved: 50%-75%, no effect: < 50%). CGI-SI subscale score Mental state: PANSS total score, PANSS positive subscale score, PANSS negative subscale score, PANSS general pathological subscale score Leaving the study early. Adverse effects.	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Random number table.
Allocation concealment (selection bias)	Low risk	Sealed envelope.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	High risk	There was no blinding on outcome assessment.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.
Selective reporting (reporting bias)	High risk	Data on TESS total score, blood routine, ECG, liver function, use of benzodiazepines were missing
Other bias	Low risk	None obvious.

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: six months. Design: parallel. Setting: inpatient and outpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 90. Age: aripiprazole group: mean = (25.2 ± 6.1) years; clozapine group: mean = (24.5 ± 7.2) years. Gender: aripiprazole group: 23 male, 22 female; clozapine group: 22 male, 23 female. History: aripiprazole group: mean = (1.4 ± 0.9) years; clozapine group: mean = (1.4 ± 0.8) years. Age at onset not reported
Interventions	1. Aripiprazole: Dose range: 10-30 mg/day. Mean dose: not reported. N = 45. 2. Clozapine: Dose range: 50-450 mg/day. Mean dose: not reported. N = 45
Outcomes	Mental state: PANSS total score. PANSS positive subscale score, PANSS negative subscale score, PANSS general psychogenic pathological subscale score, anxiety - labelled as "adverse effect" Quality of life: WHO-QOL-100. Adverse effects: central nervous system (headache, dizziness, somnolence, insomnia), gastrointestinal (salivate, constipation), ECG(QTc) abnormal, weight gain, appetite decrease, blood glucose increase Unable to use - Adverse effects: TESS total score, urine routine, hepatorenal function and EEG (no data)
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Unclear if there were incomplete data.

Wei 2007 (Continued)

Selective reporting (reporting bias)	High risk	Although TESS was used to assess adverse effects, no data on scores were available. Data on urine routine, hepatorenal function and EEG were missing
Other bias	Low risk	None obvious.

Wei 2009

Methods	Allocation: randomised, random number table. Blindness: unclear. Duration: one week wash out period + eight weeks intervention. Design: parallel. Setting: inpatient and outpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS more than 60 years. N = 102. Age: aripiprazole group: 19- 57 years, mean = (28.2 ± 3.9) years; olanzapine group: 20 - 58 years, mean = (28.4 ± 4.7) years Gender: 80 female. History: aripiprazole group: 3 months- 8 years, mean = (2.4 ± 1.4) years; olanzapine group: 3 months- 6 years, mean = (2.1 ± 1.1) years. Age at onset not reported
Interventions	1. Aripiprazole: Dose range: 10-30 mg/day. Mean dose: not reported. N = 51. 2. Olanzapine: Dose range: 10-20 mg/day. Mean dose: not reported. N = 51
Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 75%, improved: 50%-75%, no effect: < 50%) Mental state: PANSS total score, PANSS positive subscale score, PANSS negative subscale score, PANSS general psychogenic pathological subscale score Adverse effects.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.

Wei 2009 (Continued)

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Unclear if there were incomplete data.
Selective reporting (reporting bias)	High risk	Data on Global state, TESS total score, excitement or agitation insomnia, somnolence, myotonia, akathisia, tremors, use of benzodiazepines were missing
Other bias	Low risk	None obvious.

Wen 2009

Methods	Allocation: randomised, random permutation table. Blindness: unclear. Duration: eight weeks. Design: parallel. Setting: inpatient, China.	
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 60. Age: aripiprazole group: 18- 45 years, mean = (26.2 ± 3.7) years; risperidone group: 19 - 44 years, mean = (26.3 ± 3.3) years Gender: 60 female. History: aripiprazole group: 5-13 weeks, mean = (7.4 ± 4.3) weeks; risperidone group: 4-17 weeks, mean = (7.2 ± 4.7) weeks. Age at onset not reported	
Interventions	1. Aripiprazole: Dose range: 5-30 mg/day. Mean =(24.11 ± 6.32) mg/day. N = 30. 2. Risperidone: Dose range: 1-6 mg/day. Mean = (4.01 ± 1.89) mg/day. N = 30	
Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 75%, markedly improved: 50%-74%, improved: 25%-49%, no effect: < 25%) Mental state: PANSS total score, PANSS positive subscale score, PANSS negative subscale score, PANSS general pathological subscale score, PANSS general psychogenic pathological subscale score Leaving the study early. Adverse effects. Unable to use - Adverse effects: TESS total score, use of benzodiazepines and other medicines (no data)	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement

Wen 2009 (Continued)

Random sequence generation (selection bias)	Low risk	Random permutation table.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.
Selective reporting (reporting bias)	High risk	Data on TESS total score, use of benzodiazepines and other medicines were missing
Other bias	Low risk	None obvious.

Wen 2009a

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: eight weeks. Design: parallel. Setting: inpatient and outpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 80. Age: aripiprazole group: mean = (44.5 ± 3.0) years; risperidone group: mean = (43.9 ± 3.5) years Gender: 80 female. History: aripiprazole group: mean = (6.5 ± 1.6) years; risperidone group: mean = (6.9 ± 1.7) years. Age at onset not reported
Interventions	1. Aripiprazole: Dose range: 5-30 mg/day. Mean = (16.5 ± 5.5) mg/day. N = 40. 2. Risperidone: Dose range: 2-6 mg/day. Mean = (4.22 ± 1.51) mg/day. N = 40
Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 75%, markedly improved: 50%-75%, improved: 25%-50%, no effect: < 25%) Mental state: PANSS total score, PANSS positive subscale score, PANSS negative subscale score, PANSS general pathological subscale score, PANSS general psychogenic pathological subscale score Adverse effects. Unable to use - Adverse effects: TESS total score, blood and urine routine, renal unction, use of benzo-

Wen 2009a (Continued)

	diazepines and anticholinergic medicines (no data)	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.
Selective reporting (reporting bias)	High risk	Data on TESS total score, blood and urine routine, renal unction, use of benzodiazepines and anticholinergic medicines were missing
Other bias	Low risk	None obvious.

Włodziewicz 2006

Methods	Allocation: random, no further details. Blindness: open label. Duration: 52 weeks optional extension to a 26 week multicentre, randomised, double blind placebo controlled trial of aripiprazole. Location: multicentre.
Participants	Diagnosis: schizophrenia -chronic stable or acutely psychotic meeting criteria for relapse and had completed at least 2 weeks of double-blind therapy. N = 214. Gender: M = 116, F = 98. History: duration of illness not reported. Setting: not reported.
Interventions	1. Aripiprazole: 15-30 mg/day. Mean dose: 22.0 mg/day. N = 104. 2. Olanzapine: 10-20 mg/day. Mean dose: 14.2 mg/day. N = 110

Włodzimirz 2006 (Continued)

Outcomes	Leaving the study early: any reason, adverse events, inefficacy. Global state: CGI. Mental state: PANSS total score. Adverse effects	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Randomised, no further details.
Allocation concealment (selection bias)	High risk	Open label.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open label.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open label.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	LOCF method used to account for people leaving the study early
Selective reporting (reporting bias)	High risk	Adverse events were reported if they were > 5%. Scales if used were not reported
Other bias	High risk	Industry sponsored.

Wolf 2007

Methods	Allocation: random. Blindness: open label. Duration: 8 weeks. Design: prospective Location: multicentric
Participants	Diagnosis: Schizophrenia (DSM IV), required initiation of antipsychotics, antipsychotic switch clinically appropriate N = 833. Age: 18-65 years. History: duration of illness not reported, age at onset not reported. Setting: outpatient.

Wolf 2007 (Continued)

Interventions	1. Aripiprazole: 10 mg-30 mg/day (mean 19.1 mg/day). N = 680. 2. Other antipsychotic: recommended dose N = 153.
Outcomes	Global state: CGI-I. Adverse effects: At least one adverse effect, extrapyramidal adverse effects, prolactin-associated adverse effects. Others: POM, IAQ.
Notes	Primary goal was evaluating the effectiveness of aripiprazole in general psychiatric setting in Europe. Data from patients in UK was not reported. Unable to use data from CGI-I, POM and IAQ

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	4:1 computer-generated using Interactive Voice Response System
Allocation concealment (selection bias)	High risk	Open label.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open label.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open label.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	LOCF method used to account for people leaving the study early
Selective reporting (reporting bias)	High risk	Adverse events were reported if they were > 5%. Scales if used were not reported
Other bias	High risk	Industry sponsored.

Wu 2008

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: one week wash-out period + twelve weeks intervention. Design: parallel. Setting: inpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 98.

	Age: aripiprazole group: mean = (63.5 ± 4.2) years; risperidone group: mean = (27.8 ± 9.6) years Gender: not reported. History: aripiprazole group: mean = (26.7 ± 6.2) years; risperidone group: mean = (26.5 ± 6.4) years. Age at onset not reported	
Interventions	1. Aripiprazole: Dose range: 2.5-30 mg/day. Mean dose: not reported. N = 49. 2. Risperidon: Dose range: 0.5-6 mg/day. Mean dose: not reported. N = 49	
Outcomes	Mental state: PANSS total score, PANSS positive subscale score, PANSS negative subscale score, PANSS general pathological subscale score Adverse effects. Unable to use- Adverse effects: TESS score, blood routine, hepatorenal function, electrolyte (no data)	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Unclear if there was drop-out.
Selective reporting (reporting bias)	High risk	The data on TESS score, blood routine, hepatorenal function, electrolyte were missing
Other bias	High risk	None obvious.

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: twelve weeks. Design: parallel. Setting: inpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3 and ICD- 10). PANSS score of 60 or more. N = 72. Age: aripiprazole: 16- 55 years, mean = (29.7 ± 19.6) years; clozapine: 18- 58 years, mean = (28.6 ± 18.1) years. Gender: aripiprazole group: 16 male, 20 female; clozapine group: 16 male, 20 female . History: aripiprazole group: 1 months- 21 years, mean = (5.4 ± 3.4) years; clozapine group: 1.5 months - 20years, mean = (5.5 ± 2.7) years. Age at onset not reported
Interventions	1. Aripiprazole: Dose range: 10-25 mg/day. Mean dose: not reported. N = 36. 2. Clozapine: Dose range: 50-450 mg/day. Mean dose: not reported. N = 36
Outcomes	Mental state: PANSS total score. PANSS positive subscale score, PANSS negative subscale score, PANSS general psychogenic pathological subscale score; BPRS score Quality of life: WHO-QOL-100. Adverse effects.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Unclear if there were incomplete data.
Selective reporting (reporting bias)	High risk	The data on use of benzhexol, propranolol and benzodiazepines were missing
Other bias	Low risk	None obvious.

Xie 2008

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: twelve weeks. Design: parallel. Setting: inpatient, China.	
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 84. Age: 25- 40 years. Gender: 84 male. History: not reported. Age at onset not reported.	
Interventions	1. Aripiprazole: Dose range:10-20 mg/day. Mean dose: not reported. N = 42. 2. Risperidon: Dose range: 2-4 mg/day. Mean dose: not reported. N = 42	
Outcomes	Global state: PANSS score decreased rate (recovery: $\geq 75\%$, markedly improved: 50%-75%, improved: 25%-50%, no effect: $< 25\%$) Mental state: PANSS total score, PANSS positive subscale score, PANSS negative subscale score, PANSS general pathological subscale score Adverse effects. Unable to use - Sexual desire - unvalidated scale.	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.
Selective reporting (reporting bias)	Low risk	No imported outcome were missing.
Other bias	Low risk	None obvious.

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: eight weeks. Design: parallel. Setting: inpatient, China.	
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 80. Age: aripiprazole group 18- 65 years, mean = (33.4 ± 9.1) years; risperidone group 18 ~ 63 years, mean = (32.4 ± 8.2) years Gender: aripiprazole group: 22 male, 18 female; risperidone group: 21 male, 19 female. History: aripiprazole group 1~ 22 months, mean = (13.1 ± 2.1) months; risperidone group 1~ 23 months, mean = (12.6 ± 3.6) months. Age at onset not reported	
Interventions	1. Aripiprazole: Dose range: 5-30 mg/day. Mean dose: (21 ± 10.4) mg/day. N = 40. 2. Risperidone: Dose range: 1-6 mg/day. Mean dose: (4 ± 1.6) mg/day. N = 40	
Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 75%, markedly improved: 50%-75%, improved: 25%-50%, no effect: < 25%) Mental state: PANSS total score, PANSS positive subscale score, PANSS negative subscale score, PANSS general pathological subscale score Adverse effects. Unable to use - Adverse effects: TESS total score, blood routine, use of benzodiazepines and other medicines (no data)	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.

Xie 2010 (Continued)

Selective reporting (reporting bias)	High risk	Although TESS was used to assess adverse effects, no data on scores were available. Data on blood routine, use of benzodiazepines and other medicines were missing
Other bias	Low risk	None obvious.

Xu 2007

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: eight weeks. Design: parallel. Setting: inpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). BPRS score of 35 or more. N = 70. Age: Aripiprazole: mean = (28 ± 6) years; Clozapine: mean = (29 ± 5) years. Gender: Aripiprazole group: 18 male, 17 female; Clozapine group: 19 male, 16 female. History: Aripiprazole group: mean = (3.5 ± 1.5) years; Clozapine group: 1.5 months - 20 years, mean = (3.8 ± 1.4) years. Age at onset not reported Setting: inpatient.
Interventions	1. Aripiprazole: Dose range: 10-30 mg/day. Mean dose: not reported. N = 35. 2. Clozapine: Dose range: 25-400 mg/day. Mean dose: not reported. N = 35
Outcomes	Global state: BPRS score decreased rate (recovery: ≥ 75%, markedly improved: 50%-75%, improved: 25%-50%, no effect: < 25%) Mental state: BPRS total score. Adverse effects. Unable to use - Adverse effects: TESS total score, use of benzhexol and benzodiazepines (no data)
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.

Xu 2007 (Continued)

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.
Selective reporting (reporting bias)	High risk	Although TESS was used to assess adverse effects, no data on scores were available. Data on use of benzhexol and benzodiazepines were missing
Other bias	Low risk	None obvious.

Xu 2010

Methods	Allocation: randomised, no further details. Blindness: double. Duration: 3-7 days wash-out period + six weeks intervention. Design: parallel. Setting: not reported, China.	
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 52. Age: 18- 65 years, aripiprazole group: mean = (35.4 ± 8.8) years; risperidone group: mean= (40.1 ± 13.3) years Gender: aripiprazole group: 11 male, 15 female; risperidone group: 12 male, 14 female. History: aripiprazole group: mean = (6.5 ± 6.7) years; risperidone group: mean = (8.5 ± 9.4) years. Age at onset not reported	
Interventions	1. Aripiprazole: Dose range: 10-30 mg/day. Mean dose: not reported. N = 26. 2. Risperidone: Dose range: 2-6 mg/day. Mean dose: not reported. N = 26	
Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 80%, markedly improved: 50%-80%, improved: 30%-50%, no effect: < 30%). CGI-I, CGI-S score Mental state: PANSS total score. Leaving the study early. Adverse effects. Unable to use - Adverse effects: TESS total score, Extrapyramidal reaction scale score, BARS score (no data)	
Notes		
Risk of bias		
Bias	Authors' judgement	Support for judgement

Xu 2010 (Continued)

Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Total proportion of drop-out was 7.7% (2/26 vs. 2/26). Aripiprazole group: 1 because of violation of study scheme, 1 because of bad compliance; risperidone group: 1 because of violation of study scheme, 1 because of drug combination; 1 because of effect
Selective reporting (reporting bias)	High risk	Data on TESS total score, Extrapyramidal reaction scale score, BARS scores were not reported
Other bias	Low risk	None obvious.

Yan 2007

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: six months. Design: parallel. Location: inpatient and outpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 86, completed study: N = 74. Age: aripiprazole group: mean = (32.5 ± 6.8) years; clozapine group: mean = (28.2 ± 2.8) years. Gender: aripiprazole group: 19 female, 19 male; clozapine group: 18 male, 18 female. History: Not reported. Age at onset not reported.
Interventions	1. Aripiprazole: Dose range: 15-30 mg/day. Mean dose: not reported. N = 43. 2. Clozapine: Dose range: 200-500 mg/day. Mean dose: not reported. N = 43
Outcomes	Mental state: PANSS total score. PANSS positive subscale score, PANSS negative subscale score, PANSS general psychogenic pathological subscale score Quality of life: WHO-QOL-100

Yan 2007 (Continued)

	Unable to use - Adverse effects: TESS total score and use of benzodiazepine (no data)	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Double.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Total proportion of drop-out was 7.7% (2/26 vs. 2/26). Aripiprazole group: 1 because of violation of study scheme, 1 because of bad compliance; risperidone group: 1 because of violation of study scheme, 1 because of drug combination; 1 because of effect
Selective reporting (reporting bias)	High risk	Data on TESS total score, Extrapyramidal reaction scale score, BARS scores were not reported
Other bias	Low risk	None obvious.

Yan 2008

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: eight weeks. Design: parallel. Setting: inpatient and outpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 60. Age: aripiprazole group: mean = (13.0 ± 2.3) years; risperidone group: mean = (13.0 ± 2.6) years Gender: aripiprazole group: 14 male, 16 female; risperidone group: 13 male, 17 female.

	History: aripiprazole group: mean = (10. 6 ± 6. 0) years; risperidone group: mean = (8. 2 ± 5. 2) years. Age at onset not reported.	
Interventions	1. Aripiprazole: Dose range: 2.5-25 mg/day. Mean dose: not reported. N = 30. 2. Risperidone: Dose range: 0.5-6 mg/day. Mean dose: not reported. N = 30	
Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 75%, markedly improved: 50%-75%, improved: 25%-50%, no effect: < 25%). CGI-SI score Mental state: PANSS total score, PANSS positive subscale score, PANSS negative subscale score, PANSS general pathological subscale score Leaving the study early: no patient. Adverse effects. Unable to use- Adverse effects: TESS score, blood routine, hepatorenal function, EEG, and weight (no data)	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.
Selective reporting (reporting bias)	High risk	Although TESS was used to assess adverse effects, no data on scores were available. Data on blood routine, hepatorenal function, EEG, and weight were missing
Other bias	Low risk	None obvious.

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: six weeks. Design: parallel. Setting: not reported, China.	
Participants	Diagnosis: schizophrenia (CCMD-3), BPRS total score of 35 or more. N = 100. Age: 18- 56 years, mean = (28.6 ± 11.3) years. Gender: 54 male, 46 female. History: mean = (14.5 ± 6.3) years. Age at onset not reported Setting: not reported.	
Interventions	1. Aripiprazole: Dose range: 5-30 mg/day. Mean dose: (22.5 ± 7.5) mg/day. N = 50. 2. Clozapine: Initial dose: 25-50 mg/day. Mean dose: not reported. N = 50	
Outcomes	Global state: BPRS score decreased rate (recovery: ≥ 80%, markedly improved: 50%-80%, improved: 25%-50%, no effect: < 25%) Mental state: BPRS total score. Adverse effects.	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.
Selective reporting (reporting bias)	High risk	Although TESS was used to assess adverse effects, no data on scores were available. Data on dizziness, salivate, constipation, weight gain, and renal function were deficient. Data on use of benzodiazepines were also missing

Yan 2008a (Continued)

Other bias	Low risk	None obvious.
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Yan 2010

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: twelve weeks. Design: parallel. Setting: inpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 100. Age: aripiprazole group: 18- 43 years, mean = (33.40 ± 7.09) years; risperidone group: 21 - 44 years, mean = (32.17 ± 5.13) years Gender: aripiprazole group: 27 male, 23 female; risperidone group: 24 male, 26 female. History: aripiprazole group: 1- 13 months, mean = (5.94 ± 2.79) months; risperidone group: 1- 11 months, mean = (5.46 ± 2.47) months. Age at onset not reported
Interventions	1. Aripiprazole: Dose range: 5-30 mg/day. Mean dose: not reported. N = 50. 2. Risperidone: Dose range: 1-8 mg/day. Mean dose: not reported. N = 50
Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 80%, markedly improved: 50%-79%, improved: 30%-49%, no effect: < 30%) Mental state: PANSS total score, PANSS total score decreased rate Leaving the study early. Adverse effects.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.

Incomplete outcome data (attrition bias) All outcomes	Low risk	The total proportion of loss to follow up was 6% (4/50 vs. 2/50). Aripiprazole group: 2 cases because of drug combination, 1 case because of adverse effect, 1 case due to family demanded; risperidone group: 2 cases because of drug combination
Selective reporting (reporting bias)	High risk	Data on number of no effect, blood and urine routine, renal function, use of benzodiazepines and other medicines were missing
Other bias	Low risk	None obvious.

Yang 2006

Methods	Allocation: randomised, no further detail. Blindness: unclear. Duration: eight weeks. Design: parallel. Setting: inpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS score of 60 or more. N = 100*. Age: Aripiprazole: 20- 62 years, mean = (43 ± 22) years; Clozapine: 22- 59 years, mean = (40 ± 20) years. Gender: Aripiprazole group: 29 male, 18 female; Clozapine group: 26 male, 17 female . History: Aripiprazole group: mean = (25 ± 31) months; Clozapine group: mean = (28.4 ± 33) months. Age at onset not reported Setting: inpatient.
Interventions	1. Aripiprazole: Dose range: 10-30 mg/day. Mean dose: not reported. N = 47. 2. Clozapine: Dose range: 50-450 mg/day. Mean dose: not reported. N = 43
Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 75%, markedly improved: 50%-75%, improved: 25%-50%, no effect: < 25%). GGI-SI Mental state: PANSS total score. PANSS positive subscale score, PANSS negative subscale score, PANSS general psychogenic pathological subscale score. anxiety - labelled as "adverse effect" Adverse effects.
Notes	* There is a discrepancy of 10 people between the number of people selected for the study (100) and the numbers randomised into each group (47:43). Since the report consistently reported the N numbers in each group as 47:43 in the result and discussion sections of the paper, we assume these are the N numbers of the trial

Risk of bias

Yang 2006 (Continued)

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not stated.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not stated.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete outcome.
Selective reporting (reporting bias)	Low risk	No evidence of selective reporting.
Other bias	Low risk	None obvious.

Yang 2007

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: six weeks. Design: parallel. Setting: inpatient and outpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS score of 60 or more. N = 60. Age: not reported. Gender: not reported. History: not reported.
Interventions	1. Aripiprazole: Started dose: 5 mg/day. Maximum dose: (15 ± 5. 5) mg/day. N = 30. 2. Clozapine: Started dose: 50 mg/day. Maximum dose: (269. 8 ± 132. 5) mg/day. N = 30
Outcomes	Global state: markedly improved, improved, no effect. Mental state: PANSS total score, anxiety - labelled as "adverse effect" Adverse effects. Unable to use - Adverse effects: TESS total score and hepatorenal function (no data)
Notes	

<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Unclear if there was drop-out.
Selective reporting (reporting bias)	High risk	Data on TESS total score and hepatorenal function were missing
Other bias	Low risk	None obvious.

Yang 2008

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: one week wash-out period + eight weeks intervention. Design: parallel. Setting: inpatient and outpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 60. Age: aripiprazole group: mean = (32.7 ± 5.9) years; ziprasidone group: mean = (31.2 ± 6.8) years Gender: aripiprazole group: 20 male, 10 female; ziprasidone group: 10 male, 11 female. History: aripiprazole group: mean = (5.5 ± 4.1) years; ziprasidone group: mean = (5.2 ± 3.9) years. Age at onset not reported
Interventions	1. Aripiprazole: Dose range: 10-30 mg/day, mean dose: not reported. N = 30. 2. Ziprasidone: Dose range: 20-160 mg/day, mean dose: not reported. N = 30
Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 75%, markedly improved: 50%-75%, improved: 25%-50%, no effect: < 25%) Mental state: PANSS total score, PANSS positive subscale score, PANSS negative subscale score, PANSS general psychogenic pathological subscale score

Yang 2008 (Continued)

	Leaving the study early. Adverse effects.	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	There were no incomplete data.
Selective reporting (reporting bias)	High risk	Data on TESS score, RSESE score, blood and urine routine,hepatorenal function, drugs for adverse events were missing
Other bias	Low risk	None obvious.

Yang 2008a

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: eight weeks. Design: parallel. Setting: inpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 60. Age: aripiprazole group: mean = (28.2 ± 10.3) years; risperidone group: mean = (27.8 ± 9.6) years Gender: aripiprazole group: 21 male, 9 female; risperidone group: 20 male, 10 female. History: aripiprazole group: mean = (2.6 ± 1.8) years; risperidone group: mean = (2.8 ± 2.0) years. Age at onset not reported

Interventions	1. Aripiprazole: Dose range: 5-25 mg/day. Mean = (16.5 ± 5.5) mg/day. N = 30. 2. Risperidon: Dose range: 1-5 mg/day. Mean = (3.8 ± 1.6) mg/day. N = 30	
Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 75%, markedly improved: 50%-75%, improved: 25%-50%, no effect: < 25%). CGI-SI score Mental state: PANSS total score, PANSS positive subscale score, PANSS negative subscale score, PANSS general pathological subscale score Leaving the study early: no patient. Adverse effects. Unable to use- Adverse effects: Blood and urine routine, liver function, ECG, weight and other adverse effect, use of benzodiazepines and anticholinergic medication (no data)	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	There were no incomplete data.
Selective reporting (reporting bias)	High risk	Although blood and urine routine, liver function, ECG, weight and other adverse effect, use of benzodiazepines and anticholinergic medication were missing
Other bias	Low risk	None obvious.

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: eight weeks. Design: parallel. Setting: inpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 90. Age: aripiprazole group: 18- 52 years. mean = (26.7 ± 8.5) years; risperidone group: 18 ~ 51 years, mean = (26.2 ± 8.3) years Gender: aripiprazole group: 45 female; risperidone group: 45 female. History: aripiprazole group: 1- 52 months, mean = (15.2 ± 16.7) months; risperidone group: 1- 49 months, mean = (14.9 ± 17.1) months. Age at onset not reported
Interventions	1. Aripiprazole: Dose range: 10-30 mg/day. Mean dose: not reported. N = 45. 2. Risperidone: Dose range: 1-6 mg/day. Mean dose: not reported. N = 45
Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 75%, markedly improved: 50%-75%, improved: 25%-50%, no effect: < 25%) Mental state: PANSS total score, PANSS positive subscale score, PANSS negative subscale score, PANSS psychopathological subscale score. z Adverse effects. Unable to use - Adverse effects: TESS total score, blood routine, liver function, blood glucose, weight, use of benzodiazepines and anticholinergic medication (no data)
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	There was no drop-out.

Yang 2008b (Continued)

Selective reporting (reporting bias)	High risk	Data on TESS total score, blood routine, liver function, blood glucose, weight, use of benzodiazepines and anticholinergic medication were missing
Other bias	Low risk	None obvious.

Yang 2009

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: twelve weeks. Design: parallel. Setting: inpatient and outpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). N = 60. Age: 18- 45 years, aripiprazole group: mean = (29.6 ± 7.3) years; olanzapine group: mean = (28.9 ± 6.6) years Gender: aripiprazole group: 16 male, 14 female; olanzapine group: 15 male, 15 female. History: aripiprazole group: mean = (10.2 ± 5.0) years; olanzapine group: mean = (10.4 ± 5.8) years. Age at onset not reported
Interventions	1. Aripiprazole: Initial dose: 10 mg/day. Mean = (20.8 ± 6.2) mg/day. N = 30. 2. Olanzapine: Initial dose: 5 mg/day. Mean = (14.3 ± 5) mg/day. N = 30
Outcomes	Adverse effects: weight gain, blood glucose.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomisation, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.

Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Unclear if there were incomplete data.
Selective reporting (reporting bias)	Low risk	No selective reporting.
Other bias	Low risk	None obvious.

Ye 2005

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: eight weeks. Design: parallel. Setting: inpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 68. Age: aripiprazole group: 18- 52 years, mean = (28. 6 ± 16. 8) years; risperidone group: 19 ~ 55 years, mean = (31.9 ± 15.7) years Gender: aripiprazole group: 20 male, 14 female; risperidone group: 24 male, 10 female. History: not reported. Age at onset not reported.
Interventions	1. Aripiprazole: Dose range: 5-30 mg/day. Mean = (17.5 ± 6.5) mg/day. N = 34. 2. Risperidone: Dose range: 1-6 mg/day. Mean = (4.1 ± 1.8) mg/day. N = 34
Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 75%, markedly improved: 50%-75%, improved: 25%-50%, no effect: < 25%) Mental state: PANSS total score, PANSS positive subscale score, PANSS negative subscale score, PANSS general pathological subscale score, agitation labelled as “adverse effect” Adverse effects. Unable to use- Adverse effects: TESS score, blood and urine routine, liver function, blood glucose (no data)
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.

Ye 2005 (Continued)

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.
Selective reporting (reporting bias)	High risk	Data on TESS total score and blood and urine routine, liver function, blood glucose were missing
Other bias	Low risk	None obvious.

Ye 2005a

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: one week washout + six weeks intervention. Design: parallel. Setting: inpatient, China.	
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. BPRS of 40 or more. N = 60. Age: aripiprazole group: 18- 65 years, mean = (28.3 ± 10.6) years; olanzapine group: 18 ~ 56 years, mean = (26.5 ± 11.3) years Gender: aripiprazole group: 20 male, 10 female; olanzapine group: 19 male, 11 female. History: aripiprazole group: 0.3~ 18 years, mean = (6.3 ± 6.9) years; olanzapine group: 0.5 ~ 15 years, mean = (5.7 ± 6.1) years. Age at onset not reported	
Interventions	1. Aripiprazole: Dose range: 10-30 mg/day. Mean dose: not reported. N = 30. 2. Olanzapine: Dose range: 5-10 mg/day. Mean dose: not reported. N = 30	
Outcomes	Global state: PANSS score decreased rate (recovery: 80≥ %, markedly improved: 60%-70%, improved: 30%-59%, no effect: < 30%). CGI score Mental state: PANSS total decreased score, PANSS positive decreased subscale score, PANSS negative decreased subscale score, PANSS psychopathological decreased subscale score Leaving the study early. Adverse effects. Unable to use - Adverse effects: TESS total score, blood and urine routine, weight gain, extrapyramidal effects, constipation, somnolence, use of benzodiazepines and other medicine (no data)	
Notes		
Risk of bias		
Bias	Authors' judgement	Support for judgement

Ye 2005a (Continued)

Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Two people were lost to follow-up (1/30 VS.1/30) in the two groups, one because of early discharge, one due to refusing further therapy
Selective reporting (reporting bias)	High risk	Data on TESS total score, blood and urine routine, weight gain, extrapyramidal effects, constipation, somnolence, use of benzodiazepines and other medicine were missing
Other bias	Low risk	None obvious.

Yi 2007

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: twelve weeks. Design: parallel. Setting: inpatients, China.
Participants	Diagnosis: schizophrenia (CCMD-3). N = 60. Age: mean = (30.1 ± 9.7) years. Gender: 34 male, 26 female. History: mean = (32 ± 10.5) years. Age at onset: mean = (29.7 ± 9.5) years
Interventions	1. Aripiprazole: Dose range: 10-30 mg/day. Mean = (17.6 ± 4.5) mg/day. N = 30. 2. Clozapine: Dose range: 300-600 mg/day. Mean = (370 ± 82) mg/day. N = 30
Outcomes	Adverse events: Fasting plasma glucose (FPG), C-peptide.
Notes	
<i>Risk of bias</i>	

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Unclear if there were incomplete data.
Selective reporting (reporting bias)	Low risk	No selective reporting.
Other bias	Low risk	None obvious.

Yu 2006

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: eight weeks. Design: parallel. Setting: inpatient, China.
Participants	Diagnosis: treatment resistant schizophrenia (CCMD-3). PANSS score of 60 or more. N = 53. Age: aripiprazole group: 18- 59 years, mean = (32.8 ± 6.2) years; clozapine group: 17 ~ 58 years, mean = (30.6 ± 7.8) years. Gender: aripiprazole group: 17 male, 9 female; clozapine group: 10 male, 12 female . History: aripiprazole group: 1 month-9 years, mean = (4.2 ± 3.9) years; clozapine group: 1 month- 11years, mean = (5.2 ± 3.4) years. Age at onset not reported
Interventions	1. Aripiprazole: Dose range: 5-30 mg/day. Mean = (15 ± 5) mg/day. N = 26. 2. Clozapine: Dose range: 50-500 mg/day. Mean = (400 ± 125) mg/day. N = 22
Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 75%, markedly improved: 50%-75%, improved: 25%-50%, no effect: < 25%) Mental state: PANSS positive subscale score, PANSS negative subscale score Adverse effects. Unable to use - Leaving the study early: 5 people dropped out, but it did not report which group they were from

Yu 2006 (Continued)

	Adverse effects: TESS total score and hepatorenal function (no data)	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	High risk	Five people were excluded from analysis due to incomplete outcome data. It is unclear which group these 5 people belonged to
Selective reporting (reporting bias)	High risk	Data on TESS total score and hepatorenal function were missing
Other bias	Low risk	None obvious.

Yu 2006a

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: eight weeks. Design: parallel. Location: inpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). N = 74. Age: aripiprazole group: mean = (23.69 ± 11.67) years; clozapine group: mean = (25.61 ± 6.4) years. Gender: aripiprazole group: 18 male, 18 female; clozapine group: 19 male, 19 female . History: aripiprazole group: mean = (7.5 ± 2.3) months; clozapine group: mean = (8.92 ± 3.3) months. Age at onset not reported

Yu 2006a (Continued)

Interventions	1. Aripiprazole: Dose range: 10-40 mg/day. Mean dose: not reported. N = 36. 2. Clozapine: Dose range: 75-550 mg/day. Mean dose: not reported. N = 38	
Outcomes	Adverse effect: change of ECG and blood glucose.	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Unclear if there was incomplete data.
Selective reporting (reporting bias)	Low risk	No selective reporting.
Other bias	Low risk	None obvious.

Yu 2007

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: eight weeks. Design: parallel. Location: inpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS score of 60 or more. N = 74. Age: aripiprazole group: mean = (23.69 ± 11.67) years; clozapine group: mean = (25.61 ± 6.4) years. Gender: aripiprazole group: 18 male, 18 female; clozapine group: 19 male, 19 female. History: aripiprazole group: mean = (7.5 ± 2.3) months; clozapine group: mean = (8.92 ± 3.3) months. Age at onset not reported

Interventions	1. Aripiprazole: Dose range: 10-40 mg/day. Mean dose: not reported. N = 36. 2. Clozapine: Dose range: 75-550 mg/day. Mean dose: not reported. N = 38	
Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 75%, markedly improved: 50%-75%, improved: 25%-50%, no effect: < 25%) Mental state: PANSS total score, PANSS positive subscale score, PANSS negative subscale score Adverse effect. Unable to use - Adverse effects: TESS total score, liver function and blood glucose (no data) Mental state: BPRS and PANSS subscale scores - unvalidated subscales	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.
Selective reporting (reporting bias)	High risk	Although TESS was used to assess adverse effects, no data on scores were available. Data on liver function and blood glucose were missing
Other bias	Low risk	None obvious.

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: eight weeks. Design: parallel. Setting: inpatient, China.	
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 100. Age: aripiprazole group: 18- 65 years, mean = (36.3 ± 4.1) years; risperidone group: 16 ~ 60 years, mean = (34.5 ± 12.7) years Gender: aripiprazole group: 32 male, 18 female; risperidone group: 30 male, 20 female. History: aripiprazole group: 3 months- 10 years, mean = (3.0 ± 1.9) years. risperidone group: 2 months- 15 years, mean = (3. 2 ±2. 5) years. Age at onset not reported	
Interventions	1. Aripiprazole: Dose range: 5-30 mg/day. Mean= (22.3 ± 3.2) mg/day. N = 50. 2. Risperidone: Dose range: 1-6 mg/day. Mean= (3.8 ±1.33) mg/day. N = 50	
Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 75%, markedly improved: 50%-74%, improved: 25%-49%, no effect: < 25%) Mental state: PANSS total score, PANSS positive subscale score, PANSS negative subscale score, PANSS general pathological subscale score Adverse effects. Unable to use- Adverse effects: TESS score, blood and urine routine, renal function (no data)	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.
Selective reporting (reporting bias)	High risk	Data on TESS score, blood and urine routine, and renal function were missing

Yu 2008 (Continued)

Other bias	Low risk	None obvious.
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Yu 2009

Methods	Allocation: randomised, stratified random. Blindness: unclear. Duration: twelve weeks. Design: parallel. Setting: inpatients, China.
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS total score of 60 or more. N = 60. Age: aripiprazole group: 22- 57 years, mean = (34. 63 ± 9. 86) years; clozapine group: 23 - 59 years, mean = (9. 49 ± 4.33) years. Gender: aripiprazole group: 19 M, 11 F; clozapine group: 22 M, 8 F. History: aripiprazole group: 5- 21 years, mean = (9.15 ± 4.31) years; clozapine group: 5.25- 23 years, mean = (9.49 ± 4.33) years. Age at onset not reported
Interventions	1. Aripiprazole: Dose range: 5-30 mg/day. Mean = (16.75 ± 3.55) mg/day. N = 30. 2. Clozapine: Dose range: 50-600 mg/day. Mean = (398.33 ± 74.84) mg/day. N = 30
Outcomes	Mental state: PANSS total score, PANSS positive subscore, PANSS negative subscore Adverse effects. Unable to use - Adverse effects: TESS total score, EEG, and drugs for adverse events (no data)
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Stratified randomisation.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.

Yu 2009 (Continued)

Selective reporting (reporting bias)	High risk	Although TESS was used to assess adverse effects, no data on scores were available. Data on EEG and drugs for adverse events were missing
Other bias	Low risk	None obvious.

Yu ZG 2007

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: eight weeks. Design: parallel. Setting: inpatients, China.
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS total score of 60 or more. N = 60. Age: aripiprazole group: 18- 54 years, mean = (34. 5 ± 4.7) years; clozapine group: 18 - 51 years, mean = (33.6 ± 5.2) years. Gender: aripiprazole group: 17 M, 13 F; clozapine group: 18 M, 12 F. History: aripiprazole group: 4 months- 6 years; clozapine group: 2 months- 4 years . Age at onset not reported
Interventions	1. Aripiprazole: Dose range: 5-30 mg/day. Mean = (22.1 ± 3.4) mg/ day. N = 30. 2. Clozapine: Dose range: 50-500 mg/day. Mean = (336 ± 4.7) mg/ day. N = 30
Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 75%, markedly improved: 50%-74%, improved: 25%-49%, no effect: < 25%) Mental state: PANSS total score. PANSS positive subscale score, PANSS negative subscale score, PANSS general psychogenic pathological subscale score Adverse effects. Unable to use - Adverse effects: blood routine, urine routine, blood glucose, and hepatorenal function (no data)
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.

Yu ZG 2007 (Continued)

Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.
Selective reporting (reporting bias)	High risk	Data on blood routine, urine routine, blood glucose, and hepatorenal function were missing
Other bias	Low risk	None obvious.

Zhang 2006

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: eight weeks. Design: parallel. Location: inpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS total score of 60 or more. N = 112. Age: aripiprazole group: 15~ 60 years, mean = (25.7 ± 7.9) years; risperidone group: 15~ 60 years, mean = (26.1 ± 8.2) years. Gender: aripiprazole group: 30 Male, 26 Female; Risperidon group: 29 Male, 27 Female History: aripiprazole group: 1 month- 10 years, mean = (4.8 ± 2.6) years; risperidone group: 1 month- 9 years, mean = (4.6 ± 2.8) years. Age at onset not reported
Interventions	1. Aripiprazole: Dose range: 5-30 mg/day. Mean = (21.4 ± 3.1) mg/day. N = 56. 2. Risperidone: Dose range: 1-6 mg/day. Mean = (3.9 ± 1.7) mg/day. N = 56
Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 75%, markedly improved: 50%-75%, improved: 30%-50%, no effect: < 30%) Mental state: PANSS total score, PANSS score decreased rate: PANSS positive subscore, PANSS negative subscore, PANSS cognitive score, PANSS excited subscore, PANSS depressed subscore Adverse effects. Unable to use - Adverse effects: TESS total score, use of benzhexol and benzodiazepines (no data)
Notes	

Zhang 2006 (Continued)

<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	There were no incomplete data.
Selective reporting (reporting bias)	High risk	Although TESS was used to assess adverse effects, no data on scores were available. Data on use of benzhexol and benzodiazepines were missing
Other bias	Low risk	None obvious.

Zhang 2006a

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: one week washout + eight weeks intervention. Design: parallel. Setting: inpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 104. Age: aripiprazole group: 18- 62 years, mean = (28.1 ± 6.3) years; olanzapine group: 19 - 65 years, mean = (32.6 ± 5.4) years Gender: aripiprazole group: 29 male, 23 female; olanzapine group: 27 male, 25 female. History: aripiprazole group: mean = (2.8 ± 4.6) years; olanzapine group: mean = (3.5 ± 5.2) years. Age at onset not reported
Interventions	1. Aripiprazole: Dose range: 5-25 mg/day. Mean = (16.53 ± 4.7) mg/day. N = 52. 2. Olanzapine: Dose range: 5-25 mg/day. Mean = (17.3 ± 6.4) mg/day. N = 52

Zhang 2006a (Continued)

Outcomes	Global state: PANSS score decreased rate (recovery: $80 \geq$ %, markedly improved: 50%-80%, improved: 30%-50%, no effect: $< 30\%$) Mental state: PANSS total score, PANSS positive subscale score, PANSS negative subscale score, PANSS psychopathological subscale score Adverse effects.	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.
Selective reporting (reporting bias)	High risk	Data on blood and urine routine, liver function, ECG, use of benzodiazepines and benzhexol were missing
Other bias	Low risk	None obvious.

Zhang 2007

Methods	<p>Allocation: randomised, no further details.</p> <p>Blindness: unclear.</p> <p>Duration: eight weeks.</p> <p>Design: parallel.</p> <p>Location: inpatient, China.</p>
Participants	<p>Diagnosis: schizophrenia (CCMD-3).</p> <p>N = 97.</p> <p>Age: aripiprazole group: 18- 74 years, mean = (31.7 ± 11.6) years; clozapine group: 18 ~ 67 years, mean = (34.3 ± 11.4) years</p> <p>Gender: aripiprazole group: 24 male, 26 female; clozapine group: 23 male, 24 female.</p> <p>History: aripiprazole group: mean = (7.4 ± 6.1) years; clozapine group: mean = $(7.4 \pm 4.$</p>

Zhang 2007 (Continued)

	2) months. Age at onset not reported. Setting: inpatient.	
Interventions	1. Aripiprazole: Dose range: 5-30 mg/day. Mean dose:not reported. N = 50. 2. Clozapine: Dose range: 25-400 mg/day. Mean dose:not reported. N = 47	
Outcomes	Adverse effect: change of ECG (ECG abnormal, tachycardia and others)	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Unclear if there were incomplete data.
Selective reporting (reporting bias)	Low risk	No selective reporting.
Other bias	Low risk	None obvious.

Zhang 2007a

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: eight weeks. Design: parallel. Location: inpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS total score of 60 or more. N = 50. Age: aripiprazole group: mean = (10.07 ± 2.35) years; risperidone group: mean = (9.37 ± 4.08) years. Gender: aripiprazole group: 11 Male, 14 Female; risperidone group: 10 Male, 15 Female .

	History: aripiprazole group: mean = (1.64 ± 3.74) months; risperidone group: mean = (1.87 ± 2.96) months. Age at onset not reported	
Interventions	1. Aripiprazole: Dose range: 5-20 mg/day. Mean dose: not reported. N = 25. 2. Risperidone: Dose range: 1-4 mg/day. Mean dose: not reported. N = 25	
Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 75%, markedly improved: 50%-75%, improved: 25%-50%, no effect: < 25%) Mental state: PANSS total score, PANSS positive subscale score, PANSS negative subscale score, PANSS general psychogenic pathological subscale score Adverse effects. Unable to use - Adverse effects: blood and urine routines, EEG, use of anticholinergic drug and benzodiazepines (no data)	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.
Selective reporting (reporting bias)	High risk	Data on blood and urine routines, EEG, use of anticholinergic drug and benzodiazepines were missing
Other bias	Low risk	None obvious.

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: six weeks. Design: parallel. Setting: outpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). BPRS of 35 or more. N = 60. Age: aripiprazole group: mean = (28.2 ± 10.3) years; risperidone group: mean = (27.8 ± 9.6) years Gender: aripiprazole group: 20 male, 10 female; risperidone: 20 male, 10 female. History: aripiprazole group: mean = (2.6 ± 10.8) years; risperidone group: mean = (2.8 ± 2.0) years. Age at onset not reported
Interventions	1. Aripiprazole: Dose range: 5-25 mg/day. mean = (16.5 ± 5.5) mg/day. N=30. 2. Risperidone: Dose range: 1-5mg/day. mean = (3.8 ± 1.6) mg/day. N=30
Outcomes	Global state: BPRS score decreased rate (recovery: ≥75%, markedly improved: 50%-75%, improved: 30%-50%, no effect: < 30%) Mental state: BPRS score. Leaving the study early: no patient. Adverse effect: TESS total score. Unable to use - Various specific adverse effects (no data).
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.
Selective reporting (reporting bias)	High risk	Data on various specific adverse effects were missing.

Zhang 2007b (Continued)

Other bias	Low risk	None obvious.
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Zhang 2008

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: one week washout period + eight weeks intervention. Design: parallel. Setting: inpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 60. Age: aripiprazole group: mean = (36.3 ± 8.2) years; risperidone group: mean = (37.3 ± 8.7) years Gender: aripiprazole group: 23 male, 7 female; risperidone: 21 male, 9 female. History: aripiprazole group: 1 month-30 years; risperidone group: 2 months - 29 years. Age at onset not reported
Interventions	1. Aripiprazole: Dose range: 5-30 mg/day. Mean dose: not reported. N = 30. 2. Risperidone: Dose range: 1-6 mg/day. Mean dose: not reported. N = 30
Outcomes	Global state: PANSS score decreased rate (recovery: ≥75%, markedly improved: 50%-75%, improved: 25%-50%, no effect: < 25%). CGI score Mental state: PANSS total score, PANSS positive subscore, PANSS negative subscore Adverse effects. Unable to use - Adverse effects: TESS total score(no data).
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.

Zhang 2008 (Continued)

Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.
Selective reporting (reporting bias)	High risk	Although ESRS was used to assess adverse effects, no data on scores were available
Other bias	Low risk	None obvious.

Zhang 2008a

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: six weeks. Design: parallel. Location: inpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS total score of 60 or more. N = 60. Age: aripiprazole group: 18-58 years, mean = (32.8 ± 6.9) years; risperidone group: 20-56 years, mean = (33.4 ± 5.8) years. Gender: aripiprazole group: 18 Male, 12 Female; risperidone group: 16 Male, 14 Female. History: aripiprazole group: 1 month-8 years, mean = (4.8 ± 3.2) years; risperidone group: 2 months-7 years, mean = (4.6 ± 3.8) years. Age at onset not reported
Interventions	1. Aripiprazole: Dose range: 10-30 mg/day. Mean = (15 ± 5) mg/day. N = 30. 2. Risperidone: Dose range: 1-6 mg/day. Mean = (3.5 ± 1.6) mg/day. N = 30
Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 75%, markedly improved: 50%-75%, improved: 30%-50%, no effect: < 30%) Mental state: PANSS total score. Adverse effects. Unable to use - Adverse effects: TESS total score, blood and urine routine, liver function (no data)
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.

Zhang 2008a (Continued)

Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.
Selective reporting (reporting bias)	High risk	Although ESRS was used to assess adverse effects, no data on scores were available
Other bias	Low risk	None obvious.

Zhang 2008b

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: six weeks. Design: parallel. Location: inpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). N = 40. Age: aripiprazole group: 18-58 years, mean = (33.2 ± 7.8) years; risperidone group: 18-65 years, mean = (34.5 ± 8.7) years. Gender: aripiprazole group: 8 Male, 12 Female; risperidone group: 10 Male, 10 Female History: aripiprazole group: 1 month-5 years, mean = (2.8 ± 3.6) years; risperidone group: 2 months-7 years, mean = (3.7 ± 4.2) years. Age at onset not reported
Interventions	1. Aripiprazole: Dose range: 5-30 mg/day. Mean = (10 ± 5.22) mg/day. N = 20. 2. Risperidone: Dose range: 1-6 mg/day. Mean = (3.5 ± 0.8) mg/day. N = 20
Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 75%, markedly improved: 50%-75%, improved: 20%-50%, no effect: < 25%) Mental state: PANSS total score, PANSS positive subscale score, PANSS negative subscale score, PANSS general psychogenic pathological subscale score Adverse effects. Unable to use - Adverse effects: TESS total score, endocrine change, laboratory tests (no data)
Notes	
<i>Risk of bias</i>	

Zhang 2008b (Continued)

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.
Selective reporting (reporting bias)	High risk	Data on TESS score, endocrine change, laboratory tests were missing. No data of Quality of life GQOLI - 74
Other bias	Low risk	None obvious.

Zhang 2009

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: twelve weeks. Design: parallel. Setting: not reported, China.
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. Refractory schizophrenia (TRS). N = 72. Age: aripiprazole group: 25-54 years, mean = 34.4years; clozapine group: 24-58 years, mean = 33.8 years. Gender: aripiprazole group: 21 female, 15 male; clozapine group: 22 male, 14 female. History: aripiprazole group: 5.8-26 years, mean = 8.6 years; clozapine group: 5.5-28 years, mean = 8.9 years. Age at onset not reported
Interventions	1. Aripiprazole: Dose range: 10-30 mg/day. Mean dose: not reported. N = 36. 2. Clozapine: Dose range: 200-500 mg/day. Mean dose: not reported. N = 36
Outcomes	Global state: PANSS score decreased rate (recovery: > 75%, markedly improved: 51%-74%, improved: 26%-50%, no effect: < 25%) Mental state: PANSS total score. PANSS positive subscale score, PANSS negative subscale score, PANSS general psychogenic pathological subscale score

Zhang 2009 (Continued)

	Adverse effects.	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.
Selective reporting (reporting bias)	High risk	Data on TESS, use of benzhexol and benzodiazepines were missing
Other bias	Low risk	None obvious.

Zhang 2009a

Methods	Allocation: randomised, random number table. Blindness: single. Duration: eight weeks. Design: parallel. Setting: inpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 60. Age: aripiprazole group: mean = (31.3 ± 8.7) years; risperidone group: mean = (30.4 ± 8.7) years Gender: 60 male. History: not reported. Age at onset not reported.
Interventions	1. Aripiprazole: Dose range: 5-20 mg/day. Mean dose: not reported. N = 30. 2. Risperidone: Dose range: 1-4 mg/day. Mean dose: not reported. N = 30

Zhang 2009a (Continued)

Outcomes	Mental state: PANSS total score. Adverse effects: blood glucose and cholesterol.	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, random number table.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Single, if the blinding was performed well was unknown.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	unclear if there were no incomplete data.
Selective reporting (reporting bias)	Low risk	No evidence of selective reporting.
Other bias	Low risk	None obvious.

Zhang 2009b

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: one week wash out + eight weeks intervention. Design: parallel. Setting: inpatient and outpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 60. Age: aripiprazole group: mean = (37 ± 7) years; risperidone group: mean = (36 ± 7) years Gender: aripiprazole group: 18 male, 12 female; risperidone group: 19 male, 11 female. History: not reported. Age at onset not reported.
Interventions	1. Aripiprazole: Dose range: 10-30 mg/day. Mean dose: not reported. N = 30. 2. Risperidone: Dose range: 4-6 mg/day. Mean dose: not reported. N = 30

Zhang 2009b (Continued)

Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 75%, markedly improved: 50%-74%, improved: 25%-49%, no effect: < 25%) Mental state: PANSS total score, PANSS positive subscale score, PANSS negative subscale score,PANSS general pathological subscale score, PANSS general psychogenic pathological subscale score Adverse effects. Unable to use - Adverse effects: TESS total score, blood and urine routine, blood glucose, use of benzo-diazepines and other medicines (no data)	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.
Selective reporting (reporting bias)	High risk	Data on TESS total score, blood and urine routine, blood glucose, use of benzodiazepines and other medicines were missing
Other bias	Low risk	None obvious.

Zhang 2010

Methods	<p>Allocation: Random permutation table.</p> <p>Blindness: unclear.</p> <p>Duration: eight weeks.</p> <p>Design: parallel.</p> <p>Setting: inpatient, China.</p>
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Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more.Refractory schizophrenia (TRS). N = 120. Age: aripiprazole group 18- 55 years, mean= 33 years; clozapine group: 21- 53 years, mean = 34 years. Gender: aripiprazole group: 21 female, 15 male; clozapine group: 22 male, 14 female. History: aripiprazole group: 2- 16 years, mean = 7 years; clozapine group: 4- 19 years, mean = 6 years. Age at onset not reported	
Interventions	1. Aripiprazole: Dose range: 20-30 mg/day. Mean= (22. 1 ± 5. 4) mg/day. N = 60. 2. Clozapine: Dose range: 300-600 mg/day. Mean= (354. 5 ± 84. 9) mg/day. N = 60	
Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 75%, markedly improved: 50%-74%, improved: 25%-49%, no effect: < 25%) Mental state: PANSS total score. PANSS positive subscale score, PANSS negative subscale score, PANSS general psychogenic pathological subscale score Adverse effects: central nervous system (headache, insomnia, somnolence), gastrointestinal(nausea, constipation), weight gain, extrapyramidal side-effects (tremor, akathisia), tachycardia Unable to use - Adverse effects: TESS total score, use of benzhexol and benzodiazepines (no data). The data of at least one adverse effect	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Random permutation table.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	No incomplete data.
Selective reporting (reporting bias)	High risk	Although TESS was used to assess adverse effects, no data on scores were available. Data on use of benzhexol and benzodiazepines were missing

Zhang 2010 (Continued)

Other bias	Low risk	None obvious.
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Zhang 2010a

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: eight weeks. Design: parallel. Setting: inpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 100. Age: 19- 64 years. Gender: not reported. History: not reported. Age at onset not reported.
Interventions	1. Aripiprazole: Dose range: 5-25 mg/day. Mean dose: not reported. N = 50. 2. Risperidone: Dose range: 1-4 mg/day. Mean dose: not reported. N = 50
Outcomes	Mental state: PANSS total score. Adverse effects: TESS total score, Unable to use - Quality of life: GQOLI - 74 Adverse effects: anxiety, EPS, ECG abnormal, mouth dry, liver function, use of benzo-diazepines and other medicines
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Unclear if there were incomplete data.

Zhang 2010a (Continued)

Selective reporting (reporting bias)	High risk	Data on GQOLI - 74 score, anxiety, EPS, ECG abnormal, mouth dry, liver function, use of benzodiazepines and other medicines were missing
Other bias	Low risk	None obvious.

Zhao 2006

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: eight weeks. Design: parallel. Setting: inpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 68. Age: aripiprazole group: mean = (24.3 ± 9.4) years; quetiapine group: 18-51 years, mean = (26.7 ± 8.4) years Gender: male and female History: aripiprazole group: mean = (23 ± 13) months; quetiapine group: mean = (4.5 ± 2.9) years. Age at onset not reported
Interventions	1. Aripiprazole: Dose range: 10-30 mg/day. Mean dose = not reported. N = 34. 2. Quetiapine: Dose range: 100-750 mg/day. Mean dose = (465 ± 132) mg/day. N = 34
Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 75%, markedly improved: 50%-75%, improved: 30%-50%, no effect: < 30%) Mental state: PANSS total score. Unable to use - Mental state: PANSS positive subscale score, PANSS negative subscale score, PANSS general psychogenic pathological subscale score
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not described.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not described.

Zhao 2006 (Continued)

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not described.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete outcome data.
Selective reporting (reporting bias)	High risk	TESS score was measured, but not reported.
Other bias	Low risk	None obvious.

Zhao 2007

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: eight weeks. Design: parallel. Setting: inpatient, China.	
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 80. Age: aripiprazole group: 17- 62 years, mean = (29.5 ± 11.7) years; risperidone group: 16 - 60 years, mean = (29.3 ± 10.6) years. Gender: aripiprazole group: 19 Male, 21 Female; risperidone group: 21 Male, 19 Female. History: aripiprazole group: 1 month- 10 years, mean =6.4 years; risperidone group: 1. 5 months- 13 years, mean = 6.3 years. Age at onset not reported	
Interventions	1. Aripiprazole: Dose range: 5-30 mg/day. Mean: not reported. N = 40. 2. Risperidone: Dose range: 0.5-6 mg/day. Mean: not reported. N = 40	
Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 75%, markedly improved: 50%-75%, improved: 25%-50%, no effect: < 25%) Mental state: PANSS total score, PANSS positive subscale score, PANSS negative subscale score, PANSS general pathological subscale score. agitation labelled as “adverse effect” Adverse effects.	
Notes		
<i>Risk of bias</i>		
Bias	Authors’ judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.

Zhao 2007 (Continued)

Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.
Selective reporting (reporting bias)	High risk	Data on TESS score, use of benzodiazepines, benzhexol and propranolol were missing
Other bias	Low risk	None obvious.

Zhi 2005

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: eight weeks. Design: parallel. Setting: inpatient, China.	
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 80. Age: aripiprazole group: 18- 35 years, mean = (22.0 ± 6.08) years; risperidone group: 18 ~ 33 years, mean = (24.56 ± 8.68) years. Gender: 80 female. History: aripiprazole group: 1 month- 15 years, mean = (8.42 ± 6.83) years; risperidone group: 1 month- 14 years, mean = (8.02 ± 7.32) years. Age at onset not reported	
Interventions	1. Aripiprazole: Dose range: 5-30 mg/day. Mean = (21.0 ± 6. 17) mg/day. N = 40. 2. Risperidone: Dose range: 1-6 mg/day. Mean = (4.46 ± 1.03) mg/day. N = 40	
Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 75%, markedly improved: 50%-75%, improved: 25%-50%, no effect: < 25%) Mental state: PANSS total score, PANSS positive subscale score, PANSS negative subscale score, PANSS general pathological subscale score Adverse effects.	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement

Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.
Selective reporting (reporting bias)	High risk	Data on TESS total score, use of benzodiazepines, benzhexol and propranolol were missing
Other bias	Low risk	None obvious.

Zhou 2007

Methods	Allocation: Random permutation table. Blindness: unclear. Duration: one week washout period + eight weeks intervention. Design: parallel. Setting: inpatient and outpatient patient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 92, complete study: N = 90. Age: aripiprazole group: mean = (35.2 ± 8.5) years; clozapine group: mean = (34.3 ± 7.9) years. Gender: aripiprazole group: 20 female, 25 male; clozapine: 23 male, 22 female. History: aripiprazole group: mean = (3.3 ± 2.8) years; clozapine group: mean = (3.4 ± 2.9) years. Age at onset not reported
Interventions	1. Aripiprazole: Dose range: 5-30 mg/day. Mean dose: not reported. N = 45. 2. Clozapine: Dose range: 50-400 mg/day. Mean dose: not reported. N = 47
Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 75%, markedly improved: 50%-74%, improved: 25%-49%, no effect: < 25%) Mental state: PANSS total score. anxiety - labelled as "adverse effect" Leaving the study early. Adverse effects. Unable to use - Mental state: PANSS negative subscore, cognitive factor, affective symptoms (no data)

Zhou 2007 (Continued)

	Adverse effects: TESS total score, hepatorenal function, use of benzhexol and benzodiazepines (no data)	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Random permutation table.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.
Selective reporting (reporting bias)	High risk	Data on TESS score, PANSS negative subscore, cognitive factor, affective symptoms, hepatorenal function, use of benzhexol and benzodiazepines were missing
Other bias	Low risk	None obvious.

Zhou 2007a

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: six weeks. Design: parallel. Setting: inpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 62. Age: aripiprazole group: mean = (37.5 ± 8.1) years; risperidone group: mean = (39.2 ± 10.3) years. Gender: aripiprazole group: 9 Male, 22 Female; risperidone group: 7 Male, 24 Female. History: not reported. Age at onset not reported.

Interventions	1. Aripiprazole: Dose range: 5-30 mg/day. Mean = 10.2 mg/day. N = 31. 2. Risperidone: Dose range: 0.5-6 mg/day. Mean = 3.5 mg/day. N = 31	
Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 75%, markedly improved: 50%-75%, improved: 25%-50%, no effect: < 25%) Mental state: PANSS total score, PANSS positive subscale score, PANSS negative subscale score, PANSS general pathological subscale score Adverse effects. Unable to use - Adverse effects: TESS total score, use of benzodiazepines and anticholinergic medication (no data)	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	There were no incomplete data.
Selective reporting (reporting bias)	High risk	Data on TESS total score, use of benzodiazepines and anticholinergic medication were missing
Other bias	Low risk	None obvious.

Zhou 2007b

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: eight weeks. Design: parallel. Setting: inpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 60. Age: 18- 60 years. Gender: aripiprazole group: 20 male, 10 female; risperidone group: 18 male, 12 female. History: not reported. Age at onset not reported.
Interventions	1. Aripiprazole: Dose range: 5-25 mg/day. Mean dose: not reported. N = 30. 2. Risperidon: Dose range: 1-4 mg/day. Mean dose: not reported. N = 30
Outcomes	Mental state: PANSS total score. Adverse effects. Unable to use - Quality of life: GQOLI - 74 (no data). Adverse effects: use of benzodiazepines and other medicines (no data)
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Unclear if there were no incomplete data.
Selective reporting (reporting bias)	High risk	Data on GQOLI - 74 score, use of benzodiazepines and other medicines were missing
Other bias	Low risk	None obvious.

Zhou 2008

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: eight weeks. Design: multi-centre, parallel. Setting: inpatient, China.	
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. N = 140. Age: aripiprazole group: 10- 50 years, mean = (28.7 ± 7.8) years; risperidone group: 18 - 49 years, mean = (28.1 ± 7.8) years. Gender: aripiprazole group: 36 Male, 34 Female; risperidone group: 35 Male, 35 Female. History: aripiprazole group: 1 month- 3 years, mean = (3.0 ± 1.4) years; risperidone group: 1 month- 3 years, mean = (3.1 ± 2.3) years. Age at onset not reported	
Interventions	1. Aripiprazole: Dose range: 10-30 mg/day. Mean = (22. 4 ± 3. 4) mg/day. N = 70. 2. Risperidone: Dose range: 1-4 mg/day. Mean dose = (4. 3 ± 1. 7) mg/day. N = 70	
Outcomes	Global state: PANSS score decreased rate (recovery: ≥ 75%, markedly improved: 50%-75%, improved: 25%-50%, no effect: < 25%) Mental state: PANSS total score. PANSS positive subscale score, PANSS negative subscale score, PANSS general psychogenic pathological subscale score Adverse effects. Unable to use: Adverse effects: TESS total score, EEG, use of benzodiazepines, benzhexol and propranolol (no data)	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	There were no incomplete data.

Zhou 2008 (Continued)

Selective reporting (reporting bias)	High risk	Data on TESS total score, EEG, use of benzodiazepines, benzhexol and propranolol were missing
Other bias	Low risk	None obvious.

Zhu 2005

Methods	Allocation: randomised, no further details. Blindness: single. Duration: eight weeks. Design: parallel. Setting: inpatient and outpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). BPRS total score of 40 or more. N = 80. Age: aripiprazole group: 16~ 57 years, mean = (28.3 ± 10.2) years; clozapine group: 17 ~ 58 years, mean = (27.8 ± 8.2) years. Gender: aripiprazole group: 22 M, 18 F; clozapine group: 20 M, 20 F. History: aripiprazole group: 2 months~ 8 years, mean = (6.2 ± 3.7) years; clozapine group: 3 months~ 9 years, mean = (6.7 ± 5.8) years. Age at onset not reported
Interventions	1. Aripiprazole: Dose range: 5-20 mg/day. Mean dose: not reported. N = 40. 2. Clozapine: Dose range: 50-500 mg/day. Mean dose: not reported. N = 40
Outcomes	Global state: PANSS score decreased rate (markedly improved: ≥60%, improved: 20%-59%, no effect: < 20%) Mental state: PANSS total score. PANSS positive subscale score, PANSS negative subscale score, PANSS general pathological subscale score. BPRS total score Adverse effects.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Single blind, but whether the blindness was performed well was unclear

Zhu 2005 (Continued)

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	There were drop-outs, but specific digital was not obtained.
Selective reporting (reporting bias)	High risk	Data on blood and urine routine, liver function were missing
Other bias	Low risk	None obvious.

Zhu 2008

Allocation: randomised, no further details.
 Blindness: unclear.
 Duration: six weeks.
 Design: parallel.
 Setting: inpatient, China.

Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. BPRS of 40 or more.
 N = 60.
 Age: aripiprazole group: 18- 65 years. mean = (28.3 ± 10.6) years; quetiapine group: 18-56 years, mean = (26.5 ± 11.3) years
 Gender: aripiprazole group: 20 male, 10 female; quetiapine group: 19 male, 11 female.
 History: aripiprazole group: mean = (6.3 ± 6.9) years; quetiapine group: mean = (5.7 ± 6.1) years. Age at onset not reported

1. Aripiprazole: Dose range: 10-30 mg/day. Mean dose: not reported. N = 30.
 2. Quetiapine: Dose range: 200-700 mg/day. Mean dose: not reported. N = 30

Global state: PANSS score decreased rate (recovery: ≥ 80%, markedly improved: 50%-80%, improved: 30%-50%, no effect: < 30%)
 Mental state: PANSS total score. PANSS positive subscale score, PANSS negative subscale score, PANSS general psychogenic pathological subscale score. BPRS total score

Notes

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.

Zhu 2008 (Continued)

Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Total proportion of drop-out was 3.3% and the data of the two groups were balanced (1/30: 1/30)
Selective reporting (reporting bias)	High risk	Data on CGI score, TESS total score, akathisia, tremor, insomnia, constipation, drowsiness sleepiness, weight gain, EEG, blood routine, urine routine, use of benzo-diazepine and propranolol were missing
Other bias	Low risk	None obvious.

Zhu 2010

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: six months. Design: trial with three arms. Setting: inpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS of 60 or more. SANS of 60 or more. N = 81; Number of people completed study: N = 76. Age: 40- 65 years. Gender: not reported. History: not reported. Age at onset not reported.
Interventions	1. Aripiprazole: Dose range: 10-30 mg/day. Mean = (18.3 ± 2.9) mg/day. N: not reported, complete study: N = 22. 2. Risperidone: Dose range: 1-5 mg/day. Mean = (4.2 ± 0.4) mg/day. N: not reported, complete study: N = 28 3. Olanzapine: Dose range: 5-20 mg/day. Mean = (12.6 ± 2.6) mg/day. N: not reported, complete study: N = 26
Outcomes	Mental state: PANSS total score, PANSS positive subscale score, PANSS negative subscale score, PANSS general psychogenic pathological subscale score. SANS total score Adverse effects. Unable to use - BPRS and SANS subscale score - unvalidated subscales. Leaving the study early - unclear from which group people were dropped out

Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.
Incomplete outcome data (attrition bias) All outcomes	High risk	The total proportion of loss to follow-up was 6.2% (5 people), but it was unclear proportion in every group
Selective reporting (reporting bias)	High risk	Data on TESS total score, use of benzodiazepines and other medicines were missing
Other bias	Low risk	None obvious.

Zimbroff 2007

Methods	Allocation: random, computer-generated, centre blocked Blindness: double, dummy administration. Duration: four weeks. Location: multicentre.
Participants	Diagnosis: schizophrenia or schizoaffective disorder (DSM-IV). N = 256. Age: 18-70 years. Gender: 169 M, 57 F. History: duration of illness not reported, age at onset not reported, hospitalised > 14 consecutive days prior to screening, PANSS $\geq$ 80, 4/more on 2+ PANSS positive items, score of $\geq$ 4 on CGI-S Setting: inpatient.
Interventions	1. Aripiprazole: dose 15 mg/day first 14 days, up to 30 mg/day thereafter, mean 21 mg/day (SD 7). N = 129. 2. Ziprasidone: dose 80 mg/day on first 14 days, up to 160 mg/day thereafter mean 149 mg/day (SD 25): N = 127

Outcomes	Leaving the study early. Global state: CGI-S. Mental state: BPRS, PANSS. Adverse effects: system-specific effects, AIMS, BAS, SAS. Unable to use - Global state: ORDQ. Mental state: CDSS (no numerical data). Adverse effects: SAS (reported as zero difference with P value - not credible data), weight, glucose, blood lipids (median reported with no other data). Adverse effects: AIMS, BAS (P values, and numbers that did allow calculation of SD).*
Notes	* These data, although possible to report, carried assumptions on numbers of people from which they were derived, identical SDs per group, normality of data on top of other assumptions usually associated with scale-derived numbers. We feel that these are assumptions too far

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Random, computer-generated, blocked by centre.
Allocation concealment (selection bias)	Unclear risk	No further details.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double, double dummy administration. Whether blinding was successful has not been examined, but both compounds have similar adverse effects
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Objective outcomes such as laboratory measures or death are unlikely to have been much affected by lack of blinding
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	LOCF method used to account for people leaving the study early
Selective reporting (reporting bias)	High risk	Only adverse events with an incidence of more than 5% were reported. This procedure may have missed important adverse events CDSS and ORDQ - no numerical data reported because "no statistically significant differences were observed. . ." AIMS, BAS, SAS were portrayed very differently to other scales - allowing computation of data but not giving clear person-based numbers for the ratings

Zimbroff 2007 (Continued)

Other bias	High risk	Random sequence generation (selection bias)
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Zou 2006

Methods	Allocation: randomised, no further details. Blindness: unclear. Duration: six weeks. Design: parallel. Setting: inpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). PANSS total score of 60 or more, BPRS total score of 36 or more, TESS total score of 1 or less. N = 62. Age: aripiprazole group: mean = (45.99 ± 6.89) years; clozapine group: mean = (45.81 ± 9.2) years. Gender: aripiprazole group: 20 M, 11 F; clozapine group: 18 M, 13 F. History: aripiprazole group: mean = (16.99 ± 8.64) years; clozapine group: mean = (15.98 ± 3.5) years. Age at onset not reported
Interventions	1. Aripiprazole: Dose range: 5-15 mg/day. Mean dose: not reported. N = 30. 2. Clozapine: Dose range: 25-400 mg/day. Mean dose: not reported. N = 30
Outcomes	Mental state: PANSS total score. PANSS positive subscale score, PANSS negative subscale score, PANSS general pathological subscale score. BPRS total score Adverse effects: TESS scale (poisoning symptoms, laboratory abnormalities, nervous system, autonomic nervous system, cardiovascular system, other) Unable to use: Mental state: BPRS and PANSS subscale scores - unvalidated subscale
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if outcome was assessed blindly.

Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Unclear if there was drop-out.
Selective reporting (reporting bias)	Low risk	No selective reporting.
Other bias	Low risk	None obvious.

Diagnostic tools and scales

CCMD: Classification of Mental Disorders

DSM IV: Diagnostic and Statistical Manual, 4th edition

Rating Scales

Global rating scales:

CGI: Clinical Global Impressions.

CGI-S: Clinical Global Impression-Severity.

CGI-I: Clinical Global Impression-Improvement

ORDQ: Outcome Resource Discharge Questionnaire

ASEX: Arizona Sexual Experience Scale. .

Mental state

BPRS: Brief Psychiatric Rating Scale.

MADRS: Montgomery-Asberg Depression Rating Scale.

MMSE: Wiing Mini Mental State Examination.

PANSS: Positive and Negative Syndrome Scale.

PANSS-EC: Positive and Negative Syndrome Scale-Excited Component.

SANS: Scale for the Assessment of Negative Symptoms.

SAPS: Scale for the Assessment of Positive Symptoms.

CDSS:Calgary Depression Scale for Schizophrenia

Side effects

AIMS: Abnormal Involuntary Movement Scale.

BAS: Barnes Akathisia Scale.

ESRS: Extrapyramidal Syndrome Rating Scale.

SAS: Simpson-Angus Index - for neurological side effects.

TESS: Treatment Emergent Symptom Scale

UKU: Udvalg for kliniske ndersogelser Side Effect Rating Scale -side effect rating scale.

Quality of Life

QLS: Quality of Life Scale.

IWQoL-Lite: Impact of Wiegth on Quality of Life

Other

BMI: body mass index

ECG: electrocardiogram

EPS: extrapyramidal symptoms

LOCF: last observation carried forward

SD: standard deviation

TG: triglyceride

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Ai 2008	Allocation: not randomised - randomisation allocation according to admission order
Allen 2007	Allocation: not randomised, review.
Anon 2008	Allocation: randomised. Participants: people with schizophrenia. Interventions: aripiprazole + psychosocial intervention vs aripiprazole, not aripiprazole vs other atypical antipsychotics
Bao 2007	Allocation: randomised. Participants: people with schizophrenia Intervention: aripiprazole + clonazepam vs clozapine
Bergman 2007	Allocation: randomised. Participants: people with schizophrenia. Interventions: aripiprazole + guanfacine vs aripiprazole, not aripiprazole vs other atypical antipsychotics
Bristol-Myers 2006	Allocation: randomised. Participants: people with schizophrenia. Interventions: aripiprazole as augmenter of atypical antipsychotics, not aripiprazole vs other atypical antipsychotics
Carson 2000	Allocation: randomised. Participants: people with schizophrenia. Interventions: aripiprazole vs haloperidol vs placebo, not aripiprazole vs other atypical antipsychotics
Casey 2003	Allocation: pooled analysis.
Chen 2005	Allocation: not randomised.
Chen 2007	Allocation: not randomised - randomisation allocation according to admission order
Chen 2008	Allocation: not randomised - randomisation allocation according to admission order
Chen LJ 2010	Allocation: not randomised - randomisation allocation according to admission order
Chen YH 2010	Allocation: not randomised - randomisation allocation according to admission order
Colombo 2008	Allocation: randomised. Participants: metabolic syndrome incidence not schizophrenia. Interventions: aripiprazole vs olanzapine.
Cornblatt 2002	Allocation: randomised open label. Participants: people with schizophrenia. Interventions: aripiprazole vs olanzapine.

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	Outcome: No usable data available.
Fawzi 2009	Allocation: randomised open label. Participants: people with schizophrenia. Interventions: aripiprazole vs olanzapine vs olanzapine + clomipramine. Outcome: No usable data available.
Fleischhacker 2008a	Allocation: randomised double blind then open label extension. Participants: people with schizophrenia. Interventions: aripiprazole + clozapine vs placebo + clozapine, not aripiprazole vs other atypical antipsychotics
Geng 2009	Allocation: not randomised - randomisation allocation according to admission order
Guan 2007	Allocation: not randomised - randomisation allocation according to admission order
Han HF 2010	Allocation: not randomised - randomisation allocation according to admission order
Hatta 2009	Allocation: randomised. Participants: people with schizophrenia. Interventions: aripiprazole vs olanzapine vs risperidone vs quetiapine. Outcome: No usable data available.
Henderson 2009	Allocation: randomised. Participants: people with schizophrenia. Interventions: aripiprazole vs placebo, not aripiprazole vs other atypical antipsychotics
Huang 2008	Allocation: not randomised - randomisation allocation according to admission order
Janssen 2005	Allocation: randomised. Participants: people with schizophrenia. Interventions: switch treatment with aripiprazole in patients while on risperidone, not aripiprazole vs other atypical antipsychotics
Jiang 2007	Allocation: not randomised - randomisation allocation according to admission order
Ju 2009	Allocation: not randomised - randomisation allocation according to admission order
Kim 2006	Allocation: randomised. Participants: people with schizophrenia. Interventions: aripiprazole + clozapine vs clozapine, not aripiprazole vs other atypical antipsychotics
Kim 2009	Allocation: randomised. Participants: people with schizophrenia. Interventions: aripiprazole vs other atypical antipsychotics. Outcome: No usable data available.
Lan 2008	Allocation: randomised. Participants: people with schizophrenia. Interventions: shift from other antipsychotics to aripiprazole, not aripiprazole vs other drugs

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Li 2007e	Allocation: not randomised - randomisation allocation according to admission order
Li 2007f	Allocation: not randomised - randomisation allocation according to admission order
Li C 2010	Allocation: not randomised - randomisation allocation according to admission order
Liang 2005	Allocation: randomised. Participants: people with schizophrenia. Interventions: aripiprazole vs risperidone. Outcome: no usable data available.
Liemburg 2011	Allocation: randomised. Participants: people with schizophrenia. Interventions: aripiprazole vs risperidone. Outcome: no usable data available.
Lin 2006	Allocation: not randomised - randomisation allocation according to admission order
Lin Y 2009	Allocation: not randomised - randomisation allocation according to admission order
Liu 2007a	Allocation: not randomised - randomisation allocation according to admission order
Liu 2007b	Allocation: not randomised - randomisation allocation according to admission order
Liu XH 2009	Allocation: not randomised - randomisation allocation according to admission order
Lu 2008	Allocation: not randomised - randomisation allocation according to admission order
Lv 2006	Allocation: not randomised - randomisation allocation according to admission order
Ma 2007	Allocation: randomised. Participants: people with schizophrenia. Interventions: aripiprazole + clozapine vs clozapine, not aripiprazole vs other atypical antipsychotics
Ma 2009b	Allocation: not randomised - randomisation allocation according to admission order
Medori 2008	Allocation: not randomised. Participants: people with schizophrenia. Interventions: risperidone (RLAI) vs quetiapine, not aripiprazole vs other atypical antipsychotics
Millar 2008	Allocation: randomised. Participants: people with schizophrenia. Interventions: clozapine + placebo vs clozapine + aripiprazole, not aripiprazole vs other drugs
Mortimer 2004	Allocation: randomised. Participants: people with schizophrenia. Interventions: aripiprazole vs placebo, not aripiprazole vs other atypical antipsychotics

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Mossner 2009	Allocation: randomised. Participants: people with schizophrenia. Interventions: risperidone vs haloperidol, not aripiprazole vs other drugs
Namey 2006	Allocation: randomised. Participants: people with schizophrenia. Interventions: clozapine + placebo vs clozapine + aripiprazole, not aripiprazole vs other drugs
Newcomer 2006	Allocation: not randomised - pooled analysis.
Newcomer 2008	Allocation: not randomised, pooled analysis.
Newcomer 2008c	Allocation: not randomised, pooled analysis.
Pae 2009a	Allocation: randomised. Participants: people with schizophrenia. Interventions: aripiprazole vs aripiprazole + another antipsychotic (reducing dose over 4 weeks) vs aripiprazole + another antipsychotic (reducing dose over 6 weeks), not aripiprazole alone vs other drugs
Ray 2004	Allocation: not randomised, cohort study.
Remington 2009	Allocation: randomised. Participants: people with schizophrenia. Interventions: aripiprazole + clozapine vs clozapine + placebo, not aripiprazole alone vs other drugs
Schreiner 2009	Allocation: randomised. Participants: people with schizophrenia, schizo-affective disorder. Interventions: switching treatment for patients on oral risperidone, olanzapine and conventional antipsychotics to RLAI vs quetiapine and aripiprazole, not aripiprazole vs other drugs
Shen 2006	Allocation: not randomised - randomisation allocation according to admission order
Shim 2006	Allocation: "double blind", unclear if randomised. Participants: people with schizophrenia. Interventions: aripiprazole + haloperidol vs haloperidol + placebo, not aripiprazole alone vs other drugs
Sun 2006a	Allocation: open label controlled clinical trial, not RCT.
Sun P 2009	Allocation: not randomised - randomisation allocation according to admission order
Takeuchi 2008	Allocation: randomised. Participants: people with schizophrenia. Interventions: two switching strategies of aripiprazole, not aripiprazole vs other drugs
Talbott 2007	Allocation: randomised. Participants: people with schizophrenia. Interventions: pooled post-hoc analysis aripiprazole vs haloperidol and aripiprazole vs olanzapine

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Taylor 2007	Allocation: randomised, open label. Participants: schizophrenia. Interventions: aripiprazole vs olanzapine vs risperidone vs haloperidol vs quetiapine vs ziprasidone, not aripiprazole vs other atypicals. Outcome: no usable data.
Wang 2006e	Allocation: not randomised - randomisation allocation according to admission order
Wang 2007b	Allocation: not randomised - randomisation allocation according to admission order
Wang 2007c	Allocation: not randomised - randomisation allocation according to admission order
Watts 2006a	Allocation: randomised, open label. Participants: schizophrenia. Interventions: aripiprazole vs ziprasidone. Outcome: no usable data, study terminated.
Xu 2008	Allocation: not randomised - randomisation allocation according to admission order
Yang 2007a	Allocation: not randomised - randomisation allocation according to admission order
Yang 2007b	Allocation: not randomised.
Yu 2007a	Allocation: not randomised - randomisation allocation according to admission order
Zeng 2006	Allocation: not randomised - randomisation allocation according to admission order
Zhang 2006b	Allocation: not randomised - randomisation allocation according to admission order
Zhang F 2009	Allocation: not randomised - randomisation allocation according to admission order
Zhang RK 2008	Allocation: not randomised - randomisation allocation according to admission order
Zhang XL 2007	Allocation: not randomised - randomisation allocation according to admission order
Zhao GW 2009	Allocation: not randomised - randomisation allocation according to admission order
Zhao JY 2009	Allocation: not randomised - randomisation allocation according to admission order
Zhe 2007	Allocation: not randomised - randomisation allocation according to admission order
Zhi 2010	Allocation: not randomised - randomisation allocation according to admission order

RCT: randomised controlled trial

RLAI: Risperidone Long-acting Injection

vs: versus

Characteristics of studies awaiting assessment *[ordered by study ID]*

Wang 2006f

Methods	Allocation: randomised (no further description). Blinding: not stated. Duration: 8 weeks. Setting: inpatients, China.
Participants	Diagnosis: chronic schizophrenia (CCMD-3). N = 50. Sex: male and female. Age: 20 to 58 years. History: 5 to 18 years.
Interventions	1. Aripiprazole: 5-30 mg/day, n = 25*. 2. Risperidone: 0.5-5 mg/day, n = 25.
Outcomes	Global state: curative effect. Mental state: PANSS score. Adverse events*.
Notes	N number in various outcomes are inconsistent. We, therefore, decided not to include this trial, until we acquire further clarification from authors

Zhao 2006a

Methods	Allocation: randomised (no further description). Blinding: not stated. Duration: 8 weeks. Setting: inpatients, China.
Participants	Diagnosis: first episode schizophrenia (CCMD-3). N = 68. Sex: male and female. Age: 24.3 ± 9.4 years in aripiprazole group; 28 ± 10 years in quetiapine group History: mean ~24 months, SD ~14 months.
Interventions	1. Aripiprazole: 10-30 mg/day, n = 34*. 2. Quetiapine: 100-750 mg/day, n = 34.
Outcomes	Global state: curative effect*. Mental state: PANSS score. Adverse events.
Notes	* reported N numbers and their corresponding percentage of the same outcome are inconsistent. We, therefore, decided not to include this trial, until we acquire further clarification from authors

Zheng XR 2008

Methods	Allocation: randomised (no further description). Blinding: not stated. Duration: 8 weeks. Setting: inpatients, China.
Participants	Diagnosis: schizophrenia (CCMD-3). N = 68. Sex: male and female. Age: 16 to 58 years. History: median ~ 5 months; range 1~32 months.
Interventions	1. Aripiprazole: 5~30 mg/day, n = 30*. 2. Risperidone: 1~5 mg/day, n = 34.
Outcomes	Global state: curative effect*. Adverse events*.
Notes	The total number of participants (n = 64) is inconsistent with the total number of people randomised (n = 68). We, therefore, decided not to include this trial, until we acquire further clarification from authors

陶建青, 2007

Methods	Allocation: unclear
Participants	Participants: schizophrenia
Interventions	Aripiprazole vs Risperidone
Outcomes	
Notes	No full-text article.

CCMD-3: Chinese Classification of Mental Disorders third version

PANSS: Positive And Negative Symptom Scale

vs: versus

Characteristics of ongoing studies [ordered by study ID]**Bristol-Myers 2009**

Trial name or title	NCT 00857818
Methods	Allocation: random. Blindness: open label. Duration: 16 weeks. Design: parallel.

Bristol-Myers 2009 (Continued)

	Location: not reported.
Participants	Diagnosis: schizophrenia, bipolar 1 disorder. Age 18-65 years. Gender: both. History: duration of illness not reported. Setting: not reported
Interventions	1. Aripiprazole. 2. Olanzapine. 3. Risperidone. 4. Quetiapine
Outcomes	Long-time effectiveness and tolerability. Global state: CGI, PG-I. Quality of life: IWQoL -Lite. Percent change in fasting lipids from baseline. Change in fasting glucose, levels weight, BMI. Change in fasting non- HDL Cholesterol level from baseline.
Starting date	April 2009.
Contact information	Bristol-Myers Squibb.
Notes	Not open for participant recruitment.

Eli Lilly 2003

Trial name or title	Trial 8047 F1D-MC-HGLB
Methods	Allocation: random, no further details. Blindness: double, no further details. Duration: 28 weeks. Design: parallel. Location: not reported.
Participants	Diagnosis: schizophrenia. Age 18-65 years. Gender: not reported. History: duration of illness not reported. Setting: in- and outpatient.
Interventions	1. Aripiprazole. 2. Olanzapine.

Eli Lilly 2003 (Continued)

Outcomes	Long-time effectiveness and tolerability. Global state: CGI, PG-I. General Mental State: PANSS. Depression: MADRS. Quality of life: SWN-S, SF-36. Cognitive functioning: MOS. Sexual functioning: GISF. Health resource utilisation and resource utilisation costs, hospitalisation time. Treatment-emergent adverse events: EPS (SAS, BAS, AIMS). Laboratory values. Vital signs.
Starting date	October 2003.
Contact information	Eli Lilly and Company.
Notes	

Essock 2002

Trial name or title	NCT 00044655
Methods	Allocation: random, no further details Blindness: single, no further details. Duration: unclear. Design: parallel. Location: multiple.
Participants	Diagnosis: schizophrenia, schizoaffective disorder or schizophreniform disorder. Age 18-65 years. Gender: male/female participants. History: duration of illness not reported. Setting: outpatient.
Interventions	1. Aripiprazole. 2. Olanzapine. 3. Risperidone. 4. Quetiapine. 5. Ziprasidone.
Outcomes	Efficacy, safety, adverse effects.
Starting date	July 2001.
Contact information	NIMH. United States Federal Government

Essock 2002 (Continued)

Notes	
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Glorioso 2005

Trial name or title	NCT 00245206 ID: R01MH71536
Methods	Allocation: random, no further details Blindness: open label. Duration: 5 years Design: parallel. Location: unclear.
Participants	Diagnosis: schizophrenia. Age ≥ 45 years. Gender: male/female participants. History: duration of illness not reported. Setting: not reported.
Interventions	1. Aripiprazole. 2. Olanzapine. 3. Risperidone. 4. Quetiapine.
Outcomes	Metabolic, cardiovascular and cerebrovascular effects.
Starting date	August 2005.
Contact information	University of California
Notes	

Hanssens 2007

Trial name or title	NCT 00508157 CN 138-489
Methods	Allocation: random, no further details Blindness: open label. Duration: 16 weeks. Design: parallel. Location: multicentre.
Participants	Diagnosis: schizophrenia. Age 18-65 years. Gender: male/female participants. History: duration of illness not reported. Setting: not reported.

Hanssens 2007 (Continued)

Interventions	1. Aripiprazole. 2. Olanzapine. 3. Risperidone. 4. Quetiapine.
Outcomes	Change from baseline in fasting non- HDL cholesterol.
Starting date	July 2007.
Contact information	Bristol -Myers Squibb.
Notes	

Johnson 2006

Trial name or title	Study ID- CR006121 NCT- 00299702
Methods	Allocation: random. Blindness: open label. Duration: 2 years. Design: parallel. Location: multicentre.
Participants	Diagnosis: schizophrenia. Age 18-65 years. Gender: male and female participants. History: duration of illness not reported. Setting: not specified.
Interventions	1. Aripiprazole. 2. Risperidal Consta.
Outcomes	Time to relapse, long-time effectiveness and tolerability.
Starting date	February 2006.
Contact information	Johnson and Johnson.
Notes	

Lehrer 2008

Trial name or title	NCT- 00712270
Methods	Allocation: random. Blindness: double blind. Duration: 16 weeks. Design: parallel.
Participants	Diagnosis: schizophrenia. Age 18-55 years. Gender: male and female participants. History: duration of illness not reported. Setting: not specified.
Interventions	1. Aripiprazole. 2. Risperidone.
Outcomes	Predict differential antipsychotic drug treatment response using PET and MRI
Starting date	April 2005
Contact information	Kettring Health Network
Notes	

Lin 2009

Trial name or title	NCT- 00956189
Methods	Allocation: random. Blindness: single blind. Duration: 1 year. Design: parallel.
Participants	Diagnosis: schizophrenia. Age 18-65 years. Gender: male and female participants. History: duration of illness not reported. Setting: not specified.
Interventions	1. Aripiprazole. 2. Amisulpiride.
Outcomes	Metabolic profile and clinical efficacy.
Starting date	August 2009.
Contact information	National Taiwan University Hospital.

Lin 2009 (Continued)

Notes	
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Livingston 2007

Trial name or title	NCT 00423878
Methods	Allocation: random. Blindness: single blind. Duration: 6 months. Design: parallel. Location: unclear.
Participants	Diagnosis: schizophrenia. Age: 16-65 years. Gender: male/female participants. History: duration of illness not reported. Setting: not reported.
Interventions	1. Aripiprazole. 2. Risperidone. 3. Quetiapine. 4. Olanzapine.
Outcomes	Metabolic effects, adverse events, clinical efficacy and tolerability
Starting date	January 2007.
Contact information	
Notes	

McCormack 2006

Trial name or title	NCT - 00320671
Methods	Allocation: random. Blindness: double blind. Duration: 12 weeks. Design: parallel. Location: unclear.
Participants	Diagnosis: schizophrenia. Age: 16-40 years. Gender: male/female participants. History: duration of illness not reported. Setting: not reported.

McCormack 2006 (Continued)

Interventions	1. Aripiprazole. 2. Risperidone.
Outcomes	Metabolic effects, adverse events, substance use.
Starting date	2005 - December.
Contact information	United States Health Authority
Notes	

McEvoy 2007

Trial name or title	NCT00466310
Methods	Allocation: random. Blindness: open label. Duration: 4 weeks. Design: parallel. Location: multicentre.
Participants	Diagnosis: schizophrenia. Age 18-60 years. Gender: male and female participants. History: duration of illness not reported. Setting: not specified.
Interventions	1. Aripiprazole. 2. Risperidone.
Outcomes	Metabolic adverse effects.
Starting date	February 2007
Contact information	Duke University.
Notes	

Montoya 2006

Trial name or title	NCT00330863
Methods	Allocation: random. Blindness: open label. Duration: 30 months. Design: parallel. Location: multicentre.

Montoya 2006 (Continued)

Participants	Diagnosis: schizophrenia. Age 18-65 years. Gender: male and female participants. History: duration of illness not reported. Setting: not specified.
Interventions	1. Aripiprazole. 2. Risperidone. 3. Quetiapine. 4. Ziprasidone. 5. Olanzapine. 6. Risperidone microspheres.
Outcomes	Time to relapse, long-time effectiveness and tolerability.
Starting date	May 2006
Contact information	United States of America
Notes	

Schweiger 2005

Trial name or title	NCT-00205660
Methods	Allocation: random. Blindness: open label. Duration: 12 weeks. Design: parallel. Location: multicentre.
Participants	Diagnosis: schizophrenia. Age: 18-60 years. Gender: male and female participants. History: duration of illness not reported. Setting: not specified.
Interventions	1. Aripiprazole. 2. Olanzapine. 3. Quetiapine. 4. Risperidone. 5. Ziprasidone.
Outcomes	Metabolic adverse effects. Long-time effectiveness, safety and tolerability
Starting date	February 2005.

Schweiger 2005 (Continued)

Contact information	Bristol-Myers Squibb
Notes	

Stroup 2007

Trial name or title	NCT-00423878
Methods	Allocation: random. Blindness: single blind. Duration: 6 months. Design: parallel. Location: multicentre.
Participants	Diagnosis: schizophrenia. Age: 18-65 years. Gender: male and female participants. History: duration of illness not reported. Setting: not specified.
Interventions	1. Aripiprazole. 2. Olanzapine. 3. Quetiapine. 4. Risperidone.
Outcomes	Changes in cholesterol level. Long-time effectiveness, safety and tolerability
Starting date	January 2007.
Contact information	Duke University , U. S. A.
Notes	

Swartz 2008b

Trial name or title	NCT- 00802100
Methods	Allocation: random. Blindness: single blind. Duration: 28- 30 weeks. Design: parallel. Location: multicentre.
Participants	Diagnosis: schizophrenia. Age: 18-40 years. Gender: male and female participants. History: duration of illness not reported.

Swartz 2008b (Continued)

	Setting: not specified.
Interventions	1. Aripiprazole. 2. Olanzapine. 3. Perphenazine.
Outcomes	Long-time effectiveness, safety and tolerability, use other medication to limit side effects
Starting date	December 2008.
Contact information	Duke University , U. S. A.
Notes	

Vontur 2005

Trial name or title	NCT00223418
Methods	Allocation: random. Blindness: open label. Duration: unspecified. Design: parallel.
Participants	Diagnosis: schizophrenia. Age 18-52 years. Gender: male and female participants. History: duration of illness not reported. Setting: not specified.
Interventions	1. Aripiprazole. 2. Olanzapine.
Outcomes	Improvement in cognitive functions, long-time effectiveness and tolerability, social and occupational functioning
Starting date	September 2005.
Contact information	United States of America.
Notes	

Global rating scales

CGI: Clinical Global Impressions

PGI-I: Patient's Global Impressions of Improvement

Mental state:

MADRS: Montgomery-Asberg Depression Rating Scale

PANSS: Positive and Negative Syndrome Scale

Depression:

MADRS: Montgomery-Åsberg Depression Rating Scale

Sexual functioning:

GISF: Global Impressions of Sexual Function

Side effects:

AIMS: Abnormal Involuntary Movement Scale

BAS: Barnes Akathisia Scale

SAS: Simpson-Angus Index - for neurological side effects

Quality of Life:

IWQoL-Lite: Impact of Weight on Quality of Life

SF-36: Short form 36

SWN-S: subjective well-being

Other

BMI: body mass index

EPS: extrapyramidal symptoms

HDL: high-density lipoprotein

MOS: Medical Outcomes Study

MRI: magnetic resonance imaging

PET: positron emission tomography

DATA AND ANALYSES

Comparison 1. COMPARISON 1. ARIPIPRAZOLE versus CLOZAPINE

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Global state: 1. No clinically significant response (as defined by the original studies)	29	2132	Risk Ratio (M-H, Random, 95% CI)	1.05 [0.87, 1.27]
2 Mental state: 1. Specific - binary outcomes	11		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 anxiety (short term, up to 12 weeks)	11	732	Risk Ratio (M-H, Random, 95% CI)	2.62 [1.21, 5.70]
2.2 anxiety (medium term, 12 to 26 weeks)	1	90	Risk Ratio (M-H, Random, 95% CI)	0.33 [0.04, 3.08]
2.3 agitation (short term, up to 12 weeks)	1	60	Risk Ratio (M-H, Random, 95% CI)	1.87 [0.18, 19.55]
3 Mental state: 2. Average endpoint scores of various scales (short term, up to 12 weeks, high=poor)	27		Mean Difference (IV, Random, 95% CI)	Subtotals only
3.1 BPRS	5	426	Mean Difference (IV, Random, 95% CI)	-0.22 [-1.44, 1.00]
3.2 PANSS	23	1638	Mean Difference (IV, Random, 95% CI)	-0.10 [-1.41, 1.22]
3.3 SANS	1	50	Mean Difference (IV, Random, 95% CI)	-2.27 [-6.27, 1.73]
4 Mental state: 3. Average endpoint scores of various scales (medium term, 12 to 26 weeks, high=poor)	3		Mean Difference (IV, Random, 95% CI)	Subtotals only
4.1 PANSS	3	236	Mean Difference (IV, Random, 95% CI)	-5.41 [-8.42, -2.41]
5 Mental state: 4. Average endpoint scores of various scales (skewed data, high=poor)			Other data	No numeric data
5.1 BPRS			Other data	No numeric data
5.2 PANSS			Other data	No numeric data
5.3 PANSS negative symptom subscale score			Other data	No numeric data
6 Mental state: 5. Specific - average endpoint positive score (PANSS, high=poor)	22	1523	Mean Difference (IV, Random, 95% CI)	0.27 [-0.48, 1.02]
6.1 by up to 12 weeks - short term	19	1287	Mean Difference (IV, Random, 95% CI)	0.35 [-0.50, 1.20]
6.2 from 12-26 weeks - medium term	3	236	Mean Difference (IV, Random, 95% CI)	-0.23 [-1.79, 1.34]
7 Mental state: 6. Specific - average endpoint negative score (PANSS, high=poor)	23	1640	Mean Difference (IV, Random, 95% CI)	-0.61 [-1.53, 0.30]
7.1 up to 12 weeks - short term	20	1404	Mean Difference (IV, Random, 95% CI)	-0.04 [-0.79, 0.71]

7.2 from 12-26 weeks - medium term	3	236	Mean Difference (IV, Random, 95% CI)	-3.24 [-5.82, -0.67]
8 Mental state: 7. Specific - average endpoint general psychopathological score (PANSS, high=poor)	19	1330	Mean Difference (IV, Random, 95% CI)	-0.27 [-0.78, 0.23]
8.1 up to 12 weeks - short term	16	1094	Mean Difference (IV, Random, 95% CI)	-0.08 [-0.62, 0.45]
8.2 from 12-26 weeks - medium term	3	236	Mean Difference (IV, Random, 95% CI)	-1.89 [-3.45, -0.34]
9 Mental state: 8. Specific - average total score decreased rate (PANSS, low=poor)	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
9.1 by up to 12 weeks	1	118	Mean Difference (IV, Random, 95% CI)	0.06 [-0.03, 0.15]
10 Mental state: 9. Specific - average positive score decreased rate (PANSS, low=poor)	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
10.1 by up to 12 weeks - short term	1	118	Mean Difference (IV, Random, 95% CI)	-0.01 [-0.10, 0.08]
11 Leaving the study early	4		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
11.1 Any reason	3	240	Risk Ratio (M-H, Random, 95% CI)	1.41 [0.46, 4.29]
11.2 Adverse events	3	212	Risk Ratio (M-H, Random, 95% CI)	0.76 [0.20, 2.92]
11.3 Economic issues	1	120	Risk Ratio (M-H, Random, 95% CI)	2.0 [0.38, 10.51]
12 Quality of life: 1a. Average scores (short term, up to 12 weeks, WHO-QOL-100, low=poor)	4		Mean Difference (IV, Random, 95% CI)	Subtotals only
12.1 endpoint scale score	2	132	Mean Difference (IV, Random, 95% CI)	2.59 [1.43, 3.74]
12.2 physical health	2	132	Mean Difference (IV, Random, 95% CI)	7.73 [1.51, 13.94]
12.3 mental health	2	132	Mean Difference (IV, Random, 95% CI)	9.21 [4.74, 13.68]
12.4 social function	2	132	Mean Difference (IV, Random, 95% CI)	7.78 [-0.98, 16.54]
12.5 external environmental	3	248	Mean Difference (IV, Random, 95% CI)	13.82 [8.69, 18.94]
12.6 independence	1	72	Mean Difference (IV, Random, 95% CI)	0.08 [-1.62, 1.78]
12.7 spiritual support	1	72	Mean Difference (IV, Random, 95% CI)	6.61 [4.25, 8.97]
13 Quality of life: 1b. Average scores (medium term, 12 to 24 weeks, WHO-QOL-100, low=poor)	3		Mean Difference (IV, Random, 95% CI)	Subtotals only
13.1 endpoint scale score	2	176	Mean Difference (IV, Random, 95% CI)	2.75 [1.98, 3.53]
13.2 physical health	3	256	Mean Difference (IV, Random, 95% CI)	4.89 [0.22, 9.56]
13.3 mental health	3	256	Mean Difference (IV, Random, 95% CI)	7.39 [5.26, 9.53]
13.4 social function	3	256	Mean Difference (IV, Random, 95% CI)	6.68 [2.79, 10.56]
13.5 material life	1	80	Mean Difference (IV, Random, 95% CI)	-0.80 [-2.00, 2.40]
13.6 independence	2	176	Mean Difference (IV, Random, 95% CI)	6.71 [4.76, 8.66]
13.7 spiritual support	2	176	Mean Difference (IV, Random, 95% CI)	-0.31 [-1.37, 0.75]
14 Quality of life: 2. Average endpoint general quality of life score (GQOLI - 74, low=poor)	2		Mean Difference (IV, Random, 95% CI)	Subtotals only
14.1 Total score	1	114	Mean Difference (IV, Random, 95% CI)	0.5 [-3.40, 4.40]
14.2 Physical health	1	120	Mean Difference (IV, Random, 95% CI)	7.70 [2.95, 12.45]
14.3 Mental health	1	120	Mean Difference (IV, Random, 95% CI)	2.70 [-2.30, 7.70]
14.4 Social function	1	120	Mean Difference (IV, Random, 95% CI)	6.60 [3.15, 10.05]

14.5 Material life	1	120	Mean Difference (IV, Random, 95% CI)	0.10 [-5.30, 5.50]
14.6 Environmental area (medium term)	1	90	Mean Difference (IV, Random, 95% CI)	11.5 [5.55, 17.45]
14.7 Independence (medium term)	1	90	Mean Difference (IV, Random, 95% CI)	6.16 [2.84, 9.48]
15 Adverse effects: 1. At least one adverse effect	15	1582	Risk Ratio (M-H, Random, 95% CI)	0.62 [0.47, 0.81]
15.1 Non-specific	7	574	Risk Ratio (M-H, Random, 95% CI)	0.67 [0.48, 0.95]
15.2 epilepsy	1	60	Risk Ratio (M-H, Random, 95% CI)	0.33 [0.01, 7.87]
15.3 liver function abnormal	5	364	Risk Ratio (M-H, Random, 95% CI)	0.49 [0.16, 1.56]
15.4 stuffy nose	3	258	Risk Ratio (M-H, Random, 95% CI)	0.50 [0.21, 1.20]
15.5 sweating	1	74	Risk Ratio (M-H, Random, 95% CI)	0.35 [0.04, 3.23]
15.6 urinary retention	2	132	Risk Ratio (M-H, Random, 95% CI)	1.00 [0.11, 9.39]
15.7 urinary incontinence	2	120	Risk Ratio (M-H, Random, 95% CI)	0.18 [0.02, 1.54]
16 Adverse effects: 2. Cardiac effects	25		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
16.1 abnormal ECG (short term, up to 12 weeks)	12	921	Risk Ratio (M-H, Random, 95% CI)	0.38 [0.29, 0.51]
16.2 blood pressure- decrease (short term, up to 12 weeks)	3	194	Risk Ratio (M-H, Random, 95% CI)	0.57 [0.23, 1.43]
16.3 general adverse cardiac events (short term, up to 12 weeks)	1	62	Risk Ratio (M-H, Random, 95% CI)	0.32 [0.17, 0.60]
16.4 QTc prolongation (short term, up to 12 weeks)	4	334	Risk Ratio (M-H, Random, 95% CI)	0.16 [0.05, 0.49]
16.5 tachycardia (short term, up to 12 weeks)	15	1104	Risk Ratio (M-H, Random, 95% CI)	0.29 [0.22, 0.38]
16.6 QTc prolongation (medium term, 12 to 24 weeks)	1	90	Risk Ratio (M-H, Random, 95% CI)	0.05 [0.00, 0.79]
16.7 tachycardia (medium term, 12 to 24 weeks)	1	60	Risk Ratio (M-H, Random, 95% CI)	0.09 [0.01, 1.57]
17 Adverse effects: 3. Central / peripheral nervous system	26		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
17.1 activity- decrease (short term, up to 12 weeks)	1	120	Risk Ratio (M-H, Random, 95% CI)	0.21 [0.10, 0.48]
17.2 activity- increase (short term, up to 12 weeks)	1	48	Risk Ratio (M-H, Random, 95% CI)	4.26 [0.22, 84.28]
17.3 blurred vision (short term, up to 12 weeks)	6	472	Risk Ratio (M-H, Random, 95% CI)	0.29 [0.12, 0.66]
17.4 dizziness (short term, up to 12 weeks)	9	698	Risk Ratio (M-H, Random, 95% CI)	0.60 [0.36, 1.00]
17.5 fatigue (short term, up to 12 weeks)	4	300	Risk Ratio (M-H, Random, 95% CI)	0.57 [0.27, 1.23]
17.6 general central nervous system adverse reaction (short term, up to 12 weeks)	1	62	Risk Ratio (M-H, Random, 95% CI)	2.0 [0.55, 7.29]
17.7 general vegetative nervous system adverse reaction (short term, up to 12 weeks)	1	62	Risk Ratio (M-H, Random, 95% CI)	0.48 [0.27, 0.84]
17.8 headache (short term, up to 12 weeks)	16	1102	Risk Ratio (M-H, Random, 95% CI)	2.28 [1.07, 4.86]

17.9 hyper-salivation (short term, up to 12 weeks)	16	1074	Risk Ratio (M-H, Random, 95% CI)	0.06 [0.03, 0.10]
17.10 insomnia (short term, up to 12 weeks)	14	990	Risk Ratio (M-H, Random, 95% CI)	5.62 [2.90, 10.91]
17.11 irritability (short term, up to 12 weeks)	2	120	Risk Ratio (M-H, Random, 95% CI)	6.77 [0.82, 55.80]
17.12 memory decline (short term, up to 12 weeks)	1	80	Risk Ratio (M-H, Random, 95% CI)	0.13 [0.02, 0.95]
17.13 sedation (short term, up to 12 weeks)	1	80	Risk Ratio (M-H, Random, 95% CI)	0.03 [0.00, 0.52]
17.14 somnolence (short term, up to 12 weeks)	21	1492	Risk Ratio (M-H, Random, 95% CI)	0.15 [0.09, 0.24]
17.15 insomnia (medium term, 12 to 24 weeks)	1	90	Risk Ratio (M-H, Random, 95% CI)	3.0 [0.13, 71.74]
17.16 headache (medium term, 12 to 24 weeks)	1	90	Risk Ratio (M-H, Random, 95% CI)	0.5 [0.10, 2.59]
18 Adverse effects: 4. Extrapyramidal effects	21		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
18.1 akathisia (short term, up to 12 weeks)	13	916	Risk Ratio (M-H, Random, 95% CI)	1.21 [0.54, 2.68]
18.2 dystonia (short term, up to 12 weeks)	5	374	Risk Ratio (M-H, Random, 95% CI)	3.24 [1.29, 8.12]
18.3 general extrapyramidal symptoms (short term, up to 12 weeks)	8	520	Risk Ratio (M-H, Random, 95% CI)	1.91 [0.75, 4.85]
18.4 tardive dyskinesia (short term, up to 12 weeks)	1	72	Risk Ratio (M-H, Random, 95% CI)	1.0 [0.15, 6.72]
18.5 tremor (short term, up to 12 weeks)	6	460	Risk Ratio (M-H, Random, 95% CI)	1.99 [0.72, 5.48]
18.6 use of antiparkinson medication (short term, up to 12 weeks)	2	140	Risk Ratio (M-H, Random, 95% CI)	2.84 [0.07, 117.07]
18.7 akathisia (medium term, 12 to 24 weeks)	1	80	Risk Ratio (M-H, Random, 95% CI)	0.33 [0.04, 3.07]
18.8 dystonia (medium term, 12 to 24 weeks)	1	80	Risk Ratio (M-H, Random, 95% CI)	0.5 [0.05, 5.30]
18.9 spasmodic torticollis (medium term, 12 to 24 weeks)	1	80	Risk Ratio (M-H, Random, 95% CI)	0.33 [0.01, 7.95]
18.10 tremor (medium term, 12 to 24 weeks)	1	80	Risk Ratio (M-H, Random, 95% CI)	1.0 [0.15, 6.76]
19 Adverse effects: 6. Haematological	17		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
19.1 abnormal blood routine (short term, up to 12 weeks)	5	368	Risk Ratio (M-H, Random, 95% CI)	0.16 [0.04, 0.60]
19.2 leucopenia (short term, up to 12 weeks)	10	726	Risk Ratio (M-H, Random, 95% CI)	0.21 [0.08, 0.56]
19.3 abnormal blood routine (medium term, 12 to 24 weeks)	2	152	Risk Ratio (M-H, Random, 95% CI)	0.32 [0.14, 0.75]
20 Adverse effects: 5. Gastrointestinal	22		Risk Ratio (M-H, Random, 95% CI)	Subtotals only

20.1 abdominal discomfort / pain (short term, up to 12 weeks)	2	132	Risk Ratio (M-H, Random, 95% CI)	10.21 [1.32, 79.12]
20.2 constipation (short term, up to 12 weeks)	19	1390	Risk Ratio (M-H, Random, 95% CI)	0.15 [0.08, 0.31]
20.3 dry mouth (short term, up to 12 weeks)	4	268	Risk Ratio (M-H, Random, 95% CI)	0.64 [0.08, 5.38]
20.4 general gastrointestinal adverse reaction (short term, up to 12 weeks)	2	130	Risk Ratio (M-H, Random, 95% CI)	1.17 [0.41, 3.39]
20.5 indigestion (short term, up to 12 weeks)	1	60	Risk Ratio (M-H, Random, 95% CI)	0.47 [0.04, 4.89]
20.6 nausea / vomiting (short term, up to 12 weeks)	10	790	Risk Ratio (M-H, Random, 95% CI)	1.55 [0.71, 3.38]
20.7 constipation (medium term, 12 to 24 weeks)	1	90	Risk Ratio (M-H, Random, 95% CI)	0.02 [0.00, 0.36]
20.8 hyper-salivation (medium term, 12 to 24 weeks)	1	90	Risk Ratio (M-H, Random, 95% CI)	0.02 [0.00, 0.29]
21 Adverse effects: 7. Hormonal	3		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
21.1 lactation/menstrual changes (short term, up to 12 weeks)	3	214	Risk Ratio (M-H, Random, 95% CI)	0.11 [0.03, 0.47]
22 Adverse effects: 8a. Metabolic - binary measures	20		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
22.1 blood glucose - increased (short term, up to 12 weeks)	5	410	Risk Ratio (M-H, Random, 95% CI)	0.12 [0.04, 0.37]
22.2 C-peptide (short term, up to 12 weeks)	1	60	Risk Ratio (M-H, Random, 95% CI)	0.03 [0.00, 0.45]
22.3 decreased appetite (short term, up to 12 weeks)	2	130	Risk Ratio (M-H, Random, 95% CI)	0.07 [0.01, 0.54]
22.4 postural hypotension (short term, up to 12 weeks)	5	344	Risk Ratio (M-H, Random, 95% CI)	0.16 [0.07, 0.39]
22.5 PRL- increase (short term, up to 12 weeks)	1	48	Risk Ratio (M-H, Random, 95% CI)	0.05 [0.00, 0.82]
22.6 weight gain (short term, up to 12 weeks)	18	1318	Risk Ratio (M-H, Random, 95% CI)	0.13 [0.08, 0.22]
22.7 blood glucose - increased (medium term, 12 to 24 weeks)	1	90	Risk Ratio (M-H, Random, 95% CI)	0.08 [0.00, 1.33]
22.8 decreased appetite (medium term, 12 to 24 weeks)	1	90	Risk Ratio (M-H, Random, 95% CI)	0.06 [0.00, 0.99]
22.9 weight gain (medium term, 12 to 24 weeks)	1	90	Risk Ratio (M-H, Random, 95% CI)	0.02 [0.00, 0.39]
23 Adverse effects: 8b. Metabolic - continuous measures (short term, up to 12 weeks, high=poor)	3		Mean Difference (IV, Random, 95% CI)	Subtotals only
23.1 blood glucose - FPG in HbA1c normal group (in mmol/l)	1	36	Mean Difference (IV, Random, 95% CI)	0.0 [-0.39, 0.39]

23.2 blood glucose - FPG in HbA1c abnormal group (in mmol/l)	1	19	Mean Difference (IV, Random, 95% CI)	0.0 [-0.61, 0.61]
23.3 blood glucose - PBG in HbA1c normal group (in mmol/l)	1	36	Mean Difference (IV, Random, 95% CI)	-0.20 [-0.66, 0.26]
23.4 blood glucose - PBG in HbA1c abnormal group (in mmol/l)	1	19	Mean Difference (IV, Random, 95% CI)	-1.90 [-2.63, -1.17]
23.5 blood glucose - FPG average endpoint (in mmol/l)	2	134	Mean Difference (IV, Random, 95% CI)	-0.52 [-0.83, -0.22]
23.6 blood glucose - C-peptide average endpoint (in mg/dlmmol/l)	1	60	Mean Difference (IV, Random, 95% CI)	-0.72 [-1.45, 0.01]
23.7 weight gain - average endpoint level (in kg)	1	74	Mean Difference (IV, Random, 95% CI)	-1.99 [-5.56, 1.58]
24 Cost effectiveness analysis (high=poor, data skewed)			Other data	No numeric data
24.1 Cost of hospitalisation (in RMB)			Other data	No numeric data
24.2 Cost of drug (in RMB)			Other data	No numeric data
24.3 Length of hospitalisation (day)			Other data	No numeric data

Comparison 2. COMPARISON 2. ARIPIPRAZOLE versus QUETIAPINE

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Global state: 1.No clinically significant response (as defined by original studies)	12	991	Risk Ratio (M-H, Random, 95% CI)	0.92 [0.64, 1.32]
2 Global state: 2a. Average endpoint total score (short term, up to 12 weeks, high=poor)	11	991	Mean Difference (IV, Random, 95% CI)	-1.00 [-2.58, 0.57]
2.1 CGI	1	80	Mean Difference (IV, Random, 95% CI)	0.10 [-0.49, 0.69]
2.2 PANSS	10	831	Mean Difference (IV, Random, 95% CI)	-0.88 [-3.15, 1.40]
2.3 BPRS	1	80	Mean Difference (IV, Random, 95% CI)	-2.63 [-4.55, -0.71]
3 Global state: 2b. Average endpoint scale score (medium term, 12 to 24 weeks, high=poor)	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
3.1 PANSS	1	100	Mean Difference (IV, Random, 95% CI)	-1.20 [-5.67, 3.27]
4 Global state: 3. Average endpoint SI score (CGI, high=poor)	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
4.1 up to 12 weeks -short term	1	108	Mean Difference (IV, Random, 95% CI)	0.10 [-0.41, 0.61]
5 Mental state: 2a. Specific - binary outcomes	8		Risk Ratio (M-H, Random, 95% CI)	Subtotals only

5.1 agitation (short term, up to 12 weeks)	5	423	Risk Ratio (M-H, Random, 95% CI)	1.29 [0.27, 6.27]
5.2 anxiety (short term, up to 12 weeks)	2	168	Risk Ratio (M-H, Random, 95% CI)	2.18 [0.51, 9.35]
5.3 depression (short term, up to 12 weeks)	1	108	Risk Ratio (M-H, Random, 95% CI)	0.33 [0.01, 8.01]
5.4 agitation (medium term, 12 to 26 weeks)	1	100	Risk Ratio (M-H, Random, 95% CI)	0.33 [0.01, 7.99]
6 Mental state: 3. Specific - average endpoint positive score (PANSS, high=poor)	8	683	Mean Difference (IV, Random, 95% CI)	-0.83 [-1.99, 0.32]
6.1 by up to 12 weeks - short term	7	583	Mean Difference (IV, Random, 95% CI)	-0.97 [-2.34, 0.41]
6.2 from 12-26 weeks - medium term	1	100	Mean Difference (IV, Random, 95% CI)	-0.10 [-1.32, 1.12]
7 Mental state: 4. Specific - average endpoint negative score (PANSS, high=poor)	7	543	Mean Difference (IV, Random, 95% CI)	-0.48 [-1.17, 0.21]
7.1 up to 12 weeks - short term	6	443	Mean Difference (IV, Random, 95% CI)	-0.68 [-1.52, 0.17]
7.2 from 12-26 weeks - medium term	1	100	Mean Difference (IV, Random, 95% CI)	0.0 [-1.23, 1.23]
8 Mental state: 5. Specific - average endpoint general pathological score (PANSS, high=poor)	11	931	Mean Difference (IV, Random, 95% CI)	-1.69 [-3.81, 0.43]
8.1 up to 12 weeks - short term	10	831	Mean Difference (IV, Random, 95% CI)	-1.83 [-4.19, 0.54]
8.2 from 12-26 weeks - medium term	1	100	Mean Difference (IV, Random, 95% CI)	-0.40 [-2.52, 1.72]
9 Mental state: 6. average scores of various scales (high=poor, skewed data)			Other data	No numeric data
9.1 BPRS endpoint scale score			Other data	No numeric data
9.2 PANSS general pathology subscale score			Other data	No numeric data
9.3 PANSS negative subscale score			Other data	No numeric data
9.4 PANSS positive subscale score			Other data	No numeric data
9.5 PANSS total endpoint scale score			Other data	No numeric data
10 Leaving the study early	2		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
10.1 any reason	2	168	Risk Ratio (M-H, Random, 95% CI)	0.80 [0.22, 2.87]
10.2 no effect	1	108	Risk Ratio (M-H, Random, 95% CI)	0.33 [0.01, 8.01]
10.3 early discharge	1	60	Risk Ratio (M-H, Random, 95% CI)	3.0 [0.13, 70.83]
10.4 early treatment termination	2	168	Risk Ratio (M-H, Random, 95% CI)	1.35 [0.09, 19.24]
10.5 violation of test scheme	1	108	Risk Ratio (M-H, Random, 95% CI)	5.0 [0.25, 101.77]
10.6 withdrew informed consent	1	108	Risk Ratio (M-H, Random, 95% CI)	0.33 [0.01, 8.01]

11 Quality of life: Average score (medium term, 12 to 24 weeks, WHO-QOL-100, low=poor)	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
11.1 Total score	1	100	Mean Difference (IV, Random, 95% CI)	2.60 [1.31, 3.89]
11.2 Physical health	1	100	Mean Difference (IV, Random, 95% CI)	6.0 [4.38, 7.62]
11.3 Mental health	1	100	Mean Difference (IV, Random, 95% CI)	9.10 [5.92, 12.28]
11.4 Social function	1	100	Mean Difference (IV, Random, 95% CI)	5.60 [3.33, 7.87]
11.5 Spiritual pillar	1	100	Mean Difference (IV, Random, 95% CI)	0.10 [-1.49, 1.69]
11.6 Environmental area	1	100	Mean Difference (IV, Random, 95% CI)	11.5 [5.86, 17.14]
11.7 Independence	1	100	Mean Difference (IV, Random, 95% CI)	6.20 [3.05, 9.35]
12 Adverse effects: 1. At least one adverse effect	8	1362	Risk Ratio (M-H, Random, 95% CI)	0.89 [0.66, 1.20]
12.1 non-specific	3	258	Risk Ratio (M-H, Random, 95% CI)	0.98 [0.70, 1.37]
12.2 abnormal urinary test result	1	108	Risk Ratio (M-H, Random, 95% CI)	0.33 [0.01, 8.01]
12.3 liver function abnormal	8	658	Risk Ratio (M-H, Random, 95% CI)	0.54 [0.26, 1.13]
12.4 stuffy nose	2	188	Risk Ratio (M-H, Random, 95% CI)	3.0 [0.32, 28.32]
12.5 sweating	1	70	Risk Ratio (M-H, Random, 95% CI)	1.0 [0.07, 15.36]
12.6 urine routine abnormal	1	80	Risk Ratio (M-H, Random, 95% CI)	0.33 [0.01, 7.95]
13 Adverse effects: 2. Cardiac effects (short term, up to 12 weeks)	9		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
13.1 abnormal ECG	6	528	Risk Ratio (M-H, Random, 95% CI)	0.95 [0.40, 2.26]
13.2 blood pressure- decrease	4	348	Risk Ratio (M-H, Random, 95% CI)	0.52 [0.20, 1.32]
13.3 QTc prolongation	3	225	Risk Ratio (M-H, Random, 95% CI)	0.34 [0.08, 1.39]
13.4 tachycardia	8	643	Risk Ratio (M-H, Random, 95% CI)	0.35 [0.18, 0.69]
14 Adverse effects: 3. Central / peripheral nervous system	10		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
14.1 blurred vision (short term, up to 12 weeks)	6	521	Risk Ratio (M-H, Random, 95% CI)	0.88 [0.31, 2.49]
14.2 dizziness (short term, up to 12 weeks)	8	671	Risk Ratio (M-H, Random, 95% CI)	0.64 [0.34, 1.22]
14.3 headache (short term, up to 12 weeks)	5	436	Risk Ratio (M-H, Random, 95% CI)	3.15 [0.52, 18.94]
14.4 insomnia (short term, up to 12 weeks)	7	591	Risk Ratio (M-H, Random, 95% CI)	2.12 [0.88, 5.10]
14.5 somnolence (short term, up to 12 weeks)	9	731	Risk Ratio (M-H, Random, 95% CI)	0.34 [0.15, 0.77]
14.6 dizziness (medium term, 12 to 24 weeks)	1	100	Risk Ratio (M-H, Random, 95% CI)	0.86 [0.31, 2.37]
14.7 headache (medium term, 12 to 24 weeks)	1	100	Risk Ratio (M-H, Random, 95% CI)	9.00 [1.18, 68.42]
14.8 insomnia (medium term, 12 to 24 weeks)	1	100	Risk Ratio (M-H, Random, 95% CI)	2.0 [0.19, 21.36]
14.9 somnolence (medium term, 12 to 24 weeks)	1	100	Risk Ratio (M-H, Random, 95% CI)	0.8 [0.34, 1.86]
15 Adverse effects: 4. Extrapyramidal symptoms - various (short term, up to 12 weeks)	10		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
15.1 akathisia	7	571	Risk Ratio (M-H, Random, 95% CI)	1.15 [0.49, 2.70]

15.2 dystonia	2	145	Risk Ratio (M-H, Random, 95% CI)	0.47 [0.06, 3.53]
15.3 general extrapyramidal symptoms	4	348	Risk Ratio (M-H, Random, 95% CI)	2.80 [0.64, 12.31]
15.4 tremor	4	343	Risk Ratio (M-H, Random, 95% CI)	0.44 [0.09, 2.07]
16 Adverse effects: 5. Gastrointestinal	8		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
16.1 constipation (short term, up to 12 weeks)	7	591	Risk Ratio (M-H, Random, 95% CI)	0.38 [0.19, 0.75]
16.2 dry mouth (short term, up to 12 weeks)	7	611	Risk Ratio (M-H, Random, 95% CI)	0.23 [0.10, 0.53]
16.3 nausea / vomiting (short term, up to 12 weeks)	7	611	Risk Ratio (M-H, Random, 95% CI)	2.68 [1.36, 5.26]
16.4 dry mouth (medium term, 12 to 24 weeks)	1	100	Risk Ratio (M-H, Random, 95% CI)	0.11 [0.01, 0.84]
16.5 nausea / vomiting (medium term, 12 to 24 weeks)	1	100	Risk Ratio (M-H, Random, 95% CI)	7.00 [0.89, 54.83]
17 Adverse effects: 6. Haematological	3		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
17.1 blood routine abnormal (short term, up to 12 weeks)	1	85	Risk Ratio (M-H, Random, 95% CI)	0.31 [0.01, 7.43]
17.2 leucopenia (short term, up to 12 weeks)	2	140	Risk Ratio (M-H, Random, 95% CI)	1.0 [0.07, 15.26]
18 Adverse events: 7. Hormonal	7		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
18.1 menstrual disorder (short term, up to 12 weeks)	6	518	Risk Ratio (M-H, Random, 95% CI)	0.58 [0.20, 1.64]
18.2 menstrual disorder (medium term, 12 to 24 weeks)	1	100	Risk Ratio (M-H, Random, 95% CI)	0.5 [0.05, 5.34]
19 Adverse effects: 8a. Metabolic - binary measures	11		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
19.1 decreased appetite (short term, up to 12 weeks)	4	328	Risk Ratio (M-H, Random, 95% CI)	0.28 [0.06, 1.39]
19.2 lactation (short term, up to 12 weeks)	5	383	Risk Ratio (M-H, Random, 95% CI)	0.57 [0.17, 1.92]
19.3 weight gain (short term, up to 12 weeks)	10	823	Risk Ratio (M-H, Random, 95% CI)	0.45 [0.24, 0.85]
19.4 decreased appetite (medium term, 12 to 24 weeks)	1	100	Risk Ratio (M-H, Random, 95% CI)	0.13 [0.02, 0.96]
19.5 lactation (medium term, 12 to 24 weeks)	1	100	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
19.6 weight gain (medium term, 12 to 24 weeks)	1	100	Risk Ratio (M-H, Random, 95% CI)	0.5 [0.05, 5.34]
20 Adverse effects: 8b. Metabolic - continuous measure	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
20.1 cholesterol - TC average endpoint level (in mmol/L, high=poor)	1	180	Mean Difference (IV, Random, 95% CI)	-0.19 [-0.36, -0.02]
20.2 cholesterol-TG average endpoint level (in mmol/L, high=poor)	1	180	Mean Difference (IV, Random, 95% CI)	-0.04 [-0.21, 0.13]

20.3 cholesterol - LDL average endpoint level (in mmol/L, high=poor)	1	180	Mean Difference (IV, Random, 95% CI)	-0.12 [-0.26, 0.02]
20.4 waistline- average endpoint level (in cm, high=poor)	1	180	Mean Difference (IV, Random, 95% CI)	-1.80 [-3.88, 0.28]
20.5 weight- average endpoint level (in Kg, high=poor)	1	180	Mean Difference (IV, Random, 95% CI)	1.30 [-1.30, 3.90]
20.6 cholesterol - HDL average endpoint (in mmol/L, low=poor))	1	180	Mean Difference (IV, Random, 95% CI)	-0.02 [-0.11, 0.07]

Comparison 3. COMPARISON 3. ARIPIRAZOLE versus RISPERIDONE

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Global state: 1. No clinically significant response (as defined by the original studies)	80		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
1.1 by up to 12 weeks -- short term	80	6381	Risk Ratio (M-H, Random, 95% CI)	1.08 [0.96, 1.21]
2 Global state: 2. Average endpoint total score(short term, up to 12 weeks, CGI, high=poor)	2	196	Mean Difference (IV, Random, 95% CI)	0.35 [0.09, 0.61]
3 Global state: 3. Average CGI subscale scores (short term, up to 12 weeks, high=poor)	1	240	Mean Difference (IV, Random, 95% CI)	0.44 [0.22, 0.66]
3.1 CGI-EI	1	120	Mean Difference (IV, Random, 95% CI)	0.5 [0.14, 0.86]
3.2 CGI-SI	1	120	Mean Difference (IV, Random, 95% CI)	0.40 [0.12, 0.68]
4 Global state: 4. average endpoint data of various scales (high=poor, data skewed)			Other data	No numeric data
4.1 CGI-GI			Other data	No numeric data
4.2 CGI-SI			Other data	No numeric data
4.3 CGI			Other data	No numeric data
5 Mental state: 1. Specific - binary outcomes (short term, up to 12 weeks)	34		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
5.1 anxiety	9	744	Risk Ratio (M-H, Random, 95% CI)	1.81 [1.12, 2.94]
5.2 agitation/excitement	26	2038	Risk Ratio (M-H, Random, 95% CI)	1.26 [0.86, 1.84]
5.3 irritability	1	100	Risk Ratio (M-H, Random, 95% CI)	1.0 [0.06, 15.55]
6 Mental state: 2. Average endpoint scale score	82		Mean Difference (IV, Random, 95% CI)	Subtotals only
6.1 BPRS (short term, up to 12 weeks, high=poor)	5	570	Mean Difference (IV, Random, 95% CI)	-1.33 [-2.24, -0.42]
6.2 PANSS (short term, up to 12 weeks, high=poor)	77	5733	Mean Difference (IV, Random, 95% CI)	-0.80 [-1.58, -0.02]

6.3 PANSS (medium term, 12 to 24 weeks, high=poor)	1	50	Mean Difference (IV, Random, 95% CI)	-0.15 [-8.03, 7.73]
6.4 SANS (medium term, 12 to 24 weeks, high=poor)	1	50	Mean Difference (IV, Random, 95% CI)	-0.55 [-3.72, 2.62]
7 Mental state: 3. Specific - average endpoint positive score (PANSS, high=poor)	40	3205	Mean Difference (IV, Random, 95% CI)	0.02 [-0.37, 0.41]
7.1 short term (up to 12 weeks)	39	3155	Mean Difference (IV, Random, 95% CI)	0.03 [-0.38, 0.43]
7.2 medium term (12-26 weeks)	1	50	Mean Difference (IV, Random, 95% CI)	-0.21 [-2.38, 1.96]
8 Mental state: 4. Specific - average endpoint negative score (PANSS, high=poor)	37		Mean Difference (IV, Random, 95% CI)	Subtotals only
8.1 short term (up to 12 weeks)	37	2976	Mean Difference (IV, Random, 95% CI)	-0.64 [-1.04, -0.25]
9 Mental state: 5. Specific - average endpoint general psychopathological score (PANSS, high=poor)	58	4243	Mean Difference (IV, Random, 95% CI)	-0.25 [-0.71, 0.20]
9.1 by up to 12 weeks - short term	57	4193	Mean Difference (IV, Random, 95% CI)	-0.27 [-0.74, 0.19]
9.2 12- 26 weeks - medium term	1	50	Mean Difference (IV, Random, 95% CI)	1.52 [-2.66, 5.70]
10 Mental state: 6. PANSS average score decreased rate (short term, up to 12 weeks, low=poor)	5		Mean Difference (IV, Random, 95% CI)	Subtotals only
10.1 total scale score decreased rate	3	219	Mean Difference (IV, Random, 95% CI)	3.06 [0.24, 5.87]
10.2 negative symptom subscale score decreased rate	3	216	Mean Difference (IV, Random, 95% CI)	-0.02 [-0.11, 0.08]
10.3 positive symptom subscale score decreased rate	3	216	Mean Difference (IV, Random, 95% CI)	-0.01 [-0.10, 0.08]
10.4 general pathology subscale score decreased rate	1	50	Mean Difference (IV, Random, 95% CI)	2.38 [-0.33, 5.09]
11 Mental state: 7. BPRS total score decreased rate (short term, up to 12 weeks, high=poor)	2	132	Mean Difference (IV, Random, 95% CI)	-2.97 [-6.61, 0.67]
12 Mental state: 8. General - average total score (PANSS, high=poor)	2		Mean Difference (IV, Random, 95% CI)	Subtotals only
12.1 up to 12 weeks (short-term)	2	372	Mean Difference (IV, Random, 95% CI)	1.5 [-2.96, 5.96]
13 Mental state: 9. average scores of various scale (high=poor, skewed data)			Other data	No numeric data
13.1 SANS endpoint scale score			Other data	No numeric data
13.2 PANSS general pathology subscale score			Other data	No numeric data

13.3 PANSS negative symptom subscale score			Other data	No numeric data
13.4 PANSS positive symptom subscale score			Other data	No numeric data
14 Leaving the study early	17		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
14.1 Any reason	12	1239	Risk Ratio (M-H, Random, 95% CI)	1.02 [0.79, 1.32]
14.2 Progressive disease	2	188	Risk Ratio (M-H, Random, 95% CI)	0.86 [0.14, 5.09]
14.3 Not insisting follow up	2	146	Risk Ratio (M-H, Random, 95% CI)	1.48 [0.49, 4.44]
14.4 Termination treatment early	1	100	Risk Ratio (M-H, Random, 95% CI)	3.0 [0.13, 71.92]
14.5 Violation of study scheme	2	152	Risk Ratio (M-H, Random, 95% CI)	1.32 [0.30, 5.83]
14.6 Incomplete data	1	180	Risk Ratio (M-H, Random, 95% CI)	5.0 [0.24, 102.71]
14.7 Adverse effect	9	1272	Risk Ratio (M-H, Random, 95% CI)	1.15 [0.64, 2.06]
14.8 Economic issue	2	160	Risk Ratio (M-H, Random, 95% CI)	1.02 [0.11, 9.60]
14.9 No effect	5	681	Risk Ratio (M-H, Random, 95% CI)	0.99 [0.49, 2.01]
15 Adverse effects: 1. At least one adverse effect, non-specific	51		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
15.1 non-specific	28	2361	Risk Ratio (M-H, Random, 95% CI)	0.81 [0.73, 0.91]
15.2 liver function abnormal	29	2300	Risk Ratio (M-H, Random, 95% CI)	0.63 [0.46, 0.86]
15.3 hyper-salivation	7	554	Risk Ratio (M-H, Random, 95% CI)	0.63 [0.22, 1.80]
15.4 myalgia/ostealgia	2	100	Risk Ratio (M-H, Random, 95% CI)	1.95 [0.51, 7.46]
15.5 renal function abnormal	1	100	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
15.6 sexual desire change	8	614	Risk Ratio (M-H, Random, 95% CI)	0.11 [0.04, 0.30]
15.7 sweating- increase	4	278	Risk Ratio (M-H, Random, 95% CI)	0.65 [0.16, 2.59]
15.8 stuffy nose	2	165	Risk Ratio (M-H, Random, 95% CI)	3.90 [0.44, 34.47]
16 Adverse effects: 2a.Cardiac effects (short term, up to 12 weeks)	61		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
16.1 abnormal ECG	12	1032	Risk Ratio (M-H, Random, 95% CI)	0.66 [0.41, 1.05]
16.2 blood pressure decline or rise	5	363	Risk Ratio (M-H, Random, 95% CI)	1.54 [0.46, 5.15]
16.3 blood pressure- increase	1	80	Risk Ratio (M-H, Random, 95% CI)	1.0 [0.06, 15.44]
16.4 blood pressure- decrease	6	504	Risk Ratio (M-H, Random, 95% CI)	1.15 [0.45, 2.90]
16.5 EEG abnormal	1	120	Risk Ratio (M-H, Random, 95% CI)	0.67 [0.12, 3.85]
16.6 postural hypotension	6	399	Risk Ratio (M-H, Random, 95% CI)	0.94 [0.46, 1.93]
16.7 QTc prolongation	5	649	Risk Ratio (M-H, Random, 95% CI)	0.37 [0.13, 1.09]
16.8 tachycardia	49	3835	Risk Ratio (M-H, Random, 95% CI)	0.76 [0.61, 0.96]
17 Adverse effects: 2b. Cardiac - QTc change from baseline (in ms)	2	383	Mean Difference (IV, Random, 95% CI)	-7.19 [-12.19, -2.19]
18 Adverse effects: 3. Central / peripheral nervous system (short term, up to 12 weeks)	63		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
18.1 acute onset of schizophrenia	2	120	Risk Ratio (M-H, Random, 95% CI)	1.33 [0.49, 3.64]
18.2 dizziness	23	1896	Risk Ratio (M-H, Random, 95% CI)	1.06 [0.72, 1.54]
18.3 blurred vision	39	3272	Risk Ratio (M-H, Random, 95% CI)	0.96 [0.70, 1.32]
18.4 fatigue	5	369	Risk Ratio (M-H, Random, 95% CI)	0.62 [0.29, 1.35]
18.5 headache	20	1505	Risk Ratio (M-H, Random, 95% CI)	1.91 [1.31, 2.78]
18.6 headache/dizziness	20	1486	Risk Ratio (M-H, Random, 95% CI)	1.29 [0.93, 1.79]
18.7 insomnia	54	4209	Risk Ratio (M-H, Random, 95% CI)	1.17 [0.98, 1.39]

18.8 memory decrease	1	60	Risk Ratio (M-H, Random, 95% CI)	0.22 [0.05, 0.94]
18.9 sedation	2	170	Risk Ratio (M-H, Random, 95% CI)	0.20 [0.04, 1.18]
18.10 sleep disorder	2	152	Risk Ratio (M-H, Random, 95% CI)	0.85 [0.39, 1.86]
18.11 somnolence	35	2779	Risk Ratio (M-H, Random, 95% CI)	0.95 [0.74, 1.22]
19 Adverse effects: 3a. Endocrine - Prolactin - average change (ng/ml)	2	383	Mean Difference (IV, Random, 95% CI)	-54.71 [-60.06, -49.36]
20 Adverse effects: 3b. Endocrine - Prolactin-associated	1		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
20.1 abnormally high prolactin value	1	301	Risk Ratio (M-H, Random, 95% CI)	0.04 [0.02, 0.08]
20.2 dysmenorrhoea	1	91	Risk Ratio (M-H, Random, 95% CI)	3.17 [0.17, 59.43]
21 Adverse effects: 4. Various extrapyramidal symptoms (short term, up to 12 weeks)	64		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
21.1 akathisia	42	3501	Risk Ratio (M-H, Random, 95% CI)	0.60 [0.48, 0.74]
21.2 tremor	36	2799	Risk Ratio (M-H, Random, 95% CI)	0.35 [0.27, 0.45]
21.3 dystonia	32	2640	Risk Ratio (M-H, Random, 95% CI)	0.35 [0.25, 0.49]
21.4 parkinsonism	1	301	Risk Ratio (M-H, Random, 95% CI)	7.39 [0.43, 128.08]
21.5 use of antiparkinson medication	1	83	Risk Ratio (M-H, Random, 95% CI)	0.59 [0.32, 1.12]
21.6 extrapyramidal symptoms	31	2605	Risk Ratio (M-H, Random, 95% CI)	0.39 [0.31, 0.50]
21.7 torsion spasm	3	200	Risk Ratio (M-H, Random, 95% CI)	0.52 [0.04, 7.18]
21.8 tremor	2	391	Risk Ratio (M-H, Random, 95% CI)	1.21 [0.07, 21.13]
21.9 increase activities	1	64	Risk Ratio (M-H, Random, 95% CI)	5.0 [0.25, 100.20]
22 Adverse effects: 4b. Extrapyramidal - average score	2		Mean Difference (IV, Random, 95% CI)	Subtotals only
22.1 Abnormal Involuntary Movement Scale (high=poor)	2	383	Mean Difference (IV, Random, 95% CI)	-0.25 [-1.24, 0.75]
22.2 Barnes Akathisia Scale (high=poor)	2	383	Mean Difference (IV, Random, 95% CI)	-0.11 [-0.49, 0.27]
22.3 Simpson-Angus Scale (high=poor)	2	383	Mean Difference (IV, Random, 95% CI)	-0.70 [-2.22, 0.82]
23 Adverse effects: 5. Gastrointestinal	46		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
23.1 constipation	27	2067	Risk Ratio (M-H, Random, 95% CI)	0.75 [0.52, 1.08]
23.2 dry mouth	33	2658	Risk Ratio (M-H, Random, 95% CI)	1.20 [0.86, 1.69]
23.3 gastrointestinal reaction	3	300	Risk Ratio (M-H, Random, 95% CI)	2.01 [0.76, 5.37]
23.4 nausea / vomiting	28	2180	Risk Ratio (M-H, Random, 95% CI)	1.84 [1.31, 2.56]
24 Adverse effects: 6. Haematological	8		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
24.1 blood routine abnormal	6	515	Risk Ratio (M-H, Random, 95% CI)	0.45 [0.20, 1.02]
24.2 leucopenia	1	60	Risk Ratio (M-H, Random, 95% CI)	0.33 [0.01, 7.87]
24.3 blood lipid abnormal	1	80	Risk Ratio (M-H, Random, 95% CI)	2.0 [0.19, 21.18]
25 Adverse effects: 7a. Metabolic - binary measures (short term, up to 12 weeks)	62		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
25.1 appetite- decrease	2	204	Risk Ratio (M-H, Random, 95% CI)	0.26 [0.07, 1.03]
25.2 blood glucose- increase	5	358	Risk Ratio (M-H, Random, 95% CI)	0.28 [0.09, 0.82]
25.3 endocrine disorder	9	642	Risk Ratio (M-H, Random, 95% CI)	0.07 [0.03, 0.17]

25.4 lactation	3	216	Risk Ratio (M-H, Random, 95% CI)	0.11 [0.02, 0.60]
25.5 menstrual disorder/ lactation	29	2278	Risk Ratio (M-H, Random, 95% CI)	0.10 [0.06, 0.16]
25.6 menstrual disorder or sexual function change	1	68	Risk Ratio (M-H, Random, 95% CI)	0.07 [0.00, 1.12]
25.7 menstrual disorder	9	655	Risk Ratio (M-H, Random, 95% CI)	0.13 [0.06, 0.27]
25.8 skin symptom	9	778	Risk Ratio (M-H, Random, 95% CI)	0.32 [0.12, 0.86]
25.9 PRL-increase	3	184	Risk Ratio (M-H, Random, 95% CI)	0.07 [0.01, 0.38]
25.10 obesity	1	72	Risk Ratio (M-H, Random, 95% CI)	0.95 [0.14, 6.35]
25.11 vaginal bleeding	1	72	Risk Ratio (M-H, Random, 95% CI)	2.84 [0.12, 67.53]
25.12 weight gain	58	4623	Risk Ratio (M-H, Random, 95% CI)	0.22 [0.17, 0.29]
25.13 weight loss	1	101	Risk Ratio (M-H, Random, 95% CI)	2.94 [0.12, 70.56]
26 Adverse effects: 7b. Metabolic - continuous measures (high=poor)	7		Mean Difference (IV, Random, 95% CI)	Subtotals only
26.1 endpoint average weight (in kg)	5	465	Mean Difference (IV, Random, 95% CI)	-2.30 [-4.17, -0.44]
26.2 weight change from baseline (in kg)	1	100	Mean Difference (IV, Random, 95% CI)	-1.50 [-1.84, -1.16]
26.3 average endpoint BMI of male (in kg/m2)	1	60	Mean Difference (IV, Random, 95% CI)	-2.46 [-4.08, -0.84]
26.4 average endpoint BMI of female (in kg/m2)	2	124	Mean Difference (IV, Random, 95% CI)	-1.47 [-3.55, 0.60]
26.5 average endpoint blood glucose of female (in mmol/L)	1	60	Mean Difference (IV, Random, 95% CI)	4.29 [3.97, 4.61]
26.6 average endpoint blood glucose of male (in mmol/L)	1	60	Mean Difference (IV, Random, 95% CI)	0.28 [-0.04, 0.60]
26.7 average endpoint blood glucose FBG (in mg/dl)	1	60	Mean Difference (IV, Random, 95% CI)	-0.08 [-0.37, 0.21]
26.8 average endpoint cholesterol - TC of female (in mmol/L)	1	60	Mean Difference (IV, Random, 95% CI)	-0.51 [-0.96, -0.06]
26.9 average endpoint cholesterol - TC of male (in mmol/L)	1	60	Mean Difference (IV, Random, 95% CI)	-0.48 [-0.96, -0.00]
26.10 average endpoint cholesterol - TC level (in mmol/L)	2	240	Mean Difference (IV, Random, 95% CI)	-0.02 [-0.19, 0.14]
26.11 average endpoint cholesterol-TG level (in mmol/ L)	1	60	Mean Difference (IV, Random, 95% CI)	-0.07 [-0.21, 0.07]
26.12 average endpoint cholesterol - LDL level (in mmol/L)	2	240	Mean Difference (IV, Random, 95% CI)	0.07 [-0.11, 0.26]
26.13 average endpoint waistline (in cm)	1	180	Mean Difference (IV, Random, 95% CI)	-3.30 [-5.47, -1.13]
27 Adverse effect : 7c. Metabolic - continuous measures	4	789	Mean Difference (IV, Random, 95% CI)	-0.01 [-0.22, 0.21]
27.1 average endpoint cholesterol- HDL level (in mmol/L)	2	240	Mean Difference (IV, Random, 95% CI)	0.06 [-0.03, 0.14]

27.2 cholesterol - change from baseline (in mg/dl)	1	83	Mean Difference (IV, Random, 95% CI)	-22.3 [-39.69, -4.91]
27.3 glucose - change from baseline (in mg/dl)	1	83	Mean Difference (IV, Random, 95% CI)	6.8 [-6.10, 19.70]
27.4 weight gain - change from baseline (in kg)	2	383	Mean Difference (IV, Random, 95% CI)	-0.54 [-1.24, 0.15]
28 Adverse effect: 8. required additional drug combination	2		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
28.1 benzodiazepines	2	138	Risk Ratio (M-H, Random, 95% CI)	1.07 [0.73, 1.58]
28.2 benzhexol	1	69	Risk Ratio (M-H, Random, 95% CI)	0.34 [0.12, 0.93]
28.3 benzhexol/propranolol	1	69	Risk Ratio (M-H, Random, 95% CI)	1.11 [0.45, 2.72]
29 Adverse effects: 9. TESS score (short term, up to 12 weeks, high=poor)	4	250	Mean Difference (IV, Random, 95% CI)	-1.34 [-2.30, -0.39]
30 Adverse effects: 10. TESS score (short term, up to 12 weeks, high=poor, data skewed)			Other data	No numeric data
31 Adverse effects: 11. weight gain (in KG, high=poor, data skewed)			Other data	No numeric data
32 Cognitive functioning: 1. Specific - average endpoint total score	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
32.1 (short term, up to 12 weeks, WMS, low= poor)	1	72	Mean Difference (IV, Random, 95% CI)	-1.56 [-7.95, 4.83]
32.2 (short term, up to 12 weeks, WAIS-RC, low=poor)	1	72	Mean Difference (IV, Random, 95% CI)	-1.57 [-8.92, 5.78]
33 Cost effectiveness analysis (high=poor, data skewed)			Other data	No numeric data
33.1 Cost of hospitalisation (in RMB)			Other data	No numeric data
33.2 Cost of drug (in RMB)			Other data	No numeric data
33.3 Length of hospitalisation (day)			Other data	No numeric data

Comparison 4. COMPARISON 4. ARIPIRAZOLE versus ZIPRASIDONE

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Global state: 1. No clinically significant response (as defined by the original studies)	6		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
1.1 up to 12 weeks - short term	6	442	Risk Ratio (M-H, Random, 95% CI)	0.97 [0.62, 1.52]
2 Global state: 2. Average endpoint CGI-GI score (short term, up to 12 weeks, high=poor)	1		Mean Difference (IV, Random, 95% CI)	Subtotals only

3 Global state: 3. Average change score (CGI-S, decline=good)	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
4 Mental state: 1. Average endpoint total score (short term, up to 12 weeks, high=poor)	7		Mean Difference (IV, Random, 95% CI)	Subtotals only
4.1 PANSS	7	689	Mean Difference (IV, Random, 95% CI)	-1.74 [-3.68, 0.20]
4.2 SANS	3	238	Mean Difference (IV, Random, 95% CI)	-1.39 [-2.56, -0.22]
4.3 BPRS	1	247	Mean Difference (IV, Random, 95% CI)	-2.20 [-4.97, 0.57]
5 Mental state: 2. Specific - binary outcomes (up to 12 weeks - short term)	3		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
5.1 anxiety - labelled as "adverse effect"	1	86	Risk Ratio (M-H, Random, 95% CI)	3.0 [0.64, 14.04]
5.2 agitation - labelled as "adverse effect"	2	150	Risk Ratio (M-H, Random, 95% CI)	1.00 [0.11, 9.42]
6 Mental state: 3. Specific - average endpoint PANSS subscale scores (short term, high=poor)	6		Mean Difference (IV, Random, 95% CI)	Subtotals only
6.1 positive symptom scores	2	146	Mean Difference (IV, Random, 95% CI)	-0.16 [-1.36, 1.04]
6.2 negative symptom scores	4	272	Mean Difference (IV, Random, 95% CI)	-0.31 [-1.23, 0.61]
6.3 general pathology scores	5	382	Mean Difference (IV, Random, 95% CI)	-0.35 [-1.73, 1.04]
7 Mental state: endpoint scores of various scales (high=poor, data skewed)			Other data	No numeric data
7.1 PANSS negative symptom subscale score			Other data	No numeric data
7.2 PANSS positive symptom subscale score			Other data	No numeric data
8 Leaving the study early	2		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
8.1 any reason	2	316	Risk Ratio (M-H, Random, 95% CI)	0.94 [0.66, 1.34]
8.2 adverse events	1	256	Risk Ratio (M-H, Random, 95% CI)	0.44 [0.14, 1.38]
8.3 defaulted	1	256	Risk Ratio (M-H, Random, 95% CI)	0.98 [0.58, 1.66]
8.4 inefficacy	1	256	Risk Ratio (M-H, Random, 95% CI)	1.48 [0.54, 4.03]
8.5 other/withdrew	1	256	Risk Ratio (M-H, Random, 95% CI)	0.98 [0.25, 3.85]
9 Adverse effects: 1. At least one adverse effect, non-specific	8		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
9.1 non-specific	2	126	Risk Ratio (M-H, Random, 95% CI)	1.23 [0.85, 1.78]
9.2 endocrine disorder	1	84	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
9.3 liver function abnormal	1	84	Risk Ratio (M-H, Random, 95% CI)	3.0 [0.13, 71.61]
9.4 respiratory tract infection	1	253	Risk Ratio (M-H, Random, 95% CI)	0.33 [0.09, 1.17]
9.5 sexual function change	2	172	Risk Ratio (M-H, Random, 95% CI)	8.00 [2.96, 21.65]
9.6 skin rash	1	60	Risk Ratio (M-H, Random, 95% CI)	0.33 [0.01, 7.87]
9.7 stuffy nose	1	84	Risk Ratio (M-H, Random, 95% CI)	1.0 [0.06, 15.47]
9.8 sweating	1	70	Risk Ratio (M-H, Random, 95% CI)	1.0 [0.07, 15.36]
9.9 urine routine abnormal	1	80	Risk Ratio (M-H, Random, 95% CI)	0.33 [0.01, 7.95]
10 Adverse effects: 2. Cardiac effects (short term, up to 12 weeks)	7		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
10.1 abnormal ECG	4	296	Risk Ratio (M-H, Random, 95% CI)	0.60 [0.22, 1.68]
10.2 QTc prolongation	2	145	Risk Ratio (M-H, Random, 95% CI)	0.42 [0.06, 2.79]
10.3 tachycardia	3	230	Risk Ratio (M-H, Random, 95% CI)	1.16 [0.43, 3.16]
10.4 blood pressure- decrease	2	144	Risk Ratio (M-H, Random, 95% CI)	3.92 [0.44, 34.66]

11 Adverse effects: 3. Central / peripheral nervous system (short term, up to 12 weeks)	6		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
11.1 blurred vision	1	84	Risk Ratio (M-H, Random, 95% CI)	7.0 [0.90, 54.44]
11.2 dizziness	5	376	Risk Ratio (M-H, Random, 95% CI)	3.24 [1.57, 6.70]
11.3 headache	2	150	Risk Ratio (M-H, Random, 95% CI)	4.92 [0.96, 25.27]
11.4 insomnia	5	382	Risk Ratio (M-H, Random, 95% CI)	2.93 [1.17, 7.30]
11.5 somnolence	4	296	Risk Ratio (M-H, Random, 95% CI)	1.45 [0.62, 3.39]
12 Adverse effects: 4. Various extrapyramidal symptoms (short term, up to 12 weeks)	9		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
12.1 akathisia	3	423	Risk Ratio (M-H, Random, 95% CI)	0.80 [0.25, 2.61]
12.2 activity-decrease	1	86	Risk Ratio (M-H, Random, 95% CI)	3.0 [0.13, 71.65]
12.3 dystonia	1	84	Risk Ratio (M-H, Random, 95% CI)	0.07 [0.00, 1.13]
12.4 general extrapyramidal symptoms	2	120	Risk Ratio (M-H, Random, 95% CI)	0.77 [0.37, 1.62]
12.5 tremor	2	152	Risk Ratio (M-H, Random, 95% CI)	3.0 [0.32, 28.21]
12.6 spasmodic torticollis	1	80	Risk Ratio (M-H, Random, 95% CI)	0.33 [0.01, 7.95]
12.7 use of antiparkinson medication	2	140	Risk Ratio (M-H, Random, 95% CI)	2.84 [0.07, 117.07]
13 Adverse effects: 5. Gastrointestinal (short term, up to 12 weeks)	6		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
13.1 appetite-decrease	1	86	Risk Ratio (M-H, Random, 95% CI)	2.0 [0.39, 10.35]
13.2 constipation	3	230	Risk Ratio (M-H, Random, 95% CI)	0.63 [0.13, 2.97]
13.3 dry mouth	4	296	Risk Ratio (M-H, Random, 95% CI)	0.54 [0.10, 2.80]
13.4 hyper-salivation	1	86	Risk Ratio (M-H, Random, 95% CI)	2.0 [0.19, 21.24]
13.5 nausea / vomiting	6	442	Risk Ratio (M-H, Random, 95% CI)	2.53 [0.91, 7.09]
14 Adverse effects: 6. Haematological	2		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
14.1 leucopenia	2	140	Risk Ratio (M-H, Random, 95% CI)	1.0 [0.07, 15.26]
15 Adverse effects: 7. Hormonal	6		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
15.1 menstrual disorder	6	538	Risk Ratio (M-H, Random, 95% CI)	0.74 [0.28, 1.93]
16 Adverse effects: 8a. Metabolic - binary measures	5		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
16.1 appetite-decrease	2	152	Risk Ratio (M-H, Random, 95% CI)	0.57 [0.04, 7.93]
16.2 blood routine abnormal	1	85	Risk Ratio (M-H, Random, 95% CI)	0.31 [0.01, 7.43]
16.3 lactation	1	66	Risk Ratio (M-H, Random, 95% CI)	3.0 [0.13, 71.07]
16.4 weight gain	3	232	Risk Ratio (M-H, Random, 95% CI)	4.01 [1.10, 14.60]
17 Adverse effects: 8b. Metabolic - continuous measures	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
17.1 cholesterol - TG average endpoint level (in mmol/L, high= poor)	1	180	Mean Difference (IV, Random, 95% CI)	-0.04 [-0.21, 0.13]
17.2 cholesterol - TC average endpoint level (in mmol/L, high= poor)	1	180	Mean Difference (IV, Random, 95% CI)	0.0 [-0.17, 0.17]
17.3 cholesterol - LDL average endpoint level (in mmol/L, high= poor)	1	180	Mean Difference (IV, Random, 95% CI)	0.13 [-0.04, 0.30]
17.4 HDL (low=poor)	1	180	Mean Difference (IV, Random, 95% CI)	0.10 [0.01, 0.19]

17.5 waistline- average endpoint level (in cm, high= poor)	1	180	Mean Difference (IV, Random, 95% CI)	-3.40 [-5.29, -1.51]
17.6 weight- average endpoint level (in kg, high= poor)	1	180	Mean Difference (IV, Random, 95% CI)	-2.5 [-5.06, 0.06]

Comparison 5. COMPARISON 5. ARIPIPRAZOLE versus OLANZAPINE

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Global state: 1.No clinically significant response (as defined by the original studies)	11	1739	Risk Ratio (M-H, Random, 95% CI)	1.06 [0.96, 1.17]
1.1 up to 12 weeks- short term	10	1422	Risk Ratio (M-H, Random, 95% CI)	1.02 [0.86, 1.21]
1.2 from 12 to 26 weeks (medium-term)	1	317	Risk Ratio (M-H, Random, 95% CI)	1.08 [0.95, 1.22]
2 Global state: 2. Not responded (decline in PANSS of 30% or more)	1		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 by up to 12 weeks (short-term)	1	566	Risk Ratio (M-H, Random, 95% CI)	1.16 [1.01, 1.34]
2.2 more than 26 weeks (long-term)	1	566	Risk Ratio (M-H, Random, 95% CI)	1.13 [1.00, 1.27]
3 Global state: 3. Remission not achieved (as defined in the study)	1		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
3.1 by up to 12 weeks (short-term)	1	566	Risk Ratio (M-H, Random, 95% CI)	1.01 [0.91, 1.13]
3.2 more than 26 weeks (long-term)	1	566	Risk Ratio (M-H, Random, 95% CI)	1.38 [1.23, 1.56]
4 Global state: 4. Average endpoint EI score (CGI, high=poor)	2		Mean Difference (IV, Random, 95% CI)	Subtotals only
4.1 up to 12 weeks - short term	2	180	Mean Difference (IV, Random, 95% CI)	0.0 [-0.16, 0.16]
5 Global state: 5. Average endpoint CGI score decreased rate (short term, low=poor)	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
6 Global state: 6. Average change score (CGI-S, decline=best)	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
6.1 more than 26 weeks (long-term)	1	566	Mean Difference (IV, Random, 95% CI)	0.10 [-0.12, 0.32]
7 Global state: 7. Improvement (CGI-I, high=poor)	1	566	Mean Difference (IV, Random, 95% CI)	0.10 [-0.12, 0.32]
8 Mental state: 1. Average endpoint scale score (PANSS, high=poor)	13		Mean Difference (IV, Random, 95% CI)	Subtotals only
8.1 up to 12 weeks - short term	11	1500	Mean Difference (IV, Random, 95% CI)	0.61 [-0.23, 1.46]

8.2 12- 26 weeks - medium term	2	139	Mean Difference (IV, Random, 95% CI)	0.80 [-5.26, 6.87]
8.3 more than 26 weeks (long-term)	1	566	Mean Difference (IV, Random, 95% CI)	4.20 [0.10, 8.30]
9 Mental state: 2. Average endpoint scale score (SANS, high=poor)	2	137	Mean Difference (IV, Random, 95% CI)	-0.04 [-2.04, 1.97]
9.1 up to 12 weeks - short term	1	89	Mean Difference (IV, Random, 95% CI)	-0.04 [-2.52, 2.44]
9.2 more than 26 weeks - long term	1	48	Mean Difference (IV, Random, 95% CI)	-0.03 [-3.45, 3.39]
10 Mental state: 3. average endpoint score (PANSS, high=poor, data skewed)			Other data	No numeric data
10.1 PANSS total			Other data	No numeric data
10.2 PANSS negative symptom subscale score			Other data	No numeric data
10.3 PANSS positive symptom subscale score			Other data	No numeric data
11 Mental state: 4. Specific - average endpoint positive score (PANSS, high=poor)	7	1043	Mean Difference (IV, Random, 95% CI)	0.71 [0.17, 1.26]
11.1 by up to 12 weeks - short term	5	429	Mean Difference (IV, Random, 95% CI)	0.77 [-0.16, 1.70]
11.2 12- 26 weeks - medium term	1	48	Mean Difference (IV, Random, 95% CI)	0.66 [-1.54, 2.86]
11.3 more than 26 weeks	1	566	Mean Difference (IV, Random, 95% CI)	0.80 [-0.03, 1.63]
12 Mental state: 5. Specific - average endpoint negative subscale score (PANSS, high=poor)	6	967	Mean Difference (IV, Random, 95% CI)	0.42 [-0.25, 1.09]
12.1 up to 12 weeks - short term	5	401	Mean Difference (IV, Random, 95% CI)	0.16 [-0.59, 0.92]
12.2 more than 26 weeks	1	566	Mean Difference (IV, Random, 95% CI)	1.40 [-0.07, 2.87]
13 Mental state: 6. Specific - average endpoint general pathological score (PANSS, high=poor)	8	642	Mean Difference (IV, Random, 95% CI)	-0.80 [-2.24, 0.64]
13.1 up to 12 weeks - short term	7	594	Mean Difference (IV, Random, 95% CI)	-0.94 [-2.49, 0.60]
13.2 12- 26 weeks - medium term	1	48	Mean Difference (IV, Random, 95% CI)	0.80 [-3.08, 4.68]
14 Mental state: 7. Specific - binary outcomes	2		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
14.1 anxiety - labelled as "adverse effect"	2	778	Risk Ratio (M-H, Random, 95% CI)	1.23 [0.79, 1.90]
14.2 depression - labelled as "adverse effect"	1	566	Risk Ratio (M-H, Random, 95% CI)	0.27 [0.08, 0.95]
14.3 exacerbation of schizophrenia - labelled as "adverse effect"	2	778	Risk Ratio (M-H, Random, 95% CI)	0.89 [0.50, 1.56]

15 Mental state: 8. Various scale scores decreased rate (low=poor, data skewed)			Other data	No numeric data
15.1 PANSS positive symptom subscale			Other data	No numeric data
15.2 PANSS negative symptom subscale			Other data	No numeric data
15.3 PANSS general pathology subscale			Other data	No numeric data
15.4 BPRS total			Other data	No numeric data
15.5 PANSS total			Other data	No numeric data
16 Adverse effects: 1. At least one adverse effect	9		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
16.1 non-specific	1	75	Risk Ratio (M-H, Random, 95% CI)	0.95 [0.69, 1.30]
16.2 endocrine dyscrasia	1	80	Risk Ratio (M-H, Random, 95% CI)	0.08 [0.01, 0.61]
16.3 high prolactin level	1	317	Risk Ratio (M-H, Random, 95% CI)	0.27 [0.12, 0.60]
16.4 liver function abnormal	5	348	Risk Ratio (M-H, Random, 95% CI)	0.46 [0.20, 1.07]
16.5 skin adverse reaction	1	89	Risk Ratio (M-H, Random, 95% CI)	1.63 [0.41, 6.41]
16.6 sweating- increase	2	138	Risk Ratio (M-H, Random, 95% CI)	3.0 [0.32, 28.16]
16.7 flu syndrome	1	212	Risk Ratio (M-H, Random, 95% CI)	0.49 [0.16, 1.54]
16.8 respiratory infection	1	212	Risk Ratio (M-H, Random, 95% CI)	1.54 [0.50, 4.69]
17 Adverse effects: 2. Cardiac effects	8		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
17.1 abnormal ECG	2	121	Risk Ratio (M-H, Random, 95% CI)	0.96 [0.15, 6.29]
17.2 blood pressure- decrease	1	89	Risk Ratio (M-H, Random, 95% CI)	0.33 [0.01, 7.80]
17.3 QTc prolongation	3	618	Risk Ratio (M-H, Random, 95% CI)	0.40 [0.11, 1.38]
17.4 tachycardia	5	339	Risk Ratio (M-H, Random, 95% CI)	0.91 [0.39, 2.08]
18 Adverse effects: 3a. Cardiac - QTc change from baseline (in ms)	1	317	Mean Difference (IV, Random, 95% CI)	-3.70 [-9.51, 2.11]
19 Adverse effects: 3b. Central / peripheral nervous system	9		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
19.1 dizziness	6	1057	Risk Ratio (M-H, Random, 95% CI)	0.98 [0.62, 1.53]
19.2 blurred vision	1	75	Risk Ratio (M-H, Random, 95% CI)	0.13 [0.01, 2.35]
19.3 headache	5	991	Risk Ratio (M-H, Random, 95% CI)	2.03 [0.82, 5.07]
19.4 fatigue	3	721	Risk Ratio (M-H, Random, 95% CI)	0.58 [0.21, 1.62]
19.5 insomnia	7	1141	Risk Ratio (M-H, Random, 95% CI)	1.81 [0.95, 3.45]
19.6 somnolence	5	1003	Risk Ratio (M-H, Random, 95% CI)	0.65 [0.42, 1.01]
19.7 headache/dizziness	1	89	Risk Ratio (M-H, Random, 95% CI)	0.29 [0.09, 1.00]
19.8 sedation	2	883	Risk Ratio (M-H, Random, 95% CI)	0.37 [0.23, 0.60]
19.9 nervousness	1	212	Risk Ratio (M-H, Random, 95% CI)	1.32 [0.42, 4.19]
19.10 CNS stimulation	1	212	Risk Ratio (M-H, Random, 95% CI)	0.73 [0.21, 2.52]
20 Adverse effects: 4. Endocrine - Prolactin - average increase	1	566	Mean Difference (IV, Random, 95% CI)	-8.89 [-12.96, -4.82]
21 Adverse effects: 5. Extrapyramidal - various	8		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
21.1 Akathisia	6	1320	Risk Ratio (M-H, Random, 95% CI)	1.56 [0.67, 3.60]
21.2 Tremor	1	61	Risk Ratio (M-H, Random, 95% CI)	7.23 [0.95, 55.31]
21.3 Extrapyramidal symptoms	4	667	Risk Ratio (M-H, Random, 95% CI)	0.99 [0.62, 1.59]
21.4 Parkinsonism	3	618	Risk Ratio (M-H, Random, 95% CI)	0.80 [0.46, 1.38]

22 Adverse effects: 6. Gastrointestinal	7		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
22.1 nausea / vomiting	6	948	Risk Ratio (M-H, Random, 95% CI)	1.34 [0.80, 2.26]
22.2 constipation	6	443	Risk Ratio (M-H, Random, 95% CI)	0.46 [0.21, 1.04]
22.3 dry mouth	5	854	Risk Ratio (M-H, Random, 95% CI)	0.67 [0.38, 1.19]
22.4 abdominal pain - upper	1	566	Risk Ratio (M-H, Random, 95% CI)	2.96 [1.09, 8.03]
23 Adverse effects: 7. Hormonal	3		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
23.1 menstrual changes	3	198	Risk Ratio (M-H, Random, 95% CI)	0.20 [0.04, 1.13]
24 Adverse effects: 8a. Metabolic - binary measures	10		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
24.1 appetite- increase	2	655	Risk Ratio (M-H, Random, 95% CI)	0.33 [0.06, 2.00]
24.2 blood glucose - increase	3	227	Risk Ratio (M-H, Random, 95% CI)	0.12 [0.03, 0.44]
24.3 cholesterol - abnormally high cholesterol value	1	223	Risk Ratio (M-H, Random, 95% CI)	0.32 [0.19, 0.54]
24.4 lactation	1	60	Risk Ratio (M-H, Random, 95% CI)	0.33 [0.01, 7.87]
24.5 PRL- increase	1	89	Risk Ratio (M-H, Random, 95% CI)	0.09 [0.01, 1.56]
24.6 weight gain	9	1538	Risk Ratio (M-H, Random, 95% CI)	0.25 [0.15, 0.43]
25 Adverse effects: 8b. Metabolic - continuous measures (high=poor)	5		Mean Difference (IV, Random, 95% CI)	Subtotals only
25.1 weight - average endpoint level (in kg)	3	242	Mean Difference (IV, Random, 95% CI)	-7.43 [-9.21, -5.65]
25.2 weight gain - change from baseline (in kg)	2	656	Mean Difference (IV, Random, 95% CI)	-3.03 [-7.35, 1.29]
25.3 cholesterol - change from baseline (in mg/dl)	2	789	Mean Difference (IV, Random, 95% CI)	-15.37 [-21.62, -9.11]
25.4 cholesterol - TC average endpoint level (in mmol/L)	2	182	Mean Difference (IV, Random, 95% CI)	-1.00 [-1.44, -0.56]
25.5 cholesterol - TG average endpoint level (in mmol/L)	1	102	Mean Difference (IV, Random, 95% CI)	-1.0 [-1.31, -0.69]
25.6 blood glucose - PBG average endpoint level (in mg/dl)	1	60	Mean Difference (IV, Random, 95% CI)	-0.95 [-1.27, -0.63]
25.7 glucose - change from baseline (in mg/dl)	2	883	Mean Difference (IV, Random, 95% CI)	-3.39 [-7.98, 1.19]
26 Adverse effects: 9. Average endpoint scale score (TESS, high=poor, data skewed)			Other data	No numeric data
27 Leaving the study early	9		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
27.1 Any reason	9	2331	Risk Ratio (M-H, Random, 95% CI)	1.15 [1.05, 1.25]
27.2 Economic issues	1	80	Risk Ratio (M-H, Random, 95% CI)	3.0 [0.13, 71.51]
27.3 Early discharge	1	60	Risk Ratio (M-H, Random, 95% CI)	3.0 [0.13, 70.83]
27.4 Refusing therapy	1	60	Risk Ratio (M-H, Random, 95% CI)	0.33 [0.01, 7.87]
27.5 adverse events	4	1352	Risk Ratio (M-H, Random, 95% CI)	1.20 [0.92, 1.59]
27.6 inefficacy	4	1352	Risk Ratio (M-H, Random, 95% CI)	1.81 [1.23, 2.67]
27.7 lost to follow-up	2	821	Risk Ratio (M-H, Random, 95% CI)	0.74 [0.46, 1.17]
27.8 medication noncompliance	1	255	Risk Ratio (M-H, Random, 95% CI)	2.23 [0.71, 7.06]
27.9 others	2	780	Risk Ratio (M-H, Random, 95% CI)	2.21 [0.77, 6.34]
27.10 patient decision	3	1035	Risk Ratio (M-H, Random, 95% CI)	1.04 [0.60, 1.81]
27.11 protocol entry or interim criteria not met	1	566	Risk Ratio (M-H, Random, 95% CI)	0.20 [0.02, 1.68]

27.12 protocol violation	2	821	Risk Ratio (M-H, Random, 95% CI)	0.80 [0.42, 1.53]
27.13 sponsor decision	1	566	Risk Ratio (M-H, Random, 95% CI)	0.33 [0.01, 8.03]
27.14 death	1	214	Risk Ratio (M-H, Random, 95% CI)	0.35 [0.01, 8.55]
28 Quality of life: 1. Average endpoint general quality of life score (GQOLI-74, low=poor)	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
28.1 Total score	1	68	Mean Difference (IV, Random, 95% CI)	-1.26 [-6.37, 3.85]
28.2 Physical health	1	68	Mean Difference (IV, Random, 95% CI)	-0.19 [-4.72, 4.34]
28.3 Mental health	1	68	Mean Difference (IV, Random, 95% CI)	-2.46 [-8.20, 3.28]
28.4 Social function	1	68	Mean Difference (IV, Random, 95% CI)	1.21 [-3.41, 5.83]
28.5 Material life	1	68	Mean Difference (IV, Random, 95% CI)	-0.77 [-4.62, 3.08]

Comparison 6. COMPARISON 6. ARIPIPRAZOLE versus OLANZAPINE (acutely agitated people - all data by 5 days)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Global state: Average improvement (BPRS, high=good)	1	471	Mean Difference (IV, Random, 95% CI)	-0.18 [-0.79, 0.43]
2 Mental state: Specific - binary outcomes	1		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 agitation - no change - (change defined as $\geq$ 40%reduction in PANSS-EC)	1	604	Risk Ratio (M-H, Random, 95% CI)	0.92 [0.76, 1.12]
2.2 agitation - labelled as "adverse effect"	1	578	Risk Ratio (M-H, Random, 95% CI)	0.25 [0.05, 1.17]
2.3 anxiety - labelled as "adverse effect"	1	604	Risk Ratio (M-H, Random, 95% CI)	0.93 [0.40, 2.17]
2.4 exacerbation of schizophrenia - labelled as "adverse effect"	1	604	Risk Ratio (M-H, Random, 95% CI)	5.13 [0.25, 106.49]
3 Leaving the study early	1		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
3.1 adverse events	1	604	Risk Ratio (M-H, Random, 95% CI)	0.68 [0.12, 4.07]
4 Adverse effects: 1. Central nervous system	1		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
4.1 dizziness	1	578	Risk Ratio (M-H, Random, 95% CI)	0.29 [0.06, 1.36]
4.2 headache	1	578	Risk Ratio (M-H, Random, 95% CI)	2.43 [1.02, 5.77]
4.3 lethargy	1	578	Risk Ratio (M-H, Random, 95% CI)	1.33 [0.30, 5.90]
4.4 sedation	1	578	Risk Ratio (M-H, Random, 95% CI)	0.71 [0.23, 2.22]
4.5 sleep - insomnia	1	604	Risk Ratio (M-H, Random, 95% CI)	1.60 [0.87, 2.94]
4.6 somnolence	1	578	Risk Ratio (M-H, Random, 95% CI)	0.14 [0.02, 1.15]
5 Adverse effects: 2. Endocrine - Prolactin - average increase	1	604	Mean Difference (IV, Random, 95% CI)	-15.76 [-19.18, -12.34]
6 Adverse effects: 3a. Extrapyramidal - various	1		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
6.1 akathisia	1	604	Risk Ratio (M-H, Random, 95% CI)	1.43 [0.79, 2.56]
6.2 parkinsonism	1	604	Risk Ratio (M-H, Random, 95% CI)	1.71 [0.41, 7.10]

7 Adverse effects: 3b. Extrapyramidal - average score	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
7.1 Barnes Akathisia Scale (high=poor)	1	604	Mean Difference (IV, Random, 95% CI)	0.07 [-0.24, 0.38]
7.2 Simpson-Angus Scale (high=poor)	1	604	Mean Difference (IV, Random, 95% CI)	-0.05 [-0.13, 0.03]
8 Adverse effects: 4. Gastrointestinal	1		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
8.1 nausea / dyspepsia	1	578	Risk Ratio (M-H, Random, 95% CI)	0.5 [0.09, 2.71]
8.2 salivation - dry mouth	1	578	Risk Ratio (M-H, Random, 95% CI)	1.0 [0.20, 4.91]
9 Adverse effects: 5. Metabolic - continuous measures	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
9.1 triglycerides - fasting, increase	1	604	Mean Difference (IV, Random, 95% CI)	-35.62 [-49.25, -21.99]

Comparison 7. COMPARISON 7. ARIPIPRAZOLE versus OTHER ANTIPSYCHOTIC DRUGS

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Global state: 1. No change (as defined in the study, measured by IAQ)	1		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
1.1 cognition	1	523	Risk Ratio (M-H, Random, 95% CI)	0.95 [0.82, 1.11]
1.2 energy	1	523	Risk Ratio (M-H, Random, 95% CI)	0.69 [0.56, 0.84]
1.3 mood	1	523	Risk Ratio (M-H, Random, 95% CI)	0.77 [0.65, 0.92]
1.4 negative symptoms	1	523	Risk Ratio (M-H, Random, 95% CI)	0.82 [0.68, 0.99]
1.5 somnolence	1	523	Risk Ratio (M-H, Random, 95% CI)	0.80 [0.69, 0.93]
1.6 weight gain	1	523	Risk Ratio (M-H, Random, 95% CI)	0.84 [0.76, 0.94]
2 Global state: 2. Change in sexual dysfunction (ASEX)	1	85	Mean Difference (IV, Fixed, 95% CI)	-1.43 [-2.97, 0.11]
3 Mental state: Specific - binary outcomes	3	5338	Risk Ratio (M-H, Fixed, 95% CI)	1.20 [0.96, 1.51]
3.1 Anxiety - labelled as "adverse effects"	2	1361	Risk Ratio (M-H, Fixed, 95% CI)	1.33 [0.94, 1.90]
3.2 Agitation - labelled as "adverse effects"	1	548	Risk Ratio (M-H, Fixed, 95% CI)	2.64 [0.96, 7.23]
3.3 Schizophrenia - labelled as "adverse effects"	1	548	Risk Ratio (M-H, Fixed, 95% CI)	0.94 [0.49, 1.81]
3.4 Psychotic disorder - labelled as "adverse effects"	3	2881	Risk Ratio (M-H, Fixed, 95% CI)	1.03 [0.73, 1.48]
4 Preference: Study medication worse than or equal to previous medication	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
4.1 patient - by up to 12 weeks (short-term)	1	446	Risk Ratio (M-H, Fixed, 95% CI)	0.67 [0.49, 0.91]
4.2 care giver - by up to 12 weeks (short-term)	1	121	Risk Ratio (M-H, Fixed, 95% CI)	0.86 [0.52, 1.43]

4.3 patient - from 12 to 26 weeks (medium-term)	1	330	Risk Ratio (M-H, Fixed, 95% CI)	0.39 [0.25, 0.61]
4.4 care giver - from 12 to 26 weeks (medium-term)	1	80	Risk Ratio (M-H, Fixed, 95% CI)	0.44 [0.15, 1.33]
5 Quality of life: 1. Unsatisfactory response on health dimension scale	1	329	Risk Ratio (M-H, Fixed, 95% CI)	0.29 [0.13, 0.66]
6 Quality of life: 3. Average change score (QLS, high=better)	1	326	Mean Difference (IV, Fixed, 95% CI)	6.20 [3.08, 9.32]
7 Quality of life: 2. Average score (EQ-5D utility score, high=better)	1	329	Mean Difference (IV, Fixed, 95% CI)	0.01 [-0.04, 0.05]
8 Quality of life: 4a. Weight related - No meaningful change (IWQOL-Lite)	1	327	Risk Ratio (M-H, Fixed, 95% CI)	0.92 [0.83, 1.01]
9 Quality of life: 4b. Weight related - average score (IWQOL-Lite, high=better)	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
9.1 short-term	1	443	Mean Difference (IV, Fixed, 95% CI)	1.16 [-1.84, 4.16]
9.2 medium-term	1	328	Mean Difference (IV, Fixed, 95% CI)	2.50 [1.04, 3.96]
10 Leaving the study early	3		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
10.1 any reason	3	2908	Risk Ratio (M-H, Random, 95% CI)	0.97 [0.78, 1.19]
10.2 administrative reasons	1	833	Risk Ratio (M-H, Random, 95% CI)	0.08 [0.00, 1.84]
10.3 adverse events	3	2908	Risk Ratio (M-H, Random, 95% CI)	1.40 [1.11, 1.76]
10.4 death	1	555	Risk Ratio (M-H, Random, 95% CI)	0.48 [0.04, 5.23]
10.5 inefficacy	3	2908	Risk Ratio (M-H, Random, 95% CI)	0.94 [0.45, 1.96]
10.6 lost to follow-up	2	1388	Risk Ratio (M-H, Random, 95% CI)	0.85 [0.34, 2.13]
10.7 no longer meets criteria	2	1388	Risk Ratio (M-H, Random, 95% CI)	0.65 [0.16, 2.63]
10.8 other	2	1388	Risk Ratio (M-H, Random, 95% CI)	0.62 [0.10, 3.80]
10.9 poor/non compliance	2	1388	Risk Ratio (M-H, Random, 95% CI)	1.10 [0.53, 2.32]
10.10 pregnancy	1	555	Risk Ratio (M-H, Random, 95% CI)	0.95 [0.14, 6.73]
10.11 withdrew	3	2908	Risk Ratio (M-H, Random, 95% CI)	0.48 [0.36, 0.66]
11 Adverse effects: 1. At least one adverse effect	2	2333	Risk Ratio (M-H, Random, 95% CI)	1.14 [1.05, 1.23]
12 Adverse effects: 2. Central nervous system	3	11524	Risk Ratio (M-H, Fixed, 95% CI)	1.29 [1.12, 1.49]
12.1 sleep disorder	1	813	Risk Ratio (M-H, Fixed, 95% CI)	1.79 [0.78, 4.10]
12.2 insomnia	3	2881	Risk Ratio (M-H, Fixed, 95% CI)	2.09 [1.65, 2.66]
12.3 somnolence	3	2881	Risk Ratio (M-H, Fixed, 95% CI)	0.52 [0.39, 0.71]
12.4 headache	3	2881	Risk Ratio (M-H, Fixed, 95% CI)	1.47 [1.09, 1.99]
12.5 fatigue	1	548	Risk Ratio (M-H, Fixed, 95% CI)	0.59 [0.27, 1.28]
12.6 Lightheadedness	1	1520	Risk Ratio (M-H, Fixed, 95% CI)	0.99 [0.59, 1.67]
13 Adverse effects: 3a. Endocrine - Prolactin - increase in level	1	548	Risk Ratio (M-H, Fixed, 95% CI)	0.31 [0.23, 0.41]
14 Adverse effects: 3b. Endocrine - Prolactin - Change in level	1	94	Mean Difference (IV, Fixed, 95% CI)	-8.60 [-19.14, 1.94]
15 Adverse effects: 4. Extrapyramidal - akathisia	3		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
15.1 homogeneous data	2	1361	Risk Ratio (M-H, Random, 95% CI)	2.77 [1.28, 5.99]
15.2 outlying study	1	1520	Risk Ratio (M-H, Random, 95% CI)	0.17 [0.12, 0.22]
16 Adverse effects: 5. Gastrointestinal	3	2881	Risk Ratio (M-H, Fixed, 95% CI)	3.13 [2.12, 4.61]

16.1 nausea	3	2881	Risk Ratio (M-H, Fixed, 95% CI)	3.13 [2.12, 4.61]
17 Adverse effects: 6a. Metabolic-binary measures	1	2517	Risk Ratio (M-H, Fixed, 95% CI)	0.73 [0.65, 0.82]
17.1 weight gain (7% or more of total body weight at 26 weeks - medium-term)	1	330	Risk Ratio (M-H, Fixed, 95% CI)	0.35 [0.19, 0.64]
17.2 weight loss (7% or more of total body weight at 26 weeks - medium-term)	1	330	Risk Ratio (M-H, Fixed, 95% CI)	1.75 [0.97, 3.19]
17.3 average weight gain	1	548	Risk Ratio (M-H, Fixed, 95% CI)	0.11 [0.03, 0.37]
17.4 total cholesterol increase	1	269	Risk Ratio (M-H, Fixed, 95% CI)	0.75 [0.62, 0.91]
17.5 LDL increase	1	268	Risk Ratio (M-H, Fixed, 95% CI)	0.65 [0.51, 0.84]
17.6 HDL increase	1	269	Risk Ratio (M-H, Fixed, 95% CI)	0.87 [0.61, 1.22]
17.7 triglyceride increase	1	267	Risk Ratio (M-H, Fixed, 95% CI)	0.80 [0.64, 1.00]
17.8 fasting glucose (increase)	1	236	Risk Ratio (M-H, Fixed, 95% CI)	0.95 [0.62, 1.47]
18 Adverse effects: 6b. Metabolic - continuous measures	1	1796	Mean Difference (IV, Fixed, 95% CI)	-2.97 [-3.48, -2.46]
18.1 weight change (no risk)	1	537	Mean Difference (IV, Fixed, 95% CI)	-2.7 [-3.68, -1.72]
18.2 % weight change from baseline- up to 12 weeks (short-term)	1	441	Mean Difference (IV, Fixed, 95% CI)	-2.48 [-3.30, -1.66]
18.3 % weight change from baseline - from 12 to 26 weeks (medium-term)	1	327	Mean Difference (IV, Fixed, 95% CI)	-3.74 [-4.65, -2.83]
18.4 no change in fasting total cholesterol	1	262	Mean Difference (IV, Fixed, 95% CI)	-9.70 [-16.07, -3.33]
18.5 no change in fasting total glucose	1	229	Mean Difference (IV, Fixed, 95% CI)	-1.9 [-5.78, 1.98]

Analysis 1.1. Comparison 1 COMPARISON 1. ARIPIPRAZOLE versus CLOZAPINE, Outcome 1 Global state: 1. No clinically significant response (as defined by the original studies).

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 1 COMPARISON 1. ARIPIPRAZOLE versus CLOZAPINE

Outcome: 1 Global state: 1. No clinically significant response (as defined by the original studies)

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Analysis 1.2. Comparison 1 COMPARISON 1. ARIPIPRAZOLE versus CLOZAPINE, Outcome 2 Mental state: 1. Specific - binary outcomes.

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 1 COMPARISON 1. ARIPIPRAZOLE versus CLOZAPINE

Outcome: 2 Mental state: 1. Specific - binary outcomes

Analysis 1.3. Comparison 1 COMPARISON 1. ARIPIPRAZOLE versus CLOZAPINE, Outcome 3 Mental state: 2. Average endpoint scores of various scales (short term, up to 12 weeks, high=poor).

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 1 COMPARISON 1. ARIPIPRAZOLE versus CLOZAPINE

Outcome: 3 Mental state: 2. Average endpoint scores of various scales (short term, up to 12 weeks, high=poor)

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Analysis 1.4. Comparison 1 COMPARISON 1. ARIPIPRAZOLE versus CLOZAPINE, Outcome 4 Mental state: 3. Average endpoint scores of various scales (medium term, 12 to 26 weeks, high=poor).

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 1 COMPARISON 1. ARIPIPRAZOLE versus CLOZAPINE

Outcome: 4 Mental state: 3. Average endpoint scores of various scales (medium term, 12 to 26 weeks, high=poor)

Analysis 1.5. Comparison 1 COMPARISON 1. ARIPIPRAZOLE versus CLOZAPINE, Outcome 5 Mental state: 4. Average endpoint scores of various scales (skewed data, high=poor).

Mental state: 4. Average endpoint scores of various scales (skewed data, high=poor)

Study	Intervention	Mean	SD	N	Notes
BPRS					
Xiao 2007	Aripiprazole	15.33	7.96	36	
Xiao 2007	Clozapine	15.91	11.22	36	
PANSS					
Jiang 2009	Aripiprazole	53.2	13.9	40	
Jiang 2009	Clozapine	11.2	5.9	40	
PANSS negative symptom subscale score					
Jiang 2009	Aripiprazole	16.4	6.5	40	
Jiang 2009	Clozapine	11.2	5.9	40	

Mental state: 4. Average endpoint scores of various scales (skewed data, high=poor) (Continued)

Liu 2008	Aripiprazole	11.71	7.60	31	
Liu 2008	Clozapine	11.82	6.77	31	
Xiao 2007	Aripiprazole	6.31	5.24	36	
Xiao 2007	Clozapine	13.37	5.15	36	

Analysis 1.6. Comparison 1 COMPARISON 1. ARIPIPRAZOLE versus CLOZAPINE, Outcome 6 Mental state: 5. Specific - average endpoint positive score (PANSS, high=poor).

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 1 COMPARISON 1. ARIPIPRAZOLE versus CLOZAPINE

Outcome: 6 Mental state: 5. Specific - average endpoint positive score (PANSS, high=poor)

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Analysis 1.7. Comparison 1 COMPARISON 1. ARIPIRAZOLE versus CLOZAPINE, Outcome 7 Mental state: 6. Specific - average endpoint negative score (PANSS, high=poor).

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 1 COMPARISON 1. ARIPIRAZOLE versus CLOZAPINE

Outcome: 7 Mental state: 6. Specific - average endpoint negative score (PANSS, high=poor)

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Analysis 1.8. Comparison 1 COMPARISON 1. ARIPIPRAZOLE versus CLOZAPINE, Outcome 8 Mental state: 7. Specific - average endpoint general psychopathological score (PANSS, high=poor).

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 1 COMPARISON 1. ARIPIPRAZOLE versus CLOZAPINE

Outcome: 8 Mental state: 7. Specific - average endpoint general psychopathological score (PANSS, high=poor)

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Analysis 1.9. Comparison 1 COMPARISON 1. ARIPIPRAZOLE versus CLOZAPINE, Outcome 9 Mental state: 8. Specific - average total score decreased rate (PANSS, low=poor).

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 1 COMPARISON 1. ARIPIPRAZOLE versus CLOZAPINE

Outcome: 9 Mental state: 8. Specific - average total score decreased rate (PANSS, low=poor)

Analysis 1.10. Comparison 1 COMPARISON 1. ARIPIPRAZOLE versus CLOZAPINE, Outcome 10 Mental state: 9. Specific - average positive score decreased rate (PANSS, low=poor).

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 1 COMPARISON 1. ARIPIPRAZOLE versus CLOZAPINE

Outcome: 10 Mental state: 9. Specific - average positive score decreased rate (PANSS, low=poor)

Analysis 1.11. Comparison 1 COMPARISON 1. ARIPIRAZOLE versus CLOZAPINE, Outcome 11 Leaving the study early.

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 1 COMPARISON 1. ARIPIRAZOLE versus CLOZAPINE

Outcome: 11 Leaving the study early

Analysis 1.12. Comparison 1 COMPARISON 1. ARIPIPRAZOLE versus CLOZAPINE, Outcome 12 Quality of life: 1a. Average scores (short term, up to 12 weeks, WHO-QOL-100, low=poor).

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 1 COMPARISON 1. ARIPIPRAZOLE versus CLOZAPINE

Outcome: 12 Quality of life: 1a. Average scores (short term, up to 12 weeks, WHO-QOL-100, low=poor)

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Analysis 1.13. Comparison 1 COMPARISON 1. ARIPIPRAZOLE versus CLOZAPINE, Outcome 13 Quality of life: 1b. Average scores (medium term, 12 to 24 weeks, WHO-QOL-100, low=poor).

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 1 COMPARISON 1. ARIPIPRAZOLE versus CLOZAPINE

Outcome: 13 Quality of life: 1b. Average scores (medium term, 12 to 24 weeks, WHO-QOL-100, low=poor)

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Analysis 1.14. Comparison 1 COMPARISON 1. ARIPIRAZOLE versus CLOZAPINE, Outcome 14 Quality of life: 2. Average endpoint general quality of life score (GQOLI - 74, low=poor).

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 1 COMPARISON 1. ARIPIRAZOLE versus CLOZAPINE

Outcome: 14 Quality of life: 2. Average endpoint general quality of life score (GQOLI - 74, low=poor)

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Analysis 1.15. Comparison 1 COMPARISON 1. ARIPIPRAZOLE versus CLOZAPINE, Outcome 15 Adverse effects: 1. At least one adverse effect.

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 1 COMPARISON 1. ARIPIPRAZOLE versus CLOZAPINE

Outcome: 15 Adverse effects: 1. At least one adverse effect

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Analysis 1.16. Comparison 1 COMPARISON 1. ARIPIPRAZOLE versus CLOZAPINE, Outcome 16 Adverse effects: 2. Cardiac effects.

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 1 COMPARISON 1. ARIPIPRAZOLE versus CLOZAPINE

Outcome: 16 Adverse effects: 2. Cardiac effects

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Analysis 1.17. Comparison 1 COMPARISON 1. ARIPIRAZOLE versus CLOZAPINE, Outcome 17 Adverse effects: 3. Central / peripheral nervous system.

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 1 COMPARISON 1. ARIPIRAZOLE versus CLOZAPINE

Outcome: 17 Adverse effects: 3. Central / peripheral nervous system

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Analysis 1.18. Comparison 1 COMPARISON 1. ARIPIPRAZOLE versus CLOZAPINE, Outcome 18 Adverse effects: 4. Extrapyramidal effects.

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 1 COMPARISON 1. ARIPIPRAZOLE versus CLOZAPINE

Outcome: 18 Adverse effects: 4. Extrapyramidal effects

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Analysis 1.19. Comparison 1 COMPARISON 1. ARIPIPRAZOLE versus CLOZAPINE, Outcome 19 Adverse effects: 6. Haematological.

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 1 COMPARISON 1. ARIPIPRAZOLE versus CLOZAPINE

Outcome: 19 Adverse effects: 6. Haematological

(Continued . . .)

Analysis 1.20. Comparison 1 COMPARISON 1. ARIPIPRAZOLE versus CLOZAPINE, Outcome 20 Adverse effects: 5. Gastrointestinal.

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 1 COMPARISON 1. ARIPIPRAZOLE versus CLOZAPINE

Outcome: 20 Adverse effects: 5. Gastrointestinal

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Analysis 1.21. Comparison 1 COMPARISON 1. ARIPIPRAZOLE versus CLOZAPINE, Outcome 21 Adverse effects: 7. Hormonal.

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 1 COMPARISON 1. ARIPIPRAZOLE versus CLOZAPINE

Outcome: 21 Adverse effects: 7. Hormonal

Analysis 1.22. Comparison 1 COMPARISON 1. ARIPIRAZOLE versus CLOZAPINE, Outcome 22 Adverse effects: 8a. Metabolic - binary measures.

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 1 COMPARISON 1. ARIPIRAZOLE versus CLOZAPINE

Outcome: 22 Adverse effects: 8a. Metabolic - binary measures

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Analysis 1.23. Comparison 1 COMPARISON 1. ARIPIRAZOLE versus CLOZAPINE, Outcome 23 Adverse effects: 8b. Metabolic - continuous measures (short term, up to 12 weeks, high=poor).

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 1 COMPARISON 1. ARIPIRAZOLE versus CLOZAPINE

Outcome: 23 Adverse effects: 8b. Metabolic - continuous measures (short term, up to 12 weeks, high=poor)

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Analysis 1.24. Comparison 1 COMPARISON 1. ARIPIPRAZOLE versus CLOZAPINE, Outcome 24 Cost effectiveness analysis (high=poor, data skewed).

Cost effectiveness analysis (high=poor, data skewed)

Study	Intervention	Mean	SD	N	Note
Cost of hospitalisation (in RMB)					
Liu 2010	Aripiprazole	3413.66	1815.05	30	
Liu 2010	Clozapine	4582.00	3372.42	28	
Cost of drug (in RMB)					
Liu 2010	Aripiprazole	418.13	326.43	30	
Liu 2010	Clozapine	210.39	300.32	28	
Length of hospitalisation (day)					
Liu 2010	Aripiprazole	33.19	16.71	30	
Liu 2010	Clozapine	49.50	30.83	28	

Analysis 2.1. Comparison 2 COMPARISON 2. ARIPIRAZOLE versus QUETIAPINE, Outcome 1 Global state: 1.No clinically significant response (as defined by original studies).

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 2 COMPARISON 2. ARIPIRAZOLE versus QUETIAPINE

Outcome: 1 Global state: 1.No clinically significant response (as defined by original studies)

Analysis 2.2. Comparison 2 COMPARISON 2. ARIPIPRAZOLE versus QUETIAPINE, Outcome 2 Global state: 2a. Average endpoint total score (short term, up to 12 weeks, high=poor).

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 2 COMPARISON 2. ARIPIPRAZOLE versus QUETIAPINE

Outcome: 2 Global state: 2a. Average endpoint total score (short term, up to 12 weeks, high=poor)

Analysis 2.3. Comparison 2 COMPARISON 2. ARIPIRAZOLE versus QUETIAPINE, Outcome 3 Global state: 2b. Average endpoint scale score (medium term, 12 to 24 weeks, high=poor).

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 2 COMPARISON 2. ARIPIRAZOLE versus QUETIAPINE

Outcome: 3 Global state: 2b. Average endpoint scale score (medium term, 12 to 24 weeks, high=poor)

Analysis 2.4. Comparison 2 COMPARISON 2. ARIPIRAZOLE versus QUETIAPINE, Outcome 4 Global state: 3. Average endpoint SI score (CGI, high=poor).

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 2 COMPARISON 2. ARIPIRAZOLE versus QUETIAPINE

Outcome: 4 Global state: 3. Average endpoint SI score (CGI, high=poor)

Analysis 2.5. Comparison 2 COMPARISON 2. ARIPIRAZOLE versus QUETIAPINE, Outcome 5 Mental state: 2a. Specific - binary outcomes.

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 2 COMPARISON 2. ARIPIRAZOLE versus QUETIAPINE

Outcome: 5 Mental state: 2a. Specific - binary outcomes

Analysis 2.6. Comparison 2 COMPARISON 2. ARIPIRAZOLE versus QUETIAPINE, Outcome 6 Mental state: 3. Specific - average endpoint positive score (PANSS, high=poor).

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 2 COMPARISON 2. ARIPIRAZOLE versus QUETIAPINE

Outcome: 6 Mental state: 3. Specific - average endpoint positive score (PANSS, high=poor)

Analysis 2.7. Comparison 2 COMPARISON 2. ARIPIRAZOLE versus QUETIAPINE, Outcome 7 Mental state: 4. Specific - average endpoint negative score (PANSS, high=poor).

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 2 COMPARISON 2. ARIPIRAZOLE versus QUETIAPINE

Outcome: 7 Mental state: 4. Specific - average endpoint negative score (PANSS, high=poor)

Analysis 2.8. Comparison 2 COMPARISON 2. ARIPIRAZOLE versus QUETIAPINE, Outcome 8 Mental state: 5. Specific - average endpoint general pathological score (PANSS, high=poor).

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 2 COMPARISON 2. ARIPIRAZOLE versus QUETIAPINE

Outcome: 8 Mental state: 5. Specific - average endpoint general pathological score (PANSS, high=poor)

Analysis 2.9. Comparison 2 COMPARISON 2. ARIPIRAZOLE versus QUETIAPINE, Outcome 9 Mental state: 6. average scores of various scales (high=poor, skewed data).

Mental state: 6. average scores of various scales (high=poor, skewed data)

Study	Intervention	Mean	SD	N	Note
BPRS endpoint scale score					
Zhu 2008	Aripiprazole	23.8	14.3	29	
Zhu 2008	Quetiapine	23.9	13.7	29	
PANSS general pathology subscale score					
Zhu 2008	Aripiprazole	19.4	11.7	29	
Zhu 2008	Quetiapine	19.5	11.3	29	
PANSS negative subscale score					
Dai 2005	Aripiprazole	11.8	7.1	40	
Dai 2005	Quetiapine	11.7	7.6	40	
Ge 2010	Aripiprazole	12.88	3.54	40	
Ge 2010	Quetiapine	15.12	8.15	40	
Wei 2006	Aripiprazole	11.9	7.2	54	
Wei 2006	Quetiapine	11.8	7.6	54	
Zhu 2008	Aripiprazole	10.9	8.1	29	
Zhu 2008	Quetiapine	11.4	7.4	29	
PANSS positive subscale score					
Chen 2009	Aripiprazole	10.1	5.1	30	
Chen 2009	Quetiapine	10.7	6.2	30	
Dai 2005	Aripiprazole	12.3	6.9	40	
Dai 2005	Quetiapine	12.6	7.1	40	
Wei 2006	Aripiprazole	12.4	6.9	54	

Mental state: 6. average scores of various scales (high=poor, skewed data) (Continued)

Wei 2006	Quetiapine	12.5	7.1	54	
Zhu 2008	Aripiprazole	12.8	8.3	29	
Zhu 2008	Quetiapine	14.3	7.9	29	
PANSS total endpoint scale score					
Zhu 2008	Aripiprazole	44.2	23.6	29	
Zhu 2008	Quetiapine	4.38	24.2	29	

Analysis 2.10. Comparison 2 COMPARISON 2. ARIPIPRAZOLE versus QUETIAPINE, Outcome 10
Leaving the study early.

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 2 COMPARISON 2. ARIPIPRAZOLE versus QUETIAPINE

Outcome: 10 Leaving the study early

(Continued ...)

Analysis 2.11. Comparison 2 COMPARISON 2. ARIPIRAZOLE versus QUETIAPINE, Outcome 11 Quality of life: Average score (medium term, 12 to 24 weeks, WHO-QOL-100, low=poor).

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 2 COMPARISON 2. ARIPIRAZOLE versus QUETIAPINE

Outcome: 11 Quality of life: Average score (medium term, 12 to 24 weeks, WHO-QOL-100, low=poor)

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Analysis 2.12. Comparison 2 COMPARISON 2. ARIPIPRAZOLE versus QUETIAPINE, Outcome 12 Adverse effects:1. At least one adverse effect.

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 2 COMPARISON 2. ARIPIPRAZOLE versus QUETIAPINE

Outcome: 12 Adverse effects:1. At least one adverse effect

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Analysis 2.13. Comparison 2 COMPARISON 2. ARIPIRAZOLE versus QUETIAPINE, Outcome 13 Adverse effects: 2. Cardiac effects (short term, up to 12 weeks).

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 2 COMPARISON 2. ARIPIRAZOLE versus QUETIAPINE

Outcome: 13 Adverse effects: 2. Cardiac effects (short term, up to 12 weeks)

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Analysis 2.14. Comparison 2 COMPARISON 2. ARIPIRAZOLE versus QUETIAPINE, Outcome 14
Adverse effects: 3. Central / peripheral nervous system.

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 2 COMPARISON 2. ARIPIRAZOLE versus QUETIAPINE

Outcome: 14 Adverse effects: 3. Central / peripheral nervous system

(Continued ...)

**Analysis 2.15. Comparison 2 COMPARISON 2. ARIPIRAZOLE versus QUETIAPINE, Outcome 15
Adverse effects: 4. Extrapyramidal symptoms - various (short term, up to 12 weeks).**

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 2 COMPARISON 2. ARIPIRAZOLE versus QUETIAPINE

Outcome: 15 Adverse effects: 4. Extrapyramidal symptoms - various (short term, up to 12 weeks)

(Continued ...)

Analysis 2.16. Comparison 2 COMPARISON 2. ARIPIPRAZOLE versus QUETIAPINE, Outcome 16 Adverse effects: 5. Gastrointestinal.

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 2 COMPARISON 2. ARIPIPRAZOLE versus QUETIAPINE

Outcome: 16 Adverse effects: 5. Gastrointestinal

(Continued . . .)

Analysis 2.17. Comparison 2 COMPARISON 2. ARIPIRAZOLE versus QUETIAPINE, Outcome 17 Adverse effects: 6. Haematological.

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 2 COMPARISON 2. ARIPIRAZOLE versus QUETIAPINE

Outcome: 17 Adverse effects: 6. Haematological

Analysis 2.18. Comparison 2 COMPARISON 2. ARIPIRAZOLE versus QUETIAPINE, Outcome 18 Adverse events: 7. Hormonal.

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 2 COMPARISON 2. ARIPIRAZOLE versus QUETIAPINE

Outcome: 18 Adverse events: 7. Hormonal

Analysis 2.19. Comparison 2 COMPARISON 2. ARIPIRAZOLE versus QUETIAPINE, Outcome 19 Adverse effects: 8a. Metabolic - binary measures.

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 2 COMPARISON 2. ARIPIRAZOLE versus QUETIAPINE

Outcome: 19 Adverse effects: 8a. Metabolic - binary measures

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Analysis 2.20. Comparison 2 COMPARISON 2. ARIPIRAZOLE versus QUETIAPINE, Outcome 20
Adverse effects: 8b. Metabolic - continuous measure.

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 2 COMPARISON 2. ARIPIRAZOLE versus QUETIAPINE

Outcome: 20 Adverse effects: 8b. Metabolic - continuous measure

Analysis 3.1. Comparison 3 COMPARISON 3. ARIPIRAZOLE versus RISPERIDONE, Outcome 1 Global state: 1. No clinically significant response (as defined by the original studies).

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 3 COMPARISON 3. ARIPIRAZOLE versus RISPERIDONE

Outcome: 1 Global state: 1. No clinically significant response (as defined by the original studies)

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Analysis 3.2. Comparison 3 COMPARISON 3. ARIPIRAZOLE versus RISPERIDONE, Outcome 2 Global state: 2. Average endpoint total score(short term, up to 12 weeks, CGI, high=poor).

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 3 COMPARISON 3. ARIPIRAZOLE versus RISPERIDONE

Outcome: 2 Global state: 2. Average endpoint total score(short term, up to 12 weeks, CGI, high=poor)

Analysis 3.3. Comparison 3 COMPARISON 3. ARIPIRAZOLE versus RISPERIDONE, Outcome 3 Global state: 3. Average CGI subscale scores (short term, up to 12 weeks, high=poor).

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 3 COMPARISON 3. ARIPIRAZOLE versus RISPERIDONE

Outcome: 3 Global state: 3. Average CGI subscale scores (short term, up to 12 weeks, high=poor)

Analysis 3.4. Comparison 3 COMPARISON 3. ARIPIRAZOLE versus RISPERIDONE, Outcome 4 Global state: 4. average endpoint data of various scales (high=poor, data skewed).

Global state: 4. average endpoint data of various scales (high=poor, data skewed)

Study	Intervention	Mean	SD	N	Note
CGI-GI					
Chen 2006	Aripiprazole	1.7	0.9	51	
Chen 2006	Risperidone	1.6	1.2	50	
CGI-SI					
Chen 2006	Aripiprazole	2.5	1.4	51	
Chen 2006	Risperidone	2.3	1.2	50	

Global state: 4. average endpoint data of various scales (high=poor, data skewed) (Continued)

Yang 2008a	Aripiprazole	2.22	1.28	30	
Yang 2008a	Risperidone	2.35	1.16	30	
CGI					
Feng 2006		1.49	1.05	35	
Feng 2006		1.44	1.2	34	
Zhang 2008	Aripiprazole	6.65	4.88	30	
Zhang 2008	Risperidone	7.51	5.76	30	

Analysis 3.5. Comparison 3 COMPARISON 3. ARIPIRAZOLE versus RISPERIDONE, Outcome 5 Mental state: I. Specific - binary outcomes (short term, up to 12 weeks).

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 3 COMPARISON 3. ARIPIRAZOLE versus RISPERIDONE

Outcome: 5 Mental state: I. Specific - binary outcomes (short term, up to 12 weeks)

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Analysis 3.6. Comparison 3 COMPARISON 3. ARIPIRAZOLE versus RISPERIDONE, Outcome 6 Mental state: 2. Average endpoint scale score.

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 3 COMPARISON 3. ARIPIRAZOLE versus RISPERIDONE

Outcome: 6 Mental state: 2. Average endpoint scale score

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Analysis 3.7. Comparison 3 COMPARISON 3. ARIPIRAZOLE versus RISPERIDONE, Outcome 7 Mental state: 3. Specific - average endpoint positive score (PANSS, high=poor).

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 3 COMPARISON 3. ARIPIRAZOLE versus RISPERIDONE

Outcome: 7 Mental state: 3. Specific - average endpoint positive score (PANSS, high=poor)

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Analysis 3.8. Comparison 3 COMPARISON 3. ARIPIRAZOLE versus RISPERIDONE, Outcome 8 Mental state: 4. Specific - average endpoint negative score (PANSS, high=poor).

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 3 COMPARISON 3. ARIPIRAZOLE versus RISPERIDONE

Outcome: 8 Mental state: 4. Specific - average endpoint negative score (PANSS, high=poor)

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Analysis 3.9. Comparison 3 COMPARISON 3. ARIPIRAZOLE versus RISPERIDONE, Outcome 9 Mental state: 5. Specific - average endpoint general psychopathological score (PANSS, high=poor).

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 3 COMPARISON 3. ARIPIRAZOLE versus RISPERIDONE

Outcome: 9 Mental state: 5. Specific - average endpoint general psychopathological score (PANSS, high=poor)

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Analysis 3.10. Comparison 3 COMPARISON 3. ARIPIRAZOLE versus RISPERIDONE, Outcome 10 Mental state: 6. PANSS average score decreased rate (short term, up to 12 weeks, low=poor).

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 3 COMPARISON 3. ARIPIRAZOLE versus RISPERIDONE

Outcome: 10 Mental state: 6. PANSS average score decreased rate (short term, up to 12 weeks, low=poor)

**Analysis 3.11. Comparison 3 COMPARISON 3. ARIPIPRAZOLE versus RISPERIDONE, Outcome 11
Mental state: 7. BPRS total score decreased rate (short term, up to 12 weeks, high=poor).**

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 3 COMPARISON 3. ARIPIPRAZOLE versus RISPERIDONE

Outcome: 11 Mental state: 7. BPRS total score decreased rate (short term, up to 12 weeks, high=poor)

**Analysis 3.12. Comparison 3 COMPARISON 3. ARIPIPRAZOLE versus RISPERIDONE, Outcome 12
Mental state: 8. General - average total score (PANSS, high=poor).**

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 3 COMPARISON 3. ARIPIPRAZOLE versus RISPERIDONE

Outcome: 12 Mental state: 8. General - average total score (PANSS, high=poor)

Analysis 3.13. Comparison 3 COMPARISON 3. ARIPIPRAZOLE versus RISPERIDONE, Outcome 13
Mental state: 9. average scores of various scale (high=poor, skewed data).

Mental state: 9. average scores of various scale (high=poor, skewed data)

Study	Intervention	Mean	SD	N	Note
SANS endpoint scale score					
Tong 2007	Aripiprazole	10. 6	14. 4	36	
Tong 2007	Risperidone	14. 2	20. 3	32	
PANSS general pathology subscale score					
Chang 2007	Aripiprazole	18.65	11.64	50	
Chang 2007	Risperidone	19.15	10.95	50	
Xie 2008	Aripiprazole	19. 24	12. 18	42	
Xie 2008	Risperidone	19. 36	10. 71	42	
PANSS negative symptom subscale score					
Chang 2007	Aripiprazole	12.04	6.46	50	
Chang 2007	Risperidone	12.08	6.56	50	
CuiMeng 2008	Aripiprazole	9. 2	8. 7	60	
CuiMeng 2008	Ziprasidone	12. 3	8. 2	60	
Deng 2008	Aripiprazole	14.89	3.89	25	
Deng 2008	Risperidone	13.01	7.362	25	
Guo 2006	Aripiprazole	12.4	3.9	18	
Guo 2006	Risperidone	15.8	9.2	20	
Ji 2007	Aripiprazole	12.71	4.58	32	
Ji 2007	Risperidone	15.19	9.57	32	
Li 2007d	Aripiprazole	15.9	5.8	60	
Li 2007d	Risperidone	12.3	6.6	60	

Mental state: 9. average scores of various scale (high=poor, skewed data) (Continued)

Li 2009b	Aripiprazole	11.1	6.2	30	
Li 2009b	Risperidone	11.1	6.1	30	
Li X 2007	Aripiprazole	12.2	7.2	36	
Li X 2007	Risperidone	12.5	8.4	35	
Liu 2006a	Aripiprazole	11.3	7.4	45	
Liu 2006a	Risperidone	10.8	7.7	45	
Lv 2007	Aripiprazole	11. 5	3. 8	40	
Lv 2007	Risperidone	12. 5	6. 8	40	
Mai 2005	Aripiprazole	12. 9	7. 1	36	
Mai 2005	Risperidone	13. 9	6. 1	36	
Pan 2007	Aripiprazole	11.9	7.2	30	
Pan 2007	Risperidone	13.9	6.1	30	
Shan 2008	Aripiprazole	11.2	5.8	30	
Shan 2008	Risperidone	11.4	5.4	30	
Song 2009	Aripiprazole	11.7	6.5	30	
Song 2009	Risperidone	12.8	5.9	30	
Su 2007	Aripiprazole	11. 4	7. 6	39	
Su 2007	Risperidone	12. 6	6. 7	39	
Tang 2006	Aripiprazole	10.9	5.3	37	
Tang 2006	Risperidone	11.1	5.8	35	
Tang 2007	Aripiprazole	11.9	5.7	30	
Tang 2007	Risperidone	11.2	5.8	30	
Tu 2009	Aripiprazole	11.3	6.5	35	

Mental state: 9. average scores of various scale (high=poor, skewed data) (Continued)

Tu 2009	Risperidone	13.8	6.7	33	
Wen 2009a	Aripiprazole	14.89	3.88	40	
Wen 2009a	Risperidone	13.02	7.34	40	
Xie 2008	Aripiprazole	11.95	5.69	42	
Xie 2008	Risperidone	12.32	6.17	42	
Xie 2010	Aripiprazole	10.76	4.53	40	
Xie 2010	Risperidone	10.78	6.11	40	
Yang 2008b	Aripiprazole	12.1	6.9	45	
Yang 2008b	Risperidone	11.9	7.1	45	
Ye 2005a	Aripiprazole	11.8	4.3	29	
Ye 2005a	Risperidone	12.3	8.2	29	
Zhang 2008b	Aripiprazole	9.2	8.7	20	
Zhang 2008b	Risperidone	13.5	6.9	20	
Zhi 2005	Aripiprazole	10.7	6.5	40	
Zhi 2005	Risperidone	12.8	5.9	40	
Zhou 2008	Aripiprazole	10.8	5.5	70	
Zhou 2008	Risperidone	11.2	5.7	70	
Zhu 2010	Aripiprazole	10.40	6.57	22	
Zhu 2010	Risperidone	11.67	4.31	28	
PANSS positive symptom subscale score					
Chang 2007	Aripiprazole	16.82	11.66	50	
Chang 2007	Risperidone	17.64	11.76	50	
Chen 2010	Aripiprazole	10.58	5.33	32	

Mental state: 9. average scores of various scale (high=poor, skewed data) (Continued)

Chen 2010	Risperidone	11.31	5.33	32	
Fan 2010	Aripiprazole	10.66	4.71	30	
Fan 2010	Risperidone	8.96	4.93	30	
Feng 2006	Aripiprazole	5.18	2.04	30	
Feng 2006	Risperidone	4.91	3.14	30	
Hu 2010	Aripiprazole	10.56	4.52	25	
Hu 2010	Risperidone	11.16	6.21	25	
Li 2007a	Aripiprazole	10.39	6.02	30	
Li 2007a	Risperidone	10.31	5.11	30	
Li 2007d	Aripiprazole	17.2	9.3	60	
Li 2007d	Risperidone	12.1	3.4	60	
Li X 2007	Aripiprazole	12	8	36	
Li X 2007	Risperidone	13.2	7.3	35	
Lian 2008	Aripiprazole	8.9	4.1	43	
Lian 2008	Risperidone	11.5	5.9	43	
Liu 2006a	Aripiprazole	12.4	7.2	45	
Liu 2006a	Risperidone	12.1	7.5	45	
Liu 2008c	Aripiprazole	9.59	3.17	37	
Liu 2008c	Risperidone	10.29	5.47	35	
Mu 2008	Aripiprazole	10.95	5.07	50	
Mu 2008	Risperidone	11.50	6.02	50	
Song 2009	Aripiprazole	10.7	5.3	30	
Song 2009	Risperidone	11.3	5.9	30	

Mental state: 9. average scores of various scale (high=poor, skewed data) (Continued)

Su 2007	Aripiprazole	10.8	7.5	39	
Su 2007	Risperidone	12.2	6.8	39	
Tang 2006	Aripiprazole	10.6	5.1	37	
Tang 2006	Risperidone	11.2	6.0	35	
Tang 2007	Aripiprazole	10.1	5.3	30	
Tang 2007	Risperidone	8.6	6.5	30	
Tang 2010	Aripiprazole	10.2	4.1	38	
Tang 2010	Risperidone	10.6	5.8	40	
Wang 2007e	Aripiprazole	9.7	5.8	30	
Wang 2007e	Risperidone	10.1	5.6	30	
Xie 2008	Aripiprazole	17.21	10.97	42	
Xie 2008	Risperidone	17.33	11.82	42	
Xie 2010	Aripiprazole	8.94	2.13	40	
Xie 2010	Risperidone	9.41	4.78	40	
Yang 2008b	Aripiprazole	12.2	6.8	45	
Yang 2008b	Risperidone	12.3	7.1	45	
Yu 2008	Aripiprazole	9.7	5.53	50	
Yu 2008	Risperidone	10.1	5.8	50	
Zhang 2007a	Aripiprazole	8.0	2.4	25	
Zhang 2007a	Risperidone	9.31	5.12	25	
Zhang 2008	Aripiprazole	9.77	6.78	30	
Zhang 2008	Risperidone	11.17	5.75	30	
Zhang 2008b	Aripiprazole	13.1	8.6	20	

Mental state: 9. average scores of various scale (high=poor, skewed data) (Continued)

Zhang 2008b	Risperidone	9.1	7.6	20	
Zhi 2005	Aripiprazole	10.7	5.3	40	
Zhi 2005	Risperidone	11.3	5.9	40	

Analysis 3.14. Comparison 3 COMPARISON 3. ARIPIPRAZOLE versus RISPERIDONE, Outcome 14
Leaving the study early.

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 3 COMPARISON 3. ARIPIPRAZOLE versus RISPERIDONE

Outcome: 14 Leaving the study early

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Analysis 3.15. Comparison 3 COMPARISON 3. ARIPIRAZOLE versus RISPERIDONE, Outcome 15
Adverse effects: 1. At least one adverse effect, non-specific.

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 3 COMPARISON 3. ARIPIRAZOLE versus RISPERIDONE

Outcome: 15 Adverse effects: 1. At least one adverse effect, non-specific

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Analysis 3.16. Comparison 3 COMPARISON 3. ARIPIRAZOLE versus RISPERIDONE, Outcome 16 Adverse effects: 2a.Cardiac effects (short term, up to 12 weeks).

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 3 COMPARISON 3. ARIPIRAZOLE versus RISPERIDONE

Outcome: 16 Adverse effects: 2a.Cardiac effects (short term, up to 12 weeks)

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**Analysis 3.17. Comparison 3 COMPARISON 3. ARIPIRAZOLE versus RISPERIDONE, Outcome 17
Adverse effects: 2b. Cardiac - QTc change from baseline (in ms).**

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 3 COMPARISON 3. ARIPIRAZOLE versus RISPERIDONE

Outcome: 17 Adverse effects: 2b. Cardiac - QTc change from baseline (in ms)

Analysis 3.18. Comparison 3 COMPARISON 3. ARIPIRAZOLE versus RISPERIDONE, Outcome 18
Adverse effects: 3. Central / peripheral nervous system (short term, up to 12 weeks).

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 3 COMPARISON 3. ARIPIRAZOLE versus RISPERIDONE

Outcome: 18 Adverse effects: 3. Central / peripheral nervous system (short term, up to 12 weeks)

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Analysis 3.19. Comparison 3 COMPARISON 3. ARIPIPRAZOLE versus RISPERIDONE, Outcome 19
Adverse effects: 3a. Endocrine - Prolactin - average change (ng/ml).

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 3 COMPARISON 3. ARIPIPRAZOLE versus RISPERIDONE

Outcome: 19 Adverse effects: 3a. Endocrine - Prolactin - average change (ng/ml)

Analysis 3.20. Comparison 3 COMPARISON 3. ARIPIPRAZOLE versus RISPERIDONE, Outcome 20
Adverse effects: 3b. Endocrine - Prolactin-associated.

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 3 COMPARISON 3. ARIPIPRAZOLE versus RISPERIDONE

Outcome: 20 Adverse effects: 3b. Endocrine - Prolactin-associated

**Analysis 3.21. Comparison 3 COMPARISON 3. ARIPIRAZOLE versus RISPERIDONE, Outcome 21
Adverse effects: 4. Various extrapyramidal symptoms (short term, up to 12 weeks).**

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 3 COMPARISON 3. ARIPIRAZOLE versus RISPERIDONE

Outcome: 21 Adverse effects: 4. Various extrapyramidal symptoms (short term, up to 12 weeks)

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Analysis 3.22. Comparison 3 COMPARISON 3. ARIPIPRAZOLE versus RISPERIDONE, Outcome 22
Adverse effects: 4b. Extrapyramidal - average score.

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 3 COMPARISON 3. ARIPIPRAZOLE versus RISPERIDONE

Outcome: 22 Adverse effects: 4b. Extrapyramidal - average score

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Analysis 3.23. Comparison 3 COMPARISON 3. ARIPIPRAZOLE versus RISPERIDONE, Outcome 23 Adverse effects: 5. Gastrointestinal.

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 3 COMPARISON 3. ARIPIPRAZOLE versus RISPERIDONE

Outcome: 23 Adverse effects: 5. Gastrointestinal

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Analysis 3.24. Comparison 3 COMPARISON 3. ARIPIRAZOLE versus RISPERIDONE, Outcome 24
Adverse effects: 6. Haematological.

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 3 COMPARISON 3. ARIPIRAZOLE versus RISPERIDONE

Outcome: 24 Adverse effects: 6. Haematological

Analysis 3.25. Comparison 3 COMPARISON 3. ARIPIPRAZOLE versus RISPERIDONE, Outcome 25
Adverse effects: 7a. Metabolic - binary measures (short term, up to 12 weeks).

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 3 COMPARISON 3. ARIPIPRAZOLE versus RISPERIDONE

Outcome: 25 Adverse effects: 7a. Metabolic - binary measures (short term, up to 12 weeks)

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Analysis 3.26. Comparison 3 COMPARISON 3. ARIPIPRAZOLE versus RISPERIDONE, Outcome 26
Adverse effects: 7b. Metabolic - continuous measures (high=poor).

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 3 COMPARISON 3. ARIPIPRAZOLE versus RISPERIDONE

Outcome: 26 Adverse effects: 7b. Metabolic - continuous measures (high=poor)

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Analysis 3.27. Comparison 3 COMPARISON 3. ARIPIPRAZOLE versus RISPERIDONE, Outcome 27 Adverse effect : 7c. Metabolic - continuous measures.

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 3 COMPARISON 3. ARIPIPRAZOLE versus RISPERIDONE

Outcome: 27 Adverse effect : 7c. Metabolic - continuous measures

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Analysis 3.28. Comparison 3 COMPARISON 3. ARIPIPRAZOLE versus RISPERIDONE, Outcome 28
Adverse effect: 8. required additional drug combination.

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 3 COMPARISON 3. ARIPIPRAZOLE versus RISPERIDONE

Outcome: 28 Adverse effect: 8. required additional drug combination

**Analysis 3.29. Comparison 3 COMPARISON 3. ARIPIPRAZOLE versus RISPERIDONE, Outcome 29
Adverse effects: 9. TESS score (short term, up to 12 weeks, high=poor).**

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 3 COMPARISON 3. ARIPIPRAZOLE versus RISPERIDONE

Outcome: 29 Adverse effects: 9. TESS score (short term, up to 12 weeks, high=poor)

**Analysis 3.30. Comparison 3 COMPARISON 3. ARIPIPRAZOLE versus RISPERIDONE, Outcome 30
Adverse effects: 10. TESS score (short term, up to 12 weeks, high=poor, data skewed).**

Adverse effects: 10. TESS score (short term, up to 12 weeks, high=poor, data skewed)

Study	Intervention	Mean	SD	N	Note
Chen 2006	Aripiprazole	0.2	0.5	51	
Chen 2006	Risperidone	0.1	0.4	50	
CuiMeng 2008	Aripiprazole	5.35	4.25	60	
CuiMeng 2008	Risperidone	7.95	5.15	60	
Mu 2010	Aripiprazole	3.59	2.08	129	
Mu 2010	Risperidone	3.62	2.14	129	
Qu 2009	Aripiprazole	5.35	4.2	30	
Qu 2009	Risperidone	7.95	5.1	30	
Yan 2010	Aripiprazole	3.42	2.34	50	

Adverse effects: 10. TESS score (short term, up to 12 weeks, high=poor, data skewed) (Continued)

Yan 2010	Risperidone	4.45	1.92	50	
Zhang 2010a	Aripiprazole	5.35	4.25	50	
Zhang 2010a	Risperidone	7.95	5.15	50	
Zhou 2007b	Aripiprazole	5.35	4.25	30	
Zhou 2007b	Risperidone	7.95	5.15	30	

Analysis 3.31. Comparison 3 COMPARISON 3. ARIPIPRAZOLE versus RISPERIDONE, Outcome 31
Adverse effects: 11. weight gain (in KG, high=poor, data skewed).

Adverse effects: 11. weight gain (in KG, high=poor, data skewed)

Study	Heading 1	Heading 2	Heading 3	Heading 4	Heading 5
Chen 2006	Aripiprazole	1.1	1.5	51	
Chen 2006	Risperidone	1.8	1.4	50	
Tao 2008	Aripiprazole	2.06	2.67	90	
Tao 2008	Risperidone	2.73	2.43	90	
Wang 2007e	Aripiprazole	0.3	1.97	30	
Wang 2007e	Risperidone	1.0	3.1	30	

Analysis 3.32. Comparison 3 COMPARISON 3. ARIPIPRAZOLE versus RISPERIDONE, Outcome 32 Cognitive functioning: I. Specific - average endpoint total score.

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia
 Comparison: 3 COMPARISON 3. ARIPIPRAZOLE versus RISPERIDONE
 Outcome: 32 Cognitive functioning: I. Specific - average endpoint total score

Analysis 3.33. Comparison 3 COMPARISON 3. ARIPIPRAZOLE versus RISPERIDONE, Outcome 33 Cost effectiveness analysis (high=poor, data skewed).

Cost effectiveness analysis (high=poor, data skewed)

Study	Intervention	Mean	SD	N	Note
Cost of hospitalisation (in RMB)					
Liu 2010	Aripiprazole	3413.66	1815.05	30	
Liu 2010	Risperidone	4551.41	3024.38	54	
Cost of drug (in RMB)					
Liu 2010	Aripiprazole	418.13	326.43	30	
Liu 2010	Risperidone	685.00	493.02	54	
Length of hospitalisation (day)					

Cost effectiveness analysis (high=poor, data skewed) (Continued)

Liu 2010	Aripiprazole	33.19	16.71	30	
Liu 2010	Risperidone	50.84	40.85	28	

Analysis 4.1. Comparison 4 COMPARISON 4. ARIPIPAZOLE versus ZIPRASIDONE, Outcome 1 Global state: 1. No clinically significant response (as defined by the original studies).

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 4 COMPARISON 4. ARIPIPAZOLE versus ZIPRASIDONE

Outcome: 1 Global state: 1. No clinically significant response (as defined by the original studies)

Analysis 4.2. Comparison 4 COMPARISON 4. ARIPIRAZOLE versus ZIPRASIDONE, Outcome 2 Global state: 2. Average endpoint CGI-GI score (short term, up to 12 weeks, high=poor).

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 4 COMPARISON 4. ARIPIRAZOLE versus ZIPRASIDONE

Outcome: 2 Global state: 2. Average endpoint CGI-GI score (short term, up to 12 weeks, high=poor)

Analysis 4.3. Comparison 4 COMPARISON 4. ARIPIRAZOLE versus ZIPRASIDONE, Outcome 3 Global state: 3. Average change score (CGI-S, decline=good).

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 4 COMPARISON 4. ARIPIRAZOLE versus ZIPRASIDONE

Outcome: 3 Global state: 3. Average change score (CGI-S, decline=good)

Analysis 4.4. Comparison 4 COMPARISON 4. ARIPIRAZOLE versus ZIPRASIDONE, Outcome 4 Mental state: 1. Average endpoint total score (short term, up to 12 weeks, high=poor).

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 4 COMPARISON 4. ARIPIRAZOLE versus ZIPRASIDONE

Outcome: 4 Mental state: 1. Average endpoint total score (short term, up to 12 weeks, high=poor)

Analysis 4.5. Comparison 4 COMPARISON 4. ARIPIRAZOLE versus ZIPRASIDONE, Outcome 5 Mental state: 2. Specific - binary outcomes (up to 12 weeks - short term).

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia
 Comparison: 4 COMPARISON 4. ARIPIRAZOLE versus ZIPRASIDONE
 Outcome: 5 Mental state: 2. Specific - binary outcomes (up to 12 weeks - short term)

Analysis 4.6. Comparison 4 COMPARISON 4. ARIPIRAZOLE versus ZIPRASIDONE, Outcome 6 Mental state: 3. Specific - average endpoint PANSS subscale scores (short term, high=poor).

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 4 COMPARISON 4. ARIPIRAZOLE versus ZIPRASIDONE

Outcome: 6 Mental state: 3. Specific - average endpoint PANSS subscale scores (short term, high=poor)

Analysis 4.7. Comparison 4 COMPARISON 4. ARIPIRAZOLE versus ZIPRASIDONE, Outcome 7 Mental state: endpoint scores of various scales (high=poor, data skewed).

Mental state: endpoint scores of various scales (high=poor, data skewed)

Study	Intervention	Mean	SD	N	Note
PANSS negative symptom subscale score					
Cheng 2009	Aripiprazole	14.56	9.51	43	
Cheng 2009	Ziprasidone	13.12	5.16	43	
PANSS positive symptom subscale score					
Liu 2008a	Aripiprazole	14.21	5.45	33	
Liu 2008a	Ziprasidone	12.96	8.43	33	
Wang 2008c	Aripiprazole	13.12	5.16	43	
Wang 2008c	Ziprasidone	14.56	9.51	43	
Yang 2008	Aripiprazole	11.3	5.7	30	
Yang 2008	Ziprasidone	11.5	3.9	30	

Analysis 4.8. Comparison 4 COMPARISON 4. ARIPIPRAZOLE versus ZIPRASIDONE, Outcome 8 Leaving the study early.

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 4 COMPARISON 4. ARIPIPRAZOLE versus ZIPRASIDONE

Outcome: 8 Leaving the study early

Analysis 4.9. Comparison 4 COMPARISON 4. ARIPIPRAZOLE versus ZIPRASIDONE, Outcome 9 Adverse effects: 1. At least one adverse effect, non-specific.

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 4 COMPARISON 4. ARIPIPRAZOLE versus ZIPRASIDONE

Outcome: 9 Adverse effects: 1. At least one adverse effect, non-specific

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Analysis 4.10. Comparison 4 COMPARISON 4. ARIPIPRAZOLE versus ZIPRASIDONE, Outcome 10
Adverse effects: 2. Cardiac effects (short term, up to 12 weeks).

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 4 COMPARISON 4. ARIPIPRAZOLE versus ZIPRASIDONE

Outcome: 10 Adverse effects: 2. Cardiac effects (short term, up to 12 weeks)

**Analysis 4.11. Comparison 4 COMPARISON 4. ARIPIPRAZOLE versus ZIPRASIDONE, Outcome 11
Adverse effects: 3. Central / peripheral nervous system (short term, up to 12 weeks).**

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 4 COMPARISON 4. ARIPIPRAZOLE versus ZIPRASIDONE

Outcome: 11 Adverse effects: 3. Central / peripheral nervous system (short term, up to 12 weeks)

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Analysis 4.12. Comparison 4 COMPARISON 4. ARIPIRAZOLE versus ZIPRASIDONE, Outcome 12
Adverse effects: 4. Various extrapyramidal symptoms (short term, up to 12 weeks).

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 4 COMPARISON 4. ARIPIRAZOLE versus ZIPRASIDONE

Outcome: 12 Adverse effects: 4. Various extrapyramidal symptoms (short term, up to 12 weeks)

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Analysis 4.13. Comparison 4 COMPARISON 4. ARIPIRAZOLE versus ZIPRASIDONE, Outcome 13
Adverse effects: 5. Gastrointestinal (short term, up to 12 weeks).

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 4 COMPARISON 4. ARIPIRAZOLE versus ZIPRASIDONE

Outcome: 13 Adverse effects: 5. Gastrointestinal (short term, up to 12 weeks)

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Analysis 4.14. Comparison 4 COMPARISON 4. ARIPIPRAZOLE versus ZIPRASIDONE, Outcome 14 Adverse effects: 6. Haematological.

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 4 COMPARISON 4. ARIPIPRAZOLE versus ZIPRASIDONE

Outcome: 14 Adverse effects: 6. Haematological

Analysis 4.15. Comparison 4 COMPARISON 4. ARIPIPRAZOLE versus ZIPRASIDONE, Outcome 15 **Adverse effects: 7. Hormonal.**

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 4 COMPARISON 4. ARIPIPRAZOLE versus ZIPRASIDONE

Outcome: 15 Adverse effects: 7. Hormonal

Analysis 4.16. Comparison 4 COMPARISON 4. ARIPIRAZOLE versus ZIPRASIDONE, Outcome 16
Adverse effects: 8a. Metabolic - binary measures.

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 4 COMPARISON 4. ARIPIRAZOLE versus ZIPRASIDONE

Outcome: 16 Adverse effects: 8a. Metabolic - binary measures

Analysis 4.17. Comparison 4 COMPARISON 4. ARIPIRAZOLE versus ZIPRASIDONE, Outcome 17
Adverse effects: 8b. Metabolic - continuous measures.

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 4 COMPARISON 4. ARIPIRAZOLE versus ZIPRASIDONE

Outcome: 17 Adverse effects: 8b. Metabolic - continuous measures

Analysis 5.1. Comparison 5 COMPARISON 5. ARIPIRAZOLE versus OLANZAPINE, Outcome 1 Global state: 1.No clinically significant response (as defined by the original studies).

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 5 COMPARISON 5. ARIPIRAZOLE versus OLANZAPINE

Outcome: 1 Global state: 1.No clinically significant response (as defined by the original studies)

Analysis 5.2. Comparison 5 COMPARISON 5. ARIPIRAZOLE versus OLANZAPINE, Outcome 2 Global state: 2. Not responded (decline in PANSS of 30% or more).

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 5 COMPARISON 5. ARIPIRAZOLE versus OLANZAPINE

Outcome: 2 Global state: 2. Not responded (decline in PANSS of 30% or more)

Analysis 5.3. Comparison 5 COMPARISON 5. ARIPIRAZOLE versus OLANZAPINE, Outcome 3 Global state: 3. Remission not achieved (as defined in the study).

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 5 COMPARISON 5. ARIPIRAZOLE versus OLANZAPINE

Outcome: 3 Global state: 3. Remission not achieved (as defined in the study)

Analysis 5.4. Comparison 5 COMPARISON 5. ARIPIRAZOLE versus OLANZAPINE, Outcome 4 Global state: 4. Average endpoint EI score (CGI, high=poor).

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 5 COMPARISON 5. ARIPIRAZOLE versus OLANZAPINE

Outcome: 4 Global state: 4. Average endpoint EI score (CGI, high=poor)

Analysis 5.5. Comparison 5 COMPARISON 5. ARIPIRAZOLE versus OLANZAPINE, Outcome 5 Global state: 5. Average endpoint CGI score decreased rate (short term, low=poor).

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 5 COMPARISON 5. ARIPIRAZOLE versus OLANZAPINE

Outcome: 5 Global state: 5. Average endpoint CGI score decreased rate (short term, low=poor)

Analysis 5.6. Comparison 5 COMPARISON 5. ARIPIRAZOLE versus OLANZAPINE, Outcome 6 Global state: 6. Average change score (CGI-S, decline=best).

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 5 COMPARISON 5. ARIPIRAZOLE versus OLANZAPINE

Outcome: 6 Global state: 6. Average change score (CGI-S, decline=best)

Analysis 5.7. Comparison 5 COMPARISON 5. ARIPIRAZOLE versus OLANZAPINE, Outcome 7 Global state: 7. Improvement (CGI-I, high=poor).

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 5 COMPARISON 5. ARIPIRAZOLE versus OLANZAPINE

Outcome: 7 Global state: 7. Improvement (CGI-I, high=poor)

Analysis 5.8. Comparison 5 COMPARISON 5. ARIPIRAZOLE versus OLANZAPINE, Outcome 8 Mental state: I. Average endpoint scale score (PANSS, high=poor).

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 5 COMPARISON 5. ARIPIRAZOLE versus OLANZAPINE

Outcome: 8 Mental state: I. Average endpoint scale score (PANSS, high=poor)

Analysis 5.9. Comparison 5 COMPARISON 5. ARIPIRAZOLE versus OLANZAPINE, Outcome 9 Mental state: 2. Average endpoint scale score (SANS, high=poor).

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 5 COMPARISON 5. ARIPIRAZOLE versus OLANZAPINE

Outcome: 9 Mental state: 2. Average endpoint scale score (SANS, high=poor)

Analysis 5.10. Comparison 5 COMPARISON 5. ARIPIRAZOLE versus OLANZAPINE, Outcome 10 Mental state: 3. average endpoint score (PANSS, high=poor, data skewed).

Mental state: 3. average endpoint score (PANSS, high=poor, data skewed)

Study	Intervention	Mean	SD	N	Note
PANSS total					
Bai 2007	Aripiprazole	11.26	5.07	59	
Bai 2007	Olanzapine	10.24	5.85	59	
PANSS negative symptom subscale score					
Han 2007	Aripiprazole	12.7	3.8	30	
Han 2007	Ziprasidone	12.6	6.8	30	

Mental state: 3. average endpoint score (PANSS, high=poor, data skewed) (Continued)

PANSS positive symptom subscale score				
Han 2007		11.3	4.3	30
Han 2007		11.5	6.7	30

Analysis 5.11. Comparison 5 COMPARISON 5. ARIPIPRAZOLE versus OLANZAPINE, Outcome 11
Mental state: 4. Specific - average endpoint positive score (PANSS, high=poor).

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 5 COMPARISON 5. ARIPIPRAZOLE versus OLANZAPINE

Outcome: 11 Mental state: 4. Specific - average endpoint positive score (PANSS, high=poor)

Analysis 5.12. Comparison 5 COMPARISON 5. ARIPIPRAZOLE versus OLANZAPINE, Outcome 12 Mental state: 5. Specific - average endpoint negative subscale score (PANSS, high=poor).

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 5 COMPARISON 5. ARIPIPRAZOLE versus OLANZAPINE

Outcome: 12 Mental state: 5. Specific - average endpoint negative subscale score (PANSS, high=poor)

Analysis 5.13. Comparison 5 COMPARISON 5. ARIPIRAZOLE versus OLANZAPINE, Outcome 13 Mental state: 6. Specific - average endpoint general pathological score (PANSS, high=poor).

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 5 COMPARISON 5. ARIPIRAZOLE versus OLANZAPINE

Outcome: 13 Mental state: 6. Specific - average endpoint general pathological score (PANSS, high=poor)

Analysis 5.14. Comparison 5 COMPARISON 5. ARIPIPRAZOLE versus OLANZAPINE, Outcome 14 Mental state: 7. Specific - binary outcomes.

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 5 COMPARISON 5. ARIPIPRAZOLE versus OLANZAPINE

Outcome: 14 Mental state: 7. Specific - binary outcomes

Analysis 5.15. Comparison 5 COMPARISON 5. ARIPIPRAZOLE versus OLANZAPINE, Outcome 15 Mental state: 8. Various scale scores decreased rate (low=poor, data skewed).

Mental state: 8. Various scale scores decreased rate (low=poor, data skewed)

Study	Heading 1	Heading 2	Heading 3	Heading 4	Heading 5
PANSS positive symptom subscale					
Ye 2005a	Aripiprazole	12.8	8.4	34	
PANSS negative symptom subscale					

Mental state: 8. Various scale scores decreased rate (low=poor, data skewed) (Continued)

Ye 2005a	Aripiprazole	10.9	8.1	34	
PANSS general pathology subscale					
Ye 2005a	Aripiprazole	19.4	11.8	34	
BPRS total					
Ye 2005a	Aripiprazole	24.8	4.3	34	
PANSS total					
Ye 2005a	Aripiprazole	44.1	23.8	34	

Analysis 5.16. Comparison 5 COMPARISON 5. ARIPIPRAZOLE versus OLANZAPINE, Outcome 16
Adverse effects: 1. At least one adverse effect.

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 5 COMPARISON 5. ARIPIPRAZOLE versus OLANZAPINE

Outcome: 16 Adverse effects: 1. At least one adverse effect

(Continued ...)

(... Continued)

Analysis 5.17. Comparison 5 COMPARISON 5. ARIPIPRAZOLE versus OLANZAPINE, Outcome 17
Adverse effects: 2. Cardiac effects.

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 5 COMPARISON 5. ARIPIPRAZOLE versus OLANZAPINE

Outcome: 17 Adverse effects: 2. Cardiac effects

(Continued ...)

Analysis 5.18. Comparison 5 COMPARISON 5. ARIPIPRAZOLE versus OLANZAPINE, Outcome 18
Adverse effects: 3a. Cardiac - QTc change from baseline (in ms).

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia
 Comparison: 5 COMPARISON 5. ARIPIPRAZOLE versus OLANZAPINE
 Outcome: 18 Adverse effects: 3a. Cardiac - QTc change from baseline (in ms)

Analysis 5.19. Comparison 5 COMPARISON 5. ARIPIRAZOLE versus OLANZAPINE, Outcome 19 Adverse effects: 3b. Central / peripheral nervous system.

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 5 COMPARISON 5. ARIPIRAZOLE versus OLANZAPINE

Outcome: 19 Adverse effects: 3b. Central / peripheral nervous system

(Continued ...)

(Continued . . .)

Analysis 5.20. Comparison 5 COMPARISON 5. ARIPIPRAZOLE versus OLANZAPINE, Outcome 20
Adverse effects: 4. Endocrine - Prolactin - average increase.

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 5 COMPARISON 5. ARIPIPRAZOLE versus OLANZAPINE

Outcome: 20 Adverse effects: 4. Endocrine - Prolactin - average increase

**Analysis 5.21. Comparison 5 COMPARISON 5. ARIPIPRAZOLE versus OLANZAPINE, Outcome 21
Adverse effects: 5. Extrapyramidal - various.**

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 5 COMPARISON 5. ARIPIPRAZOLE versus OLANZAPINE

Outcome: 21 Adverse effects: 5. Extrapyramidal - various

(Continued ...)

Analysis 5.22. Comparison 5 COMPARISON 5. ARIPIPRAZOLE versus OLANZAPINE, Outcome 22 Adverse effects: 6. Gastrointestinal.

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 5 COMPARISON 5. ARIPIPRAZOLE versus OLANZAPINE

Outcome: 22 Adverse effects: 6. Gastrointestinal

(Continued . . .)

Analysis 5.23. Comparison 5 COMPARISON 5. ARIPIRAZOLE versus OLANZAPINE, Outcome 23
Adverse effects: 7. Hormonal.

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 5 COMPARISON 5. ARIPIRAZOLE versus OLANZAPINE

Outcome: 23 Adverse effects: 7. Hormonal

Analysis 5.24. Comparison 5 COMPARISON 5. ARIPIRAZOLE versus OLANZAPINE, Outcome 24
Adverse effects: 8a. Metabolic - binary measures.

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 5 COMPARISON 5. ARIPIRAZOLE versus OLANZAPINE

Outcome: 24 Adverse effects: 8a. Metabolic - binary measures

(Continued ...)

Analysis 5.25. Comparison 5 COMPARISON 5. ARIPIRAZOLE versus OLANZAPINE, Outcome 25
Adverse effects: 8b. Metabolic - continuous measures (high=poor).

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 5 COMPARISON 5. ARIPIRAZOLE versus OLANZAPINE

Outcome: 25 Adverse effects: 8b. Metabolic - continuous measures (high=poor)

(Continued ...)

(... Continued)

Analysis 5.26. Comparison 5 COMPARISON 5. ARIPIPRAZOLE versus OLANZAPINE, Outcome 26
Adverse effects: 9. Average endpoint scale score (TESS, high=poor, data skewed).

Adverse effects: 9. Average endpoint scale score (TESS, high=poor, data skewed)

Study	Intervention	Mean	SD	N	Note
Zhang 2006a	Aripiprazole	4.43	4.03	52	
Zhang 2006a	Olanzapine	5.54	4.33	52	

Analysis 5.27. Comparison 5 COMPARISON 5. ARIPIRAZOLE versus OLANZAPINE, Outcome 27 **Leaving the study early.**

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 5 COMPARISON 5. ARIPIRAZOLE versus OLANZAPINE

Outcome: 27 Leaving the study early

(Continued ...)

Analysis 5.28. Comparison 5 COMPARISON 5. ARIPIRAZOLE versus OLANZAPINE, Outcome 28
Quality of life: I. Average endpoint general quality of life score (GQOLI-74, low=poor).

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 5 COMPARISON 5. ARIPIRAZOLE versus OLANZAPINE

Outcome: 28 Quality of life: I. Average endpoint general quality of life score (GQOLI-74, low=poor)

Analysis 6.1. Comparison 6 COMPARISON 6. ARIPIRAZOLE versus OLANZAPINE (acutely agitated people - all data by 5 days), Outcome 1 Global state: Average improvement (BPRS, high=good).

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 6 COMPARISON 6. ARIPIRAZOLE versus OLANZAPINE (acutely agitated people - all data by 5 days)

Outcome: 1 Global state: Average improvement (BPRS, high=good)

Analysis 6.2. Comparison 6 COMPARISON 6. ARIPIRAZOLE versus OLANZAPINE (acutely agitated people - all data by 5 days), Outcome 2 Mental state: Specific - binary outcomes.

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 6 COMPARISON 6. ARIPIRAZOLE versus OLANZAPINE (acutely agitated people - all data by 5 days)

Outcome: 2 Mental state: Specific - binary outcomes

(Continued ...)

Analysis 6.3. Comparison 6 COMPARISON 6. ARIPIPRAZOLE versus OLANZAPINE (acutely agitated people - all data by 5 days), Outcome 3 Leaving the study early.

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 6 COMPARISON 6. ARIPIPRAZOLE versus OLANZAPINE (acutely agitated people - all data by 5 days)

Outcome: 3 Leaving the study early

Analysis 6.4. Comparison 6 COMPARISON 6. ARIPIPRAZOLE versus OLANZAPINE (acutely agitated people - all data by 5 days), Outcome 4 Adverse effects: 1. Central nervous system.

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 6 COMPARISON 6. ARIPIPRAZOLE versus OLANZAPINE (acutely agitated people - all data by 5 days)

Outcome: 4 Adverse effects: 1. Central nervous system

(Continued ...)

Analysis 6.5. Comparison 6 COMPARISON 6. ARIPIPRAZOLE versus OLANZAPINE (acutely agitated people - all data by 5 days), Outcome 5 Adverse effects: 2. Endocrine - Prolactin - average increase.

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 6 COMPARISON 6. ARIPIPRAZOLE versus OLANZAPINE (acutely agitated people - all data by 5 days)

Outcome: 5 Adverse effects: 2. Endocrine - Prolactin - average increase

Analysis 6.6. Comparison 6 COMPARISON 6. ARIPIRAZOLE versus OLANZAPINE (acutely agitated people - all data by 5 days), Outcome 6 Adverse effects: 3a. Extrapyramidal - various.

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 6 COMPARISON 6. ARIPIRAZOLE versus OLANZAPINE (acutely agitated people - all data by 5 days)

Outcome: 6 Adverse effects: 3a. Extrapyramidal - various

Analysis 6.7. Comparison 6 COMPARISON 6. ARIPIPRAZOLE versus OLANZAPINE (acutely agitated people - all data by 5 days), Outcome 7 Adverse effects: 3b. Extrapyramidal - average score.

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 6 COMPARISON 6. ARIPIPRAZOLE versus OLANZAPINE (acutely agitated people - all data by 5 days)

Outcome: 7 Adverse effects: 3b. Extrapyramidal - average score

Analysis 6.8. Comparison 6 COMPARISON 6. ARIPIPRAZOLE versus OLANZAPINE (acutely agitated people - all data by 5 days), Outcome 8 Adverse effects: 4. Gastrointestinal.

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 6 COMPARISON 6. ARIPIPRAZOLE versus OLANZAPINE (acutely agitated people - all data by 5 days)

Outcome: 8 Adverse effects: 4. Gastrointestinal

Analysis 6.9. Comparison 6 COMPARISON 6. ARIPIRAZOLE versus OLANZAPINE (acutely agitated people - all data by 5 days), Outcome 9 Adverse effects: 5. Metabolic - continuous measures.

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 6 COMPARISON 6. ARIPIRAZOLE versus OLANZAPINE (acutely agitated people - all data by 5 days)

Outcome: 9 Adverse effects: 5. Metabolic - continuous measures

Analysis 7.1. Comparison 7 COMPARISON 7. ARIPIRAZOLE versus OTHER ANTIPSYCHOTIC DRUGS, Outcome 1 Global state: 1. No change (as defined in the study, measured by IAQ).

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 7 COMPARISON 7. ARIPIRAZOLE versus OTHER ANTIPSYCHOTIC DRUGS

Outcome: 1 Global state: 1. No change (as defined in the study, measured by IAQ)

(Continued ...)

Analysis 7.2. Comparison 7 COMPARISON 7. ARIPIPRAZOLE versus OTHER ANTIPSYCHOTIC DRUGS, Outcome 2 Global state: 2. Change in sexual dysfunction (ASEX).

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 7 COMPARISON 7. ARIPIPRAZOLE versus OTHER ANTIPSYCHOTIC DRUGS

Outcome: 2 Global state: 2. Change in sexual dysfunction (ASEX)

Analysis 7.3. Comparison 7 COMPARISON 7. ARIPIPRAZOLE versus OTHER ANTIPSYCHOTIC DRUGS, Outcome 3 Mental state: Specific - binary outcomes.

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 7 COMPARISON 7. ARIPIPRAZOLE versus OTHER ANTIPSYCHOTIC DRUGS

Outcome: 3 Mental state: Specific - binary outcomes

(Continued ...)

Analysis 7.4. Comparison 7 COMPARISON 7. ARIPIPRAZOLE versus OTHER ANTIPSYCHOTIC DRUGS, Outcome 4 Preference: Study medication worse than or equal to previous medication.

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 7 COMPARISON 7. ARIPIPRAZOLE versus OTHER ANTIPSYCHOTIC DRUGS

Outcome: 4 Preference: Study medication worse than or equal to previous medication

Analysis 7.5. Comparison 7 COMPARISON 7. ARIPIPRAZOLE versus OTHER ANTIPSYCHOTIC DRUGS, Outcome 5 Quality of life: 1. Unsatisfactory response on health dimension scale.

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 7 COMPARISON 7. ARIPIPRAZOLE versus OTHER ANTIPSYCHOTIC DRUGS

Outcome: 5 Quality of life: 1. Unsatisfactory response on health dimension scale

Analysis 7.6. Comparison 7 COMPARISON 7. ARIPIPRAZOLE versus OTHER ANTIPSYCHOTIC DRUGS, Outcome 6 Quality of life: 3. Average change score (QLS, high=better)).

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 7 COMPARISON 7. ARIPIPRAZOLE versus OTHER ANTIPSYCHOTIC DRUGS

Outcome: 6 Quality of life: 3. Average change score (QLS, high=better))

Analysis 7.7. Comparison 7 COMPARISON 7. ARIPIPRAZOLE versus OTHER ANTIPSYCHOTIC DRUGS, Outcome 7 Quality of life: 2. Average score (EQ-5D utility score, high=better).

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 7 COMPARISON 7. ARIPIPRAZOLE versus OTHER ANTIPSYCHOTIC DRUGS

Outcome: 7 Quality of life: 2. Average score (EQ-5D utility score, high=better)

Analysis 7.8. Comparison 7 COMPARISON 7. ARIPIPRAZOLE versus OTHER ANTIPSYCHOTIC DRUGS, Outcome 8 Quality of life: 4a. Weight related - No meaningful change (IWQOL-Lite).

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 7 COMPARISON 7. ARIPIPRAZOLE versus OTHER ANTIPSYCHOTIC DRUGS

Outcome: 8 Quality of life: 4a. Weight related - No meaningful change (IWQOL-Lite)

Analysis 7.9. Comparison 7 COMPARISON 7. ARIPIPRAZOLE versus OTHER ANTIPSYCHOTIC DRUGS, Outcome 9 Quality of life: 4b. Weight related - average score (IWQOL-Lite, high=better).

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 7 COMPARISON 7. ARIPIPRAZOLE versus OTHER ANTIPSYCHOTIC DRUGS

Outcome: 9 Quality of life: 4b. Weight related - average score (IWQOL-Lite, high=better)

Analysis 7.10. Comparison 7 COMPARISON 7. ARIPIRAZOLE versus OTHER ANTIPSYCHOTIC DRUGS, Outcome 10 Leaving the study early.

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 7 COMPARISON 7. ARIPIRAZOLE versus OTHER ANTIPSYCHOTIC DRUGS

Outcome: 10 Leaving the study early

(Continued ...)

(Continued . . .)

Analysis 7.11. Comparison 7 COMPARISON 7. ARIPIPRAZOLE versus OTHER ANTIPSYCHOTIC DRUGS, Outcome 11 Adverse effects: 1. At least one adverse effect.

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 7 COMPARISON 7. ARIPIPRAZOLE versus OTHER ANTIPSYCHOTIC DRUGS

Outcome: 11 Adverse effects: 1. At least one adverse effect

Analysis 7.12. Comparison 7 COMPARISON 7. ARIPIRAZOLE versus OTHER ANTIPSYCHOTIC DRUGS, Outcome 12 Adverse effects: 2. Central nervous system.

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 7 COMPARISON 7. ARIPIRAZOLE versus OTHER ANTIPSYCHOTIC DRUGS

Outcome: 12 Adverse effects: 2. Central nervous system

(Continued ...)

Analysis 7.13. Comparison 7 COMPARISON 7. ARIPIPRAZOLE versus OTHER ANTIPSYCHOTIC DRUGS, Outcome 13 Adverse effects: 3a. Endocrine - Prolactin - increase in level.

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 7 COMPARISON 7. ARIPIPRAZOLE versus OTHER ANTIPSYCHOTIC DRUGS

Outcome: 13 Adverse effects: 3a. Endocrine - Prolactin - increase in level

Analysis 7.14. Comparison 7 COMPARISON 7. ARIPIRAZOLE versus OTHER ANTIPSYCHOTIC DRUGS, Outcome 14 Adverse effects: 3b. Endocrine - Prolactin - Change in level.

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 7 COMPARISON 7. ARIPIRAZOLE versus OTHER ANTIPSYCHOTIC DRUGS

Outcome: 14 Adverse effects: 3b. Endocrine - Prolactin - Change in level

Analysis 7.15. Comparison 7 COMPARISON 7. ARIPIRAZOLE versus OTHER ANTIPSYCHOTIC DRUGS, Outcome 15 Adverse effects: 4. Extrapyramidal - akathisia.

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 7 COMPARISON 7. ARIPIRAZOLE versus OTHER ANTIPSYCHOTIC DRUGS

Outcome: 15 Adverse effects: 4. Extrapyramidal - akathisia

(Continued ...)

Analysis 7.16. Comparison 7 COMPARISON 7. ARIPIPRAZOLE versus OTHER ANTIPSYCHOTIC DRUGS, Outcome 16 Adverse effects: 5. Gastrointestinal.

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 7 COMPARISON 7. ARIPIPRAZOLE versus OTHER ANTIPSYCHOTIC DRUGS

Outcome: 16 Adverse effects: 5. Gastrointestinal

Analysis 7.17. Comparison 7 COMPARISON 7. ARIPIRAZOLE versus OTHER ANTIPSYCHOTIC DRUGS, Outcome 17 Adverse effects: 6a. Metabolic- binary measures.

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 7 COMPARISON 7. ARIPIRAZOLE versus OTHER ANTIPSYCHOTIC DRUGS

Outcome: 17 Adverse effects: 6a. Metabolic- binary measures

(Continued ...)

Analysis 7.18. Comparison 7 COMPARISON 7. ARIPIRAZOLE versus OTHER ANTIPSYCHOTIC DRUGS, Outcome 18 Adverse effects: 6b. Metabolic - continuous measures.

Review: Aripiprazole versus other atypical antipsychotics for schizophrenia

Comparison: 7 COMPARISON 7. ARIPIRAZOLE versus OTHER ANTIPSYCHOTIC DRUGS

Outcome: 18 Adverse effects: 6b. Metabolic - continuous measures

ADDITIONAL TABLES

Table 1. Titles for reviews suggested by excluded studies

Suggested title/ongoing title	Excluded study	Reference to relevant ongoing Cochrane title*
Alpha-receptor agonists for schizophrenia	Bergman 2007	Currently no review.
Antidepressant augmentation of antipsychotic drugs for schizophrenia	Fawzi 2009	Whitehead 2002
Aripiprazole augmentation of other antipsychotics for schizophrenia	Bristol-Myers 2006 , Shim 2006	Maayan 2011
Aripiprazole for people with metabolic syndrome	Colombo 2008	Mukundan 2010
Aripiprazole versus first generation antipsychotics for schizophrenia	Carson 2000 , Mossner 2009 , Talbot 2007 , Taylor 2007	Bhattacharjee 2008
Aripiprazole versus placebo for schizophrenia	Carson 2000 , Henderson 2009 , Mortimer 2004	Belgamwar 2011
Augmentation of clozapine for schizophrenia	Fleischhacker 2008a , Kim 2006 , Ma 2007 , Millar 2008 , Namey 2006 , Remington 2009	Cipriani 2009
Psychosocial intervention for schizophrenia	Anon 2008	Unclear which of the many reviews would be relevant.
Switching from other antipsychotics to aripiprazole for schizophrenia	Janssen 2005 , Lan 2008 , Pae 2009a , Schreiner 2009 , Takeuchi 2008	Mukundan 2010

* It is possible that these studies could also contribute to other titles not referenced in this column.

Table 2. Suggested design of future study

Methods	Allocation: randomised - clearly described generation of sequence and concealment of allocation. Blindness: double - described and tested. Duration: six months minimum.
Participants	Diagnosis: schizophrenia (operational criteria). N = 2700.* Age: any. Gender: both. History: any.
Interventions	1. Aripiprazole: dose ~ 10-30 mg/day. N = 300. 2. Amisulpride: dose ~ 400-800 mg/day. N = 300.

Table 2. Suggested design of future study (Continued)

	3. Clozapine: dose ~ 300-800 mg/day. N = 300. 4. Olanzapine: dose ~ 10-20 mg/day. N = 300. 5. Quetiapine: dose ~300-800 mg/day. N = 300. 6. Risperidone: dose ~ 4-8 mg/day. N = 300. 7. Sertindole: dose ~ 12-24 mg/day. N = 300. 8. Ziprasidone: dose ~ 120-160 mg/day. N = 300. 9. Zotepine: dose ~ 100-300 mg/day. N = 300.
Outcomes	Leaving study early (any reason, adverse events, inefficacy). Service outcomes: hospitalised, time in hospital, attending out patient clinics. Global impression: CGI**, relapse. Mental state: PANSS. Adverse events/effects: UKU, major adverse event/effect. Employment, living independently, family satisfaction, patient satisfaction

* power calculation suggested 300/group would allow good chance of showing a 10% difference between groups for primary outcome.

** Primary outcome

CGI: Clinical Global Impression Scale

PANSS: Positive and Negative Syndrome Scale

UKU: Udvalg for kliniske undersøgelser Side Effect Rating Scale -side effect rating scale

APPENDICES

Appendix I. Previous searches

1. Update of 2011

We searched the Cochrane Schizophrenia Group Trials Register (November 2011) using the phrase

[(aripiprazol* AND (amisulprid* OR clozapin* OR olanzapin* OR quetiapin* OR risperidon* OR sertindol* OR ziprasidon* OR zotepin*)) in title, abstract or index terms of REFERENCE) or ((aripiprazol* AND (amisulprid* OR clozapin* OR olanzapin* OR quetiapin* OR risperidon* OR sertindol* OR ziprasidon* OR zotepin*)) in interventions of STUDY)]

The Cochrane Schizophrenia Group's Trials Register is compiled by systematic searches of major databases, handsearches of journals and conference proceedings (see [Group Module](#)). Incoming trials are assigned to relevant existing or new review titles.

2. Update of 2007

We searched the Cochrane Schizophrenia Group Trials Register (March 2007) using the phrase:

[(aripiprazol* AND (amisulprid* OR clozapin* OR olanzapin* OR quetiapin* OR risperidon* OR sertindol* OR ziprasidon* OR zotepin*)) in title, abstract or index terms of REFERENCE) or ((aripiprazol* AND (amisulprid* OR clozapin* OR olanzapin* OR quetiapin* OR risperidon* OR sertindol* OR ziprasidon* OR zotepin*)) in interventions of STUDY)]

This register is compiled by systematic searches of major databases, handsearches and conference proceedings (see [Group Module](#)).

The Cochrane Schizophrenia Group Trials Register is maintained on Meerkat 1.5. This version of Meerkat stores references as studies. When an individual reference is selected through a search all references which have been identified as the same study are also selected

3. Initial search

We searched the Cochrane Schizophrenia Group Trials Register (August 2005) using the phrase:

[(aripiprazol* AND (amisulprid* OR clozapin* OR olanzapin* OR quetiapin* OR risperidon* OR sertindol* OR ziprasidon* OR zotepin*)) in title, abstract or index terms of REFERENCE].

Appendix 2. Previous data collection and analysis

1. Data extraction

We independently extracted data from selected trials. When disputes arose we attempted to resolve these by discussion. When this was not possible and further information was necessary to resolve the dilemma, we did not enter data and added the trial to the list of those awaiting assessment.

2. Management

We extracted the data onto standard simple forms. Where possible, we entered data in such a way that the area to the left of the line of no effect indicated a favourable outcome for aripiprazole.

3. Rating scales

A wide range of instruments are available to measure outcomes in mental health studies. These instruments vary in quality and many are not validated or are even ad hoc. It is accepted generally that measuring instruments should have the properties of reliability (the extent to which a test effectively measures anything at all) and validity (the extent to which a test measures that which it is supposed to measure) (Rust 1989). Unpublished scales are known to be subject to bias in trials of treatments for schizophrenia (Marshall 2000). Therefore continuous data from rating scales were included only if the measuring instrument had been described in a peer-reviewed journal. In addition, the following minimum standards for instruments were set: the instrument should either be (a) a self-report or (b) completed by an independent rater or relative (not the therapist) and (c) the instrument should be a global assessment of an area of functioning.

Assessment of risk of bias in included studies

Again working independently, PK, KK and SL assessed the risk of bias using the tool described in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). This tool encourages consideration of how the sequence was generated, how allocation was concealed, the integrity of blinding at outcome, the completeness of outcome data, selective reporting and other biases.

The risk of bias in each domain and overall were assessed and categorised into:

- A. Low risk of bias: plausible bias unlikely to seriously alter the results (categorised as 'Yes' in Risk of Bias table)
- B. High risk of bias: plausible bias that seriously weakens confidence in the results (categorised as 'No' in Risk of Bias table)
- C. Unclear risk of bias: plausible bias that raises some doubt about the results (categorised as 'Unclear' in Risk of Bias table)

Trials with a high risk of bias (defined as at least three out of five domains were categorised as 'No') or where allocation was clearly not concealed were not included in the review. If the raters disagreed, the final rating was made by consensus with the involvement of another member of the review group. Where inadequate details of randomisation and other characteristics of trials are provided, authors of the studies were contacted in order to obtain further information. Non-concurrence in quality assessment was reported.

Measures of treatment effect

1. Data types

We assessed outcomes using continuous (for example changes on a behaviour scale), categorical (for example, one of three categories on a behaviour scale, such as 'little change', 'moderate change' or 'much change') or dichotomous (for example, either 'no important changes' or 'important change' in a person's behaviour) measures. Currently RevMan does not support categorical data so we were unable to analyse this.

2. Dichotomous-yes/no-data

We carried out an intention-to-treat analysis. Everyone allocated to the intervention were counted, whether they completed the follow-up or not. It was assumed that those who left early had no change in their outcome. This rule is conservative concerning response to treatment, because it assumes that those discontinuing the studies would not have responded. It is not conservative concerning adverse effects, but we felt that assuming that all those leaving early would have developed adverse effects would overestimate risk. Where possible, efforts were made to convert outcome measures to dichotomous data. This can be done by identifying cut-off points on rating scales and dividing participants accordingly into 'clinically improved' or 'not clinically improved'. It was generally assumed that if there had been a 50% reduction in a scale-derived score such as the Brief Psychiatric Rating Scale (BPRS, Overall 1962) or the Positive and Negative Syndrome Scale (PANSS, Kay 1986), this could be considered as a clinically significant response (Leucht 2005, Leucht 2005a). If data based on these thresholds were not available, we used the primary cut-off presented by the original authors. We calculated the relative risk (RR) and its 95% confidence interval (CI) based on the random-effects model, as this takes into account any differences between studies even if there is no statistically significant heterogeneity. It has been shown that RR is more intuitive (Boissel 1999) than odds ratios and that odds ratios tend to be interpreted as RR by clinicians (Deeks 2000). This misinterpretation then leads to an overestimate of the impression of the effect. When the overall results were significant we calculated the number needed to treat (NNT) and the number needed to harm (NNH) as the inverse of the risk difference.

3. Continuous data

3.1 Normal distribution of the data

The meta-analytic formulas applied by RevMan Analyses (the statistical programme included in RevMan) require a normal distribution of data. The software is robust towards some skew but to which degree of skewness meta-analytic calculations can still be reliably carried out is unclear. On the other hand, excluding all studies on the basis of estimates of the normal distribution of the data also leads to a bias, because a considerable amount of data may be lost leading to a selection bias. Therefore, we included all studies in the primary analysis. In a sensitivity analysis we excluded potentially skewed data applying the following rules:

- a) When a scale started from the finite number zero the standard deviation, when multiplied by two, was more than the mean (as otherwise the mean is unlikely to be an appropriate measure of the centre of the distribution, Altman 1996).
- b) If a scale started from a positive value (such as PANSS which can have values from 30 to 210) the calculation described above was modified to take the scale starting point into account. In these cases skew is present if $2SD > (S - S_{min})$, where S is the mean score and S_{min} is the minimum score). In large studies (as a cut-off we used 200 participants) skewed data pose less of a problem. In these cases we entered the data in a synthesis and no sensitivity analysis was applied.
- d) The rules explained in a) and b) do not apply to change data. The reason is that when continuous data are presented on a scale which includes a possibility of negative values, it is difficult to tell whether data are non-normally distributed (skewed) or not. This is also the case for change data (endpoint minus baseline). In the absence of individual patient data it is impossible to know if data are skewed, though this is likely. After consulting the ALLSTAT electronic statistics mailing list, we presented change data in RevMan Analyses in order to summarise available information. In doing this, it was assumed either that data were not skewed or that the analysis could cope with the unknown degree of skew. Without individual patient data it is impossible to test this assumption. We therefore included change data and did not apply a sensitivity analysis. For continuous outcomes we estimated a mean difference (MD) between groups. MDs were again based on the random-effects model, as this takes into account any differences between studies even if there is no statistically significant heterogeneity. We combined both endpoint data and change data in the analysis because there is no principal statistical reason why endpoint and change data should measure different effects (Higgins 2011). When standard errors instead of standard deviations (SD) were presented, we converted the former to standard deviations. If both were missing we estimated SDs from p-values or used the average SD of the other studies (Furukawa 2006).

Unit of analysis issues

1. Cluster trials

Studies increasingly employ cluster randomisation (such as randomisation by clinician or practice) but analysis and pooling of clustered data poses problems. Authors often fail to account for intra class correlation in clustered studies, leading to a unit of analysis error

(Divine 1992) whereby P values are spuriously low, confidence intervals unduly narrow and statistical significance overestimated. This can cause Type I errors (Bland 1997, Gulliford 1999).

Where clustering was not accounted for in primary studies, we presented the data in a table, with a (*) symbol to indicate the presence of a probable unit of analysis error. In subsequent versions of this review we will seek to contact first authors of studies to obtain intra class correlation coefficients of their clustered data and to adjust for this using accepted methods (Gulliford 1999). Where clustering has been incorporated into the analysis of primary studies, we will also present these data as if from a non-cluster randomised study, but adjusted for the clustering effect.

We have sought statistical advice and have been advised that the binary data as presented in a report should be divided by a design effect. This is calculated using the mean number of participants per cluster (m) and the intra class correlation coefficient (ICC) [Design effect = $1 + (m-1) \times \text{ICC}$] (Donner 2002). If the ICC was not reported it was assumed to be 0.1 (Ukoumunne 1999).

If cluster studies had been appropriately analysed taking into account intra class correlation coefficients and relevant data documented in the report, we synthesised these with other studies using the generic inverse variance technique.

2. Cross-over trials

A major concern of cross-over trials is the carry-over effect. It occurs if an effect (e.g. pharmacological, physiological or psychological) of the treatment in the first phase is carried over to the second phase. As a consequence on entry to the second phase the participants can differ systematically from their initial state despite a wash-out phase. For the same reason cross-over trials are not appropriate if the condition of interest is unstable (Elbourne 2002). As both effects are very likely in schizophrenia, we will only use data of the first phase of cross-over studies.

3. Studies with multiple treatment groups

Where a study involved more than two treatment groups, if relevant, the additional treatment groups were presented in additional relevant comparisons. Data were not double counted. Where the additional treatment groups were not relevant, these data were not reproduced.

Dealing with missing data

At some degree of loss of follow-up, data must lose credibility (Xia 2007). Although high rates of premature discontinuation are a major problem in this field, we felt that it was unclear which degree of attrition leads to a high degree of bias. We, therefore, did not exclude outcomes on the basis of the percentage of participants completing them. However we addressed the drop-out problem in all parts of the review, including the abstract. For this purpose we calculated, presented and commented on frequency statistics (overall rates of leaving the studies early in all studies and comparators pooled and their ranges).

We assumed that the people who discontinued the studies for any reason did not show any response to the treatment.

Assessment of heterogeneity

1. Clinical heterogeneity

We considered all the included studies within any comparison to judge for clinical heterogeneity.

2. Statistical

2.1 Visual inspection

We visually inspected graphs to investigate the possibility of statistical heterogeneity.

2.2 Employing the I^2 statistic

Visual inspection was supplemented using, primarily, the I^2 statistic. This provides an estimate of the percentage of variability due to heterogeneity rather than chance alone. Where the I^2 estimate was greater than or equal to 50% we interpreted this as indicating the presence of considerable levels of heterogeneity (Higgins 2011).

Assessment of reporting biases

Reporting biases arise when the dissemination of research findings is influenced by the nature and direction of results (Egger 1997). These are described in section 10.1 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). We are aware that funnel plots may be useful in investigating small-study effects but are of limited power to detect such effects when there are few studies. We entered data from all identified and selected trials into a funnel graph (trial effect versus trial size) in an attempt to investigate the likelihood of overt publication bias. We did not undertake a formal test for funnel plot asymmetry.

Data synthesis

Where possible for both dichotomous and continuous data we used the random-effects model for data synthesis as this takes into account any differences between studies even if there is no statistically significant heterogeneity. We understand that there is no closed argument for preference for use of fixed or random-effects models. The random-effects method incorporates an assumption that the different studies are estimating different, yet related, intervention effects. This does seem true to us, however, random-effects does put added weight onto the smaller of the studies - those trials that are most vulnerable to bias.

Subgroup analysis and investigation of heterogeneity

1. Subgroup

We did not anticipate any subgroup analyses.

2. Heterogeneity

If data are clearly heterogeneous we checked that data are correctly extracted and entered and that we had made no unit of analysis errors. If inconsistency was high and clear reasons explaining the heterogeneity were found, we presented the data separately. If not, we commented on the heterogeneity of the data.

Sensitivity analysis

We planned sensitivity analyses a priority for examining the change in the robustness of the sensitivity to including studies with potentially skewed data. A recent report showed that some of the comparisons of atypical antipsychotics may have been biased by using inappropriate comparator doses (Heres 2006). We, therefore, also analysed whether the exclusion of studies with inappropriate comparator doses changed the results of the primary outcome and the general mental state.

FEEDBACK

New Feedback, 4 August 2016

Summary

I would like to bring the authors attention to a possible error in their review report.

I believe that the a result in [Analysis 3.6](#) (aripiprazole versus risperidone), (Mental state: 2 average endpoint scale), subgroup 2 (PANSS [short term, up to 12 weeks, high=poor]) contain an extra study in error. The study in question, [Zhang 2009](#), appears to compare aripiprazole with clozapine, and not with risperidone. As such, it should not be included in this analysis.

For this analysis the authors report no significant difference between aripiprazole and risperidone for PANSS short term (78 RCTs, n= 5793, -0.69 CI -1.49 to 0.11) with considerable heterogeneity ($\text{Chi}^2 = 161.78$; $\text{df} = 76$; $P=0.00001$; $I^2=53\%$). However, after excluding [Zhang 2009](#) and replicating the analysis, significant results in favour of aripiprazole are observed (77 RCTs, n = 5733, MD -0.80 CI -1.58 to -0.02, $Z = 2.01$, $P = 0.04$) with considerable heterogeneity ($\text{Chi}^2 = 145.74$; $\text{df} = 76$; $P<0.00001$; $I^2=48\%$).

Conclusions elsewhere in the report may also need reconsideration.

Reply

Thank you for bring this to our attention. Following your query, I have checked through these data and found that [Zhang 2009a](#) which has the correct control group, has accidentally been entered twice. For some reason the duplicate entry was added as [Zhang 2009](#). My guess is the software didn't allow the same study to be entered twice in the same outcome, hence the reviewer mistook [Zhang 2009](#) as [Zhang 2009a](#). To rectify the error, I have removed study [Zhang 2009](#) from this outcome. The result does became statistically significant and the results section has changed, but this significance is only marginal, upper CI is -0.02. As statistically significant results do not always necessarily have clinical significance, and as this is a marginal change, I feel the overall conclusions of the review should remain the same.

Contributors

Claire Ainsworth: commentator.

Jun Xia: review author.

WHAT'S NEW

Date	Event	Description
18 October 2016	Feedback has been incorporated	Feedback received and authors have amended data input for a mental state outcome (Analysis 3.6). Data have changed and result is now significant, but overall conclusions of review remain unchanged. See Feedback 1 .

HISTORY

Protocol first published: Issue 3, 2007

Review first published: Issue 4, 2009

Date	Event	Description
24 October 2013	New citation required but conclusions have not changed	No overall change to conclusions.
25 June 2013	New search has been performed	New search run in November 2012. Trials assessed and new data added to review (162 new trials), but no changes to overall conclusions
16 October 2012	New citation required but conclusions have not changed	New search and data added, no major changes to conclusions.
24 January 2012	New search has been performed	This is a major update, eight new trials have been included.
4 September 2008	Amended	Converted to new review format.

CONTRIBUTIONS OF AUTHORS

Tao Suo - study selection (2012 update), data extraction, report writing.

Priya Khanna - study selection (2011 update), data extraction, report writing.

Katja Komossa - protocol development, searching, study selection, data extraction, report writing.

Huai-xing Ma - study selection (2012 update), data extraction, report writing.

Stefan Leucht - protocol development, searching, study selection, data extraction, report writing.

Hany George El Sayeh - protocol development, 2011 update - help with write up.

Jun Xia - help with study selection (2012 update), data extraction, report writing.

DECLARATIONS OF INTEREST

Tao Suo - none known.

Priya Khanna - none known.

Katja Komossa - none known.

Huai-xing Ma - none know.*

Stefan Leucht - has received honoraria for lectures from Abbvie, Astra Zeneca, BristolMyersSquibb, ICON, EliLilly, Janssen, Johnson & Johnson, Roche, SanofiAventis, Lundbeck and Pfizer; honoraria for consulting/advisory boards from Roche, EliLilly, Medavante, BristolMyersSquibb, Alkermes, Janssen, Johnson & Johnson and Lundbeck. EliLilly has provided medication for a study with Stefan Leucht as primary investigator.

Christine Rummel - has received lecture honoraria and travel grants to attend scientific meetings from AstraZenca, JanssenCilag, EliLilly and Pfizer.

Heike Hunger - none known.

Sandra Schwarz - none known.

Hany George El-Sayeh - none known.

Jun Xia - none known.*

* no conflict of interest but authors work for a professional review company that received an incentive to complete this update (see also [Sources of support](#)).

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- National Institute of Health Research, UK.

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DIFFERENCES BETWEEN PROTOCOL AND REVIEW

The review was slightly adapted to new formatting and functions available in Review Manager 5, notably the 'Risk of bias' tables. In the first version of this review, we planned to undertake a sensitivity analysis and exclude studies with 'inappropriate comparator doses'; however, this was not defined. In the current review, we have defined this in the [Sensitivity analysis](#) section.

INDEX TERMS

Medical Subject Headings (MeSH)

Antipsychotic Agents [*therapeutic use]; Aripiprazole; Benzodiazepines [therapeutic use]; Piperazines [*therapeutic use]; Quinolones [*therapeutic use]; Randomized Controlled Trials as Topic; Schizophrenia [*drug therapy]

MeSH check words

Humans