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Saha, Kumar, Bo, Li, Zhao, Sai et al. (3 more authors) (2016) Chlorpromazine versus atypical antipsychotic drugs for schizophrenia. Cochrane Database of Systematic Reviews. CD010631. ISSN 1469-493X

https://doi.org/10.1002/14651858.CD010631.pub2

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Chlorpromazine versus atypical antipsychotic drugs for schizophrenia (Review)

Saha KB, Bo L, Zhao S, Xia J, Sampson S, Zaman RU

Saha KB, Bo L, Zhao S, Xia J, Sampson S, Zaman RU. Chlorpromazine versus atypical antipsychotic drugs for schizophrenia. *Cochrane Database of Systematic Reviews* 2016, Issue 4. Art. No.: CD010631. DOI: 10.1002/14651858.CD010631.pub2.

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[Intervention Review]

Chlorpromazine versus atypical antipsychotic drugs for schizophrenia

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Editorial group: Cochrane Schizophrenia Group. Publication status and date: New, published in Issue 4, 2016.

Citation: Saha KB, Bo L, Zhao S, Xia J, Sampson S, Zaman RU. Chlorpromazine versus atypical antipsychotic drugs for schizophrenia. *Cochrane Database of Systematic Reviews* 2016, Issue 4. Art. No.: CD010631. DOI: 10.1002/14651858.CD010631.pub2.

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ABSTRACT

Background

Chlorpromazine is an aliphatic phenothiazine, which is one of the widely-used typical antipsychotic drugs. Chlorpromazine is reliable for its efficacy and one of the most tested first generation antipsychotic drugs. It has been used as a 'gold standard' to compare the efficacy of older and newer antipsychotic drugs. Expensive new generation drugs are heavily marketed worldwide as a better treatment for schizophrenia, but this may not be the case and an unnecessary drain on very limited resources.

Objectives

To compare the effects of chlorpromazine with atypical or second generation antipsychotic drugs, for the treatment of people with schizophrenia.

Search methods

We searched the Cochrane Schizophrenia Group's Trials Register up to 23 September 2013.

Selection criteria

We included randomised controlled trials (RCTs) that compared chlorpromazine with any other atypical antipsychotic drugs for treating people with schizophrenia. Adults (as defined in each trial) diagnosed with schizophrenia, including schizophreniform, schizoaffective and delusional disorders were included in this review.

Data collection and analysis

At least two review authors independently screened the articles identified in the literature search against the inclusion criteria and extracted data from included trials. For homogeneous dichotomous data, we calculated the risk ratio (RR) and the 95% confidence intervals (CIs). For continuous data, we determined the mean difference (MD) values and 95% CIs. We assessed the risk of bias in included studies and rated the quality of the evidence using the GRADE approach.

Main results

This review includes 71 studies comparing chlorpromazine to olanzapine, risperidone or quetiapine. None of the included trials reported any data on economic costs.

1. Chlorpromazine versus olanzapine

In the short term, there appeared to be a significantly greater clinical response (as defined in each study) in people receiving olanzapine (3 RCTs, N = 204; RR 2.34, 95% CI 1.37 to 3.99, *low quality evidence*). There was no difference between drugs for relapse (1 RCT, N = 70; RR 1.5, 95% CI 0.46 to 4.86, *very low quality evidence*), nor in average endpoint score using the Brief Psychiatric Rating Scale (BPRS) for mental state (4 RCTs, N = 245; MD 3.21, 95% CI -0.62 to 7.05, *very low quality evidence*). There were significantly more extrapyramidal symptoms experienced amongst people receiving chlorpromazine (2 RCTs, N = 298; RR 34.47, 95% CI 4.79 to 248.30, *very low quality evidence*). Quality of life ratings using the general quality of life interview (GQOLI) - physical health subscale were more favourable with people receiving olanzapine (1 RCT, N = 61; MD -10.10, 95% CI -13.93 to -6.27, *very low quality evidence*). There was no difference between groups for people leaving the studies early (3 RCTs, N = 139; RR 1.69, 95% CI 0.45 to 6.40, *very low quality evidence*).

2. Chlorpromazine versus risperidone

In the short term, there appeared to be no difference in clinical response (as defined in each study) between chlorpromazine or risperidone (7 RCTs, N = 475; RR 0.84, 95% CI 0.53 to 1.34, *low quality of evidence*), nor in average endpoint score using the BPRS for mental state 4 RCTs, N = 247; MD 0.90, 95% CI -3.49 to 5.28, *very low quality evidence*), or any observed extrapyramidal adverse effects (3 RCTs, N = 235; RR 1.7, 95% CI 0.85 to 3.40,*very low quality evidence*). Quality of life ratings using the QOL scale were significantly more favourable with people receiving risperidone (1 RCT, N = 100; MD -14.2, 95% CI -20.50 to -7.90, *very low quality evidence*). There was no difference between groups for people leaving the studies early (one RCT, N = 41; RR 0.21, 95% CI 0.01 to 4.11, *very low quality evidence*).

3. Chlorpromazine versus quetiapine

In the short term, there appeared to be no difference in clinical response (as defined in each study) between chlorpromazine or quetiapine (28 RCTs, N = 3241; RR 0.93, 95% CI 0.81 to 1.06, *moderate quality evidence*) nor in average endpoint score using the BPRS for mental state (6 RCTs, N = 548; MD – 0.18, 95% CI – 1.23 to 0.88, *very low quality evidence*). Quality of life ratings using the GQOL1-74 scale were significantly more favourable with people receiving quetiapine (1 RCT, N = 59; MD – 6.49, 95% CI – 11.30 to – 1.68, *very low quality evidence*). Significantly more people receiving chlorpromazine experienced extrapyramidal adverse effects (8 RCTs, N = 644; RR 8.03, 95% CI 4.78 to 13.51, *low quality of evidence*). There was no difference between groups for people leaving the studies early in the short term (12 RCTs, N = 1223; RR 1.04, 95% CI 0.77 to 1.41,*moderate quality evidence*).

Authors' conclusions

Most included trials included inpatients from hospitals in China. Therefore the results of this Cochrane review are more applicable to the Chinese population. Mostincluded trials were short term studies, therefore we cannot comment on the medium and long term use of chlorpromazine compared to atypical antipsychotics. Low qualityy evidence suggests chlorpromazine causes more extrapyramidal adverse effects. However, all studiesused varying dose ranges, and higher doses would be expected to be associated with more adverse events.

PLAIN LANGUAGE SUMMARY

Chlorpromazine compared with newer atypical antipsychotics

People with schizophrenia often hear voices or see things (hallucinations) and have strange beliefs (delusions). The main treatment for people with these symptoms of schizophrenia is antipsychotic drugs. Chlorpromazine was one of the first drugs discovered to be effective for treating people with schizophrenia. It remains one of the most commonly used and inexpensive treatments. However, being an older drug (typical or first generation) it also has serious side effects, including blurred vision, a dry mouth, tremors or uncontrollable shaking, depression, muscle stiffness and restlessness.

In this Cochrane review we examined the effects of chlorpromazine for treating people with schizophrenia compared with newer antipsychotic drugs.

We searched the literature for randomised controlled trials up to 23 September 2013, and included 71 trials. The included studies compared chlorpromazine with three newer antipsychotics: risperidone, quetiapine or olanzapine. Most included trials were short term studies and undertaken in China. Based on low quality evidence, we found that chlorpromazine is not much different to risperidone or quetiapine but is associated with more side effects. More favourable results were found for olanzapine with those receiving olanzapine experiencing fewer side effects and greater improvements in global state and quality of life than those receiving chlorpromazine, but again this is based on low quality evidence. Larger, longer, better conducted and reported trials should focus on important outcomes such as quality of life, levels of satisfaction with treatment or care, relapse, costs and hospital discharge or admission. Also, more international studies are needed. Outpatient treatment was under-represented in the included studies, and future research should also include work with this group of people.

Due to the limitations of evidence in this Cochrane review, it is difficult to draw firm conclusions. Chlorpormazine is available widely, is comparable with the newer antipsychotics and is relatively cheap so despite its propensity to cause side effects, is likely to remain one of the benchmark antipsychotics.

The plain language summary has been written by a consumer. Ben Gray: Senior Peer Researcher, McPin Foundation. http://mcpin.org/.

Chlorpromazine versus olanzapine for schizophrenia Patient or population: people with schizophrenia Settings: inpatient and outpatient Intervention: chlorpromazine Comparison: olanzapine Illustrative comparative risks* (95% CI) Number of participants Quality of the evidence Comments **Relative effect** Outcomes (GRADE) (95% CI) (studies) Assumed risk Corresponding risk Olanzapine Chlorpromazine No significant clinical Low¹ RR 2.34 204 $\oplus \oplus \bigcirc \bigcirc$ response: short term (1.37 to 3.99) (3 studies) low^{2,3} 1000 per 1000 700 per 1000 (up to 6 months) (959 to 1000) Follow-up: 6 to 12 weeks High¹ 190 per 1000 445 per 1000 (260 to 758)

Relapse: long RR 1.5 70 term Study population $\oplus 000$ (over 12 months) very low^{3,4} (0.46 to 4.86) (1 study) Follow-up: mean 2 114 per 1000 171 per 1000 (53 to 555) years Moderate 114 per 1000 171 per 1000 (52 to 554)

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SUMMARY OF FINDINGS FOR THE MAIN COMPARISON [Explanation]

4

Mental state: short term (up to 6 months) BRPS average endpoint score (high = poor) Follow-up: 6 to 12 weeks		The mean mental state: short term (up to 6 months) in the interven- tion groups was 3.21 higher (0.62 lower to 7.05 higher)		245 (4 studies)	⊕○○○ - very low ^{2,3,5,6,7}	
Adverse effects: any	Low		RR 34.47	298	⊕000 -	
observed extrapyrami- dal symptoms - short term (up to 6 months)	10 per 1000	345 per 1000 (48 to 1000)	(4.79 to 248.3)	(2 studies)	very low ^{2,3,8}	
Follow-up: mean 8 weeks	Moderate					
	100 per 1000	1000 per 1000 (479 to 1000)				
	High					
	250 per 1000	1000 per 1000 (1000 to 1000)				
Quality of life: short term (up to 6 months) GQOLI-physical health subscale score (high = good) Follow-up: mean 8 weeks		The mean quality of life: short term (up to 6 months) in the interven- tion groups was 10.10 lower (13.93 to 6.27 lower)		61 (1 study)	⊕○○○ - very low ^{2,3,7,9,10}	
Leaving the study early due to any reason: short term (up to 6 months) Follow-up: mean 6 weeks	Study population ¹¹		RR 1.69 (0.45 to 6.4)	139 (3 studies)	⊕○○○ - very low ^{3,12,13}	

1	59 per 1000	268 per 1000 (71 to 1000)	
N	<i>l</i> oderate ¹¹		
2	29 per 1000	387 per 1000 (103 to 1000)	
	oup and the relative	dian control group risk acros e effect of the intervention (a	tudies) is provided in footnotes. The corresponding risk (and its 95% CI) is based on the assume its 95% CI).
GPADE Working Group are	dos of ovidence		
GRADE Working Group gra		y to change our confidence ir	ne estimate of effect.
			our confidence in the estimate of effect and may change the estimate.
Low quality: Further resea	arch is very likely to		ur confidence in the estimate of effect and is likely to change the estimate.
			al connucied in the continue of circot and is intery to change the continue.
Very low quality: We are v	very uncertain abou	ut the estimate.	
	-		
¹ Control risk: the control ri	sks are representa	tive of the control group risks	f the study population.
¹ Control risk: the control ris ² Risk of bias: rated serious	sks are representa - most included st	tive of the control group risks	f the study population. terms of allocation and blinding, hence selection
¹ Control risk: the control ris ² Risk of bias: rated serious and detection bias are likel ³ Publication bias: strongly	sks are representa - most included st ly to be present. Tv	tive of the control group risks udies had unclear risk of bias vo studies also had high risk	f the study population. terms of allocation and blinding, hence selection
¹ Control risk: the control ris ² Risk of bias: rated serious and detection bias are likel ³ Publication bias: strongly suspected.	sks are representa - most included st ly to be present. Tv suspected - we ide	tive of the control group risks udies had unclear risk of bias vo studies also had high risk entified only small trial(s) fron	f the study population. terms of allocation and blinding, hence selection reporting bias. China for this outcome. Publication bias is highly
¹ Control risk: the control ris ² Risk of bias: rated serious and detection bias are likel ³ Publication bias: strongly suspected. ⁴ Imprecision: serious - only	sks are representa - most included st ly to be present. Ty suspected - we ide y one small trial wi	tive of the control group risks udies had unclear risk of bias vo studies also had high risk entified only small trial(s) fron th unclear risk of selection ar	f the study population. terms of allocation and blinding, hence selection reporting bias.
¹ Control risk: the control ris ² Risk of bias: rated serious and detection bias are likel ³ Publication bias: strongly suspected. ⁴ Imprecision: serious - only The result was imprecise w	sks are representa - most included st ly to be present. Ty suspected - we ide y one small trial wi yith few event and	tive of the control group risks udies had unclear risk of bias wo studies also had high risk entified only small trial(s) fron th unclear risk of selection ar a wide Cl.	f the study population. terms of allocation and blinding, hence selection reporting bias. China for this outcome. Publication bias is highly detection bias contributed data to this outcome.
¹ Control risk: the control ris ² Risk of bias: rated serious and detection bias are likel ³ Publication bias: strongly suspected. ⁴ Imprecision: serious - only The result was imprecise w ⁵ Inconsistency: serious - un	sks are representa - most included st ly to be present. Ty suspected - we ide y one small trial wi vith few event and nexplained heterog	tive of the control group risks udies had unclear risk of bias wo studies also had high risk entified only small trial(s) fron th unclear risk of selection ar a wide Cl. geneity present, suggesting di	f the study population. terms of allocation and blinding, hence selection reporting bias. China for this outcome. Publication bias is highly detection bias contributed data to this outcome. erent magnitude of effect.
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¹²Risk of bias: serious - most included studies that contributed data to this outcome had high risk of bias with the selection, detection and reporting of the result.
 ¹³Imprecision: serious - estimate of effect was not significant and the total sample size is smaller than the desired optimal

information size.

7

BACKGROUND

Description of the condition

Schizophrenia is a severe form of mental health disorder. It has a high lifetime prevalence rate, affecting (4 per 1000 people (Saha 2005), but low incident rate because of the chronic nature of the illness. The median incident rate of schizophrenia is 15.2 per 100,000 people (McGrath 2008).

The International Classification of Diseases (ICD) classifies the illness into categories F20 to F29 as 'schizophrenia, schizotypal and delusional disorder' (ICD-10 1992), particularly 'schizophrenia' in F20. The ICD-10 states that "schizophrenic disorders are characterized in general by fundamental and characteristic distortions of thinking and perception, and affects that are inappropriate or blunted". The Diagnostic and Statistical Manual of the American Psychiatric Association has also used the term 'schizophrenia' (DSM-IV-TR 2000).

The prognosis of schizophrenia is quite variable, and in the past psychiatrists were not very optimistic about its treatment (Kraeplin 1919). However, recent studies show that the outcome of schizophrenia treatment is better than previously thought. The use of phenothiazines may have contributed to this as well as other factors, such as improving community services (Bland 1978).

Description of the intervention

Psychiatrists have prescribed typical antipsychotic drugs since the 1950s, when the first antipsychotic medication, chlorpromazine, was synthesized. Chlorpromazine was first used as an antihistaminic agent to treat allergies. Later, surgeons used it as a presurgical medication to sedate people before surgical procedures (Laborit 1951). In 1952, Paul Charpentier, from Laboratories Rhône-Poulenc in France, and Delay and Deniker's team described the antipsychotic properties of chlorpromazine (Delay 1952). Chlorpromazine is considered a pivotal discovery in the field of psychosis treatment, with other antipsychotics often measured in 'chlorpromazine equivalents' (Turner 2007; Yorston 2000).

There are now many antipsychotic drugs available. They are broadly divided into two groups: 'typical antipsychotic drugs' and 'atypical antipsychotic drugs'. Typical antipsychotic drugs are also known as 'first generation', 'conventional' or 'classical' antipsychotic drugs, e.g. chlorpromazine and haloperidol. Atypical antipsychotic drugs are also known as 'second generation' or 'newer antipsychotic drugs', e.g. clozapine, risperidone, quetiapine and olanzapine. Typical antipsychotic drugs have a good reputation regarding their efficacy in treating the 'positive' symptoms of schizophrenia (e.g. delusions and hallucinations) (Mathews 2007). They are also well known for their adverse effects, such as movement disorders (extrapyramidal symptoms (EPS) or extrapyramidal side effects (EPSE)), sedation, metabolic syndromes and sometimes potentially fatal conditions, such as neuroleptic malignant syndrome (Arana 2000). The second generation antipsychotic drugs arrived on the market, claiming notable differences. They had a reputed low side-effect profile and, according to pharmaceutical companies, higher efficacy (Janssen 1988). However, research funded independently of pharmaceutical companies has suggested that there may be little difference between the older and newer drugs (Adams 2014). This has subsequently fuelled debate as to whether new atypical antipsychotics are more effective than older established first-generation antipsychotics, and whether questioning the efficacy of the two classifications of drugs creates an improper generalisation of antipsychotics that do not form a homogenous class (Leucht 2009). Against this backdrop, chlorpromazine remains a benchmark drug in the treatment of schizophrenia. Although imperfect, it is relatively inexpensive and remains one of the most common drugs used for treating people with schizophrenia worldwide (Adams 2005).

How the intervention might work

Chlorpromazine is an aliphatic phenothiazine, which is one of the widely-used typical antipsychotic drugs. Chlorpromazine is reliable for its efficacy and one of the most tested first generation antipsychotic drugs. It has been used as a 'gold standard' to compare the efficacy of older and newer antipsychotic drugs. It blocks alpha 1, 5HT2A, D2 and D1 receptors in the brain, and thus it works as an antipsychotic. It also has effect on muscarinic, serotonin and H1 receptors. By blocking D2 receptor it can also cause extrapyramidal side effects. Other adverse effects include dry mouth, blurred vision, restlessness, sedation, neuroleptic malignant syndrome (DSM-IV 1994) etc. On the other hand, atypical antipsychotic drugs by definition may cause decreased or no extrapyramidal side effects (Kinon 1996). Different atypical antipsychotic drugs act in different ways; for example, clozapine blocks D2 and 5HT2 receptors (Meltzer 1989). Both clozapine and quetiapine blocks more 5HT2 receptors than D2 receptors. olanzapine blocks 5HT2A, 5HT6, D1, D2, D3 and muscarinic receptors (Zhang 1999).

Why it is important to do this review

This is one of a family of related Cochrane reviews on this important compound (Table 1).

Chlorpromazine is one of two oral antipsychotic drugs on the World Health Organization's Essential Drug list (WHO 2011). It is globally accessible and has been known for its effectiveness in schizophrenia treatment since the 1950s (Adams 2014), and it is also the most commonly used and inexpensive treatment for schizophrenia (Odejide 1982). Expensive new generation drugs are heavily marketed worldwide as a better treatment for schizophrenia. However, this may not be the case and may be an unnecessary drain on very limited resources (Adams 2006). Also,

comparisons with new generation drugs, which are coming offpatent and are therefore more accessible, are important to assist informed and independent choice of treatment for people with schizophrenia.

OBJECTIVES

To compare the effects of chlorpromazine with atypical or second generation antipsychotic drugs, for treatment of people with schizophrenia (seeDifferences between protocol and review).

METHODS

Criteria for considering studies for this review

Types of studies

We included all relevant randomised controlled trials (RCTs). If a trial was described as double-blind but implied randomisation, we included such trials in a sensitivity analysis (see Sensitivity analysis). If their inclusion did not result in a substantive difference, we kept these trials in the analyses. If their inclusion resulted in statistically significant differences, we did not add the data from these lower quality studies to the results of the better trials, but presented such data within a subcategory. We excluded quasi-RCTs (e.g. allocating by alternate days of the week). Where people were given additional treatments within the chlorpromazine and atypical antipsychotic groups, we only included data if the adjunct treatment was evenly distributed between groups and only the chlorpromazine and atypical antipsychotic groups were randomised.

Types of participants

Adults (as defined in each trial) diagnosed with schizophrenia, including schizophreniform, schizoaffective and delusional disorders (any means of diagnosis, including operational criteria (DSM-IV 1994; ICD-10 1992) or clinical opinion).

We are interested in making sure that information is as relevant to the current care of people with schizophrenia as possible so if the information was reported we clearly highlighted in the Characteristics of included studies and Description of studies, the current clinical state (acute, early post - acute, partial remission, remission) as well as the stage (prodromal, first episode, early illness, persistent) and as to whether the studies primarily focused on people with particular problems (for example, negative symptoms, treatment-resistant illnesses).

Types of interventions

I. Chlorpromazine

Any dose and any route of administration.

2. Any atypical antipsychotic

Atypical antipsychotic drugs including: amisulpride, aripiprazole, asenapine (Smith 2010), clozapine, clothiapine or clotiapine (Toren 1995), iloperidone (Caccia 2010), lurasidone (Risbood 2012), mosapramine (Takahashi 1999), olanzapine, paliperidone, perospirone (Bian 2008), quetiapine, remoxipride (Nadal 2001), risperidone, sertindole (Cincotta 2010), sulpiride (Rzewuska 1988), ziprasidone and zotepine (list non-exhaustive). Any dose and any route of administration.

Types of outcome measures

If possible, we divided outcomes into short term (up to six months), medium term (seven to 12 months) and long term (over one year).

Primary outcomes

1. Clinical response

Clinically significant improvement as defined by each included trial.

2. Relapse

As defined by each trial.

Secondary outcomes

1. Death: natural death or suicide

2. Global state

- 2.1 Any change in global state.
- 2.2 Deterioration.
- 2.3 Need for additional antipsychotic drugs.
- 2.4 Need for additional benzodiazepines.
- 2.5 Poor compliance.

3. Mental state

3.1 General symptoms

3.1.1 Any change in general symptoms.3.1.2 Average endpoint general symptom score.

3.1.3 Average change in general symptom score.

3.2 Specific symptoms (positive and negative symptoms of schizophrenia, depression and mania/hypomania)

3.2.1 Any change of specific symptoms.

3.2.2 Average endpoint specific symptom score.

3.2.3 Average change specific symptom score.

4. Service involvement

- 4.1 Duration of hospital stay.
- 4.2 Re-hospitalisation.
- 4.3 Engagement with community services.
- 4.4 Engagement with inpatient/outpatient services.

5. Functioning

5.1 General functioning

5.1.1 Any change in general functioning.

- 5.1.2 Average endpoint score in general functioning.
- 5.1.3 Average change score in general functioning.

5.2 Social functioning

5.1.1 Any change in social functioning.

5.1.2 Average endpoint score in social functioning.

5.1.3 Average change score in social functioning

5.3 Employment status

5.1.1 Any change in employment status.5.1.2 Average endpoint score in employment functioning.5.1.3 Average change score in employment functioning.

6. Behaviour

6.1 General behaviour.

6.2 Any improvement in behaviour, as defined in each trial.6.3 Specific behaviour (e.g. agitation, aggression, violent incidents).

- 6.4 Average endpoint in behaviour scores.
- 6.5 Average change in behaviour scores.

7. Adverse effects

- 7.1 Anticholinergic.
- 7.2 Cardiovascular.
- 7.3 Central nervous system.
- 7.4 Gastrointestinal.

7.5 Endocrine (e.g. amenorrhoea, galactorrhoea, hyperlipidaemia, hyperglycaemia, hyperinsulinemia).

7.6 Haematology (e.g. haemogram, leukopenia, agranulocytosis/ neutropenia).

7.7 Hepatitic (e.g. abnormal transaminase, abnormal liver function).

7.8 Metabolic.

- 7.9 Movement disorders.
- 7.10 Various other.

8. Satisfaction

- 8.1 Patient satisfaction.
- 8.2 Carer satisfaction.
- 8.3 Professional satisfaction (managers/doctors/nurses).

9. Economic outcomes

- 9.1 Direct costs, as defined in each study.
- 9.2 Indirect costs, as defined in each study.
- 9.3 Cost-effectiveness, as defined in each study.

10. Quality of life

- 10.1 Average endpoint score in quality of life.
- 10.2 Average change score in quality of life.
- 10.3 Any improvement in quality of life.

11. Leaving the study early

'Summary of findings' tables

We used the GRADE approach to interpret findings (Schünemann 2008) and used GRADE profiler (GRADEPRO) to import data from RevMan 5 (Teview Manager) 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 aimed to select the following main outcomes for inclusion in the 'Summary of findings' tables:

- Clinical response: clinically significant improvement (as defined by each of the studies) by medium term.
 - Relapse (as defined by each of the studies) by medium term.
- Mental state: average endpoint score (Brief Psychiatric Rating Scale (BPRS)) by medium term.

• Adverse effects: extrapyramidal side effects: reported by the number participants by medium term.

• Quality of life: improvement as defined by each of the study by medium term.

• Participants leaving the study early by medium term.

• Economic outcomes: cost effectiveness (as defined in each study) by long term.

Search methods for identification of studies

Electronic searches

I. Cochrane Schizophrenia Group Trials Register

We searched the Cochrane Schizophrenia Group's Trials Register up to 23 September 2013 using the phrase:

[((*chlorpromazine* AND (*amisulprid* or *aripiprazol* or *clozapin* or *olanzapin* or *quetiapin* or *risperidon* or *sertindol* or *ziprasidon* or *zotepin* or *sulpiride* or *remoxipride* or *paliperidone* or *perospirone* or asenapine or clothiapine or clotiapine or iloperidone or lurasidone or mosapramine or ((Atypical or (Second NEXT generation)) and antipsychotic*))) in title, abstract or index terms of REFERENCE or interventions of STUDY)]

The Cochrane Schizophrenia Group's Trials Register is compiled by systematic searches of major databases, handsearches and conference proceedings (see Group Module).

The seatch strategy was changed after protocol publication and we added new search terms to the strategy. The search strategy in protocol step is in Appendix 1.

Searching other resources

I. Reference searching

We inspected references of all included trials for further relevant studies published in any language.

2. Personal contact

If necessary we contacted the first author, relevant pharmaceutical companies, and drug approval agencies of trials for additional information.

Data collection and analysis

Selection of studies

Two review authors (BL and SZ) independently inspected citations from the searches and identified relevant abstracts. JX independently re-inspected a random 20% sample to ensure reliability. Where disputes arose, the full report was acquired for more detailed scrutiny. BL obtained and inspected full reports of the abstracts meeting the review criteria and JX re-inspected a random 20% of these reports in order to ensure reliable selection. Where it was not possible to resolve disagreement by discussion, we attempted to contact the authors of the study for clarification.

Data extraction and management

I. Extraction

Two review authors (BL and SZ) extracted data from all included trials. To ensure reliability of data extraction, JX independently extracted data from a random sample of these studies, comprising 10% of the total. We discussed and documented any disagreements. Another review author (SS) helped to clarify any remaining issues and we documented these final decisions. If possible, we extracted data presented only in graphs and figures, but only included this data if two review authors independently had the same result. If necessary, we attempted to contact the trial authors through an open-ended request in order to obtain missing information or for clarification whenever necessary.

2. Management

2.1 Forms

We extracted data onto standard, pre-designed simple forms.

2.2 Scale-derived data

We included continuous data from rating scales only if:

• The psychometric properties of the measuring instrument had been described in a peer-reviewed journal (Marshall 2000); and

• The measuring instrument had 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 noted in the 'Description of studies' if this was the case or not.

2.3 Endpoint versus change data

There are advantages to both endpoint and change data. Change data can remove a component of between person variability from the analysis. However, calculation of change requires two assessments (baseline and endpoint), which can be difficult in unstable and difficult to measure conditions, such as schizophrenia.

We decided to primarily use endpoint data, and only use change data if the former were unavailable. We combined endpoint and change data in the analysis as we preferred to use MD rather than standardised mean difference (SMD) values throughout (Higgins 2011).

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 applied the following standards to all data before inclusion:

For change data:

We entered change data, as 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 presented and entered change data into statistical analyses.

For endpoint data:

a) When a scale started from the finite number 0, we subtracted the lowest possible value from the mean, and divided this by the SD. If this value was < 1, it strongly suggested a skew, and we excluded the study. If this ratio was higher than 1 but below 2, there was suggestion of skew. We entered the study and tested whether its inclusion or exclusion would change the results substantially. Finally, if the ratio was > 2, we included the study because skew was less likely (Altman 1996; Higgins 2011).

b) If a scale started from a positive value (such as the Positive and Negative Syndrome Scale (PANSS), which can have values from 30 to 210) (Kay 1986), we modified the calculation described above to take into account the scale starting point. In such cases skew was present if $2 \text{ SD} > (S - S_{min})$, where S is the mean score and S_{min} is the minimum score.

(Please note, irrespective of the above rules, we entered endpoint data from studies of at least 200 participants in the analysis because skewed data pose less of a problem in large studies).

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). However, we did not identify such data.

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 BPRS (Overall 1962) or the PANSS (Kay 1986), this could be considered a clinically significant response (Leucht 2005a; Leucht 2005b).

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 indicates a favourable outcome for chlorpromazine. Where keeping to this made it impossible to avoid outcome titles with clumsy double-negatives (e.g. 'not unimproved') we reported data where the left of the line indicates an unfavourable outcome. We have noted this in the relevant graphs.

Assessment of risk of bias in included studies

Two review authors (BL and SZ) independently assessed the risk of bias of included trials by using criteria described in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). This set of criteria is based on evidence of association 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.

If the two review authors disagreed, we made the final rating by consensus, with the involvement of another review author from the team. Where inadequate details of randomisation and other characteristics of trials were provided, we contacted trial authors for further information. We reported non-concurrence in quality assessment, but if disputes arose as to which category a trial was to be allocated, again, we resolved this by discussion.

We described the results of the 'Risk of bias' assessments in both the review text and in the 'Summary of findings' tables.

Measures of treatment effect

I. 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 (ORs) and that ORs tend to be interpreted as RRs by clinicians (Decks 2000). The number needed to treat for an additional beneficial outcome (NNTB)/number needed to treat for an additional harmful outcome (NNTH) statistic with its CIs 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' table(s), where possible, we calculated illustrative comparative risks.

2. Continuous data

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

Unit of analysis issues

I. Cluster trials

Studies increasingly employ 'cluster randomisation' (such as randomisation by clinician or practice) but analysis and pooling of clustered data poses problems. Firstly, study 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). We did not identify any cluster-randomised studies. However, if we identify such studies in future updates of this Cochrane review where clustering is not accounted for in primary studies, we will present data in a table, with an asterisk (*) to indicate the presence of a probable unit of analysis error. In updates of this review we will try to contact first authors of such studies to obtain intraclass correlation coefficients (ICCs) for their clustered data and to adjust for this by using accepted methods (Gulliford 1999).

Where clustering was incorporated into the analysis of primary studies, we presented these data as if from a non-cluster randomised study, but adjusted for the clustering effect.

We received statistical advice that binary data 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)*ICC] (Donner 2002). If the ICC was not reported, we assumed it was 0.1 (Ukoumunne 1999).

Where cluster studies had been appropriately analysed taking into account ICCs and relevant data documented in the report, synthesis with other studies was 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, we planned to only use data from the first phase of cross-over studies. However, we did not identify any cross-over trials for inclusion in this review.

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 within the two-by-two table. If data were continuous, we had planned to combine data following the formula in Section 7.7.3.8 (Combining groups) of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011a). Where the additional treatment arms were irrelevant, we did not reproduce these data.

Dealing with missing data

I. Overall loss of credibility

At some degree of loss of follow-up, data must lose credibility (Xia 2009). We chose that, for any particular outcome, should more than 50% of data be unaccounted for, we would not reproduce these data or use them within analyses. If more than 50% of those in one arm of a study were lost but the total loss was less than 50%, we addressed this within the 'Summary of findings' table(s) by downgrading the quality of the evidence. We also downgraded the quality of the evidence within the 'Summary of findings' table(s) where loss was 25% to 50% in total.

2. Binary

In the case where attrition for a binary outcome was between 0% and 50% and where these data were not clearly described, we presented these data on a 'once-randomised-always-analyse' basis (an intention-to-treat (ITT) analysis). We assumed all those leaving the study early to have the same rates of negative outcome as those who completed, with the exception of the outcome of death and adverse effects. For these outcomes, we used the rate of those who stayed in the study in that particular arm of the trial for those who did not. We undertook a sensitivity analysis to test how prone the primary outcomes were to change when 'completer' data only were compared to the ITT analysis using the above assumptions.

3. Continuous

3.1 Attrition

In cases where attrition for a continuous outcome was between 0% and 50% and completer-only data was reported, we reproduced these.

3.2 Standard deviations

If SD values were not reported, we first tried to obtain the missing values from the trial authors. If unavailable, where there were missing measures of variance for continuous data, but an exact standard error (SE) and CIs available for group means, and either 'P' value or 't' value available for differences in mean, we calculated them according to the Cochrane Handbook for Systematic Reviews of Interventions (Higgins 2011): when only the standard error (SE) is reported, SDs are calculated by the formula SD = SE * square root (n). Chapters 7.7.3 and 16.1.3 of the Cochrane Handbook for Systematic Reviews of Interventions (Higgins 2011a; Higgins 2011b) present detailed formulae for estimating SDs from P values, t or F values, CIs, ranges or other statistics. If these formula did not apply, we 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 did not impute any continuous data in this review.

3.3 Last observation carried forward

We anticipated that in some studies would employ the method of last observation carried forward (LOCF) 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). Therefore, where LOCF data were used in the trial, if less than 50% of the data had been assumed, we reproduced these data and indicated that they were the product of LOCF assumptions.

Assessment of heterogeneity

I. 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 and discussed these.

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, and discussed.

3. Statistical heterogeneity

3.1 Visual inspection

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

3.2 Employing the I² statistic

We investigated heterogeneity between studies by considering the I² statistic alongside the Chi² test P value. The I² statistic provides an estimate of the percentage of inconsistency thought to be due to chance (Higgins 2003). The importance of the observed I² statistic value depends on: i. magnitude and direction of effects; and ii. strength of evidence for heterogeneity (e.g. P value from the Chi² test, or a CI for I² statistic). We interpreted an I² statistic estimate \geq around 50% accompanied by a statistically significant Chi² test as evidence of substantial levels of heterogeneity (Section 9.5.2 - Deeks 2011). When we found substantial levels of heterogeneity in the primary outcome, we explored reasons for heterogeneity (Subgroup analysis and investigation of heterogeneity).

Assessment of reporting biases

I. Protocol versus full study

Reporting biases arise when the dissemination of research findings is influenced by the nature and direction of results. These are described in Section 10.1 (Sterne 2011). We tried to locate protocols of included RCTs. If the protocol was available, we compared outcomes in the protocol and in the published report. If the protocol was unavailable, we compared outcomes listed in the methods section of the trial report with actually reported results.

2. Funnel plot

Reporting biases arise when the dissemination of research findings is influenced by the nature and direction of results (Egger 1997). These are again described in Section 10 of the *Cochrane Handbook for Systematic Reviews of Interventions* (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 are 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. However, there is 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. We used the random-effects model for all analyses.

Subgroup analysis and investigation of heterogeneity

I. Subgroup analyses

1.1 Primary outcomes

We did not anticipate any subgroup analyses.

1.2 Clinical state, stage or problem

We proposed to provide an overview of the effects of chlorpromazine versus atypical antipsychotic drugs for people with schizophrenia in general in this Cochrane review. In addition, we tried to report data on subgroups of people in the same clinical state, stage and with similar problems.

2. Investigation of heterogeneity

We reported if inconsistency in trial results was high. 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 Cochrane 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 presented these data. If not, we did not pool these data and discussed any issues. We know of no supporting research for this 10% cut-off but are investigating use of prediction intervals as an alternative to this unsatisfactory state. If we observed obvious unanticipated clinical or methodological heterogeneity, we simply stated hypotheses regarding these for future reviews or versions of this Cochrane review. We did not anticipate undertaking analyses relating to these.

Sensitivity analysis

I. Implication of randomisation

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

2. Assumptions for lost binary data

Where assumptions have 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 assumption compared with completer data only. 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 on primary outcomes when we used our assumption compared with completer data only. We performed a sensitivity analysis testing how prone results were to change when 'completer' 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 we judged to be at 'high' risk of bias across one or more of the domains of randomisation (implied as randomised with no further detail 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 had also 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-RCTs. However, we did not impute any values in this Cochrane review.

5. Fixed-effect and random-effects

We synthesised all data using a random-effects model. However, we also synthesised data for the primary outcome using a fixedeffect model to evaluate whether this altered the significance of the results.

RESULTS

Description of studies

Results of the search

We identified 444 references following our literature search, of which we excluded 298 after screening by title/abstract. For this

Cochrane review with the three comparisons of olanzapine, risperidone and quetiapine, we obtained and scrutinised 146 full-text articles. Of these, 42 articles did not meet the inclusion criteria (see Characteristics of excluded studies) and were excluded. We included 71 trials (Figure 1). In the same literature search, we identified 33 more studies comparing chlorpromazine to atypical antipsychotics, including aripiprazole, clotiapine, clozapine, iloperidone, remoxipride, sulpiride, ziprasidone and zotepine. We will include all of these comparisons in a future update of this Cochrane review.

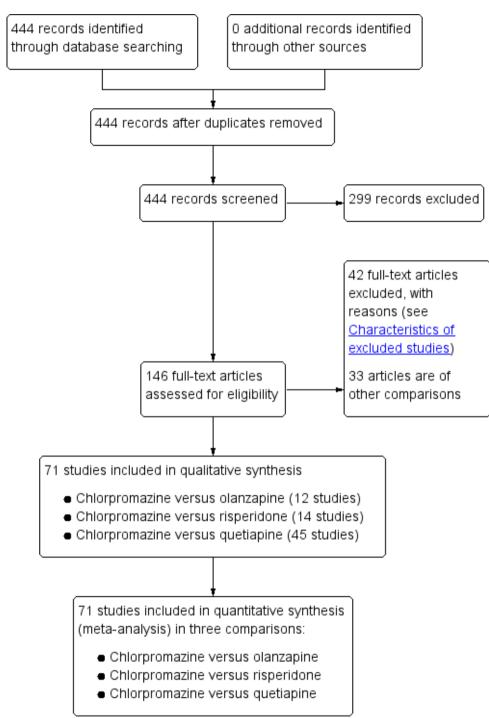


Figure I. Study flow diagram.

Included studies

I. Chlorpromazine versus olanzapine

For this comparison, we included 12 studies (total N = 919; chlorpromazine N = 432 and olanzapine N = 487).

1. Trial length

Most included studies were eight weeks in duration (vs OLZ -Chang 2003; vs OLZ - Chen 2006; vs OLZ - He 2003; vs OLZ -Luo 2007; vs OLZ - Wang 2002; vs OLZ - Wang 2008; vs OLZ -Zhao 2006), with three studies at six weeks in duration (HGCQ (Turkey) 2000; HGDV (Morocco) 1999; vs OLZ - Loza 1999 (HGDT)). The final two studies were 12 weeks (vs OLZ - Wu 2008) and two years (vs OLZ - An 2006) in duration. Therefore most included studies provided data for our short term outcome, with only one study providing any data for the long term.

2. Design

All included studies were parallel arm RCTs. Four out of the 12 studies provided information as to randomisation methods, which included methods such as computer-generated randomisation and random number tables (HGCQ (Turkey) 2000; HGDV (Morocco) 1999; vs OLZ - Chang 2003; vs OLZ - Luo 2007).

3. Participants

All included participants had a diagnosis of schizophrenia; diagnostic criteria used included DSM-IV (HGCQ (Turkey) 2000; HGDV (Morocco) 1999; vs OLZ - Loza 1999 (HGDT)) and CCMD (vs OLZ - An 2006; vs OLZ - Wang 2008; vs OLZ - Wu 2008; vs OLZ - Zhao 2006). Diagnostic criteria were unclear in the remaining studies, with participants described either as having 'schizophrenia' (vs OLZ - Chang 2003; vs OLZ - Chen 2006; vs OLZ - He 2003) or 'first-episode schizophrenia (vs OLZ - Luo 2007; vs OLZ - Wang 2002).

4. Setting

Nine of the included studies were undertaken in China, and included both inpatient and outpatient settings. Other studies were completed in Turkey (HGCQ (Turkey) 2000), Morocco (HGDV (Morocco) 1999) and Egypt (vs OLZ - Loza 1999 (HGDT)).

5. Study size

Study sizes ranged from 30 (HGCQ (Turkey) 2000) to 100 participants (vs OLZ - Wu 2008); and the mean sample size was 77 participants.

6. Interventions

6.1 Chlorpromazine

Chlorpromazine doses ranged from 25 to 600 mg/day (vs OLZ - Wang 2002) to 200 to 800 mg/day (HGCQ (Turkey) 2000; HGDV (Morocco) 1999; vs OLZ - Chen 2006; vs OLZ - Loza 1999 (HGDT)). Doses tended to be fairy consistent between studies.

6.2 Olanzapine

Olanzapine doses between studies were largely uniform, with a range in 10 of the included studies of 5 mg/day to 20 mg/day, and in vs OLZ - Luo 2007 the range was 5 mg/day to 25 mg/day, with vs OLZ - Wang 2008 using a range of 5 mg/day to 15 mg/day.

7. Outcomes

7.1 General remarks

The included studies for this comparison provided generally wellreported outcomes, including clinical response, global state outcomes, relapse rates and adverse events. Death was not reported in any of the included studies for any reason.

7.2 Acceptability and efficacy

Each included study provided data regarding mental and global state outcomes (widely accepted rating scales, including the BPRS, PANSS and CGI). However, some of these data were skewed and were presented in an additional table.

7.3 Adverse events

Adverse events, including extrapyramidal averse effects, anticholinergic effect, cardiovascular effects, gastrointestinal effects and 'others' were generally well-reported in the included studies.

7.4 Outcome scales

7.4.1 Global state

i) Clinical Global Impression (CGI)

This is a rating instrument that enables clinicians to quantify severity of illness and overall clinical improvement during therapy (Guy 1976). A 7-point scoring system is usually used, with low scores indicating decreased severity or greater recovery, or both.

7.4.2 Mental state

i) Brief Psychiatric Rating Scale (BPRS)

This scale is used to assess the severity of abnormal mental states (Overall 1962). The original scale has 16 items, but a revised 18item scale is commonly used. Each item is defined on a seven-point scale varying from 'not present' to 'extremely severe', scoring from zero to six or one to seven. Scores can range from 0 to 108 or 18 to 126, respectively. High scores indicate more severe symptoms. The BPRS-positive cluster comprises four items, which are conceptual disorganisation, suspiciousness, hallucinatory behaviour and unusual thought content. The BPRS-negative cluster comprises only three items, which are emotional withdrawal, motor retardation and blunted affect.

ii) Hamilton Anxiety Scale (HAMA)

HAMA is a rating scale developed to quantify the severity of anxiety symptomatology and consists of 14 items, each defined by a series of symptoms (Maier 1988). Each item is rated on a 5-point scale, ranging from zero (not present) to four (severe).

iii) Montgomery-Åsberg Depression Rating Scale (MADRS)

The MADRS is a 10- item clinician-administered diagnostic questionnaire used to measure the severity of depressive episodes (Montgomery 1979). There are 10 items (including apparent sadness, reported sadness, inner tension, reduced sleep, reduced appetite, concentration difficulties, lassitude, inability to feel, pessimistic thoughts and suicidal thoughts), each rated zero (absent) to six (severe). Overall scores range from zero to 60.

iv) Nurses' Observation Scale for Inpatient Evaluation (NOSIE)

This scale assesses the behaviour of patients on an inpatient unit (Honigfeld 1965). The scale has 30 items, each rated from zero (not present) to four (markedly present), and includes such behaviours as 'gets angry or annoyed easily', 'cries' or 'is impatient'.

iv) Positive and Negative Syndrome Scale (PANSS)

The PANSS was originated as a method for evaluating positive, negative and other symptom dimensions in schizophrenia (Kay 1987). The scale has 30 items, and each item can be rated on a 7-point scoring system varying from one (absent) to seven (extreme). This scale can be divided into three subscales for measuring the severity of general psychopathology, positive symptoms (PANSS-P) and negative symptoms (PANSS-N). A low score indicates low levels of symptoms.

v) Scale for Assessment of Positive Symptoms (SAPS)

This scale measures the positive symptoms of schizophrenia and is split into four items including hallucinations, delusions, bizarre behaviour and positive formal thought disorder, each rated on a scale of zero (absent) to five (severe) (Andreasen 1984).

7.4.3 Functioning

i) Wisconsin Card Sorting Test (WCST-IQ/MQ)

The WCST is a neuropsychological test in which participants are expected to organise a set of specifically-designed cards, without instruction (Monchi 2001). The test is a measure of executive functioning, assessing primarily strategic planning, organized searching, utilizing environmental feedback to shift cognitive sets, directing behavior toward achieving a goal, and modulating impulsive responding.

7.4.4 Adverse events

i) Extrapyramidal Symptom Rating Scale (ESRS)

The ESRS is a physical examination with 12 items that include both subjective and objective assessments (Chouinard 1980).

iii) Leeds Sleep Evaluation Questionnaire (LSEQ)

The LSEQ is a 10-item, self-rating measurement designed to assess changes in sleep quality over the course of psychopharmacological treatment (Parrott 1980). Four domains are rated, including 'ease of initiating sleep', 'quality of sleep', 'ease of waking' and 'behaviour following wakefulness'.

7.4.5 Quality of life

i) Gothenburg Quality of Life Instrument (GQOLI/ GQOL1 - 74) This scale assesses overall sleep quality; participants respond on a 7point Linkert-type scale with one (excellent) and seven (very poor) (Sullivan 1993). Participants also rate other aspects of quality of life, including a self-evaluation of their economic situation, social and friendship situation and home/family situation.

ii) Quality of life scale (QoL)

The QoL scale is a 16-item instrument that measures six conceptual domains of quality of life: material and physical well-being, relationships with other people, social, community and civic activities, personal development and fulfilment, recreation and independence (Flanagan 1982). Scores range from 16 to 112, with a higher score indicating a better outcome.

7.5 Missing outcomes

Studies did not provide vast amounts of data, nor even measured in many instances, outcomes including service involvement, functioning, behaviour, satisfaction with treatment, or economic outcomes.

2. Chlorpromazine versus risperidone

For this comparison, we included 14 studies, with a total of 991 participants (chlorpromazine N = 474; risperidone N = 517).

1. Trial length

Duration of included studies ranged from three weeks (vs RPD -Liu 2005) to five months (vs RPD - Chang 1998). The average length of studies was around eight weeks, therefore all included studies provided only short term data.

2. Design

All included studies were parallel-arm RCTs. No included study adequately described randomisation methods.

3. Participants

All participants were diagnosed with schizophrenia according to Chinese Classification of Mental Disorders (CCMD) criteria (Chen 2002).

4. Setting

All included studies were undertaken in China with inpatient and outpatient settings both represented.

5. Study size

Sample sizes between studies ranged from 32 (vs RPD - Liu 2000) to 107 participants (vs RPD - Luo 2001), with a mean sample size of 70 participants.

6. Interventions

6.1 Chlorpromazine

All studies used different dosage ranges, and included 25 to 450 mg/day (vs RPD - Wang 2005); 100 to 450 mg/day (vs RPD - Lin 2005); 300/400 to 600 mg/day (vs RPD - Wu 2002; vs RPD - Wu 2004); and 100 to 700 mg/day (vs RPD - Luo 2001). Not all studies reported mean doses, with only vs RPD - Cui 2001 and vs RPD - Feng 2003 using a mean dose of 426 mg/day and 355 mg/day respectively.

6.2 Risperidone

Risperidone doses also varied between studies, with the highest range of 1 mg/day to 9 mg/day used in vs RPD - Ma 2004; most included studies used a range of risperidone up to 6 mg/day (vs RPD - Chang 1998; vs RPD - He 1999; vs RPD - Wang 2005; vs RPD - Wu 2002; vs RPD - Wu 2004; vs RPD - Zheng 2001). Again, only two studies described the mean doses used in the studies (vs RPD - Cui 2001; vs RPD - Feng 2003) of 4.19 mg/ day and 3.62 mg/day respectively.

7. Outcomes

7.1 General remarks

The included studies for this comparison provided generally wellreported outcomes, including clinical response, global state outcomes and adverse events. Death was not reported in any of the included studies for any reason.

7.2 Acceptability and efficacy

Data regarding mental and global state outcomes were measured using widely accepted rating scales, including the BPRS, PANSS and CGI. However some of these data were skewed and were presented in an additional table.

7.3 Adverse events

Adverse events, including extrapyramidal averse effects, anticholinergic effect, cardiovascular effects, gastrointestinal effects and 'others' were generally well reported in the included studies.

7.4 Outcome scales presenting useable data

7.4.1 Global state

i) Clinical Global Impression (CGI)

This is a rating instrument that enables clinicians to quantify severity of illness and overall clinical improvement during therapy (Guy 1976). A 7-point scoring system is usually used with low scores indicating decreased severity or greater recovery, or both.

7.4.2 Mental state

i) Brief Psychiatric Rating Scale (BPRS)

This scale is used to assess the severity of abnormal mental states (Overall 1962). The original scale has 16 items, but a revised 18item scale is commonly used. Each item is defined on a 7-point scale varying from 'not present' to 'extremely severe', scoring from zero to six or one to seven. Scores can range from zero to 108 or 18 to 126, respectively. High scores indicate more severe symptoms. The BPRS-positive cluster comprises four items, which are conceptual disorganisation, suspiciousness, hallucinatory behaviour and unusual thought content. The BPRS-negative cluster comprises only three items, which are emotional withdrawal, motor retardation and blunted affect.

ii) Positive and Negative Syndrome Scale (PANSS)

The PANSS was originated as a method for evaluating positive, negative and other symptom dimensions in schizophrenia (Kay 1987). The scale has 30 items, and each item can be rated on a 7-point scoring system varying from one (absent) to seven (extreme). This scale can be divided into three subscales for measuring the severity of general psychopathology, positive symptoms (PANSS-P) and negative symptoms (PANSS-N). A low score indicates low levels of symptoms.

iii) Scale for Assessment of Negative Symptoms (SANS)

The SANS measures the incidence and severity of negative symptoms using a 25-item scale, using a six-point scoring system, of zero (= better) to five (= worse), where a higher score equals a more severe experience of negative symptoms (Andreasen 1982). *iv) Scale for Assessment of Positive Symptoms (SAPS)*

This scale measures the positive symptoms of schizophrenia and is split into four items including hallucinations, delusions, bizarre behaviour and positive formal thought disorder, each rated on a scale of zero (absent) to five (severe) (Andreasen 1984).

7.4.3 Functioning

i) Wisconsin Card Sorting Test (WCST-IQ/MQ)

The WCST is a neuropsychological test in which participants are expected to organise a set of specifically-designed cards, without instruction (Monchi 2001). The test is a measure of executive functioning, assessing primarily strategic planning, organized searching, utilizing environmental feedback to shift cognitive sets, directing behavior toward achieving a goal, and modulating impulsive responding.

7.4.4 Adverse events

i) Treatment-Emergent Signs and Symptoms (TESS)

The ICH E3 1995 guideline has stated that 'treatment-emergent signs and symptoms' (TESS) are to be defined as "events not seen at baseline and events that worsened even if present at baseline". It can be difficult to document this accurately taking into account

variables in time, dosage, adverse events and severity. Generally, TESS scores for particular adverse events are categorised as 'mild', 'moderate' or 'severe', with an appropriate action taken (e.g. none, discontinued, dose changed', hospitalisation and additional medication given). It is not often that studies publish continuous data from these measurements, with the more common presentation of dichotomised TESS ratings.

7.4.5 Quality of life

i) Quality of life scale (QoL)

The QoL scale is a 16-item instrument that measures six conceptual domains of quality of life: material and physical well-being; relationships with other people; social, community and civic activities; personal development and fulfilment; recreation and independence (Flanagan 1982). Scores range from 16 to 112, with a higher score indicating a better outcome.

7.5 Missing outcomes

Studies did not report any data for relapse rates, service use, behaviour, satisfaction with care or treatment, or economic outcomes.

3. Chlorpromazine versus quetiapine

For this comparison, we included 45 studies with a total of 4388 participants (chlorpromazine N = 2183; quetiapine N = 2205).

1. Trial length

Thirty-seven of the 45 studies were under eight weeks in length. The shortest study was 42 days in length (vs QTP - Peng 2006). The longest study was six months long (vs QTP - Li 2003) and was the only study to provide data at the medium term. All other outcomes were reported at short term (< six months).

2. Design

All included studies were parallel-arm RCTs. No included study adequately described randomisation methods.

3. Participants

All participants had a diagnosis of schizophrenia, with diagnosis using the Chinese Classification of Mental Disorders (CCMD) employed in 42 included studies. Two studies used DSM criteria to diagnose schizophrenia (vs QTP - Hu 2003; vs QTP - Peuskens 1997), and one study used a combination of CCMD and ICD-10 criteria (vs QTP - Zhou 2004).

4. Setting

All included studies were undertaken in China with both inpatient and outpatient settings represented.

5. Study size

Sample sizes between studies ranged from 30 (vs QTP - Kong 2003) to 237 participants (vs QTP - Zhang 2003).

6. Interventions

6.1 Chlorpromazine

The most common dose range between groups was between 300 to 600 mg/day. Only one study stated dosages used were 'less than 1000 mg/day' (vs QTP - Guo 2008), with other maximum doses stated as 750 mg/day (vs QTP - Peuskens 1997).

6.2 Quetiapine

Quetiapine doses were mostly between 300 and 700 mg/day. One study did not state the dosages used in either group (vs QTP - Zhou 2003).

7. Outcomes

7.1 General remarks

The included studies for this comparison generally provided wellreported outcomes, including clinical response, global state outcomes and adverse events. Death was not reported in any of the included studies for any reason. Most outcomes were reported using measurement scales, although we ensured they had been peerreviewed as the lack of dichotomous outcomes makes valuable interpretation of these results difficult.

7.2 Acceptability and efficacy

Data regarding mental and global state outcomes were reported using widely accepted rating scales, including the BPRS, PANSS and CGI. However some of these data were skewed and were presented in an additional table.

7.3 Adverse events

Adverse events, including extrapyramidal averse effects, anticholinergic effect, cardiovascular effects, gastrointestinal effects and 'others' were generally well reported in the included studies.

7.4 Outcome scales

7.4.1 Global state

i) Clinical Global Impression (CGI)

This is a rating instrument that enables clinicians to quantify severity of illness and overall clinical improvement during therapy (Guy 1976). A 7-point scoring system is usually used with low scores indicating decreased severity or greater recovery, or both.

7.4.2 Mental state

i) Brief Psychiatric Rating Scale (BPRS)

This scale is used to assess the severity of abnormal mental states (Overall 1962). The original scale has 16 items, but a revised 18item scale is commonly used. Each item is defined on a 7-point scale varying from 'not present' to 'extremely severe', scoring from zero to six or one to seven. Scores can range from zero to 108 or 18 to 126, respectively. High scores indicate more severe symptoms. The BPRS-positive cluster comprises four items, which are conceptual disorganisation, suspiciousness, hallucinatory behaviour and unusual thought content. The BPRS-negative cluster comprises only three items, which are emotional withdrawal, motor retardation and blunted affect.

ii) Hamilton Rating Scale for Depression (HAMD)

The HAMD rates severity of depression in adults including items of mood, feelings of guilt, suicide ideation, insomnia, agitation or retardation, anxiety, weight loss and somatic symptoms (Hamilton 1960). There are 20 items rated on a Linket-type scale, where zero equals an absence of symptoms and a higher score indicates a worse outcome.

iii) Positive and Negative Syndrome Scale (PANSS)

The PANSS was originated as a method for evaluating positive, negative and other symptom dimensions in schizophrenia (Kay 1987). The scale has 30 items, and each item can be rated on a 7-point scoring system varying from one (absent) to seven (extreme). This scale can be divided into three subscales for measuring the severity of general psychopathology, positive symptoms (PANSS-P) and negative symptoms (PANSS-N). A low score indicates low levels of symptoms.

7.4.3 Functioning

i) Wisconsin Card Sorting Test (WCST-IQ/MQ)

The WCST is a neuropsychological test in which participants are expected to organise a set of specifically-designed cards, without instruction (Monchi 2001). The test is a measure of executive functioning, assessing primarily strategic planning, organized searching, utilizing environmental feedback to shift cognitive sets, directing behaviour toward achieving a goal and modulating impulsive responding.

ii) Wechsler Memory Scale-revised (WMS-RC)

The WMS-RC is a neuropsychological test that is used to measure a person's memory functions (WMS-IV 2009). The scale consists of seven subtests: spatial addition, symbol span, design memory, general cognitive screener, logical memory, verbal paired associates and visual reproduction. A high score indicates a better outcome.

7.4.4 Adverse events

i) Treatment-Emergent Signs and Symptoms (TESS)

The ICH E3 1995 guideline has stated that 'treatment-emergent signs and symptoms' (TESS) are to be defined as "events not seen at baseline and events that worsened even if present at baseline". It can be difficult to document this accurately taking into account variables in time, dosage, adverse events and severity. Generally, TESS scores for particular adverse events are categorised as 'mild', 'moderate' or 'severe', with an appropriate action taken (e.g. none, discontinued, dose changed' hospitalisation, and additional medication given). It is not often that studies publish continuous data from these measurements, with the more common presentation of dichotomised TESS ratings.

7.4.5 Quality of life

i) Gothenburg Quality of Life Instrument (GQOLI/ GQOL1-74) This scale assesses overall sleep quality; participants respond on a 7-point Linkert-type scale ranging from one('excellent') and seven ('very poor') (Sullivan 1993). Participants also rate other aspects of quality of life, including a self-evaluation of their economic situation, social and friendship situation and home/family situation.

7.5 Missing outcomes

Excluded studies

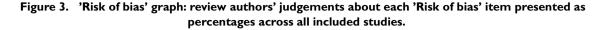
We excluded 42 studies; for details please consult the Characteristics of excluded studies section,

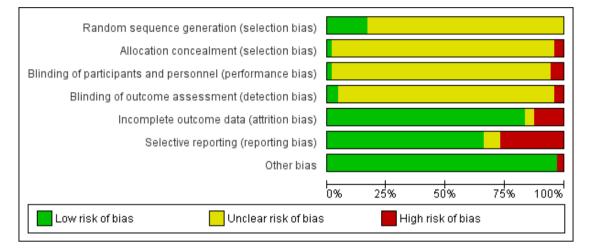
Risk of bias in included studies

For a graphical overview, please see Figure 2 and Figure 3.

Figure 2. 'Risk of bias' summary: review authors' judgements about each 'Risk of bias' item for each included study.







Allocation

I. Chlorpromazine versus olanzapine

Only four included studies provided adequate information regarding randomisation, which included methods such as a computergenerated randomisation and random number tables (HGCQ (Turkey) 2000; HGDV (Morocco) 1999; vs OLZ - Chang 2003; vs OLZ - Luo 2007). We judged each of these studies as at 'low' risk of bias. The remaining studies in this comparison were rated as at 'unclear' risk of bias, as 'randomisation' or 'random allocated' was stated, however no description was provided. However, three studies were rated as a 'high' risk of bias due to the lack of allocation concealment (HGCQ (Turkey) 2000; HGDV (Morocco) 1999; vs OLZ - Loza 1999 (HGDT)); each study stated that "the [study drug] bottles were labelled 'Olanzapine' or 'Chlorpromazine' in addition to the study number". We rated all other studies as 'unclear' for allocation bias.

2. Chlorpromazine versus risperidone

None of the included studies provided details as to randomisation methods and therefore we rated each as at 'unclear' risk of bias, since 'randomisation' or 'random allocated' was stated but no description was provided.

3. Chlorpromazine versus quetiapine

Only eight of the 45 included studies provided adequate data as to randomisation methods; five studies used a random number table (vs QTP - Chen 2001; vs QTP - Guo 2008; vs QTP - Peng 2006; vs QTP - Wang 2005; vs QTP - Zhou 2003), two studies randomised by tossing a coin (vs QTP - Guo 2003a; vs QTP - Zhang 2002) and one study randomised through computer-generated random numbers (vs QTP - Zhang 2003). We rated these studies at 'low' risk of bias, with the remaining studies rated at 'unclear' risk.

Blinding

I. Chlorpromazine versus olanzapine

We rated four studies at 'high' risk of bias for blinding and detection bias (HGCQ (Turkey) 2000; HGDV (Morocco) 1999; vs OLZ - Loza 1999 (HGDT); vs OLZ - Wang 2002). Each of these were open label studies where both participant and study investigator knew what was being given and received. All other studies were rated at 'unclear' risk of bias.

2. Chlorpromazine versus risperidone

Only two studies were rated at 'low' risk of bias for performance and detection bias in blinding (vs RPD - Cui 2001; vs RPD -

Feng 2003). Double blinding was used via, identical study drugs, dispensed by an independent pharmacist. All other studies were rated as at 'unclear' risk of bias.

3. Chlorpromazine versus quetiapine

We rated only one study as at 'low' risk of bias, since it specified assessor blinding (vs QTP - Peng 2006). All other studies were rated at 'unclear' risk of bias.

Incomplete outcome data

I. Chlorpromazine versus olanzapine

All studies apart from one were rated at 'low' risk of attrition bias either because all participants were stated to have complete the study, or those that left the study early were included in the final analysis. We rated only one study as a 'high' risk of bias because 13 and 11 people dropped out of the olanzapine and chlorpromazine groups respectively (vs OLZ - Wang 2008). These people were excluded from the final analysis and reasons for dropout were not given.

2. Chlorpromazine versus risperidone

We rated all but two studies as at 'low' risk of attrition bias either because all participants were stated to have completed the study, or those that left the study early were included in the final analysis. We rated two studies as at 'unclear' risk (vs RPD - Feng 2003; vs RPD - Wang 2005) as there were dropouts, however it was unclear whether these were included in the final analysis.

3. Chlorpromazine versus quetiapine

Thirty-seven included studies were rated as at 'low' risk of attrition bias either because all participants were stated to have complete the study, or those that left the study early were included in the final analysis. We rated eight studies as at 'high' risk of attrition bias (vs QTP - Cao 2005; vs QTP - Cheng 2003; vs QTP - Guo 2003b; vs QTP - Ji 2004; vs QTP - Li 2003; vs QTP - NCT00882518; vs QTP - Wang 2005; vs QTP - Yang 2007) either because it was unclear if these were included in the final analysis, or dropouts were excluded from the analysis.

Selective reporting

I. Chlorpromazine versus olanzapine

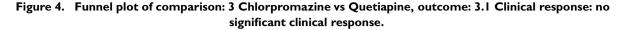
We rated five studies at 'high' risk of bias for selective reporting (HGCQ (Turkey) 2000; vs OLZ - Chang 2003; vs OLZ - Chen 2006; vs OLZ - Loza 1999 (HGDT); vs OLZ - Wang 2002) due to pre-specified outcomes in each study not being fully reported, or partially reported. One study was rated as at 'unclear' risk of bias (vs OLZ - Wu 2008) as it was not explicit whether all outcomes were reported. We rated all remaining studies as at 'low' risk of bias.

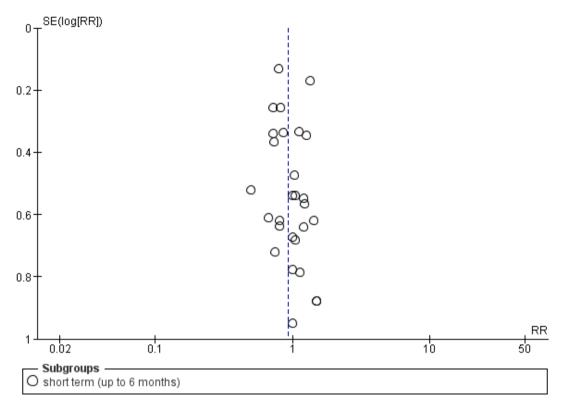
2. Chlorpromazine versus risperidone

We rated two studies as at 'high' risk of bias for selective reporting due to pre-specified outcomes in each study not being fully reported or partially reported (vs RPD - Lin 2005; vs RPD - Zheng 2001). Two studies were rated as at 'unclear' risk of bias as it was not explicit whether all outcomes were reported (vs RPD - Feng 2003; vs RPD - Liu 2000). We rated all other studies as at 'low' risk of bias.

3. Chlorpromazine versus quetiapine

Twelve studies were rated as at 'high' risk of bias for selective reporting due to pre-specified outcomes in each study not being fully reported, or partially reported (vs QTP - Ai 2007; vs QTP - Chen 2007; vs QTP - Chen 2008; vs QTP - Deng 2004; vs QTP - Guo 2007; vs QTP - Jiang 2006; vs QTP - Jiang 2008; vs QTP - Jiang 2007; vs QTP - Nai 2007; vs QTP - Wan 2002; vs QTP - Zhang 2003; vs QTP - Zou 2006). We rated one study as at 'unclear' risk of bias as it was not explicit whether all outcomes were reported (vs QTP - Liu 2003). We rated all other studies as at 'low' risk of bias. See Figure 4.





Other potential sources of bias

I. Chlorpromazine versus olanzapine

All studies were rated at 'low' risk of other potential sources of bias, since we did not detect any obvious bias.

2. Chlorpromazine versus risperidone

We rated all studies at 'low' risk of other potential sources of bias, since we did not detect any obvious bias.

3. Chlorpromazine versus quetiapine

We rated two studies at 'high' risk of bias as they were both funded by the pharmaceutical company AstraZeneca, the manufacturers of quetiapine (vs QTP - Peuskens 1997; vs QTP -NCT00882518). All remaining studies were rated at 'low' risk of other potential sources of bias, since we did not detect any obvious bias.

Effects of interventions

See: Summary of findings for the main comparison CHLORPROMAZINE versus OLANZAPINE for schizophrenia; Summary of findings 2 CHLORPROMAZINE versus RISPERIDONE for schizophrenia; Summary of findings 3 CHLORPROMAZINE versus QUETIAPINE for schizophrenia

Comparison I: CHLORPROMAZINE versus OLANZAPINE

1.1 Clinical response: 1. No significant clinical response

1.1.1 short term - up to 6 months

In this subgroup we found three relevant trials (N = 204). There was a statistically significant difference (P = 0.002) in favour of olanzapine (RR 2.34, 95% CI 1.37 to 3.99; Analysis 1.1).

1.1.2 long term - over 12 months

We only found one relevant trial in this subgroup (N = 70) (vs OLZ - An 2006). There was no significant difference between chlorpromazine and olanzapine (RR 1.83, 95% CI 0.76 to 4.41; Analysis 1.1).

1.1.3 total

Overall there was a statistically significant difference in favour of olanzapine in both short and long term (4 RCTs, N = 274; RR 2.19, 95% CI 1.39 to 3.45; P = 0.0008; Analysis 1.1)

I.2 Clinical response: 2. Average endpoint score of CGI (high = poor) - short term (up to 6 months)

In this subgroup we included three trials (N = 110). There was a statistically significant difference in favour of olanzapine (MD 0.93, 95% CI 0.36 to 1.51; P = 0.002; Analysis 1.2). This subgroup had moderate levels of heterogeneity (Chi² test = 3.9; df = 2; P = 0.142; I² statistic = 49%).

1.3 Clinical response: 3. Relapse - long term (over 12 months)

In this subgroup we only found one relevant trial (N = 70) (vs OLZ - An 2006). There was no significant difference between chlorpromazine and olanzapine (RR 1.5, 95% CI 0.46 to 4.86; Analysis 1.3).

1.4 Mental state: I. Average endpoint score of various scales (high = poor) - short term (up to 6 months)

1.4.1 BPRS total

In this subgroup we found four relevant trials (N = 245). There was no significant difference between chlorpromazine and olanzapine (MD 3.21, 95% CI -0.62 to 7.05; Analysis 1.4). This subgroup had important levels of heterogeneity (Chi² test = 23.38; df = 3; P = 0.0; I² statistic = 87%).

1.4.2 BPRS activation subscale

In this subgroup we found two relevant trials (N = 299). There was a statistically significant difference in favour of olanzapine (MD 0.47, 95% CI 0.27 to 0.67; P < 0.00001; Analysis 1.4).

1.4.3 BPRS anxiety-depression subscale

In this subgroup we only included one trial (N = 213) (vs OLZ - Wang 2008). There was a statistically significant difference in favour of olanzapine (MD 1.57, 95% CI 1.36 to 1.78; P < 0.00001; Analysis 1.4).

1.4.4 BPRS hostile-suspiciousness subscale

In this subgroup we found two relevant trials (N = 299). There was no significant difference between chlorpromazine and olanzapine (MD -0.31, 95% CI -1.98 to 1.35; Analysis 1.4). This subgroup had important levels of heterogeneity (Chi² test = 16.24; df = 1; P = 0.0; I² statistic = 94%).

1.4.5 BPRS thinking disorder subscale

We found two relevant trials in this subgroup (N = 299). There was no significant difference between chlorpromazine and olanzapine (MD -0.8, 95% CI -2.66 to 1.06; Analysis 1.4). This subgroup had important levels of heterogeneity (Chi² test = 16.59; df = 1; P = 0.0; I² statistic = 94%).

1.4.6 BPRS withdraw-retardation subscale

In this subgroup we found two relevant trials (N = 299). There was no significant difference between chlorpromazine and olanzapine (MD -0.49 95% CI -2.25 to 1.26; Analysis 1.4). This subgroup had important levels of heterogeneity (Chi² test = 53.34; df = 1; P = 0.0; I² statistic = 98%).

1.4.7 NOSIE total

We only included one trial in this subgroup (N = 213) (vs OLZ - Wang 2008). There was a statistically significant difference in favour of chlorpromazine (MD -18.36, 95% CI -22.39 to -14.33; P < 0.00001; Analysis 1.4).

1.4.8 PANSS total

In this subgroup we included six trials (N = 351). There was a statistically significant difference in favour of olanzapine (MD 10.46, 95% CI 4.49 to 16.43; P = 0.006; Analysis 1.4). This subgroup had important levels of heterogeneity (Chi² test = 15.31; df = 5; P = 0.009; I² statistic = 67%).

1.4.9 PANSS general pathology subscale

In this subgroup we only found one relevant trial (N = 100) (vs OLZ - Wu 2008). There was no significant difference between chlorpromazine and olanzapine (MD 1.31, 95% CI -0.32 to 2.94; Analysis 1.4).

1.4.10 PANSS negative symptom subscale

In this subgroup we found two relevant trials (N = 141). There was a statistically significant difference in favour of olanzapine (MD 2.38, 95% CI 0.31 to 4.45; P = 0.02; Analysis 1.4).

1.4.11 PANSS positive symptom subscale

We found two relevant trials in this subgroup (N = 161). There was no significant difference between chlorpromazine and olanzapine (MD 0.91, 95% CI -0.30 to 2.11; Analysis 1.4).

1.4.12 SAPS total

In this subgroup we only found one relevant trial (n = 86) (vs OLZ - Chen 2006). There was no significant difference between chlorpromazine and olanzapine (MD -2.1, 95% CI -4.53 to 0.33; Analysis 1.4).

1.5 Mental state: 3. Average endpoint score (BPRS, high = poor) - medium term (7 - 12 months)

In this subgroup we only found one relevant trial (N = 60) (vs OLZ - Wang 2002). There was a statistically significant difference in favour of olanzapine (MD 8.60, 95% CI 5.94 to 11.26; P < 0.00001; Analysis 1.5).

1.6 Mental state: 2. Average endpoint score of various scales (high = poor) - skewed data

Data using the various mental state scales, including the BPRS, PANSS, MADRS and HAMA, were skewed and are best inspected by viewing (Analysis 1.6).

1.7 Service involvement: 1. Re-hospitalisation

1.7.1 long term (over 12 months)

We found only one trial in this subgroup (N = 70) (vs OLZ - An 2006). There was no significant difference between chlorpromazine and olanzapine (RR 1.50, 95% CI 0.46 to 4.86; Analysis 1.7).

1.8 Functioning: 1. Executive function - average endpoint score (WCST, high = poor)

1.8.1 short term (up to 6 months)

In this subgroup we only found one relevant trial (N = 53) (vs OLZ - An 2006). There was a statistically significant difference in favour of olanzapine (MD 10.96, 95% CI 1.01 to 20.91; P = 0.03; Analysis 1.8).

1.9 Adverse effects: 1. Anticholinergic - short term (up to 6 months)

1.9.1 blurred vision

In this subgroup we found three relevant trials (N = 241). There was no significant difference between chlorpromazine and olanzapine (RR 2.59, 95% CI 0.66 to 10.22; Analysis 1.9). This subgroup had moderate levels of heterogeneity (Chi² test = 3.4; df = 2; P = 0.183; I² statistic = 41%).

1.9.2 dry mouth

In this subgroup we found five relevant trials (N = 536). There was no significant difference between chlorpromazine and olanzapine (RR 1.13, 95% CI 0.29 to 4.45; Analysis 1.9). This subgroup had important levels of heterogeneity (Chi² test = 18.59; df = 4; P = 0.001; I² statistic = 78%).

1.9.3 excessive sweating

We included two relevant trials in this subgroup (N = 180). There was no significant difference between chlorpromazine and olanzapine (RR 3.00, 95% CI 0.62 to 14.46; Analysis 1.9).

1.9.4 hypersalivation

In this subgroup we found two relevant trials (N = 166). There was a statistically significant difference in favour of olanzapine (RR 10.99, 95% CI 4.14 to 29.17; P < 0.00001; Analysis 1.9).

1.9.5 stuffy nose

In this subgroup we only found one relevant trial (N = 80) (vs OLZ - He 2003). There was a statistically significant difference in favour of olanzapine (RR 3.00, 95% CI 1.06 to 8.52; P = 0.04; Analysis 1.9).

1.10 Adverse effects: 2. Cardiovascular - short term (up to 6 months)

1.10.1 abnormal ECG

In this subgroup we found two relevant trials (N = 180). There was no significant difference between chlorpromazine and olanzapine (RR 3.60, 95% CI 0.60 to 21.55; Analysis 1.10).

1.10.2 apathism - short term (up to six months)

In this subgroup we included only one relevant trial (N = 100) (vs OLZ - Wu 2008). There was a statistically significant difference in favour of olanzapine (RR 5.00, 95% CI 1.15 to 21.67; P = 0.03; Analysis 1.10).

1.10.3 blood pressure (drop)

We included two trials in this subgroup (N = 180). There was a statistically significant difference in favour of olanzapine (RR 8.82, 95% CI 1.13 to 68.52 Analysis 1.10.

1.10.4 orthostatic hypotension

In this subgroup we found five relevant trials (N = 561). There was a statistically significant difference in favour of olanzapine (RR 9.78, 95% CI 2.68 to 35.71; P = 0.006; Analysis 1.10).

1.10.5 palpitation

In this subgroup we only found one relevant trial (N = 237) (vs OLZ - Wang 2008). There was a statistically significant difference in favour of olanzapine (RR 40.66, 95% CI 2.49 to 664.56; P = 0.009; Analysis 1.10).

1.10.6 tachycardia

In this subgroup we found three relevant trials (N = 241). There was a statistically significant difference in favour of olanzapine (RR 3.53, 95% CI 1.66 to 7.48; P = 0.001; Analysis 1.10).

1.11 Adverse effects: 3. Central nervous system - short term (up to 6 months)

1.11.1 dizziness

We included two trials in this subgroup (N = 180). There was a statistically significant difference in favour of olanzapine (RR 3.85, 95% CI 1.11 to 13.32; P = 0.03; Analysis 1.11).

1.11.2 drowsiness

In this subgroup we found five relevant trials (N = 536). There was a statistically significant difference in favour of olanzapine (RR 2.46, 95% CI 1.66 to 3.64; P < 0.00001; Analysis 1.11).

1.11.3 fatigue

In this subgroup we found two relevant trials (N = 161). There was no significant difference between chlorpromazine and olanzapine (RR 1.00, 95% CI 0.13 to 7.66; Analysis 1.11). This subgroup had moderate levels of heterogeneity (Chi² test = 1.79; df = 1; P = 0.181; I² statistic = 44%).

1.12 Adverse effects: 4. Gastrointestinal - short term (up to 6 months)

1.12.1 appetite loss

In this subgroup we found two relevant trials (N = 180). There was a statistically significant difference in favour of olanzapine (RR 11.01, 95% CI 2.82 to 42.94; P = 0.0006; Analysis 1.12). This subgroup had moderate levels of heterogeneity (Chi² test = 1.78; df = 1; P = 0.182; I² statistic = 44%).

1.12.2 constipation

In this subgroup we found six relevant trials (N = 622). There was a statistically significant difference in favour of olanzapine (RR 4.29, 95% CI 2.61 to 7.05; P < 0.00001; Analysis 1.12).

1.12.3 diarrhoea

We found only one trial in this subgroup (N = 80) (vs OLZ - He 2003). There was no significant difference between chlorpromazine and olanzapine (RR 5.00, 95% CI 0.25 to 100.97; Analysis 1.12).

1.12.4 dysphagia

We found only one relevant trial in this subgroup (N = 100) (vs OLZ - Wu 2008). There was no significant difference between chlorpromazine and olanzapine (RR 3.00, 95% CI 0.13 to 71.92; Analysis 1.12).

1.12.5 nausea/vomiting

We included two relevant trials in this subgroup (N = 180). There was no significant difference between chlorpromazine and olanzapine (RR 1.49, 95% CI 0.43 to 5.20; Analysis 1.12).

1.13 Adverse effects: 5. Haematology - - short term (up to 6 months)

1.13.1 abnormal haemogram

In this subgroup we found two relevant trials (N = 180). There was no significant difference between chlorpromazine and olanzapine (RR 4.00, 95% CI 0.87 to 18.31; Analysis 1.13).

1.13.2 leukopenia

In this subgroup we only found one relevant trial (N = 86) (vs OLZ - Chen 2006). There was no significant difference between chlorpromazine and olanzapine (RR 6.69, 95% CI 0.36 to 125.71; Analysis 1.13).

1.14.1 abnormal liver function

In this subgroup we only found one relevant trial (N = 100) (vs OLZ - Wu 2008). There was no significant difference between chlorpromazine and olanzapine (RR 5.00, 95% CI 0.25 to 101.58; Analysis 1.14).

1.14.2 abnormal transaminase

In this subgroup we found two relevant trials (N = 147). There was no significant difference between chlorpromazine and olanzapine (RR 0.88, 95% CI 0.01 to 150.45; Analysis 1.14). This subgroup had important levels of heterogeneity (Chi² test = 6.56; df = 1; P = 0.01; I² statistic = 85%).

1.15 Adverse effects: 7a Metabolic - weight gain - short term (up to 6 months)

In this subgroup we found five relevant trials (N = 536). There was no significant difference between chlorpromazine and olanzapine (RR 0.70, 95% CI 0.25 to 1.96; Analysis 1.15). This subgroup had important levels of heterogeneity (Chi² test = 12.17; df = 4; P = 0.016; I² statistic = 67%).

1.16 Adverse effects: 7b. Metabolic - weight gain - continuous measures

1.16.1 short term (up to to 6 months)

In this subgroup we found four relevant trials (N = 160). There was a statistically significant difference in favour of chlorpromazine (MD -5.11, 95% CI -9.15 to -1.07; P = 0.01; Analysis 1.16).

1.16.1 medium term (7 to 12 months)

We included only one trial in this subgroup (N = 50) (vs OLZ - Luo 2007). There was no significant difference between chlorpromazine and olanzapine (MD 0.59, 95% CI -11.87 to 13.05; Analysis 1.16).

1.17 Adverse effects: 7c. Metabolic - other - continuous measures

1.17.1 cholesterol (TC) - short term (up to 6 months)

In this subgroup we included one relevant trial (N = 50) (vs OLZ - Luo 2007). There was no significant difference between

chlorpromazine and olanzapine (MD -0.40, 95% CI -1.02 to 0.22; Analysis 1.17).

1.17.2 high-density lipoprotein (HDL) - short term (up to 6 months)

We only found one trial in this subgroup (N = 50) (vs OLZ - Luo 2007). There was no significant difference between chlorpromazine and olanzapine (MD 0.05, 95% CI -0.12 to 0.22; Analysis 1.17).

1.17.3 low-density lipoprotein (LDL) - short term (up to 6 months)

We found only one relevant trial in this subgroup (N = 50) (vs OLZ - Luo 2007). There was no significant difference between chlorpromazine and olanzapine (MD -0.01, 95% CI -0.31 to 0.29; Analysis 1.17).

1.17.4 low-density lipoprotein (LDL) - medium term (7 to 12 months)

In this subgroup we only found one relevant trial (N = 50) (vs OLZ - Luo 2007). There was no significant difference between chlorpromazine and olanzapine (MD 0.06, 95% CI -0.41 to 0.53; Analysis 1.16).

1.18 Adverse effects: 7d. Metabolic - other - average endpoint scores - skewed data

Data for endpoint scores in cholesterol, high-density lipoprotein and triglyceride are skewed and are best inspected by viewing Analysis 1.18.

1.19 Adverse effects: 8a. Movement disorders extrapyramidal symptoms - short term (up to 6 months)

1.19.1 akathisia

In this subgroup we found three relevant trials (N = 417). There was no significant difference between chlorpromazine and olanzapine (RR 1.86, 95% CI 0.29 to 11.84; Analysis 1.19). This subgroup had important levels of heterogeneity (Chi² test = 5.51; df = 2; P = 0.064; I² statistic = 64%).

1.19.2 any EPS symptoms

In this subgroup we found two relevant trials (N = 298). There was a statistically significant difference in favour of olanzapine (RR 34.47, 95% CI 4.79 to 248.3; P = 0.0004; Analysis 1.19).

1.19.3 muscle stiffness

In this subgroup we found two relevant trials (N = 180). There was no significant difference between chlorpromazine and olanzapine (RR 6.13, 95% CI 0.73 to 51.45; Analysis 1.19).

1.19.4 tremor

In this subgroup we found two relevant trials (N = 180). There was no significant difference between chlorpromazine and olanzapine (RR 6.78, 95% CI 0.84 to 54.57; Analysis 1.19).

1.20 Adverse effects: 8b. Movement disorders extrapyramidal symptoms - average endpoint score (ESRS, high = poor)

1.20.1 short term (up to 6 months)

We included two relevant trials in this subgroup (N = 80). There was a statistically significant difference in favour of olanzapine (MD 0.9, 95% CI 0.14 to 1.66; P = 0.02; Analysis 1.20)

1.21 Adverse effects: 9a. Various other - sleep - average endpoint score (LSEQ, high = better) - short term (up to 6 months)

1.21.1 awaking from sleep

We found only one relevant trial in this subgroup (N = 30) (HGCQ (Turkey) 2000). There was no significant difference between chlorpromazine and olanzapine (MD -5.30, 95% CI -21.91 to 11.31; Analysis 1.21).

1.21.2 getting to sleep score

In this subgroup we only found one relevant trial (N = 30) (HGCQ (Turkey) 2000). There was no significant difference between chlorpromazine and olanzapine (MD -0.60, 95% CI -19.88 to 18.68; Analysis 1.21).

1.21.3 quality of sleep

In this subgroup we only found one relevant trial (N = 30) (HGCQ (Turkey) 2000). There was no significant difference between chlorpromazine and olanzapine (MD -15.00, 95% CI -33.07 to 3.07; Analysis 1.21).

1.22 Adverse effects: 9b. Various other - sleep - average length of sleep (hour/day)

1.22.1 short term (up to 6 months)

We found one trial in this subgroup (N = 50) (vs OLZ - Luo 2007). There was a statistically significant difference in favour of olanzapine (MD 3.63, 95% CI 2.08 to 5.18; P < 0.00001; Analysis 1.22).

1.22.2 medium term (7 to 12 months)

In this subgroup we only found one relevant trial (N = 50) (vs OLZ - Luo 2007). There was a statistically significant difference in favour of olanzapine (MD 4.41, 95% CI 2.82 to 6.00; P < 0.00001; Analysis 1.22).

1.23 Adverse effects: 9c. Various other - sleep - average score - behaviour following waking - skewed data

Data for this study are skewed and are best inspected by viewing Analysis 1.23.

1.24 Adverse effects: 9d. Various other - rash

1.24.1 short term (up to 6 months)

We included one relevant trial in this subgroup (N = 30) (HGCQ (Turkey) 2000). There was no significant difference between chlorpromazine and olanzapine (RR 2.00, 95% CI 0.14 to 28.76; Analysis 1.24).

1.25 Quality of life: 1 a. Average endpoint scores (various scales, high = better) - short term (up to 6 months)

1.25.1 GQOLI - living condition

In this subgroup we only found one relevant trial (N = 61) (vs OLZ - Zhao 2006). There was no significant difference between chlorpromazine and olanzapine (MD -1.00, 95% CI -4.21 to 2.21; Analysis 1.25).

1.25.2 GQOLI - physical health

In this subgroup we only found one relevant trial (N = 61) (vs OLZ - Zhao 2006). There was a statistically significant difference in favour of olanzapine (MD -10.10, 95% CI -13.93 to -6.27; P < 0.00001; Analysis 1.25).

1.25.3 GQOLI - psychological health

In this subgroup we only found one relevant trial (N = 61) (vs OLZ - Zhao 2006). There was a statistically significant difference in favour of olanzapine (MD -22.60, 95% CI -25.94 to -19.26; P < 0.00001; Analysis 1.25).

1.25.4 GQOLI - social function

In this subgroup we only found one relevant trial (N = 61) (vs OLZ - Zhao 2006). There was a statistically significant difference in favour of olanzapine (MD -18.20, 95% CI -20.51 to -15.89; P < 0.00001; Analysis 1.25).

1.26 Quality of life: 1b. Average endpoint score (QoL, high = better) - skewed data

Data for this outcome are skewed, and are best inspected by viewing Analysis 1.25.

1.27 Leaving the study early - short term (up to 6 months)

1.27.1 due to any reason

In this subgroup we found three relevant trials (N = 139). There was no significant difference between chlorpromazine and olanzapine (RR 1.69, 95% CI 0.45 to 6.40; Analysis 1.27). This subgroup had moderate levels of heterogeneity (Chi² test = 3.64; df = 2; P = 0.162; I² statistic = 45%).

1.27.2 due to lack of efficacy

In this subgroup we found two relevant trials (N = 71). There was no significant difference between chlorpromazine and olanzapine (RR 0.47, 95% CI 0.08 to 2.66; Analysis 1.27).

Comparison 2: CHLORPROMAZINE versus RISPERIDONE

2.1 Clinical response: 1. No significant clinical response

2.1.1 short term (up to 6 months)

In this subgroup we found seven relevant trials (N = 475). There was no significant difference between chlorpromazine and risperidone (RR 0.84, 95% CI 0.53 to 1.34; Analysis 2.1).

2.2 Global state: I. Average endpoint score (CGI-CI, high = poor) - skewed data

Data for this outcome are skewed and are best inspected by viewing Analysis 2.2.

2.3 Global state: 2. Need of additional benzhexol

2.3.1 short term (up to 6 months)

We included two trials in this subgroup (N = 137). There was no significant difference between chlorpromazine and risperidone (RR 1.20, 95% CI 0.26 to 5.53; Analysis 2.3). This subgroup had important levels of heterogeneity (Chi² test = 2.36; df = 1; P = 0.124; I² statistic = 58%).

2.4 Mental state: I a. Average endpoint score (various scales, high = poor) short term (up to 6 months)

2.4.1 BPRS total

In this subgroup we found four relevant trials (N = 247). There was no significant difference between chlorpromazine and risperidone (MD 0.90, 95% CI -3.49 to 5.28; Analysis 2.4). This subgroup had important levels of heterogeneity (Chi² test = 14.61; df = 3; P = 0.002; I² statistic = 79%).

2.4.2 BPRS activation subscale

In this subgroup we found two relevant trials (N = 130). There was no significant difference between chlorpromazine and risperidone (MD 0.41, 95% CI -0.81 to 1.63; Analysis 2.4). This subgroup had important levels of heterogeneity (Chi² test = 4.41; df = 1; P = 0.036; I² statistic = 77%).

2.4.3 BPRS anxiety-depression subscale

In this subgroup we found two relevant trials (N = 130). There was no significant difference between chlorpromazine and risperidone (MD 0.09, 95% CI -1.56 to 1.73; Analysis 2.4). This subgroup had important levels of heterogeneity (Chi² test = 11.14; df = 1; P = 0.001; I² statistic = 91%).

2.4.4 BPRS hostile-suspiciousness subscale

We found two relevant trials in this subgroup (N = 130). There was no significant difference between chlorpromazine and risperidone groups (MD 0.89, 95% CI -1.41 to 3.18; Analysis 2.4). This subgroup had important levels of heterogeneity (Chi² test = 12.36; df = 1; P = 0.0; I² statistic = 92%).

2.4.5 NORS total

In this subgroup we only found one relevant trial (N = 39) (vs RPD - He 1999). There was no significant difference between chlorpromazine and risperidone (MD 1.80, 95% CI -2.53 to 6.13; Analysis 2.4).

2.4.6 PANSS total

In this subgroup we found five relevant trials (N = 397). There was no significant difference between chlorpromazine and risperidone (MD -1.95, 95% CI -5.58 to 1.69; Analysis 2.4). This subgroup had important levels of heterogeneity (Chi² test = 8.7; df = 4; P = 0.069; I² statistic = 54%).

2.4.7 PANSS positive symptom subscale

In this subgroup we found four relevant trials (N = 337). There was no significant difference between chlorpromazine and risperidone (MD 0.03, 95% CI -1.67 to 1.74; Analysis 2.4). This subgroup had important levels of heterogeneity (Chi² test = 11.12; df = 3; P = 0.011; I² statistic = 73%).

2.4.8 PANSS negative symptom subscale

We found three relevant trials in this subgroup (N = 230). There was no significant difference between chlorpromazine and risperidone (MD 3.16, 95% CI -1.57 to 7.89; Analysis 2.4). This subgroup had important levels of heterogeneity (Chi² test = 40.11; df = 2; P = 0.0; I² statistic = 95%).

2.4.9 PANSS general pathology subscale

In this subgroup we found three relevant trials (N = 267). There was no significant difference between chlorpromazine and risperidone (MD -0.85, 95% CI -2.15 to 0.46; Analysis 2.4).

2.4.10 SANS total

In this subgroup we found two relevant trials (N = 71). There was no significant difference between chlorpromazine and risperidone (MD 10.89, 95% CI -4.49 to 26.27; Analysis 2.4). This subgroup had important levels of heterogeneity (Chi² test = 13.51; df = 1; P = 0.0; I² statistic = 93%).

2.5 Mental state: Ib. Average endpoint score (various scales, high = poor) - skewed data

Data for this outcome are skewed and are best inspected by viewing Analysis 2.5.

2.6 Mental state: 2. Average change score - decreased rate (various scales, high = poor) - short term (up to 6 months)

2.6.1 PANSS total

In this subgroup we only found one relevant trial (N = 57) (vs RPD - Wang 2002). There was no significant difference between chlorpromazine and risperidone (MD -0.11, 95% CI -0.23 to 0.01; Analysis 2.6).

2.6.2 PANSS negative subscale

In this subgroup we only found one relevant trial (N = 57) (vs RPD - Wang 2002). There was no significant difference between chlorpromazine and risperidone (MD -0.21, 95% CI -0.44 to 0.02; Analysis 2.6).

2.6.3 PANSS positive subscale

We only found one relevant trial in this subgroup (N = 57) (vs RPD - Wang 2002). There was no significant difference between chlorpromazine and risperidone (MD -0.07, 95% CI -0.36 to 0.22; Analysis 2.6).

2.7 Functioning: average endpoint score (WCST subscales, high = good) - short term (up to 6 months)

2.7.1 WCST-IQ

In this subgroup we only found one relevant trial (N = 100) (vs RPD - Wang 2005). There was a statistically significant difference in favour of risperidone (MD -11.30, 95% CI -18.34 to -4.26; P = 0.002; Analysis 2.7).

2.7.2 WCST-MQ

We only found one relevant trial in this subgroup (N = 100) (vs RPD - Wang 2005). There was a statistically significant difference in favour of risperidone (MD -19.6, 95% CI -28.83 to -10.37; P < 0.0001; Analysis 2.7).

2.8 Adverse effects: I. Anticholinergic - short term (up to 6 months)

2.8.1 blurred vision

In this subgroup we found five relevant trials (N = 387). There was a statistically significant difference in favour of risperidone (RR 2.44, 95% CI 1.32 to 4.50; P = 0.004; Analysis 2.8).

2.8.2 dry mouth

There were nine relevant trials in this subgroup (N = 852). There was no significant difference between chlorpromazine and risperidone (RR 2.00, 95% CI 0.88 to 4.51; Analysis 2.8). This subgroup had important levels of heterogeneity (Chi² test = 28.49; df = 8; P = 0.0; I² statistic = 72%).

2.8.3 excessive sweating

In this subgroup we found two relevant trials (N = 180). There was no significant difference between chlorpromazine and risperidone (RR 3.00, 95% CI 0.62 to 14.46; Analysis 2.8).

2.8.4 hypersalivation

In this subgroup we found five relevant trials (N = 373). There was a statistically significant difference in favour of risperidone (RR 8.67, 95% CI 3.80 to 19.8; P < 0.00001; Analysis 2.8).

2.8.5 stuffy nose

In this subgroup we only found one relevant trial (N = 80) (vs OLZ - He 2003). There was a statistically significant difference in favour of risperidone (RR 3.00, 95% CI 1.06 to 8.52; P = 0.04; Analysis 2.8).

2.9 Adverse effects: 2a. Cardiovascular - short term (up to 6 months)

2.9.1 abnormal ECG

In this subgroup we found three relevant trials (N = 229). There was no significant difference between chlorpromazine and risperidone (RR 2.41, 95% CI 0.96 to 6.06; Analysis 2.9).

2.9.2 apathism

In this subgroup we only found one relevant trial (N = 100) (vs RPD - Wu 2004). There was a statistically significant difference in favour of risperidone (RR 6.25, 95% CI 2.35 to 16.65; P = 0.0002; Analysis 2.9).

2.9.3 bood pressure drop

In this subgroup we found three relevant trials (N = 250). There was a statistically significant difference in favour of risperidone (RR 8.25, 95% CI 2.61 to 26.12; P = 0.0003; Analysis 2.9).

2.9.4 bradycardia

In this subgroup we only found one relevant trial (N = 100) (vs RPD - Wu 2004). There was no significant difference between chlorpromazine and risperidone (RR 0.50, 95% CI 0.05 to 5.34; Analysis 2.9).

2.9.5 orthostatic hypotension

In this subgroup we found five relevant trials (N = 546). There was a statistically significant difference in favour of risperidone (RR 5.74, 95% CI 2.28 to 14.44; P = 0.0002; Analysis 2.9).

2.9.6 palpitation

We only found one relevant trial in this subgroup (N = 237) (vs OLZ - Wang 2008). There was a statistically significant difference in favour of risperidone (RR 40.66, 95% CI 2.49 to 664.56; P = 0.009; Analysis 2.9).

2.9.7 sinus tachycardia

In this subgroup we only found one relevant trial (N = 51) (vs RPD - Zheng 2001). There was no significant difference between chlorpromazine and risperidone (RR 3.12, 95% CI 0.35 to 28.03; Analysis 2.9).

2.9.8 tachycardia

In this subgroup we found seven relevant trials (N = 557). There was a statistically significant difference in favour of risperidone (RR 2.64, 95% CI 1.64 to 4.26; $P \le 0.0001$; Analysis 2.9).

2.10 Adverse effects: 2b. Cardiovascular - continuous measures - short term (up to 6 months)

2.10.1 cardiac rate (upright position)

In this subgroup we only found one relevant trial (N = 100) (vs RPD - Liu 2005). There was no significant difference between chlorpromazine and risperidone (MD 3.90, 95% CI -1.57 to 9.37; Analysis 2.10).

2.10.2 cardiac rate (horizontal position)

In this subgroup we only found one relevant trial (N = 100) (vs RPD - Liu 2005). There was a statistically significant difference in favour of risperidone (MD 7.42, 95% CI 3.47 to 11.37; P = 0.0002; Analysis 2.10).

2.10.3 contractive blood pressure (upright position)

In this subgroup we only found one relevant trial (N = 100) (vs RPD - Liu 2005). There was no significant difference between chlorpromazine and risperidone (MD -1.06, 95% CI -2.20 to 0.08; Analysis 2.10).

2.10.4 ontractive blood pressure (horizontal position)

In this subgroup we only found one relevant trial (N = 100) (vs RPD - Liu 2005). There was a statistically significant difference in favour of risperidone (MD 1.38, 95% CI 0.61 to 2.15; P = 0.0005; Analysis 2.10).

2.10.5 diastolic blood pressure (upright position)

In this subgroup we only found one relevant trial (N = 100) (vs RPD - Liu 2005). There was no significant difference between chlorpromazine and risperidone (MD -0.53, 95% CI -1.29 to 0.23; Analysis 2.10).

2.10.6 diastolic blood pressure (horizontal position)

We only found one relevant trial in this subgroup (N = 100) (vs RPD - Liu 2005). There was no significant difference between chlorpromazine and risperidone (MD 0.39, 95% CI -0.18 to 0.96; Analysis 2.10).

2.11 Adverse effects: 3. Central nervous system - short term (up to 6 months)

2.11.1 agitation

In this subgroup we only found one relevant trial (N = 65) (vs RPD - Feng 2003). There was no significant difference between chlorpromazine and risperidone (RR 0.32, 95% CI 0.01 to 7.66; Analysis 2.11).

2.11.2 dizziness

We found four relevant trials in this subgroup (N = 299). There was a statistically significant difference between chlorpromazine and risperidone (RR 2.37, 95% CI 1.38 to 4.07; Analysis 2.11).

2.11.3 drowsiness

In this subgroup we found four relevant trials (N = 307). There was a statistically significant difference in favour of risperidone (RR 3.62, 95% CI 1.56 to 8.39; P = 0.003; Analysis 2.11). This subgroup had moderate levels of heterogeneity (Chi² test = 5.14; df = 3; P = 0.162; I² statistic = 42%).

2.11.4 fatigue

We only found one relevant trial in this subgroup (N = 100) (vs RPD - Wu 2004). There was a statistically significant difference in favour of risperidone (RR 2.69, 95% CI 1.77 to 4.09; P < 0.00001; Analysis 2.11).

2.11.4 insomnia

In this subgroup we found five relevant trials (N = 342). There was a statistically significant difference in favour of chlorpromazine (RR 0.33, 95% CI 0.12 to 0.91; P = 0.03; Analysis 2.11).

2.11.5 reduced activity

We only found one relevant trial in this subgroup (N = 78) (vs RPD - Ma 2004). There was no significant difference between chlorpromazine and risperidone (RR 2.00, 95% CI 0.19 to 21.16; Analysis 2.11).

2.12 Adverse effects: 4. Gastrointestinal- short term (up to 6 months)

2.12.1 constipation

In this subgroup we found nine relevant trials (N = 868). There was a statistically significant difference in favour of risperidone (RR 3.00, 95% CI 2.05 to 4.39; P < 0.00001; Analysis 2.12).

2.12.2 diarrhoea

In this subgroup we only found one relevant trial (N = 80) (vs OLZ - He 2003). There was no significant difference between chlorpromazine and risperidone (RR 5.00, 95% CI 0.25 to 100.97; Analysis 2.12).

2.12.3 dysphagia

In this subgroup we only found one relevant trial (N = 100) (vs RPD - Wu 2004). There was a statistically significant difference (P = 0.04) in favour of risperidone (RR 3.67, 95% CI 1.09 to 12.36; Analysis 2.12).

2.12.4 loss of appetite

In this subgroup we found two relevant trials (N = 180). There was a statistically significant difference in favour of risperidone (RR 11.01, 95% CI 2.82 to 42.94; P = 0.0006; Analysis 2.12). This subgroup had moderate levels of heterogeneity (Chi² test = 1.78; df = 1; P = 0.182; I² statistic = 44%).

2.12.5 nausea/vomiting

We found four relevant trials in this subgroup (N = 350). There was no significant difference between chlorpromazine and risperidone (RR 0.85, 95% CI 0.37 to 1.91; Analysis 2.12).

2.13 Adverse effects: 5. Haematology - short term (up to 6 months)

2.13.1 Abnormal haemogram

In this subgroup we found two relevant trials (N = 180). There was no significant difference between chlorpromazine and risperidone (RR 4.00, 95% CI 0.87 to 18.31; Analysis 2.13).

2.13.2 leukopenia

We only found one relevant trial in this subgroup (N = 86) (vs OLZ - Chen 2006). There was no significant difference between chlorpromazine and risperidone (RR 6.69, 95% CI 0.36 to 125.71; Analysis 2.13).

2.14 Adverse effects: 6. Hepatitic - short term (up to 6 months)

2.14.1 abnormal liver function - short term (up to six months)

In this subgroup we only found one relevant trial (N = 78) (vs RPD - Ma 2004). There was no significant difference between chlorpromazine and risperidone (RR 5.00, 95% CI 0.25 to 100.89; Analysis 2.14).

2.14.2 abnormal transaminase - short term (up to six months)

We found three relevant trials in this subgroup (N = 229). There was no significant difference between chlorpromazine and risperidone (RR 0.88, 95% CI 0.07 to 11.58; Analysis 2.14). This subgroup had important levels of heterogeneity (Chi² test = 6.3; df = 2; P = 0.043; I² statistic = 68%).

2.15 Adverse effects: 7. Metabolic - weight gain

2.15.1 short term (up to six months)

In this subgroup we found four relevant trials (N = 302). There was no significant difference between chlorpromazine and risperidone (RR 1.36, 95% CI 0.52 to 3.59; Analysis 2.15). This subgroup had important levels of heterogeneity (Chi² test = 6.75; df = 3; P = 0.08; I² statistic = 56%).

2.16 Adverse effects: 8. Movement disorders - short term (up to 6 months)

2.16.1 akathisia

In this subgroup we found six relevant trials (N = 435). There was a statistically significant difference in favour of risperidone (RR 2.37, 95% CI 1.46 to 3.85; P = 0.0005; Analysis 2.16).

2.16.2 any EPS symptoms

In this subgroup we found three relevant trials (N = 235). There was no significant difference between chlorpromazine and risperidone (RR 1.70, 95% CI 0.85 to 3.40; Analysis 2.16). This subgroup had important levels of heterogeneity (Chi² test = 4.33; df = 2; P = 0.115; I² statistic = 54%).

2.16.3 dystonia

In this subgroup we found three relevant trials (N = 228). There was no significant difference between chlorpromazine and risperidone (RR 1.61, 95% CI 0.97 to 2.66; Analysis 2.16).

2.16.4 muscle stiffness

In this subgroup we found five relevant trials (N = 335). There was no significant difference between chlorpromazine and risperidone (RR 2.96, 95% CI 0.92 to 9.49; Analysis 2.16). This subgroup had important levels of heterogeneity (Chi² test = 8.82; df = 4; P = 0.066; I² statistic = 55%).

2.16.5 torsion movements

We only found one relevant trial in this subgroup (N = 78) (vs RPD - Ma 2004). There was no significant difference between chlorpromazine and risperidone (RR 9.00, 95% CI 0.50 to 161.73; Analysis 2.16).

2.16.6 tremor

In this subgroup we found six relevant trials (N = 435). There was a statistically significant difference in favour of risperidone (RR 2.15, 95% CI 1.47 to 3.14, P < 0.0001; Analysis 2.16).

2.17 Adverse effects: 9. Average endpoint score (TESS) - skewed data

Data for this outcome are skewed and are best inspected by viewing Analysis 2.17.

2.18 Adverse effects: 10. Various - short term (up to 6 months)

2.18.1 concentration (poor)

In this subgroup we only found one relevant trial (N = 100) (vs RPD - Wu 2004). There was a statistically significant difference in favour of risperidone (RR 1.95, 95% CI 1.35 to 2.82; P = 0.0003; Analysis 2.18).

2.18.2 memory deterioration

In this subgroup we only found one relevant trial (N = 100) (vs RPD - Wu 2004). There was a statistically significant difference in favour of risperidone (RR 1.95, 95% CI 1.35 to 2.82; P = 0.0004; Analysis 2.18).

2.18.3 sexual dysfunction

In this subgroup we only found one relevant trial (N = 100) (vs RPD - Wu 2004). There was a statistically significant difference in favour of risperidone (RR 2.55, 95% CI 1.43 to 4.53; P = 0.002; Analysis 2.18).

2.18.4 unspecified

In this subgroup we only found one relevant trial (N = 100) (vs RPD - Wang 2005). There was no significant difference between chlorpromazine and risperidone (RR 1.38, 95% CI 0.97 to 1.95; Analysis 2.18).

2.19 Quality of life: 1. Average endpoint scale score (QOL, high = good)

2.19.1 short term (up to 6 months)

In this subgroup we only found one relevant trial (N = 100) (vs RPD - Wu 2004). There was a statistically significant difference in favour of risperidone (MD -14.20, 95% CI -20.50 to -7.90; P < 0.00001; Analysis 2.19).

2.20 Leaving the study early - short term (up to 6 months)

2.20.1 due to adverse events

In this subgroup we only found one relevant trial (N = 41) (vs RPD - He 1999). There was no significant difference between chlorpromazine and risperidone (RR 0.21, 95% CI 0.01 to 4.11; Analysis 2.20).

Comparison 3: CHLORPROMAZINE versus QUETIAPINE

3.1 Clinical response: No significant clinical response

3.1.1 short term (up to six months)

In this subgroup we found 28 relevant trials (N = 3241). There was no significant difference between chlorpromazine and quetiapine (RR 0.93, 95% CI 0.81 to 1.06; Analysis 3.1).

3.2 Global state: 1. Need of additional benzodiazepines/benzhexol

3.2.1 short term (up to 6 months)

In this subgroup we found two relevant trials (N = 290). There was a statistically significant difference in favour of quetiapine (RR 1.39, 95% CI 1.1 to 1.75; Analysis 3.2).

3.3 Global state: 2a. Average endpoint scores (various scales, high = poor) - short term (up to 6 months)

3.3.1 CGI-SI

In this subgroup we found two relevant trials (N = 177). There was no significant difference between chlorpromazine and quetiapine (MD 0.01, 95% CI -0.82 to 0.84; Analysis 3.3. This subgroup had important levels of heterogeneity (Chi² test = 5.67; df = 1; P = 0.017; I² statistic = 82%).

3.3.2 CGI-GI

In this subgroup we found three relevant trials (N = 229). There was no significant difference between chlorpromazine and quetiapine (MD -0.11, 95% CI -0.33 to 0.11; Analysis 3.3).

3.4 Global state: 2b. Average endpoint score (CGI-SI, high = poor) - skewed data

Data for this outcome are skewed and are best inspected by viewing Analysis 3.4.

3.5 Global state: 3. Average change scores (CGI-SI, high = poor)

3.5.1 short term (up to six months)

We only found one relevant trial in this subgroup (N = 384) (vs QTP - NCT00882518). There was a statistically significant difference in favour of chlorpromazine (MD -0.30, 95% CI -0.32 to -0.28; P < 0.00001; Analysis 3.5).

3.6 Mental state: Ia. Average endpoint scores (various scale, high = poor) - short term (up to 6 months)

3.6.1 BPRS total

In this subgroup we found six relevant trials (N = 548). There was no significant difference between chlorpromazine and quetiapine (MD -0.18, 95% CI -1.23 to 0.88; Analysis 3.6).

3.6.2 BPRS anxiety-depression subscale

In this subgroup we only found one relevant trial (N = 60) (vs QTP - Yang 2007). There was no significant difference between chlorpromazine and quetiapine (MD -0.27, 95% CI -1.16 to 0.62; Analysis 3.6).

3.6.3 BPRS activation subscale

In this subgroup we only found one relevant trial (N = 60) (vs QTP - Yang 2007). There was no significant difference between chlorpromazine and quetiapine (MD 0.22, 95% CI -0.26 to 0.70; Analysis 3.6).

3.6.4 BPRS hostile-suspiciousness subscale

In this subgroup we only found one relevant trial (N = 60) (vs QTP - Yang 2007). There was no significant difference between chlorpromazine and quetiapine (MD -0.09, 95% CI -1.15 to 0.97; Analysis 3.6).

3.6.5 BPRS thinking disorder subscale

We only found one relevant trial in this subgroup (N = 60) (vs QTP - Yang 2007). There was no significant difference between chlorpromazine and quetiapine (MD -0.15, 95% CI -1.39 to 1.09; Analysis 3.6).

3.6.6 BPRS withdraw-retardation subscale

In this subgroup we only found one relevant trial (N = 60) (vs QTP - Yang 2007). There was no significant difference between chlorpromazine and quetiapine (MD -0.10, 95% CI -0.76 to 0.56; Analysis 3.6).

3.6.7 PANSS total

In this subgroup we found 25 relevant trials (N = 2049). There was no significant difference between chlorpromazine and quetiapine (MD -0.05, 95% CI -2.3 to 2.19; Analysis 3.6). This subgroup had important levels of heterogeneity (Chi² test = 102.88; df = 24; P = 0.0; I² statistic = 77%).

3.6.8 PANSS positive symptom

In this subgroup we found 13 relevant trials (N = 1102). There was no significant difference between chlorpromazine and quetiapine (MD 0.39, 95% CI -0.11 to 0.88; Analysis 3.6).

3.6.9 PANSS negative symptoms

In this subgroup we found 17 relevant trials (N = 1361). There was a statistically significant difference in favour of quetiapine (MD 1.05, 95% CI 0.13 to 1.98; P = 0.03; Analysis 3.6). This subgroup had important levels of heterogeneity (Chi² test = 54.37; df = 16; P = 0.0; I² statistic = 71%).

3.6.10 PANSS general pathology

In this subgroup we found 18 relevant trials (N = 1530). There was no significant difference between chlorpromazine and quetiapine (MD -1.11, 95% CI -3.06 to 0.84; Analysis 3.6). This subgroup had important levels of heterogeneity (Chi² test = 160.66; df = 17; P = 0.0; I² statistic = 89%).

3.6.11 HAMD total

In this subgroup we only found one relevant trial (N = 63) (vs QTP - Li 2010). There was a statistically significant difference in favour of quetiapine (MD 7.40, 95% CI 5.13 to 9.67; P < 0.00001; Analysis 3.6).

3.7 Mental state: Ib. Average endpoint scores (various scales, high = poor) - medium term (6 to 12 months)

3.7.1 PANSS total

In this subgroup we only found one relevant trial (N = 41) (vs QTP - Li 2003). There was a statistically significant difference in favour of quetiapine (MD 4.90, 95% CI 1.74 to 8.06; P = 0.002; Analysis 3.7).

3.7.2 PANSS general pathology

We only found one relevant trial in this subgroup (N = 41) (vs QTP - Li 2003). There was no significant difference between chlorpromazine and quetiapine (MD -0.20, 95% CI -4.34 to 3.94; Analysis 3.7).

3.7.3 PANSS negative symptoms

In this subgroup we only found one relevant trial (N = 77) (vs QTP - Li 2003). There was a statistically significant difference in favour of quetiapine (MD 2.70, 95% CI 0.44 to 4.96; P = 0.02; Analysis 3.7).

3.8 Mental state: Ic. Average endpoint scores (various scales, high = poor) - skewed data

Data for this outcome are skewed and are best inspected be viewing Analysis 3.8.

3.9 Mental state: Average change score (various scales, high = poor) - short term (up to 6 months)

3.9.1 PANSS total

In this subgroup we found two relevant trials (N = 426). There was a statistically significant difference in favour of chlorpromazine (MD -2.50, 95% CI -2.82 to -2.19; P < 0.00001; Analysis 3.9).

3.9.2 PANSS positive symptoms

In this subgroup we only found one relevant trial (N = 384) (vs QTP - NCT00882518). There was a statistically significant difference in favour of quetiapine (MD 1.20, 95% CI 1.10 to 1.30, Analysis 3.9).

3.9.3 PANSS negative symptom

In this subgroup we only found one relevant trial (N = 384) (vs QTP - NCT00882518). There was a statistically significant difference) in favour of quetiapine (MD 0.80, 95% CI 0.70 to 0.90; P < 0.00001; Analysis 3.9).

3.9.4 PANSS general pathology

In this subgroup we only found one relevant trial (N = 384) (vs QTP - NCT00882518). There was a statistically significant differenc in favour of quetiapine (MD 1.00, 95% CI 0.85 to 1.15; P < 0.00001; Analysis 3.9). 3.10 Mental state: I.e. Average score decreased rate of BPRS/PANSS (%) - short term (up to 6 months)

3.10.1 BPRS

In this subgroup we only found one relevant trial (N = 197) (vs QTP - Cai 2006). There was no significant difference between chlorpromazine and quetiapine (MD -0.80, 95% CI -4.86 to 3.26; Analysis 3.10).

3.10.2 PANSS

In this subgroup we found six relevant trials (N = 782). There was no significant difference between chlorpromazine and quetiapine (MD -1.96, 95% CI -7.20 to 3.28; Analysis 3.10). This subgroup had important levels of heterogeneity (Chi² test = 18.14; df = 5; P = 0.003; I² statistic = 72%).

3.11 Functioning: 1. Average endpoint score (various scales, high = better) - short term (up to 6 months)

3.11.1 WCST-IQ

In this subgroup we only found one relevant trial (N = 120) (vs QTP - Nai 2007). There was a statistically significant difference in favour of quetiapine (MD -11.30, 95% CI -17.62 to -4.98; P = 0.0005; Analysis 3.11).

3.11.2 WCST-MQ

In this subgroup we only found one relevant trial (N = 120) (vs QTP - Nai 2007). There was a statistically significant difference in favour of quetiapine (MD -19.6, 95% CI -27.37 to -11.83; P < 0.00001; Analysis 3.11).

3.12 Cognitive function: I. Average endpoint scores (various scales, high = better) short term (up to 6 months)

3.12.1 WCST

In this subgroup we found two relevant trials (N = 123). There was a statistically significant difference in favour of quetiapine (MD 8.92, 95% CI 0.40 to 17.43; P = 0.04; Analysis 3.12).

3.12.2 WMS-RC

In this subgroup we only found one relevant trial (N = 71) (vs QTP - Sun 2006). There was a statistically significant difference in favour of chlorpromazine (MD -9.34, 95% CI -17.53 to -1.15; P = 0.03; Analysis 3.12).

3.13 Adverse effects: 1. Anticholinergic - short term (up to 6 months)

3.13.1 blurred vision

In this subgroup we found 18 relevant trials (N = 1780). There was a statistically significant difference in favour of quetiapine (RR 5.00, 95% CI 3.46 to 7.22; P < 0.00001; Analysis 3.13).

3.13.2 dry mouth

In this subgroup we found 18 relevant trials (N = 1682). There was a statistically significant difference (P < 0.0001) in favour of quetiapine (RR 2.34, 95% CI 1.54 to 3.54; Analysis 3.13). This subgroup had moderate levels of heterogeneity (Chi² test = 32.99; df = 17; P = 0.011; I² statistic = 48%).

3.13.2 excessive sweating

In this subgroup we found three relevant trials (N = 162). There was no significant difference between chlorpromazine and quetiapine (RR 3.91, 95% CI 0.84 to 18.19; Analysis 3.13).

3.13.3 hypersalivation

We found 11 relevant trials in this subgroup (N = 1135). There was a statistically significant difference in favour of quetiapine (RR 3.85, 95% CI 2.36 to 6.28; P < 0.0001; Analysis 3.13).

3.13.4 stuffy nose

In this subgroup we found eight relevant trials (N = 972). There was no significant difference between chlorpromazine and quetiapine (RR 0.69, 95% CI 0.45 to 1.06; Analysis 3.13).

3.14 Adverse effects: 2. Cardiovascular - short term (up to 6 months)

3.14.1 abnormal ECG

In this subgroup we found seven relevant trials (N = 708). There was a statistically significant difference in favour of quetiapine (RR 1.82, 95% CI 1.11 to 2.98; P = 0.02; Analysis 3.14).

3.14.2 blood pressure drop

In this subgroup we found eight relevant trials (N = 690). There was no significant difference between chlorpromazine and quetiapine (RR 0.97, 95% CI 0.53 to 1.79; Analysis 3.14). This subgroup had moderate levels of heterogeneity (Chi² test = 13.18; df = 7; P = 0.068; I² statistic = 47%).

3.14.3 orthostatic hypotension

In this subgroup we found seven relevant trials (N = 605). There was a statistically significant difference in favour of quetiapine (RR 2.64, 95% CI 1.14 to 6.12; P = 0.02; Analysis 3.14).

3.14.4 tachycardia

In this subgroup we found 17 relevant trials (N = 1752). There was a statistically significant difference in favour of quetiapine (RR 1.70, 95% CI 1.33 to 2.18; P < 0.0001; Analysis 3.14).

3.15 Adverse effects: 3. Central nervous system - short term (up to 6 months)

3.15.1 dizziness

In this subgroup we found 12 relevant trials (N = 1206). There was no significant difference between chlorpromazine and quetiapine (RR 1.40, 95% CI 0.83 to 2.35; Analysis 3.15). This subgroup had moderate levels of heterogeneity (Chi² test = 16.88; df = 11; P = 0.111; I² statistic = 35%).

3.15.2 drowsiness

In this subgroup we found 17 relevant trials (N = 1677). There was a statistically significant difference in favour of quetiapine (RR 2.28, 95% CI 1.51 to 3.45; P < 0.0001; Analysis 3.15). This subgroup had moderate levels of heterogeneity (Chi² test = 31.15; df = 16; P = 0.013; I² statistic = 49%).

3.15.3 headache

In this subgroup we found three relevant trials (N = 192). There was no significant difference between chlorpromazine and quetiapine (RR 0.74, 95% CI 0.13 to 4.18; Analysis 3.15).

3.15.4 insomnia

In this subgroup we found nine relevant trials (N = 867). There was no significant difference between chlorpromazine and quetiapine (RR 0.92, 95% CI 0.55 to 1.54; Analysis 3.15).

3.15.5 reduced activity

In this subgroup we found eight relevant trials (N = 788). There was a statistically significant difference in favour of quetiapine (RR 7.80, 95% CI 3.05 to 19.92; P < 0.0001; Analysis 3.15).

3.15.6 sedation

In this subgroup we only found one relevant trial (N = 40) (vs QTP - He 2003). There was no significant difference between chlorpromazine and quetiapine (RR 0.33, 95% CI 0.01 to 7.72; Analysis 3.15).

3.16 Adverse effects: 4. Gastrointestinal - short term (up to 6 months)

3.16.1 constipation

In this subgroup we found 22 relevant trials (N = 2048). There was a statistically significant difference in favour of quetiapine (RR 2.55, 95% CI 2.04 to 3.20; P < 0.00001; Analysis 3.16).

3.16.2 diarrhoea

In this subgroup we only found one relevant trial (N = 62) (vs QTP - Chen 2007). There was no significant difference between chlorpromazine and quetiapine (RR 5.32, 95% CI 0.27 to 106.54; Analysis 3.16).

3.16.3 loss of appetite

In this subgroup we found five relevant trials (N = 472). There was no significant difference between chlorpromazine and quetiapine (RR 2.52, 95% CI 0.82 to 7.72; Analysis 3.16). This subgroup had moderate levels of heterogeneity (Chi² test = 7.06; df = 4; P = 0.133; I² statistic = 43%).

3.16.4 nausea/vomiting

In this subgroup we found nine relevant trials (N = 819). There was no significant difference between chlorpromazine and quetiapine (RR 1.23, 95% CI 0.58 to 2.63; Analysis 3.16).

3.17 Adverse effects: 5a. Endocrine - various - short term (up to 6 months)

3.17.2 gynaecomastia, galactorrhoea

In this subgroup we only found one relevant trial (N = 83) (vs QTP - Guo 2008). There was no significant difference between chlorpromazine and quetiapine (RR 5.37, 95% CI 0.27 to 108.47; Analysis 3.17).

3.17.2 hyperprolactinemia

In this subgroup we found two relevant trials (N = 277). There was a statistically significant difference in favour of quetiapine (RR 5.69, 95% CI 2.74 to 11.79; P < 0.00001; Analysis 3.17).

3.17.3 menstrual irregularities

In this subgroup we only found one relevant trial (N = 52) (vs QTP - Guo 2007). There was no significant difference between chlorpromazine and quetiapine (RR 5.00, 95% CI 0.25 to 99.34; Analysis 3.17).

3.18 Adverse effects: 5b. Endocrine - average endpoint - short term (up to 6 months)

3.1.18 prolactin level (ng/mL)

In this subgroup we only found one relevant trial (n = 30) (vs QTP - Kong 2003). There was a statistically significant difference in favour of quetiapine (MD 24.62, 95% CI 17.76 to 31.48; P < 0.00001; Analysis 3.18).

3.19 Adverse effect: 5c. Endocrine - skewed data - short term (up to 6 months)

3.19.1 average prolactin level (ng/mL)

Data for this outcome are skewed and are best inspected by viewing Analysis 3.19.

3.20 Adverse effects: 6a. Haematology - short term (up to 6 months)

3.20.1 elevated ALT

In this subgroup we found eight relevant trials (N = 775). There was no significant difference between chlorpromazine and quetiapine (RR 1.62, 95% CI 0.92 to 2.87; Analysis 3.20).

3.20.2 decreased white blood cell count

In this subgroup we found four relevant trials (N = 427). There was no significant difference between chlorpromazine and quetiapine (RR 1.02, 95% CI 0.43 to 2.42; Analysis 3.20).

3.20.3 increased white blood cell count

We only found one relevant trial in this subgroup (N = 79) (vs QTP - Zhou 2004). There was no significant difference between chlorpromazine and quetiapine (RR 2.05, 95% CI 0.40 to 10.56; Analysis 3.20).

3.21 Adverse effects: 6b. Haematology - average endpoint - short term (up to 6 months)

3.21.1 blood glucose

In this subgroup we only found one relevant trial (N = 130) (vs QTP - Guo 2006). There was no significant difference between chlorpromazine and quetiapine (MD 0.10, 95% CI -0.18 to 0.38; Analysis 3.21).

3.21.2 blood TG

In this subgroup we only found one relevant trial (N = 130) (vs QTP - Guo 2006). There was no significant difference between chlorpromazine and quetiapine (MD 0.00, 95% CI -0.28 to 0.28; Analysis 3.21).

3.21.3 blood TC

We only found one relevant trial (N = 130) in this subgroup (vs QTP - Guo 2006). There was no significant difference between chlorpromazine and quetiapine (MD 0.20, 95% CI -0.11 to 0.51; Analysis 3.21).

3.22 Adverse effects: 7. Hepatitic - short term (up to 6 months)

3.22.1 abnormal liver function

In this subgroup we found five relevant trials (N = 561). There was a statistically significant difference in favour of quetiapine (RR 2.10, 95% CI 1.32 to 3.33; P = 0.002; Analysis 3.22).

3.23 Adverse effects: 8. Movement disorders - short term (up to 6 months)

3.23.1 agitation

We found five relevant trials in this subgroup (N = 313). There was a statistically significant difference in favour of chlorpromazine (RR 0.36, 95% CI 0.14 to 0.95; P = 0.04; Analysis 3.23).

3.23.2 akathisia

In this subgroup we found 17 relevant trials (N = 1757). There was a statistically significant difference in favour of quetiapine (RR 3.73, 95% CI 2.55 to 5.47; P < 0.00001; Analysis 3.23).

3.23.3 any EPS symptoms

In this subgroup we found eight relevant trials (N = 644). There was a statistically significant difference in favour of quetiapine (RR 8.03, 95% CI 4.78 to 13.51; P < 0.00001; Analysis 3.23).

3.23.4 dystonia

In this subgroup we only found one relevant trial (N = 201) (vs QTP - Peuskens 1997). There was no significant difference between chlorpromazine and quetiapine (RR 0.33, 95% CI 0.01 to 8.01; Analysis 3.23).

3.23.5 myotonia

In this subgroup we found 12 relevant trials (N = 1257). There was a statistically significant difference in favour of quetiapine (RR 4.59, 95% CI 3.18 to 6.64; P < 0.00001; Analysis 3.23).

3.23.6 need additional medication for EPS symptoms

We only found one relevant trial in this subgroup (N = 202) (vs QTP - Peuskens 1997). There was no significant difference between chlorpromazine and quetiapine (RR 1.50, 95% CI 0.71 to 3.18; Analysis 3.23).

3.23.7 torsion movement

In this subgroup we found nine relevant trials (N = 1063). There was a statistically significant difference in favour of quetiapine (RR 5.81, 95% CI 2.76 to 12.23; P < 0.00001; Analysis 3.23).

3.23.8 tremor

In this subgroup we found 13 relevant trials (N = 1343). There was a statistically significant difference in favour of quetiapine (RR 2.90, 95% CI 1.89 to 4.45; P < 0.00001; Analysis 3.23).

3.24 Adverse effects: 9a. Metabolic - weight gain

3.24.1 short term (up to six months)

In this subgroup we found 15 relevant trials (N = 1259). There was a statistically significant difference in favour of quetiapine (RR 1.67, 95% CI 1.17 to 2.39; P = 0.005; Analysis 3.24).

3.25 Adverse effects: 9b. Metabolic - continuous - short term (up to 6 months)

3.25.1 average BMI

In this subgroup we only found one relevant trial (N = 105) (vs QTP - Wang 2005). There was no significant difference between chlorpromazine and quetiapine (MD 0.50, 95% CI -0.67 to 1.67; Analysis 3.25).

3.25.2 average weight (KG)

In this subgroup we only found one relevant trial (N = 130) (vs QTP - Guo 2006). There was no significant difference between chlorpromazine and quetiapine (MD -1.00, 95% CI -4.68 to 2.68; Analysis 3.25).

3.26 Adverse effects: 10. Various other - short term (up to 6 months)

3.26.1 unspecified adverse effects

In this subgroup we found four relevant trials (N = 560). There was a statistically significant difference (P = 0.004) in favour of quetiapine (RR 1.73, 95% CI 1.20 to 2.51; Analysis 3.26). This subgroup had important levels of heterogeneity (Chi² test = 10.42; df = 3; P = 0.015; I² statistic = 71%).

3.27 Adverse effects: 11. Average endpoint score (TESS, high = poor) - skewed data

Data for this outcome are skewed and are best inspected by viewing Analysis 3.27.

3.28 Quality of life: 1. General - average endpoint score (GQOLI - 74, high = better)

3.28.1 short term (up to 6 months)

In this subgroup we only found one relevant trial (N = 59) (vs QTP - Ji 2004). There was a statistically significant difference in favour of quetiapine (MD -6.49, 95% CI -11.3 to -1.68; P = 0.008; Analysis 3.28).

3.29 Leaving the study early: Ia. Short term (up to six months)

3.29.1 due to adverse effect

In this subgroup we found ten relevant trials (N = 1680). There was a statistically significant difference in favour of quetiapine (RR 1.43, 95% CI 1.04 to 1.98; P = 0.03; Analysis 3.29).

3.29.2 due to inefficacy

In this subgroup we found three relevant trials (N = 695). There was no significant difference between chlorpromazine and quetiapine (RR 1.42, 95% CI 0.68 to 2.96; Analysis 3.29).

3.29.3 due to any other reason

We found 12 relevant trials in this subgroup (N = 1223). There was no significant difference between chlorpromazine and quetiapine (RR 1.04, 95% CI 0.77 to 1.41; Analysis 3.29).

3.29.4 due to lost to follow-up

In this subgroup we found two relevant trials (N = 400). There was no significant difference between chlorpromazine and quetiapine (RR 0.56, 95% CI 0.23 to 1.37; Analysis 3.29).

3.30 Leaving the study early: 1b. Medium term (seven to 12 months)

For this outcome we only found one relevant trial (N = 103) (vs QTP - Li 2003). There was no significant difference between chlorpromazine and quetiapine (RR 1.19, 95% CI 0.61 to 2.32; Analysis 3.30).

4. Sensitivity analysis

I. Implication of randomisation

1.1 Chlorpromazine versus olanzapine - clinical response: no significant clinical response

After removing studies that did not adequately explain randomisation methods, there was no substantial difference in the estimate of the effect, with results statistically significant in favour of olanzapine (1 RCT, N = 58; RR 2.49, 95% CI 1.10 to 5.64).

1.2 Chlorpromazine versus risperidone - clinical response: no significant clinical response

After removing studies that did not adequately explain randomisation methods, there were no data left in the short term outcome to compare, since all included studies did not provide explanation.

1.3 Chlorpromazine versus quetiapine - clinical response: no significant clinical response

After removing studies that did not adequately explain randomisation methods, there was no substantial difference in the estimate of the effect.

2. Assumptions for lost binary data

We did not assume any binary data from the included studies.

3. Risk of bias

3.1 Chlorpromazine versus olanzapine - clinical response: no significant clinical response

After we removed studies that were rated as 'high' across one or more of the 'Risk of bias' domains, there were no data left in the short-term outcome to compare, since all included studies were rated as 'high' (vs OLZ - Chang 2003; vs OLZ - Chen 2006; vs OLZ - Wang 2002). However, there was no difference in longterm outcome.

3.2 Chlorpromazine versus risperidone - clinical response: no significant clinical response

After we removed studies that we had rated as 'high' across one or more of the 'Risk of bias' domains, there was no substantial difference in the estimate of the effect.

3.3 Chlorpromazine versus quetiapine - clinical response: no significant clinical response

After removing studies that rated as 'high' across one or more of the 'Risk of bias' domains, there was no substantial difference in the estimate of the effect.

4. Imputed values

We had also 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-RCTs. However, we did not impute any values in this Cochrane review.

5. Fixed-effect and random-effects

5.1 Chlorpromazine versus olanzapine - clinical response: no significant clinical response

There was no difference in the estimate of effect if a fixed-effect model was used in place of the random-effects model.

5.2 Chlorpromazine versus risperidone - clinical response: no significant clinical response

There was no difference in the estimate of effect if a fixed-effect model was used in place of the random-effects model.

5.3 Chlorpromazine versus quetiapine - clinical response: no significant clinical response

There was no difference in the estimate of effect if a fixed-effect model was used in place of the random-effects model.

Chlorpromazine versus	risperidone for schi	zophrenia				
Patient or population: p Settings: inpatient and Intervention: chlorprom Comparison: risperidon	outpatient azine	renia				
Outcomes	Illustrative compar	ative risks* (95% CI)	Relative effect (95% CI)	Number of participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Risperidone	Chlorpromazine				
No significant clinical response - short term (up to 6 months) Follow-up: median 8 to 12 weeks	Low ¹		RR 0.84	475	$\Phi \Phi \bigcirc \bigcirc$	-
	60 per 1000	50 per 1000 (32 to 80)	(0.53 to 1.34)	(7 studies)	low ^{2,3}	
	Moderate ¹					
	114 per 1000	96 per 1000 (60 to 153)				
	High ¹					
	240 per 1000	202 per 1000 (127 to 322)				
Mental state: short term (up to 6 months) BPRS endpoint scale score (high = poor)		The mean mental state: short term (up to 6 months) in the interven- tion groups was		247 (4 studies)	⊕○○○ very low ^{2,4,5,6,7}	-

Adverse effects: any observed extrapyrami- dal symptoms - short term (up to 6 months) Follow-up: 8 to 12 weeks			RR 1.7	235	0 00 -
	130 per 1000 221 pe (111 to	221 per 1000 (111 to 442)	(0.85 to 3.4)	(3 studies)	very low ^{2,6,7}
	High ¹				
	240 per 1000	408 per 1000 (204 to 816)			
Quality of life: short term (up to 6 months) QOL endpoint scale score (high = good) Follow-up: mean 12 weeks		The mean quality of life: short term (up to 6 months) in the interven- tion groups was 14.2 lower (20.5 to 7.9 lower)		100 (1 study)	⊕ very low ^{7,8,9,10}
Leaving the study early	Study population		RR 0.21	41 (1. sturb)	⊕000 ·
due to adverse effects - short term (up to 6 months) Follow-up: mean 8 weeks	95 per 1000	20 per 1000 (1 to 391)	(0.01 to 4.11)	(1 study)	very low ^{7,10}
	Moderate				
	95 per 1000	20 per 1000 (1 to 390)			
	roup and the relativ	edian control group risk across e effect of the intervention (an		l in footnotes. The corre	esponding risk (and its 95% Cl) is based on the assume
Moderate quality: furthe	earch is very unlikel er research is likely t	y to change our confidence in o have an important impact or	n our confidence in t	he estimate of effect ar	nd may change the estimate. d is likely to change the estimate.

¹Control risk: the control risks are representative of those observed in the study population.

²Risk of bias: serious - most of the included studies had unclear risk of bias in terms of allocation and blinding, hence selection and detection bias are likely to be present. Some of the studies also had high risk of reporting bias.

³Publication bias: strongly suspected - only Chinese studies with relatively small sample size were identified. Publication bias is highly likely.

⁴Inconsistency: serious - unexplained heterogeneity present, suggesting different magnitude of effect.

⁵Indirectness: serious - binary outcome assessing mental state is unavailable. We, therefore, employed BPRS score as an alternative indicator.

⁶Imprecision: serious - although the CI around the estimate of effect relatively tight, the result was not significant and sample size was smaller than the optimal information size.

⁷Publication bias: strongly suspected - only one study with unclear risk of selection and detection bias available for this outcome.

⁸Indirectness: serious - binary outcome for quality of life was not available. Therefore, we adopted QOL score as an indicator. ⁹Imprecision: serious - estimate of effect was significant with tight CI, but the study sample size is smaller than the optimal information size.

¹⁰Imprecision: serious - estimate of effect was not significant and with relatively wide CI. Sample size was smaller than the optimal information size.

Chlorpromazine versus quetiapine for schizophrenia					
eople with schizophre outpatient azine	enia				
Illustrative compara	tive risks* (95% CI)	Relative effect (95% Cl)	Number of participants (studies)	Quality of the evidence (GRADE)	Comments
Assumed risk	Corresponding risk				
Quetiapine	Chlorpromazine				
Low ¹		RR 0.93 3241		⊕⊕⊕⊖ -	
70 per 1000	65 per 1000 (57 to 74)	(0.81 to 1.06)	(28 studies)	moderate ²	
Moderate ¹					
128 per 1000	119 per 1000 (104 to 136)				
High ¹		_			
360 per 1000	335 per 1000 (292 to 382)				
	short term (up to 6		548 (6 studies)	\bigcirc very low ^{2,3,4,5}	-
	eople with schizophre azine Illustrative compara Assumed risk Quetiapine Low ¹ 70 per 1000 Moderate ¹ 128 per 1000 High ¹	eople with schizophrenia hutpatient azine Illustrative comparative risks* (95% Cl) Assumed risk Corresponding risk Quetiapine Chlorpromazine Low ¹ Chlorpromazine 70 per 1000 65 per 1000 (57 to 74) Moderate ¹ 119 per 1000 (104 to 136) High ¹ 360 per 1000 360 per 1000 335 per 1000 (292 to 382) The mean mental state: short term (up to 6 months) in the interven- tion groups was 0.18 lower (1.23 lower to 0.88	eople with schizophrenia autpatient azine Illustrative comparative risks* (95% Cl) Relative effect (95% Cl) Assumed risk Corresponding risk Quetiapine Chlorpromazine Low ¹ RR 0.93 (0.81 to 1.06) 70 per 1000 65 per 1000 (57 to 74) Moderate ¹ (0.81 to 1.06) 128 per 1000 119 per 1000 (104 to 136) High ¹ 360 per 1000 (292 to 382) The mean mental state: short term (up to 6 months) in the intervention groups was 0.18 lower (1.23 lower to 0.88	active intervention is a serie of the set of t	abopte with schizophrenia utpatient zizine Illustrative comparative risks* (95% Cl) Relative effect (95% Cl) Relative effect (95% Cl) Number of participants (studies) Quality of the evidence (studies) Quality of the evidence (GRADE) Assumed risk Corresponding risk Quetiapine Chlorpromazine Low ¹ Chlorpromazine Low ¹ FR 0.93 (0.81 to 1.06) (28 studies) Moderate ¹ 128 per 1000 (19 per 1000 (104 to 136) High ¹ 360 per 1000 335 per 1000 (292 to 382) The mean mental state: short term (up to 6 months) in the interven- tion groups was 0.18 lower (1.23 lower to 0.88 Relative effect Number of participants Quality of the evidence (studies) Number of participants Quality of the evidence (studies) S241 (28 studies) S241 (28 studies)

Chlorpromazine versus atypical antipsychotic drugs for schizophrenia (Review) Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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Quality of life: short term (up to 6 months) GQOL1-74 end- point scale score (high = good) Follow-up: mean 12 weeks		The mean quality of life: short term (up to 6 months) in the interven- tion groups was 6.49 lower (11.3 to 1.68 lower)		59 (1 study)	⊕○○○ - very low ^{6,7,8,9}
Adverse effects: any			RR 8.03	644	⊕⊕⊖⊖ - low ^{2,5}
observed extrapyrami- dal symptoms - short term (up to 6 months) Follow-up: 6 to 8 weeks	36 per 1000	293 per 1000 (174 to 493)	(4.78 to 13.51)	(8 studies)	IOW-12
Follow-up. 6 to 6 weeks	Moderate				
	0 per 1000	0 per 1000 (0 to 0)			
	High				
	80 per 1000	642 per 1000 (382 to 1000)			
Leaving the study early			RR 1.04	1223	
due to any reason short term (up to 6 months) Follow-up: 6 to 16 weeks	93 per 1000	97 per 1000 (72 to 131)	(0.77 to 1.41)	(12 studies)	moderate ²
	High ¹				
	280 per 1000	291 per 1000 (216 to 395)			

*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% CI) 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.

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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.

¹Control risk: are representative of those observed in the study population.

²Risk of bias: serious - most of the included studies had unclear risk of bias in terms of allocation and blinding, hence selection and detection bias are likely to be present. Some of the studies also had high risk of reporting bias.

³Indirectness: serious - binary outcome on mental state is not available. Thus we employed BPRS rating as an indicator.

⁴Imprecision: serious - although the estimate of effect was not significant, the CI was relatively tight around the point of

estimate. The sample size is also relatively large and exceed the calculated optimal information size.

⁵Publication bias: strongly suspected - only Chinese trials with small sample size were identified for this outcome.

⁶Risk of bias: serious - the only study contributed data to this outcome had unclear risk of selection and detection bias. It also had attrition data that we excluded from the final analysis.

⁷Indirectness: serious - there was no binary measurement available on quality of life. Therefore, we used GQOLI-74 as an alternative indicator.

⁸Imprecision: serious - sample size was smaller than the optimal information size.

⁹Publication bias: strongly suspected - we only identified a Chinese trial with a small sample size with positive findings for this outcome.

DISCUSSION

Summary of main results

I. Chlorpromazine versus olanzapine

1.1 Clinical response

Data from included studies indicate that olanzapine is more effective than chlorpromazine when it comes to 'clinical response' outcomes, at least in the short term, since long-term data are equivocal. Notably, each study providing data defined 'clinical response' differently; one study classified response as a decrease in BPRS score, while another measured the number of people who became stabilised on their study medication. The remaining studies did not explain how clinical response was measured. However, regarding average endpoint scores using the CGI, scores were significantly lower in the olanzapine groups. Disappointingly, only one small study (N = 70) provided data for relapse, which demonstrated no significant difference between groups; a result that will need to be confirmed by future large, high-quality RCTs.

1.2 Mental state

These outcomes were difficult to interpret, with most included studies using a different scale of measurement to rate mental state in participants. Clearly there was no significant difference between the two compounds regarding total mean BPRS scores. However there was a significant level of heterogeneity in the studies. The source of this heterogeneity was vs OLZ - Chen 2006 and removal of this study demonstrated a statistically significant difference between groups, in favour of olanzapine. The reasons for this heterogeneity have not been confirmed, since all studies shared a similar setting and used differing dose ranges of chlorpromazine (either 25 to 600 mg/day or 200 to 800 mg/day) and its olanzapine comparator. These findings need clarifying in future studies, as only a small sample provided data (N = 245). Changes in PANSS score were significant, with a greater decrease seen in people receiving olanzapine (N = 351).

1.3 Service involvement

Unfortunately, data for service usage/involvement was seriously lacking; the only study that provided data for re-hospitalisation rates (N = 70) demonstrated an equivocal result between groups.

I.4 Functioning

Data from one study (N = 53) suggest that olanzapine is significantly better at improving functioning, using the WCST. A naturalistic study has suggested that people who received atypicals showed a better cognitive pattern in terms of WCST performance than those on typical antipsychotics (Rossi 2006). However, although this is a test that is generally accepted in schizophrenia research, it has not been widely used in the included studies, making it difficult to confirm this result.

I.5 Adverse effects

Extrapyramidal adverse effects were largely equivocal; only data for 'any observed EPS' event were significant, with more events in people receiving chlorpromazine; however, this finding is based on only two studies (N = 298). There is a strong dataset indicating that chlorpromazine causes significantly greater instances of drowsiness and constipation. Other significant findings, particularly associated with cardiovascular outcomes (palpitation, tachycardia and blood pressure decrease) are only based on the findings of two small RCTs.

1.6 Quality of life

Two different rating scales were used in the two studies that provided data, neither of which were meta-analysed, with skewed data only available using the QoL scale. GQOLI scores show that ratings on specific areas of quality of life (including physical health, psychological health and social functioning) were significantly better in people receiving olanzapine. Again, this is a result that will need to be confirmed with future studies reporting data using these validated scales.

1.7 Leaving the study early

There was no difference between groups for people leaving the studies early for any reason.

2. Chlorpromazine versus risperidone

2.1 Clinical response

Data from the seven included RCTs (N = 475) indicate there is no significant difference between compounds in 'clinical response' (as defined in the different studies). Other global state outcomes are equivocal, with skewed data only available using the CGI, and data equivocal for amounts of participants requiring additional antiparkinsonian medication.

2.2 Mental state

Most included studies measured mental state outcomes using one of the widely-accepted rating scales (BPRS, PANSS or SANS), with data for each subscale demonstrating no significant difference between groups.

2.3 Functioning

Data show significantly better scores for improvement in functioning using the WCST when receiving risperidone. Again, as only one small study reported data for two subscales of the WCST, it is impossible to make a generalisation with this result.

2.4 Adverse effects

Extrapyramidal adverse effects were largely equivocal; however, akathisia was significantly more prominent in people receiving chlorpromazine (31% versus 13%), as was tremor (32% versus 14%). vs RPD - Wang 2002 was the source of heterogeneity in the two aforementioned significant findings, and this was the only study to use a fixed dose of chlorpromazine (400 mg/day) and two further treatment arms of risperidone (4 mg/day or 6 mg/day). Chlorpromazine was also associated significantly with more events of constipation (N = 868), loss of appetite (N = 180), tachycardia (N = 557), hypersalivation (N = 373), blurred vision (N = 387), drop of blood pressure (N = 250) and orthostatic hypotension (N = 546), drowsiness (N = 307) and dizziness (N = 299). However, significantly more people receiving risperidone experienced insomnia (N = 342).

2.5 Quality of life

With only one study providing data using the QoL scale demonstrating significantly greater improvement in people receiving risperidone (N = 100), it is difficult to generalise this finding to a real-world setting.

2.6 Leaving the study early

There was no difference between groups for people leaving the studies early for any reason with roughly equal numbers of participants leaving their groups.

3. Chlorpromazine versus quetiapine

3.1 Clinical response

Data from the 28 included RCTs (N = 3241) indicate there is no significant difference in 'clinical response' (as defined in the different studies) between compounds; however, significantly more people receiving chlorpromazine required additional benzodiazepines or antiparkinsonian drugs. Furthermore, global state outcomes using the CGI are largely equivocal, making it difficult to weigh up any further benefits of either drug taking into account the fact that there was no difference in clinical response.

3.2 Mental state

Mental state outcomes using either the BPRS or PANSS were largely equivocal again, with no significant difference between groups. There were some results that suggested quetiapine was significantly more effective at reducing negative symptoms (using PANSS). However, there was a significant degree of heterogeneity in these results.

3.3 Functioning

Data showed significantly better scores for improvement in functioning using the WCST when receiving quetiapine. Again, with only one small study reporting data for two subscales of the WCST, it is impossible to make a generalisation with this result.

3.4 Adverse effects

Extrapryamidal symptoms were significantly more prominent in people receiving chlorpromazine, particularly with akathisia (N = 1757), 'any' EPS symptom (N = 644), myotonia (N = 1257), torsion movement (N = 1063) and tremor (N = 1343). However, levels of agitation tended to be higher in people receiving quetiapine. Other specific adverse effects, including drowsiness, reduced activity, weight gain, constipation, orthostatic hypotension, tachycardia, hypersalivation, blurred vision and dry mouth, were significantly greater in people receiving chlorpromazine.

3.5 Quality of life

GQOLI scores show that ratings on QoL were significantly better in people receiving quetiapine. Again, this needs to be confirmed with future studies reporting data using this validated scale.

3.6 Leaving the study early

More people left their study early due to adverse effects if they were receiving chlorpromazine; a finding that reflects the expected tolerability of this drug based on the adverse events recorded above. Leaving the studies early for other reasons were not significantly different between groups in the short or medium term.

Overall completeness and applicability of evidence

None of the included studies provided measured outcomes for economic consideration, nor behaviour or satisfaction with treatment or care. These outcomes are important for managers and policy makers' consideration, as well as for carers. Cearly data for 'satisfaction of treatment or care' would provide a basis for evidence of patient acceptability of either compound. No study reported the outcome of death. Reported outcomes were largely clinician oriented, and outcomes including service involvement was underreported, and future studies would need to address this patient

important, policy important outcome. The majority of included studies provided data at the short term only (less than six months), making it impossible to assess any medium or long-term effect either compound has on patients. Several studies were excluded because they did not provide any useable data.

Most included studies included inpatients from hospitals in China. Therefore the results of this Cochrane review are more applicable to the Chinese population and are not particularly suitable to apply to community-treated patients. The dose range employed in most studies was as high as 1000 mg/day, which is far beyond the maximum BNF recommended dosage (BNF 2014). As most studies provided a range as opposed to a mean dosage, it is not possible to generalise these findings to other populations.

Quality of the evidence

Unfortunately, the overall quality of the evidence was poor (see Figure 2; Figure 3 for a graphical overview and summary). No included studies provided details as to randomisation methods and selective reporting was relatively prominent in most included studies. Furthermore, as most studies were undertaken in China (concerns have previously been raised about the quality of reporting in Chinese studies; Anon 2010; Wu 2006), this data requires interpreting with caution as biases may have inflated the estimate of effect in statistically significant outcomes. We identified duplicated data in two studies (vs OLZ - Wu 2008; vs RPD - Wu 2004) where these two studies compared chlorpromazine to olanzapine and risperidone, respectively. vs OLZ - Wu 2008 measured quality of life using the SF-36 scale, and vs RPD - Wu 2004 measured QoL using the GQOLI scale; however the data for these are identical in both studies. The mean scores, SDs and sample size in each group were identical; and we therefore strongly suspect reporting biases, but need to clarify this with the trial authors. In the meantime, we have included the QoL data from vs RPD - Wu 2004, and cross-checked all other data between studies and found no further duplication.

Potential biases in the review process

Chlorpromazine is an old antipsychotic drug that has been extensively compared with other compounds. There exists the possibility that there are unpublished, unidentified studies that we have not included in this review. We strictly adhered to our protocol regarding data extraction and data management. However, we have presented comparisons with chlorpromazine with the specific name of the comparator drug, instead of the planned, generic 'chlorpromazine versus atypical antipsychotics'. We have only included data for three of the drug comparisons and plan in future updated of this Cochrane review to include all other comparator atypical antipsychotics. We also note that due to the size of the 2012 search results, the search date for this review is out-of-date. We intend to re-run a search this year and republish as soon as possible.

Agreements and disagreements with other studies or reviews

This Cochrane review clarifies the evidence relating to the effects of chlorpromazine versus three comparator atypical antipsychotics, namely olanzapine, risperidone and quetiapine. It provides the evidence base for the disputed adverse effect profile, which has been claimed to be more severe in the older, atypical antipsychotics as compared to the newer compounds. However, 96% of the studies from which this data have been derived were undertaken in Chinese hospitals making it difficult to generalise the finding.

AUTHORS' CONCLUSIONS

Implications for practice

I. For people with schizophrenia

Based on weak evidence, chlorpromazine is not much different to risperidone or quetiapine and slightly less effective than olanzapine for levels of clinical response. Chlorpromazine was associated with more extrapyramidal adverse effects, particularly akathisia and tremor compared to risperidone and quetiapine. Risperidone has a lower adverse event profile than any of the other atypical comparators. Generally, chlorpromazine was associated with more, and varied adverse effects. There is a lack of evidence relating to patient-oriented outcomes, including satisfaction with treatment or care and well-reported QoL outcomes.

2. For clinicians

It is surprising how few studies outside of China have investigated the effects of chlorpromazine versus other atypical antipsychotics on people with schizophrenia. Most data relate only to short-term studies; therefore it is impossible to comment on the medium and long-term use of chlorpromazine in the research setting. Chlorpromazine was generally associated with more adverse events. However all studies made use of varying dose ranges; and the use of higher doses would be expected to be associated with greater adverse events. As included studies did not provide mean doses, we could not perform a sensitivity analysis to assess such differences in the results.

3. For managers or policy makers

Included studies reported no data relating to service utilisation, functioning in the community or cost features. Chlorpromazine is a cheap drug compared to new 'atypical' antipsychotics. Therefore, investing some money in research on this drug could be cost saving in the long run.

Implications for research

I. General

Future studies in this area need to be well reported, long term (> one year) and adhere to the Consolidated Standards of Reporting Trials (CONSORT) statement (CONSORT; Moher 2001). This states that all research needs to be clearly and transparently reported, and be accompanied by a flow diagram to simply display the study progress and process.

2. Specific

The trials that met the inclusion criteria of this Cochrane review were all undertaken in China, predominantly in an inpatient surrounding, and focused only on short-term outcomes (average of eight weeks). Further research should be international in scope and fairly representative of other healthcare systems. Outpatient treatment was under-represented in the included studies, and future research should work with this population. More participant focused outcomes (e.g. functioning in social, occupational, family life, satisfaction with care, etc.) and economic considerations could be addressed.

ACKNOWLEDGEMENTS

The editorial base of the Cochrane Schizophrenia Group (Nottingham, UK) produces and maintains standard text for use in the Methods section of their Cochrane reviews. We have used this text and adapted it as required.

We thank Khaled Turkmani for peer reviewing the Cochrane protocol, Martina Rojnic Kuzman for peer reviewing this review version. We would also like to thank Deirdre Walshe for copy editing.

"This project was supported by the National Institute for Health Research, via Cochrane Infrastructure funding to the Schizophrenia Group. The views and opinions expressed therein are those of the authors and do not necessarily reflect those of the Systematic Reviews Programme, NIHR, NHS or the Department of Health."

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies [ordered by study ID]

HGCQ (Turkey) 2000

Methods	Allocation: randomised, blocks, computer-generated, 2:1 for each investigator, concealed from investigators. Blindness: double, medication kits issued. Duration: 6 weeks. Design: parallel 2 centres, Turkey. Setting: inpatients and outpatients.
Participants	Diagnosis: schizophrenia (DSM-IV). Length of illness: informed consent obtained. N = 30. Age: range 18 to 47 years, mean 32.8 years. Sex: male = 17, female = 13. Inclusion criteria: CGI severity at least 4. Excluded: pregnant, seriously unstable illness, including hepatic, renal, gastroenterologic, respiratory, cardiovascular, endocrinologic, neurologic or hematologic disease, glaucoma, uncontrolled thyroid disease, myasthenia gravis, urinary retention, seizures, leucopenia
Interventions	 Chlorpromazine: dose range 200 to 800 mg/day. N = 10. Olanzapine: dose range 5 to 20 mg/day. N = 20.
Outcomes	Leaving the study early. Mental state: BPRS, PANSS. Global state: CGI. Adverse events: ESRS, COSTART list, weight change. Quality of life: VPS, LSEQ. Unable to use: Adverse events: UKU, weight change (no data).

Notes

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer generated randomisation.
Allocation concealment (selection bias)	High risk	No concealment of allocation. Quote: "the bottles were labelled 'Olanzapine' or 'Chlorpromazine' in addition to the study number"

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Risk of bias

HGCQ (Turkey) 2000 (Continued)

Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding.
Blinding of outcome assessment (detection bias) All outcomes	High risk	No blinding, which may introduce detec- tion bias, especially, for those subjective outcomes involving rating scales
Incomplete outcome data (attrition bias) All outcomes	Low risk	Attrition was included in the final analysis.
Selective reporting (reporting bias)	High risk	UKU adverse effect rating scale data and weight change data were not reported
Other bias	Low risk	None obvious.

HGDV (Morocco) 1999

Notes Risk of bias	Adverse events: ESRS, COSTART list, weig		Risk of bias
Outcomes	Leaving study early. Mental state: BPRS, PANSS, MADRS, HAMA. Global state: CGI.		
Interventions	 Olanzapine: dose range 5 to 20 mg/day. N = 27. Chlorpromazine: dose range 200 to 800 mg/day. N = 13. 		
Participants	Diagnosis: schizophrenia (DSM-IV). Length of illness: previously hospitalised (mean ~ 1.5 times), informed consent obtained. N = 40. Age: 18 to 47. Sex: 6 male, 33 female. Setting: inpatients and outpatients. Inclusion criteria: initial CGI severity score of 4. Excluded: pregnant, seriously unstable illness, including hepatic, renal, gastroenterologic, respiratory, cardiovascular, endocrinologic, neurologic or hematologic disease; glaucoma, uncontrolled thyroid disease, myasthenia gravis, urinary retention, seizures, leucopenia		
Methods	Allocation: randomised, computer-generated, blocks for each investigator, 2:1, olanza- pine to chlorpromazine. Blindness: open-label, medication kits issued. Duration: 6 weeks (preceded by washout phase; extension for responders). Design: single centre Morocco.		

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HGDV (Morocco) 1999 (Continued)

Random sequence generation (selection bias)	Low risk	Computer generated randomisation.
Allocation concealment (selection bias)	High risk	No concealment of allocation. Quote: "the bottles were labelled 'Olanzapine' or 'Chlorpromazine' in addition to the study number"
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding. Quote: "This is an open label studypersonnel at the study site, patients and personnel at Lilly were not blinded as to the treatment being administered."
Blinding of outcome assessment (detection bias) All outcomes	High risk	No blinding, which may introduce detec- tion bias, especially, for those subjective outcomes involving rating scales
Incomplete outcome data (attrition bias) All outcomes	Low risk	Two participants left chlorpromazine group early, but were included in the final analysis
Selective reporting (reporting bias)	Low risk	It appears that all measured outcomes were reported.
Other bias	Low risk	None obvious.

vs OLZ - An 2006

Methods	Allocation: randomised, no further information. Blinding: not stated. Duration: 2 years. Design: parallel. Setting: inpatients, China.
Participants	Diagnosis: schizophrenia (CCMD-3). N = 70. Age: mean ~ 27 years, SD ~ 6 years. Sex: male and female. Length of illness: mean ~ 32 months, SD ~ 13 months. Inclusion criteria: PANSS ≥ 60 , length of illness less than 5 years, without organic dis- eases, without history of drug or alcohol dependence, clear of any antipsychotic medi- cation for at least 1 month prior to hospital admission, able to complete cognitive test and consent to participation to the study
Interventions	 Olanzapine: dose range 10.3 ± 4.2 mg/d. N = 35. Chlorpromazine: dose range 240 ± 53 mg/d. N = 35.

vs OLZ - An 2006 (Continued)

Clinical response: number of people stabilised on current medication
Relapse.
Service involvement: re-hospitalisation.
Functioning: executive functioning as measured by WCST.
Leaving the study early.
Unable to use:
Functioning: executive functioning WCST subscale score. The subscales are not validated

Notes

Risk of bias

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, but no detail provided.
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	Eight and 16 people dropped out of olan- zapine and chlorpromazine group respec- tively. The drop out is unlikely to have had any impact on the outcomes measured, ex- cept for WCST (executive functioning) test
Selective reporting (reporting bias)	Low risk	All measured outcomes were reported.
Other bias	Low risk	None obvious.

vs OLZ - Chang 2003

Methods	Allocation: randomised with random number table. Blindness: not reported. Duration: 8 weeks. Design: parallel group. Setting: hospital and community, China.
Participants	Diagnosis: schizophrenia. N = 62. Age: 18 to 53 years.

vs OLZ - Chang 2003 (Continued)

	Sex: male and female. Length of illness: 4 to 5 years. Inclusion criteria: not reported.
Interventions	 Olanzapine: 5 to 20 mg/day. N = 32. Chlorpromazine: 25 to 600 mg/day. N = 30.
Outcomes	Clinical response: no clinically significant improvement*. Mental state: BPRS. Adverse effects.
Notes	*BPRS scale score decreased rate $\leq 29\%$.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomised with random number table.
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 data.
Selective reporting (reporting bias)	High risk	TESS was measured, but not reported.
Other bias	Low risk	None obvious.

vs OLZ - Chen 2006

Methods	Allocation: randomised, no further detail. Blindness: not reported. Duration: 8 weeks. Design: parallel group. Setting: inpatients, China.
Participants	Diagnosis: schizophrenia. N = 86. Age: 20 to 55 years. Sex: male and female.

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vs OLZ - Chen 2006 (Continued)

	Length of illness: 3 months to 5 years; median 2 years. Inclusion criteria: BPRS \geq 30, SAPS \geq 28, SANS \leq 12. Exclusion criteria: severe physical impairment, history of drug or alcohol abuse, pregnant or lactating women
Interventions	 Chlorpromazine: 200 to 800 mg/day. N = 44. Olanzapine: 5 to 20 mg/day. N = 42.
Outcomes	Clinical response: no clinically significant improvement*. Mental state: BPRS and SAPS endpoint scale score. Adverse effects. Unable to use: Mental state: BPRS anxiety - depression subscale data, as it was skewed
Notes	*Unclear how this was assessed.

Risk of bias

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further description.
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 data.
Selective reporting (reporting bias)	High risk	TESS was measured, but not reported.
Other bias	Low risk	None obvious.

vs	OLZ -	He	2003
•••		110	2005

Methods	Allocation: randomised, no further detail. Blindness: not reported. Duration: 8 weeks. Design: parallel group. Setting: inpatients, China.
Participants	Diagnosis: schizophrenia. N = 80. Age: 20 to 55 years. Sex: male and female. Length of illness: olanzapine group = 1.5 ± 3.2 years; chlorpromazine group = 2.2 ± 3.0 years. Inclusion criteria: PANSS ≥ 60 Exclusion criteria: severe liver, renal, heart, haematological diseases; people with glaucoma or history of drug or alcohol abuse, pregnant or lactating women
Interventions	 Chlorpromazine: 100 to 600 mg/day. N = 40. Olanzapine: 5 to 30 mg/day. N = 42.
Outcomes	Mental state: PANSS endpoint scale score, subscale scores. Adverse events.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further description.
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 data.
Selective reporting (reporting bias)	Low risk	All measured outcomes were reported.
Other bias	Low risk	None obvious.

Methods	Allocation: randomised, computer-generated, blocks for each investigator, 2:1, olanza- pine to chlorpromazine, concealed from investigators. Blindness: open label. Duration: 6 weeks (preceded by washout phase of 2 to 9 days; extension for responders) Setting: inpatients and outpatients, multi-centre: two sites, Egypt
Participants	Diagnosis: schizophrenia (DSM-IV). N = 41. Age: range 17 to 47 years, mean 32.3. Sex: male 33, female 8. Inclusion criteria: initial score of at least four on the CGI severity scale. Excluded: pregnant, seriously unstable illness, including hepatic, renal, gastroenterologic, respiratory, cardiovascular, endocrinologic, neurologic or hematologic disease; glaucoma, uncontrolled thyroid disease, myasthenia gravis, urinary retention, seizures, leucopenia
Interventions	 Olanzapine: dose range 5 to 20 mg/day. N = 27. Chlorpromazine: dose range 200 to 800 mg/day. N = 14.
Outcomes	Leaving study early. Mental state: BPRS, PANSS. Global state: CGI-S. Quality of Life Scale: QoL. Adverse events: ESRS, COSTART list, weight change. Unable to use: Adverse events: UKU (no data). Hospital status: (no data). Laboratory tests & physiological measures: (no data).

Notes

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	It's unclear if appropriate tools/methods were used to facility the random allocation. Quote: "qualified patients were assigned by random allocation at Visit 2 to one of the two treatment groups. Randomisation was performed at 2:1 ratio."
Allocation concealment (selection bias)	High risk	No concealment of allocation. Quote: "Medication was dispensed to the patients by the study sitethe bottles were labelled 'Olanzapine' or 'Chlorpromazine' in addi- tion to the study number"

vs OLZ - Loza 1999 (HGDT) (Continued)

Blinding of participants and personnel (performance bias) All outcomes	High risk	This is an open label study.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open label study.
Incomplete outcome data (attrition bias) All outcomes	Low risk	LOCF was used to account for any missing values in the final analysis
Selective reporting (reporting bias)	High risk	Laboratory tests, physiological measures and hospital status, as well as UKU Side Ef- fect Rating Scale scores were not reported
Other bias	Low risk	None obvious.

vs OLZ - Luo 2007

Methods	Allocation: randomised, using computer generated random numbers. Blindness: not reported. Duration: 8 weeks trial period, plus 52 weeks follow-up. Design: parallel group. Setting: inpatients, China.	
Participants	Diagnosis: first episode schizophrenia. N = 50. Age: 18 to 60 years. Sex: male and female. Length of illness: unclear, but stated as first episode schizophrenia. Inclusion criteria: CCMD-3 diagnosed schizophrenia, not receiving any other antipsy- chotic medications in combination Exclusion criteria: simple obesity, hypertension, hypothyroidism, severe heart, liver or renal disease	
Interventions	 Chlorpromazine: 50 to 400 mg/day. N = 20. Olanzapine: 5 to 25 mg/day. N = 30. 	
Outcomes	Cholesterol analysis: TC, TG, LDL, HDL. Adverse effects: weight, sleep time.	
Notes		
Risk of bias	Risk	of bias
Bias	Authors' judgement Support for judgement	

vs OLZ - Luo 2007 (Continued)

Random sequence generation (selection bias)	Low risk	Randomised with computer generated ran- dom numbers.
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	Low risk	Not stated, but most of the outcomes re- ported are objective lab test results, which is unlikely to introduce bias to the study
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete outcome data.
Selective reporting (reporting bias)	Low risk	All measured outcomes are reported.
Other bias	Low risk	None obvious.

vs OLZ - Wang 2002

Methods	Allocation: randomised, using computer generated random numbers. Blindness: not reported. Duration: 8 weeks trial period, plus 52 weeks follow-up. Design: parallel group. Setting: inpatients, China.
Participants	Diagnosis: first episode schizophrenia. N = 60. Age: 18 to 60 years. Sex: male and female. Length of illness: unclear, but stated as first episode schizophrenia. Inclusion criteria: CCMD-3 diagnosed schizophrenia, BPRS > 30 Exclusion criteria: severe organic disease, heart, liver or renal disease, substance misuse induced mental disorders
Interventions	 Chlorpromazine: 25 to 600 mg/day. N = 28. Olanzapine: 5 to 20 mg/day. N = 32.
Outcomes	Clinical response: no significant clinical response*. Mental state: BPRS Adverse effects. Unable to use: Mental state: 'BPRS reducing score', as it's unclear what the trial author meant by this. We are uncertain as to how the score is calculated or what it means
Notes	*Paper did not report on how they measured significant clinical response

vs OLZ - Wang 2002 (Continued)

Risk of bias

Risk of bias			Risk of
Bias	Authors' judgement	Support for judgement	
Random sequence generation (selection bias)	Unclear risk	Randomised, no further information.	
Allocation concealment (selection bias)	Unclear risk	Not stated.	
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open label. Quote: "test and control drugs were administrated openly." p2665	
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated, but most of the outcomes re- ported are objective laboratory test results, which is unlikely to introduce bias to the study	
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete outcome data.	
Selective reporting (reporting bias)	High risk	TESS is measured, but not reported.	
Other bias	Low risk	None obvious.	

vs OLZ - Wang 2008

Methods	Allocation: randomised, no further information. Blindness: not reported. Duration: 1 week washout period, plus 8 weeks trial. Design: parallel group. Setting: inpatients and community patients, China.
Participants	Diagnosis: schizophrenia (CCMD-3). N = 237. Age: mean age ~ 27 years, SD ~ 10 years. Sex: male and female. Length of illness: mean ~ 4 years, SD ~ 5 years. Inclusion criteria: CCMD-3 diagnosed schizophrenia, BPRS > 36, obtained informed consent, lab test results within normal range Exclusion criteria: severe organic disease, heart, liver or renal disease and any other severe mental disorders
Interventions	 Chlorpromazine: 200 to 700 mg/day. N = 119. Olanzapine: 5 to 15 mg/day. N = 118.

vs OLZ - Wang 2008 (Continued)

Outcomes	Mental state: BPRS subscale and endpoint scale score*. NOSIE endpoint scale score* Adverse effects. Leaving the study early. Unable to use: Mental state: unvalidated NOSIE subscale scores.
Notes	*The published BPRS and NOSIE endpoint scale score were implied as 'mean \pm SD', but we suspect they are 'mean \pm SE' for the SDs are extremely tight around the mean. Therefore, we converted these reported SE to SD following SD = SEM X sq rt (N)

Risk of bias

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further information.
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	High risk	Thirteen and 11 people dropped out of Olazapine and chlorpromazine group re- spectively. These people were excluded from final analysis. Reason for drop out were not given
Selective reporting (reporting bias)	Low risk	None obvious. All measured outcomes ap- pear to be reported.
Other bias	Low risk	None obvious.

vs OLZ - Wu 2008

Methods	Allocation: randomised, no further information.
	Blindness: not reported.
	Duration: twelve weeks trial.
	Design: parallel group.
	Setting: inpatients, China.

vs OLZ - Wu 2008 (Continued)

Participants	Diagnosis: schizophrenia (CCMD-3). N = 100. Age: 18 to 60 years. Sex: male and female. Length of illness: mean ~ 4 years, SD ~ 5 years. Inclusion criteria: CCMD-3 diagnosed schizophrenia, PANSS > 60, obtained informed consent Exclusion criteria: severe organic disease, drug or alcohol dependence
Interventions	 Chlorpromazine: 50 to 600 mg/day. N = 50. Olanzapine: 5 to 20 mg/day. N = 50.
Outcomes	Mental state: PANSS subscale and endpoint scale score. NOSIE endpoint scale score Adverse effects. Leaving the study early. Unable to use: Mental state: invalidated SF-36 subscale scores. Quality of life: SF-36 total scale score*.
Notes	*Data derived from this scale overlapped with the QOL data reported in another study published by the same author. Therefore, we decided to report the QOL data that was published earlier (published in 2004) than this paper

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further information.
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 data.
Selective reporting (reporting bias)	Unclear risk	None obvious. All measured outcomes ap- pear to be reported.
Other bias	Low risk	None obvious.

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Methods	Allocation: randomised, no further information. Blindness: not reported. Duration: 8 weeks trial. Design: parallel group. Setting: inpatients and community patients, China.
Participants	Diagnosis: schizophrenia (CCMD-3). N = 61. Age: mean ~ 30 years, SD ~ 9.6 years. Sex: male and female. Length of illness: mean ~ 1.5 years, SD ~ 3 years. Inclusion criteria: CCMD-3 diagnosed schizophrenia, PANSS > 60, obtained informed consent Exclusion criteria: severe organic disease, drug or alcohol dependence, pregnant or lac- tating women, learning disability
Interventions	 Chlorpromazine: 50 to 600 mg/day. N = 29. Olanzapine: 5 to 20 mg/day. N = 32.
Outcomes	Mental state: PANSS subscale and endpoint scale score. Quality of life: QGOLI score. Adverse effects.
Notes	

Risk of bias

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further information.
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 data.
Selective reporting (reporting bias)	Low risk	None obvious. All measured outcomes appear to be reported.
Other bias	Low risk	None obvious.

vs	QTP	- Ai	2007
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Methods	Allocation: randomised, no further detail. Blinding: not reported. Duration: 12 weeks. Setting: inpatients, China.		
Participants	Diagnosis: schizophrenia (CCMD-3). N = 85. Sex: male = 44, female = 41. Age: mean ~ 30 years, SD ~ 11 years. Length of illness: mean ~ 5.8 years, SD ~ 3.3 years. Inclusion criteria: schizophrenia (CCMD-3). Exclusion criteria: severe physical illness.		
Interventions	 Chlorpromazine: 400 to 550 mg/day. Quetiapine: 400 to 750 mg/day. N = 4 		
Outcomes	Clinical response: no clinical improvement*. Mental state: BPRS. Adverse effects.		
Notes	* BPRS decreased rate < 25%.		
Risk of bias			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 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 data.	
Selective reporting (reporting bias)	High risk	TESS measured, but not reported fully.	
Other bias	Low risk	None obvious.	

Methods	Allocation: randomised, no further information. Blindness: not stated. Duration: 8 weeks. Design: parallel. Setting: inpatients, China.
Participants	Diagnosis: schizophrenia (CCMD-2-R). N = 60. Age: 23.7 \pm 5.4 years. Sex*: male = 45, female = 12. Length of illness: 0.8 \pm 0.6 years. Inclusion criteria: first episode schizophrenia (CCMD-2-R), did not receive systematic treatment prior to admission, PANSS \geq 60, length of illness less than 2 years, laboratory tests normal Exclusion criteria: patients with physical or organic diseases
Interventions	 Chlorpromazine: titrated over a 1 week period to a treatment dosage of 200 to 400 mg/d, a further 7 weeks fixed dosage. N = 30. Quetiapine: titrated over one week period to a treatment dosage of 300 to 500 mg/d, followed by a further 7 weeks fixed dosage. N = 30.
Outcomes	Mental state: PANSS positive, negative, general pathology and total score Function: general function as measured by WAIS - RC endpoint subscale score, WMS endpoint subscale score Uable to use unvalidated WMS subscale score.
Notes	*We contacted the trial author for clarification of the number of male and female par- ticipants but didn't receive any reply

Risk of bias

Bias Authors' judgement Support for judgement Random sequence generation (selection Unclear risk Randomised, no further information. bias) Allocation concealment (selection bias) Unclear risk Not stated. Blinding of participants and personnel Unclear risk Not stated. (performance bias) All outcomes Not stated. Blinding of outcome assessment (detection Unclear risk bias) All outcomes Incomplete outcome data (attrition bias) Low risk All patients completed the trial. All outcomes

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vs QTP - An 2005 (Continued)

Selective reporting (reporting bias)	Low risk	All measured outcomes were well reported.
Other bias	Low risk	None obvious.

vs QTP - Cai 2006

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Methods	Allocation: randomised. Blindness: not stated. Duration: 1 week wash out, plus 8 weeks trial. Design: parallel. Setting: inpatients from 8 hospitals, China.
Participants	Diagnosis: schizophrenia (CCMD-3). N = 197. Age: mean ~ 31.1 years, SD ~ 10.1 years. Sex: male = 109, female = 88. Length of illness: mean ~ 5.6 years. Inclusion criteria: BRPS score \geq 36. Exclusion criteria: patients with severe physical diseases, organic disease or pregnant women
Interventions	 Chlorpromazine: chlorpromazine was titrated to a treatment dosage (decided by the doctor). N = 96, no further details were provided. Quetiapine: quetiapine was titrated from 100 mg/d to a treatment dosage (decided by the doctor) which is usually < 800 mg/d. N = 101, no further detail were provided. No ECT or any other antipsychotic medication were combined during the treatment, but benzodiazepine or other medications for adverse effects were allowed
Outcomes	Mental state: decreased rate of BPRS score. Leave the study early**. Adverse effect. Unable to use. Clinical response: no clinical improvement*.
Notes	*The total N of this outcome exceeded the total number of people randomised, therefore, we are unable to determine the true proportion of cases without clinical improvement **We adopted 96 and 101 as the number of participants in the chlorpromazine and quetiapine groups respectively, rather than using 100 and 109 as reported in the paper, as the total of the latter exceeds the number of people randomised

Risk	of bias
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Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details were reported.

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vs QTP - Cai 2006 (Continued)

Allocation concealment (selection bias)	Unclear risk	Not reported.
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	Twelve cases left the study early with no reason reported, but ITT analysis was con- ducted
Selective reporting (reporting bias)	Low risk	All outcomes were reported.
Other bias	Low risk	None obvious.

vs QTP - Cai 2007

Methods	Allocation: randomised, no further detail were reported. Blindness: not reported. Duration: 1 week washout period, plus 8 week trial. Design: parallel. Setting: inpatients, China.
Participants	Diagnosis: schizophrenia (CCMD-3). N = 94. Age: Quetiapine group, range: 18 to 68 years, average: 37.6 ± 15.3 years; chlorpromazine group, range: 19 to 65 years, average: 34 ± 10.5 years Sex: Quetiapine group, male 35, female 13; chlorpromazine group, male 32, female 14. Length of illness: quetiapine group, range: 2 months to 15 years, average: 3.3 ± 3.5 years; chlorpromazine group, range: 3 months to 16 years, average: 3.6 ± 4.3 years Inclusion criteria: PANSS score ≥ 60 . Exclusion criteria: patients with organic mental disorder, alcohol abuse or other drugs abuse, with learning disability, pregnant or breastfeeding women. Patients on slow release depot antipsychotic
Interventions	 Chlorpromazine: chlorpromazine was titrated from a dosage of 100 mg/d to a maximum dosage of 700 mg/d, frequency. N = 46. Quetiapine: Quetiapine was titrated from a dosage of 100 mg/d to a treatment dosage which should be less than 700 mg/d. N = 48.
Outcomes	Clinical response:no clinical improvement*, decreased rate of PANSS score Mental state: PANSS endpoint scale score decreased rate, positive subscale score decreased rate, negative subscale score decreased rate Adverse effect: TESS. Unable to use:

vs QTP - Cai 2007 (Continued)

	Mental state: PANSS subscale scores on cognitive function, agitation and depression. These subscales are not validated
Notes	*Decreased rate of PANSS score: < 25%.

Risk of bias

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further detail were reported.
Allocation concealment (selection bias)	Unclear risk	Not reported.
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	All the patients completed the study.
Selective reporting (reporting bias)	Low risk	All the outcomes were well reported.
Other bias	Low risk	None obvious.

vs QTP - Cao 2005

Methods	Allocation: randomised, no further detail. Blinding: open label. Duration: 16 weeks. Setting: inpatients, China.
Participants	Diagnosis: schizophrenia (CCMD-3). N = 50. Age: 25 to 40 years. Sex: male. Length of illness: not stated. Exclusion: having other mental health problems, other physical illness, drug/alcohol dependent, abnormal lab test results, problematic marital relationships
Interventions	 Chlorpromazine: dosage not stated. N = 25. Quetiapine: dosage not stated. N = 25.

vs QTP - Cao 2005 (Continued)

Outcomes	Leaving the study early. Unable to use: Adverse effects - continuous data was repor Sexual arousal, and other sexual related outco scale	rted, but the scale used was unclear. omes that were measured using an invalidated	_
Notes	Only male participants were included in th	e study; therefore, gender bias is likely	
Risk of bias			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 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	High risk	Drop outs were excluded from analysis.	
Selective reporting (reporting bias)	Low risk	All measured outcomes reported.	
Other bias	Low risk	None obvious.	

vs QTP - Chen 2001

Methods	Allocation: randomised by using random number table. Blinding: double blind, no further detail. Duration: 1 week washout period, plus 8 weeks intervention. Setting: inpatients, multi-centre, China.
Participants	Diagnosis: schizophrenia (CCMD-2-R). N = 221. Sex: male = 113 and female = 108. Age: mean ~ 35 years, SD ~ 11 years. Length of illness: not stated. Inclusion criteria: CCMD-3 diagnosed schizophrenia, BPRS \geq 36. Exclusion criteria: severe heart, renal, liver illness, nerve system illness, hypertension, blood disease, pregnant/lactating women, received ECT within 2 weeks prior to current study, suicidal patients, participated in other clinical trials within 1 month prior to

vs QTP - Chen 2001 (Continued)

	current study
Interventions	 Quetiapine: 200 to 800 mg/day. N = 114. Chlorpromazine: 200 to 800 mg/day. N = 107.
Outcomes	Clinical response: no clinical improvement*, decreased rate of PANSS score Global state: poor compliance, leave the study early. Mental state: BPRS, PANSS. Adverse events.
Notes	*Decreased rate of PANSS score < 25%.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomised using random number table.
Allocation concealment (selection bias)	Low risk	Pharmacist produced identical pills, only they know which pill contains experimen- tal drug
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	ITT was used.
Selective reporting (reporting bias)	Low risk	Outcomes reported as measured.
Other bias	Low risk	None obvious.

vs QTP - Chen 2007

Methods	Allocation: randomised, no further detail. Blinding: not reported. Duration: 3 months. Setting: inpatients and outpatients, Xuzhou, Jiangsu province, China
Participants	Diagnosis: schizophrenia (CCMD-3). N = 62. Sex: male = 33 and female = 29.

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vs QTP - Chen 2007 (Continued)

	Age: mean ~ 20.1 years, SD ~ 2.1 years. Length of illness: average, mean 1.6 years, SD 0.8 years. Inclusion criteria: length of illness between 6 months to 7 years. Exclusion criteria: severe physical illness, drug/alcohol dependent, pregnant/lactating women
Interventions	 Chlorpromazine: 360.3 ± 82.5 mg/day. N = 30. Quetiapine: 300.7 ± 00.3 mg/day. N = 32.
Outcomes	Mental state: PANSS, BPRS. Adverse events. Unable to use: GQOLI-74. Only subscale scores were reported. The subscales were not validated
Notes	*Decreased rate of PANSS score < 25%.

Risk of bias

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomisation, no further detail.
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 data.
Selective reporting (reporting bias)	High risk	Clinical response was measured, but not reported.
Other bias	Low risk	None obvious.

vs QTP	-	Chen	2008
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Methods	Allocation: randomised, no further detail. Blindness: no further detail. Duration: 3 days wash out period, plus 8 weeks trial. Design: parallel. Setting: inpatients, China.		
Participants	Diagnosis: schizophrenia (CCMD-3). N = 60. Age: 18 to 50 years. Sex: male = 33, female = 27. Length of illness: mean ~ 21.25 months, SD ~ 13.90 months; Inclusion criteria: PANSS score ≥ 60 . Exclusion criteria: severe physical diseases or other mental diseases, pregnant or breast- feeding women, allergic to medication		
Interventions	 Chlorpromazine: titrated over a 1 week period from 100 mg/d to 400 to 600 mg/ d. N = 30. Quetiapine: titrated over a 1 week period from 50 mg/d to 300 to 500 mg/d. N = 30. During 8 weeks treatment period, benzodiazepine or anticholinergics agents were used when necessary 		
Outcomes	Clinical response: no clinical improvement* Mental health: PANSS scale score; PANSS negative.		
Notes	*Decreased rate of PANSS score: < 25%		
Risk of bias			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.	

bias)
All outcomesLow riskAll patients completed the trial.Incomplete outcome data (attrition bias)
All outcomesLow riskAll patients completed the trial.Selective reporting (reporting bias)High riskTESS were not fully reported.

Not reported.

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Blinding of outcome assessment (detection Unclear risk

vs QTP - Chen 2008 (Continued)

Other bias	Low risk	None obvious.
vs QTP - Cheng 2003		
Methods	Allocation: Randomised, no further detail. Blindness: not reported. Duration: 8 weeks. Design: parallel. Setting: inpatients, China.	
Participants	Diagnosis: schizophrenia (CCMD-2-R). N = 89. Age: average, 33.1 \pm 10.3 years; chlorpromazine group:34.8 \pm 10.5 years. Sex: quetiapine group: male 20, female 24; chlorpromazine group: male 22, female 23. Length of illness: quetiapine group: 6.4 \pm 5.8 years; chlorpromazine group: 6.4 \pm 5.7 years Inclusion criteria: PANSS score \geq 60. Exclusion criteria: physical impairment.	
Interventions	Chlorpromazine: titrated over a 1 week period from 50 mg/d to 200 mg/d, average dosage in the end of the 4th week post treatment was 400 \pm 150 mg/d and 250 \pm 100 mg/d at the end of 8th week. N = 45 Quetiapine: titrated over a 1 week period from 50 mg/d to 200 mg/d, average dosage in the end of the 4th week post treatment was 450 \pm 250 mg/d and 260 \pm 110 mg/d at the end of 8th week. N = 44	
Outcomes	Global state: CGI*, need of additional non-antipsychotic drugs Mental state: PANSS* Adverse effect: TESS. Leaving the study early. Uable to use: Clinical response, the total number of patients in each group doesn't match the number reported at baseline. We contacted the trial author, but did not receive any response	
Notes		hese two studies were not clearly stated in the paper. We e same number of participants as when randomised
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.

vs QTP - Cheng 2003 (Continued)

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	High risk	Three cases left study early in the quetiap- ine group because of advanced condition; 2 cases left the study early in the chlor- promazine group because of adverse effects. Unclear if these were included in the final analysis
Selective reporting (reporting bias)	Low risk	All the outcomes were well reported.
Other bias	Low risk	None obvious.

vs QTP - Deng 2004

Methods	Allocation: Randomised, no further detail. Blindness: double blind, the medication was put into capsules. Duration: 3 to 7 days of wash out period, plus 12 weeks trial. Design: parallel. Setting: inpatients, China.
Participants	 Diagnosis: schizophrenia (CCMD-2) N = 90. Age: Quetiapine group, range: 18 to 70 years, average: 37.6 ± 15.5 years; chlorpromazine group, range: 20 to 65 years, average: 34.2 ± 10.6 years Sex: quetiapine group: male 20, female 25; chlorpromazine group: male 26, female 19 Length of illness: quetiapine group, 3.3 ± 3.6 years; chlorpromazine group, 3.5 ± 4.2 years Inclusion criteria: Schizophrenia, CCMD-2. BPRS score ≥ 35. Exclusion criteria: severe physical diseases, extremely agitated or restless
Interventions	Chlorpromazine: dosage started from 50 mg/d and increased to 100 mg/d on the 3rd day of treatment, then 150 mg/d on the 5th day. Maintenance dosage: 200 to 800 mg/d. N = 45 Quetiapine: dosage started from 50 mg/d increased to 100 mg/d on the third day of treatment, then 150 mg/d on the fifth day. Maintenance dosage 200 to 800 mg/d. N = 45 Benzodiazepine or benzhexol were used when necessary. Without combination with other antipsychotic drugs

vs QTP - Deng 2004 (Continued)

Outcomes	Clinical response: no clinical improvement*. Effects on physiology: blood test result, liver function.		
Notes	*Decreased rate of BPRS score: < 30%.		
Risk of bias			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	Not reported.	
Incomplete outcome data (attrition bias) All outcomes	Low risk	All included patients completed the trial.	
Selective reporting (reporting bias)	High risk	Clinical response, BPRS, SANS, SAPS and TESS were not reported	
Other bias	Low risk	None obvious.	

vs QTP - Guo 2003a

Methods	Allocation: randomised (by tossing a coin). Blinding: not reported. Duration: 8 weeks. Setting: outpatients, China.
Participants	Diagnosis: schizophrenia (CCMD-3). N = 148. Sex: male (N = 74) and female (N = 74). Age: 18 to 55 years. Length of illness: range, 3 months to 1 year, mean 0.1 year, SD 0.5 year Inclusion: PANSS \geq 60, length of illness < 1 year, not receiving long-acting antipsychotic drugs. Exclusion: severe physical illness, drug/alcohol dependent.
Interventions	 Chlorpromazine: 600 ± 50 mg/day. N = 73. Quetiapine: 450 ± 25 mg/day. N = 75.

vs QTP - Guo 2003a (Continued)

Outcomes	Clinical response: no clinical improvement*, decreased rate of PANSS score Mental state: PANSS (total, positive and negative score). Adverse events. Effects on physiology: laboratory findings. liver function.
Notes	*Decreased rate of PANSS score < 25%.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomised by tossing a coin.
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 data.
Selective reporting (reporting bias)	Low risk	All the outcomes were well reported.
Other bias	Low risk	None obvious.

vs QTP - Guo 2003b

Methods	Allocation: randomised, no further detail. Blinding: single blind, assessor blind. Duration: 3 months. Setting: inpatients, China.
Participants	Diagnosis: schizophrenia (CCMD-3). N = 71. Sex*: male 28 and female 31. Age: 17 to 58 years, mean ~ 26.22 years, SD ~ 6.73 years. Length of illness: mean 5.72 months, SD 3.97 months. Inclusion: PANSS > 60, length of illness < 2 years. Exclusion: severe physical illness, pregnant or breast feeding women

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vs QTP - Guo 2003b (Continued)

Interventions	 Quetiapine: titration period :1 to 2 weeks, average dosage: 300.72 ± 101.25 mg/ d. N = 35. Chlorpromazine: titration period :1 to 2 weeks, average dosage: 360.28 ± 82.45 mg/d. N = 35. Antan was used when EPS appears, no other antipsychotic drugs were used during treatment
Outcomes	Mental state: PANSS (total, positive and negative score). Leave the study early. Adverse events. Effects on physiology: laboratory findings. liver function. Unable to use: WHO-QOL-100, no scale scores reported and the subscales were not validated
Notes	*The total number of male and female participants does not match to the total number randomised

Risk of bias

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further detail.
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	High risk	Five patients left the study early in the que- tiapine group, 6 patients left the study early in the chlorpromazine group, without any reason reported. No ITT analysis was ap- plied
Selective reporting (reporting bias)	Low risk	All the outcomes were well reported
Other bias	Low risk	None obvious.

Methods	Allocation: randomised, no further detail reported. Blindness: not stated. Duration: 3 days wash out period, plus 8 weeks trial. Design: parallel. Setting: inpatients, China.
Participants	Diagnosis: schizophrenia (CCMD-3). N = 80. Age: 16 to 57 years, mean ~ 28.3 years, SD ~ 10.2 years. Sex: male = 42, female = 38. Length of illness: 2 months to 10 years; mean ~ 6.5 years, SD ~ 5.9 years Inclusion criteria: PANSS \geq 60. Exclusion criteria: severe physical impairment or other mental disorders, pregnant or breastfeeding women, allergic to medication
Interventions	1. Chlorpromazine: titrated over a 1 week period from 100 mg/d to a treatment dosage of 400 to 600 mg/d. N = 40. 2. Quetiapine: titrated over a 1 week period from 50 mg/d to a treatment dosage of 300 to 500 mg/d. N = 40. Antan was used for EPS; alprazolam was used for insomnia or anxiety; β -blokers was used for tachycardia Liver function, ECG and blood test were measured at baseline, 2, 4 and 8 weeks post- treatment
Outcomes	Clinical response: no clinical improvement*. Globle state: need for non-antipsychotic drugs. Mental state: PANSS scale score, positive score, negative score, general pathological score Adverse effects: TESS.
Notes	*Decreased rate of PANSS score < 20%.

Risk of bias

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details reported.
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	All the patients completed the trial.

vs QTP - Guo 2005 (Continued)

Selective reporting (reporting bias)	Low risk	All measured outcomes were reported.
Other bias	Low risk	None obvious.

vs QTP - Guo 2006

Methods	Allocation: randomised, no further details. Blindness: not stated. Duration: 8 weeks. Design: parallel. Setting: inpatients, China.
Participants	Diagnosis: schizophrenia (CCMD-3). N = 130. Age: mean ~ 33 years, SD ~ 11 years. Sex: male = 57, female = 73. Length of illness: not stated. Inclusion criteria: FBG < 6.7 mmol/L, without use of antipsychotic, antidepressant or any other medication having an influence on the metabolites of blood glucose or blood lipid Exclusion criteria: disturbance of carbohydrate or lipid metabolics, severe physical im- pairments
Interventions	 Chlorpromazine: chlorpromazine titrated over a 2-week period from 50 mg/d to 200 to 800 mg/d. N = 65. Quetiapine: quetiapine titrated over a 2-week period from 50 mg/d to 200 to 800 mg/d. N = 65. Without combination of antipsychotic, antidepressant, or any other medication having a influence on the metabolites of blood glucose or blood lipid
Outcomes	Adverse effects: weight gain/loss. Effects on physiology: blood glucose, cholesterol.
Notes	This trial was funded by the National Science and Technology Research Fund

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.

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vs QTP - Guo 2006 (Continued)

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported.
Incomplete outcome data (attrition bias) All outcomes	Low risk	All randomised patients completed this trial.
Selective reporting (reporting bias)	Low risk	All outcomes were reported.
Other bias	Low risk	None obvious.

vs QTP - Guo 2007

Methods	Allocation: randomised, no further detail. Blinding: not reported. Duration: 8 weeks. Setting: inpatients and outpatients, Kangning hospital, Guangzhou city, China
Participants	Diagnosis: schizophrenia (CCMD-3). N = 52. Age: 18 to 40 years, mean ~ 26.8 years, SD ~ 4.2 years. Sex: male = 23, female = 29. Length of illness: 0.5 to 2 years, mean ~ 1.1 years, SD ~ 0.6 years Inclusion: PANSS \geq 60, CGI-SI \geq 4. Exclusion: organic brain diseases, severe physical illness, drug/alcohol dependent, preg- nant/lactating women
Interventions	 Chlorpromazine: 300 to 500 mg/day. N = 26. Quetiapine: 600 to 800 mg/day. N = 26. Antan or propranolol were used when necessary.
Outcomes	Global state: CGI-S, CGI-I. Mental state: PANSS. Function: global function WCST. Adverse events. Unable to use: WCST subcale score, as it is not validated.
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 stated.
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vs QTP - Guo 2007 (Continued)

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 data.
Selective reporting (reporting bias)	High risk	TESS was measured, but not reported.
Other bias	Low risk	None obvious.

vs QTP - Guo 2008

Methods	Allocation: randomised, using random number table. Blindness: double-blind, patients and assessor were blinded. Duration: 16 weeks. Design: parallel. Setting: inpatients, China.
Participants	Diagnosis: schizophrenia (CCMD-3). N = 86. Age: mean ~ 30 years, SD ~ 10 years. Sex: male = 39, female = 44. Length of illness: less than 1 year: 57 cases; more than 1 year: 26 cases Inclusion criteria: PANSS \geq 60. Exclusion criteria: organic diseases or severe cardiac, liver, kidney diseases, patients re- ceiving 2 or more antipsychotic drugs, patients taking antipsychotic drugs 1 week before randomisation
Interventions	 Chlorpromazine: < 1000 mg. N = 40. Quetiapine: initial dosage is 100 mg/d, titrated to a treatment dosage (exact dosage not reported), N = 46.
Outcomes	Clinical response: no clinical improvement* Mental state: PANSS. Quality of life: WHO-QOL-100 endpoint scale score. Adverse effect: TESS. Effects of physiology: laboratory findings,blood count, cholesterol, glucose, liver function Leave the study early. Unable to use: WHO-QOL-100 subscale score. The subscales were not validated
Notes	*Decreased rate of PANSS score < 50%.

vs QTP - Guo 2008 (Continued)

Risk of bias

Risk of bias		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomised by using random number ta- ble.
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	A total of 3 patients in the quetiapine group left the study early: 1 case left due lack of efficacy, 2 cases due to adverse effects. ITT was employed in the final result analysis
Selective reporting (reporting bias)	Low risk	All the outcomes were reported.
Other bias	Low risk	None obvious.

vs QTP - He 2003

Methods	Allocation: randomised, no further details. Blinding: open label. Duration: six weeks. Setting: Jiangsu City, China.
Participants	Diagnosis: schizophrenia (CCMD-2-R). N = 40. Sex: male 24, female 16. Age: 18 to 50 years, mean ~ 32.4 years, SD ~ 8.1 years. Length of illness: one month to 10 years, mean 4.3 years, SD 3.4 years Inclusion criteria: PANSS $\geq 60.$ Exclusion criteria: severe physical illness, alcohol/drug abuse, pregnant/lactating women
Interventions	 Chlorpromazine: 468 ± 39 mg/day. N = 20. Quetiapine: 433 ± 19 mg/day. N = 20.
Outcomes	Clinical improvement: no clinical improvement*. Mental state: PANSS endpoint scale score, positive, negative, general pathology score Adverse effects.

vs QTP - He 2003 (Continued)

Notes	*Decreased rate of PANSS score < 40%.		
Risk of bias			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 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 data.	
Selective reporting (reporting bias)	Low risk	All the outcomes were well reported.	
Other bias	Low risk	None obvious.	

vs QTP - Hu 2003

Methods	Allocation: randomised, no further detail. Blinding: not reported. Duration: 4 weeks. Setting: inpatients, Mental health centre, Sichuan, China.
Participants	Diagnosis: schizophrenia (DSM-IV), first onset, inpatients. N = 41. Sex: male Age: mean ~ 26.94 years, SD ~ 8.82 years. Length of illness: not reported. Exclusion: severe physical illness, lactating/pregnant women
Interventions	 Chlorpromazine: 350 ± 67.8 mg/d. N = 19. Quetiapine: 410 ± 108.77 mg/d. N = 22.
Outcomes	Mental state: PANSS (positive, negative, general psychopathology subscale) Adverse effects: TESS, RSESE. Unable to use: GAF score - some data missing.
Notes	

vs QTP - Hu 2003 (Continued)

Risk of bias

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 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 data.
Selective reporting (reporting bias)	Low risk	Evidence of selective reporting was no found.
Other bias	Low risk	None obvious.

vs QTP - Ji 2004

Methods	Allocation: randomised, no further detail. Blinding: not reported. Duration: 3 months. Setting: inpatients, China.
Participants	Diagnosis: schizophrenia (CCMD-3). N = 66. Age: 18 to 45 years, mean ~ 25.6 years, SD ~ 7 years. Sex: male = 33 and female = 26. Length of illness: mean ~ 1.6 years, SD ~ 0.5 years. Inclusion: PANSS \geq 60. Exclusion: patients with severe physical illnesses, drug or alcohol dependency, pregnant or lactating women
Interventions	 Chlorpromazine: average dosage, 507 ± 27.8 mg/d. N = 33. Quetiapine: average dosage,501.2 ± 31.2 mg/d. N = 33.
Outcomes	Global state: poor compliance, leave the study early. Mental state: PANSS total, negative, positive, general psychopathology score. Quality of life: GQOLI - 74 endpoint scale score. Adverse effects.

vs QTP - Ji 2004 (Continued)

Uable to use: Quality of life:GQOLI - 74 subscale score. These subscales were not validated

Notes

Risk of bias

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 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	High risk	Four patients in the chlorpromazine group left the study early, 3 patients in the que- tiapine group left the study early, all due to adverse effects. Dropouts were excluded from analysis	
Selective reporting (reporting bias)	Low risk	Evidence of selective reporting was not found.	
Other bias	Low risk	None obvious.	

vs QTP - Jiang 2006

Methods	Allocation: randomised, no further details. Blinding: not reported. Duration: 8 weeks. Setting: inpatients, China.
Participants	Diagnosis: schizophrenia (CCMD-3). N = 191. Age: mean ~ 34 years, SD ~ 9.7 years. Sex: not reported. Length of illness: duration ill mean 58 months, SD 68 months Inclusion: PANSS \geq 60, or a score of at least 3 on two or more of the PANSS items 'delusion', 'hallucination', 'Incoherence', 'suspiciousness', 'persecution'. Exclusion: severe physical illness, drug/alcohol dependent, received experimental drugs within 4 weeks prior to the trial

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vs QTP - Jiang 2006 (Continued)

Interventions	 Chlorpromazine: 100 to 600 mg/d. N = 97. Quetiapine: 100 to 800 mg/d. N = 94.
Outcomes	Clinical response: no clinical improvement*. Adverse events: TESS. Effects on physiology: laboratory findings. Leave the study early. Unable to use: PANSS score, this data is not reported.
Notes	*No clinical improvement: decreased rate of PANSS score < 30%

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	Not reported.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Twenty-one cases in the quetiapine group left the study early, 5 cases because of agi- tation, 10 because of abnormal liver func- tion, 1 because of orthostatic hypotension, 5 cases lost to follow-up. Twenty cases in the chlorpromazine group left the study early: 17 cases because of adverse effects and 3 were lost to follow-up. The drop-out cases were also reported
Selective reporting (reporting bias)	High risk	PANSS measured, but not reported.
Other bias	Low risk	None obvious.

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Methods	Allocation: randomised, no further detail. Blinding: not stated. Duration: 6 weeks. Setting: inpatient, China.
Participants	Diagnosis: schizophrenia (CCMD-3). Sex: male = 36, female = 24. Age: 18 to 60 years, mean ~ 33.54 years, SD ~ 5.26 years N = 60. Length of illness: mean ~ 8.24 years, SD ~ 3.15 years. Inclusion criteria: PANSS \geq 60, patients who weren't receiving any antipsychotic drugs before randomisation, or with a suspension of antipsychotic drugs at least 1 week before randomisation. Exclusion criteria: severe physical illness, organic brain disease, drug abuse, pregnant/ lactating women, allergic to the medication
Interventions	 Chlorpromazine: 300 to 800 mg/d. N = 30. Quetiapine: 300 to 800 mg/d. N = 30. Antan or benzodiazepine were used when necessary, no other antipsychotic medication were used during treatment course
Outcomes	Clinical improvement: no clinical improvement*. Mental state: PANSS and BPRS endpoint total score. Measured at baseline, 2, 4 and 6 weeks post treatment. Adverse events: TESS.
Notes	*Decreased rate of PANSS score < 25%.

Risk of bias

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	Not reported.
Incomplete outcome data (attrition bias) All outcomes	Low risk	All included patients completed the trial.
Selective reporting (reporting bias)	High risk	TESS were not fully reported.

vs QTP - Jiang 2008 (Continued)

Other bias	Low risk	None obvious.	
vs QTP - Jin 2007			
Methods	Allocation: randomised, no further details. Blinding: not reported. Duration: 4 weeks. Setting: outpatients and inpatients, Hebei province, China.		
Participants	Diagnosis: schizophrenia (CCMD-3). N = 60. Sex: male = 33 and female = 27. Age: 18 to 60 years. Length of illness: 1 to 24 months. Exclusion: severe physical illness, drug abuse, pregnant/lactating women, allergic to either of the intervention drugs		
Interventions	 Chlorpromazine: 200 to 600 mg/day. N = 30. Quetiapine: 200 to 800 mg/day. N = 30. 		
Outcomes	Clinical response: no clinical improvement*, decreased rate of PANSS score Adverse effects.		
Notes	*Decreased rate of PANSS score < 25%.		
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 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 data.	
Selective reporting (reporting bias)	High risk	TESS measured, but not reported.	
Other bias	Low risk	None obvious.	

vs QTP -	Kong 2003
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Methods	Allocation: randomised, no further details. Blinding: not reported. Duration: 6 weeks. Setting: outpatients, China.		
Participants	Diagnosis: schizophrenia (CCMD-3). N = 30. Sex: male 8, female 22. Age: mean 26 to 38 years. Length of illness: 0.5 to 5 years. Inclusion: patients did not take antipsychotic drugs 1 week before randomisation, with- out cardiac, liver, kidney or endocrine diseases. Exclusion: lactating/pregnant women.		
Interventions	 Chlorpromazine: 200 to 400 mg/d. N Quetiapine: 300 to 500 mg/d. N = 15 		_
Outcomes	Effects on physiology: laboratory findings.		_
Notes			
Risk of bias		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	Not reported.	
Incomplete outcome data (attrition bias) All outcomes	Low risk	All included patients completed the trial.	
Selective reporting (reporting bias)	Low risk	All outcomes were reported.	_
Other bias	Low risk	None obvious.	

vs QTP - Li	2003
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Methods	Allocation: randomised, no further details. Blinding: not reported. Duration: 6 months. Setting: inpatients and outpatients, mental health centre, Shandong, China		
Participants	Diagnosis: schizophrenia (CCMD-2-R). N = 103. Sex: male 36, female 31. Age: 18 to 56 years, mean ~ 31.3 years, SD ~ 9.5 years. Length of illness: mean ~ 1.3 years, SD ~ 2.0 years. Inclusion: schizophrenia, CCMD-3; PANSS ≥ 60. Exclusion: severe physical illness, drug/alcohol dependent, pregnant/lactating women		
Interventions	 Chlorpromazine: 503 ± 134 mg/day. N = 51. Quetiapine: 482 ± 124 mg/day. N = 52. 		
Outcomes	Mental state: PANSS scores. Adverse effects: TESS scores. Unable to use: Quality of life: WHO-QOL-100 subscale scores. The subscales were not validated		
Notes			
Risk of bias			Risk of bias
Bias	Authors' judgement	Support for judgement	
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details.	

bias)		
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	High risk	Twelve cases left the study early in quetiap- ine group; 14 patients left the study early in chlorpromazine group. The reasons for dropout were either lack of efficacy or ad- verse effects. ITT was not used
Selective reporting (reporting bias)	Low risk	We did not find any evidence of selective reporting.

vs QTP - Li 2003 (Continued)

Other bias	Low risk	None obvious.
vs QTP - Li 2010		
Methods	Allocation: randomised, no further de Blinding: not reported. Duration: 6 weeks. Setting: inpatients, China.	tail.
Participants	Diagnosis: schizophrenia (CCMD-3). N = 64. Sex: male = 37 and female = 27. Age: mean ~ 27.9 years, SD ~ 7.22 ye Length of illness: mean 32 months, SI Inclusion: schizophrenia, CCMD-3. Exclusion: not reported.	ars.
Interventions	 Chlorpromazine: 550 ± 12.5 mg Quetiapine: 500 ± 17.5 mg/day. 	
Outcomes	Leave the study early. Mental state: HAMD scores.	
Notes		
Risk of bias		H
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	One case in the chlorpromazine group left the study early. Reason not stated, neither was it included in the final analysis
Selective reporting (reporting bias)	Low risk	All the outcomes were well reported.

vs QTP - Li 2010 (Continued)

Other bias	Low risk	None obvious.	
vs QTP - Liu 2003			
Methods	Allocation: randomised, no Blinding: not reported. Duration: 6 weeks. Setting: inpatients, China.	Duration: 6 weeks.	
Participants	e	= 38.	
Interventions	day. N = 44.	2. Chlorpromazine: titrated upwards from initial dosage of 50 mg/d to 200 to 350	
Outcomes	Clinical response: no clinica Mental state: PANSS scores Adverse effects: TESS score Effects on physiology: labor	- 3.	
Notes	*Decreased rate of PANSS	score < 40%.	

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	Not reported.
Incomplete outcome data (attrition bias) All outcomes	Low risk	All included patients completed the trial.

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vs QTP - Liu 2003 (Continued)

Selective reporting (reporting bias)	Unclear risk	TESS were not well reported.
Other bias	Low risk	None obvious.

vs QTP - Mei 2007

Methods	Allocation: randomised, no further details. Blinding: not reported. Duration: 3 days wash out period, plus 8 weeks trial. Setting: inpatients, China.
Participants	Diagnosis: schizophrenia (CCMD-3). N = 96. Sex: male = 43, female = 53. Age: 17 to 60 years, mean ~ 29.4 years, SD ~ 11.5 years. Length of illness: 3 months to 12 years, median = 6.1 years. Inclusion: PANSS \geq 60, patients did not take antipsychotic drugs within 1 week before admission. patients did not accept long-acting antipsychotic drugs within one month before admission. Exclusion: severe physical illness, organic brain diseases, drug/alcohol dependent, preg- nant or breastfeeding women
Interventions	 Chlorpromazine: 425 ± 106 mg/day. N = 49. Quetiapine: 600 ± 50 mg/day. N = 47. No other antipsychotic drugs were used during treatment, but some medications was used for EPS
Outcomes	Clinical response: no clinical improvement*. Mental state: PANSS. Adverse events. Effects of physiology: Laboratory findings.(blood glucose, serum prolactin)
Notes	*PANSS decreased rate < 25%.

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 stated.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not stated.

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vs QTP - Mei 2007 (Continued)

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.
Selective reporting (reporting bias)	Low risk	All outcomes were reported.
Other bias	Low risk	None obvious.

vs QTP - Nai 2007

Methods	Allocation: randomised, no further details. Blinding: not reported. Duration: 3 days wash out period, plus 8 weeks trial. Setting: inpatients, China.
Participants	Diagnosis: schizophrenia (CCMD-3). N = 120. Sex: male = 63, female = 57. Age: 18 to 45 years, mean ~ 28 years, SD ~ 7.9 years. Length of illness: 1 month to 24 months. Inclusion: primary schizophrenia, without taking any antipsychotic drugs, PANSS \geq 60, did not take antipsychotic drugs within 1 week before admission, did not accept long-acting antipsychotic drugs within one month before admission. Exclusion: severe physical illness, pregnant or breastfeeding women
Interventions	 Chlorpromazine: 100 to 450 mg/day. N = 60. Quetiapine: 300 to 750 mg/day. N = 60. No other antipsychotic drugs will be used during treatment course, but Antan or benzodiazepine were used when necessary
Outcomes	Function: global function, WCST-IQ, WCST-MQ scores. Unable to use: WCST subscale scores were not validated.
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 stated.

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vs QTP - Nai 2007 (Continued)

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	All included patients completed the trial.
Selective reporting (reporting bias)	High risk	PANSS were not well reported.
Other bias	Low risk	None obvious.

vs QTP - NCT00882518

Methods	Allocation: randomised, no further detail reported. Blindness: double-blind, patients, caregiver and investigator were blinded. Duration: 6 weeks. Design: parallel. Setting: inpatients, China.
Participants	Diagnosis: schizophrenia. N = 388. Age: mean ~ 32.5 years, SD ~ 10.52 years. Sex: male = 202, female = 182. Length of illness: not reported. Inclusion criteria: patients gave written informed consent. Exclusion criteria: AIDs or hepatitis, History of epilepsy, hospitalised for schizophrenic disorder 1 month prior to entering into study
Interventions	 Chlorpromazine: The initial dose was 50 to 100 mg/d then increased to a treatment dosage varying between 300 to 600 mg/d. N = 192. Quetiapine: the initial dose was 300 mg/d then increased to a treatment dosage varying between 400 to 800 mg/d. N = 196.
Outcomes	Clinical response: no clinical improvement [*] . Global state: CGI, CGI severity of illness score, poor compliance, leave the study early ^{**} Mental state: PANSS scale score, positive score, negative score, general pathological score. PANSS aggression score, depression clusters score Adverse effects. Unable to use: PANSS aggression score, depression clusters score. The subscale is not validated
Notes	*Decreased rate of PANSS score < 30%. **Patients who left the study early were categorised by the following reasons: "withdrawal by subject" , "severe non - compliance to protocol" , "incorrect enrolment" , "central lab

vs QTP - NCT00882518 (Continued)

closure for national day" as "any reason" in our meta analysis. We added the number of these patients and imputed the total number into our meta analysis

Risk of bias		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details were re- ported.
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	High risk	Thirty-eight patients in the quetiapine group and 44 patients in the chlorpro- mazine group left the study early and no ITT analysis were applied. Among them, 9 patients in the quetiapine group and 18 patients in the chlorpromazine group left because of adverse effects. Twelve patients in the quetiapine group and 9 patients in the chlorpromazine group left due to lack of efficacy
Selective reporting (reporting bias)	Low risk	All the outcomes were well reported.
Other bias	High risk	The study was sponsored by AstraZenenca- -the producer of quetiapine fumarate ex- tended-release (SEROQUEL-XR)

vs QTP - Peng 2006

Methods	Allocation: randomised using random number table. Blinding: double-blind, patients, investigator and assessor were blinded. Duration: 42 days. Setting: inpatients, West China Hospital, Sichuan, China.
Participants	Diagnosis: schizophrenia (CCMD-3). N = 40. Age: mean ~ 30.6 years, SD ~ 11.26 years. Sex: male and female

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vs QTP - Peng 2006 (Continued)

	Length of illness: mean ~ 28.5 years, SD ~ 6.45years Exclusion: not stated.
Interventions	 Chlorpromazine: 473.61 ± 107.26 mg/day. N = 20. Quetiapine: 555.56 ± 137.74 mg/day. N = 20.
Outcomes	Globle state: poor compliance, leaving the study early. Unable to use: PANSS, BPRS, TESS, RSESE scores - no SD reported.
Notes	

Risk of bias

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomised using random number table.
Allocation concealment (selection bias)	Unclear risk	Not stated.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Double blind, but untested.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Assessor blind.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Unclear whether people dropped out are included in the analysis
Selective reporting (reporting bias)	Low risk	No evidence of selective reporting.
Other bias	Low risk	None obvious.

vs QTP - Peuskens 1997

Methods	Allocation: randomised, no further detail. Blinding: double blind, investigator-blinded, no further details. Duration: six weeks. Design: parallel, multicentre. Setting: Belgium, UK, Spain, France, South Africa.
Participants	Diagnosis: schizophrenia, schizophreniform disorder (DSM-III-R). N = 201. Sex: male = 129, female = 72. Age: 18 to 65 years.

vs QTP - Peuskens 1997 (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	Not reported.

vs QTP - Peuskens 1997 (Continued)

Incomplete outcome data (attrition bias) All outcomes	Low risk	Data for leaving study early were available. ITT method was not used but overall dis- continuation rate was low (2.5%)
Selective reporting (reporting bias)	Low risk	Evidence of selective reporting was not found.
Other bias	High risk	Sponsored by manufacturer of quetiapine AstraZenenca.

vs QTP - Sun 2006

Methods	Allocation: randomised, no further details. Blinding: not reported. Duration: 8 weeks. Setting: inpatients, China.
Participants	Diagnosis: schizophrenia (CCMD-3). N = 71. Sex: male = 46 and female = 25. Age: mean ~ 26.3 years, SD ~ 5.9 years. Length of illness: mean ~ 1.2 years, SD ~ 0.6 years. Inclusion: first episode schizophrenia and no history of taking antipsychotic drugs, PANSS \geq 60. Exclusion: severe physical disease, pregnant or breastfeeding women, allergic to the related medication
Interventions	 Chlorpromazine: mean ~ 485 mg/d, SD ~ 132 mg/d. N = 36. Quetiapine: mean ~ 530 mg/d, SD ~ 128 mg/d. N = 35. No combination with other antipsychotic drugs.Benzodiazepine, anticholinergic medication or propranolol was used for adverse effects
Outcomes	Mental state: PANSS total score, positive score, negative score, general pathological score Function: Global function-WCST endpoint total score, WMS-RC endpoint total score Unable to use: WCST, WMS-RS subscale score. The subscale is not validated. NCT total and subscale score. The NCT scale is not validated
Notes	

Risk of bias

Risk of bias

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

vs QTP - Sun 2006 (Continued)

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	All included patients completed this trial.
Selective reporting (reporting bias)	Low risk	All outcomes were reported.
Other bias	Low risk	None obvious.

vs QTP - Tian 2006

Methods	Allocation: randomised, no further details reported. Blinding: not reported. Duration: 8 weeks. Setting: inpatients and outpatients, China.		
Participants	Diagnosis: schizophrenia (CCMD-3). Paticipant: N = 92. Sex: male = 35 and female = 57. Age: 18 to 61 years, mean ~ 27.8 years, SD ~ 8.4 years. Length of illness: mean ~ 6.2 years, SD ~ 4.2 years. Inclusion: schizophrenia. Exclusion: severe physical illness, drug/alcohol dependent, pregnant/lactating women, aggressive and suicidal patients		
Interventions	 Chlorpromazine: 420 ± 67.2 mg/day. N = 46. Quetiapine: 421 ± 18 mg/day. N = 46. 		
Outcomes	Clinical response: no clinical improvement [*] . Mental state: PANSS score,positive score, negative score and general pathological score Adverse effects.		
Notes	*Decreased rate of PANSS score < 25%.		
Risk of bias	Ris		Risk of bias
Bias	Authors' judgement	Support for judgement	
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details provided.	
Allocation concealment (selection bias)	Unclear risk	Not stated.	

vs QTP - Tian 2006 (Continued)

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 data.
Selective reporting (reporting bias)	Low risk	We did not find any evidence of selective reporting.
Other bias	Low risk	None obvious.

vs QTP - Wan 2002

Bias	Authors' judgement	Support	for judgement	
Risk of bias		H		Risk of bias
Notes	*No clinical improvement: decrease oration	*No clinical improvement: decreased rate of PANSS score \leq 29% or symptoms deterioration		
Outcomes		Clinical response: no clinical improvement*. Mental state: PANSS scores (total, positive, negative and general pathological) Adverse effect: TESS.		_
Interventions	2. Quetiapine: 300 to 750 mg/d. No other antipsychotic drugs were	 Chlorpromazine: 300 to 750 mg/d. N = 30. Quetiapine: 300 to 750 mg/d. N = 30. No other antipsychotic drugs were used during treatment course, but Antan or benzo- diazepine were used when necessary 		
Participants	N = 60. Sex: not reported. Age: 18 to 60 years. Length of illness: not reported. Inclusion: first episode schizophren	Sex: not reported. Age: 18 to 60 years. Length of illness: not reported. Inclusion: first episode schizophrenia, PANSS ≥ 60 . Exclusion: organic diseases, severe physical illness, alcohol or drug abuse, pregnant or		
Methods	Allocation: randomised, no further Blinding: double-blind. Duration: 6 weeks. Setting: inpatients, China.	Duration: 6 weeks.		_

vs QTP - Wan 2002 (Continued)

Random sequence generation (selection bias)	Unclear risk	Randomised, no further information.
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	All included patients completed the trial.
Selective reporting (reporting bias)	High risk	SAS were not reported.
Other bias	Low risk	None obvious.

vs QTP - Wan 2008

Methods	Allocation: randomised, no further information. Blinding: not reported. Duration: 6 weeks. Setting: inpatients, China.
Participants	Diagnosis: schizophrenia (CCMD-3). N = 60. Sex: male = 32, female = 28. Age: 18 to 60 years, mean ~ 33.54 years, SD ~ 5.26 years. Length of illness: mean ~ 8.24 years, SD ~ 3.15 years. Inclusion: PANSS ≥ 60 , have no history of taking antipsychotic drugs or suspended antipsychotic drugs for 1 week before randomisation. Exclusion: organic brain diseases, severe physical illness, alcohol or drug abuse, pregnant or breastfeeding women
Interventions	 Chlorpromazine: 300 to 800 mg/d. N = 30. Quetiapine: 300 to 800 mg/d. N = 30. No other antipsychotic drugs were used during treatment course, but Antan or benzo- diazepine were used when necessary
Outcomes	Clinical response: no clinical improvement*. Mental state: PANSS total score,BPRS total score. Adverse effect: TESS
Notes	*Decreased rate of PANSS score \leq 29% or symptoms deterioration

vs QTP - Wan 2008 (Continued)

Risk of bias

Risk of bias		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further information pro- vided.
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	All the patients completed the trial.
Selective reporting (reporting bias)	Low risk	All the outcomes were well reported.
Other bias	Low risk	None obvious.

vs QTP - Wang 2004

Methods	Allocation: randomised, no further details provided. Blinding: no details. Duration: 6 weeks. Setting: inpatients, Guangzhou Mental Health Hospital, China
Participants	Diagnosis: schizophrenia (CCMD-3). N = 96. Sex: male and female. Age: 19 to 58 years. Length of illness: 2 months to 14 years. Exclusion criteria: pregnant/lactating women, drug/alcohol dependent patients, severe physical illness, took quetiapine or chlorpromazine within 4 weeks prior to the study, suicidal, allergic to any of the intervention drugs, participated in other clinical trials within 30 days prior to the current study
Interventions	 Chlorpromazine: 300 to 750 mg/day. N = 48. Quetiapine: 300 to 750 mg/day. N = 48.
Outcomes	Leaving the study early. Mental state: PANSS (total, positive, negative,general psychopathology subscale) Global state: CGI endpoint total improvement score, illness severity score, no clinical improvement*

vs QTP - Wang 2004 (Continued)

	Adverse effects.		
Notes	*PANSS decreased rate < 30%.		
Risk of bias			Ris
Bias	Authors' judgement	Support for judgement	
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details provided.	
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	ITT was used.	
Selective reporting (reporting bias)	Low risk	We did not find any evidence of selective reporting.	
Other bias	Low risk	None obvious.	

vs QTP - Wang 2005

Methods	Allocation: randomised, randomised by the random number. Blinding: open label. Duration: 3 days washout period, plus 8 weeks trial. Setting: inpatients, China.
Participants	Diagnosis: schizophrenia (CCMD-3). N = 112. Age: mean 33.3 years, SD 11.7 years. Sex: not stated. Length of illness: mean ~ 65.1 days, SD ~ 8.4 days. Inclusion: PANSS score \geq 60, score of at least 4 on 2 or more of the PANSS items 'delusion', 'hallucination behavior', 'Incoherence', 'suspiciousness', 'persecution'. Exclusion: drug/alcohol dependent patients, severe physical illness, accept quetiapine or chlorpromazine within 4 weeks prior to the study and have no response to both of them
Interventions	 Chlorpromazine: 100 to 600 mg/day. N = 57. Quetiapine: 400 to 750 mg/day. N = 48.

vs QTP - Wang 2005 (Continued)

Outcomes	Clinical response:no clinical improvement*.
	Mental state: PANSS scores (total, positive, negative and general pathological)
	Adverse effect: TESS, weight gain/loss.
	Effects on physiology: laboratory findings, blood glucose and PRL
	Unable to use:
	Leaving the study early: 7 cases left the study early because of poor compliance, use other
	medication, withdrew informed consent. We were unable to use this data, as it is not
	reported by groups and we were unable to separate them
Notes	*decreased rate of PANSS score < 25%.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation, randomised by the ran- dom number.
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	High risk	Seven patients left the study early because of poor compliance, or lost to follow-up. They were not included in the final analysis Twenty-three patients left the study but were included in the adverse effects analy- sis: 12 cases from the chlorpromazine group and 11 cases from the quetiapine group
Selective reporting (reporting bias)	Low risk	All outcomes were reported.
Other bias	Low risk	None obvious.

Methods	Allocation: randomised, no further detail. Blindness: not reported. Duration: 8 weeks. Design: parallel. Setting: outpatients and inpatients, China.
Participants	Diagnosis: schizophrenia (CCMD-3). N = 63. Age: mean ~ 33.1 years, SD ~ 9.69 years Sex: male = 35, female = 28. Length of illness: mean ~ 4.90 months, SD ~ 3.60 months. Inclusion criteria: BPRS score > 35, did not take any antipsychotic drugs within 2 weeks before randomisation Exclusion criteria: severe physical impairment or organic brain diseases, alcohol or drug abuse, pregnant or breastfeeding women
Interventions	 Chlorpromazine: titrated over a 2 week period from 50 mg/d to 300 to 600 mg/d, average dosage, mean ~ 474.19 mg/d, SD ~ 99.89 mg/d. N = 32. Quetiapine: titrated over a two week period from 50 mg/d to 300 to 750 mg/d, average dosage, mean ~ 595.16 mg/d, SD ~ 126.72 mg/d. N = 31.
Outcomes	Clinical response: no clinical improvement*. Leave the study early. Mental state: BPRS Adverse effect: TESS
Notes	*Decreased rate of BPRS score < 25%

Risk of bias

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details provided.
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	High risk	One patient in the quetiapine group and 2 patients in the chlorpromazine group left the study early. No reason given and no ITT analysis was applied

vs QTP - Yang 2007 (Continued)

Selective reporting (reporting bias)	Low risk	All the patients completed the trial.
Other bias	Low risk	None obvious.

vs QTP - Zhang 2002

Methods	Allocation: randomised (by tossing a coin). Blinding: double-blind, investigator was blinded. Duration: 8 weeks. Setting: inpatients, China.
Participants	Diagnosis: schizophrenia (CCMD-2-R). N = 117. Sex: male 89 and female 28. Age: average, mean 23.89 years, SD 5.63 years. Length of illness: mean 3.87 years, SD 1.03 years. Exclusion criteria: length of illness > 5 years, with severe physical or neurological illness, pregnant or lactating women
Interventions	 Chlorpromazine: 300 mg to 550 mg/day. N = 57. Quetiapine: 300 mg to 550 mg/day. N = 60.
Outcomes	Clinical response: no clinical improvement*. Mental state: PANSS positive, negative, general psychopathology and endpoint score. Adverse event: TESS endpoint score.
Notes	*Decreased rate of PANSS score < 25%.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomised by tossing a coin.
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	All included patients completed the trial.

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vs QTP - Zhang 2002 (Continued)

Selective reporting (reporting bias)	Low risk	All outcomes were reported.
Other bias	Low risk	None obvious.

vs QTP - Zhang 2003

this study. Interventions 1. Chlorpromazine: first week 75 mg to 300 mg/day, second week onwards 300 mg to 750 mg/day. N = 118. 2. Quetiapine: first week 75 mg to 300 mg/day, second week onwards 300 mg to 750 mg/day. N = 119. Outcomes Clinical response:no clinical improvement*, decreased rate of PANSS score Globel state: poor compliance, leave the study early. Mental state, PANSS endpoint score. Adverse effect: weight gain/loss_ECG_Tachycaridia	Interventions 1. Chlorpromazine: first week 75 mg to 300 mg/day, second week onwards		
Globel state: poor compliance, leave the study early. Mental state, PANSS endpoint score.	2. Quetiapine: first week 75 mg to 300 mg/day, second week onwards 300	N = 118. : first week 75 mg to 300 mg/day, second week onwards 300 mg to	this study
Effects on physiology: pulse, blood pressure, laboratory findings	Outcomes Clinical response:no clinical improvement*, decreased rate of PANSS score Globel state: poor compliance, leave the study early.		Interventions 1. Chlorpromazine: first week 75 mg to 300 m to 750 mg/day. N = 118. 2. Quetiapine: first week 75 mg to 300 mg/day
Notes *Decreased rate of PANSS score < 30%.	Adverse effect: weight gain/loss, ECG, Tachycaridia. Effects on physiology: pulse, blood pressure, laboratory findings	or compliance, leave the study early. NSS endpoint score. eight gain/loss, ECG, Tachycaridia.	Interventions 1. Chlorpromazine: first week 75 mg to 300 m to 750 mg/day. N = 118. 2. Quetiapine: first week 75 mg to 300 mg/day 750 mg/day. N = 119. Outcomes Clinical response:no clinical improvement*, decree Globel state: poor compliance, leave the study ear Mental state, PANSS endpoint score. Adverse effect: weight gain/loss, ECG, Tachycarid
Notes*Decreased rate of PANSS score < 30%.		or compliance, leave the study early. NSS endpoint score. eight gain/loss, ECG, Tachycaridia.	Interventions 1. Chlorpromazine: first week 75 mg to 300 m to 750 mg/day. N = 118. 2. Quetiapine: first week 75 mg to 300 mg/day 750 mg/day. N = 119. Outcomes Clinical response:no clinical improvement*, decree Globel state: poor compliance, leave the study ear Mental state, PANSS endpoint score. Adverse effect: weight gain/loss, ECG, Tachycarid
		or compliance, leave the study early. NSS endpoint score. eight gain/loss, ECG, Tachycaridia.	Interventions 1. Chlorpromazine: first week 75 mg to 300 m to 750 mg/day. N = 118. 2. Quetiapine: first week 75 mg to 300 mg/day 750 mg/day. N = 119. Outcomes Clinical response:no clinical improvement*, decree Globel state: poor compliance, leave the study ear Mental state, PANSS endpoint score. Adverse effect: weight gain/loss, ECG, Tachycarid
	Effects on physiology: pulse, blood pressure, laboratory findings	or compliance, leave the study early. NSS endpoint score. eight gain/loss, ECG, Tachycaridia. ology: pulse, blood pressure, laboratory findings	Interventions 1. Chlorpromazine: first week 75 mg to 300 m to 750 mg/day. N = 118. 2. Quetiapine: first week 75 mg to 300 mg/day. 750 mg/day. N = 119. Outcomes Clinical response:no clinical improvement*, decree Globel state: poor compliance, leave the study ear Mental state, PANSS endpoint score. Adverse effect: weight gain/loss, ECG, Tachycarid Effects on physiology: pulse, blood pressure, labor
	Effects on physiology: pulse, blood pressure, laboratory findings	or compliance, leave the study early. NSS endpoint score. eight gain/loss, ECG, Tachycaridia. ology: pulse, blood pressure, laboratory findings	Interventions 1. Chlorpromazine: first week 75 mg to 300 m to 750 mg/day. N = 118. 2. Quetiapine: first week 75 mg to 300 mg/day 750 mg/day. N = 119. Outcomes Clinical response:no clinical improvement*, decree Globel state: poor compliance, leave the study ear Mental state, PANSS endpoint score. Adverse effect: weight gain/loss, ECG, Tachycarid Effects on physiology: pulse, blood pressure, labor
	Effects on physiology: pulse, blood pressure, laboratory findings	or compliance, leave the study early. NSS endpoint score. eight gain/loss, ECG, Tachycaridia. ology: pulse, blood pressure, laboratory findings	Interventions 1. Chlorpromazine: first week 75 mg to 300 m to 750 mg/day. N = 118. 2. Quetiapine: first week 75 mg to 300 mg/day 750 mg/day. N = 119. Outcomes Clinical response:no clinical improvement*, decred Globel state: poor compliance, leave the study ear Mental state, PANSS endpoint score. Adverse effect: weight gain/loss, ECG, Tachycarid Effects on physiology: pulse, blood pressure, labor

vs QTP - Zhang 2003 (Continued)

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	Twenty-eight patients left the study early with reasons reported in the study. ITT was used
Selective reporting (reporting bias)	High risk	CGI and adverse events were measured, but data were not reported
Other bias	Low risk	None obvious.

vs QTP - Zhang 2006

Methods	Allocation: randomised, no further details reported. Blindness: single blinded, assessor was blinded. Duration: 2 weeks wash out period, plus 8 weeks trial. Design: parallel. Setting: inpatients, China.	
Participants	Diagnosis: schizophrenia (CCMD-3). N = 61. Age: 18 to 59 years. Sex: not reported. Length of illness: < 2 years. Inclusion criteria: length of illness < 2 years, PANSS $\geq 60.$ Exclusion criteria: patients with severe physical impairment or abnormal laboratory findings, pregnant or breastfeeding women, allergic to quetiapine or chlorpromazine, patients with long-acting antipsychotic drugs treatment at present	-
Interventions	 Chlorpromazine: mean ~ 404.55 mg/d, SD ~ 66.42 mg/d. N = 33. Quetiapine: mean ~ 484.10 mg/d, SD ~ 143.54 mg/d. N = 28. 	
Outcomes	Clinical response: no clinical improvement*, decreased rate of PANSS score Mental state: PANSS scale score, positive score, negative score, general pathological score Adverse effects: TESS.	-
Notes	*Decreased rate of PANSS score < 30%.	
Risk of bias		Risk of bias

vs QTP - Zhang 2006 (Continued)

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details were re- ported.
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	All included patients completed the trial.
Selective reporting (reporting bias)	Low risk	All outcomes were reported.
Other bias	Low risk	None obvious.

vs QTP - Zhang 2008

Methods	Allocation: randomised, no further details were reported. Blinding: not reported. Duration: 8 weeks. Setting: inpatients, China.
Participants	Diagnosis: schizophrenia (CCMD-3). Paticipan: N = 60. Sex: male 45 and female 15. Age: mean 35.6 years, SD 9.7 years. Length of illness:4 to 17 years. Inclusion: PANSS score \geq 60. Exclusion: patients with severe physical illnesses, pregnant or lactating women, alcohol or drug dependent patients, patients with allergy to quetiapine and chlorpromazine
Interventions	 Chlorpromazine: titration period: 2 weeks, from 75 mg/d to a treatment dosage of 350 to 550 mg/d. N = 30. Quetiapine: titration period: two weeks, from 100 mg/d to a treatment dosage of 400 to 800 mg/d. N = 30.
Outcomes	Clinical response:no clinical improvement*. Mental state, PANSS endpoint total score. Adverse effects: TESS.
Notes	*Decreased rate of PANSS score < 25%.

vs QTP - Zhang 2008 (Continued)

Risk of bias

Risk of bias		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details were reported.
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	All included patients completed the trial.
Selective reporting (reporting bias)	Low risk	All outcomes were reported.
Other bias	Low risk	None obvious.

vs QTP - Zhou 2003

Methods	Allocation: randomised, using a random number table. Blinding: assessors were blinded, unclear if the patients were. Duration: 6 weeks. Setting: inpatients, Mental health centre, Sichuan, China.	
Participants	Diagnosis: schizophrenia (CCMD-3), inpatients. N = 40. Sex: male and female. Age: mean ~ 28, SD ~ 10 years. Length of illness: mean ~ 25 years, SD ~ 6 years. Exclusion: not described.	-
Interventions	 Chlorpromazine: dosage not stated. N = 20. Quetiapine: dosage not stated. N = 20. 	
Outcomes	Leave the study early. Unable to use: WCST subscale scores, as they are not validated	
Notes		
Risk of bias		Risk of bias

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vs QTP - Zhou 2003 (Continued)

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomised using a random number table.
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	One case of early discharge due to family emergency, 3 other patients withdrew for their family members were unsatisfied with the efficacy. The above drop out reasons are unlikely to have an impact on the outcome reported in this study
Selective reporting (reporting bias)	Low risk	Evidence of selective reporting was not found.
Other bias	Low risk	None obvious.

vs QTP - Zhou 2004

Methods	Allocation: randomised, no further details provided. Blinding: not reported. Duration: 12 weeks. Setting: inpatients, Jinan psychiatric hospital, Shandong province, China
Participants	Diagnosis: schizophrenia (ICD-10, CCMD-3). N = 83. Age: 17 to 51 years old. Sex: male and female. Length of illness: 4 months to 21 years. Inclusion: without receiving antipsychotic drugs, PANSS ≥ 60 ; patients without severe physical diseases and organic brain diseases, learning disability, allergic to quetiapine or chlorpormazine, abnormal laboratory findings; Exclusion: pregnant or breast feeding women.
Interventions	 Chlorpromazine: 200 to 600 mg/d. N = 41. Quetiapine: 300 to 400 mg/d. N = 42.

vs QTP - Zhou 2004 (Continued)

Outcomes	Clinical response: no clinical improvement* Leave the study early. Mental state: PANSS positive, negative, general psychopathology, total score Adverse events: TESS score. Unable to use GQOLI subscale score. These subscales were not validated.
Notes	*PANSS decreased rate < 25%.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details provided.
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	Four patients left the study early because of discharge or financial problems. They were not included in the efficacy and adverse ef- fect analysis, but this should have minimal influence in the accuracy of results
Selective reporting (reporting bias)	Low risk	Evidence of selective reporting was unclear.
Other bias	Low risk	None obvious.

vs QTP - Zou 2006

Methods	Allocation: randomised, no further details provided. Blinding: not reported. Duration: 8 weeks. Setting: Community and hospital, Zhejiang, China.
Participants	Diagnosis: schizophrenia (CCMD-3). N = 86. Age: 17 to 56 years. Sex: male and female. Length of illness: < 10 years.

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vs QTP - Zou 2006 (Continued)

	Exclusion: severe physical illness, drug/alcohol dependent, pregnant/lactating women, allergic to experimental drugs
Interventions	 Quetiapine: 483.1 ± 25.5 mg/day. N = 43. Chlorpromazine: 450.2 ± 30.2 mg/day. N = 43.
Outcomes	Clinical response: no clinical improvement*. Mental state: PANSS scores. Adverse events.
Notes	*Decreased rate of PANSS score < 25%.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further details provided.
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 data.
Selective reporting (reporting bias)	High risk	TESS scores measured, but not reported.
Other bias	Low risk	None obvious.

vs RPD - Chang 1998

Methods	Allocation: randomised, no further information. Blinding: not stated. Duration: 21 weeks. Design: parallel. Setting: China.
Participants	Diagnosis: schizophrenia (CCMD). N = 58. Age: mean ~ 35 years, SD ~ 7 years. Sex: male and female.

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vs RPD - Chang 1998 (Continued)

	Length of illness: mean ~ 12 years, SD ~ 7 Inclusion criteria: without organic diseases.		
Interventions	 Chlorpromazine: dose range 0.6g/d, N Risperidone: dose range 1 to 6mg/d, N 		
Outcomes	Clinical response: no significant clinical res Adverse effects.	ponse.	
Notes			
Risk of bias			Risk of bias
Bias	Authors' judgement	Support for judgement	
Random sequence generation (selection bias)	Unclear risk	Randomised, but no detail provided.	
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 data.	
Selective reporting (reporting bias)	Unclear risk	Unclear what the study intended to mea- sure, as we were unable to obtain its proto- col	
Other bias	Low risk	None obvious.	
	LOW HIGH	10110 0071003.	

vs RPD - Cui 2001

Methods	Allocation: randomised, no further information. Blindness: not reported. Duration: 1 week wash out period, plus 6 weeks trial. Design: parallel group. Setting: inpatients, China.
Participants	Diagnosis: schizophrenia (CCMD-2-R). N = 60. Age: 18 to 57 years. Sex: male and female.

vs RPD - Cui 2001 (Continued)

	Length of illness: in risperidone group mean ~ 69 months, SD ~ 82 months; in chlor- promazine group mean ~ 59 months, SD ~ 77 months. Inclusion criteria: BPRS > 35, without antipsychotic medication one week prior to trial, blood test normal, ECG and EEG normal Exclusion criteria: nervous system and endocrine system disease, heart, liver, renal disease, pregnant and lactating women
Interventions	 Chlorpromazine: 426.67 ± 81.38 mg/day. N = 30. Risperidone: 4.19 ± 0.68 mg/day. N = 30.
Outcomes	Clinical response: no significant clinical response*. Mental state: BPRS. Adverse effects.
Notes	*BPRS score decreased rate <30% is regarded as no significant clinical response

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further detail.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double blind (clinician and patients are blinded). Quote "risperidone and chlorpro- mazine were placed into capsules of equal size and same colour, dispensed by pharma- cist. Neither patients or clinician are aware of the content of the capsule." p206
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete outcome data.
Selective reporting (reporting bias)	Low risk	it appears that all measured outcomes were reported.
Other bias	Low risk	None obvious.

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Methods	Allocation: randomised, no further information. Blindness: not reported. Duration: three months. Design: parallel group. Setting: inpatients, China.
Participants	Diagnosis: schizophrenia (CCMD-2-R). N = 65. Age: mean ~ 26 years, SD ~ 8 years. Sex: male and female. Length of illness: in chlorpromazine group mean ~ 5.82 months, SD ~ 3.97 months; in risperidone group mean ~ 6.02 months, SD ~ 4.38 months. Inclusion criteria: PANSS > 60, without systematic antipsychotic treatment, length of illness is within two years Exclusion criteria: severe physical impairment, heart, liver, renal disease, drug or alcohol dependence, pregnant and lactating women
Interventions	 Chlorpromazine: 355.79 ± 82.45 mg/day. N = 33. Risperidone: 3.62 ± 1.07 mg/day. N = 32.
Outcomes	Mental state: PANSS. Adverse effects. Quality of life: QOL-100. Leaving the study early. Unable to use: Adverse effects: we were unable to report on the following adverse effects for their data were pooled together - fatigue, drowsiness, constipation, dry mouth, tachycardia, deteriorated memory, blurred vision

Notes

Risk of bias

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further detail.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Double-blind, but untested.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double-blinded.

vs RPD - Feng 2003 (Continued)

Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Three and 2 people dropped out of chlor- promazine and risperidone groups respec- tively. Trial authors did not report the rea- son for drop out. It's unclear if these par- ticipants were included in the final analysis
Selective reporting (reporting bias)	Unclear risk	It appears that all measured outcomes were reported.
Other bias	Low risk	None obvious.

vs RPD - He 1999

Methods	Allocation: randomised, no further information. Blindness: not reported. Duration: 1 week wash out period, plus 8 weeks trial. Design: parallel group. Setting: inpatients, China.
Participants	Diagnosis: schizophrenia (CCMD-2-R). N = 41. Age: mean ~ 45 years, SD ~ 11 years. Sex: male and female. Length of illness: mean ~ 16 years, SD ~ 10 years. Inclusion criteria: CCMD-2-R diagnosed schizophrenia. Exclusion criteria: severe organic or heart, liver, renal disease
Interventions	 Chlorpromazine: 100 to 600 mg/day. N = 20. Risperidone: 2 to 6 mg/day. N = 21.
Outcomes	Clinical response: no significant clinical response*. Mental state: BPRS, SAPS, SANS, NORS. Adverse effects: TESS. Leaving the study early. Unable to use: Mental state: unvalidated SAPS and SANS subscale scores.
Notes	*BPRS score decreased rate < 50% is regarded as no significant clinical response

Risk of bias

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

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vs RPD - He 1999 (Continued)

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	Two people dropped out of risperidone group due to agitation and severe nausea. This is unlikely to have any serious impact on other outcomes assessed
Selective reporting (reporting bias)	Low risk	It appears that all measured outcomes were reported.
Other bias	Low risk	None obvious.
	DP 1 1 1	
Participants	Blindness: not reported. Duration: 8 weeks trial. Design: parallel group. Setting: inpatients, China. Diagnosis: first episode schizophrenia (CON = 70. Age: mean ~ 32 years, SD ~ 14 years. Sex: male and female. Length of illness: chlorpromazine group 59 ± 45.80 months.	CMD-3). 25.19 ± 42.54 months; risperidone group 32.
Participants	Duration: 8 weeks trial. Design: parallel group. Setting: inpatients, China. Diagnosis: first episode schizophrenia (CON = 70. Age: mean ~ 32 years, SD ~ 14 years. Sex: male and female. Length of illness: chlorpromazine group 59 ± 45.80 months. Inclusion criteria: first episode schizophre one week prior to trial, or depot antipsyct	
Participants	Duration: 8 weeks trial. Design: parallel group. Setting: inpatients, China. Diagnosis: first episode schizophrenia (CON = 70. Age: mean ~ 32 years, SD ~ 14 years. Sex: male and female. Length of illness: chlorpromazine group 59 ± 45.80 months. Inclusion criteria: first episode schizophre one week prior to trial, or depot antipsyct Exclusion criteria: severe organic or hea	25.19 ± 42.54 months; risperidone group 32. nia, without receiving oral antipsychotic drugs hotic one month prior to trial, PANSS > 60 .rt, liver, renal disease, pregnant or lactating y. N = 35.
-	Duration: 8 weeks trial. Design: parallel group. Setting: inpatients, China. Diagnosis: first episode schizophrenia (CON = 70. Age: mean ~ 32 years, SD ~ 14 years. Sex: male and female. Length of illness: chlorpromazine group 59 ± 45.80 months. Inclusion criteria: first episode schizophre one week prior to trial, or depot antipsyct Exclusion criteria: severe organic or heat women, or abnormal ECG 1. Chlorpromazine: 100 to 450 mg/da	25.19 ± 42.54 months; risperidone group 32. nia, without receiving oral antipsychotic drugs hotic one month prior to trial, PANSS > 60 rt, liver, renal disease, pregnant or lactating y. N = 35.

Chlorpromazine versus atypical antipsychotic drugs for schizophrenia (Review) Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd. Risk of bias

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vs RPD - Lin 2005 (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	Not reported.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.
Selective reporting (reporting bias)	High risk	CGI was measured, but not reported.
Other bias	Low risk	None obvious.

vs RPD - Liu 2000

Methods	Allocation: randomised, no further information. Blindness: not reported. Duration: 3 months. Design: parallel group. Setting: inpatients, China.
Participants	Diagnosis: first episode schizophrenia (CCMD-2). N = 32. Age: 18 to 45 years. Sex: male and female. Length of illness: < 5 years. Inclusion criteria: no history of substance misuse prior to admission, without the use of antipsychotic drugs at least two weeks prior to admission, Exclusion criteria: severe physical impairment or central nervous system disease or trau- matic head injury
Interventions	 Chlorpromazine: 500 to 700 mg/day. N = 15. Risperidone: 3 to 4.5 mg/day. N = 17.
Outcomes	Mental state: SANS. Unable to use: Mental state: unvalidated SANS subscale scores.
Notes	

vs RPD - Liu 2000 (Continued)

Risk of bias

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	Not reported.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.
Selective reporting (reporting bias)	Unclear risk	Not enough information to make a judge- ment.
Other bias	Low risk	None obvious.

vs RPD - Liu 2005

Methods	Allocation: randomised, no further information. Blindness: not reported. Duration: 21 days. Design: parallel group. Setting: inpatients, China.
Participants	Diagnosis: schizophrenia (CCMD-2-R). N = 100. Age: 18 to 59 years. Sex: male only. Length of illness: not stated. Inclusion criteria: no severe physical impairment or primary hypotension Exclusion criteria: severe organic or heart, liver, renal disease
Interventions	 Chlorpromazine: 50 to 450 mg/day. N = 50. Risperidone: 1 to 4 mg/day. N = 50.
Outcomes	Adverse effects. Blood pressure. Unable to use: Adverse effects: TESS subscale score.

vs RPD - Liu 2005 (Continued)

Notes

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further detail.
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 data.
Selective reporting (reporting bias)	Low risk	All measured outcomes are reported.
Other bias	Low risk	None obvious.

vs RPD - Luo 2001

Methods	Allocation: randomised, no further information. Blindness: double-blind, but untested. Duration: 8 weeks trial. Design: parallel group. Setting: inpatients, China.
Participants	Diagnosis: schizophrenia (CCMD-2-R). N = 107. Age: 15 to 46 years. Sex: male and female. Length of illness: mean ~ 3 years, SD ~ 4 years. Inclusion criteria: not stated. Exclusion criteria: severe organic or heart, liver, renal disease, substance misuse, epilepsy, pregnant or lactating women
Interventions	 Chlorpromazine: 100 to 700 mg/day. N = 52. Risperidone: 1 to 7 mg/day. N = 55.
Outcomes	Clinical response: no significant clinical response*. Mental state: PANSS

vs RPD - Luo 2001 (Continued)

Notes	*PANSS score decreased rate < 30%.		
Risk of bias			Risk of bias
Bias	Authors' judgement	Support for judgement	
Random sequence generation (selection bias)	Unclear risk	Randomised, no further detail.	
Allocation concealment (selection bias)	Unclear risk	Not reported.	
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Double blind, but untested.	_
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported.	_
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.	
Selective reporting (reporting bias)	Low risk	All measured outcomes are reported.	
Other bias	Low risk	None obvious.	

vs RPD - Ma 2004

Methods	Allocation: randomised, no further information. Blindness: not reported. Duration: 1 week wash out period, plus 12 weeks trial. Design: parallel group. Setting: inpatients, China.
Participants	Diagnosis: schizophrenia (CCMD-3). N = 78. Age: 19 to 65 years. Sex: male and female. Length of illness: mean ~ 6.6 years. Inclusion criteria: no severe physical impairment of chronic diseases, no epilepsy or history of organic disease; blood, urine test normal, liver function normal, ECG and EEG normal, BPRS > 35
Interventions	 Chlorpromazine: average dose 475 mg/day. N = 39. Risperidone: 1 to 9 mg/day. N = 39.

vs RPD - Ma 2004 (Continued)

Outcomes	Global state: CGI-SI (skewed data), need of additional Benzhexol Mental state: BPRS. Adverse effects.

Notes

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, no further detail.
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 data.
Selective reporting (reporting bias)	Low risk	All measured outcomes are reported.
Other bias	Low risk	None obvious.

vs RPD - Wang 2002

Methods	Allocation: randomised, no further information. Blindness: not reported. Duration: 8 weeks trial. Design: parallel group. Setting: inpatients, China.
Participants	Diagnosis: schizophrenia (CCMD-2-R). N = 59. Age: 18 to 58 years. Sex: male and female. Length of illness: mean ~ 100 months, SD ~ 85 months. Inclusion criteria: without intake of antipsychotic medication one week prior to trial, or slow release depot antipsychotic one month prior to trial, PANSS > 60 Exclusion criteria: severe organic, brain or other disease.

Risk of bias

vs RPD - Wang 2002 (Continued)

Interventions	 Chlorpromazine: 400 mg/day. N = 20. Risperidone: 4 mg/day. N = 19.** Risperidone: 6 mg/day. N = 20.**
Outcomes	Clinical response: no significant clinical response*. Global state: need of additional Benzhexol. Mental state: PANSS change score. Adverse effects. Unable to use. Mental state: PANSS score at week 1. This is an eight weeks trial, but there was no endpoint PANSS score reported at week 8, instead the author reported improved PANSS score measured at week 1
Notes	*Paper did not report on how this is measured. **We combined the 4 mg and 6 mg risperidone group, when reporting their outcomes

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	Not reported.
Incomplete outcome data (attrition bias) All outcomes	Low risk	One case was discharged early from risperi- done (4 mg group), but it is unlikely to have had any significant impact on other outcome assessments such as PANSS score
Selective reporting (reporting bias)	Low risk	All measured outcomes are reported.
Other bias	Low risk	None obvious.

Risk of bias

vs RPD - Wang 2005

Methods	Allocation: randomised, no further informa Blindness: not reported. Duration: 8 weeks trial. Design: parallel group. Setting: inpatients, China.	ation.	
Participants	Diagnosis: first episode schizophrenia (CCI N = 100. Age: 18 to 45 years. Sex: male and female. Length of illness: 1 to 24 months. Inclusion criteria: not stated. Exclusion criteria: not stated.	MD-3).	_
Interventions	 Chlorpromazine: 25 to 450 mg/day. N Risperidone: 0.5 to 6 mg/day. N = 50 		
Outcomes	Functioning: WCST IQ and MQ score. Adverse effects.		
Notes			
Risk of bias			Risk of bias
Bias	Authors' judgement	Support for judgement	
Random sequence generation (selection bias)	Unclear risk	Randomised, no further detail.	
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	Unclear risk	No incomplete outcome data.	
Selective reporting (reporting bias)	Low risk	All measured outcomes are reported.	
Other bias	Low risk	None obvious.	

vs RPD - Wu 2002

Methods	Allocation: randomised, no further informa Blindness: not reported. Duration: 12 weeks trial. Design: parallel group. Setting: inpatients, China.	tion.	
Participants	Diagnosis: chronic schizophrenia (CCMD- N = 70. Age: 21 to 60 years. Sex: male and female. Length of illness: 5 to 23 years. Inclusion criteria: BPRS > 38. Exclusion criteria: severe physical impairme		
Interventions	 Chlorpromazine: 400 to 600 mg/day. Risperidone: 4 to 6 mg/day. N = 35. 	N = 35.	
Outcomes	Clinical response: no significant clinical resp Adverse effects.	ponse*.	
Notes	*The paper did not report on how this is de	etermined.	
Risk of bias			Risk of bias
Bias	Authors' judgement	Support for judgement	
Random sequence generation (selection bias)	Unclear risk	Randomised, no further detail.	
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)	Low risk	All measured outcomes are reported.	
Other bias	Low risk	None obvious.	

vs RPD - Wu 2004

Methods	Allocation: randomised, no furth Blindness: not reported. Duration: 3 months. Design: parallel group. Setting: inpatients, China.	er information.	
Participants			
Interventions		 Chlorpromazine: 300 to 600 mg/day. N = 50. Risperidone: 3 to 6 mg/day. N = 50. 	
Outcomes	Mental state: PANSS. Quality of life: QOL. Adverse effects.		
Notes			
Risk of bias			
Bias	Authors' judgement	Support for judgement	
Random sequence generation (selection bias)	Unclear risk	Randomised, no further detail.	
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)	Low risk	All measured outcomes are reported.	
Other bias	Low risk	None obvious.	

vs RPD - Zheng 2	001	
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Methods	Allocation: randomised, no further informa Blindness: not reported.	Allocation: randomised, no further information.	
	Duration: 1 week washout period, plus 8 weeks trial.		
	Design: parallel group.		
	Setting: inpatients, China.		
Participants	Diagnosis: schizophrenia (CCMD-2-R). N = 51. Age: mean ~ 45 years, SD ~ 11 years.		
	Sex: male and female.		
	Length of illness: mean ~ 16 years, SD ~ 10) years.	
	Inclusion criteria: not stated.		
	Exclusion criteria: severe organic or heart, l	iver, renal disease	
Interventions	 Chlorpromazine: 100 to 600 mg/day. Risperidone: 5 to 6 mg/day. N = 26. 	N = 25.	
Outcomes	Clinical response: no significant clinical res Adverse effects.	ponse*.	
Notes	*BPRS score decreased rate < 50% is regard	led as no significant clinical response	
Risk of bias			Risk of bias
Bias	Authors' judgement	Support for judgement	
Random sequence generation (selection bias)	Unclear risk	Randomised, no further information.	
Allocation concealment (selection bias)	Unclear risk	Not stated.	
Blinding of participants and personnel	Unclear risk		
(performance bias) All outcomes		Not stated.	
-		Not stated.	
All outcomes Blinding of outcome assessment (detection bias)			

Abbreviations: AIMS = Abnormal Involuntary Movement Scale

Other bias

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Low risk

None obvious.

BAS = Barne's Akathisa Scale BPRS = Brief Psychiatric Rating Scale CCMD = Chinese Classification of Mental Disorders CGI = Clinical Global Impression COSTART = Coding Symbols for a Thesaurus of Adverse Reaction Terms DSM = Diagnositc Statistics Manual ECG = Electrocardiogram EPS = Extrapyramidal Symptoms ESRS = Extrapyramidal Symptom Rating Scale FBG = fasting blood glucose GAF = Global Assessment of Functioning GQOL = General Quality of Life Scale HAMA = Hamilton Rating Scale for Anxiety HAMD = Hamilton Rating Scale for Depression HDL = High-density lipoprotein LDL = Low-density lipoprotein LSEQ = Leeds Sleep Evaluation Questionnaire MADRS = Montgomery-Åsberg Depression Rating Scale NORS = Nurse Observation Rating Scale NOSIE = Nurses' Observation Scale for Inpatient Evaluation PANSS = Positive and Negative Syndrome Scale PRL = prolactin QoL = Quality of Life RSESE = Rating Scale for Extrapyramidal Side Effects SANS = Scale for the Assessment of Negative Symptoms SAPS = Scale for the Assessment of Positive Symptoms SAS = Simpson-Angus Extrapyramidal Side-Effects scale SF-36 = SF-36 Health Survey TC = Total Cholesterol TESS = Treatment-Emergent Signs and Symptoms TG = triglycerides UKU = Undersogelser side effect rating scale VPS = Vitality Plus Scale WAIS-RC = Wechsler Adult Intelligence Scale-Revised WCST = Wisconsin Card Sorting Test WHO-QOL = World Health Organisation Quality of Life scale WMS = Wechsler Memory Scale

Characteristics of excluded studies [ordered by study ID]

Study	Reason for exclusion
Appelberg 2004	Allocation: randomised. Participants: schizophrenia. Intervention: olanzapine versus conventional neuroleptics (which may or may not include chlorpro- mazine)
Beuzen 1998 (HGCF)	Allocation: randomised. Participants: treatment-resistant schizophrenia.

(Continued)

Bouchard 1998	Allocation: randomised. Participants: treatment-resistant schizophrenia.
Chen 2001	Allocation: not randomised, summary of several trials.
Conley 1998	Allocation: randomised. Participants: treatment-resistant schizophrenia.
Czekalla 2001	Allocation: randomised. Participants: schizophrenia. Intervention: olanzapine versus placebo versus haloperidol versus risperidone
de Jesus Mari 2004	Allocation: randomised. Participants: schizophrenia. Intervention: olanzapine versus conventional treatment (including chlorpromazine, as well as other drugs). Results cannot be separated
Edgell 1998	Allocation: randomised. Participants: schizophrenia. Intervention: olanzapine versus risperidone.
Feng 2001	Allocation: randomised. Participants: treatment-resistant schizophrenia.
Hu 2005	Allocation: randomised. Participants: treatment-resistant schizophrenia.
Huang 2000a	Allocation: quasi-randomisation. Randomised according to admission order
Huang 2000b	Allocation: randomised. Participants: schizophrenia. Intervention: risperidone versus chlorpromazine versus olanzapine Outcome: no usable data reported.
Kostakoglu 2001	Allocation: unclear. Participants: not stated. Intervention: olanzapine versus chlorpromazine. Outcome: no usable data.
Li 2007	Allocation: quasi-randomisation. Randomised according the odd and even numbers of hospital ad- mission order
Pappas 1997	Allocation: unclear. Participants: acute schizophrenia. Intervention: risperidone versus haloperidol versus chlorpromazine Outcome: no usable data reported.
Qu 2006	Allocation: quasi-randomisation, according to odd and even admission numbers

(Continued)

Shi 2007	Allocation: randomised. Participants: schizophrenia. Intervention: chlorpromazine versus risperidone. Outcome: no usable data. Paper reported on tracked eye movement only
Su 2002	Allocation: quasi-randomisation, according to hospital admission order
Tian 2005	Allocation: randomised. Participants: schizophrenia. Intervention: risperidone and chlorpromazine versus risperidone and benzodiazepines
vs QTP - Arvanitis 1996	Allocation: double-blind, randomised, multicentre. Patients: schizophrenia. Intervention: five fixed dose of quetiapine versus a standard dose of haloperidol or placebo
vs QTP - AstraZeneca 2000	Allocation: randomised multicentre, double-blind, parallel-group trial Patients: treatment-resistant schizophrenia.
vs QTP - AstraZeneca 2005	Allocation: randomised multicentre, double-blind, parallel-group trial Patients: treatment-resistant schizophrenia.
vs QTP - Bai 2006	Allocation: not randomised. The randomisation was based on the admission sequence
vs QTP - Cai 2008	Allocation: not randomised. The randomisation was based on the admission sequence
vs QTP - Du 2004	Allocation: not randomised. The randomisation was based on the admission sequence
vs QTP - Jiang 2004	Allocation: randomised. Participants: schizophrenia. Intervention: chlorpromazine versus quetiapine. Outome: no usable outcome data reported.
vs QTP - Li 2005	Allocation: not randomised. The randomisation was based on the admission sequence
vs QTP - Ma 2004	Allocation: not randomised.
vs QTP - Ning 2008	Allocation: randomised, no further information. Participants: schizophrenia, CCMD - 3. Intervention: chlorpromazine versus quetaipine. The data is unable to use, as the number of each group is inconsistent in the result reporting and method statement
vs QTP - Tang 2004	Allocation: not randomised. The randomisation was based on the admission sequence
vs QTP - Tang 2008	Allocation: not randomised. The randomisation was based on the requirement (unclear from patients or physician) and patients financial capacity

(Continued)

vs QTP - Wang 2007	Allocation: not randomised. The randomisation was based on the admission sequence
vs QTP - Zhang 2007	Allocation: not randomised. The randomisation was based on the admission number
vs QTP - Zhong 2005	Allocation: double-blind, randomised, multicentre. Participants: schizophrenia, age range of 16 to 60 years but no average data reported
Wang 1998	Allocation: randomised. Participants: patients with schizophrenia aged between 16 and 62. The average age is approximately 24 years with a SD of 12.9 years. we consulted statistician and were unable to determine the proportion of people under 18 involved in this trial
Wang 2004	Allocation: randomised. Participants: treatment-resistant schizophrenia.
Wang 2006	Allocation: quasi-randomisation, according to the odd and even numbers of hospital admission order
Xiong 2004	Allocation: randomised. Participants: children with schizophrenia (7 to 16 years).
Yu 2001	Allocation: quasi-randomisation, according to the odd and even numbers of hospital admission number
Yuan 2006	Allocation: quasi-randomisation, according to the odd and even numbers of hospital admission number
Zou 2005	Allocation: quasi-randomisation, according to the odd and even numbers of hospital admission number

DATA AND ANALYSES

Comparison 1. CHLORPROMAZINE versus OLANZAPINE

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Clinical response: 1. No significant clinical response	4	274	Risk Ratio (M-H, Random, 95% CI)	2.19 [1.39, 3.45]
1.1 short term - up to 6 months	3	204	Risk Ratio (M-H, Random, 95% CI)	2.34 [1.37, 3.99]
1.2 long term - over 12 months	1	70	Risk Ratio (M-H, Random, 95% CI)	1.83 [0.76, 4.41]
2 Clinical response: 2. Average endpoint score (CGI, high = poor) - short term (up to 6 months)	3	110	Mean Difference (IV, Random, 95% CI)	0.93 [0.36, 1.51]
3 Clinical response: 3. Relapse - long term (over 12 months)	1	70	Risk Ratio (M-H, Random, 95% CI)	1.5 [0.46, 4.86]
4 Mental state: 1. Average endpoint score (various scales, high = poor) - short term (up to 6 months)	10		Mean Difference (IV, Random, 95% CI)	Subtotals only
4.1 BPRS total	4	245	Mean Difference (IV, Random, 95% CI)	3.21 [-0.62, 7.05]
4.2 BPRS activation subscale	2	299	Mean Difference (IV, Random, 95% CI)	0.47 [0.27, 0.67]
4.3 BPRS anxiety-depression subscale	1	213	Mean Difference (IV, Random, 95% CI)	1.57 [1.36, 1.78]
4.4 BPRS hostile-suspiciousness subscale	2	299	Mean Difference (IV, Random, 95% CI)	-0.31 [-1.98, 1.35]
4.5 BPRS thinking disorder subscale	2	299	Mean Difference (IV, Random, 95% CI)	-0.80 [-2.66, 1.06]
4.6 BPRS withdraw-retardation subscale	2	299	Mean Difference (IV, Random, 95% CI)	-0.49 [-2.25, 1.26]
4.7 NOSIE total	1	213	Mean Difference (IV, Random, 95% CI)	-18.36 [-22.39, -14. 33]
4.8 PANSS total	6	351	Mean Difference (IV, Random, 95% CI)	10.46 [4.49, 16.43]
4.9 PANSS general pathology subscale	1	100	Mean Difference (IV, Random, 95% CI)	1.31 [-0.32, 2.94]
4.10 PANSS negative symptom subscale	2	141	Mean Difference (IV, Random, 95% CI)	2.38 [0.31, 4.45]
4.11 PANSS positive symptom subscale	2	161	Mean Difference (IV, Random, 95% CI)	0.91 [-0.30, 2.11]
4.12 SAPS total	1	86	Mean Difference (IV, Random, 95% CI)	-2.10 [-4.53, 0.33]
5 Mental state: 2. Average endpoint score (BPRS, high = poor) - medium term (7 to 12 months)	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
5.1 BPRS total	1	60	Mean Difference (IV, Random, 95% CI)	8.60 [5.94, 11.26]

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6 Mental state: 3. Average			Other data	No numeric data
endpoint score (various scales,				
high = poor) - skewed data				
6.1 BPRS total			Other data	No numeric data
6.2 HAMA (anxiety)			Other data	No numeric data
6.3 MADRS (depression)			Other data	No numeric data
6.4 PANSS negative symptom			Other data	No numeric data
subscale				
6.5 PANSS positive symptom			Other data	No numeric data
subscale				
7 Service involvement: 1.	1		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
Re-hospitalisation				
7.1 long term (over 12	1	70	Risk Ratio (M-H, Random, 95% CI)	1.5 [0.46, 4.86]
months)				
8 Functioning: 1. Executive	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
function - average endpoint				
score (WCST, high = poor)				
8.1 short term (up to 6	1	53	Mean Difference (IV, Random, 95% CI)	10.96 [1.01, 20.91]
months)				
9 Adverse effects: 1.	6		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
Anticholinergic - short term				
(up to 6 months)				
9.1 blurred vision	3	241	Risk Ratio (M-H, Random, 95% CI)	2.59 [0.66, 10.22]
9.2 dry mouth	5	536	Risk Ratio (M-H, Random, 95% CI)	1.13 [0.29, 4.45]
9.3 excessive sweating	2	180	Risk Ratio (M-H, Random, 95% CI)	3.0 [0.62, 14.46]
9.4 hypersalivation	2	166	Risk Ratio (M-H, Random, 95% CI)	10.99 [4.14, 29.17]
9.5 stuffy nose	1	80	Risk Ratio (M-H, Random, 95% CI)	3.0 [1.06, 8.52]
10 Adverse effects: 2.	6		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
Cardiovascular - short term (up				
to 6 months)				
10.1 abnormal ECG	2	180	Risk Ratio (M-H, Random, 95% CI)	3.60 [0.60, 21.55]
10.2 apathism	1	100	Risk Ratio (M-H, Random, 95% CI)	5.0 [1.15, 21.67]
10.3 blood pressure (drop)	2	180	Risk Ratio (M-H, Random, 95% CI)	8.82 [1.13, 68.52]
10.4 orthostatic hypotension	5	561	Risk Ratio (M-H, Random, 95% CI)	9.78 [2.68, 35.71]
10.5 palpitation	1	237	Risk Ratio (M-H, Random, 95% CI)	40.66 [2.49, 664.56]
10.6 tachycardia	3	241	Risk Ratio (M-H, Random, 95% CI)	3.53 [1.66, 7.48]
11 Adverse effects: 3. Central	5		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
nervous system - short term				
(up to 6 months)	2	100		2.05 [1.11.12.22]
11.1 dizziness	2	180	Risk Ratio (M-H, Random, 95% CI)	3.85 [1.11, 13.32]
11.2 drowsiness	5	536	Risk Ratio (M-H, Random, 95% CI)	2.46 [1.66, 3.64]
11.3 fatigue	2	161	Risk Ratio (M-H, Random, 95% CI)	1.00 [0.13, 7.66]
12 Adverse effects: 4.	6		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
Gastrointestinal - short term				
(up to 6 months)	2	100	Did Datis (M H Dandam, 050/ CI)	11.01 [2.92 (2.04]
12.1 appetite loss	2	180	Risk Ratio (M-H, Random, 95% CI)	11.01 [2.82, 42.94] 4.29 [2.61, 7.05]
12.2 constipation 12.3 diarrhoea	6 1	622 80	Risk Ratio (M-H, Random, 95% CI) Risk Ratio (M-H, Random, 95% CI)	4.29 [2.61, 7.05] 5.0 [0.25, 100.97]
12.5 diarnoea 12.4 dysphagia	1	100	Risk Ratio (M-H, Random, 95% CI)	3.0 [0.13, 71.92]
12.5 nausea/vomiting	2	180	Risk Ratio (M-H, Random, 95% CI)	1.49 [0.43, 5.20]
13 Adverse effects: 5. Haematology	2	266	Risk Ratio (M-H, Random, 95% CI)	4.46 [1.16, 17.22]
- short term (up to 6 months)	5	200	Now Natio (191-11, Ndildolli, 7570 CI)	ד.דן טד.ד[1.10, 1/.22]
- shore term (up to 0 monuis)				

13.1 abnormal haemogram	2	180	Risk Ratio (M-H, Random, 95% CI)	4.0 [0.87, 18.31]
13.2 leukopenia	1	86	Risk Ratio (M-H, Random, 95% CI)	6.69 [0.36, 125.71]
14 Adverse effects: 6. Hepatitic -	3		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
short term (up to 6 months)				
14.1 abnormal liver function	1	100	Risk Ratio (M-H, Random, 95% CI)	5.00 [0.25, 101.58]
14.2 abnormal transaminase	2	147	Risk Ratio (M-H, Random, 95% CI)	0.88 [0.01, 150.45]
15 Adverse effects: 7a. Metabolic -	5	536	Risk Ratio (M-H, Random, 95% CI)	0.70 [0.25, 1.96]
weight gain - short term (up to				
6 months)				
16 Adverse effects: 7b. Metabolic	4		Mean Difference (IV, Random, 95% CI)	Subtotals only
- weight gain - continuous				
measures				
16.1 short term (up to 6	4	160	Mean Difference (IV, Random, 95% CI)	-5.11 [-9.15, -1.07]
months)				
16.2 medium term (7 to 12	1	50	Mean Difference (IV, Random, 95% CI)	0.59 [-11.87, 13.05]
months)				
17 Adverse effects: 7c. Metabolic -	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
other - continuous measures				
17.1 cholesterol (TC) - short	1	50	Mean Difference (IV, Random, 95% CI)	-0.40 [-1.02, 0.22]
term (up to 6 months)				
17.2 high-density lipoprotein	1	50	Mean Difference (IV, Random, 95% CI)	0.05 [-0.12, 0.22]
(HDL) - short term (up to 6				
months)	_	-		
17.3 low-density lipoprotein	1	50	Mean Difference (IV, Random, 95% CI)	-0.01 [-0.31, 0.29]
(LDL) - short term (up to 6				
months)	1	50		0.0([0.41.0.52]
17.4 low-density lipoprotein	1	50	Mean Difference (IV, Random, 95% CI)	0.06 [-0.41, 0.53]
(LDL) - medium term (7 to 12 months)				
18 Adverse effects: 7d. Metabolic -			Other data	No numeric data
other - average endpoint scores			Other data	no numeric data
- skewed data				
18.1 cholesterol (TC) -			Other data	No numeric data
medium term (7 to 12 months)			O ther data	i to indificile data
18.2 high-density lipoprotein			Other data	No numeric data
(HDL) - short term (up to 6				
months)				
18.3 triglyceride (TG) - short			Other data	No numeric data
term (up to 6 months)				
18.4 triglyceride (TG) -			Other data	No numeric data
medium term (7 to 12 months)				
19 Adverse effects: 8a. Movement	4		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
disorders - extrapyramidal				
symptoms - short term (up to 6				
months)				
19.1 akathisia	3	417	Risk Ratio (M-H, Random, 95% CI)	1.86 [0.29, 11.84]
19.2 any EPS symptoms	2	298	Risk Ratio (M-H, Random, 95% CI)	34.47 [4.79, 248.30]
19.3 muscle stiffness	2	180	Risk Ratio (M-H, Random, 95% CI)	6.13 [0.73, 51.45]
19.4 tremor	2	180	Risk Ratio (M-H, Random, 95% CI)	6.78 [0.84, 54.57]

20 Adverse effects: 8b. Movement disorders - extrapyramidal symptoms - average endpoint score (ESRS, high = poor)	2		Mean Difference (IV, Random, 95% CI)	Subtotals only
20.1 short term (up to 6 months)	2	80	Mean Difference (IV, Random, 95% CI)	0.90 [0.14, 1.66]
21 Adverse effects: 9a. Various other - sleep - average endpoint score (LSEQ, high = better) - short term (up to 6 months)	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
21.1 awaking from sleep	1	30	Mean Difference (IV, Random, 95% CI)	-5.30 [-21.91, 11. 31]
21.2 getting to sleep score	1	30	Mean Difference (IV, Random, 95% CI)	-0.60 [-19.88, 18. 68]
21.3 quality of sleep	1	30	Mean Difference (IV, Random, 95% CI)	-15.0 [-33.07, 3.07]
22 Adverse effects: 9b. Various other - sleep - average length of sleep (hour/day)	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
22.1 short term (up to 6 months)	1	50	Mean Difference (IV, Random, 95% CI)	3.63 [2.08, 5.18]
22.2 medium term (7 to 12 months)	1	50	Mean Difference (IV, Random, 95% CI)	4.41 [2.82, 6.00]
23 Adverse effects: 9c. Various other - sleep - behaviour following waking (LSEQ) - skewed data			Other data	No numeric data
23.1 short term (up to 6 months)			Other data	No numeric data
24 Adverse effects: 9b. Various other - rash	1	30	Risk Ratio (M-H, Random, 95% CI)	2.0 [0.14, 28.76]
24.1 short term (up to 6 months)	1	30	Risk Ratio (M-H, Random, 95% CI)	2.0 [0.14, 28.76]
25 Quality of life: 1a. Average endpoint scores (various scales, high = better) - short term (up to 6 months)	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
25.1 GQOLI - living condition	1	61	Mean Difference (IV, Random, 95% CI)	-1.0 [-4.21, 2.21]
25.2 GQOLI - physical health	1	61	Mean Difference (IV, Random, 95% CI)	-10.10 [-13.93, -6. 27]
		<i></i>		22 (0 [25 0/ 10
25.3 GQOLI - psychological health	1	61	Mean Difference (IV, Random, 95% CI)	-22.60 [-25.94, -19. 26]
	1	61 61	Mean Difference (IV, Random, 95% CI) Mean Difference (IV, Random, 95% CI)	
health				26] -18.20 [-20.51, -15.
health 25.4 GQOLI - social function 26 Quality of life: 1b. Average endpoint score (QoL, high =			Mean Difference (IV, Random, 95% CI)	26] -18.20 [-20.51, -15. 89]

27.1 due to any reason	3	139	Risk Ratio (M-H, Random, 95% CI)	1.69 [0.45, 6.40]
27.2 due to lack of efficacy	2	71	Risk Ratio (M-H, Random, 95% CI)	0.47 [0.08, 2.66]

Comparison 2. CHLORPROMAZINE versus RISPERIDONE

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Clinical response: 1. No significant clinical response	7	475	Risk Ratio (M-H, Random, 95% CI)	0.84 [0.53, 1.34]
1.1 short term (up to 6 months)	7	475	Risk Ratio (M-H, Random, 95% CI)	0.84 [0.53, 1.34]
2 Global state: 1. Average endpoint score (CGI-CI, high = poor) - skewed data			Other data	No numeric data
2.1 short term (up to 6 months)			Other data	No numeric data
3 Global state: 2. Need of additional benzhexol	2	137	Risk Ratio (M-H, Random, 95% CI)	1.20 [0.26, 5.53]
3.1 short term (up to 6 months)	2	137	Risk Ratio (M-H, Random, 95% CI)	1.20 [0.26, 5.53]
4 Mental state: 1a. Average endpoint score (various scales, high = poor) - short term (up to 6 months)	9		Mean Difference (IV, Random, 95% CI)	Subtotals only
4.1 BPRS total	4	247	Mean Difference (IV, Random, 95% CI)	0.90 [-3.49, 5.28]
4.2 BPRS activation subscale	2	130	Mean Difference (IV, Random, 95% CI)	0.41 [-0.81, 1.63]
4.3 BPRS anxiety-depression subscale	2	130	Mean Difference (IV, Random, 95% CI)	0.09 [-1.56, 1.73]
4.4 BPRS	2	130	Mean Difference (IV, Random, 95% CI)	0.89 [-1.41, 3.18]
hostile-suspiciousness subscale				
4.5 NORS total	1	39	Mean Difference (IV, Random, 95% CI)	1.80 [-2.53, 6.13]
4.6 PANSS total	5	397	Mean Difference (IV, Random, 95% CI)	-1.95 [-5.58, 1.69]
4.7 PANSS positive symptom subscale	4	337	Mean Difference (IV, Random, 95% CI)	0.03 [-1.67, 1.74]
4.8 PANSS negative symptom subscale	3	230	Mean Difference (IV, Random, 95% CI)	3.16 [-1.57, 7.89]
4.9 PANSS general pathology subscale	3	267	Mean Difference (IV, Random, 95% CI)	-0.85 [-2.15, 0.46]
4.10 SANS total	2	71	Mean Difference (IV, Random, 95% CI)	10.89 [-4.49, 26.27]
5 Mental state: 1b. Average endpoint score (various scales, high = poor) - skewed data - short term (up to 6 months)			Other data	No numeric data
5.1 BPRS thinking disorder subscale			Other data	No numeric data
5.2 BPRS withdraw-retardation subscale			Other data	No numeric data

				NT 1 1
5.3 PANSS general pathology			Other data	No numeric data
subscale				
5.4 PANSS negative symptom			Other data	No numeric data
subscale				
5.5 PANSS positive symptom			Other data	No numeric data
subscale				
5.6 SAPS total			Other data	No numeric data
6 Mental state: 2. Average change	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
score - decreased rate (various				
scales, high = poor) - short term				
(up to 6 months)				
6.1 PANSS total	1	57	Mean Difference (IV, Random, 95% CI)	-0.11 [-0.23, 0.01]
6.2 PANSS negative subscale	1	57	Mean Difference (IV, Random, 95% CI)	-0.21 [-0.44, 0.02]
6.3 PANSS positive subscale	1	57	Mean Difference (IV, Random, 95% CI)	-0.07 [-0.36, 0.22]
7 Functioning: 1. Average	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
endpoint score (WCST				
subscales, high = good) - short				
term (up to 6 months)				
7.1 WCST-IQ	1	100	Mean Difference (IV, Random, 95% CI)	-11.30 [-18.34, -4.
				26]
7.2 WCST-MQ	1	100	Mean Difference (IV, Random, 95% CI)	-19.60 [-28.83, -10.
				37]
8 Adverse effects: 1.	10		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
Anticholinergic - short term				
(up to 6 months)				
8.1 blurred vision	5	387	Risk Ratio (M-H, Random, 95% CI)	2.44 [1.32, 4.50]
8.2 dry mouth	9	852	Risk Ratio (M-H, Random, 95% CI)	2.00 [0.88, 4.51]
8.3 excessive sweating	2	180	Risk Ratio (M-H, Random, 95% CI)	3.0 [0.62, 14.46]
8.4 hypersalivation	5	373	Risk Ratio (M-H, Random, 95% CI)	8.67 [3.80, 19.80]
8.5 stuffy nose	1	80	Risk Ratio (M-H, Random, 95% CI)	3.0 [1.06, 8.52]
9 Adverse effects: 2a.	13		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
Cardiovascular - short term (up				
to 6 months)				
9.1 abnormal ECG	3	229	Risk Ratio (M-H, Random, 95% CI)	2.41 [0.96, 6.06]
9.2 apathism	1	100	Risk Ratio (M-H, Random, 95% CI)	6.25 [2.35, 16.65]
9.3 blood pressure drop	3	250	Risk Ratio (M-H, Random, 95% CI)	8.25 [2.61, 26.12]
9.4 bradycardia	1	100	Risk Ratio (M-H, Random, 95% CI)	0.5 [0.05, 5.34]
9.5 orthostatic hypotension	5	546	Risk Ratio (M-H, Random, 95% CI)	5.74 [2.28, 14.44]
9.6 palpitation	1	237	Risk Ratio (M-H, Random, 95% CI)	40.66 [2.49, 664.56]
9.7 sinus tachycardia	1	51	Risk Ratio (M-H, Random, 95% CI)	3.12 [0.35, 28.03]
9.8 tachycardia	7	557	Risk Ratio (M-H, Random, 95% CI)	2.64 [1.64, 4.26]
10 Adverse effects: 2b.	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
Cardiovascular - continuous				
measures - short term (up to 6				
months)				
10.1 cardiac rate (upright	1	100	Mean Difference (IV, Random, 95% CI)	3.90 [-1.57, 9.37]
position)				
10.2 cardiac rate (horizontal	1	100	Mean Difference (IV, Random, 95% CI)	7.42 [3.47, 11.37]
position)				-
10.3 contractive blood	1	100	Mean Difference (IV, Random, 95% CI)	-1.06 [-2.20, 0.08]
pressure (upright position)			,	

10.4 contractive blood	1	100	Mean Difference (IV, Random, 95% CI)	1.38 [0.61, 2.15]
pressure (horizontal position)	1	100	$M_{\text{res}} = D(M_{\text{res}} - M_{\text{res}}) = 0.50/(CD)$	0.52 [1.20, 0.22]
10.5 diastolic blood pressure	1	100	Mean Difference (IV, Random, 95% CI)	-0.53 [-1.29, 0.23]
(upright position)	1	100	Mean Difference (IV, Random, 95% CI)	0.20[0.10_0.07]
10.6 diastolic blood pressure (horizontal position)	1	100	Mean Difference (IV, Random, 93% CI)	0.39 [-0.18, 0.96]
11 Adverse effects: 3. Central	6	1191	Odds Ratio (M-H, Random, 95% CI)	1.96 [0.92, 4.22]
nervous system - short term	0	11/1		1.70 [0.72, 4.22]
(up to 6 months)				
11.1 agitation	1	65	Odds Ratio (M-H, Random, 95% CI)	0.31 [0.01, 7.98]
11.2 dizziness	4	299	Odds Ratio (M-H, Random, 95% CI)	3.57 [1.75, 7.30]
11.3 drowsiness	4	307	Odds Ratio (M-H, Random, 95% CI)	4.93 [1.49, 16.32]
11.4 fatigue	1	100	Odds Ratio (M-H, Random, 95% CI)	13.05 [4.82, 35.33]
11.5 insomnia	5	342	Odds Ratio (M-H, Random, 95% CI)	0.29 [0.10, 0.90]
11.6 reduced activity	1	78	Odds Ratio (M-H, Random, 95% CI)	2.05 [0.18, 23.63]
12 Adverse effects: 4.	9		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
Gastrointestinal - short term	-		(,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,	j
(up to 6 months)				
12.1 constipation	9	868	Risk Ratio (M-H, Random, 95% CI)	3.00 [2.05, 4.39]
12.2 diarrhoea	1	80	Risk Ratio (M-H, Random, 95% CI)	5.0 [0.25, 100.97]
12.3 dysphagia	1	100	Risk Ratio (M-H, Random, 95% CI)	3.67 [1.09, 12.36]
12.4 loss of appetite	2	180	Risk Ratio (M-H, Random, 95% CI)	11.01 [2.82, 42.94]
12.5 nausea/vomiting	4	350	Risk Ratio (M-H, Random, 95% CI)	0.85 [0.37, 1.91]
13 Adverse effects: 5. Haematology	3	266	Risk Ratio (M-H, Random, 95% CI)	4.46 [1.16, 17.22]
- short term (up to 6 months)				
13.1 abnormal haemogram	2	180	Risk Ratio (M-H, Random, 95% CI)	4.0 [0.87, 18.31]
13.2 leukopenia	1	86	Risk Ratio (M-H, Random, 95% CI)	6.69 [0.36, 125.71]
14 Adverse effects: 6. Hepatitic -	3	307	Risk Ratio (M-H, Random, 95% CI)	1.30 [0.17, 10.09]
short term (up to 6 months)				
14.1 abnormal liver function	1	78	Risk Ratio (M-H, Random, 95% CI)	5.0 [0.25, 100.89]
14.2 abnormal transaminase	3	229	Risk Ratio (M-H, Random, 95% CI)	0.88 [0.07, 11.58]
15 Adverse effects: 7. Metabolic -	4	302	Risk Ratio (M-H, Random, 95% CI)	1.36 [0.52, 3.59]
weight gain				
15.1 short term (up to 6	4	302	Risk Ratio (M-H, Random, 95% CI)	1.36 [0.52, 3.59]
months)				
16 Adverse effects: 8. Movement	8		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
disorders - short term (up to 6				,
months)				
16.1 akathisia	6	435	Risk Ratio (M-H, Random, 95% CI)	2.37 [1.46, 3.85]
16.2 any EPS symptoms	3	235	Risk Ratio (M-H, Random, 95% CI)	1.70 [0.85, 3.40]
16.3 dystonia	3	228	Risk Ratio (M-H, Random, 95% CI)	1.61 [0.97, 2.66]
16.4 muscle stiffness	5	335	Risk Ratio (M-H, Random, 95% CI)	2.96 [0.92, 9.49]
16.5 torsion movements	1	78	Risk Ratio (M-H, Random, 95% CI)	9.00 [0.50, 161.73]
16.6 tremor	6	435	Risk Ratio (M-H, Random, 95% CI)	2.15 [1.47, 3.14]
17 Adverse events: 9. Average			Other data	No numeric data
endpoint score (TESS) -				
skewed data				
17.1 short term (up to 6			Other data	No numeric data
•				
months)				
	2		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
18 Adverse effects: 10. Various other - short term (up to 6	2		Risk Ratio (M-H, Random, 95% CI)	Subtotals only

18.1 concentration (poor)	1	100	Risk Ratio (M-H, Random, 95% CI)	1.95 [1.35, 2.82]
18.2 memory deterioration	1	100	Risk Ratio (M-H, Random, 95% CI)	1.95 [1.35, 2.82]
18.3 sexual dysfunction	1	100	Risk Ratio (M-H, Random, 95% CI)	2.55 [1.43, 4.53]
18.4 unspecified	1	100	Risk Ratio (M-H, Random, 95% CI)	1.38 [0.97, 1.95]
19 Quality of life: 1. Average endpoint score (QOL, high = good)	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
19.1 short term (up to 6 months)	1	100	Mean Difference (IV, Random, 95% CI)	-14.20 [-20.50, -7. 90]
20 Leaving the study early - short term (up to 6 months)	1		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
20.1 due to adverse events	1	41	Risk Ratio (M-H, Random, 95% CI)	0.21 [0.01, 4.11]

Comparison 3. CHLORPROMAZINE versus QUETIAPINE

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Clinical response: 1. No significant clinical response	28		Risk Ratio (IV, Random, 95% CI)	Subtotals only
1.1 short term (up to 6 months)	28	3241	Risk Ratio (IV, Random, 95% CI)	0.93 [0.81, 1.06]
2 Global state: 1. Need of additional benzodiazepines/benzhexol	2		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 short term (up to 6 months)	2	290	Risk Ratio (M-H, Random, 95% CI)	1.39 [1.10, 1.75]
3 Global state: 2a. Average endpoint scores (various scales, high = poor) - short term (up to 6 months)	3		Mean Difference (IV, Random, 95% CI)	Subtotals only
3.1 CGI-SI	2	177	Mean Difference (IV, Random, 95% CI)	0.01 [-0.82, 0.84]
3.2 CGI-GI	3	229	Mean Difference (IV, Random, 95% CI)	-0.11 [-0.33, 0.11]
4 Global state: 2b. Average endpoint score (CGI-SI, high = poor) - skewed data)			Other data	No numeric data
4.1 short term (up to 6 months)			Other data	No numeric data
5 Global state: 3. Average change scores (CGI-SI, high = poor)	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
5.1 short term (up to 6 months)	1	384	Mean Difference (IV, Random, 95% CI)	-0.30 [-0.32, -0.28]
6 Mental state: 1a. Average endpoint scores (various scales, high = poor) - short term (up to 6 months)	31		Mean Difference (IV, Random, 95% CI)	Subtotals only
6.1 BPRS total	6	548	Mean Difference (IV, Random, 95% CI)	-0.18 [-1.23, 0.88]
6.2 BPRS anxiety-depression subscale	1	60	Mean Difference (IV, Random, 95% CI)	-0.27 [-1.16, 0.62]

6.3 BPRS activation subscale	1	60	Mean Difference (IV, Random, 95% CI)	0.22 [-0.26, 0.70]
6.4 BPRS	1	60	Mean Difference (IV, Random, 95% CI)	-0.09 [-1.15, 0.97]
hostile-suspiciousness subscale				
6.5 BPRS thinking disorder	1	60	Mean Difference (IV, Random, 95% CI)	-0.15 [-1.39, 1.09]
subscale				
6.6 BPRS	1	60	Mean Difference (IV, Random, 95% CI)	-0.10 [-0.76, 0.56]
withdraw-retardation subscale				
6.7 PANSS total	25	2049	Mean Difference (IV, Random, 95% CI)	-0.05 [-2.30, 2.19]
6.8 PANSS positive symptoms	13	1102	Mean Difference (IV, Random, 95% CI)	0.39 [-0.11, 0.88]
6.9 PANSS negative	17	1361	Mean Difference (IV, Random, 95% CI)	1.05 [0.13, 1.98]
symptoms				
6.10 PANSS general	18	1530	Mean Difference (IV, Random, 95% CI)	-1.11 [-3.06, 0.84]
pathology				
6.11 HAMD total	1	63	Mean Difference (IV, Random, 95% CI)	7.4 [5.13, 9.67]
7 Mental state: 1b. Average	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
endpoint scores (various scales,				
high = poor) - medium term (6				
to 12 months)				
7.1 PANSS total	1	41	Mean Difference (IV, Random, 95% CI)	4.90 [1.74, 8.06]
7.2 PANSS general pathology	1	41	Mean Difference (IV, Random, 95% CI)	-0.20 [-4.34, 3.94]
7.3 PANSS negative	1	77	Mean Difference (IV, Random, 95% CI)	2.70 [0.44, 4.96]
symptoms				
8 Mental state: 1c. Average			Other data	No numeric data
endpoint scores (various scales,				
high = poor) -skewed data				
8.1 PANSS total - short term			Other data	No numeric data
(up to 6 months)				
8.2 PANSS positive symptoms			Other data	No numeric data
- short term (up to 6 months)				
8.3 PANSS negative			Other data	No numeric data
symptoms - short term (up to 6				
months)				
8.4 PANSS general pathology			Other data	No numeric data
- short term (up to 6 months				
9 Mental state: 1d. Average change	2		Mean Difference (IV, Random, 95% CI)	Subtotals only
score (various scales, high =				
poor) - short term (up to 6				
months)		1		
9.1 PANSS total	2	426	Mean Difference (IV, Random, 95% CI)	-2.50 [-2.82, -2.19]
9.2 PANSS positive symptoms	1	384	Mean Difference (IV, Random, 95% CI)	1.20 [1.10, 1.30]
9.3 PANSS negative	1	384	Mean Difference (IV, Random, 95% CI)	0.80 [0.70, 0.90]
symptoms		20/		
9.4 PANSS general pathology	1	384	Mean Difference (IV, Random, 95% CI)	1.0 [0.85, 1.15]
10 Mental state: 1e. Average score	7		Mean Difference (IV, Random, 95% CI)	Subtotals only
decreased rate of BPRS/PANSS				
(%) - short term (up to 6				
months)	1	107	Mean Difference (IV, Random, 95% CI)	0.00[/.0(2.2()
10.1 BPRS 10.2 PANSS	1 6	197 782	Mean Difference (IV, Random, 95% CI) Mean Difference (IV, Random, 95% CI)	-0.80 [-4.86, 3.26] -1.96 [-7.20, 3.28]
10.2 1711055	0	/ 02	wear Difference (17, Nationii, 7970 CI)	-1.70 [-7.20, 3.20]

11 Functioning: 1. Average endpoint score (various scales, high = better) - short term (up to 6 months)	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
11.1 WCST-IQ	1	120	Mean Difference (IV, Random, 95% CI)	-11.30 [-17.62, -4. 98]
11.2 WCST-MQ	1	120	Mean Difference (IV, Random, 95% CI)	-19.60 [-27.37, -11. 83]
12 Cognitive function: 1. Average endpoint score (various scales, high = better) - short term (up to 6 months)	2		Mean Difference (IV, Random, 95% CI)	Subtotals only
12.1 WCST	2	123	Mean Difference (IV, Random, 95% CI)	8.92 [0.40, 17.43]
12.2 WMS-RC	1	71	Mean Difference (IV, Random, 95% CI)	-9.34 [-17.53, -1.15]
13 Adverse effects: 1.	22	, -	Risk Ratio (M-H, Random, 95% CI)	Subtotals only
Anticholinergic - short term	22			Subtotals only
(up to 6 months)				
13.1 blurred vision	18	1780	Risk Ratio (M-H, Random, 95% CI)	5.00 [3.46, 7.22]
13.2 dry mouth	18	1682	Risk Ratio (M-H, Random, 95% CI)	2.34 [1.54, 3.54]
13.3 excessive sweating	3	162	Risk Ratio (M-H, Random, 95% CI)	3.91 [0.84, 18.19]
13.4 hypersalivation	11	1135	Risk Ratio (M-H, Random, 95% CI)	3.85 [2.36, 6.28]
13.5 stuffy nose	8	972	Risk Ratio (M-H, Random, 95% CI)	0.69 [0.45, 1.06]
14 Adverse effects: 2.	22		Risk Ratio (IV, Random, 95% CI)	Subtotals only
Cardiovascular - short term (up				,
to 6 months)				
14.1 abnormal ECG	7	708	Risk Ratio (IV, Random, 95% CI)	1.82 [1.11, 2.98]
14.2 blood pressure drop	8	690	Risk Ratio (IV, Random, 95% CI)	0.97 [0.53, 1.79]
14.3 orthostatic hypotension	7	605	Risk Ratio (IV, Random, 95% CI)	2.64 [1.14, 6.12]
14.4 tachycardia	17	1752	Risk Ratio (IV, Random, 95% CI)	1.70 [1.33, 2.18]
15 Adverse effects: 3. Central	21		Risk Ratio (IV, Random, 95% CI)	Subtotals only
nervous system - short term				
(up to 6 months)				
15.1 dizziness	12	1206	Risk Ratio (IV, Random, 95% CI)	1.40 [0.83, 2.35]
15.2 drowsiness	17	1677	Risk Ratio (IV, Random, 95% CI)	2.28 [1.51, 3.45]
15.3 headache	3	192	Risk Ratio (IV, Random, 95% CI)	0.74 [0.13, 4.18]
15.4 insomnia	9	867	Risk Ratio (IV, Random, 95% CI)	0.92 [0.55, 1.54]
15.5 reduced activity	8	788	Risk Ratio (IV, Random, 95% CI)	7.80 [3.05, 19.92]
15.6 sedation	1	40	Risk Ratio (IV, Random, 95% CI)	0.33 [0.01, 7.72]
16 Adverse effects: 4.	22		Risk Ratio (IV, Random, 95% CI)	Subtotals only
Gastrointestinal - short term				
(up to 6 months)				
16.1 constipation	22	2048	Risk Ratio (IV, Random, 95% CI)	2.55 [2.04, 3.20]
16.2 diarrhoea	1	62	Risk Ratio (IV, Random, 95% CI)	5.32 [0.27, 106.54]
16.3 loss of appetite	5	472	Risk Ratio (IV, Random, 95% CI)	2.52 [0.82, 7.72]
16.4 nausea/vomiting	9	819	Risk Ratio (IV, Random, 95% CI)	1.23 [0.58, 2.63]
17 Adverse effects: 5a. Endocrine -	4		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
various - short term (up to 6				
months)				
17.1 gynaecomastia,	1	83	Risk Ratio (M-H, Random, 95% CI)	5.37 [0.27, 108.47]
galactorrhoea				
17.2 hyperprolactinemia	2	277	Risk Ratio (M-H, Random, 95% CI)	5.69 [2.74, 11.79]
17.3 menstrual irregularities	1	52	Risk Ratio (M-H, Random, 95% CI)	5.0 [0.25, 99.34]

18 Adverse effects: 5b. Endocrine - average endpoint - short term (up to 6 months)	1	30	Mean Difference (IV, Random, 95% CI)	24.62 [17.76, 31.48]
 18.1 prolactin level (ng/mL) 19 Adverse effects: 5c. Endocrine - skewed data - short term (up to 6 months) 	1	30	Mean Difference (IV, Random, 95% CI) Other data	24.62 [17.76, 31.48] No numeric data
19.1 average prolactin level (ng/mL)			Other data	No numeric data
20 Adverse effects: 6a. Haematology - short term (up to 6 months)	10		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
20.1 elevated ALT	8	775	Risk Ratio (M-H, Random, 95% CI)	1.62 [0.92, 2.87]
20.2 decreased white blood cell count	4	427	Risk Ratio (M-H, Random, 95% CI)	1.02 [0.43, 2.42]
20.3 increased white blood cell count	1	79	Risk Ratio (M-H, Random, 95% CI)	2.05 [0.40, 10.56]
21 Adverse effects: 6b. Haematology - average endpoint - short term (up to 6 months)	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
21.1 blood glucose	1	130	Mean Difference (IV, Random, 95% CI)	0.10 [-0.18, 0.38]
21.2 blood TG	1	130	Mean Difference (IV, Random, 95% CI)	0.0 [-0.28, 0.28]
21.3 blood TC	1	130	Mean Difference (IV, Random, 95% CI)	0.20 [-0.11, 0.51]
22 Adverse effects: 7. Hepatitic - short term (up to 6 months)	5		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
22.1 abnormal liver function	5	561	Risk Ratio (M-H, Random, 95% CI)	2.10 [1.32, 3.33]
23 Adverse effects: 8. Movement disorders - short term (up to 6 months)	24		Risk Ratio (IV, Random, 95% CI)	Subtotals only
23.1 agitation	5	313	Risk Ratio (IV, Random, 95% CI)	0.36 [0.14, 0.95]
23.2 akathisia	17	1757	Risk Ratio (IV, Random, 95% CI)	3.73 [2.55, 5.47]
23.3 any EPS symptoms	8	644	Risk Ratio (IV, Random, 95% CI)	8.03 [4.78, 13.51]
23.4 dystonia	1	201	Risk Ratio (IV, Random, 95% CI)	0.33 [0.01, 8.01]
23.5 myotonia	12	1257	Risk Ratio (IV, Random, 95% CI)	4.59 [3.18, 6.64]
23.6 need additional medication for EPS symptoms	1	202	Risk Ratio (IV, Random, 95% CI)	1.5 [0.71, 3.18]
23.7 torsion movement	9	1063	Risk Ratio (IV, Random, 95% CI)	5.81 [2.76, 12.23]
23.8 tremor	13	1343	Risk Ratio (IV, Random, 95% CI)	2.90 [1.89, 4.45]
24 Adverse effects: 9a. Metabolic - weight gain	15	1259	Risk Ratio (M-H, Random, 95% CI)	1.67 [1.17, 2.39]
24.1 weight gain	15	1259	Risk Ratio (M-H, Random, 95% CI)	1.67 [1.17, 2.39]
25 Adverse effects: 9b. Metabolic - short term (up to 6 months)	2		Mean Difference (IV, Random, 95% CI)	Subtotals only
25.1 average BMI	1	105	Mean Difference (IV, Random, 95% CI)	0.5 [-0.67, 1.67]
25.2 average weight (KG)	1	130	Mean Difference (IV, Random, 95% CI)	-1.0 [-4.68, 2.68]
26 Adverse effects: 10. Various other - short term (up to 6 months)	4	560	Risk Ratio (M-H, Random, 95% CI)	1.73 [1.19, 2.52]
26.1 unspecified adverse effects	4	560	Risk Ratio (M-H, Random, 95% CI)	1.73 [1.19, 2.52]

27 Adverse effects: 11. Average endpoint score (TESS, high = poor) - skewed data			Other data	No numeric data
27.1 short term (up to 6 months)			Other data	No numeric data
27.2 medium term (7 to 12 months)			Other data	No numeric data
28 Quality of life: 1. General - average endpoint score (GQOL1 - 74, high = better)	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
28.1 short term (up to 6 months)	1	59	Mean Difference (IV, Random, 95% CI)	-6.49 [-11.30, -1.68]
29 Leaving the study early: 1a. Short term (up to 6 months)	19		Risk Ratio (IV, Random, 95% CI)	Subtotals only
29.1 due to adverse effect	10	1680	Risk Ratio (IV, Random, 95% CI)	1.43 [1.04, 1.98]
29.2 due to inefficacy	3	695	Risk Ratio (IV, Random, 95% CI)	1.42 [0.68, 2.96]
29.3 due to any other reason	12	1223	Risk Ratio (IV, Random, 95% CI)	1.04 [0.77, 1.41]
29.4 due to loss to follow-up	2	400	Risk Ratio (IV, Random, 95% CI)	0.56 [0.23, 1.37]
30 Leaving the study early: 1b.	1	103	Risk Ratio (IV, Random, 95% CI)	1.19 [0.61, 2.32]
Medium term (7 to 12 months)				

Analysis 1.1. Comparison | CHLORPROMAZINE versus OLANZAPINE, Outcome | Clinical response: 1. No significant clinical response.

Review: Chlorpromazine versus atypical antipsychotic drugs for schizophrenia

Comparison: I CHLORPROMAZINE versus OLANZAPINE

Outcome: I Clinical response: I. No significant clinical response

Study or subgroup	Chlorpromazine	Olanzapine	Risk Ratio M-	Weight	Risk Ratio M-
	n/N	n/N	H,Random,95% Cl		H,Random,95% Cl
I short term - up to 6 mon	ths				
vs OLZ - Chang 2003	13/27	6/31		31.1 %	2.49 [1.10, 5.64]
vs OLZ - Chen 2006	4/44	3/42	_ _	10.1 %	1.27 [0.30, 5.35]
vs OLZ - Wang 2002	14/28	6/32		31.7 %	2.67 [1.19, 6.00]
Subtotal (95% CI)	99	105	•	72.9 %	2.34 [1.37, 3.99]
Total events: 31 (Chlorpron	nazine), 15 (Olanzapine)				
Heterogeneity: $Tau^2 = 0.0$;	$Chi^2 = 0.82, df = 2 (P = 0.6)$	6); l ² =0.0%			
Test for overall effect: $Z = 3$	8.11 (P = 0.0019)				
2 long term - over 12 mont	hs				
vs OLZ - An 2006	11/35	6/35		27.1 %	1.83 [0.76, 4.41]
			0.01 0.1 1 10 100		
			Chlorpromazine Olanzapine		
					(Continued)

						(Continued)
Study or subgroup	Chlorpromazine	Olanzapine		Risk Ratio M-	Weight	Risk Ratio
			H,Random,95%			M- H,Random,95%
	n/N	n/N		CI		
Subtotal (95% CI)	35	35		•	27.1 %	1.83 [0.76, 4.41]
Total events: II (Chlorprom	nazine), 6 (Olanzapine)					
Heterogeneity: not applicabl	e					
Test for overall effect: Z = 1.35 (P	.35 (P = 0.18)					
Total (95% CI)	134	140		•	100.0 %	2.19 [1.39, 3.45]
Total events: 42 (Chlorprom	nazine), 21 (Olanzapine)					
Heterogeneity: $Tau^2 = 0.0$; (Chi ² = 1.03, df = 3 (P = 0.7	9); l ² =0.0%				
Test for overall effect: $Z = 3$.36 (P = 0.00077)					
Test for subgroup difference	s: $Chi^2 = 0.2I$, $df = I$ (P =	0.64), I ² =0.0%				
			0.01 0.1	I IO IOO		
			Chlorpromazine	Olanzapine		

Analysis 1.2. Comparison I CHLORPROMAZINE versus OLANZAPINE, Outcome 2 Clinical response: 2. Average endpoint score (CGI, high = poor) - short term (up to 6 months).

Review: Chlorpromazine versus atypical antipsychotic drugs for schizophrenia

Comparison: I CHLORPROMAZINE versus OLANZAPINE

Outcome: 2 Clinical response: 2. Average endpoint score (CGI, high = poor) - short term (up to 6 months)

Study or subgroup	Chlorpromazine		Olanzapine		C	Mean Difference	Weight	Mean Difference
	Ν	Mean(SD)	Ν	Mean(SD)	IV,Rai	ndom,95% Cl		IV,Random,95% CI
HGCQ (Turkey) 2000	10	4.6 (1.1)	20	4 (1.4)			25.1 %	0.60 [-0.32, 1.52]
HGDV (Morocco) 1999	12	4.3 (0.9)	27	2.9 (0.6)			- 41.7 %	1.40 [0.84, 1.96]
vs OLZ - Loza 1999 (HGD ⁻	Г) 14	4.6 (1)	27	4 (1.3)			33.2 %	0.60 [-0.12, 1.32]
Total (95% CI)	36		74			-	100.0 %	0.93 [0.36, 1.51]
Heterogeneity: $Tau^2 = 0.13$; Ch	$m^2 = 3.90$, df = 2 (P =	= 0.14); 12 =499	6					
Test for overall effect: $Z = 3.17$	(P = 0.0015)							
Test for subgroup differences: N	Vot applicable							
				-	2 -1	0 I	2	
				Chl	orpromazine	Olanzapine		

Analysis 1.3. Comparison I CHLORPROMAZINE versus OLANZAPINE, Outcome 3 Clinical response: 3. Relapse - long term (over 12 months).

Review: Chlorpromazine versus atypical antipsychotic drugs for schizophrenia

Comparison: I CHLORPROMAZINE versus OLANZAPINE

Outcome: 3 Clinical response: 3. Relapse - long term (over 12 months)

Study or subgroup	Chlorpromazine	Olanzapine	Risk Ratio	Weight	Risk Ratio M-
	n/N	n/N	H,Random,95% Cl		H,Random,95% Cl
vs OLZ - An 2006	6/35	4/35		100.0 %	1.50 [0.46, 4.86]
Total (95% CI)	35	35	-	100.0 %	1.50 [0.46, 4.86]
Total events: 6 (Chlorpro	mazine), 4 (Olanzapine)				
Heterogeneity: not applic	able				
Test for overall effect: Z =	= 0.68 (P = 0.50)				
Test for subgroup differen	ices: Not applicable				
			0.01 0.1 1 10 100		
		(Chlorpromazine Olanzapine		

Analysis 1.4. Comparison I CHLORPROMAZINE versus OLANZAPINE, Outcome 4 Mental state: 1. Average endpoint score (various scales, high = poor) - short term (up to 6 months).

Review: Chlorpromazine versus atypical antipsychotic drugs for schizophrenia

Comparison: I CHLORPROMAZINE versus OLANZAPINE

Outcome: 4 Mental state: I. Average endpoint score (various scales, high = poor) - short term (up to 6 months)

Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI	Mean(SD)	Olanzapine N	Mean(SD)	Chlorpromazine N	Study or subgroup
			. ,		. ,		I BPRS total
5.00 [3.16, 6.84]	30.9 %	-	22 (3)	31	27 (4)	27	vs OLZ - Chang 2003
-4.60 [-8.51, -0.69]	24.7 %		29.4 (11.3)	42	24.8 (6.4)	44	vs OLZ - Chen 2006
8.60 [0.18, 17.02]	12.8 %		35.4 (16)	27	44 (11.2)	DT) 14	vs OLZ - Loza 1999 (HGDT
5.40 [3.87, 6.93]	31.6 %	-	21.7 (2.5)	32	27.1 (3.4)	28	vs OLZ - Wang 2002
3.21 [-0.62, 7.05]	100.0 %	•		132 1 ² =87%	P = 0.00003);		Subtotal (95% CI) Heterogeneity: Tau ² = 11.52; C Test for overall effect: Z = 1.64
0.40 [-0.19, 0.99]	11.1 %		4.9 (1.8)	42	5.3 (0.8)	44	2 BPRS activation subscale vs OLZ - Chen 2006
0.48 [0.27, 0.69]	88.9 %		3.67 (0.57)	105	4.15 (0.95)	108	vs OLZ - Wang 2008
0.47 [0.27, 0.67]	100.0 %		5.6 (0.79)	147		152 hi ² = 0.06, df = 1 (P = 7 (P < 0.00001)	Subtotal (95% CI) Heterogeneity: Tau ² = 0.0; Chi ² Test for overall effect: Z = 4.67 3 BPRS anxiety-depression subs vs OLZ - Wang 2008
1.57 [1.36, 1.78]	100.0 %	•		105			Subtotal (95% CI) Heterogeneity: not applicable Test for overall effect: Z = 14.77
						subscale	4 BPRS hostile-suspiciousness su
	477.0/	_		40		4.4	017 Chan 200/
-1.20 [-1.97, -0.43]	47.7 %	-	5.8 (2.4)	42	4.6 (0.9)	44	vs OLZ - Chen 2006
0.50 [0.21, 0.79]	52.3 %		5.8 (2.4) 4.52 (0.78)	105	4.6 (0.9) 5.02 (1.34)	108	vs OLZ - Wang 2008
0.50 [0.21, 0.79] -0.31 [-1.98, 1.35]	52.3 % 100.0 %		4.52 (0.78)	105 147 * =94%	5.02 (1.34) = 0.00006); l ²	108 152 Chi ² = 16.24, df = 1 (P 7 (P = 0.71) cale	vs OLZ - Wang 2008 Subtotal (95% CI) Heterogeneity: Tau ² = 1.36; Ch Test for overall effect: Z = 0.37 5 BPRS thinking disorder subsca
0.50 [0.21, 0.79] -0.31 [-1.98, 1.35] -1.80 [-2.69, -0.91]	52.3 % 100.0 % 47.3 %	•	4.52 (0.78)	105 147 2 =94%	5.02 (1.34) = 0.00006); 1 ² 5.1 (0.9)	108 152 $Chi^2 = 16.24, df = 1 (P + 10, 20, 10, 10, 10, 10, 10, 10, 10, 10, 10, 1$	vs OLZ - Wang 2008 Subtotal (95% CI) Heterogeneity: Tau ² = 1.36; Ch Test for overall effect: Z = 0.37 5 BPRS thinking disorder subsca vs OLZ - Chen 2006
0.50 [0.21, 0.79] -0.31 [-1.98, 1.35]	52.3 % 100.0 %		4.52 (0.78)	105 147 * =94%	5.02 (1.34) = 0.00006); l ²	108 152 Chi ² = 16.24, df = 1 (P 7 (P = 0.71) cale	vs OLZ - Wang 2008 Subtotal (95% CI) Heterogeneity: Tau ² = 1.36; Ch Test for overall effect: Z = 0.37 5 BPRS thinking disorder subsca

(Continued . . .)

Differer	Weight	Mean Difference		Olanzapine		Chlorpromazine	Study or subgroup
IV,Random,95%	**Cigint	IV,Random,95% Cl	Mean(SD)	N	Mean(SD)	N	study of subgroup
						4 (P = 0.40)	Test for overall effect: $Z = 0.84$
							6 BPRS withdraw-retardation su
-1.40 [-1.86, -0.9	49.2 %		6.6 (1.5)	42	5.2 (0.2)	44	vs OLZ - Chen 2006
0.39 [0.24, 0.5	50.8 %		3.35 (0.51)	105	3.74 (0.58)	108	vs OLZ - Wang 2008
-0.49 [-2.25, 1.20	100.0 %	+		147		152	Subtotal (95% CI)
				=98%	2<0.00001); 12	,	Heterogeneity: Tau ² = 1.57; Ch Test for overall effect: $Z = 0.55$ 7 NOSIE total
-18.36 [-22.39, -14.3	100.0 %		287.2 (4.)	105	268.84 (15.9)	108	vs OLZ - Wang 2008
18.36 [-22.39, -14.33	100.0 % -	•	•	105		108	Subtotal (95% CI)
						2 (P < 0.00001)	Heterogeneity: not applicable Test for overall effect: Z = 8.92 8 PANSS total
5.20 [-18.16, 28.5	• 5.4 %		67.5 (30.5) -	20	72.7 (30.9)	10	HGCQ (Turkey) 2000
24.50 [10.88, 38.1	→ II.8 %		44.6 (12.8)	27	69.1 (22.5)	12	HGDV (Morocco) 1999
5.40 [-2.74, 13.5	19.5 %		54.8 (16.9)	40	60.2 (20.1)	40	vs OLZ - He 2003
3.80 [-0.83, 28.4	• 10.8 %		97.1 (29.9)	27	110.9 (17.8)	DT) 14	vs OLZ - Loza 1999 (HGDT
4.67 [1.31, 8.0	27.9 %		38.26 (9.37)	50	42.93 (7.67)	50	vs OLZ - Wu 2008
14.00 [8.65, 19.3	24.6 %		53.8 (.)	32	67.8 (10.2)	29	vs OLZ - Zhao 2006
10.46 [4.49, 16.43	100.0 %			196		155	Subtotal (95% CI)
ι, ,					$(P = 0.0 I); I^2 =$	$Chi^2 = 15.31, df = 5$	Heterogeneity: $Tau^2 = 30.32$; C Test for overall effect: Z = 3.43
							9 PANSS general pathology sub
1.31 [-0.32, 2.9	100.0 %	-	20.6 (4.11)	50	21.91 (4.23)		vs OLZ - Wu 2008
1.31 [-0.32, 2.9 1.31 [-0.32, 2.9 4	100.0 % 100.0 %	•	20.6 (4.11)	50 50	21.91 (4.23)		vs OLZ - Wu 2008
-		•	20.6 (4.11)		21.91 (4.23)	50 50	
1.31 [-0.32, 2.94	100.0 %	•				50 50 7 (P = 0.12) subscale	vs OLZ - Wu 2008 Subtotal (95% CI) Heterogeneity: not applicable Test for overall effect: Z = 1.57 10 PANSS negative symptom so
1.31 [-0.32, 2.9 4	100.0 % 29.1 %	•	22.6 (8.3)		24.2 (9.2)	50 50 7 (P = 0.12) subscale 40	vs OLZ - Wu 2008 Subtotal (95% CI) Heterogeneity: not applicable Test for overall effect: Z = 1.57 10 PANSS negative symptom so vs OLZ - He 2003
1.31 [-0.32, 2.94	100.0 %	•		50		50 50 7 (P = 0.12) subscale	vs OLZ - Wu 2008 Subtotal (95% CI) Heterogeneity: not applicable Test for overall effect: Z = 1.57 10 PANSS negative symptom so
1.31 [-0.32, 2.9 4	100.0 % 29.1 %	•	22.6 (8.3)	50 40 32 72	24.2 (9.2) 15.4 (5.7)	50 50 7 (P = 0.12) subscale 40 29 69 $i^2 = 0.22, df = (P = 1)$	vs OLZ - Wu 2008 Subtotal (95% CI) Heterogeneity: not applicable Test for overall effect: Z = 1.57 10 PANSS negative symptom so vs OLZ - He 2003
1.31 [-0.32, 2.94 1.60 [-2.24, 5.4 2.70 [0.24, 5.1	29.1 % 70.9 %	•	22.6 (8.3)	50 40 32 72	24.2 (9.2) 15.4 (5.7)	50 50 7 (P = 0.12) subscale 40 29 69 $i^2 = 0.22, df = 1 (P = 5 (P = 0.024))$	vs OLZ - Wu 2008 Subtotal (95% CI) Heterogeneity: not applicable Test for overall effect: Z = 1.57 10 PANSS negative symptom su vs OLZ - He 2003 vs OLZ - He 2003 vs OLZ - Zhao 2006 Subtotal (95% CI) Heterogeneity: Tau ² = 0.0; Chi ²
1.31 [-0.32, 2.94 1.60 [-2.24, 5.4 2.70 [0.24, 5.1 2.38 [0.31, 4.45	100.0 % 29.1 % 70.9 % 100.0 %	•	22.6 (8.3) 12.7 (3.8)	40 32 72	24.2 (9.2) 15.4 (5.7) 0.64); l ² =0.0;	50 50 7 (P = 0.12) subscale 40 29 69 $i^2 = 0.22, df = 1 (P = 5 (P = 0.024))$	vs OLZ - Wu 2008 Subtotal (95% CI) Heterogeneity: not applicable Test for overall effect: Z = 1.57 10 PANSS negative symptom su vs OLZ - He 2003 vs OLZ - Zhao 2006 Subtotal (95% CI) Heterogeneity: Tau ² = 0.0; Chi ² Test for overall effect: Z = 2.25 II PANSS positive symptom su

(Continued . . .)

							(Continued)
Study or subgroup	Chlorpromazine	0	lanzapine		Mean Difference		Mean Difference
	Ν	Mean(SD)	Ν	Mean(SD)	IV,Random,959	% Cl	IV,Random,95% CI
Heterogeneity: $Tau^2 = 0.0$; Ch Test for overall effect: $Z = 1.4$		0.47); I ² =0.0%					
12 SAPS total							
vs OLZ - Chen 2006	44	22.7 (4.4)	42	24.8 (6.8)		100.0 %	-2.10 [-4.53, 0.33]
Subtotal (95% CI)	44		42		•	100.0 %	-2.10 [-4.53, 0.33]
Heterogeneity: not applicable							
Test for overall effect: $Z = 1.6$	9 (P = 0.091)						
Test for subgroup differences:	Chi ² = 171.97, df = 11	$(P = 0.00), I^2 =$	94%				
				-20	-10 0	10 20	
				Chlor	promazine Ola	anzapine	

Analysis 1.5. Comparison | CHLORPROMAZINE versus OLANZAPINE, Outcome 5 Mental state: 2. Average endpoint score (BPRS, high = poor) - medium term (7 to 12 months).

Review: Chlorpromazine versus atypical antipsychotic drugs for schizophrenia

Comparison: I CHLORPROMAZINE versus OLANZAPINE

Outcome: 5 Mental state: 2. Average endpoint score (BPRS, high = poor) - medium term (7 to 12 months)

Study or subgroup	Chlorpromazine		Olanzapine		Dif	Mean ference	Weight	Mean Difference
	Ν	Mean(SD)	Ν	Mean(SD)	IV,Ranc	lom,95% Cl		IV,Random,95% CI
I BPRS total								
vs OLZ - Wang 2002	28	31.5 (5.6)	32	22.9 (4.8)			100.0 %	8.60 [5.94, 11.26]
Subtotal (95% CI)	28		32			-	100.0 %	8.60 [5.94, 11.26]
Heterogeneity: not applic	cable							
Test for overall effect: Z =	= 6.34 (P < 0.00001)							
Test for subgroup differer	nces: Not applicable							
						<u> </u>		
				-	-10 -5	0 5 10)	
				Cł	lorpromazine	Olanzapine		

Analysis 1.6. Comparison I CHLORPROMAZINE versus OLANZAPINE, Outcome 6 Mental state: 3. Average endpoint score (various scales, high = poor) - skewed data.

					- '
Study	Intervention	mean	SD	N	
BPRS total					BPRS total
HGCQ (Turkey) 2000	Chlorpromazine	24.7	18.4	10	
HGCQ (Turkey) 2000	Olanzapine	20.2	17.9	20	
HGDV (Morocco) 1999	Chlorpromazine	20.7	12.9	12	
HGDV (Morocco) 1999	Olanzapine	6.7	6.4	27	
vs OLZ - Wang 2008	Chlorpromazine	30.16	27.4	108	
vs OLZ - Wang 2008	Olanzapine	27.34	7.89	105	
HAMA (anxiety)					HAMA (anxiety
HGDV (Morocco) 1999	Chlorpromazine	7.6	5.8	12	
HGDV (Morocco) 1999	Olanzapine	3.3	1.8	27	
MADRS (depression)					MADRS (depre
HGDV (Morocco) 1999	Chlorpromazine	6.9	4.8	12	
HGDV (Morocco) 1999	Olanzapine	3.3	2.0	27	
PANSS negative sympto	m subscale				PANSS negative
vs OLZ - Wu 2008	Chlorpromazine	11.62	3.93	50	
vs OLZ - Wu 2008	Olanzapine	8.34	4.26	50	
PANSS positive sympton	m subscale				PANSS positive
vs OLZ - He 2003	Chlorpromazine	11.7	6.2	40	
vs OLZ - He 2003	Olanzapine	10.2	4.9	40	

Mental state: 3. Average endpoint score (various scales, high = poor) - skewed data

Analysis 1.7. Comparison I CHLORPROMAZINE versus OLANZAPINE, Outcome 7 Service involvement: I. Re-hospitalisation.

Review: Chlorpromazine versus atypical antipsychotic drugs for schizophrenia Comparison: I CHLORPROMAZINE versus OLANZAPINE Outcome: 7 Service involvement: I. Re-hospitalisation

Study or subgroup	Chlorpromazine	Olanzapine	Risk Ratio M-	Weight	Risk Ratio M-
	n/N	n/N	H,Random,95% Cl		H,Random,95%
I long term (over 12 month	ns)				
vs OLZ - An 2006	6/35	4/35		100.0 %	1.50 [0.46, 4.86]
Subtotal (95% CI)	35	35	-	100.0 %	1.50 [0.46, 4.86]
Total events: 6 (Chlorproma	azine), 4 (Olanzapine)				
Heterogeneity: not applicab	le				
Test for overall effect: $Z = C$	0.68 (P = 0.50)				
Test for subgroup difference	es: Not applicable				
			<u>, , , , , , , , , , , , , , , , , , , </u>		
		(0.01 0.1 1 10	100	

Chlorpromazine Olanzapine

Analysis 1.8. Comparison | CHLORPROMAZINE versus OLANZAPINE, Outcome 8 Functioning: 1. Executive function - average endpoint score (WCST, high = poor).

Review: Chlorpromazine versus atypical antipsychotic drugs for schizophrenia Comparison: I CHLORPROMAZINE versus OLANZAPINE

Outcome: 8 Functioning: I. Executive function - average endpoint score (WCST, high = poor)

Study or subgroup	Chlorpromazine		Olanzapine		Dif	Mean fference	Weight	Mean Difference
	Ν	Mean(SD)	Ν	Mean(SD)	IV,Rano	dom,95% Cl		IV,Random,95% CI
l short term (up to 6 m	onths)							
vs OLZ - An 2006	29	68.17 (20.31)	24	57.21 (16.63)		-	100.0 %	10.96 [1.01, 20.91]
Subtotal (95% CI)	29		24			•	100.0 %	10.96 [1.01, 20.91]
Heterogeneity: not applie	cable							
Test for overall effect: Z	= 2.16 (P = 0.031)							
Test for subgroup differe	nces: Not applicable	2						
					<u> </u>		1	
				-	100 -50	0 50	100	
				Cł	nlorpromazine	Olanzapine	e	

Analysis 1.9. Comparison I CHLORPROMAZINE versus OLANZAPINE, Outcome 9 Adverse effects: 1. Anticholinergic - short term (up to 6 months).

Review: Chlorpromazine versus atypical antipsychotic drugs for schizophrenia Comparison: I CHLORPROMAZINE versus OLANZAPINE

Outcome: 9 Adverse effects: I. Anticholinergic - short term (up to 6 months)

Study or subgroup	Chlorpromazine	Olanzapine	Risk Ratio M-	Weight	Risk Ratic M-
	n/N	n/N	H,Random,95% Cl		H,Random, C
I blurred vision					
vs OLZ - He 2003	8/40	2/40	-	41.6 %	4.00 [0.90, 17.68]
vs OLZ - Wu 2008	9/50	2/50		41.7 %	4.50 [1.02, 19.79]
vs OLZ - Zhao 2006	0/29	2/32		16.7 %	0.22 [0.01, 4.40
Subtotal (95% CI)	119	122	-	100.0 %	2.59 [0.66, 10.22]
Total events: 17 (Chlorpromaz Heterogeneity: Tau ² = 0.60; C Test for overall effect: Z = 1.3	$Chi^2 = 3.40, df = 2 (P = 0)$), 8); ² =4 %			
2 dry mouth vs OLZ - Chang 2003	1/27	7/31		16.8 %	0.16 [0.02, 1.25
vs OLZ - He 2003	26/40	5/40		24.2 %	5.20 [2.22, 12.18
vs OLZ - Wang 2008	1/119	7/118	_ _	16.5 %	0.14 [0.02, 1.13
vs OLZ - Wu 2008	8/50	2/50		20.3 %	4.00 [0.89, 17.91
vs OLZ - Zhao 2006	5/29	4/32		22.1 %	1.38 [0.41, 4.65
Subtotal (95% CI)	265	4/32 271	-	22.1 % 100.0 %	-
Subtotal (95% CI) Total events: 41 (Chlorpromaz Heterogeneity: Tau ² = 1.83; C Test for overall effect: Z = 0.13	265 zine), 25 (Olanzapine) Chi ² = 18.59, df = 4 (P =	271	-		1.13 [0.29, 4.45
Subtotal (95% CI) Total events: 41 (Chlorpromaz Heterogeneity: Tau ² = 1.83; C Test for overall effect: Z = 0.13 3 excessive sweating	265 zine), 25 (Olanzapine) Chi ² = 18.59, df = 4 (P = 8 (P = 0.86)	271 0.00095); I ² =78%		100.0 %	1.38 [0.41, 4.65 1.13 [0.29, 4.45] 3.00 [0.33, 27.63 3.00 [0.32, 27.87
Subtotal (95% CI) Total events: 41 (Chlorpromaz Heterogeneity: Tau ² = 1.83; C Test for overall effect: Z = 0.13 3 excessive sweating vs OLZ - He 2003 vs OLZ - Wu 2008 Subtotal (95% CI) Total events: 6 (Chlorpromazin Heterogeneity: Tau ² = 0.0; Ch Test for overall effect: Z = 1.3	265 zine), 25 (Olanzapine) Chi ² = 18.59, df = 4 (P = 8 (P = 0.86) 3/40 3/50 90 ne), 2 (Olanzapine) ni ² = 0.0, df = 1 (P = 1.0	271 0.00095); l ² =78% 1/40 1/50 90		100.0 %	1.13 [0.29, 4.45 3.00 [0.33, 27.63 3.00 [0.32, 27.87
Subtotal (95% CI) Total events: 41 (Chlorpromaz Heterogeneity: Tau ² = 1.83; C Test for overall effect: Z = 0.13 3 excessive sweating vs OLZ - He 2003 vs OLZ - Wu 2008 Subtotal (95% CI) Total events: 6 (Chlorpromazii Heterogeneity: Tau ² = 0.0; Ch	265 zine), 25 (Olanzapine) Chi ² = 18.59, df = 4 (P = 8 (P = 0.86) 3/40 3/50 90 ne), 2 (Olanzapine) ni ² = 0.0, df = 1 (P = 1.0	271 0.00095); l ² =78% 1/40 1/50 90		100.0 % 50.2 % 49.8 %	1.13 [0.29, 4.45] 3.00 [0.33, 27.63
Subtotal (95% CI) Total events: 41 (Chlorpromaz Heterogeneity: Tau ² = 1.83; C Test for overall effect: Z = 0.13 3 excessive sweating vs OLZ - He 2003 vs OLZ - Wu 2008 Subtotal (95% CI) Total events: 6 (Chlorpromazin Heterogeneity: Tau ² = 0.0; Ch Test for overall effect: Z = 1.37 4 hypersalivation	265 zine), 25 (Olanzapine) Chi ² = 18.59, df = 4 (P = 8 (P = 0.86) 3/40 3/50 90 ne), 2 (Olanzapine) ni ² = 0.0, df = 1 (P = 1.0 7 (P = 0.17)	271 0.00095); l ² =78% 1/40 1/50 90 D); l ² =0.0%		100.0 % 50.2 % 49.8 % 100.0 %	1.13 [0.29, 4.45 3.00 [0.33, 27.63 3.00 [0.32, 27.87 3.00 [0.62, 14.46

(Continued . . .)

						(Continued)
Study or subgroup	Chlorpromazine	Olanzapine		Risk Ratio	Weight	Risk Ratio
			H,R	M- andom,95%		M- H,Random,95%
p	n/N	n/N		Cl		Cl
Total events: 45 (Chlorpror	mazine), 4 (Olanzapine)					
Heterogeneity: $Tau^2 = 0.0$;	$Chi^2 = 0.00, df = 1 (P = 1.0)$	00); l ² =0.0%				
Test for overall effect: $Z = 4$	4.81 (P < 0.00001)					
5 stuffy nose						
vs OLZ - He 2003	12/40	4/40			100.0 %	3.00 [1.06, 8.52]
Subtotal (95% CI)	40	40		•	100.0 %	3.00 [1.06, 8.52]
Total events: 12 (Chlorpror	mazine), 4 (Olanzapine)					
Heterogeneity: not applicat	ble					
Test for overall effect: $Z = 2$	2.06 (P = 0.039)					
Test for subgroup difference	es: Chi ² = 8.13, df = 4 (P =	0.09), l ² =51%				
			0.01 0.1	I IO IOO		
			Chlorpromazine	Olanzapine		

Analysis 1.10. Comparison I CHLORPROMAZINE versus OLANZAPINE, Outcome 10 Adverse effects: 2. Cardiovascular - short term (up to 6 months).

Review: Chlorpromazine versus atypical antipsychotic drugs for schizophrenia Comparison: I CHLORPROMAZINE versus OLANZAPINE

Outcome: 10 Adverse effects: 2. Cardiovascular - short term (up to 6 months)

Study or subgroup	Chlorpromazine	Olanzapine	Risk Ratio M-	Weight	Risk Ratio M-
	n/N	n/N	H,Random,95% Cl		H,Random,95% Cl
I abnormal ECG					
vs OLZ - He 2003	2/40	0/40		35.5 %	5.00 [0.25, 100.97]
vs OLZ - Wu 2008	3/50	1/50		64.5 %	3.00 [0.32, 27.87]
Subtotal (95% CI)	90	90	-	100.0 %	3.60 [0.60, 21.55]
Total events: 5 (Chlorprom	nazine), I (Olanzapine)				
Heterogeneity: $Tau^2 = 0.0$;	$Chi^2 = 0.07, df = 1 (P = 0)$	1.79); l ² =0.0%			
Test for overall effect: Z =	1.40 (P = 0.16)				
2 apathism					
vs OLZ - Wu 2008	10/50	2/50		100.0 %	5.00 [1.15, 21.67]
Subtotal (95% CI)	50	50	-	100.0 %	5.00 [1.15, 21.67]
			0.001 0.01 0.1 1 10 100 1000	J	
			Chlorpromazine Olanzapine		(Captioned)

(Continued . . .)

Study or subgroup	Chlorpromazine	Olanzapine	Risk Ratio	Weight	(Continued Risk Ratio M-
	n/N	n/N	H,Random,95% Cl		H,Random,91 Cl
Total events: 10 (Chlorproma	zine), 2 (Olanzapine)				
Heterogeneity: not applicable					
Test for overall effect: $Z = 2.1$	15 (P = 0.031)				
3 blood pressure (drop) vs OLZ - He 2003	3/40	0/40		48.9 %	7.00 [0.37, 131.28]
vs OLZ - Wu 2008	5/50	0/50	_	51.1 %	.00 [0.62, 93.80]
Subtotal (95% CI)	90	90	-	100.0 %	8.82 [1.13, 68.52]
Total events: 8 (Chlorpromaz		70		10010 /0	0.02 [1.13, 00.92]
Heterogeneity: $Tau^2 = 0.0$; C Test for overall effect: $Z = 2.0$ 4 orthostatic hypotension	$hi^2 = 0.05, df = 1 (P = 0)$.83); I ² =0.0%			
vs OLZ - Chang 2003	6/27	0/31		20.9 %	4.86 [0.88, 252.]
vs OLZ - Chen 2006	2/44	0/42		18.5 %	4.78 [0.24, 96.68]
vs OLZ - He 2003	3/40	0/40		19.5 %	7.00 [0.37, 3 .28]
vs OLZ - Wang 2008	7/119	0/118		20.6 %	14.88 [0.86, 257.53]
vs OLZ - Wu 2008	5/50	0/50		20.4 %	.00 [0.62, 93.80]
Subtotal (95% CI)	280	281	•	100.0 %	9.78 [2.68, 35.71]
Total events: 23 (Chlorproma Heterogeneity: Tau ² = 0.0; C Test for overall effect: Z = 3.4 5 palpitation vs OLZ - Wang 2008	$hi^2 = 0.45, df = 4 (P = 0)$.98); I ² =0.0% 0/118		100.0 %	40.66 [2.49, 664.56]
Subtotal (95% CI)	119	118		100.0 %	40.66 [2.49, 664.56]
Total events: 20 (Chlorproma Heterogeneity: not applicable Test for overall effect: Z = 2.6 6 tachycardia vs OLZ - He 2003	izine), 0 (Olanzapine)	2/40		21.1 %	2.00 [0.39, 10.31]
vs OLZ - Wu 2008	7/50	3/50	+	33.8 %	2.33 [0.64, 8.51]
vs OLZ - Zhao 2006	17/29	3/32		45.2 %	6.25 [2.04, 19.16]
Subtotal (95% CI)	119	122	•	100.0 %	3.53 [1.66, 7.48]
Total events: 28 (Chlorproma Heterogeneity: Tau ² = 0.0; C Test for overall effect: $Z = 3.2$ Test for subgroup differences	$hi^2 = 1.87, df = 2 (P = 0)$ 28 (P = 0.0010)				

Chlorpromazine Olanzapine

Analysis 1.11. Comparison I CHLORPROMAZINE versus OLANZAPINE, Outcome 11 Adverse effects: 3. Central nervous system - short term (up to 6 months).

Review: Chlorpromazine versus atypical antipsychotic drugs for schizophrenia

Comparison: I CHLORPROMAZINE versus OLANZAPINE

Outcome: II Adverse effects: 3. Central nervous system - short term (up to 6 months)

Study or subgroup	Chlorpromazine	Olanzapine	Risk Ratio M-	Weight	Risk Ratio M-
	n/N	n/N	H,Random,95% Cl		H,Random,9 CI
l dizziness					
vs OLZ - He 2003	6/40	1/40		35.9 %	6.00 [0.76, 47.60]
vs OLZ - Wu 2008	6/50	2/50		64.1 %	3.00 [0.64, 14.16]
Subtotal (95% CI)	90	90	•	100.0 %	3.85 [1.11, 13.32]
Total events: 12 (Chlorproma	azine), 3 (Olanzapine)				
Heterogeneity: $Tau^2 = 0.0$; C	$Chi^2 = 0.28$, $df = 1$ (P = 0.4	50); I ² =0.0%			
Test for overall effect: $Z = 2$.	I3 (P = 0.033)				
2 drowsiness					
vs OLZ - Chang 2003	15/27	6/31	-	24.4 %	2.87 [1.30, 6.35]
vs OLZ - He 2003	6/40	2/40	+	6.5 %	3.00 [0.64, 3.98]
vs OLZ - Wang 2008	18/119	/ 8	-	30.9 %	1.62 [0.80, 3.29]
vs OLZ - Wu 2008	14/50	4/50		14.2 %	3.50 [1.24, 9.90]
vs OLZ - Zhao 2006	15/29	6/32	-	23.9 %	2.76 [1.24, 6.15]
Subtotal (95% CI)	265	271	•	100.0 %	2.46 [1.66, 3.64]
Total events: 68 (Chlorproma	azine), 29 (Olanzapine)				
Heterogeneity: Tau ² = 0.0; C	$hi^2 = 2.07, df = 4 (P = 0.7)$	72); I ² =0.0%			
Test for overall effect: $Z = 4$.	49 (P < 0.00001)				
3 fatigue					
vs OLZ - Wu 2008	6/50	3/50		68.7 %	2.00 [0.53, 7.56]
vs OLZ - Zhao 2006	0/29	2/32		31.3 %	0.22 [0.01, 4.40]
Subtotal (95% CI)	79	82	-	100.0 %	1.00 [0.13, 7.66]
Total events: 6 (Chlorpromaz	, , , , ,				
Heterogeneity: $Tau^2 = 1.11;$,	0.18); l ² =44%			
est for overall effect: $Z = 0.0$	· /				
est for subgroup differences	$: Chi^2 = 1.24, df = 2 (P =$	0.54), l ² =0.0%			

0.001 0.01 0.1 1 10 100 1000

Chlorpromazine Olanzapine

Analysis 1.12. Comparison I CHLORPROMAZINE versus OLANZAPINE, Outcome 12 Adverse effects: 4. Gastrointestinal - short term (up to 6 months).

Review: Chlorpromazine versus atypical antipsychotic drugs for schizophrenia

Comparison: I CHLORPROMAZINE versus OLANZAPINE

Outcome: 12 Adverse effects: 4. Gastrointestinal - short term (up to 6 months)

	Chlorpromazine	Olanzapine	Risk Ratio M-	Weight	Risk Ratic M
	n/N	n/N	H,Random,95% Cl		H,Random, C
appetite loss					
vs OLZ - He 2003	28/40	4/40		67.3 %	7.00 [2.70, 18.13]
vs OLZ - Wu 2008	28/50	1/50		32.7 %	28.00 [3.96, 197.94]
Subtotal (95% CI)	90	90	•	100.0 %	11.01 [2.82, 42.94]
Fotal events: 56 (Chlorprom	, , , ,				
Heterogeneity: $Tau^2 = 0.48$;		0.18); l ² =44%			
Test for overall effect: $Z = 3$.	.45 (P = 0.00055)				
2 constipation vs OLZ - Chang 2003	12/27	1/31		6.3 %	13.78 [1.91, 99.16
vs OLZ - Chen 2006	10/44	4/42	-	21.2 %	2.39 [0.81, 7.02
					L
vs OLZ - He 2003	16/40	5/40		30.3 %	3.20 [1.30, 7.90
vs OLZ - Wang 2008	4/ 9	2/118		11.6 %	6.94 [1.61, 29.87
vs OLZ - Wu 2008	18/50	4/50		24.2 %	4.50 [1.64, 12.36
vs OLZ - Zhao 2006	12/29	1/32		6.3 %	3.24 [.83, 95.63
	200	212	•	100.0 %	4.29 [2.61, 7.05
Subtotal (95% CI)	309	313	•	100.0 %	4.29 [2.01, /.09]
Fotal events: 82 (Chlorprom		515	•	100.0 %	4.29 [2.01, 7.09
. ,	azine), 17 (Olanzapine)			100.0 %	4.27 [2.01, 7.03
Fotal events: 82 (Chlorprom Heterogeneity: Tau ² = 0.0; C Fest for overall effect: $Z = 5$.	hazine), 17 (Olanzapine) Chi ² = 4.83, df = 5 (P = 0			100.0 %	4.27 [2.01, 7.03
Total events: 82 (Chlorprom Heterogeneity: Tau ² = 0.0; C Test for overall effect: $Z = 5$. 8 diarrhoea	azine), 17 (Olanzapine) Chi ² = 4.83, df = 5 (P = 0 .74 (P < 0.00001)	1.44); I ² =0.0%			
Fotal events: 82 (Chlorprom Heterogeneity: Tau ² = 0.0; C Fest for overall effect: $Z = 5$.	hazine), 17 (Olanzapine) Chi ² = 4.83, df = 5 (P = 0		-	100.0 %	
Total events: 82 (Chlorprom Heterogeneity: Tau ² = 0.0; C Test for overall effect: Z = 5. 8 diarrhoea vs OLZ - He 2003 Subtotal (95% CI)	azine), 17 (Olanzapine) Chi ² = 4.83, df = 5 (P = 0 .74 (P < 0.00001) 2/40 40	1.44); I ² =0.0%			5.00 [0.25, 100.97
Total events: 82 (Chlorprom Heterogeneity: Tau ² = 0.0; C Test for overall effect: Z = 5, 8 diarrhoea vs OLZ - He 2003 Subtotal (95% CI) Total events: 2 (Chlorproma	azine), 17 (Olanzapine) Chi ² = 4.83, df = 5 (P = 0 .74 (P < 0.00001) 2/40 40 zine), 0 (Olanzapine)	1.44); 1 ² =0.0% 0/40		100.0 %	5.00 [0.25, 100.97
Total events: 82 (Chlorprom Heterogeneity: Tau ² = 0.0; C Fest for overall effect: Z = 5. 3 diarrhoea vs OLZ - He 2003 Subtotal (95% CI) Fotal events: 2 (Chlorproma Heterogeneity: not applicabl	azine), 17 (Olanzapine) Chi ² = 4.83, df = 5 (P = 0 .74 (P < 0.00001) 2/40 40 zine), 0 (Olanzapine) e	1.44); 1 ² =0.0% 0/40		100.0 %	5.00 [0.25, 100.97
Total events: 82 (Chlorprom Heterogeneity: Tau ² = 0.0; C Fest for overall effect: Z = 5. 3 diarrhoea vs OLZ - He 2003 Subtotal (95% CI) Fotal events: 2 (Chlorproma Heterogeneity: not applicabl Fest for overall effect: Z = 1.	azine), 17 (Olanzapine) Chi ² = 4.83, df = 5 (P = 0 .74 (P < 0.00001) 2/40 40 zine), 0 (Olanzapine) e	1.44); 1 ² =0.0% 0/40		100.0 %	5.00 [0.25, 100.97
Total events: 82 (Chlorprom Heterogeneity: Tau ² = 0.0; C Fest for overall effect: Z = 5. 3 diarrhoea vs OLZ - He 2003 Subtotal (95% CI) Fotal events: 2 (Chlorproma Heterogeneity: not applicabl	azine), 17 (Olanzapine) Chi ² = 4.83, df = 5 (P = 0 .74 (P < 0.00001) 2/40 40 zine), 0 (Olanzapine) e	1.44); 1 ² =0.0% 0/40		100.0 %	5.00 [0.25, 100.97 5.00 [0.25, 100.97] 3.00 [0.13, 71.92
Total events: 82 (Chlorprom Heterogeneity: Tau ² = 0.0; C Test for overall effect: Z = 5, diarrhoea vs OLZ - He 2003 Subtotal (95% CI) Total events: 2 (Chlorproma Heterogeneity: not applicabl Test for overall effect: Z = 1, dysphagia vs OLZ - Wu 2008	azine), 17 (Olanzapine) Chi ² = 4.83, df = 5 (P = 0 .74 (P < 0.00001) 2/40 40 zine), 0 (Olanzapine) e .05 (P = 0.29)	1.44); I ² =0.0% 0/40 40		100.0 % 100.0 %	5.00 [0.25, 100.97 5.00 [0.25, 100.97 3.00 [0.13, 71.92
Total events: 82 (Chlorprom Heterogeneity: Tau ² = 0.0; C Fest for overall effect: Z = 5. 3 diarrhoea vs OLZ - He 2003 Subtotal (95% CI) Fotal events: 2 (Chlorproma Heterogeneity: not applicabl Fest for overall effect: Z = 1. 4 dysphagia	azine), 17 (Olanzapine) Chi ² = 4.83, df = 5 (P = 0 .74 (P < 0.00001) 2/40 40 zine), 0 (Olanzapine) e .05 (P = 0.29) 1/50 50	1.44); 1 ² =0.0% 0/40 40 0/50		100.0 % 100.0 % 100.0 %	5.00 [0.25, 100.97 5.00 [0.25, 100.97]
Total events: 82 (Chlorprom Heterogeneity: Tau ² = 0.0; C Fest for overall effect: Z = 5. 3 diarrhoea vs OLZ - He 2003 Subtotal (95% CI) Fotal events: 2 (Chlorproma Heterogeneity: not applicabl Fest for overall effect: Z = 1. 4 dysphagia vs OLZ - Wu 2008 Subtotal (95% CI)	azine), 17 (Olanzapine) Chi ² = 4.83, df = 5 (P = 0 .74 (P < 0.00001) 2/40 40 zine), 0 (Olanzapine) e .05 (P = 0.29) 1/50 50 zine), 0 (Olanzapine)	1.44); 1 ² =0.0% 0/40 40 0/50		100.0 % 100.0 % 100.0 %	5.00 [0.25, 100.97 5.00 [0.25, 100.97 3.00 [0.13, 71.92
Total events: 82 (Chlorprom Heterogeneity: Tau ² = 0.0; C Fest for overall effect: Z = 5. 3 diarrhoea vs OLZ - He 2003 Subtotal (95% CI) Fotal events: 2 (Chlorproma Heterogeneity: not applicabl Fest for overall effect: Z = 1. 4 dysphagia vs OLZ - Wu 2008 Subtotal (95% CI) Fotal events: 1 (Chlorproma	azine), 17 (Olanzapine) Chi ² = 4.83, df = 5 (P = 0 .74 (P < 0.00001) 2/40 40 zine), 0 (Olanzapine) e .05 (P = 0.29) 1/50 50 zine), 0 (Olanzapine) e	1.44); 1 ² =0.0% 0/40 40 0/50		100.0 % 100.0 % 100.0 %	5.00 [0.25, 100.97 5.00 [0.25, 100.97 3.00 [0.13, 71.92
Total events: 82 (Chlorprom Heterogeneity: Tau ² = 0.0; C Fest for overall effect: Z = 5. 3 diarrhoea vs OLZ - He 2003 Subtotal (95% CI) Fotal events: 2 (Chlorproma Heterogeneity: not applicabl Test for overall effect: Z = 1. 4 dysphagia vs OLZ - Wu 2008 Subtotal (95% CI) Fotal events: 1 (Chlorproma Heterogeneity: not applicabl	azine), 17 (Olanzapine) Chi ² = 4.83, df = 5 (P = 0 .74 (P < 0.00001) 2/40 40 zine), 0 (Olanzapine) e .05 (P = 0.29) 1/50 50 zine), 0 (Olanzapine) e	1.44); 1 ² =0.0% 0/40 40 0/50		100.0 % 100.0 % 100.0 %	5.00 [0.25, 100.97 5.00 [0.25, 100.97 3.00 [0.13, 71.92
Total events: 82 (Chlorprom Heterogeneity: Tau ² = 0.0; C Fest for overall effect: Z = 5. 3 diarrhoea vs OLZ - He 2003 Subtotal (95% CI) Fotal events: 2 (Chlorproma Heterogeneity: not applicabl Test for overall effect: Z = 1. 4 dysphagia vs OLZ - Wu 2008 Subtotal (95% CI) Fotal events: 1 (Chlorproma Heterogeneity: not applicabl Test for overall effect: Z = 0.	azine), 17 (Olanzapine) Chi ² = 4.83, df = 5 (P = 0 .74 (P < 0.00001) 2/40 40 zine), 0 (Olanzapine) e .05 (P = 0.29) 1/50 50 zine), 0 (Olanzapine) e	1.44); 1 ² =0.0% 0/40 40 0/50		100.0 % 100.0 % 100.0 %	5.00 [0.25, 100.97 5.00 [0.25, 100.97] 3.00 [0.13, 71.92

(Continued . . .)

Study or subgroup	Chlorpromazine	Olanzapine	Risk Ratio M-	Weight	(Continued) Risk Ratio M-
	n/N	n/N	H,Random,95% Cl		H,Random,95% Cl
vs OLZ - He 2003	4/40	2/40		57.8 %	2.00 [0.39, 10.31]
vs OLZ - Wu 2008	2/50	2/50	_	42.2 %	1.00 [0.15, 6.82]
Subtotal (95% CI)	90	90	-	100.0 %	1.49 [0.43, 5.20]
Total events: 6 (Chlorproma	azine), 4 (Olanzapine)				
Heterogeneity: $Tau^2 = 0.0;$	$Chi^2 = 0.29, df = 1 (P = 0.29)$	59); I ² =0.0%			
Test for overall effect: $Z = 0$	0.63 (P = 0.53)				
Test for subgroup difference	es: $Chi^2 = 4.63$, $df = 4$ (P =	= 0.33), I ² = I 4%			
				i	
			0.002 0.1 1 10 5	500	
			Chlorpromazine Olanzapine		

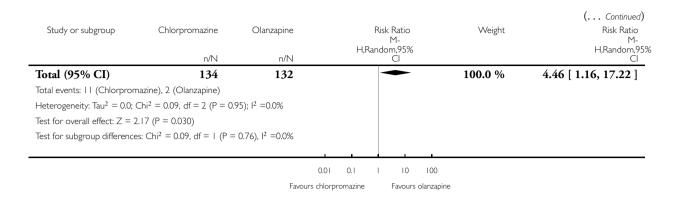
Analysis 1.13. Comparison I CHLORPROMAZINE versus OLANZAPINE, Outcome 13 Adverse effects: 5. Haematology - short term (up to 6 months).

Review: Chlorpromazine versus atypical antipsychotic drugs for schizophrenia

Comparison: I CHLORPROMAZINE versus OLANZAPINE

Outcome: 13 Adverse effects: 5. Haematology - short term (up to 6 months)

	Olanzapine	Risk Ratio M-	Weight	Risk Ratio M-
n/N	n/N	H,Random,95% Cl		H,Random,95%
4/40	1/40		39.6 %	4.00 [0.47, 34.24]
4/50	1/50		39.2 %	4.00 [0.46, 34.54]
90	90	-	7 8.8 %	4.00 [0.87, 18.31]
ne), 2 (Olanzapine) ni ² = 0.0, df = 1 (P = 1.00 9 (P = 0.074)	D); I ² =0.0%			
3/44	0/42		21.2 %	6.69 [0.36, 125.71]
44	42		21.2 %	6.69 [0.36, 125.71]
ne), 0 (Olanzapine) 7 (P = 0.20)				
			ne	(Continued)
ר יי	4/40 4/50 90 ne), 2 (Olanzapine) bi ² = 0.0, df = 1 (P = 1.00 9 (P = 0.074) 3/44 44 ne), 0 (Olanzapine)	4/40 1/40 4/50 1/50 90 90 90 90 90 90 90	n/N n/N Cl 4/40 1/40 4/50 1/50 90 90 ne). 2 (Olanzapine) $n^2 = 0.0, df = 1 (P = 1.00); l^2 = 0.0\%$ 9 (P = 0.074) 3/44 0/42 44 42 ne), 0 (Olanzapine) 7 (P = 0.20) 0.01 0.1 1 10 100	$\begin{array}{c ccccccccccccccccccccccccccccccccccc$



Analysis 1.14. Comparison I CHLORPROMAZINE versus OLANZAPINE, Outcome 14 Adverse effects: 6. Hepatitic - short term (up to 6 months).

Review: Chlorpromazine versus atypical antipsychotic drugs for schizophrenia Comparison: I CHLORPROMAZINE versus OLANZAPINE

Outcome: 14 Adverse effects: 6. Hepatitic - short term (up to 6 months)

Study or subgroup	Chlorpromazine	Olanzapine	Risk Ratio M-	Weight	Risk Ratio M-
	n/N	n/N	H,Random,95% Cl		H,Random,95% Cl
I abnormal liver function					
vs OLZ - Wu 2008	2/50	0/50		→ 100.0 %	5.00 [0.25, 101.58]
Subtotal (95% CI)	50	50		100.0 %	5.00 [0.25, 101.58]
Total events: 2 (Chlorprom	azine), 0 (Olanzapine)				
Heterogeneity: not applicab	le				
Test for overall effect: Z =	1.05 (P = 0.29)				
2 abnormal transaminase					
vs OLZ - Chen 2006	0/44	7/42	• •	50.1 %	0.06 [0.00, 1.08]
vs OLZ - Zhao 2006	5/29	0/32		→ 49.9 %	12.10 [0.70, 209.71]
Subtotal (95% CI)	73	74		100.0 %	0.88 [0.01, 150.45]
Total events: 5 (Chlorprom	azine), 7 (Olanzapine)				
Heterogeneity: $Tau^2 = 11.6$	9; Chi ² = 6.56, df = 1 (P =	= 0.01); I ² =85%			
Test for overall effect: $Z = 0$	0.05 (P = 0.96)				
Test for subgroup difference	es: Chi ² = 0.33, df = 1 (P =	= 0.57), l ² =0.0%			
				1	
			0.01 0.1 1 10	100	
		Favo	urs chlorpromazine Favours	olanzapine	

Analysis 1.15. Comparison I CHLORPROMAZINE versus OLANZAPINE, Outcome 15 Adverse effects: 7a. Metabolic - weight gain - short term (up to 6 months).

Review: Chlorpromazine versus atypical antipsychotic drugs for schizophrenia

Comparison: I CHLORPROMAZINE versus OLANZAPINE

Outcome: 15 Adverse effects: 7a. Metabolic - weight gain - short term (up to 6 months)

Study or subgroup	Chlorpromazine	Olanzapine	Risk Ratio M- H.Random,95%	Weight	Risk Ratio M- H,Random,95%
	n/N	n/N	Cl		CI
vs OLZ - Chang 2003	2/27	8/31		18.6 %	0.29 [0.07, 1.24]
vs OLZ - He 2003	10/40	3/40		21.1 %	3.33 [0.99, .22]
vs OLZ - Wang 2008	2/119	9/118		18.1 %	0.22 [0.05, 1.00]
vs OLZ - Wu 2008	6/50	4/50	-	21.2 %	1.50 [0.45, 4.99]
vs OLZ - Zhao 2006	3/29	8/32		20.9 %	0.41 [0.12, 1.41]
Total (95% CI)	265	271	•	100.0 %	0.70 [0.25, 1.96]
Total events: 23 (Chlorprom	azine), 32 (Olanzapine)				
Heterogeneity: $Tau^2 = 0.91$;	Chi ² = 12.17, df = 4 (P =	0.02); I ² =67%			
Test for overall effect: $Z = 0$.	.67 (P = 0.50)				
Test for subgroup differences	s: Not applicable				
			0.002 0.1 1 10 500		

Chlorpromazine Olanzapine

Analysis 1.16. Comparison I CHLORPROMAZINE versus OLANZAPINE, Outcome 16 Adverse effects: 7b. Metabolic - weight gain - continuous measures.

Review: Chlorpromazine versus atypical antipsychotic drugs for schizophrenia

Comparison: I CHLORPROMAZINE versus OLANZAPINE

Outcome: 16 Adverse effects: 7b. Metabolic - weight gain - continuous measures

Study or subgroup	Chlorpromazine		Olanzapine		Mean Difference	Weight	Mean Difference
	Ν	Mean(SD)	Ν	Mean(SD)	IV,Random,95% CI		IV,Random,95% CI
I short term (up to 6 months)							
HGCQ (Turkey) 2000	10	75.2 (13.19)	20	75.2 (11.38)		17.8 %	0.0 [-9.58, 9.58]
HGDV (Morocco) 1999	12	66.58 (7.62)	27	74.48 (10.73)		46.6 %	-7.90 [-13.81, -1.99]
vs OLZ - Loza 1999 (HGDT) 14	69.21 (14.86)	27	73.19 (13.47)		18.9 %	-3.98 [-13.28, 5.32]
vs OLZ - Luo 2007	20	62.3 (16.8)	30	66.35 (18.38)		16.7 %	-4.05 [-13.92, 5.82]
Subtotal (95% CI)	56		104			100.0 %	-5.11 [-9.15, -1.07]
Heterogeneity: Tau ² = 0.0; Chi ²	= 2.05, df = 3 (P =	= 0.56); l ² =0.0	%				
Test for overall effect: $Z = 2.48$	(P = 0.013)						
2 medium term (7 to 12 month	ns)						
vs OLZ - Luo 2007	20	69.13 (24.75)	30	68.54 (17.13)		→ 100.0 %	0.59 [-11.87, 13.05]
Subtotal (95% CI)	20		30	-		- 100.0 %	0.59 [-11.87, 13.05]
Heterogeneity: not applicable							
Test for overall effect: Z = 0.09	(P = 0.93)						
Test for subgroup differences: C	$chi^2 = 0.73, df = 1$ ($P = 0.39$), $ ^2 = 0.39$	0.0%				

-10 -5 0 5 10 Chlorpromazine Olanzapine

Analysis 1.17. Comparison I CHLORPROMAZINE versus OLANZAPINE, Outcome 17 Adverse effects: 7c. Metabolic - other - continuous measures.

Review: Chlorpromazine versus atypical antipsychotic drugs for schizophrenia Comparison: I CHLORPROMAZINE versus OLANZAPINE

Outcome: 17 Adverse effects: 7c. Metabolic - other - continuous measures

Study or subgroup	Chlorpromazine N	O Mean(SD)	lanzapine N	Mean(SD)	Mean Difference IV,Random,95% Cl	Weight	Mean Difference IV,Random,95% CI
I cholesterol (TC) - short	term (up to 6 mor	ths)					
vs OLZ - Luo 2007	20	4.22 (0.93)	30	4.62 (1.31)		100.0 %	-0.40 [-1.02, 0.22]
Subtotal (95% CI)	20		30			100.0 %	-0.40 [-1.02, 0.22]
Heterogeneity: not applica							
Test for overall effect: Z =	, ,						
2 high-density lipoprotein		· · · · · · · · · · · · · · · · · · ·					
vs OLZ - Luo 2007	20	1.03 (0.25)	30	0.98 (0.35)	-	100.0 %	0.05 [-0.12, 0.22]
Subtotal (95% CI)	20		30			100.0 %	0.05 [-0.12, 0.22]
Heterogeneity: not applica	able						
Test for overall effect: Z =	0.59 (P = 0.56)						
3 low-density lipoprotein	(LDL) - short term	(up to 6 months)					
vs OLZ - Luo 2007	20	2.29 (0.46)	30	2.3 (0.61)	-	100.0 %	-0.01 [-0.31, 0.29]
Subtotal (95% CI)	20		30			100.0 %	-0.01 [-0.31, 0.29]
Heterogeneity: not applica	able						
Test for overall effect: Z =	0.07 (P = 0.95)						
4 low-density lipoprotein	(LDL) - medium ter	m (7 to 12 months)				
vs OLZ - Luo 2007	20	2.38 (0.81)	30	2.32 (0.84)	-	100.0 %	0.06 [-0.41, 0.53]
Subtotal (95% CI)	20		30			100.0 %	0.06 [-0.41, 0.53]
Heterogeneity: not applica	able						
Test for overall effect: Z =	0.25 (P = 0.80)						
Test for subgroup differen	ces: Chi ² = 1.95, df	$= 3 (P = 0.58), I^2 =$	=0.0%				
						I	
				-100	0 -50 0 50	100	
				Favours chlor	rpromazine Favours ola	nzapine	

Analysis 1.18. Comparison I CHLORPROMAZINE versus OLANZAPINE, Outcome 18 Adverse effects: 7d. Metabolic - other - average endpoint scores - skewed data.

Adverse effects: 7d. Metabolic - other - average endpoint scores - skewed data

Study	Intervention	mean	SD	Ν				
cholesterol (TC) - medium term (7 to 12 months)								
vs OLZ - Luo 2007	Chlorpromazine	4.5	2.21	20				
vs OLZ - Luo 2007	Olanzapine	4.52	2.73	30				

Chlorpromazine versus atypical antipsychotic drugs for schizophrenia (Review)

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Adverse effects: 7d. Metabolic - other - average endpoint scores - skewed data (Continued)

high-density lipopro	high-density lipoprotein (HDL) - short term (up to 6 months) hig								
vs OLZ - Luo 2007	Chlorpromazine	0.89	0.33	20					
vs OLZ - Luo 2007	Olanzapine	0.89	0.45	30					
triglyceride (TG) - short term (up to 6 months) tr									
vs OLZ - Luo 2007	Chlorpromazine	1.44	1.07	20					
vs OLZ - Luo 2007	Olanzapine	2.13	2.07	30					
triglyceride (TG) - n	nedium term (7 to	12 mon	ths)		triglyceride (TG				
vs OLZ - Luo 2007	Chlorpromazine	2.26	2.04	20					
vs OLZ - Luo 2007	Olanzapine	2.32	2.14	30					

Analysis 1.19. Comparison I CHLORPROMAZINE versus OLANZAPINE, Outcome 19 Adverse effects: 8a. Movement disorders - extrapyramidal symptoms - short term (up to 6 months).

Review: Chlorpromazine versus atypical antipsychotic drugs for schizophrenia

Comparison: I CHLORPROMAZINE versus OLANZAPINE

Outcome: 19 Adverse effects: 8a. Movement disorders - extrapyramidal symptoms - short term (up to 6 months)

Study or subgroup	Chlorpromazine	Olanzapine	Olanzapine Risk Ratio M-		Risk Ratio M-	
	n/N	n/N	H,Random,95% Cl		H,Random,95% Cl	
l akathisia						
vs OLZ - He 2003	8/40	4/40		44.7 %	2.00 [0.65, 6.11]	
vs OLZ - Wang 2008	0/119	3/118		22.6 %	0.14[0.01, 2.71]	
vs OLZ - Wu 2008	10/50	1/50		32.7 %	10.00 [1.33, 75.23]	
Subtotal (95% CI)	209	208	-	100.0 %	1.86 [0.29, 11.84]	
Total events: 18 (Chlorpron	nazine), 8 (Olanzapine)					
Heterogeneity: $Tau^2 = 1.67$; $Chi^2 = 5.5 I$, $df = 2 (P =$	0.06); l ² =64%				
Test for overall effect: $Z = 0$	0.66 (P = 0.51)					
2 any EPS symptoms						
vs OLZ - Wang 2008	28/119	0/118		50.3 %	56.53 [3.49, 915.23]	
			0.001 0.01 0.1 1 10 100 1000			
			Chlorpromazine Olanzapine			
			1 F		(Continued)	

(Continued ...)

(Continued Risk Ratio M- H,Random,	Weight	Risk Ratio M- H,Random,95%	Olanzapine n/N	Chlorpromazine n/N	Study or subgroup
CI 20.90 [1.27, 343.87]	49.7 %		0/32	9/29	vs OLZ - Zhao 2006
34.47 [4.79, 248.30]	100.0 %	-	150	148	Subtotal (95% CI)
				azine), 0 (Olanzapine)	Total events: 37 (Chlorproma
			I); I ² =0.0%	$hi^2 = 0.26, df = 1 (P = 0.6)$	Heterogeneity: Tau ² = 0.0; C
				51 (P = 0.00044)	Test for overall effect: $Z = 3.1$
					3 muscle stiffness
3.00 [0.13, 71.51]	45.0 %		0/40	1/40	vs OLZ - He 2003
.00 [0.62, 93.80]	55.0 %		0/50	5/50	vs OLZ - Wu 2008
6.13 [0.73, 51.45]	100.0 %	-	90	90	Subtotal (95% CI)
				tine), 0 (Olanzapine)	Total events: 6 (Chlorpromaz
			4); I ² =0.0%	$hi^2 = 0.37, df = 1 (P = 0.5)$	Heterogeneity: Tau ² = 0.0; C
				67 (P = 0.095)	Test for overall effect: $Z = 1.6$
					4 tremor
5.00 [0.25, 100.97]	48.1 %		0/40	2/40	vs OLZ - He 2003
9.00 [0.50, 162.89]	51.9 %		0/50	4/50	vs OLZ - Wu 2008
6.78 [0.84, 54.57]	100.0 %		90	90	Subtotal (95% CI)
				tine), 0 (Olanzapine)	Total events: 6 (Chlorpromaz
			3); I ² =0.0%	$hi^2 = 0.08, df = 1 (P = 0.7)$	Heterogeneity: Tau ² = 0.0; C
				30 (P = 0.072)	Test for overall effect: $Z = 1.3$
			0.21), I ² =33%	: Chi ² = 4.49, df = 3 (P =	Test for subgroup differences

0.001 0.01 0.1 1 10 100 1000

Chlorpromazine Olanzapine

Analysis 1.20. Comparison I CHLORPROMAZINE versus OLANZAPINE, Outcome 20 Adverse effects: 8b. Movement disorders - extrapyramidal symptoms - average endpoint score (ESRS, high = poor).

Review: Chlorpromazine versus atypical antipsychotic drugs for schizophrenia

Comparison: I CHLORPROMAZINE versus OLANZAPINE

Outcome: 20 Adverse effects: 8b. Movement disorders - extrapyramidal symptoms - average endpoint score (ESRS, high = poor)

Study or subgroup	Chlorpromazine		Olanzapine		Diff	Mean ference	Weight	Mean Difference
	Ν	Mean(SD)	Ν	Mean(SD)	IV,Rand	lom,95% Cl		IV,Random,95% CI
I short term (up to 6 months)								
HGDV (Morocco) 1999	12	13.2 (1.3)	27	12.3 (0.5)			100.0 %	0.90 [0.14, 1.66]
vs OLZ - Loza 1999 (HGDT)	27	12 (0)	14	12 (0)				Not estimable
Subtotal (95% CI)	39		41				100.0 %	0.90 [0.14, 1.66]
Heterogeneity: not applicable								
Test for overall effect: $Z = 2.32$ (I	P = 0.020)							
Test for subgroup differences: No	ot applicable							
				-	2 -1	0 I	2	
				Chl	orpromazine	Olanzapine		

Analysis 1.21. Comparison | CHLORPROMAZINE versus OLANZAPINE, Outcome 21 Adverse effects: 9a. Various other - sleep - average endpoint score (LSEQ, high = better) - short term (up to 6 months).

Review: Chlorpromazine versus atypical antipsychotic drugs for schizophrenia

Comparison: I CHLORPROMAZINE versus OLANZAPINE

Outcome: 21 Adverse effects: 9a. Various other - sleep - average endpoint score (LSEQ, high = better) - short term (up to 6 months)

Study or subgroup	Chlorpromazine		Olanzapine		Mea Differenc		Mean Difference
	Ν	Mean(SD)	Ν	Mean(SD)	IV,Random,9	5% CI	IV,Random,95% CI
I awaking from sleep							
HGCQ (Turkey) 2000	10	48.4 (22.5)	20	53.7 (20.6)	-	100.0 %	-5.30 [-21.91, 11.31]
Subtotal (95% CI)	10		20		•	100.0 %	-5.30 [-21.91, 11.31]
Heterogeneity: not applica	ble						
Test for overall effect: $Z =$	0.63 (P = 0.53)						
2 getting to sleep score							
HGCQ (Turkey) 2000	10	61.3 (25.4)	20	61.9 (25.4)		100.0 %	-0.60 [-19.88, 18.68]
Subtotal (95% CI)	10		20		•	100.0 %	-0.60 [-19.88, 18.68]
Heterogeneity: not applica	ble						
Test for overall effect: $Z =$	0.06 (P = 0.95)						
3 quality of sleep					_		
HGCQ (Turkey) 2000	10	52 (23.3)	20	67 (24.8)		100.0 %	-15.00 [-33.07, 3.07]
Subtotal (95% CI)	10		20		•	100.0 %	-15.00 [-33.07, 3.07]
Heterogeneity: not applica	ble						
Test for overall effect: $Z =$	1.63 (P = 0.10)						
Test for subgroup difference	ces: $Chi^2 = 1.22$, df	= 2 (P = 0.54), l ² =0.0%				
						1 1	
				-	00 -50 0	50 100	
					Olanzapine C	Chlorpromazine	

Analysis 1.22. Comparison I CHLORPROMAZINE versus OLANZAPINE, Outcome 22 Adverse effects: 9b. Various other - sleep - average length of sleep (hour/day).

Review: Chlorpromazine versus atypical antipsychotic drugs for schizophrenia

Comparison: I CHLORPROMAZINE versus OLANZAPINE

Outcome: 22 Adverse effects: 9b. Various other - sleep - average length of sleep (hour/day)

Study or subgroup	Chlorpromazine N	Mean(SD)	Olanzapine N	Mean(SD)		Mean erence om,95% Cl	Weight	Mean Difference IV,Random,95% CI
					.,			
I short term (up to 6 mo	,							
vs OLZ - Luo 2007	20	12.4 (2.7)	30	8.77 (2.8)			100.0 %	3.63 [2.08, 5.18]
Subtotal (95% CI)	20		30			-	100.0 %	3.63 [2.08, 5.18]
Heterogeneity: not applic	able							
Test for overall effect: Z =	= 4.59 (P < 0.00001)							
2 medium term (7 to 12	months)							
vs OLZ - Luo 2007	20	13.52 (3.07)	30	9.11 (2.37)		│ →	100.0 %	4.41 [2.82, 6.00]
Subtotal (95% CI)	20		30			-	100.0 %	4.41 [2.82, 6.00]
Heterogeneity: not applic	able							
Test for overall effect: Z =	= 5.43 (P < 0.00001)							
Test for subgroup differer	nces: $Chi^2 = 0.47$, df	= I (P = 0.49),	² =0.0%					
0 1		. ,						
					-4 -2	0 2 4		
				Ch	lorpromazine	Olanzapine		

Analysis 1.23. Comparison I CHLORPROMAZINE versus OLANZAPINE, Outcome 23 Adverse effects: 9c. Various other - sleep - behaviour following waking (LSEQ) - skewed data.

Adverse effects: 9c. Various other - sleep - behaviour following waking (LSEQ) - skewed data

Study	Intervention	mean	SD	Ν				
short term (up to 6 months)								
HGCQ (Turkey) 2000	Chlorpromazine	55.1	28.3	10				
HGCQ (Turkey) 2000	Olanzapine	55.9	18.8	20				

Analysis 1.24. Comparison I CHLORPROMAZINE versus OLANZAPINE, Outcome 24 Adverse effects: 9b. Various other - rash.

Review: Chlorpromazine versus atypical antipsychotic drugs for schizophrenia Comparison: I CHLORPROMAZINE versus OLANZAPINE Outcome: 24 Adverse effects: 9b. Various other - rash

Study or subgroup	Chlorpromazine	Olanzapine	Risk Ratio M-	Weight	Risk Ratio M-
	n/N	n/N	H,Random,95% Cl		H,Random,95% Cl
I short term (up to 6 mont	:hs)				
HGCQ (Turkey) 2000	1/10	1/20		100.0 %	2.00 [0.14, 28.76]
Total (95% CI)	10	20		100.0 %	2.00 [0.14, 28.76]
Total events: I (Chlorproma	azine), I (Olanzapine)				
Heterogeneity: not applicab	le				
Test for overall effect: $Z = 0$	0.51 (P = 0.61)				
Test for subgroup difference	es: Not applicable				
		0	.01 0.1 1 10 100		
		Favours ch	lorpromazine Favours olanzap	vine	

Analysis 1.25. Comparison I CHLORPROMAZINE versus OLANZAPINE, Outcome 25 Quality of life: 1a. Average endpoint scores (various scales, high = better) - short term (up to 6 months).

Review: Chlorpromazine versus atypical antipsychotic drugs for schizophrenia

Comparison: I CHLORPROMAZINE versus OLANZAPINE

Outcome: 25 Quality of life: I a. Average endpoint scores (various scales, high = better) - short term (up to 6 months)

Study or subgroup	Chlorpromazine N	Mean(SD)	Olanzapine N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% Cl
I GQOLI - living conditio							
vs OLZ - Zhao 2006	29	25.8 (6.3)	32	26.8 (6.5)		100.0 %	-1.00 [-4.21, 2.21]
Subtotal (95% CI)	29		32		+	100.0 %	-1.00 [-4.21, 2.21]
Heterogeneity: not applic	able						
Test for overall effect: Z =	= 0.61 (P = 0.54)						
2 GQOLI - physical healt	h				_		
vs OLZ - Zhao 2006	29	33.5 (8.7)	32	43.6 (6.2)		100.0 %	-10.10 [-13.93, -6.27]
Subtotal (95% CI)	29		32		•	100.0 %	-10.10 [-13.93, -6.27]
Heterogeneity: not applic	able						
Test for overall effect: Z =	= 5.17 (P < 0.00001)					
3 GQOLI - psychological	health						
vs OLZ - Zhao 2006	29	30.2 (6.1)	32	52.8 (7.2)	•	100.0 %	-22.60 [-25.94, -19.26]
Subtotal (95% CI)	29		32			100.0 %	-22.60 [-25.94, -19.26]
Heterogeneity: not applic	able						
Test for overall effect: Z =	= 13.26 (P < 0.0000	I)					
4 GQOLI - social functio	n						
vs OLZ - Zhao 2006	29	32.7 (4.5)	32	50.9 (4.7)	•	100.0 %	-18.20 [-20.51, -15.89]
Subtotal (95% CI)	29		32		•	100.0 %	-18.20 [-20.51, -15.89]
Heterogeneity: not applic	able						
Test for overall effect: Z =	= 15.44 (P < 0.0000	I)					
Test for subgroup differer	nces: $Chi^2 = 105.01$	df = 3 (P = 0	0.00), l ² =97%				
				-2	.0 -10 0 10	20	
					Olanzapine Chlorprom	nazine	

Analysis 1.26. Comparison I CHLORPROMAZINE versus OLANZAPINE, Outcome 26 Quality of life: 1b. Average endpoint score (QoL, high = better) - skewed data.

Quality of life: 1b. Average endpoint score (QoL, high = better) - skewed data

Study	Intervention	mean	SD	Ν			
short term (up to 6 months)							
vs OLZ - Loza 1999 (HGDT)	Chlorpromazine	47.7	26.6	14			

Quality of life: 1b. Average endpoint score (QoL, high = better) - skewed data (Continued)

vs OLZ - Loza 1999 Olanzapine 56.6 31.3 27 (HGDT)

Analysis 1.27. Comparison I CHLORPROMAZINE versus OLANZAPINE, Outcome 27 Leaving the study early - short term (up to 6 months).

Review: Chlorpromazine versus atypical antipsychotic drugs for schizophrenia Comparison: I CHLORPROMAZINE versus OLANZAPINE Outcome: 27 Leaving the study early - short term (up to 6 months)

Study or subgroup	Chlorpromazine	Olanzapine	Risk Ratio M-	Weight	Risk Ratio M-
	n/N	n/N	H,Random,95% Cl		H,Random,95% Cl
I due to any reason					
HGCQ (Turkey) 2000	1/10	5/20		26.8 %	0.40 [0.05, 2.98]
HGDV (Morocco) 1999	2/12	0/27		15.6 %	10.77 [0.56, 208.71]
vs OLZ - An 2006	16/35	8/35	-	57.6 %	2.00 [0.99, 4.06]
Subtotal (95% CI)	57	82	-	100.0 %	1.69 [0.45, 6.40]
Total events: 19 (Chlorpromazine), I 3 (Olanzapine)				
Heterogeneity: $Tau^2 = 0.67$; Chi ²	= 3.64. df = 2 (P = 0.16); l	² =45%			
Test for overall effect: $Z = 0.77$ (F	· · · · · · · · · · · · · · · · · · ·				
2 due to lack of efficacy					
HGCQ (Turkey) 2000	0/10	3/20		36.3 %	0.27 [0.02, 4.82]
vs OLZ - Loza 1999 (HGDT)	1/14	3/27		63.7 %	0.64 [0.07, 5.63]
Subtotal (95% CI)	24	47	-	100.0 %	0.47 [0.08, 2.66]
Total events: I (Chlorpromazine),	6 (Olanzapine)				
Heterogeneity: Tau ² = 0.0; Chi ² =	= 0.22, df = 1 (P = 0.64); l ²	=0.0%			
Test for overall effect: $Z = 0.85$ (F	P = 0.39)				
Test for subgroup differences: Chi	$^{2} = 1.31$, df = 1 (P = 0.25)	, l ² =24%			
		0	.005 0.1 1 10 200)	

Chlorpromazine Olanzapine

Analysis 2.1. Comparison 2 CHLORPROMAZINE versus RISPERIDONE, Outcome 1 Clinical response: 1. No significant clinical response.

 Review:
 Chlorpromazine versus atypical antipsychotic drugs for schizophrenia

 Comparison:
 2 CHLORPROMAZINE versus RISPERIDONE

 Outcome:
 I Clinical response: I. No significant clinical response

Study or subgroup	Chlorpromazine	Risperidone	Risk Ratio M-	Weight	Risk Ratio M-
	n/N	n/N	H,Random,95% Cl		H,Random,95% Cl
I short term (up to 6 month	ns)				
vs RPD - Chang 1998	4/20	9/38		19.8 %	0.84 [0.30, 2.40]
vs RPD - Cui 2001	2/30	2/30		6.1 %	1.00 [0.15, 6.64]
vs RPD - He 1999	4/20	5/21		16.0 %	0.84 [0.26, 2.69]
vs RPD - Lin 2005	5/35	4/35	_	14.4 %	1.25 [0.37, 4.27]
vs RPD - Luo 2001	6/52	13/55		27.4 %	0.49 [0.20, 1.19]
vs RPD - Wang 2002	1/20	3/49		4.5 %	0.82 [0.09, 7.39]
vs RPD - Wu 2002	5/35	3/35		11.9 %	1.67 [0.43, 6.45]
Total (95% CI)	212	263	•	100.0 %	0.84 [0.53, 1.34]
Total events: 27 (Chlorproma	azine), 39 (Risperidone)				
Heterogeneity: Tau ² = 0.0; C	$Chi^2 = 2.85, df = 6 (P = 0.8)$	33); I ² =0.0%			
Test for overall effect: $Z = 0.7$	73 (P = 0.46)				
Test for subgroup differences	: Not applicable				

0.01 0.1 1 10 100

Chlorpromazine Risperidone

Analysis 2.2. Comparison 2 CHLORPROMAZINE versus RISPERIDONE, Outcome 2 Global state: 1. Average endpoint score (CGI-CI, high = poor) - skewed data.

Global state: 1. Average endpoint score (CGI-CI, high = poor) - skewed data

Study	Intervention	mean	SD	Ν				
short term (up to 6	short term (up to 6 months)							
vs RPD - Ma 2004	Chlorpromazine	2.4	3.7	39				
vs RPD - Ma 2004	Risperidone	1.8	6.6	39				

Analysis 2.3. Comparison 2 CHLORPROMAZINE versus RISPERIDONE, Outcome 3 Global state: 2. Need of additional benzhexol.

Review: Chlorpromazine versus atypical antipsychotic drugs for schizophrenia Comparison: 2 CHLORPROMAZINE versus RISPERIDONE Outcome: 3 Global state: 2. Need of additional benzhexol

Study or subgroup	Chlorpromazine	Risperidone	Risk Ratio M-	Weight	Risk Ratio M-
	n/N	n/N	H,Random,95% Cl		H,Random,95% Cl
l short term (up to 6 mon	ths)				
vs RPD - Ma 2004	24/39	2/39	-	68.6 %	2.00 [1.17, 3.41]
vs RPD - Wang 2002	1/20	5/39		31.4 %	0.39 [0.05, 3.12]
Total (95% CI)	59	78	-	100.0 %	1.20 [0.26, 5.53]
Total events: 25 (Chlorpror	nazine), 17 (Risperidone)				
Heterogeneity: Tau ² = 0.81	; $Chi^2 = 2.36$, $df = 1$ (P = C).12); 1 ² =58%			
Test for overall effect: $Z = 0$	0.23 (P = 0.82)				
Test for subgroup difference	es: Not applicable				
			0.02 0.1 1 10 50		
			Chlorpromazine Risperidone		

Analysis 2.4. Comparison 2 CHLORPROMAZINE versus RISPERIDONE, Outcome 4 Mental state: 1a. Average endpoint score (various scales, high = poor) - short term (up to 6 months).

Review: Chlorpromazine versus atypical antipsychotic drugs for schizophrenia

Comparison: 2 CHLORPROMAZINE versus RISPERIDONE

Outcome: 4 Mental state: Ia. Average endpoint score (various scales, high = poor) - short term (up to 6 months)

Study or subgroup (Chlorpromazine N	Mean(SD)	Risperidone N	Mean(SD)	Mean Difference IV,Random,95% Cl	Weight	Mear Difference IV,Random,95% C
BPRS total							
vs RPD - Cui 2001	30	24.8 (8)	30	28.07 (9.53)		24.0 %	-3.27 [-7.72, 1.18
vs RPD - He 1999	20	25.2 (5.8)	19	26.3 (7.2)		24.9 %	-1.10 [-5.22, 3.02
vs RPD - Ma 2004	39	23.2 (6.5)	39	23.3 (6.6)	-	27.9 %	-0.10 [-3.01, 2.81
vs RPD - Wu 2002	35	31.29 (11.04)	35	22.78 (8.96)		23.3 %	8.51 [3.80, 13.22
ubtotal (95% CI)	124		123		-	100.0 %	0.90 [-3.49, 5.28
eterogeneity: Tau ² = 15.7 est for overall effect: Z = 0 BPRS activation subscale		H = 3 (P = 0.00)	02); I ² =79%				
vs RPD - Cui 2001	30	3.93 (1.88)	30	4.2 (1.97)		45.5 %	-0.27 [-1.24, 0.70
vs RPD - Wu 2002	35	5 (1.65)	35	4.02 (1.01)		54.5 %	0.98 [0.34, 1.62
ubtotal (95% CI) eterogeneity: Tau ² = 0.60; est for overall effect: Z = 0	0.66 (P = 0.51)	= I (P = 0.04);	65 I ² =77%			100.0 %	0.41 [-0.81, 1.63
BPRS anxiety-depression s vs RPD - Cui 2001	subscale 30	4.5 (0.96)	30	5.27 (1.95)		48.9 %	-0.77 [-1.55, 0.01
, ,		4.5 (0.96) 5.17 (1.68)	30 35	5.27 (1.95) 4.26 (0.73)	-	48.9 % 51.1 %	L
vs RPD - Cui 2001 vs RPD - Wu 2002 ubtotal (95% CI) eterogeneity: Tau ² = 1.28; est for overall effect: Z = C BPRS hostile-suspiciousne	30 35 65 : Chi ² = 11.14, df 0.11 (P = 0.92) sss subscale	5.17 (1.68) = 1 (P = 0.000	35 65 084); I ² =91%	4.26 (0.73)	•	51.1 % 100.0 %	0.91 [0.30, 1.52
vs RPD - Cui 2001 vs RPD - VVu 2002 ubtotal (95% CI) eterogeneity: Tau ² = 1.28; est for overall effect: Z = C BPRS hostile-suspiciousne vs RPD - Cui 2001	30 35 (Chi ² = 11.14, df 0.11 (P = 0.92) ss subscale 30	5.17 (1.68) = 1 (P = 0.000 4.5 (1.96)	35 65)84); I ² =91% 30	4.26 (0.73) 4.8 (1.97)		51.1 % 100.0 % 49.3 %	0.91 [0.30, 1.52 0.09 [-1.56, 1.73 -0.30 [-1.29, 0.69
vs RPD - Cui 2001 vs RPD - Wu 2002 ubtotal (95% CI) eterogeneity: Tau ² = 1.28; est for overall effect: Z = C BPRS hostile-suspiciousne vs RPD - Cui 2001 vs RPD - Wu 2002	30 35 65 Chi ² = 11.14, df 0.11 (P = 0.92) ss subscale 30 35	5.17 (1.68) = 1 (P = 0.000	35 65 084); I ² =91% 30 35	4.26 (0.73)	•	51.1 % 100.0 % 49.3 % 50.7 %	0.91 [0.30, 1.52 0.09 [-1.56, 1.73 -0.30 [-1.29, 0.69 2.04 [1.20, 2.88
vs RPD - Cui 2001 vs RPD - Wu 2002 ubtotal (95% CI) eterogeneity: Tau ² = 1.28; est for overall effect: Z = C BPRS hostile-suspiciousne vs RPD - Cui 2001 vs RPD - Cui 2001 vs RPD - Wu 2002 ubtotal (95% CI) eterogeneity: Tau ² = 2.52; est for overall effect: Z = C NORS total	30 35 65 $(Chi^2 = 11.14, df)$ (P = 0.92) ss subscale 30 35 65 $(Chi^2 = 12.36, df)$ $(Chi^2 = 12.36, df)$ $(Chi^2 = 12.36, df)$	5.17 (1.68) = 1 (P = 0.000 4.5 (1.96) 5.98 (1.96) = 1 (P = 0.000	35 65 084); l ² =91% 30 35 65 044); l ² =92%	4.26 (0.73) 4.8 (1.97) 3.94 (1.63)		51.1 % 100.0 % 49.3 % 50.7 % 100.0 %	0.91 [0.30, 1.52 0.09 [-1.56, 1.73 -0.30 [-1.29, 0.69 2.04 [1.20, 2.88 0.89 [-1.41, 3.18
vs RPD - Cui 2001 vs RPD - Wu 2002 ubtotal (95% CI) eterogeneity: Tau ² = 1.28; est for overall effect: Z = C BPRS hostile-suspiciousne vs RPD - Cui 2001 vs RPD - Cui 2001 vs RPD - Wu 2002 ubtotal (95% CI) eterogeneity: Tau ² = 2.52; est for overall effect: Z = C	30 35 65 $(Chi^2 = 11.14, df$ (.11 (P = 0.92)) 30 35 65 $(Chi^2 = 12.36, df$	5.17 (1.68) = 1 (P = 0.000 4.5 (1.96) 5.98 (1.96)	35 65)84); l ² =91% 30 35 65	4.26 (0.73) 4.8 (1.97)		51.1 % 100.0 % 49.3 % 50.7 %	-0.77 [-1.55, 0.01 0.91 [0.30, 1.52 0.09 [-1.56, 1.73 -0.30 [-1.29, 0.69 2.04 [1.20, 2.88 0.89 [-1.41, 3.18 1.80 [-2.53, 6.13

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Study or subgroup (Chlorpromazine		Risperidone		Mean Difference	Weight	Mear Difference
study of subgroup	N	Mean(SD)	N	Mean(SD)	IV,Random,95% CI	, veight	IV,Random,95% C
6 PANSS total							,
vs RPD - Cui 2001	30	42.47 (13.79)	30	49.3 (19.15)		12.5 %	-6.83 [-15.27, 1.61
vs RPD - Feng 2003	30	48.79 (9.02)	30	44.82 (8.85)		24.3 %	3.97 [-0.55, 8.49]
vs RPD - Lin 2005	35	53.83 (10)	35	59.06 (18.59)		15.9 %	-5.23 [-12.22, 1.76]
vs RPD - Luo 2001	52	48 (14)	55	51 (19)		17.9 %	-3.00 [-9.30, 3.30
vs RPD - Wu 2004	50	38.93 (7.67)	50	41.26 (9.37)		29.3 %	-2.33 [-5.69, 1.03]
Subtotal (95% CI)	197		200		•	100.0 %	-1.95 [-5.58, 1.69]
Heterogeneity: Tau ² = 8.80; Test for overall effect: Z = 1 7 PANSS positive symptom	.05 (P = 0.29) subscale						
vs RPD - Feng 2003	30	15.28 (3.53)	30	14.06 (4.71)		22.7 %	1.22 [-0.89, 3.33]
vs RPD - Lin 2005	35	17.83 (2.64)	35	16 (4.34)	-	25.9 %	1.83 [0.15, 3.51]
vs RPD - Luo 2001	52	10 (5)	55	12 (6)	-	22.8 %	-2.00 [-4.09, 0.09]
vs RPD - Wu 2004	50	8.41 (2.94)	50	9.32 (3.84)	-	28.6 %	-0.91 [-2.25, 0.43
Heterogeneity: Tau ² = 2.18; Test for overall effect: Z = 0 8 PANSS negative symptom	0.04 (P = 0.97) n subscale	. ,		074 (2 (7)	_	22 5 94	
vs RPD - Feng 2003	30	12.09 (3.25)	30	9.74 (3.67)		33.5 %	2.35 [0.60, 4.10
vs RPD - Lin 2005	35	18.5 (5.89)	35	10.5 (2.88)		32.7 %	8.00 [5.83, 10.17
vs RPD - Wu 2004	50	9.61 (3.93)	50	10.34 (4.26)	-	33.8 %	-0.73 [-2.34, 0.88
Subtotal (95% CI) Heterogeneity: Tau ² = 16.51 Test for overall effect: Z = 1 9 PANSS general pathology	.31 (P = 0.19)	df = 2 (P<0.000	115 001); I ² =95%			100.0 %	3.16 [-1.57, 7.89
vs RPD - Feng 2003	30	19.69 (5.73)	30	20.92 (6.64)		17.3 %	-1.23 [-4.37, 1.91
vs RPD - Luo 2001	52	24 (6)	55	25 (9)		20.5 %	-1.00 [-3.88, 1.88
vs RPD - Wu 2004	50	20.91 (4.32)	50	21.6 (4.11)		62.3 %	-0.69 [-2.34, 0.96
Subtotal (95% CI) Heterogeneity: Tau ² = 0.0; G Test for overall effect: Z = 1		= 2 (P = 0.95); l ²	135 2 =0.0%		•	1 00.0 %	-0.85 [-2.15, 0.46
10 SANS total vs RPD - He 1999	20	30.1 (10.2)	19	27.3 (12.1)		48.5 %	2.80 [-4.24, 9.84
vs RPD - Liu 2000	15	52.9 (7.1)	17	34.4 (5.8)	-	51.5 %	18.50 [13.97, 23.03
Subtotal (95% CI)	35	, df = 1 (P = 0.0	36	%		- 100.0 %	10.89 [-4.49, 26.27

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									(
Study or subgroup	Chlorpromazine	Risp	peridone		[Mear Difference		Weight	Mean Difference
	Ν	Mean(SD)	Ν	Mean(SD)	IV,Ra	ndom,95	5% CI		IV,Random,95% CI
Test for overall effect: Z	= 1.39 (P = 0.17)								
Test for subgroup differe	ences: Chi ² = 8.16, df	= 9 (P = 0.52), I ² =	=0.0%						
				-20	-10	0	10	20	
				Chlor	promazine	Ri	isperidone	2	

Analysis 2.5. Comparison 2 CHLORPROMAZINE versus RISPERIDONE, Outcome 5 Mental state: 1b. Average endpoint score (various scales, high = poor) - skewed data - short term (up to 6 months).

Mental state: 1b. Average endpoint score (various scales, high = poor) - skewed data - short term (up to 6 months)

Study	Intervention	mean	SD	Ν				
BPRS thinking disorder subscale								
vs RPD - Wu 2002	Chlorpromazine	7.96	4.25	35				
vs RPD - Wu 2002	Risperidone	5.13	1.89	35				
BPRS withdraw-reta	urdation subscale				BPRS withdraw			
vs RPD - Cui 2001	Chlorpromazine	5.73	2.21	30				
vs RPD - Cui 2001	Risperidone	6.43	3.24	30				
vs RPD - Wu 2002	Chlorpromazine	7.88	3.12	35				
vs RPD - Wu 2002	Risperidone	5.02	2.87	35				
PANSS general path	ology subscale				PANSS general			
vs RPD - Cui 2001	Chlorpromazine	21.17	6.31	30				
vs RPD - Cui 2001	Risperidone	24.47	9.51	30				
PANSS negative sym	ptom subscale				PANSS negative			
vs RPD - Cui 2001	Chlorpromazine	9.5	3.53	30				
vs RPD - Cui 2001	Risperidone	12.63	7.39	30				
vs RPD - Luo 2001	Chlorpromazine	14	6	52	-			

Mental state: 1b. Average endpoint score (various scales, high = poor) - skewed data - short term (up to 6 months) (Continued)

	55	8	14	Risperidone	vs RPD - Luo 2001			
PANSS positive	PANSS positive symptom subscale							
	30	13.6	11.67	Chlorpromazine	vs RPD - Cui 2001			
	30	4.67	11.6	Risperidone	vs RPD - Cui 2001			
SAPS total					SAPS total			
	20	5.9	12.7	Chlorpromazine	vs RPD - He 1999			
	19	7.8	13.9	Risperidone	vs RPD - He 1999			

Analysis 2.6. Comparison 2 CHLORPROMAZINE versus RISPERIDONE, Outcome 6 Mental state: 2. Average change score - decreased rate (various scales, high = poor) - short term (up to 6 months).

Review: Chlorpromazine versus atypical antipsychotic drugs for schizophrenia

Comparison: 2 CHLORPROMAZINE versus RISPERIDONE

Outcome: 6 Mental state: 2. Average change score - decreased rate (various scales, high = poor) - short term (up to 6 months)

Study or subgroup	Chlorpromazine		Risperidone			Dif	Mean ference		Weight	Mean Difference
	Ν	Mean(SD)	Ν	Mean(SD)		IV,Rano	dom,95%	S CI		IV,Random,95% CI
I PANSS total										
vs RPD - Wang 2002	20	0.66 (0.22)	37	0.77 (0.2)			+		100.0 %	-0.11 [-0.23, 0.01]
Subtotal (95% CI)	20		37				•		100.0 %	-0.11 [-0.23, 0.01]
Heterogeneity: not applic	able									
Test for overall effect: Z =	= 1.86 (P = 0.063)									
2 PANSS negative subscal	e									
vs RPD - Wang 2002	20	0.58 (0.35)	37	0.79 (0.54)		-			100.0 %	-0.21 [-0.44, 0.02]
Subtotal (95% CI)	20		37			•	•		100.0 %	-0.21 [-0.44, 0.02]
Heterogeneity: not applic	able									
Test for overall effect: Z =	= 1.77 (P = 0.076)									
3 PANSS positive subscale	e									
vs RPD - Wang 2002	20	0.66 (0.25)	37	0.73 (0.84)		-			100.0 %	-0.07 [-0.36, 0.22]
Subtotal (95% CI)	20		37			-	•		100.0 %	-0.07 [-0.36, 0.22]
Heterogeneity: not applic	able									
Test for overall effect: Z =	= 0.47 (P = 0.64)									
Test for subgroup differen	ices: $Chi^2 = 0.72$, df	= 2 (P = 0.70)	, I ² =0.0%							
					-2	- 1	0	1 2		
				Ch	lorpro	mazine	Risp	eridone		

Chlorpromazine versus atypical antipsychotic drugs for schizophrenia (Review)

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Analysis 2.7. Comparison 2 CHLORPROMAZINE versus RISPERIDONE, Outcome 7 Functioning: 1. Average endpoint score (WCST subscales, high = good) - short term (up to 6 months).

Review: Chlorpromazine versus atypical antipsychotic drugs for schizophrenia

Comparison: 2 CHLORPROMAZINE versus RISPERIDONE

Outcome: 7 Functioning: I. Average endpoint score (WCST subscales, high = good) - short term (up to 6 months)

Study or subgroup	Chlorpromazine	Ri	speridone		Mean Difference		Mean Difference
	Ν	Mean(SD)	Ν	Mean(SD)	IV,Random,959	% CI	IV,Random,95% CI
I WCST-IQ							
vs RPD - Wang 2005	5 50	81.5 (18.3)	50	92.8 (17.6)		100.0 %	-11.30 [-18.34, -4.26]
Subtotal (95% CI) 50		50		•	100.0 %	-11.30 [-18.34, -4.26]
Heterogeneity: not appli	icable						
Test for overall effect: Z	= 3.15 (P = 0.0016)						
2 WCST-MQ					_		
vs RPD - Wang 2005	5 50	56.2 (25)	50	75.8 (22)	-	100.0 %	-19.60 [-28.83, -10.37]
Subtotal (95% CI) 50		50		•	100.0 %	-19.60 [-28.83, -10.37]
Heterogeneity: not appli	icable						
Test for overall effect: Z	= 4.16 (P = 0.00003	32)					
Test for subgroup differe	ences: Chi ² = 1.96, d	f = (P = 0. 6),	2 =49%				
						<u> </u>	
				-10	0 -50 0	50 100	
				I	Risperidone Ch	lorpromazine	

Analysis 2.8. Comparison 2 CHLORPROMAZINE versus RISPERIDONE, Outcome 8 Adverse effects: 1. Anticholinergic - short term (up to 6 months).

Review: Chlorpromazine versus atypical antipsychotic drugs for schizophrenia Comparison: 2 CHLORPROMAZINE versus RISPERIDONE

Outcome: 8 Adverse effects: I. Anticholinergic - short term (up to 6 months)

Study or subgroup	Chlorpromazine	Risperidone	Risk Ratio M-	Weight	Risk Ratio M-
	n/N	n/N	H,Random,95% Cl		H,Random,9 Cl
I blurred vision					
vs OLZ - He 2003	8/40	2/40		16.0 %	4.00 [0.90, 17.68]
vs OLZ - Wu 2008	9/50	2/50		16.1 %	4.50 [1.02, 19.79]
vs RPD - Ma 2004	8/39	1/39		8.8 %	8.00 [1.05, 60.97]
vs RPD - Wang 2002	2/20	3/39		12.3 %	1.30 [0.24, 7.16]
vs RPD - Wu 2002	11/35	7/35		46.7 %	1.57 [0.69, 3.58]
Subtotal (95% CI)	184	203	•	100.0 %	2.44 [1.32, 4.50]
Fotal events: 38 (Chlorpromazin Heterogeneity: Tau ² = 0.03; Chi Fest for overall effect: Z = 2.86 2 dry mouth	$i^2 = 4.25$, df = 4 (P = 0	0.37); l ² =6%			
vs OLZ - Chang 2003	1/27	7/31		8.3 %	0.16 [0.02, 1.25]
vs OLZ - He 2003	26/40	5/40		14.5 %	5.20 [2.22, 2. 8]
vs OLZ - Wang 2008	1/119	7/118		8.1 %	0.14 [0.02, 1.13]
vs OLZ - Wu 2008	8/50	2/50		10.9 %	4.00 [0.89, 7.9]
vs RPD - Lin 2005	10/35	2/35		11.2 %	5.00 [1.18, 21.19]
vs RPD - Ma 2004	6/39	3/39		11.9 %	2.00 [0.54, 7.43]
vs RPD - Wang 2002	0/20	6/39		5.6 %	0.15 [0.01, 2.48]
vs RPD - Wu 2002	16/35	5/35		14.3 %	3.20 [1.32, 7.78]
vs RPD - Wu 2004	41/50	6/50		15.0 %	6.83 [3.19, 14.64]
Subtotal (95% CI) Fotal events: 109 (Chlorpromazi Heterogeneity: Tau ² = 1.00; Chi Fest for overall effect: Z = 1.66	$i^2 = 28.49$, df = 8 (P =	437 0.00039); I ² =72%	•	100.0 %	2.00 [0.88, 4.51]
3 excessive sweating vs OLZ - He 2003	3/40	1/40		50.2 %	3.00 [0.33, 27.63]
vs OLZ - Wu 2008	3/50	1/50		49.8 %	3.00 [0.32, 27.87]
					3.00 [0.62, 14.46]

(Continued ...)

Study or subgroup	Chlorpromazine	Risperidone	Risk Ratio M- H.Random,95%	Weight	(Continued) Risk Ratio M- H,Random,95%
	n/N	n/N	Cl		Cl
Total events: 6 (Chlorproma	zine), 2 (Risperidone)				
Heterogeneity: $Tau^2 = 0.0$; C	$Chi^2 = 0.0, df = 1 (P = 1.00)$	D); I ² =0.0%			
Test for overall effect: $Z = I$.	.37 (P = 0.17)				
4 hypersalivation					
vs OLZ - Chen 2006	23/44	2/42		35.7 %	10.98 [2.76, 43.71]
vs OLZ - He 2003	22/40	2/40		35.8 %	.00 [2.77, 43.71]
vs RPD - Lin 2005	1/35	0/35		6.8 %	3.00 [0.13, 71.22]
vs RPD - Ma 2004	2/39	0/39		7.6 %	5.00 [0.25, 100.89]
vs RPD - Wang 2002	3/20	1/39	+	14.1 %	5.85 [0.65, 52.69]
Subtotal (95% CI)	178	195	•	100.0 %	8.67 [3.80, 19.80]
Total events: 51 (Chlorprom	azine), 5 (Risperidone)				
Heterogeneity: $Tau^2 = 0.0$; C	$Chi^2 = 0.93, df = 4 (P = 0.93)$	92); I ² =0.0%			
Test for overall effect: $Z = 5$.	.I3 (P < 0.0000I)				
5 stuffy nose					
vs OLZ - He 2003	12/40	4/40		100.0 %	3.00 [1.06, 8.52]
Subtotal (95% CI)	40	40	•	100.0 %	3.00 [1.06, 8.52]
Total events: 12 (Chlorprom	azine), 4 (Risperidone)				
Heterogeneity: not applicable	e				
Test for overall effect: $Z = 2$.	.06 (P = 0.039)				
Test for subgroup differences	s: Chi ² = 7.66, df = 4 (P =	0.10), l ² =48%			
			0.005 0.1 1 10 200		
			Chlorpromazine Risperidone		

Analysis 2.9. Comparison 2 CHLORPROMAZINE versus RISPERIDONE, Outcome 9 Adverse effects: 2a. Cardiovascular - short term (up to 6 months).

Review: Chlorpromazine versus atypical antipsychotic drugs for schizophrenia

Comparison: 2 CHLORPROMAZINE versus RISPERIDONE

Outcome: 9 Adverse effects: 2a. Cardiovascular - short term (up to 6 months)

Study or subgroup	Chlorpromazine	Risperidone	Risk Ratio	Weight	Risk Ratio
	n/N	n/N	M- H,Random,95% Cl		M- H,Random,9 Cl
I abnormal ECG					
vs RPD - Cui 2001	2/35	1/35		15.4 %	2.00 [0.19, 21.06]
vs RPD - Wang 2002	2/20	1/39		15.6 %	3.90 [0.38, 40.45]
vs RPD - Wu 2004	9/50	4/50		69.1 %	2.25 [0.74, 6.83]
Subtotal (95% CI)	105	124	•	100.0 %	2.41 [0.96, 6.06]
Total events: 13 (Chlorprom. Heterogeneity: Tau ² = 0.0; C Test for overall effect: Z = 1. 2 apathism	$Chi^2 = 0.20, df = 2 (P = 0.20)$	0.90); I ² =0.0%			
vs RPD - Wu 2004	25/50	4/50		100.0 %	6.25 [2.35, 16.65]
Subtotal (95% CI)	50	50	•	100.0 %	6.25 [2.35, 16.65]
Test for overall effect: Z = 3. 3 blood pressure drop vs OLZ - He 2003 vs OLZ - Wu 2008	3/40 5/50	0/40 0/50		15.5 %	7.00 [0.37, 131.28] 11.00 [0.62, 193.80]
vs RPD - Wu 2002	16/35	2/35		68.4 %	8.00 [1.99, 32.23]
Subtotal (95% CI) Total events: 24 (Chlorprom. Heterogeneity: Tau ² = 0.0; C Test for overall effect: Z = 3. 4 bradycardia vs RPD - Wu 2004	$Chi^2 = 0.05, df = 2 (P = 0.05)$	125 0.97); I ² =0.0% 2/50	-	100.0 %	8.25 [2.61, 26.12] 0.50 [0.05, 5.34]
Subtotal (95% CI)	50	50		100.0 %	0.50 [0.05, 5.34]
Total events: I (Chlorproma: Heterogeneity: not applicable Test for overall effect: Z = 0. 5 orthostatic hypotension	e				
vs OLZ - Chang 2003	6/27	0/31		10.6 %	4.86 [0.88, 252.]
vs OLZ - Chen 2006	2/44	0/42	+-	9.4 %	4.78 [0.24, 96.68]
		0	001 0.01 0.1 1 10 100 100	0	
			Chlorpromazine Risperidone	v	

(Continued . . .)

Study or subgroup	Chlorpromazine	Risperidone	Risk Ratio M- H,Random,95%	Weight	(Continued) Risk Ratio M- H,Random,95
017 14/ 2000	n/N	n/N	Cl		CI
vs OLZ - Wang 2008	7/119	0/118		10.5 %	14.88 [0.86, 257.53]
vs RPD - Feng 2003	2/33	0/32		9.5 %	4.85 [0.24, 97.31]
vs RPD - Wu 2004	13/50	3/50	-	60.0 %	4.33 [1.31, 14.28]
Subtotal (95% CI)	273	273	•	100.0 %	5.74 [2.28, 14.44]
Total events: 30 (Chlorprom Heterogeneity: Tau ² = 0.0; C Test for overall effect: $Z = 3$.	$Chi^2 = 1.17, df = 4 (P = C)$.88); I ² =0.0%			
6 palpitation vs OLZ - Wang 2008	20/119	0/118		100.0 %	40.66 [2.49, 664.56]
Subtotal (95% CI)	119	118		100.0 %	40.66 [2.49, 664.56]
Heterogeneity: not applicabl Test for overall effect: Z = 2. 7 sinus tachycardia	.60 (P = 0.0093)				
vs RPD - Zheng 2001	3/25	1/26		100.0 %	3.12 [0.35, 28.03]
Subtotal (95% CI)	25	26	-	100.0 %	3.12 [0.35, 28.03]
Total events: 3 (Chlorproma Heterogeneity: not applicabl Test for overall effect: Z = 1. 8 tachycardia vs OLZ - He 2003	e	2/40	_	8.4 %	2.00 [0.39, 10.31]
vs OLZ - Wu 2008	7/50	3/50	_ _	13.6 %	2.33 [0.64, 8.51]
vs RPD - Lin 2005	6/35	0/35		2.8 %	3.00 [0.76, 222.3]
vs RPD - Ma 2004	3/39	2/39		7.6 %	1.50 [0.27, 8.49]
vs RPD - Wang 2002	4/20	0/39		2.8 %	17.14 [0.97, 303.44]
vs RPD - Wu 2002	18/35	6/35		35.8 %	3.00 [1.35, 6.65]
vs RPD - Wu 2004	13/50	6/50		29.0 %	2.17 [0.89, 5.25]
Subtotal (95% CI)	269	288	•	100.0 %	2.64 [1.64, 4.26]
Total events: 55 (Chlorprom Heterogeneity: Tau ² = 0.0; C Test for overall effect: Z = 4. Test for subgroup difference:	$Chi^2 = 3.82, df = 6 (P = 0.000063)$				

0.001 0.01 0.1 1 10 100 1000 Chlorpromazine Risperidone

Analysis 2.10. Comparison 2 CHLORPROMAZINE versus RISPERIDONE, Outcome 10 Adverse effects: 2b. Cardiovascular - continuous measures - short term (up to 6 months).

Review: Chlorpromazine versus atypical antipsychotic drugs for schizophrenia

Comparison: 2 CHLORPROMAZINE versus RISPERIDONE

Outcome: 10 Adverse effects: 2b. Cardiovascular - continuous measures - short term (up to 6 months)

Study or subgroup	Chlorpromazine		Risperidone		Mean Difference	Weight	Mea Differenc
	N	Mean(SD)	N	Mean(SD)	IV,Random,95% Cl		IV,Random,95% (
I cardiac rate (upright posit	ion)						
vs RPD - Liu 2005	50	96.74 (14.65)	50	92.84 (13.22)	+	100.0 %	3.90 [-1.57, 9.37
Subtotal (95% CI)	50		50		-	100.0 %	3.90 [-1.57, 9.37
Heterogeneity: not applicab	le						
Test for overall effect: $Z = 1$.40 (P = 0.16)						
2 cardiac rate (horizontal po	osition)						
vs RPD - Liu 2005	50	85.36 (13.19)	50	77.94 (5.37)		100.0 %	7.42 [3.47, 11.37
Subtotal (95% CI)	50		50		•	100.0 %	7.42 [3.47, 11.37
Heterogeneity: not applicab	le						
Test for overall effect: $Z = 3$	8.68 (P = 0.00023	3)					
3 contractive blood pressur	e (upright positio	n)					
vs RPD - Liu 2005	50	12.65 (3.24)	50	13.71 (2.52)	-	100.0 %	-1.06 [-2.20, 0.08
Subtotal (95% CI)	50		50		•	100.0 %	-1.06 [-2.20, 0.08
Heterogeneity: not applicab	le						
Test for overall effect: $Z = 1$.83 (P = 0.068)						
4 contractive blood pressur	e (horizontal pos	ition)					
vs RPD - Liu 2005	50	15.52 (1.93)	50	14.14 (2.01)	-	100.0 %	1.38 [0.61, 2.15
Subtotal (95% CI)	50		50		•	100.0 %	1.38 [0.61, 2.15
Heterogeneity: not applicab	le						
Test for overall effect: $Z = 3$	8.50 (P = 0.00046	5)					
5 diastolic blood pressure (1	upright position)						
vs RPD - Liu 2005	50	8.68 (1.69)	50	9.21 (2.14)	-	100.0 %	-0.53 [-1.29, 0.23
Subtotal (95% CI)	50		50		•	100.0 %	-0.53 [-1.29, 0.23
Heterogeneity: not applicab	le						• •
Test for overall effect: $Z = 1$.37 (P = 0.17)						
6 diastolic blood pressure (I	norizontal positio	n)					
vs RPD - Liu 2005	50	10.06 (1.52)	50	9.67 (1.36)	+	100.0 %	0.39 [-0.18, 0.96
Subtotal (95% CI)	50		50		•	100.0 %	0.39 [-0.18, 0.96
Heterogeneity: not applicab	le						
Test for overall effect: $Z = 1$.35 (P = 0.18)						
Test for subgroup difference	es: Chi ² = 31.88,	df = 5 (P = 0.00)), l ² =84%				
				_			

Analysis 2.11. Comparison 2 CHLORPROMAZINE versus RISPERIDONE, Outcome 11 Adverse effects: 3. Central nervous system - short term (up to 6 months).

Review: Chlorpromazine versus atypical antipsychotic drugs for schizophrenia

Comparison: 2 CHLORPROMAZINE versus RISPERIDONE

Outcome: II Adverse effects: 3. Central nervous system - short term (up to 6 months)

Study or subgroup	Chlorpromazine	Risperidone	Odds Ratio M-	Weight	Odds Ratio M-
	n/N	n/N	H,Random,95% Cl		H,Random,S Cl
l agitation					
vs RPD - Feng 2003	0/33	1/32		3.6 %	0.31 [0.01, 7.98]
Subtotal (95% CI)	33	32		3.6 %	0.31 [0.01, 7.98]
Total events: 0 (Chlorproma	zine), I (Risperidone)				
Heterogeneity: not applicabl					
Test for overall effect: $Z = 0$.70 (P = 0.48)				
2 dizziness vs RPD - Lin 2005	8/35	3/35		7.5 %	3.16 [0.76, 13.11
vs RPD - Wang 2002	0/20	2/39		3.8 %	0.37 [0.02, 7.99
0					
vs RPD - Wu 2002	15/35	3/35		7.7 %	8.00 [2.05, 31.16]
vs RPD - Wu 2004	28/50	14/50		9.1 %	3.27 [1.42, 7.52]
Subtotal (95% CI)	140	159	•	28.1 %	3.57 [1.75, 7.30]
vs RPD - Lin 2005	7/35	2/35		6.9 %	4.13 [0.79, 21.48
3 drowsiness	7/05	2/25		(0.0)	
vs RPD - Ma 2004	5/39	3/39		7.3 %	1.76 [0.39, 7.96
vs RPD - Wang 2002	5/20	4/39		7.4 %	2.92 [0.69, 12.40]
vs RPD - Wu 2004	30/50	3/50		7.9 %	23.50 [6.42, 85.97]
Subtotal (95% CI)	144	163	•	29.5 %	4.93 [1.49, 16.32]
Total events: 47 (Chlorprom	, , , ,				
Heterogeneity: $Tau^2 = 0.93$;		0.05); l ² =62%			
Test for overall effect: $Z = 2$ 4 fatigue	.01 (1 = 0.0070)				
Test for overall effect: Z = 2 4 fatigue vs RPD - Wu 2004	43/50	16/50		8.7 %	13.05 [4.82, 35.33
4 fatigue vs RPD - Wu 2004	× ,	16/50 50	 -	8.7 % 8.7 %	-
4 fatigue vs RPD - Wu 2004 Subtotal (95% CI)	43/50 50				
4 fatigue vs RPD - Wu 2004 Subtotal (95% CI) Total events: 43 (Chlorprom Heterogeneity: not applicabl	43/50 50 nazine), 16 (Risperidone) e		 -		13.05 [4.82, 35.33]
4 fatigue vs RPD - Wu 2004 Subtotal (95% CI) Total events: 43 (Chlorprom Heterogeneity: not applicabl Test for overall effect: Z = 5	43/50 50 nazine), 16 (Risperidone) e				
4 fatigue vs RPD - Wu 2004 Subtotal (95% CI) Total events: 43 (Chlorprom Heterogeneity: not applicabl	43/50 50 nazine), 16 (Risperidone) e		 		
4 fatigue vs RPD - Wu 2004 Subtotal (95% CI) Total events: 43 (Chlorprom Heterogeneity: not applicabl Test for overall effect: Z = 5	43/50 50 nazine), 16 (Risperidone) e	50			-

(Continued . . .)

(Continued) Odds Ratio M-	Weight	Odds Ratio M-	Risperidone	Chlorpromazine	Study or subgroup
H,Random,959 Cl		H,Random,95% Cl	n/N	n/N	
0.04 [0.00, 0.78]	4.1 %		8/32	0/33	vs RPD - Feng 2003
0.31 [0.03, 3.17]	5.3 %		3/35	1/35	vs RPD - Lin 2005
2.05 [0.18, 23.63]	5.0 %		1/39	2/39	vs RPD - Ma 2004
0.13 [0.01, 2.35]	4.1 %		6/39 -	0/20	vs RPD - Wang 2002
0.29 [0.05, 1.57]	6.8 %		6/35	2/35	vs RPD - Wu 2002
0.29 [0.10, 0.90]	25.2 %	•	180	162	Subtotal (95% CI)
2.05 [0.18, 23.63]	5.0 %		1/39	5 (P = 0.032) 2/39	Test for overall effect: Z = 2.1 6 reduced activity vs RPD - Ma 2004
2					
2.05 [0.18, 23.63]	5.0 %		39	, , , ,	Subtotal (95% CI) Total events: 2 (Chlorpromazi Heterogeneity: not applicable Test for overall effect: Z = 0.5
1.96 [0.92, 4.22]	100.0 %	-	623	568	Total (95% CI)
			2 00002) 12 -700/	, , , ,	Total events: 148 (Chlorprom
			$1000071^{\circ}1^{\circ} = 70\%$		
			0.00002); I ² =70%		Heterogeneity: $Tau^2 = 1.49$; C Test for overall effect: $Z = 1.7$

Favours chlorpromazine Favours risperidone

Analysis 2.12. Comparison 2 CHLORPROMAZINE versus RISPERIDONE, Outcome 12 Adverse effects: 4. Gastrointestinal - short term (up to 6 months).

Review: Chlorpromazine versus atypical antipsychotic drugs for schizophrenia

Comparison: 2 CHLORPROMAZINE versus RISPERIDONE

Outcome: 12 Adverse effects: 4. Gastrointestinal - short term (up to 6 months)

Risk Rat	Weight	Risk Ratio M-	Risperidone	Chlorpromazine	Study or subgroup
۱ H,Randon		M- H,Random,95% Cl	n/N	n/N	
					l constipation
13.78 [1.91, 99.16	3.6 %		1/31	12/27	vs OLZ - Chang 2003
2.39 [0.81, 7.02	10.9 %		4/42	10/44	vs OLZ - Chen 2006
3.20 [1.30, 7.90	14.9 %		5/40	16/40	vs OLZ - He 2003
6.94 [1.61, 29.87	6.3 %		2/118	4/ 9	vs OLZ - Wang 2008
4.50 [1.64, 12.36	12.3 %		4/50	18/50	vs OLZ - Wu 2008
1.00 [0.15, 6.75	3.8 %		2/39	2/39	vs RPD - Ma 2004
0.27 [0.01, 5.02	1.7 %		3/39	0/20	vs RPD - Wang 2002
3.33 [1.00, 11.09	9.0 %		3/35	10/35	vs RPD - Wu 2002
		-	14/50	35/50	vs RPD - Wu 2004
2.50 [1.55, 4.04	37.7 %				
2.50 [1.55, 4.04 3.00 [2.05, 4.39 5.00 [0.25, 100.97	37.7 % 100.0 %	•	444 34); ² = 1% 0/40	$i^2 = 9.01$, df = 8 (P = 0	Total events: 117 (Chlorprom Heterogeneity: Tau ² = 0.04; C Test for overall effect: Z = 5.6
3.00 [2.05, 4.39	100.0 %	•	34); ² = %	rine), 38 (Risperidone) i ² = 9.01, df = 8 (P = 0 (P < 0.00001)	Subtotal (95% CI) Total events: 117 (Chlorprom: Heterogeneity: Tau ² = 0.04; C Test for overall effect: $Z = 5.6$ 2 diarrhoea
3.00 [2.05, 4.39	100.0 %	•	34); ² = %	tine), 38 (Risperidone) i ² = 9.01, df = 8 (P = 0 (P < 0.00001) 2/40 40	Total events: 117 (Chlorprom. Heterogeneity: Tau ² = 0.04; C Test for overall effect: Z = 5.6 2 diarrhoea vs OLZ - He 2003 Subtotal (95% CI) Total events: 2 (Chlorpromazi
3.00 [2.05, 4.39 5.00 [0.25, 100.97	100.0 %	•	34); I ² = I I% 0/40	tine), 38 (Risperidone) i ² = 9.01, df = 8 (P = 0 (P < 0.00001) 2/40 40 e), 0 (Risperidone)	Total events: 117 (Chlorprom. Heterogeneity: Tau ² = 0.04; C Test for overall effect: Z = 5.6 2 diarrhoea vs OLZ - He 2003 Subtotal (95% CI) Total events: 2 (Chlorpromazii Heterogeneity: not applicable Test for overall effect: Z = 1.0
3.00 [2.05, 4.39 5.00 [0.25, 100.97 5.00 [0.25, 100.97	100.0 %	•	34); I ² = I I% 0/40	tine), 38 (Risperidone) i ² = 9.01, df = 8 (P = 0 (P < 0.00001) 2/40 40 e), 0 (Risperidone)	Total events: 117 (Chlorprom. Heterogeneity: Tau ² = 0.04; C Test for overall effect: Z = 5.6 2 diarrhoea vs OLZ - He 2003 Subtotal (95% CI) Total events: 2 (Chlorpromazii Heterogeneity: not applicable Test for overall effect: Z = 1.0
3.00 [2.05, 4.39 5.00 [0.25, 100.97 5.00 [0.25, 100.97 3.67 [1.09, 12.36	100.0 % 100.0 % 100.0 %	•	34); ² = % 0/40 40 3/50	tine), 38 (Risperidone) $i^2 = 9.01$, df = 8 (P = 0 (P < 0.00001) 2/40 40 e), 0 (Risperidone) (P = 0.29) 11/50	Total events: 117 (Chlorprom. Heterogeneity: Tau ² = 0.04; C Test for overall effect: Z = 5.6 2 diarrhoea vs OLZ - He 2003 Subtotal (95% CI) Total events: 2 (Chlorpromazi Heterogeneity: not applicable Test for overall effect: Z = 1.0 3 dysphagia vs RPD - Wu 2004
3.00 [2.05, 4.39 5.00 [0.25, 100.97 5.00 [0.25, 100.97	100.0 % 100.0 % 100.0 %		34); ² = % 0/40 40	tine), 38 (Risperidone) i ² = 9.01, df = 8 (P = 0 (P < 0.00001) 2/40 40 e), 0 (Risperidone) (P = 0.29) 11/50 50 ne), 3 (Risperidone)	Total events: 117 (Chlorprom. Heterogeneity: Tau ² = 0.04; C Test for overall effect: Z = 5.6 2 diarrhoea vs OLZ - He 2003 Subtotal (95% CI) Total events: 2 (Chlorpromazi Heterogeneity: not applicable Test for overall effect: Z = 1.0 3 dysphagia vs RPD - Wu 2004 Subtotal (95% CI) Total events: 11 (Chlorpromazi Heterogeneity: not applicable Test for overall effect: Z = 2.1
3.00 [2.05, 4.39 5.00 [0.25, 100.97 5.00 [0.25, 100.97 3.67 [1.09, 12.36	100.0 % 100.0 % 100.0 %		34); ² = % 0/40 40 3/50	tine), 38 (Risperidone) i ² = 9.01, df = 8 (P = 0 (P < 0.00001) 2/40 40 e), 0 (Risperidone) (P = 0.29) 11/50 50 ne), 3 (Risperidone)	Total events: 117 (Chlorprom. Heterogeneity: Tau ² = 0.04; C Test for overall effect: Z = 5.6 2 diarrhoea vs OLZ - He 2003 Subtotal (95% CI) Total events: 2 (Chlorpromazi Heterogeneity: not applicable Test for overall effect: Z = 1.0 3 dysphagia vs RPD - Wu 2004 Subtotal (95% CI) Total events: 11 (Chlorpromazi Heterogeneity: not applicable
3.00 [2.05, 4.39 5.00 [0.25, 100.97 5.00 [0.25, 100.97 3.67 [1.09, 12.36 3.67 [1.09, 12.36	100.0 % 100.0 % 100.0 % 100.0 %		34); ² = % 0/40 40 3/50 50	tine), 38 (Risperidone) $i^2 = 9.01$, df = 8 (P = 0 (P < 0.00001) 2/40 40 e), 0 (Risperidone) (P = 0.29) 11/50 50 ne), 3 (Risperidone) (P = 0.036)	Total events: 117 (Chlorprom. Heterogeneity: Tau ² = 0.04; C Test for overall effect: Z = 5.6 2 diarrhoea vs OLZ - He 2003 Subtotal (95% CI) Total events: 2 (Chlorpromazi Heterogeneity: not applicable Test for overall effect: Z = 1.0 3 dysphagia vs RPD - Wu 2004 Subtotal (95% CI) Total events: 11 (Chlorpromazi Heterogeneity: not applicable Test for overall effect: Z = 2.1 Heterogeneity: not applicable Test for overall effect: Z = 2.1 4 loss of appetite

(Continued . . .)

Study or subgroup	Chlorpromazine n/N	Risperidone n/N	Risk Ratio M- H,Random,95% Cl	Weight	(Continued) Risk Ratio H,Random,95% Cl
Total events: 56 (Chlorpron	mazine), 5 (Risperidone)				
Heterogeneity: Tau ² = 0.48	$P_{\rm c}$; Chi ² = 1.78, df = 1 (P =	0.18); l ² =44%			
Test for overall effect: $Z = 3$	3.45 (P = 0.00055)				
5 nausea/vomiting					
vs OLZ - He 2003	4/40	2/40		24.7 %	2.00 [0.39, 0.3]
vs OLZ - Wu 2008	2/50	2/50		18.0 %	1.00 [0.15, 6.82]
vs RPD - Wu 2002	1/35	5/35		15.1 %	0.20 [0.02, 1.63]
vs RPD - Wu 2004	4/50	5/50		42.2 %	0.80 [0.23, 2.81]
Subtotal (95% CI)	175	175	•	100.0 %	0.85 [0.37, 1.91]
Total events: 11 (Chlorpron	, , , ,				
Heterogeneity: $Tau^2 = 0.0$;		.40); I ² =0.0%			
Test for overall effect: $Z = 0$. ,				
Test for subgroup difference	es: Chi ² = 12.58, df = 4 (P	$= 0.01$), $ ^2 = 68\%$			
			0.002 0.1 1 10 50	00	
			Chlorpromazine Risperidone		

Analysis 2.13. Comparison 2 CHLORPROMAZINE versus RISPERIDONE, Outcome 13 Adverse effects: 5. Haematology - short term (up to 6 months).

Review: Chlorpromazine versus atypical antipsychotic drugs for schizophrenia Comparison: 2 CHLORPROMAZINE versus RISPERIDONE

Outcome: 13 Adverse effects: 5. Haematology - short term (up to 6 months)

Study or subgroup	Chlorpromazine	Risperidone	Risk Ratio M-	Weight	Risk Ratio M-
	n/N	n/N	H,Random,95% Cl		H,Random,95% Cl
l abnormal haemogram					
vs OLZ - He 2003	4/40	1/40		39.6 %	4.00 [0.47, 34.24]
vs OLZ - Wu 2008	4/50	1/50		39.2 %	4.00 [0.46, 34.54]
Subtotal (95% CI)	90	90	-	7 8.8 %	4.00 [0.87, 18.31]
Total events: 8 (Chlorproma	azine), 2 (Risperidone)				
Heterogeneity: $Tau^2 = 0.0$; ($Chi^2 = 0.0, df = 1 (P = 1.0)$	00); l ² =0.0%			
Test for overall effect: $Z = I$.79 (P = 0.074)				
2 leukopenia					
vs OLZ - Chen 2006	3/44	0/42		21.2 %	6.69 [0.36, 125.71]
Subtotal (95% CI)	44	42		21.2 %	6.69 [0.36, 125.71]
Total events: 3 (Chlorproma	azine), 0 (Risperidone)				
Heterogeneity: not applicab	le				
Test for overall effect: $Z = I$.27 (P = 0.20)				
Total (95% CI)	134	132	-	100.0 %	4.46 [1.16, 17.22]
Total events: II (Chlorprom	nazine), 2 (Risperidone)				
Heterogeneity: $Tau^2 = 0.0$; ($Chi^2 = 0.09, df = 2 (P = 0)$	0.95); I ² =0.0%			
Test for overall effect: $Z = 2$	2.17 (P = 0.030)				
Test for subgroup difference	es: $Chi^2 = 0.09$, $df = 1$ (P =	= 0.76), l ² =0.0%			

0.01 0.1 1 10 100

Favours chlorpromazine Favours risperidone

Analysis 2.14. Comparison 2 CHLORPROMAZINE versus RISPERIDONE, Outcome 14 Adverse effects: 6. Hepatitic - short term (up to 6 months).

Review: Chlorpromazine versus atypical antipsychotic drugs for schizophrenia Comparison: 2 CHLORPROMAZINE versus RISPERIDONE

Outcome: 14 Adverse effects: 6. Hepatitic - short term (up to 6 months)

Study or subgroup	Chlorpromazine	Risperidone	Risk Ratio M-	Weight	Risk Ratio M-
	n/N	n/N	H,Random,95% Cl		H,Random,95 Cl
I abnormal liver function					
vs RPD - Ma 2004	2/39	0/39		22.2 %	5.00 [0.25, 100.89]
Subtotal (95% CI)	39	39		22.2 %	5.00 [0.25, 100.89]
Total events: 2 (Chlorproma	zine), 0 (Risperidone)				
Heterogeneity: not applicabl	e				
Test for overall effect: $Z = 1$.	.05 (P = 0.29)				
2 abnormal transaminase					
vs OLZ - Chen 2006	0/44	7/42	←	23.5 %	0.06 [0.00, 1.08]
vs RPD - Feng 2003	5/33	0/32		23.3 %	10.68 [0.61, 185.53]
vs RPD - Ma 2004	2/39	2/39	_	31.0 %	1.00 [0.15, 6.75]
Subtotal (95% CI)	116	113		77 .8 %	0.88 [0.07, 11.58]
Total events: 7 (Chlorproma	zine), 9 (Risperidone)				
Heterogeneity: $Tau^2 = 3.51$;	$Chi^2 = 6.30, df = 2 (P =$	0.04); l ² =68%			
Test for overall effect: $Z = 0$.	.09 (P = 0.93)				
Total (95% CI)	155	152		100.0 %	1.30 [0.17, 10.09]
Total events: 9 (Chlorproma	zine), 9 (Risperidone)				
Heterogeneity: $Tau^2 = 2.57$;	$Chi^2 = 7.40, df = 3 (P = 1)$	0.06); l ² =59%			
Test for overall effect: $Z = 0$.	.25 (P = 0.80)				
Test for subgroup difference	s: $Chi^2 = 0.74$, $df = 1$ (P =	= 0.39), I ² =0.0%			

Favours chlorpromazine

Favours risperidone

Analysis 2.15. Comparison 2 CHLORPROMAZINE versus RISPERIDONE, Outcome 15 Adverse effects: 7. Metabolic - weight gain.

 Review:
 Chlorpromazine versus atypical antipsychotic drugs for schizophrenia

 Comparison:
 2 CHLORPROMAZINE versus RISPERIDONE

 Outcome:
 15 Adverse effects: 7. Metabolic - weight gain

Study or subgroup	Chlorpromazine	Risperidone	Risk Ratio M-	Weight	Risk Ratio M-
	n/N	n/N	H,Random,95% Cl		H,Random,95% Cl
I short term (up to 6 mor	nths)				
vs RPD - Feng 2003	0/33	7/32	← ∎	9.4 %	0.06 [0.00, 1.09]
vs RPD - Ma 2004	8/39	3/39		26.8 %	2.67 [0.76, 9.31]
vs RPD - Wang 2002	2/20	3/39		19.3 %	1.30 [0.24, 7.16]
vs RPD - Wu 2004	32/50	18/50	•	44.4 %	1.78 [1.16, 2.72]
Total (95% CI)	142	160	•	100.0 %	1.36 [0.52, 3.59]
Total events: 42 (Chlorpror	mazine), 31 (Risperidone)				
Heterogeneity: Tau ² = 0.50); $Chi^2 = 6.75$, $df = 3$ (P =	0.08); I ² =56%			
Test for overall effect: Z =	0.63 (P = 0.53)				
Test for subgroup difference	es: Not applicable				
			0.01 0.1 1 10 10	0	

Favours chlorpromazine Favours risperidone

Analysis 2.16. Comparison 2 CHLORPROMAZINE versus RISPERIDONE, Outcome 16 Adverse effects: 8. Movement disorders - short term (up to 6 months).

Review: Chlorpromazine versus atypical antipsychotic drugs for schizophrenia

Comparison: 2 CHLORPROMAZINE versus RISPERIDONE

Outcome: 16 Adverse effects: 8. Movement disorders - short term (up to 6 months)

Study or subgroup	Chlorpromazine	Risperidone	Risk Ratio M-	Weight	Risk Ratio M-
	n/N	n/N	H,Random,95% Cl		H,Random,S CI
I akathisia					
vs RPD - Chang 1998	7/20	3/38		12.9 %	4.43 [1.28, 15.31]
vs RPD - Lin 2005	12/35	4/35		17.4 %	3.00 [1.07, 8.40]
vs RPD - Ma 2004	4/39	1/39		4.8 %	4.00 [0.47, 34.20]
vs RPD - Wang 2002	0/20	4/39		2.8 %	0.21 [0.01, 3.75]
vs RPD - Wu 2002	13/35	9/35	-	29.4 %	1.44 [0.71, 2.94]
vs RPD - Wu 2004	26/50	9/50	+	32.8 %	2.89 [1.51, 5.53]
Subtotal (95% CI)	199	236	•	100.0 %	2.37 [1.46, 3.85]
Heterogeneity: Tau ² = 0.08; C Test for overall effect: Z = 3.4 2 any EPS symptoms		0.27); ² =21%			
vs RPD - Feng 2003	0/33	4/32		5.4 %	0.11 [0.01, 1.93]
vs RPD - Lin 2005	20/35	11/35	=	47.1 %	1.82 [1.03, 3.21
vs RPD - Wang 2005	26/50	12/50	=	47.5 %	2.17 [1.24, 3.80
Subtotal (95% CI) Total events: 46 (Chlorproma Heterogeneity: Tau ² = 0.18; C		117	•	100.0 %	1.70 [0.85, 3.40
Test for overall effect: $Z = 1.4$		<i>,</i> ,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,			
3 dystonia vs RPD - Chang 1998	6/20	4/38		18.3 %	2.85 [0.91, 8.94
vs RPD - Wu 2002	/35	10/35	+	43.1 %	1.10 [0.54, 2.25
vs RPD - Wu 2004	15/50	8/50	-	38.6 %	1.88 [0.87, 4.02
Subtotal (95% CI) Total events: 32 (Chlorproma Heterogeneity: $Tau^2 = 0.02$; C Test for overall effect: $Z = 1.8$	$Chi^2 = 2.20, df = 2 (P =$	123 0.33); I ² =9%	•	100.0 %	1.61 [0.97, 2.66
4 muscle stiffness vs RPD - Chang 1998	8/20	2/38		24.8 %	7.60 [1.78, 32.46
vs RPD - Lin 2005	16/35	6/35	-	33.6 %	2.67 [1.18, 6.01

(Continued ...)

Study or subgroup	Chlorpromazine	Risperidone	Risk Ratio M-	Weight	(Continued Risk Ratio M-
	n/N	n/N	H,Random,95% Cl		H,Random,9 CI
vs RPD - Ma 2004	4/39	0/39		11.6 %	9.00 [0.50, 161.73]
vs RPD - Wang 2002	1/20	8/39		18.4 %	0.24 [0.03, 1.82]
vs RPD - Wu 2002	4/35	0/35	—	11.6 %	9.00 [0.50, 161.13]
Subtotal (95% CI)	149	186	•	100.0 %	2.96 [0.92, 9.49]
Total events: 33 (Chlorproma	azine), 16 (Risperidone)				
Heterogeneity: Tau ² = 0.88; (Chi ² = 8.82, df = 4 (P =	0.07); l ² =55%			
Test for overall effect: $Z = 1.8$	32 (P = 0.069)				
5 torsion movements					
vs RPD - Ma 2004	4/39	0/39		100.0 %	9.00 [0.50, 161.73]
Subtotal (95% CI)	39	39		100.0 %	9.00 [0.50, 161.73]
Total events: 4 (Chlorpromaz	tine), 0 (Risperidone)				
Heterogeneity: not applicable					
Test for overall effect: $Z = 1.4$	49 (P = 0.14)				
6 tremor					
vs RPD - Chang 1998	7/20	4/38		11.5 %	3.33 [1.10, 10.02]
vs RPD - Lin 2005	10/35	3/35		9.7 %	3.33 [1.00, 11.09]
vs RPD - Ma 2004	11/39	3/39		9.8 %	3.67 [1.11, 12.14]
vs RPD - Wang 2002	0/20	3/39		1.7 %	0.27 [0.01, 5.02]
vs RPD - Wu 2002	21/35	I 3/35	-	48.8 %	1.62 [0.97, 2.69]
vs RPD - Wu 2004	15/50	6/50		18.5 %	2.50 [1.06, 5.92]
Subtotal (95% CI)	199	236	•	100.0 %	2.15 [1.47, 3.14]
Total events: 64 (Chlorproma	azine), 32 (Risperidone)				
Heterogeneity: $Tau^2 = 0.01;$		0.39); l ² =4%			
Test for overall effect: $Z = 3.9$	· /				
Test for subgroup differences	: $Chi^2 = 2.95$, $df = 5$ (P =	= 0.7 I), I ² =0.0%			

Chlorpromazine Risperidone

Analysis 2.17. Comparison 2 CHLORPROMAZINE versus RISPERIDONE, Outcome 17 Adverse events: 9. Average endpoint score (TESS) - skewed data.

Adverse events: 9. Average endpoint score (TESS) - skewed data

Study	Intervention	mean	SD	Ν			
short term (up to 6	short term (up to 6 months)						
vs RPD - Cui 2001	Chlorpromazine	3.23	2.87	30			

Adverse events: 9. Average endpoint score (TESS) - skewed data (Continued)

vs RPD - Cui 2001	Risperidone	3.93	5.78	30
vs RPD - He 1999	Chlorpromazine	2.9	2.1	20
vs RPD - He 1999	Risperidone	2.3	2.4	19
vs RPD - Liu 2005	Chlorpromazine	2.58	2.93	50
vs RPD - Liu 2005	Risperidone	1.46	1.58	50

Analysis 2.18. Comparison 2 CHLORPROMAZINE versus RISPERIDONE, Outcome 18 Adverse effects: 10. Various other - short term (up to 6 months).

Review: Chlorpromazine versus atypical antipsychotic drugs for schizophrenia Comparison: 2 CHLORPROMAZINE versus RISPERIDONE

Outcome: 18 Adverse effects: 10. Various other - short term (up to 6 months)

Study or subgroup	Chlorpromazine	Risperidone	Risk Ratio M-	Weight	Risk Ratio
	n/N	n/N	H,Random,95% Cl		M- H,Random,95 Cl
concentration (poor)					
vs RPD - Wu 2004	39/50	20/50		100.0 %	1.95 [1.35, 2.82]
Subtotal (95% CI)	50	50	•	100.0 %	1.95 [1.35, 2.82]
Total events: 39 (Chlorpromazi	ine), 20 (Risperidone)				
Heterogeneity: not applicable					
Test for overall effect: Z = 3.54	+ (P = 0.00040)				
2 memory deterioration					
vs RPD - Wu 2004	39/50	20/50		100.0 %	1.95 [1.35, 2.82]
Subtotal (95% CI)	50	50	•	100.0 %	1.95 [1.35, 2.82]
Total events: 39 (Chlorpromazi	ine), 20 (Risperidone)				
Heterogeneity: not applicable					
Test for overall effect: Z = 3.54	+ (P = 0.00040)				
3 sexual dysfunction					
vs RPD - Wu 2004	28/50	11/50		100.0 %	2.55 [1.43, 4.53]
Subtotal (95% CI)	50	50	•	100.0 %	2.55 [1.43, 4.53]
Total events: 28 (Chlorpromazi	ine), 11 (Risperidone)				
Heterogeneity: not applicable					
Test for overall effect: Z = 3.17	(P = 0.0015)				

(Continued ...)

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Study or subgroup	Chlorpromazine	Risperidone	Risk Ratio M-	Weight	(Continued) Risk Ratio M-
	n/N	n/N	H,Random,95% Cl		H,Random,95% Cl
4 unspecified					
vs RPD - Wang 2005	33/50	24/50		100.0 %	1.38 [0.97, 1.95]
Subtotal (95% CI)	50	50	•	100.0 %	1.38 [0.97, 1.95]
Total events: 33 (Chlorprom	nazine), 24 (Risperidone)				
Heterogeneity: not applicabl	e				
Test for overall effect: $Z = I$.78 (P = 0.075)				
Test for subgroup difference	s: Chi ² = 4.01, df = 3 (P =	0.26), I ² =25%			
			0.005 0.1 I I0	200	
			Chlorpromazine Risperido	ne	

Analysis 2.19. Comparison 2 CHLORPROMAZINE versus RISPERIDONE, Outcome 19 Quality of life: 1. Average endpoint score (QOL, high = good).

Review: Chlorpromazine versus atypical antipsychotic drugs for schizophrenia Comparison: 2 CHLORPROMAZINE versus RISPERIDONE Outcome: 19 Quality of life: 1. Average endpoint score (QOL, high = good)

Study or subgroup	Chlorpromazine		Risperidone		Dif	Mean ference	Weight	Mean Difference
	Ν	Mean(SD)	Ν	Mean(SD)	IV,Rano	dom,95% Cl		IV,Random,95% CI
I short term (up to 6 m	onths)							
vs RPD - Wu 2004	50	59.04 (16.18)	50	73.24 (15.96)	←		100.0 %	-14.20 [-20.50, -7.90]
Subtotal (95% CI)	50		50		-		100.0 %	-14.20 [-20.50, -7.90]
Heterogeneity: not applie	able							
Test for overall effect: Z	= 4.42 (P < 0.0000	1)						
Test for subgroup differe	nces: Not applicable	5						
					-20 -10	0 10	20	
					Risperidone	Chlorprom	nazine	

Analysis 2.20. Comparison 2 CHLORPROMAZINE versus RISPERIDONE, Outcome 20 Leaving the study early - short term (up to 6 months).

 Review:
 Chlorpromazine versus atypical antipsychotic drugs for schizophrenia

 Comparison:
 2 CHLORPROMAZINE versus RISPERIDONE

 Outcome:
 20 Leaving the study early - short term (up to 6 months)

Study or subgroup	Chlorpromazine	Risperidone	Risk Ratio M-	Weight	Risk Ratio M-
	n/N	n/N	H,Random,95% Cl		H,Random,95% Cl
I due to adverse events					
vs RPD - He 1999	0/20	2/21		100.0 %	0.21 [0.01, 4.11]
Subtotal (95% CI)	20	21		100.0 %	0.21 [0.01, 4.11]
Total events: 0 (Chlorproma	azine), 2 (Risperidone)				
Heterogeneity: not applicab	le				
Test for overall effect: $Z = I$.03 (P = 0.30)				
Test for subgroup difference	es: Not applicable				
		0	.005 0.1 1 10 200		

Chlorpromazine Risperidone

Analysis 3.1. Comparison 3 CHLORPROMAZINE versus QUETIAPINE, Outcome 1 Clinical response: 1. No significant clinical response.

Review: Chlorpromazine versus atypical antipsychotic drugs for schizophrenia Comparison: 3 CHLORPROMAZINE versus QUETIAPINE Outcome: I Clinical response: I. No significant clinical response

Risk Ratio	Weight	Risk Ratio	Quetiapine	Chlorpromazine	Study or subgroup
IV,Random,95% CI		IV,Random,95% CI	n/N	n/N	
			5.42	(110	I short term (up to 6 months)
1.23 [0.41, 3.72]	1.5 %		5/43	6/42	vs QTP - Ai 2007
0.50 [0.18, 1.38]	1.7 %		11/109	5/100	vs QTP - Cai 2006
1.04 [0.36, 3.00]	1.6 %		6/48	6/46	vs QTP - Cai 2007
0.73 [0.36, 1.51]	3.5 %		6/ 4	11/107	vs QTP - Chen 2001
1.50 [0.27, 8.34]	0.6 %		2/30	3/30	vs QTP - Chen 2008
1.00 [0.35, 2.87]	1.6 %		6/45	6/45	vs QTP - Deng 2004
1.03 [0.41, 2.59]	2.1 %		8/75	8/73	vs QTP - Guo 2003a
1.00 [0.27, 3.72]	1.0 %		4/40	4/40	vs QTP - Guo 2005
1.27 [0.65, 2.50]	3.9 %	_ <u>+</u>	11/43	13/40	vs QTP - Guo 2008
1.00 [0.16, 6.42]	0.5 %		2/20	2/20	vs QTP - He 2003
0.72 [0.43, 1.19]	7.1 %		27/94	20/97	vs QTP - Jiang 2006
1.20 [0.41, 3.51]	1.6 %		5/30	6/30	vs QTP - Jiang 2008
0.80 [0.24, 2.69]	1.2 %		5/30	4/30	vs QTP - Jin 2007
1.13 [0.24, 5.27]	0.8 %		3/44	3/39	vs QTP - Liu 2003
1.20 [0.34, 4.19]	1.2 %		4/47	5/49	vs QTP - Mei 2007
0.80 [0.62, 1.03]	27.0 %	-	82/194	64/190	vs QTP - NCT00882518
1.35 [0.97, 1.88]	16.4 %	-	36/101	48/100	vs QTP - Peuskens 1997
0.67 [0.20, 2.21]	1.3 %	<u> </u>	6/46	4/46	vs QTP - Tian 2006
0.75 [0.18, 3.07]	0.9 %		4/30	3/30	vs QTP - Wan 2002
1.43 [0.42, 4.81]	1.2 %	<u> </u>	4/32	5/28	vs QTP - Wan 2008
0.86 [0.44, 1.66]	4.2 %		14/48	12/48	vs QTP - Wang 2004
0.72 [0.37, 1.41]	4.0 %		14/48	12/57	vs QTP - Wang 2005
1.00 [0.22, 4.56]	0.8 %		3/30	3/30	vs QTP - Yang 2007
1.05 [0.28, 4.01]	1.0 %		4/60	4/57	vs QTP - Zhang 2002
0.82 [0.50, 1.36]	7.2 %		27/119	22/118	vs QTP - Zhang 2003

(Continued ...)

					(Continued)
Study or subgroup	Chlorpromazine	Quetiapine	Risk Ri	atio Weight	Risk Ratio
	n/N	n/N	IV,Random,95	5% CI	IV,Random,95% CI
vs QTP - Zhang 2008	3/30	2/30			1.50 [0.27, 8.34]
vs QTP - Zhou 2004	3/4	12/42		4.2 %	1.11 [0.58, 2.14]
vs QTP - Zou 2006	4/43	5/43		1.2 %	0.80 [0.23, 2.78]
Subtotal (95% CI)	1606	1635	•	100.0 %	0.93 [0.81, 1.06]
Total events: 299 (Chlorproma	azine), 328 (Quetiapine)				
Heterogeneity: Tau ² = 0.0; Ch	i ² = 13.40, df = 27 (P = 0.9	99); I ² =0.0%			
Test for overall effect: $Z = 1.05$	5 (P = 0.29)				
Test for subgroup differences:	Not applicable				
			0.02 0.1 1	10 50	
			Chlorpromazine C	Quetiapine	

Analysis 3.2. Comparison 3 CHLORPROMAZINE versus QUETIAPINE, Outcome 2 Global state: 1. Need of additional benzodiazepines/benzhexol.

Review: Chlorpromazine versus atypical antipsychotic drugs for schizophrenia Comparison: 3 CHLORPROMAZINE versus QUETIAPINE

Outcome: 2 Global state: I. Need of additional benzodiazepines/benzhexol

Study or subgroup	Chlorpromazine	Quetiapine	F	lisk Ratio M-	Weight	Risk Ratio M-
	n/N	n/N	H,Ran	dom,95% Cl		H,Random,95% Cl
I short term (up to 6 months)					
vs QTP - Cheng 2003	33/45	21/44		<mark>∎</mark> _→	42.8 %	1.54 [1.08, 2.19]
vs QTP - Peuskens 1997	51/100	40/101	-		57.2 %	1.29 [0.95, 1.75]
Subtotal (95% CI)	145	145		-	100.0 %	1.39 [1.10, 1.75]
Total events: 84 (Chlorpromaz	zine), 61 (Quetiapine)					
Heterogeneity: Tau ² = 0.0; Ch	ni ² = 0.55, df = 1 (P = 0.46)	; I ² =0.0%				
Test for overall effect: $Z = 2.7$	6 (P = 0.0057)					
Test for subgroup differences:	Not applicable					
			0.5 0.7	1.5 2		
			Chlorpromazine	Quetiapine		

Analysis 3.3. Comparison 3 CHLORPROMAZINE versus QUETIAPINE, Outcome 3 Global state: 2a. Average endpoint scores (various scales, high = poor) - short term (up to 6 months).

Review: Chlorpromazine versus atypical antipsychotic drugs for schizophrenia

Comparison: 3 CHLORPROMAZINE versus QUETIAPINE

Outcome: 3 Global state: 2a. Average endpoint scores (various scales, high = poor) - short term (up to 6 months)

Study or subgroup	Chlorpromazine		Quetiapine		Mean Difference	Weight	Mean Difference
	N	Mean(SD)	N	Mean(SD)	IV,Random,95% CI	-	IV,Random,95% CI
CGI-SI							
vs QTP - Cheng 2003	45	1.8 (0.8)	44	1.4 (0.9)		54.3 %	0.40 [0.05, 0.75]
vs QTP - Wang 2004	42	3.38 (1.53)	46	3.83 (1.34)		45.7 %	-0.45 [-1.05, 0.15]
Subtotal (95% CI)	87		90			100.0 %	0.01 [-0.82, 0.84]
Heterogeneity: Tau ² = 0.30;	; Chi ² = 5.67, df =	$ (P = 0.02); ^2$	=82%				
est for overall effect: Z = 0	0.03 (P = 0.98)						
CGI-GI							
vs QTP - Cheng 2003	45	1.6 (0.8)	44	1.7 (0.5)		64.8 %	-0.10 [-0.38, 0.18]
vs QTP - Guo 2007	26	2.3 (1.6)	26	2.3 (1.1)		8.9 %	0.0 [-0.75, 0.75]
vs QTP - Wang 2004	42	2.57 (1.08)	46	2.75 (0.99)		26.3 %	-0.18 [-0.61, 0.25]
Subtotal (95% CI)	113		116		-	100.0 %	-0.11 [-0.33, 0.11]
Heterogeneity: $Tau^2 = 0.0;$	Chi ² = 0.19, df = 2	(P = 0.91); I ² =	0.0%				
est for overall effect: Z = 0).99 (P = 0.32)						
	es: $Chi^2 = 0.08$. df =	= (P = 0.78), ²	2 =0.0%				

Chlorpromazine Quetiapine

Analysis 3.4. Comparison 3 CHLORPROMAZINE versus QUETIAPINE, Outcome 4 Global state: 2b. Average endpoint score (CGI-SI, high = poor) - skewed data).

Global state: 2b. Average endpoint score (CGI-SI, high = poor) - skewed data)

Study	Intervention	Mean	SD	Ν				
short term (up to 6 months) sh								
vs QTP - Guo 2007	Chlorpromazine	1.5	1.7	26				
vs QTP - Guo 2007	Quetiapine	1.6	1.3	26				

Analysis 3.5. Comparison 3 CHLORPROMAZINE versus QUETIAPINE, Outcome 5 Global state: 3. Average change scores (CGI-SI, high = poor).

 Review:
 Chlorpromazine versus atypical antipsychotic drugs for schizophrenia

 Comparison:
 3 CHLORPROMAZINE versus QUETIAPINE

 Outcome:
 5 Global state: 3. Average change scores (CGI-SI, high = poor)

Study or subgroup	Chlorpromazine		Quetiapine		Dif	Mean ference	Weight	Mean Difference
	Ν	Mean(SD)	Ν	Mean(SD)	IV,Ranc	lom,95% Cl		IV,Random,95% CI
I short term (up to 6 mor	ths)							
vs QTP - NCT0088251	8 190	-2. (0.)	194	-1.8 (0.12)			100.0 %	-0.30 [-0.32, -0.28]
Subtotal (95% CI)	190		194				100.0 %	-0.30 [-0.32, -0.28]
Heterogeneity: not applical	ble							
Test for overall effect: $Z =$	25.55 (P < 0.00001)							
Test for subgroup difference	es: Not applicable							
							1	
				-0.	2 -0.1	0 0.1	0.2	
				Chlo	orpromazine	Quetiapine		

Analysis 3.6. Comparison 3 CHLORPROMAZINE versus QUETIAPINE, Outcome 6 Mental state: 1a. Average endpoint scores (various scales, high = poor) - short term (up to 6 months).

Review: Chlorpromazine versus atypical antipsychotic drugs for schizophrenia

Comparison: 3 CHLORPROMAZINE versus QUETIAPINE

Outcome: 6 Mental state: I a. Average endpoint scores (various scales, high = poor) - short term (up to 6 months)

Mear Difference IV,Random,95% C	Weight	Mean Difference IV,Random,95% Cl	Mean(SD)	Quetiapine N	Mean(SD)	Chlorpromazine N	Study or subgroup
							I BPRS total
0.0 [-3.23, 3.23	10.7 %	-+-	34.3 (7.6)	43	34.3 (7.6)	42	vs QTP - Ai 2007
0.0 [-2.09, 2.09	25.7 %	+	25.5 (7.6)	114	25.5 (8.2)	107	vs QTP - Chen 2001
-0.60 [-2.22, 1.02]	42.7 %	-	16.1 (3.4)	32	15.5 (3.1)	30	vs QTP - Chen 2007
1.79 [-3.17, 6.75	4.5 %		26.56 (9.48)	30	28.35 (0.)	30	vs QTP - Jiang 2008
2.05 [-3.46, 7.56	3.7 %	_ <u>+</u>	27.56 (10.68)	32	29.61 (11.04)	28	vs QTP - Wan 2008
-0.61 [-3.58, 2.36]	12.7 %		28.3 (6.5)	30	27.69 (5.18)	30	vs QTP - Yang 2007
-0.18 [-1.23, 0.88]	100.0 %	•		281		267	Subtotal (95% CI)
	100.0.0/		5 27 (1 02)			: 0.33 (P = 0.74) n subscale	Heterogeneity: $Tau^2 = 0.0$ Test for overall effect: $Z = 2$ BPRS anxiety-depression
-0.27 [-1.16, 0.62	100.0 %	-	5.37 (1.92)	30	5.1 (1.59)	30	vs QTP - Yang 2007
0.22 [-0.26, 0.70	100.0 %	_	3.47 (0.86)	30	3.69 (1.04)	0.59 (P = 0.55)	Heterogeneity: not applica Test for overall effect: Z = 3 BPRS activation subscale vs QTP - Yang 2007
0.22 [-0.26, 0.70]	100.0 %	•		30		30	Subtotal (95% CI)
						able = 0.89 (P = 0.37)	Heterogeneity: not applica Test for overall effect: Z = 4 BPRS hostile-suspiciousr
-0.09 [-1.15, 0.97	100.0 %	-	6.3 (2.23)	30	6.21 (1.93)	30	vs QTP - Yang 2007
-0.09 [-1.15, 0.97]	100.0 %	+		30		0.17 (P = 0.87)	Subtotal (95% CI) Heterogeneity: not applica Test for overall effect: Z = 5 BPRS thinking disorder s
-0.15 [-1.39, 1.09	100.0 %		7.87 (2.58)	30	7.72 (2.33)	30	vs QTP - Yang 2007
-0.15 [-1.39, 1.09]	100.0 %	•		30		0.24 (P = 0.81)	Subtotal (95% CI) Heterogeneity: not applica Test for overall effect: Z = 6 BPRS withdraw-retardat

(Continued . . .)

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Study or subgroup Chl	orpromazine	M (CD)	Quetiapine		Mean Difference	Weight	Me Differen
vs QTP - Yang 2007	N 30	Mean(SD) 5.07 (1.5)	N 30	Mean(SD) 5.17 (1.05)	IV,Random,95% CI	100.0 %	IV,Random,95% -0.10 [-0.76, 0.56
		5.07 (1.5)		5.17 (1.05)	Ţ		-
ubtotal (95% CI) leterogeneity: not applicable	30		30			100.0 %	-0.10 [-0.76, 0.56
est for overall effect: $Z = 0.30$	(P = 0.76)						
PANSS total	20	E7 (0 ()	20	EE (7 (11)		4.2.9/	2.01 [-3.58, 7.6
vs QTP - An 2005		57.68 (11.11)	30	55.67 (11)	←	4.2 %	-
vs QTP - Cai 2007	46	24.8 (8.3)	48	45.7 (13.8)		4.5 %	-20.90 [-25.48, -16.3
vs QTP - Chen 2001	107	48.1 (15.2)	114	48.5 (14.8)		4.8 %	-0.40 [-4.36, 3.5
vs QTP - Chen 2007	30	34.6 (10.7)	32	34.1 (10.2)		4.3 %	0.50 [-4.71, 5.7
vs QTP - Chen 2008	30	42.8 (4.8)	30	44.3 (4.1)		5.3 %	-1.50 [-3.76, 0.7
vs QTP - Cheng 2003	45	48.2 (15.1)	44	48 (15.2)		3.9 %	0.20 [-6.10, 6.5
vs QTP - Guo 2003a	73	46.72 (17.12)	75	47.32 (17.212)		4.2 %	-0.60 [-6.13, 4.9
vs QTP - Guo 2003b	30	48.66 (8.9)	30	45.42 (8.8)		4.6 %	3.24 [-1.24, 7.7
vs QTP - Guo 2005	40	48.1 (15.2)	40	48.6 (13.8)		3.9 %	-0.50 [-6.86, 5.8
vs QTP - Guo 2007	26	43.9 (12.3)	26	44.7 (12.2)		3.8 %	-0.80 [-7.46, 5.8
vs QTP - Guo 2008	40	52.6 (16.4)	43	42.3 (17)	<u></u>	3.6 %	10.30 [3.11, 17.4
vs QTP - He 2003	20	50 (12.9)	20	43.1 (10.2)		3.6 %	6.90 [-0.31, 14.1
vs QTP - Ji 2004	29	34.63 (10.7)	30	34.05 (10.17)		4.3 %	0.58 [-4.75, 5.9
vs QTP - Jiang 2008	30	39.24 (10.36)	30	37.21 (11.48)	<u> </u>	4.2 %	2.03 [-3.50, 7.5
vs QTP - Liu 2003	39	40.2 (13.9)	44	41.4 (14.4)		4.0 %	-1.20 [-7.29, 4.8
vs QTP - Mei 2007	49	52.9 (18.3)	47	53.2 (23.6)		3.1 %	-0.30 [-8.77, 8.1
vs QTP - Sun 2006	36	47.55 (10.63)	35	46.67 (11.4)		4.3 %	0.88 [-4.25, 6.0
vs QTP - Tian 2006	46	47.6 (17.7)	46	45.2 (19.2)		3.4 %	2.40 [-5.15, 9.9
vs QTP - Wan 2002	30	48 (14.3)	30	54.2 (14.4)		3.5 %	-6.20 [-13.46, 1.0
vs QTP - Wan 2008	28	40.13 (18.24)	32	38.57 (12.56)		3.3 %	1.56 [-6.48, 9.6
vs QTP - Wang 2004	42	58.67 (20.93)	46	61.63 (23.73)		2.9 %	-2.96 [-12.29, 6.3
vs QTP - Wang 2005	57	53.1 (18.5)	48	53.7 (23.8)	<u> </u>	3.2 %	-0.60 [-8.87, 7.6
vs QTP - Zhang 2006	33	49.9 (7.02)	28	47.1 (7.06)		4.9 %	2.80 [-0.75, 6.3
vs QTP - Zhou 2004	39	53.15 (9.84)	40	51.47 (10.62)	_ 	4.6 %	1.68 [-2.83, 6.1
vs QTP - Zou 2006	43	49.9 (14.7)	43	47.8 (15.4)		3.9 %	2.10 [-4.26, 8.4
ubtotal (95% CI)	1018		1031	. ,	•	100.0 %	-0.05 [-2.30, 2.19

Chlorpromazine Quetiapine

(Continued . . .)

Study or subgroup	Chlorpromazine		Quetiapine		Mean Difference	Weight	(Continue Mear Difference
	N	Mean(SD)	N	Mean(SD)	IV,Random,95% CI		IV,Random,95% C
PANSS positive sympton	ns						
vs QTP - An 2005	30	11.48 (4.45)	30	10.46 (4.89)	+-	4.3 %	1.02 [-1.35, 3.39
vs QTP - Chen 2001	107	11.4 (5.4)	4	.2 (4.9)	+	3. %	0.20 [-1.16, 1.56
vs QTP - Chen 2007	30	7.9 (3.3)	32	7.6 (3.2)	+	9.3 %	0.30 [-1.32, 1.92
vs QTP - Cheng 2003	45	. (4.8)	44	(5)	+	5.9 %	0.10 [-1.94, 2.14
vs QTP - Guo 2003b	30	16.01 (3.38)	30	14.03 (4.72)	-	5.6 %	1.98 [-0.10, 4.06
vs QTP - Guo 2005	40	11.4 (5.4)	40	11.3 (5.3)	+	4.4 %	0.10 [-2.24, 2.44
vs QTP - Guo 2008	40	11.2 (3.2)	43	10.8 (2.3)	+	16.7 %	0.40 [-0.81, 1.61
vs QTP - Hu 2003	19	14.64 (4.37)	22	14.09 (6.25)	<u> </u>	2.3 %	0.55 [-2.72, 3.82
vs QTP - Ji 2004	29	7.85 (3.32)	30	7.56 (3.24)	+	8.7 %	0.29 [-1.38, 1.96
vs QTP - Li 2003	37	13.5 (4.3)	40	.7 (4.2)	-	6.7 %	1.80 [-0.10, 3.70
vs QTP - Tian 2006	46	11.6 (5)	46	11.4 (5)	+	5.8 %	0.20 [-1.84, 2.24
vs QTP - Zhang 2002	57	9.97 (3.52)	60	11.08 (4.25)	-	12.2 %	-1.11 [-2.52, 0.30
vs QTP - Zhang 2006	33	13.8 (4.25)	28	12.47 (4.62)		4.8 %	1.33 [-0.91, 3.57
ubtotal (95% CI)	543		559		•	100.0 %	0.39 [-0.11, 0.88
leterogeneity: Tau ² = 0.0; est for overall effect: Z = PANSS negative symptor	I.54 (P = 0.12)	12 (P = 0.62); 1	2 =0.0%				
vs QTP - An 2005	30	22.03 (5.68)	30	21.81 (5.6)	+	4.8 %	0.22 [-2.63, 3.07
vs QTP - Chen 2001	107	12.2 (4.8)	4	13 (5.6)	-	7.4 %	-0.80 [-2.17, 0.57
vs QTP - Chen 2007	30	8.4 (3.7)	32	9.4 (3.7)	-	6.5 %	-1.00 [-2.84, 0.84
vs QTP - Cheng 2003	45	12.6 (5.3)	44	3.7 (6.2)		5.5 %	-1.10 [-3.50, 1.30
vs QTP - Guo 2003b	30	11.98 (3.24)	30	9.73 (3.67)		6.7 %	2.25 [0.50, 4.00
vs QTP - Guo 2005	40	18.5 (4.8)	40	3.2 (5.8)		5.6 %	5.30 [2.97, 7.63
vs QTP - Guo 2007	26	10.7 (3.5)	26	9.1 (3.7)	-	6.3 %	1.60 [-0.36, 3.56
vs QTP - Guo 2008	40	2. (4.3)	43	8.1 (2.6)	+	7.1 %	4.00 [2.46, 5.54
vs QTP - Hu 2003	19	14.71 (5.22)	22	14.72 (6.72)		3.7 %	-0.01 [-3.67, 3.65
vs QTP - Ji 2004	29	8.36 (3.71)	30	9.36 (3.66)	-	6.5 %	-1.00 [-2.88, 0.88
vs QTP - Sun 2006	36	10.41 (3.24)	35	9.43 (2.55)	-	7.4 %	0.98 [-0.37, 2.33
vs QTP - Tian 2006	46	14.5 (6)	46	12.4 (7)	-	5.1 %	2.10 [-0.56, 4.76
vs QTP - Wan 2002	30	15.4 (5.9)	30	17 (5.4)		4.8 %	-1.60 [-4.46, 1.26
~				(·)			L .,

-20 -10 0 10 20

Quetiapine

Chlorpromazine

(Continued . . .)

Study or subgroup (Chlorpromazine N	Mean(SD)	Quetiapine N	Mean(SD)	Mean Difference IV,Random,95% Cl	Weight	Mean Difference IV,Random,95% CI
vs QTP - Zhang 2006	33	13.23 (3.37)	28	11.47 (4.37)		6.3 %	1.76 [-0.23, 3.75]
vs QTP - Zhou 2004	39	15.55 (5.24)	40	3.78 (5.)		5.7 %	1.77 [-0.51, 4.05]
vs QTP - Zou 2006	43	I 3.6 (6.8)	43	11.5 (5.9)	+=-	5.1 %	2.10 [-0.59, 4.79]
Subtotal (95% CI)	680		681		•	100.0 %	1.05 [0.13, 1.98]
Heterogeneity: $Tau^2 = 2.55$; Test for overall effect: $Z = 2$		= 16 (P<0.000	01); I ² =71%				
10 PANSS general patholog vs QTP - An 2005	y 30	23.1 (4.23)	30	23.11 (3.4)	+	6.0 %	-0.01 [-1.95, 1.93]
vs QTP - Chen 2001	107	24.4 (7)	114	24.2 (6.7)	+	6.0 %	0.20 [-1.61, 2.01]
vs QTP - Chen 2007	30	18.4 (4.6)	32	17.1 (4.6)		5.9 %	1.30 [-0.99, 3.59]
vs QTP - Cheng 2003	45	24.5 (6.8)	44	23.3 (7)		5.6 %	1.20 [-1.67, 4.07]
vs QTP - Guo 2003b	30	20.91 (6.62)	30	19.7 (5.72)		5.5 %	1.21 [-1.92, 4.34]
vs QTP - Guo 2005	40	24.5 (6.2)	40	25.4 (7.6)		5.5 %	-0.90 [-3.94, 2.14]
vs QTP - He 2003	22	30.71 (7.14)	22	30.54 (6.18)	-	5.1 %	0.17 [-3.78, 4.12]
vs QTP - Ji 2004	29	18.42 (4.57)	30	17.13 (4.56)	-#-	5.8 %	1.29 [-1.04, 3.62]
vs QTP - Mei 2007	49	27 (8.2)	47	27.4 (11.4)		5.0 %	-0.40 [-4.39, 3.59]
vs QTP - Sun 2006	36	24.1 (3.42)	35	23.4 (5.86)	-	5.9 %	0.70 [-1.54, 2.94]
vs QTP - Tian 2006	46	21.5 (6)	46	21.4 (5)	-	5.9 %	0.10 [-2.16, 2.36]
vs QTP - Wan 2002	30	23.7 (6.2)	30	25.5 (6.7)		5.4 %	-1.80 [-5.07, 1.47]
vs QTP - Wang 2004	42	29.14 (9.79)	46	30 (9.79)		5.0 %	-0.86 [-4.96, 3.24]
vs QTP - Wang 2005	57	27.2 (8.4)	48	27.6 (11.6)	_ _	5.1 %	-0.40 [-4.34, 3.54]
vs QTP - Zhang 2002	57	24.63 (5.17)	60	26.34 (7.76)		5.8 %	-1.71 [-4.09, 0.67]
vs QTP - Zhang 2006	33	23.8 (4.1)	28	22.6 (4.08)	-#-	6.0 %	1.20 [-0.86, 3.26]
vs QTP - Zhou 2004	39	27.45 (6.1)	40	51.47 (10.62)		5.1 %	-24.02 [-27.83, -20.21]
vs QTP - Zou 2006	43	23.8 (7.8)	43	23.2 (7.6)		5.4 %	0.60 [-2.66, 3.86]
Subtotal (95% CI) Heterogeneity: $Tau^2 = 15.5$ Test for overall effect: $Z = 1$		df = 17 (P<0.0	7 65 0001); I ² =899	6	•	100.0 %	-1.11 [-3.06, 0.84]
I I HAMD total vs QTP - Li 2010	31	12.9 (4.4)	32	5.5 (4.8)	-	100.0 %	7.40 [5.13, 9.67]
Subtotal (95% CI) Heterogeneity: not applicabl Test for overall effect: $Z = 6$)	32		•	100.0 %	7.40 [5.13, 9.67]

Analysis 3.7. Comparison 3 CHLORPROMAZINE versus QUETIAPINE, Outcome 7 Mental state: 1b. Average endpoint scores (various scales, high = poor) - medium term (6 to 12 months).

Review: Chlorpromazine versus atypical antipsychotic drugs for schizophrenia

Comparison: 3 CHLORPROMAZINE versus QUETIAPINE

Outcome: 7 Mental state: Ib. Average endpoint scores (various scales, high = poor) - medium term (6 to 12 months)

Study or subgroup	Chlorpromazine		Quetiapine		Mean Difference	Weight	Mean Difference
	N	Mean(SD)	N	Mean(SD)	IV,Random,95% CI	-	IV,Random,95% CI
I PANSS total							
vs QTP - Li 2003	37	58.7 (9.8)	4	53.8 (0.1)		100.0 %	4.90 [1.74, 8.06]
Subtotal (95% CI) Heterogeneity: not applica	37 able		4		-	100.0 %	4.90 [1.74, 8.06]
Test for overall effect: Z =	3.04 (P = 0.0024)						
2 PANSS general patholog	gy						
vs QTP - Li 2003	37	22.1 (4.1)	4	22.3 (4)		100.0 %	-0.20 [-4.34, 3.94]
Subtotal (95% CI)	37		4			100.0 %	-0.20 [-4.34, 3.94]
Heterogeneity: not applica	able						
Test for overall effect: Z =	0.09 (P = 0.92)						
3 PANSS negative sympto	ms						
vs QTP - Li 2003	37	24.6 (4)	40	21.9 (6)		100.0 %	2.70 [0.44, 4.96]
Subtotal (95% CI) Heterogeneity: not applica	37 able		40		•	100.0 %	2.70 [0.44, 4.96]
Test for overall effect: Z =	2.34 (P = 0.019)						
Test for subgroup differen	ces: $Chi^2 = 3.72$, df =	= 2 (P = 0.16),	l ² =46%				
				I		1	
				-10	-5 0 5	10	
				Chlor	rpromazine Quetiapine	e	

Analysis 3.8. Comparison 3 CHLORPROMAZINE versus QUETIAPINE, Outcome 8 Mental state: 1 c. Average endpoint scores (various scales, high = poor) -skewed data.

Mental state: 1c. Average endpoint scores (various scales, high = poor) -skewed data

Study	Intervention	Mean	SD	Ν	
PANSS total - short ter	rm (up to 6 month	is)			PANSS total -

Mental state: 1c. Average endpoint scores	(various scales,	high = poor) -skewed data	(Continued)
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vs QTP - Zhang 2002	Chlorpromazine	28.39	16.57	57	
vs QTP - Zhang 2002	Quetiapine	9.27	16.36	60	
PANSS positive sympt	oms - short term (up to 6 1	nonths)		PANSS positive
vs QTP - Guo 2003a	Chlorpromazine	11.4	5.8	73	
vs QTP - Guo 2003a	Quetiapine	11.3	5.7	75	
vs QTP - Guo 2007	Chlorpromazine	9.9	5.5	26	
vs QTP - Guo 2007	Quetiapine	10.9	6.4	26	
vs QTP - Mei 2007	Chlorpromazine	11.9	6.2	49	
vs QTP - Mei 2007	Quetiapine	14.0	8.2	47	
vs QTP - Sun 2006	Chlorpromazine	9.46	4.55	36	
vs QTP - Sun 2006	Quetiapine	10.37	3.29	35	
vs QTP - Wan 2002	Chlorpromazine	11.5	6.1	30	
vs QTP - Wan 2002	Quetiapine	11.8	4.3	30	
vs QTP - Wang 2004	Chlorpromazine	11.38	4.2	42	
vs QTP - Wang 2004	Quetiapine	13.0	8.16	46	
vs QTP - Wang 2005	Chlorpromazine	12.09	6.39	57	
vs QTP - Wang 2005	Quetiapine	14.2	8.4	48	
vs QTP - Zhang 2008	Chlorpromazine	11.47	5.71	30	
vs QTP - Zhang 2008	Quetiapine	10.33	6.82	30	
vs QTP - Zhou 2004	Chlorpromazine	17.12	7.82	39	
vs QTP - Zhou 2004	Quetiapine	16.12	8.3	40	
vs QTP - Zou 2006	Chlorpromazine	10.8	6.2	43	
vs QTP - Zou 2006	Quetiapine	10.09	7.2	43	

Mental state: 1c. Average endpoint scores	(various scales, high = poor) -skewed data	(Continued)
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PANSS negative symptoms - short term (up to 6 months)							
Chlorpromazine	12.3	7.1	73				
Quetiapine	12.9	6.9	75				
Chlorpromazine	12.4	6.1	49				
Quetiapine	11.7	5.9	47				
Chlorpromazine	18.14	9.38	42				
Quetiapine	18.63	9.3	46				
Chlorpromazine	15.88	4.11	57				
Quetiapine	10.87	6.19	60				
ogy - short term (v	ip to 6 n	ionths		PANSS general			
Chlorpromazine	20.1	10.9	40				
Quetiapine	19.2	11.4	43				
	Chlorpromazine Quetiapine Chlorpromazine Quetiapine Chlorpromazine Quetiapine Chlorpromazine Quetiapine ogy - short term (u	Chlorpromazine12.3Quetiapine12.9Chlorpromazine12.4Quetiapine11.7Chlorpromazine18.14Quetiapine18.63Chlorpromazine15.88Quetiapine10.87ogy - short term (up to 6 mChlorpromazine20.1	Chlorpromazine 12.3 7.1 Quetiapine 12.9 6.9 Chlorpromazine 12.4 6.1 Quetiapine 11.7 5.9 Chlorpromazine 18.14 9.38 Quetiapine 18.63 9.3 Chlorpromazine 15.88 4.11 Quetiapine 10.87 6.19 Ouetiapine 10.87 10.9 Chlorpromazine 20.1 10.9	Chlorpromazine 12.3 7.1 73 Quetiapine 12.9 6.9 75 Chlorpromazine 12.4 6.1 49 Quetiapine 11.7 5.9 47 Chlorpromazine 18.14 9.38 42 Quetiapine 18.63 9.3 46 Chlorpromazine 15.88 4.11 57 Quetiapine 10.87 6.19 60 componazine junction of the second se			

Analysis 3.9. Comparison 3 CHLORPROMAZINE versus QUETIAPINE, Outcome 9 Mental state: Id. Average change score (various scales, high = poor) - short term (up to 6 months).

Review: Chlorpromazine versus atypical antipsychotic drugs for schizophrenia

Comparison: 3 CHLORPROMAZINE versus QUETIAPINE

Outcome: 9 Mental state: Id. Average change score (various scales, high = poor) - short term (up to 6 months)

Study or subgroup	Chlorpromazine N	Mean(SD)	Quetiapine N	Mean(SD)	Diffe	Mean rence om,95% Cl	Weight	Mean Difference IV,Random,95% CI
I PANSS total								
vs QTP - NCT00882518	150	-35.9 (1.35)	159	-33.4 (1.45)	+		99.7 %	-2.50 [-2.81, -2.19]
vs QTP - Zhang 2002	57	-43.23 (12.77)	60	-39.35 (17.63)		_	0.3 %	-3.88 [-9.44, 1.68]
Subtotal (95% CI)	207		219		•		100.0 %	-2.50 [-2.82, -2.19]
Heterogeneity: $Tau^2 = 0.0$; C	Chi ² = 0.24, df = 1	(P = 0.63); I ² =	0.0%					
Test for overall effect: $Z = 1$	5.75 (P < 0.00001)							
2 PANSS positive symptoms								
vs QTP - NCT00882518	194	-9.9 (0.53)	190	- . (0.5)			100.0 %	1.20 [1.10, 1.30]
Subtotal (95% CI)	194		190			1	100.0 %	1.20 [1.10, 1.30]
Heterogeneity: not applicable	e							
Test for overall effect: $Z = 2$	2.61 (P < 0.00001)							
3 PANSS negative symptoms	s							
vs QTP - NCT00882518	194	-5.9 (0.5)	190	-6.7 (0.48)	I	•	100.0 %	0.80 [0.70, 0.90]
Subtotal (95% CI)	194		190			,	100.0 %	0.80 [0.70, 0.90]
Heterogeneity: not applicabl	e							
Test for overall effect: $Z = 1$	6.00 (P < 0.00001)							
4 PANSS general pathology								
vs QTP - NCT00882518	194	-12.9 (0.74)	190	-13.9 (0.71)		•	100.0 %	1.00 [0.85, 1.15]
Subtotal (95% CI)	194		190			•	100.0 %	1.00 [0.85, 1.15]
Heterogeneity: not applicable	e							
Test for overall effect: $Z = 1$	3.51 (P < 0.00001)							
Test for subgroup differences	s: Chi ² = 493.44, df	T = 3 (P = 0.00)	, l ² =99%					
							1	
				-	10 -5 C	5	10	
				Ch	lorpromazine	Quetiapine	2	

Analysis 3.10. Comparison 3 CHLORPROMAZINE versus QUETIAPINE, Outcome 10 Mental state: 1e. Average score decreased rate of BPRS/PANSS (%) - short term (up to 6 months).

Review: Chlorpromazine versus atypical antipsychotic drugs for schizophrenia

Comparison: 3 CHLORPROMAZINE versus QUETIAPINE

Outcome: 10 Mental state: 1e. Average score decreased rate of BPRS/PANSS (%) - short term (up to 6 months)

Chlorpromazine N	Mean(SD)	Quetiapine N	Mean(SD)	Mean Difference IV,Random,95% Cl	Weight	Mean Difference IV,Random,95% CI
	. ,					
96	49.4 (13.1)	101	50.2 (15.9)		100.0 %	-0.80 [-4.86, 3.26]
96		101		-	100.0 %	-0.80 [-4.86, 3.26]
ole						
0.39 (P = 0.70)						
46	67 (20)	48	83 (22)	← ■───	14.8 %	-16.00 [-24.49, -7.51]
94	66.4 (26.3)	105	65.9 (27.8)		16.2 %	0.50 [-7.02, 8.02]
73	64.9 (25.3)	75	64.7 (26.5)		15.0 %	0.20 [-8.15, 8.55]
30	50.24 (6.93)	30	48.07 (6.11)		22.2 %	2.17 [-1.14, 5.48]
108	59.23 (33.61)	112	54.7 (33.83)		14.3 %	4.53 [-4.38, 3.44]
33	48.06 (13.2)	28	52.75 (3.)		17.5 %	-4.69 [-11.31, 1.93]
384		398		-	100.0 %	-1.96 [-7.20, 3.28]
1; Chi ² = 18.14, c	f = 5 (P = 0.003)	3); I ² =72%				
0.73 (P = 0.46)						
es: $Chi^2 = 0.12$, df	= I (P = 0.73),	$ ^2 = 0.0\%$				
					1	
	$\begin{array}{c} & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & $	N Mean(SD) 96 49.4 (13.1) 96 96 96 96 96 96 96 96 96 96	N Mean(SD) N 96 49.4 (13.1) 101 96 49.4 (13.1) 101 96 101 101 96 101 101 96 101 101 96 101 101 96 66.4 (26.3) 105 73 64.9 (25.3) 75 30 50.24 (6.93) 30 108 59.23 (33.61) 112 33 48.06 (13.2) 28 384 398 398 H; Chi ² = 18.14, df = 5 (P = 0.003); l ² = 72% 1	N Mean(SD) N Mean(SD) 96 49.4 (13.1) 101 50.2 (15.9) 96 101 50.2 (15.9) 96 101 50.2 (15.9) 96 101 50.2 (15.9) 96 101 50.2 (15.9) 96 101 50.2 (15.9) 96 101 50.2 (15.9) 96 101 50.2 (15.9) 96 66.7 (20) 48 83 (22) 94 66.4 (26.3) 105 65.9 (27.8) 73 64.9 (25.3) 75 64.7 (26.5) 30 50.24 (6.93) 30 48.07 (6.11) 108 59.23 (33.61) 112 54.7 (33.83) 33 48.06 (13.2) 28 52.75 (13.1) 384 398 59.8 50.73 (P = 0.46) es: Chi ² = 0.12, df = 1 (P = 0.73), l ² = 0.0% 50.2% 50.2%	N Mean(SD) N Mean(SD) IV,Random,95% CI 96 49.4 (13.1) 101 50.2 (15.9) 96 101 96 101 96 49.4 (13.1) 101 50.2 (15.9) 96 101 96 49.4 (13.1) 101 50.2 (15.9) 96 50.2 (15.9) 46 67 (20) 48 83 (22) 94 66.4 (26.3) 105 65.9 (27.8) 73 64.9 (25.3) 75 64.7 (26.5) 30 50.24 (6.93) 30 48.07 (6.11) 108 59.23 (33.61) 112 54.7 (33.83) 33 48.06 (13.2) 28 52.75 (13.1) 384 398 H; Chi ² = 18.14, df = 5 (P = 0.003); l ² =72% 0.73 (P = 0.46) es: Chi ² = 0.12, df = 1 (P = 0.73), l ² =0.0%	N Mean(SD) N Mean(SD) IV,Random,95% CI 96 49.4 (13.1) 101 50.2 (15.9) 100.0 % 96 101 100.0 % 100.0 % 96 101 100.0 % 96 101 100.0 % 96 101 100.0 % 96 101 100.0 % 96 101 100.0 % 96 101 100.0 % 96 101 100.0 % 96 105 65.9 (27.8) 73 64.9 (25.3) 75 64.7 (26.5) 30 50.24 (6.93) 30 48.07 (6.11) 108 59.23 (33.61) 112 54.7 (33.83) 33 48.06 (13.2) 28 52.75 (13.1) 413 % 33 48.06 (13.2) 28 52.75 (13.1) 41; Chi ² = 18.14, df = 5 (P = 0.003); l ² = 72% 0.73 (P = 0.46) 100.0 % es: Chi ² = 0.12, df = 1 (P = 0.73), l ² = 0.0% 100.0 % 100.0 %

Chlorpromazine Quetiapine

Analysis 3.11. Comparison 3 CHLORPROMAZINE versus QUETIAPINE, Outcome 11 Functioning: 1. Average endpoint score (various scales, high = better) - short term (up to 6 months).

Review: Chlorpromazine versus atypical antipsychotic drugs for schizophrenia

Comparison: 3 CHLORPROMAZINE versus QUETIAPINE

Outcome: 11 Functioning: 1. Average endpoint score (various scales, high = better) - short term (up to 6 months)

Study or subgroup	Chlorpromazine		Quetiapine		Mean Difference	Weight	Mean Difference
	Ν	Mean(SD)	Ν	Mean(SD)	IV,Random,95% CI		IV,Random,95% CI
i wcst-iq							
vs QTP - Nai 2007	60	81.6 (18.2)	60	92.9 (17.1)	-+-	100.0 %	-11.30 [-17.62, -4.98]
Subtotal (95% CI)	60		60		•	100.0 %	-11.30 [-17.62, -4.98]
Heterogeneity: not applic	able						
Test for overall effect: Z =	= 3.50 (P = 0.00046	5)					
2 WCST-MQ							
vs QTP - Nai 2007	60	56.3 (25.1)	60	75.9 (17.7)		100.0 %	-19.60 [-27.37, -11.83]
Subtotal (95% CI)	60		60		•	100.0 %	-19.60 [-27.37, -11.83]
Heterogeneity: not applic	able						
Test for overall effect: Z =	= 4.94 (P < 0.0000))					
Test for subgroup differer	nces: Chi ² = 2.64, d	f = (P = 0.10)), l ² =62%				
				-10	00 -50 0 50	100	

Quetiapine Chlorpromazine

Analysis 3.12. Comparison 3 CHLORPROMAZINE versus QUETIAPINE, Outcome 12 Cognitive function: 1. Average endpoint score (various scales, high = better) - short term (up to 6 months).

Review: Chlorpromazine versus atypical antipsychotic drugs for schizophrenia

Comparison: 3 CHLORPROMAZINE versus QUETIAPINE

Outcome: 12 Cognitive function: I. Average endpoint score (various scales, high = better) - short term (up to 6 months)

Study or subgroup	Chlorpromazine		Quetiapine		Mean Difference		Weight	Mean Difference
	Ν	Mean(SD)	Ν	Mean(SD)	IV,Rando	om,95% Cl		IV,Random,95% CI
I WCST								
vs QTP - Guo 2007	26	67.5 (29)	26	64.6 (27.1)		•	31.2 %	2.90 [-12.36, 18.16]
vs QTP - Sun 2006	36	79.37 (22.17)	35	67.73 (21.95)			+ 68.8 %	.64 [.38, 2 .90]
Subtotal (95% CI)	62		61				100.0 %	8.92 [0.40, 17.43]
Heterogeneity: $Tau^2 = 0$.0; Chi ² = 0.87, df =	= I (P = 0.35); I	2 =0.0%					
Test for overall effect: Z	= 2.05 (P = 0.040)							
2 WMS-RC								
vs QTP - Sun 2006	35	98.81 (16.95)	36	108.15 (18.23)			100.0 %	-9.34 [-17.53, -1.15]
Subtotal (95% CI)	35		36		-		100.0 %	-9.34 [-17.53, -1.15]
Heterogeneity: not appli	cable							
Test for overall effect: Z	= 2.24 (P = 0.025)							
Test for subgroup differe	nces: Chi ² = 9.18, c	f = 1 (P = 0.00)), I ² =89%					
					1 1			
				-	20 -10 (0 10	20	

Quetiapine Chlorpromazine

Analysis 3.13. Comparison 3 CHLORPROMAZINE versus QUETIAPINE, Outcome 13 Adverse effects: 1. Anticholinergic - short term (up to 6 months).

Review: Chlorpromazine versus atypical antipsychotic drugs for schizophrenia Comparison: 3 CHLORPROMAZINE versus QUETIAPINE Outcome: 13 Adverse effects: 1. Anticholinergic - short term (up to 6 months)

Risk Ratio Risk Ratio Study or subgroup Chlorpromazine Quetiapine Weight M-H,Random,95% M-H,Random,95% n/N n/N ĊI ĊI I blurred vision vs QTP - Cai 2006 15/96 6/101 . 16.5 % 2.63 [1.06, 6.50] 14/107 vs QTP - Chen 2001 2/114 6.4 % 7.46 [1.74, 32.05] vs QTP - Chen 2007 3.73 [0.84, 16.57] 7/30 2/32 6.1 % vs QTP - Cheng 2003 6/45 1/44 3.1 % 5.87 [0.74, 46.76] vs QTP - Guo 2003a 9.25 [1.20, 71.16] 9/73 1/75 3.2 % vs OTP - Guo 2003b 3/20 2/30 47% 2.25 [0.41, 12.28] vs QTP - Guo 2008 5.37 [0.27, 108.47] 2/40 0/43 1.5 % 1.6 % vs QTP - He 2003 3/20 0/20 7.00 [0.38, 127.32] vs QTP - Jiang 2006 28/97 4/94 -----13.3 % 6.78 [2.47, 18.60] vs QTP - Jiang 2008 1.6 % 9.00 [0.51, 160.17] 4/30 0/30 vs QTP - Jin 2007 7/30 1/30 3.3 % 7.00 [0.92, 53.47] vs QTP - Mei 2007 14/49 2/47 6.6 % 6.71 [1.61, 27.96] 15.00 [0.88, 255.20] vs OTP - Tian 2006 7/46 1.7 % 0/46 vs QTP - Wan 2008 14.79 [0.87, 251.39] 6/28 0/32 17% vs QTP - Wang 2005 14/57 2/48 6.6 % 5.89 [1.41, 24.66] vs QTP - Zhang 2006 4/33 2/28 5.1 % 1.70 [0.34, 8.58] vs OTP - Zhou 2004 10/39 2/40 64% 5.13 [1.20, 21.92] vs QTP - Zou 2006 20/43 105% 6.67 [2.14, 20.79] 3/43 Subtotal (95% CI) 883 897 ٠ 100.0 % 5.00 [3.46, 7.22] Total events: 173 (Chlorpromazine), 30 (Quetiapine) Heterogeneity: Tau² = 0.0; Chi² = 7.79, df = 17 (P = 0.97); l² =0.0% Test for overall effect: Z = 8.58 (P < 0.00001)2 dry mouth 18/101 vs QTP - Cai 2006 21/96 11.0 % 1.23 [0.70, 2.16] vs QTP - Chen 2001 14/107 6/114 8.3 % 2.49 [0.99, 6.23] vs QTP - Chen 2007 0.12 [0.01, 2.11] 0/30 4/32 1.8 %

0.001 0.01 0.1 1 10 100 1000

Chlorpromazine Quetiapine

(Continued . . .)

Study or subgroup	Chlorpromazine	Quetiapine	Risk Ratio	Weight	(Continued) Risk Ratio
	n/N	n/N	M- H,Random,95% Cl		-M- H,Random,95 Cl
vs QTP - Cheng 2003	7/45	3/44		6.0 %	2.28 [0.63, 8.26]
vs QTP - Guo 2003a	9/73	4/75		6.8 %	2.31 [0.74, 7.18]
vs QTP - Guo 2008	3/40	1/43		2.8 %	3.23 [0.35, 29.75]
vs QTP - He 2003	4/20	4/20		6.2 %	1.00 [0.29, 3.45]
vs QTP - Ji 2004	6/30	0/30		1.9 %	3.00 [0.76, 220.96]
vs QTP - Jin 2007	9/30	2/30		5.2 %	4.50 [1.06, 19.11]
vs QTP - Liu 2003	2/39	2/44	<u> </u>	3.5 %	1.13 [0.17, 7.63]
vs QTP - Mei 2007	8/49	1/47		3.2 %	7.67 [1.00, 59.01]
vs QTP - Tian 2006	31/46	0/46	· · · · · · · · · · · · · · · · · · ·	1.9 %	63.00 [3.97, 999.69]
vs QTP - Wan 2002	7/30	5/30		7.5 %	1.40 [0.50, 3.92]
vs QTP - Wan 2008	1/28	0/32		1.5 %	3.41 [0.14, 80.59]
vs QTP - Wang 2005	17/57	3/48		6.6 %	4.77 [1.49, 15.31]
vs QTP - Zhang 2006	9/33	5/28	-	7.9 %	1.53 [0.58, 4.03]
vs QTP - Zhou 2004	18/39	12/40	-	10.9 %	1.54 [0.86, 2.75]
vs QTP - Zou 2006	25/43	3/43	-	6.9 %	8.33 [2.72, 25.55]
Subtotal (95% CI)	835	847	•	100.0 %	2.34 [1.54, 3.54]
Heterogeneity: Tau ² = 0.33; Test for overall effect: Z = 4.1 3 excessive sweating vs QTP - Chen 2007	,	= 0.01); l ² =48% 1/32		48.4 %	3.20 [0.35, 29.10]
vs QTP - He 2003	1/20	0/20		23.9 %	3.00 [0.13, 69.52]
vs QTP - Wan 2002	3/30	0/30		27.7 %	7.00 [0.38, 129.93]
Subtotal (95% CI) Total events: 7 (Chlorpromaz Heterogeneity: Tau ² = 0.0; C Test for overall effect: Z = 1. 4 hypersalivation	$hi^2 = 0.22$, df = 2 (P = 0.0 74 (P = 0.082)			100.0 %	3.91 [0.84, 18.19]
vs QTP - Chen 2001	5/107	/ 4		5.3 %	5.33 [0.63, 44.86]
vs QTP - Chen 2007	23/30	2/32		13.0 %	12.27 [3.16, 47.62]
	0.115	1/44		4.3 %	1.96 [0.18, 20.80]
vs QTP - Cheng 2003	2/45				
vs QTP - Cheng 2003 vs QTP - Guo 2003a	2/45 7/73	0/75		3.0 %	5.4 [0.90, 264.93]
		0/75 0/20		3.0 % 2.4 %	3.00 [0.13, 69.52]

Chlorpromazine Quetiapine

(Continued . . .)

Study or subgroup	Chlorpromazine	Quetiapine	Risk Ratio	Weight	(Continued) Risk Ratio M-
	n/N	n/N	H,Random,95% Cl		H,Random,95% Cl
vs QTP - Mei 2007	10/49	3/47		15.9 %	3.20 [0.94, 0.90]
vs QTP - Wan 2002	3/30	0/30		2.8 %	7.00 [0.38, 129.93]
vs QTP - Wan 2008	1/28	0/32		2.4 %	3.41 [0.14, 80.59]
vs QTP - Wang 2005	7/57	2/48		10.3 %	2.95 [0.64, 13.53]
vs QTP - Yang 2007	1/32	/3		3.2 %	0.97 [0.06, 14.82]
Subtotal (95% CI)	568	567	•	100.0 %	3.85 [2.36, 6.28]
Total events: 82 (Chlorpromaz	, , , ,				
Heterogeneity: $Tau^2 = 0.0$; Chi		0.81); 12 =0.0%			
Test for overall effect: $Z = 5.39$	9 (P < 0.00001)				
5 stuffy nose					
vs QTP - Chen 2001	1/107	5/114		4.2 %	0.21 [0.03, 1.79]
vs QTP - Chen 2007	0/30	3/32		2.2 %	0.15 [0.01, 2.83]
vs QTP - Cheng 2003	1/45	2/44		3.4 %	0.49 [0.05, 5.20]
vs QTP - Guo 2003a	2/73	3/75		6.1 %	0.68 [0.12, 3.98]
vs QTP - Jiang 2006	12/97	15/94	+	38.1 %	0.78 [0.38, 1.57]
vs QTP - Jin 2007	3/30	4/30	-	9.5 %	0.75 [0.18, 3.07]
vs QTP - Mei 2007	6/49	7/47	-	18.4 %	0.82 [0.30, 2.27]
vs QTP - Wang 2005	6/57	7/48		18.1 %	0.72 [0.26, 2.00]
Subtotal (95% CI)	488	484	•	100.0 %	0.69 [0.45, 1.06]
Total events: 31 (Chlorpromaz	ine), 46 (Quetiapine)				
Heterogeneity: $Tau^2 = 0.0$; Chi	$i^2 = 2.58$, df = 7 (P = 0.9)	92); I ² =0.0%			
Test for overall effect: Z = 1.68	3 (P = 0.093)				
Test for subgroup differences: (Chi ² = 50.82, df = 4 (P =	= 0.00), I ² =92%			

0.001 0.01 0.1 1 10 100 1000

Chlorpromazine Quetiapine

Analysis 3.14. Comparison 3 CHLORPROMAZINE versus QUETIAPINE, Outcome 14 Adverse effects: 2. Cardiovascular - short term (up to 6 months).

Review: Chlorpromazine versus atypical antipsychotic drugs for schizophrenia

Comparison: 3 CHLORPROMAZINE versus QUETIAPINE

Outcome: 14 Adverse effects: 2. Cardiovascular - short term (up to 6 months)

Study or subgroup	Chlorpromazine	Quetiapine	Risk Ratio	Weight	Risk Ratio
	n/N	n/N	IV,Random,95% CI		IV,Random,95% CI
l abnormal ECG	(120	0/22		2.0.0/	
vs QTP - Chen 2007	6/30	0/32		3.0 %	3.84 [0.81, 235.53]
vs QTP - Cheng 2003	6/45	3/44		13.8 %	1.96 [0.52, 7.34]
vs QTP - Deng 2004	13/45	9/45	-	43.7 %	1.44 [0.69, 3.04]
vs QTP - Liu 2003	7/39	1/44		5.7 %	7.90 [1.02, 61.38]
vs QTP - Zhang 2003	3/118	2/119		7.7 %	1.51 [0.26, 8.89]
vs QTP - Zhang 2006	3/33	1/28		4.9 %	2.55 [0.28, 23.12]
vs QTP - Zou 2006	7/43	5/43		21.2 %	1.40 [0.48, 4.07]
Subtotal (95% CI)	353	355	•	100.0 %	1.82 [1.11, 2.98]
Heterogeneity: $Tau^2 = 0.0$; Chi Test for overall effect: $Z = 2.39$ 2 blood pressure drop	,	;; l² =0.0%			
vs QTP - Chen 2001	28/114	26/107	+	27.6 %	1.01 [0.64, 1.61]
vs QTP - Guo 2003b	9/30	1/30		7.2 %	9.00 [1.21, 66.70]
vs QTP - Guo 2007	1/26	0/26		3.3 %	3.00 [0.13, 70.42]
vs QTP - He 2003	1/20	0/20		3.3 %	3.00 [0.13, 69.52]
vs QTP - Tian 2006	6/46	15/46		19.9 %	0.40 [0.17, 0.94]
vs QTP - Wan 2008	3/28	1/32		6.2 %	3.43 [0.38, 31.12]
vs QTP - Zhou 2004	7/39	8/40	-	18.8 %	0.90 [0.36, 2.24]
vs QTP - Zou 2006	3/43	8/43		13.6 %	0.38 [0.11, 1.32]
Subtotal (95% CI)	346	344	+	100.0 %	0.97 [0.53, 1.79]
Total events: 58 (Chlorpromaz Heterogeneity: Tau ² = 0.29; Cl Test for overall effect: Z = 0.09 3 orthostatic hypotension vs QTP - Chen 2007	$hi^2 = 13.18, df = 7 (P = 0.0)$	07); I ² =47%		7.0 %	5.32 [0.27, 106.54]
vs QTP - Guo 2007	0/26	1/26	n	6.3 %	0.33 [0.01, 7.82]
vs QTP - Liu 2003	8/39	0/44		7.7 %	19.13 [1.14, 320.92]
			0.001 0.01 0.1 I 10 100 1000 Chlorpromazine Quetiapine		

(Continued . . .)

Study or subgroup	Chlorpromazine n/N	Quetiapine n/N	Risk Ratio IV,Random,95% Cl	Weight	(Continue Risk Ratio IV,Random,95% C
vs QTP - Peuskens 1997	18/100	5/101	-8-	33.8 %	3.64 [1.40, 9.42
vs QTP - Wan 2002	0/30	3/30		7.3 %	0.14 [0.01, 2.65
vs QTP - Zhang 2006	4/33	1/28		12.3 %	3.39 [0.40, 28.64
vs QTP - Zou 2006	8/43	3/43		25.5 %	2.67 [0.76, 9.38
Subtotal (95% CI)	301	304	•	100.0 %	2.64 [1.14, 6.12
Total events: 40 (Chlorpromazine Heterogeneity: Tau ² = 0.31; Chi ² Test for overall effect: Z = 2.26 (f 4 tachycardia	= 8.02, df = 6 (P = 0.24	4); l ² =25%			
vs QTP - Cai 2006	39/96	17/101	-	19.0 %	2.41 [1.47, 3.97
vs QTP - Cai 2007	6/46	4/48	- 	4.0 %	1.57 [0.47, 5.19
vs QTP - Chen 2001	18/107	12/114	-	11.3 %	1.60 [0.81, 3.16
vs QTP - Chen 2007	3/30	2/32	_ 	2.0 %	1.60 [0.29, 8.92
vs QTP - Cheng 2003	8/45	5/44		5.3 %	1.56 [0.55, 4.4
vs QTP - Guo 2003a	9/73	8/75	+	7.0 %	1.16 [0.47, 2.8]
vs QTP - Guo 2008	2/40	3/43		2.0 %	0.72 [0.13, 4.0]
vs QTP - He 2003	1/20	2/20		1.1 %	0.50 [0.05, 5.08
vs QTP - Ji 2004	4/30	2/30	- + •	2.3 %	2.00 [0.40, 10.1
vs QTP - Jiang 2008	7/30	3/30	+	3.7 %	2.33 [0.67, 8.13
vs QTP - Liu 2003	12/39	4/44		5.2 %	3.38 [1.19, 9.6
vs QTP - Tian 2006	18/46	2/46		3.0 %	9.00 [2.21, 36.55
vs QTP - Wan 2008	5/28	6/32	-	5.0 %	0.95 [0.33, 2.78
vs QTP - Zhang 2003	6/118	7/119	-	5.1 %	0.86 [0.30, 2.50
vs QTP - Zhang 2006	10/33	5/28		6.3 %	1.70 [0.66, 4.38
vs QTP - Zhou 2004	16/39	8/40	-	10.2 %	2.05 [0.99, 4.24
vs QTP - Zou 2006	8/43	9/43	-	7.6 %	0.89 [0.38, 2.09
Subtotal (95% CI) Total events: 172 (Chlorpromazin Heterogeneity: Tau ² = 0.02; Chi ² Test for overall effect: $Z = 4.22$ (f	= 17.24, df = 16 (P = 0	889 0.37); I ² =7%	•	100.0 %	1.70 [1.33, 2.18

0.001 0.01 0.1 I 10 100 1000 Chlorpromazine Quetiapine

Analysis 3.15. Comparison 3 CHLORPROMAZINE versus QUETIAPINE, Outcome 15 Adverse effects: 3. Central nervous system - short term (up to 6 months).

Review: Chlorpromazine versus atypical antipsychotic drugs for schizophrenia

Comparison: 3 CHLORPROMAZINE versus QUETIAPINE

Outcome: 15 Adverse effects: 3. Central nervous system - short term (up to 6 months)

Risk Rat	Weight	Risk Ratio	Quetiapine	Chlorpromazine	Study or subgroup
IV,Random,95% (IV,Random,95% CI	n/N	n/N	
					l dizziness
1.40 [0.76, 2.58	20.7 %	+	15/101	20/96	vs QTP - Cai 2006
8.52 [1.08, 67.01	5.2 %		/ 4	8/107	vs QTP - Chen 2001
5.33 [0.66, 43.05	5.1 %		1/32	5/30	vs QTP - Chen 2007
4.89 [0.59, 40.18	5.0 %		1/44	5/45	vs QTP - Cheng 2003
.30 [0.64, 200.7	2.9 %		0/75	5/73	vs QTP - Guo 2003a
1.33 [0.33, 5.38	9.4 %	-	3/26	4/26	vs QTP - Guo 2007
0.54 [0.05, 5.70	4.1 %		2/43	1/40	vs QTP - Guo 2008
0.45 [0.17, 1.20	14.3 %		11/46	5/46	vs QTP - Tian 2006
0.11 [0.01, 1.98	2.9 %		4/30	0/30	vs QTP - Wan 2002
3.41 [0.14, 80.59	2.5 %		0/32	1/28	vs QTP - Wan 2008
1.29 [0.31, 5.31	9.2 %		3/31	4/32	vs QTP - Yang 2007
1.23 [0.60, 2.51	18.7 %	+	10/40	12/39	vs QTP - Zhou 2004
1.40 [0.83, 2.35	100.0 %	◆	614	592	Subtotal (95% CI)
				ne), 51 (Quetiapine)	Total events: 70 (Chlorpromaz
			0.11); l ² =35%	$hi^2 = 16.88, df = 11 (P = 0)$	Heterogeneity: $Tau^2 = 0.24$; Cl
				(P = 0.21)	Test for overall effect: $Z = 1.26$
					2 drowsiness
2.56 [1.10, 5.96	8.7 %		6/43	15/42	vs QTP - Ai 2007
5.61 [2.46, 12.82	8.8 %		6/101	32/96	vs QTP - Cai 2006
1.86 [0.81, 4.27	8.8 %	-	8/114	4/ 07	vs QTP - Chen 2001
0.21 [0.01, 4.26	1.7 %		2/32	0/30	vs QTP - Chen 2007
1.96 [0.52, 7.34	5.7 %		3/44	6/45	vs QTP - Cheng 2003
2.57 [0.84, 7.82	6.8 %		4/75	10/73	vs QTP - Guo 2003a
4.75 [1.83, 12.31	7.9 %		4/30	19/30	vs QTP - Guo 2003b
1.33 [0.33, 5.38	5.3 %		3/26	4/26	vs QTP - Guo 2007
	4.7 %	<u> </u>	2/43	6/40	vs QTP - Guo 2008

0.001 0.01 0.1 1 10 100 1000 Chlorpromazine Quetiapine

(Continued . . .)

Chlorpromazine versus atypical antipsychotic drugs for schizophrenia (Review)

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Study or subgroup	Chlorpromazine	Quetiapine	Risk Ratio	Weight	(Continued Risk Ratio
	n/N	n/N	IV,Random,95% CI		IV,Random,95% CI
vs QTP - Ji 2004	7/30	0/30		1.9 %	15.00 [0.89, 251.42]
vs QTP - Jiang 2008	7/30	2/30	— •—	4.9 %	3.50 [0.79, 15.49]
vs QTP - Peuskens 1997	16/100	4/ 0	+	10.1 %	1.15 [0.60, 2.24]
vs QTP - Tian 2006	0/46	12/46	•	1.9 %	0.04 [0.00, 0.66]
vs QTP - Wan 2002	5/30	5/30	+	6.7 %	1.00 [0.32, 3.10]
vs QTP - Wan 2008	5/28	4/32		6.3 %	1.43 [0.42, 4.81]
vs QTP - Zhang 2006	6/33	1/28	+	3.1 %	5.09 [0.65, 39.79]
vs QTP - Zou 2006	20/43	3/43		6.7 %	6.67 [2.14, 20.79]
Subtotal (95% CI)	829	848	•	100.0 %	2.28 [1.51, 3.45]
Total events: 172 (Chlorpromaz	zine), 79 (Quetiapine)				
Heterogeneity: Tau ² = 0.33; Ch Test for overall effect: Z = 3.92 3 headache vs QTP - He 2003		2/20		43.3 %	
-					0.50 [0.05, 5.08]
vs QTP - Tian 2006	0/46	2/46		28.2 %	0.20 [0.01, 4.05]
vs QTP - Wan 2002	2/30	0/30		28.5 %	5.00 [0.25, 99.95]
Test for overall effect: Z = 0.34 4 insomnia vs OTP - Chen 2001		3/114	_ _ _	145%	213[055-831]
vs QTP - Chen 2001	6/107	3/114		14.5 %	2.13 [0.55, 8.31]
vs QTP - Cheng 2003	2/45	1/44		4.8 %	1.96 [0.18, 20.80]
vs QTP - Guo 2003a	3/73	2/75		8.6 %	1.54 [0.27, 8.96]
vs QTP - He 2003	5/20	4/20	-	19.9 %	1.25 [0.39, 3.99]
vs QTP - Ji 2004	0/30	5/30		3.3 %	0.09 [0.01, 1.57]
vs QTP - Liu 2003	0/39	4/44		3.2 %	0.13 [0.01, 2.25]
vs QTP - Zhang 2006	2/33	3/28		9.1 %	0.57 [0.10, 3.15]
vs QTP - Zhou 2004	3/39	4/40		13.1 %	0.77 [0.18, 3.22]
vs QTP - Zou 2006	5/43	7/43	-	23.5 %	0.71 [0.25, 2.08]
Subtotal (95% CI)	429	438	+	100.0 %	0.92 [0.55, 1.54]
Total events: 26 (Chlorpromazir Heterogeneity: Tau ² = 0.0; Chi ² Test for overall effect: Z = 0.33 5 reduced activity	² = 7.40, df = 8 (P = 0.49); I ² =0.0%			
vs QTP - Chen 2001	9/107	0/114		11.0 %	20.23 [1.19, 343.40]
			0.001 0.01 0.1 1 10 100 1000 Chlorpromazine Quetiapine		(Continued

Study or subgroup	Chlorpromazine	Quetiapine	Risk Ratio	Weight	(Continued) Risk Ratio
	n/N	n/N	IV,Random,95% CI		IV,Random,95% CI
vs QTP - Cheng 2003	4/45	0/44		10.5 %	8.80 [0.49, 58.85]
vs QTP - Guo 2003a	6/73	1/75		20.1 %	6.16 [0.76, 49.95]
vs QTP - Guo 2003b	2/30	1/30		16.0 %	2.00 [0.19, 20.90]
vs QTP - Wan 2008	2/28	0/32		9.8 %	5.69 [0.28, 3.72]
vs QTP - Yang 2007	3/32	0/31		10.3 %	6.79 [0.36, 26.24]
vs QTP - Zhang 2006	10/33	0/28		11.3 %	7.9 [.10, 292.63]
vs QTP - Zou 2006	9/43	0/43		11.1 %	19.00 [1.14, 316.52]
Subtotal (95% CI)	391	397	+	100.0 %	7.80 [3.05, 19.92]
Total events: 45 (Chlorpromaz	zine), 2 (Quetiapine)				
Heterogeneity: $Tau^2 = 0.0$; Ch	ni ² = 2.56, df = 7 (P = 0.92	l); l ² =0.0%			
Test for overall effect: $Z = 4.2$	9 (P = 0.000018)				
6 sedation					
vs QTP - He 2003	0/20	1/20		100.0 %	0.33 [0.01, 7.72]
Subtotal (95% CI)	20	20		100.0 %	0.33 [0.01, 7.72]
Total events: 0 (Chlorpromazi	ne), I (Quetiapine)				
Heterogeneity: not applicable					
Test for overall effect: $Z = 0.6$	9 (P = 0.49)				
Test for subgroup differences:	$Chi^2 = 20.04$, df = 5 (P =	0.00), l ² =75%			
			0.001 0.01 0.1 1 10 100 1000		
			Chlorpromazine Quetiapine		

Analysis 3.16. Comparison 3 CHLORPROMAZINE versus QUETIAPINE, Outcome 16 Adverse effects: 4. Gastrointestinal - short term (up to 6 months).

Review: Chlorpromazine versus atypical antipsychotic drugs for schizophrenia Comparison: 3 CHLORPROMAZINE versus QUETIAPINE

Comparison: 3 CHLORPROMAZINE Versus QUE HAPIN

Outcome: 16 Adverse effects: 4. Gastrointestinal - short term (up to 6 months)

Study or subgroup	Chlorpromazine	Quetiapine	Risk Ratio	Weight	Risk Ratio
	n/N	n/N	IV,Random,95% CI		IV,Random,95% CI
l constipation					
vs QTP - Cai 2006	20/96	12/101	•	11.6 %	1.75 [0.91, 3.39]
vs QTP - Chen 2001	11/107	4/114		4.1 %	2.93 [0.96, 8.92]
vs QTP - Chen 2007	10/30	4/32		4.6 %	2.67 [0.94, 7.60]
vs QTP - Cheng 2003	5/45	2/44		2.0 %	2.44 [0.50, 11.94]
vs QTP - Guo 2003a	8/73	2/75		2.2 %	4. [0.90, 8.7]
vs QTP - Guo 2003b	8/30	2/30		2.4 %	4.00 [0.92, 17.30]
vs QTP - Guo 2007	1/26	0/26		0.5 %	3.00 [0.13, 70.42]
vs QTP - Guo 2008	5/40	2/43		2.0 %	2.69 [0.55, 13.08]
vs QTP - He 2003	4/20	3/20	_ 	2.7 %	1.33 [0.34, 5.21]
vs QTP - Jiang 2006	47/97	13/94	+	17.0 %	3.50 [2.03, 6.04]
vs QTP - Jiang 2008	0/30	2/30		0.6 %	0.20 [0.01, 4.00]
vs QTP - Jin 2007	11/30	4/30	-+	4.8 %	2.75 [0.99, 7.68]
vs QTP - Liu 2003	4/39	2/44	<u> </u>	1.9 %	2.26 [0.44, 11.65]
vs QTP - Mei 2007	22/49	7/47	-	9.0 %	3.01 [1.42, 6.39]
vs QTP - Tian 2006	23/46	0/46		0.7 %	47.00 [2.94, 751.41]
vs QTP - Wan 2002	11/30	4/30		4.8 %	2.75 [0.99, 7.68]
vs QTP - Wan 2008	3/28	3/32		2.2 %	1.14 [0.25, 5.21]
vs QTP - Wang 2005	21/57	7/48	+	8.6 %	2.53 [1.18, 5.43]
vs QTP - Yang 2007	9/32	3/31		3.5 %	2.91 [0.87, 9.74]
vs QTP - Zhang 2006	7/33	2/28	<u></u>	2.3 %	2.97 [0.67, 13.16]
vs QTP - Zhou 2004	11/39	8/40	-	8.0 %	1.41 [0.64, 3.13]
vs QTP - Zou 2006	13/43	4/43		4.7 %	3.25 [1.15, 9.18]
Subtotal (95% CI)	1020	1028	•	100.0 %	2.55 [2.04, 3.20]
Total events: 254 (Chlorpron Heterogeneity: Tau ² = 0.0; C Fest for overall effect: $Z = 8$.	$Chi^2 = 15.01, df = 21 (P = 1)$	0.82); I ² =0.0%			

0.001 0.01 0.1 1 10 100 1000

Chlorpromazine Quetiapine

(Continued . . .)

Study or subgroup	Chlorpromazine n/N	Quetiapine n/N	Risk Ratio IV,Random,95% CI	Weight	(Continued Risk Ratio IV,Random,95% CI
2 diarrhoea					
vs QTP - Chen 2007	2/30	0/32		100.0 %	5.32 [0.27, 106.54]
Subtotal (95% CI) Total events: 2 (Chlorpromaz Heterogeneity: not applicable Test for overall effect: Z = 1.0		32		100.0 %	5.32 [0.27, 106.54]
3 loss of appetite vs QTP - Chen 2001	4/107	/ 4		17.0 %	4.26 [0.48, 37.53]
vs QTP - Chen 2007	24/30	3/32	-	32.8 %	8.53 [2.86, 25.43]
vs QTP - Cheng 2003	3/45	2/44	-	22.1 %	1.47 [0.26, 8.36]
vs QTP - Guo 2003b	1/30	1/30		12.5 %	1.00 [0.07, 15.26]
vs QTP - He 2003	1/20	2/20		15.6 %	0.50 [0.05, 5.08]
Subtotal (95% CI) Total events: 33 (Chlorproma Heterogeneity: Tau ² = 0.68; 1 Test for overall effect: $Z = 1.4$ 4 nausea/vomiting	$Chi^2 = 7.06, df = 4 (P = 0.10)$,	•	100.0 %	2.52 [0.82, 7.72]
vs QTP - Chen 2001	2/107	2/114		15.1 %	1.07 [0.15, 7.43]
vs QTP - Chen 2007	3/30	2/32		19.3 %	1.60 [0.29, 8.92]
vs QTP - Cheng 2003	1/45	1/44		7.6 %	0.98 [0.06, 15.15]
vs QTP - Guo 2003a	1/73	1/75		7.5 %	1.03 [0.07, 16.12]
vs QTP - Guo 2003b	0/30	1/30		5.7 %	0.33 [0.01, 7.87]
vs QTP - He 2003	1/20	2/20		10.6 %	0.50 [0.05, 5.08]
vs QTP - Wan 2002	2/30	2/30	-+-	15.9 %	1.00 [0.15, 6.64]
vs QTP - Wan 2008	1/28	0/32		5.7 %	3.41 [0.14, 80.59]
vs QTP - Zhou 2004	4/39	1/40		12.4 %	4.10 [0.48, 35.10]
Subtotal (95% CI) Total events: 15 (Chlorproma Heterogeneity: Tau ² = 0.0; C Test for overall effect: Z = 0. Test for subgroup differences	$hi^2 = 3.04$, $df = 8$ (P = 0. 54 (P = 0.59)		•	100.0 %	1.23 [0.58, 2.63]

0.001 0.01 0.1 1 10 100 1000

Chlorpromazine Quetiapine

Analysis 3.17. Comparison 3 CHLORPROMAZINE versus QUETIAPINE, Outcome 17 Adverse effects: 5a. Endocrine - various - short term (up to 6 months).

Review: Chlorpromazine versus atypical antipsychotic drugs for schizophrenia

Comparison: 3 CHLORPROMAZINE versus QUETIAPINE

Outcome: 17 Adverse effects: 5a. Endocrine - various - short term (up to 6 months)

n/N n/N I gynaecomastia, galactorrhoea vs QTP - Guo 2008 $2/40$ $0/43$ Subtotal (95% CI)4043Total events: 2 (Chlorpromazine), 0 (Quetiapine)Heterogeneity: not applicableTest for overall effect: $Z = 1.10$ (P = 0.27)2 hyperprolactinemia vs QTP - Jiang 2006 $38/97$ 7/94 vs QTP - Zou 2006 $8/43$ O/43Subtotal (95% CI)140137Total events: 46 (Chlorpromazine), 7 (Quetiapine)Heterogeneity: Tau ² = 0.0; Chi ² = 0.64, df = 1 (P = 0.42); l ² = 0.0%	10	93.3 % 6.7 %	M- H,Random,9 5.37 [0.27, 108.47] 37 [0.27, 108.47] 5.26 [2.47, 11.19] 17.00 [1.01, 285.60]
vs QTP - Guo 2008 $2/40$ $0/43$ Subtotal (95% CI) 40 43 Total events: 2 (Chlorpromazine), 0 (Quetiapine) Heterogeneity: not applicable Test for overall effect: Z = 1.10 (P = 0.27) 2 hyperprolactinemia vs QTP - Jiang 2006 $38/97$ $7/94$ vs QTP - Zou 2006 $8/43$ $0/43$ Subtotal (95% CI) 140 137 Total events: 46 (Chlorpromazine), 7 (Quetiapine) Heterogeneity: Tau ² = 0.0; Chi ² = 0.64, df = 1 (P = 0.42); l ² = 0.0%	10	93.3 % 6.7 %	.37 [0.27, 108.47] 5.26 [2.47, 11.19] 17.00 [1.01, 285.60]
Subtotal (95% CI)4043Total events: 2 (Chlorpromazine), 0 (Quetiapine)Heterogeneity: not applicableTest for overall effect: $Z = 1.10$ (P = 0.27)2 hyperprolactinemiavs QTP - Jiang 200638/977/94vs QTP - Zou 20068/43O/43Subtotal (95% CI)140137Total events: 46 (Chlorpromazine), 7 (Quetiapine)Heterogeneity: Tau ² = 0.0; Chi ² = 0.64, df = 1 (P = 0.42); l ² = 0.0%	10	93.3 % 6.7 %	.37 [0.27, 108.47] 5.26 [2.47, 11.19] 17.00 [1.01, 285.60]
Total events: 2 (Chlorpromazine), 0 (Quetiapine) Heterogeneity: not applicable Test for overall effect: Z = 1.10 (P = 0.27) 2 hyperprolactinemia vs QTP - Jiang 2006 38/97 7/94 vs QTP - Zou 2006 8/43 0/43 Subtotal (95% CI) 140 137 Total events: 46 (Chlorpromazine), 7 (Quetiapine) Heterogeneity: Tau ² = 0.0; Chi ² = 0.64, df = 1 (P = 0.42); l ² = 0.0%		93.3 % 6.7 %	5.26 [2.47, 11.19] 17.00 [1.01, 285.60]
2 hyperprolactinemia vs QTP - Jiang 2006 38/97 7/94 vs QTP - Zou 2006 8/43 0/43 Subtotal (95% CI) 140 137 Total events: 46 (Chlorpromazine), 7 (Quetiapine) Heterogeneity: Tau ² = 0.0; Chi ² = 0.64, df = 1 (P = 0.42); l ² = 0.0%	•	6.7 %	17.00 [1.01, 285.60]
Test for overall effect: $Z = 1.10$ (P = 0.27) 2 hyperprolactinemia vs QTP - Jiang 2006 38/97 7/94 vs QTP - Zou 2006 8/43 0/43 Subtotal (95% CI) 140 137 Total events: 46 (Chlorpromazine), 7 (Quetiapine) Heterogeneity: Tau ² = 0.0; Chi ² = 0.64, df = 1 (P = 0.42); l ² = 0.0%	•	6.7 %	17.00 [1.01, 285.60]
vs QTP - Jiang 2006 38/97 7/94 vs QTP - Zou 2006 8/43 0/43 Subtotal (95% CI) 140 137 Total events: 46 (Chlorpromazine), 7 (Quetiapine) Heterogeneity: Tau ² = 0.0; Chi ² = 0.64, df = 1 (P = 0.42); l ² = 0.0%		6.7 %	17.00 [1.01, 285.60]
vs QTP - Zou 2006 8/43 0/43 Subtotal (95% CI) 140 137 Total events: 46 (Chlorpromazine), 7 (Quetiapine) Heterogeneity: Tau ² = 0.0; Chi ² = 0.64, df = 1 (P = 0.42); l ² = 0.0%		6.7 %	17.00 [1.01, 285.60]
vs QTP - Zou 2006 8/43 0/43	.	6.7 %	17.00 [1.01, 285.60]
Subtotal (95% CI) 140 137 Total events: 46 (Chlorpromazine), 7 (Quetiapine) 1 1 Heterogeneity: Tau ² = 0.0; Chi ² = 0.64, df = 1 (P = 0.42); l ² = 0.0% 1 1			
Total events: 46 (Chlorpromazine), 7 (Quetiapine) Heterogeneity: Tau ² = 0.0; Chi ² = 0.64, df = 1 (P = 0.42); l ² =0.0%			
Heterogeneity: Tau ² = 0.0; Chi ² = 0.64, df = 1 (P = 0.42); l ² = 0.0%	- 10	0.0 %	5.69 [2.74, 11.79]
Test for overall effect: $7 = 4.67 (P < 0.00001)$			
3 menstrual irregularities			
vs QTP - Guo 2007 2/26 0/26		100.0 %	5.00 [0.25, 99.34]
Subtotal (95% CI) 26 26 -	10	0.0 %	5.00 [0.25, 99.34]
Total events: 2 (Chlorpromazine), 0 (Quetiapine)			
Heterogeneity: not applicable			
Test for overall effect: $Z = 1.06$ (P = 0.29)			
Test for subgroup differences: $Chi^2 = 0.01$, $df = 2$ (P = 1.00), $l^2 = 0.0\%$			

 0.01
 0.1
 1
 10
 100

 Favours chlorpromazine
 Favours quetiapine

Analysis 3.18. Comparison 3 CHLORPROMAZINE versus QUETIAPINE, Outcome 18 Adverse effects: 5b. Endocrine - average endpoint - short term (up to 6 months).

Review: Chlorpromazine versus atypical antipsychotic drugs for schizophrenia

Comparison: 3 CHLORPROMAZINE versus QUETIAPINE

Outcome: 18 Adverse effects: 5b. Endocrine - average endpoint - short term (up to 6 months)

Study or subgroup	Experimental		Control		Diff	Mean erence	Weight	Mean Difference
	Ν	Mean(SD)	Ν	Mean(SD)	IV,Rand	om,95% Cl		IV,Random,95% CI
l prolactin level (ng/mL))							
vs QTP - Kong 2003	15	31.83 (12.98)	15	7.21 (3.88)			100.0 %	24.62 [17.76, 31.48]
Total (95% CI)	15		15			•	100.0 %	24.62 [17.76, 31.48]
Heterogeneity: not appl	icable							
Test for overall effect: Z	= 7.04 (P < 0.00	001)						
Test for subgroup differe	ences: Not applica	ble						
							1	
				-10	-50	0 50 I	00	
				Favours chlo	orpromazine	Favours que	tiapine	

Analysis 3.19. Comparison 3 CHLORPROMAZINE versus QUETIAPINE, Outcome 19 Adverse effects: 5c. Endocrine - skewed data - short term (up to 6 months).

Adverse effects: 5c. Endocrine - skewed data - short term (up to 6 months)

Study	Intervention	Mean	SD	Ν	
average prolactin leve	l (ng/mL)				average prolact
vs QTP - Jiang 2006	Chlorpromazine	680.2	688.0	97	
vs QTP - Jiang 2006	Quetiapine	123.2	132.1	94	
vs QTP - Wang 2005	Chlorpromazine	697.21	80.26	57	
vs QTP - Wang 2005	Quetiapine	112.85	92.37	48	

Analysis 3.20. Comparison 3 CHLORPROMAZINE versus QUETIAPINE, Outcome 20 Adverse effects: 6a. Haematology - short term (up to 6 months).

Review: Chlorpromazine versus atypical antipsychotic drugs for schizophrenia Comparison: 3 CHLORPROMAZINE versus QUETIAPINE

Outcome: 20 Adverse effects: 6a. Haematology - short term (up to 6 months)

Study or subgroup	Chlorpromazine	Quetiapine	Risk Ratio M-	Weight	Risk Ratic M-
	n/N	n/N	H,Random,95% Cl		H,Random, C
I elevated ALT					
vs QTP - Cai 2007	2/46	2/48		8.9 %	1.04 [0.15, 7.10]
vs QTP - Chen 2007	0/30	3/32		3.8 %	0.15 [0.01, 2.83
vs QTP - Deng 2004	2/45	0/45		3.6 %	5.00 [0.25, 101.31]
vs QTP - Guo 2003b	2/30	2/30	_	9.1 %	1.00 [0.15, 6.64]
vs QTP - Guo 2008	2/40	0/46		3.6 %	5.73 [0.28, 115.97]
vs QTP - Wan 2002	0/30	1/30		3.3 %	0.33 [0.01, 7.87]
vs QTP - Zhang 2003	16/118	9/119	-	54.1 %	1.79 [0.83, 3.90]
vs QTP - Zou 2006	6/43	2/43		13.7 %	3.00 [0.64, 14.04]
Subtotal (95% CI)	382	393	•	100.0 %	1.62 [0.92, 2.87]
Heterogeneity: $Tau^2 = 0.0$; C Test for overall effect: $Z = 1$.	66 (P = 0.097)	56); I ² =0.0%			
Test for overall effect: $Z = 1$. 2 decreased white blood cell	66 (P = 0.097) I count		-	60.8 %	1.20 [0.39, 3.65
Test for overall effect: Z = 1. 2 decreased white blood cell vs QTP - Deng 2004	66 (P = 0.097) I count 6/45	5/45		60.8 %	
Test for overall effect: Z = 1. 2 decreased white blood cell vs QTP - Deng 2004 vs QTP - He 2003	66 (P = 0.097) I count 6/45 1/20	5/45 0/20		7.6 %	3.00 [0.13, 69.52]
Test for overall effect: Z = 1. 2 decreased white blood cell vs QTP - Deng 2004 vs QTP - He 2003 vs QTP - Wan 2002	66 (P = 0.097) I count 6/45 1/20 0/30	5/45 0/20 1/30	• 	7.6 % 7.5 %	1.20 [0.39, 3.65] 3.00 [0.13, 69.52] 0.33 [0.01, 7.87]
Test for overall effect: Z = 1. 2 decreased white blood cell vs QTP - Deng 2004 vs QTP - He 2003	66 (P = 0.097) I count 6/45 1/20	5/45 0/20	• 	7.6 %	3.00 [0.13, 69.52] 0.33 [0.01, 7.87]
Test for overall effect: Z = 1. 2 decreased white blood cell vs QTP - Deng 2004 vs QTP - He 2003 vs QTP - Wan 2002 vs QTP - Zhang 2003 Subtotal (95% CI) Total events: 9 (Chlorproma:	66 (P = 0.097) 1 count 6/45 1/20 0/30 2/118 213 zine), 9 (Quetiapine)	5/45 0/20 1/30 3/119 214		7.6 % 7.5 %	3.00 [0.13, 69.52 0.33 [0.01, 7.87 0.67 [0.11, 3.95
Test for overall effect: Z = 1. 2 decreased white blood cell vs QTP - Deng 2004 vs QTP - He 2003 vs QTP - Wan 2002 vs QTP - Zhang 2003 Subtotal (95% CI) Total events: 9 (Chlorproma: Heterogeneity: Tau ² = 0.0; C	66 (P = 0.097) 1 count 6/45 1/20 0/30 2/118 213 zine), 9 (Quetiapine) Chi ² = 1.23, df = 3 (P = 0.1)	5/45 0/20 1/30 3/119 214		7.6 % 7.5 % 24.0 %	3.00 [0.13, 69.52 0.33 [0.01, 7.87 0.67 [0.11, 3.95
Test for overall effect: Z = 1. 2 decreased white blood cell vs QTP - Deng 2004 vs QTP - He 2003 vs QTP - Wan 2002 vs QTP - Zhang 2003 Subtotal (95% CI) Total events: 9 (Chlorpromaz Heterogeneity: Tau ² = 0.0; C Test for overall effect: Z = 0.	66 (P = 0.097) 1 count 6/45 1/20 0/30 2/118 213 zine), 9 (Quetiapine) chi ² = 1.23, df = 3 (P = 0.2000) 04 (P = 0.97)	5/45 0/20 1/30 3/119 214		7.6 % 7.5 % 24.0 %	3.00 [0.13, 69.52 0.33 [0.01, 7.87 0.67 [0.11, 3.95
Test for overall effect: Z = 1. 2 decreased white blood cell vs QTP - Deng 2004 vs QTP - He 2003 vs QTP - Wan 2002 vs QTP - Zhang 2003 Subtotal (95% CI) Total events: 9 (Chlorproma: Heterogeneity: Tau ² = 0.0; C	66 (P = 0.097) 1 count 6/45 1/20 0/30 2/118 213 zine), 9 (Quetiapine) chi ² = 1.23, df = 3 (P = 0.2000) 04 (P = 0.97)	5/45 0/20 1/30 3/119 214		7.6 % 7.5 % 24.0 %	3.00 [0.13, 69.52 0.33 [0.01, 7.87 0.67 [0.11, 3.95 1.02 [0.43, 2.42]
Test for overall effect: Z = 1. 2 decreased white blood cell vs QTP - Deng 2004 vs QTP - He 2003 vs QTP - Wan 2002 vs QTP - Zhang 2003 Subtotal (95% CI) Total events: 9 (Chlorproma: Heterogeneity: Tau ² = 0.0; C Test for overall effect: Z = 0. 3 increased white blood cell vs QTP - Zhou 2004	66 (P = 0.097) 1 count 6/45 1/20 0/30 2/118 213 zine), 9 (Quetiapine) Chi ² = 1.23, df = 3 (P = 0.7) 04 (P = 0.97) count	5/45 0/20 1/30 3/119 214 75); I ² =0.0%		7.6 % 7.5 % 24.0 % 100.0 %	3.00 [0.13, 69.52 0.33 [0.01, 7.87 0.67 [0.11, 3.95 1.02 [0.43, 2.42] 2.05 [0.40, 10.56
Test for overall effect: Z = 1. 2 decreased white blood cell vs QTP - Deng 2004 vs QTP - He 2003 vs QTP - Wan 2002 vs QTP - Zhang 2003 Subtotal (95% CI) Total events: 9 (Chlorproma: Heterogeneity: Tau ² = 0.0; C Test for overall effect: Z = 0. 3 increased white blood cell	$66 (P = 0.097)$ 1 count $6/45$ $1/20$ $0/30$ $2/118$ 213 $21a$ 213 $2ine), 9 (Quetiapine)$ $Chi^{2} = 1.23, df = 3 (P = 0.23)$ $04 (P = 0.97)$ $count$ $4/39$ 39	5/45 0/20 1/30 3/119 214 75): 1 ² =0.0%		7.6 % 7.5 % 24.0 % 100.0 %	3.00 [0.13, 69.52]
Test for overall effect: Z = 1. 2 decreased white blood cell vs QTP - Deng 2004 vs QTP - He 2003 vs QTP - Wan 2002 vs QTP - Zhang 2003 Subtotal (95% CI) Total events: 9 (Chlorpromaz Heterogeneity: Tau ² = 0.0; C Test for overall effect: Z = 0. 3 increased white blood cell vs QTP - Zhou 2004 Subtotal (95% CI)	66 (P = 0.097) 1 count 6/45 1/20 0/30 2/118 213 zine), 9 (Quetiapine) chi ² = 1.23, df = 3 (P = 0.10) 04 (P = 0.97) count 4/39 39 zine), 2 (Quetiapine)	5/45 0/20 1/30 3/119 214 75): 1 ² =0.0%		7.6 % 7.5 % 24.0 % 100.0 %	3.00 [0.13, 69.52 0.33 [0.01, 7.87 0.67 [0.11, 3.95 1.02 [0.43, 2.42] 2.05 [0.40, 10.56

0.001 0.01 0.1 1 10 100 1000

Chlorpromazine Quetiapine

Analysis 3.21. Comparison 3 CHLORPROMAZINE versus QUETIAPINE, Outcome 21 Adverse effects: 6b. Haematology - average endpoint - short term (up to 6 months).

Review: Chlorpromazine versus atypical antipsychotic drugs for schizophrenia

Comparison: 3 CHLORPROMAZINE versus QUETIAPINE

Outcome: 21 Adverse effects: 6b. Haematology - average endpoint - short term (up to 6 months)

Study or subgroup	Chlorpromazine N	Mean(SD)	Quetiapine N	Mean(SD)	Mean Difference IV,Random,95% Cl	Weight	Mean Difference IV,Random,95% Cl
l blood glucose							
vs QTP - Guo 2006	65	4.9 (0.8)	65	4.8 (0.8)		100.0 %	0.10 [-0.18, 0.38]
Subtotal (95% CI) Heterogeneity: not applic	able		65		•	100.0 %	0.10 [-0.18, 0.38]
Test for overall effect: Z =	= 0.71 (P = 0.48)						
2 blood TG vs QTP - Guo 2006	65	1.4 (0.8)	65	1.4 (0.8)		100.0 %	0.0 [-0.28, 0.28]
Subtotal (95% CI) Heterogeneity: not applic Test for overall effect: Z =			65			100.0 %	0.0 [-0.28, 0.28]
3 blood TC							
vs QTP - Guo 2006	65	4.6 (0.9)	65	4.4 (0.9)	•	100.0 %	0.20 [-0.11, 0.51]
Subtotal (95% CI) Heterogeneity: not applic Test for overall effect: Z = Test for subgroup differen	= I.27 (P = 0.21)	= 2 (P = 0.64),	65 ² =0.0%			100.0 %	0.20 [-0.11, 0.51]
				-20	0 -10 0 10	20	
				Chlo	rpromazine Quetiapir	ie	

Analysis 3.22. Comparison 3 CHLORPROMAZINE versus QUETIAPINE, Outcome 22 Adverse effects: 7. Hepatitic - short term (up to 6 months).

Review: Chlorpromazine versus atypical antipsychotic drugs for schizophrenia Comparison: 3 CHLORPROMAZINE versus QUETIAPINE Outcome: 22 Adverse effects: 7. Hepatitic - short term (up to 6 months)

Study or subgroup	Chlorpromazine	Quetiapine	Risk Ratio M-	Weight	Risk Ratio M-
	n/N	n/N	H,Random,95% Cl		H,Random,95% Cl
l abnormal liver function					
vs QTP - Cai 2006	21/96	11/101		46.9 %	2.01 [1.02, 3.94]
vs QTP - Guo 2007	2/26	2/26	_	6.0 %	1.00 [0.15, 6.57]
vs QTP - Ji 2004	2/30	0/30		2.4 %	5.00 [0.25, 99.95]
vs QTP - Jiang 2006	16/97	7/94		30.1 %	2.22 [0.95, 5.14]
vs QTP - Zhang 2006	9/33	3/28		14.7 %	2.55 [0.76, 8.50]
Subtotal (95% CI)	282	279	*	100.0 %	2.10 [1.32, 3.33]
Total events: 50 (Chlorprom	azine), 23 (Quetiapine)				
Heterogeneity: $Tau^2 = 0.0$; C	Chi ² = 1.05, df = 4 (P = 0.9	90); l ² =0.0%			
Test for overall effect: $Z = 3$.	15 (P = 0.0016)				
Test for subgroup differences	s: Not applicable				
			0.01 0.1 1 10 100		
		Envolues	chlorpromozino Esucura quotior	vino	

Favours chlorpromazine Favours quetiapine

Analysis 3.23. Comparison 3 CHLORPROMAZINE versus QUETIAPINE, Outcome 23 Adverse effects: 8. Movement disorders - short term (up to 6 months).

Review: Chlorpromazine versus atypical antipsychotic drugs for schizophrenia

Comparison: 3 CHLORPROMAZINE versus QUETIAPINE

Outcome: 23 Adverse effects: 8. Movement disorders - short term (up to 6 months)

Risk Rat	Weight	Risk Ratio	Quetiapine	Chlorpromazine	Study or subgroup
IV,Random,95% (IV,Random,95% CI	n/N	n/N	
					l agitation
0.25 [0.03, 2.05	21.2 %		4/20	1/20	vs QTP - He 2003
2.00 [0.19, 20.90	17.0 %		1/30	2/30	vs QTP - Ji 2004
0.20 [0.01, 4.05	10.3 %		2/46	0/46	vs QTP - Tian 2006
0.33 [0.07, 1.52	40.6 %		6/30	2/30	vs QTP - Wan 2002
0.12 [0.01, 2.26	11.0 %		3/28	0/33	vs QTP - Zhang 2006
0.36 [0.14, 0.95	100.0 %	•	154	159	Subtotal (95% CI)
				ne), 16 (Quetiapine)	Total events: 5 (Chlorpromazir
); I ² =0.0%	$i^2 = 2.85$, df = 4 (P = 0.58)	Heterogeneity: $Tau^2 = 0.0$; Chi
				6 (P = 0.039)	Test for overall effect: $Z = 2.06$
	100.04		2414		2 akathisia
6.04 [1.82, 20.02	10.2 %		3/114	17/107	vs QTP - Chen 2001
15.97 [0.95, 268.00	1.8 %		0/32	7/30	vs QTP - Chen 2007
4.89 [1.14, 21.06	6.8 %		2/44	10/45	vs QTP - Cheng 2003
9.25 [1.20, 71.16	3.5 %		1/75	9/73	vs QTP - Guo 2003a
7.00 [0.92, 53.47	3.5 %		1/30	7/30	vs QTP - Guo 2003b
7.51 [0.40, 141.04	1.7 %		0/43	3/40	vs QTP - Guo 2008
2.00 [0.40, 10.11	5.6 %		2/30	4/30	vs QTP - Ji 2004
1.94 [0.69, 5.46	13.6 %		5/94	10/97	vs QTP - Jiang 2006
7.00 [0.92, 53.47	3.5 %		1/30	7/30	vs QTP - Jin 2007
1.92 [0.37, 9.98	5.4 %		2/47	4/49	vs QTP - Mei 2007
1.49 [0.43, 5.10	9.6 %		4/100	6/101	vs QTP - Peuskens 1997
16.00 [2.21, 115.71	3.7 %		1/46	16/46	vs QTP - Tian 2006
2.53 [0.27, 23.50	2.9 %		1/48	3/57	vs QTP - Wang 2005
12.61 [0.74, 214.70	1.8 %	<u> </u>	0/31	6/32	vs QTP - Yang 2007
7.64 [1.03, 56.63	3.6 %		1/28	9/33	vs QTP - Zhang 2006
2.05 [0.77, 5.46	15.2 %	-	5/40	10/39	vs QTP - Zhou 2004

0.001 0.01 0.1 1 10 100 1000 Chlorpromazine Quetiapine

(Continued . . .)

Study or subgroup	Chlorpromazine n/N	Quetiapine n/N	Risk Ratio IV,Random,95% Cl	Weight	(Continued Risk Ratio IV,Random,95% CI
vs QTP - Zou 2006	18/43	2/43		7.5 %	9.00 [2.22, 36.44]
Subtotal (95% CI)	882	875	•	100.0 %	3.73 [2.55, 5.47]
Total events: 146 (Chlorproma		0/)		100.0 /0	J./ J [2.J J, J.I/]
Heterogeneity: $Tau^2 = 0.0$; Ch	$i^2 = 4.7 , df = 6 (P = 0.1)$	55); I ² =0.0%			
Test for overall effect: $Z = 6.76$	5 (P < 0.00001)				
3 any EPS symptoms vs QTP - Cai 2006	43/96	8/101	-	55.0 %	5.65 [2.81, 11.40]
vs QTP - Guo 2007	3/26	0/26	,	3.2 %	7.00 [0.38, 129.11]
vs QTP - He 2003	16/20	0/20		3.6 %	33.00 [2.11, 515.02]
vs QTP - Jiang 2008	12/30	0/30		3.5 %	25.00 [1.55, 403.99]
vs QTP - Liu 2003	20/39	3/44	-	21.0 %	7.52 [2.42, 23.39]
vs QTP - Tian 2006	28/46	0/46		3.5 %	57.00 [3.58, 906.58]
vs QTP - Wan 2002	11/30	1/30		6.9 %	.00 [.5 , 79.96]
vs QTP - Wan 2008	8/28	0/32		3.4 %	19.34 [1.17, 320.74]
Subtotal (95% CI)	315	329	•	100.0 %	8.03 [4.78, 13.51]
Heterogeneity: $Tau^2 = 0.0$; Ch Test for overall effect: $Z = 7.86$,); l ² =0.0%			
Test for overall effect: Z = 7.86 4 dystonia vs QTP - Peuskens 1997	6 (P < 0.00001) 0/101	1/100		100.0 %	0.33 [0.01, 8.01]
Test for overall effect: Z = 7.86 4 dystonia vs QTP - Peuskens 1997 Subtotal (95% CI) Total events: 0 (Chlorpromazin Heterogeneity: not applicable Test for overall effect: Z = 0.66	6 (P < 0.00001) 0/101 101 ne), 1 (Quetiapine)			100.0 % 100.0 %	0.33 [0.01, 8.01] 0.33 [0.01, 8.01]
Test for overall effect: Z = 7.86 4 dystonia vs QTP - Peuskens 1997 Subtotal (95% CI) Total events: 0 (Chlorpromazin Heterogeneity: not applicable Test for overall effect: Z = 0.66	6 (P < 0.00001) 0/101 101 ne), 1 (Quetiapine)	1/100			
Test for overall effect: Z = 7.86 4 dystonia vs QTP - Peuskens 1997 Subtotal (95% CI) Total events: 0 (Chlorpromazin Heterogeneity: not applicable Test for overall effect: Z = 0.66 5 myotonia	6 (P < 0.00001) 0/101 101 ne), 1 (Quetiapine) 8 (P = 0.50)	1/100 100		100.0 %	0.33 [0.01, 8.01]
Test for overall effect: Z = 7.86 4 dystonia vs QTP - Peuskens 1997 Subtotal (95% CI) Total events: 0 (Chlorpromazir Heterogeneity: not applicable Test for overall effect: Z = 0.66 5 myotonia vs QTP - Chen 2001	6 (P < 0.00001) 0/101 101 ne), I (Quetiapine) 8 (P = 0.50) 14/107	1/100 100 7/114		100.0 % 18.0 %	0.33 [0.01, 8.01] 2.13 [0.89, 5.08]
Test for overall effect: Z = 7.86 4 dystonia vs QTP - Peuskens 1997 Subtotal (95% CI) Total events: 0 (Chlorpromazin Heterogeneity: not applicable Test for overall effect: Z = 0.66 5 myotonia vs QTP - Chen 2001 vs QTP - Chen 2007	6 (P < 0.00001) 0/101 101 ne), I (Quetiapine) 8 (P = 0.50) 14/107 1/30	1/100 100 7/114 0/32		100.0 % 18.0 % 1.4 %	0.33 [0.01, 8.01] 2.13 [0.89, 5.08] 3.19 [0.14, 75.49]
Test for overall effect: Z = 7.86 4 dystonia vs QTP - Peuskens 1997 Subtotal (95% CI) Total events: 0 (Chlorpromazin Heterogeneity: not applicable Test for overall effect: Z = 0.68 5 myotonia vs QTP - Chen 2001 vs QTP - Chen 2007 vs QTP - Cheng 2003	6 (P < 0.00001) 0/101 101 ne), 1 (Quetiapine) 8 (P = 0.50) 14/107 1/30 5/45	1/100 100 7/114 0/32 2/44		100.0 % 18.0 % 1.4 % 5.4 %	0.33 [0.01, 8.01] 2.13 [0.89, 5.08] 3.19 [0.14, 75.49] 2.44 [0.50, 11.94]
Test for overall effect: Z = 7.86 4 dystonia vs QTP - Peuskens 1997 Subtotal (95% CI) Total events: 0 (Chlorpromazin Heterogeneity: not applicable Test for overall effect: Z = 0.66 5 myotonia vs QTP - Chen 2001 vs QTP - Chen 2001 vs QTP - Chen 2007 vs QTP - Cheng 2003 vs QTP - Guo 2003a	6 (P < 0.00001) 0/101 101 ne), 1 (Quetiapine) 8 (P = 0.50) 14/107 1/30 5/45 9/73	1/100 100 7/114 0/32 2/44 4/75		100.0 % 18.0 % 1.4 % 5.4 % 10.6 %	0.33 [0.01, 8.01] 2.13 [0.89, 5.08] 3.19 [0.14, 75.49] 2.44 [0.50, 11.94] 2.31 [0.74, 7.18]
Test for overall effect: Z = 7.86 4 dystonia vs QTP - Peuskens 1997 Subtotal (95% CI) Total events: 0 (Chlorpromazin Heterogeneity: not applicable Test for overall effect: Z = 0.68 5 myotonia vs QTP - Chen 2001 vs QTP - Chen 2007 vs QTP - Chen 2007 vs QTP - Chen 2003 vs QTP - Guo 2003a vs QTP - Guo 2003b	6 (P < 0.00001) 0/101 101 ne), 1 (Quetiapine) 8 (P = 0.50) 14/107 1/30 5/45 9/73 5/30	1/100 100 7/114 0/32 2/44 4/75 0/30		100.0 % 18.0 % 1.4 % 5.4 % 10.6 % 1.7 %	0.33 [0.01, 8.01] 2.13 [0.89, 5.08] 3.19 [0.14, 75.49] 2.44 [0.50, 11.94] 2.31 [0.74, 7.18] 11.00 [0.64, 190.53]
Test for overall effect: Z = 7.86 4 dystonia vs QTP - Peuskens 1997 Subtotal (95% CI) Total events: 0 (Chlorpromazin -leterogeneity: not applicable Test for overall effect: Z = 0.68 5 myotonia vs QTP - Chen 2001 vs QTP - Chen 2007 vs QTP - Chen 2007 vs QTP - Chen 2003 vs QTP - Guo 2003a vs QTP - Guo 2003b vs QTP - Guo 2008	6 (P < 0.00001) 0/101 101 ne), I (Quetiapine) 8 (P = 0.50) 14/107 1/30 5/45 9/73 5/30 5/40	1/100 100 7/114 0/32 2/44 4/75 0/30 0/43		100.0 % 18.0 % 1.4 % 5.4 % 10.6 % 1.7 %	0.33 [0.01, 8.01] 2.13 [0.89, 5.08] 3.19 [0.14, 75.49] 2.44 [0.50, 11.94] 2.31 [0.74, 7.18] 11.00 [0.64, 190.53] 11.80 [0.67, 206.88]
Test for overall effect: Z = 7.86 4 dystonia vs QTP - Peuskens 1997 Subtotal (95% CI) Total events: 0 (Chlorpromazin Heterogeneity: not applicable Test for overall effect: Z = 0.68 5 myotonia vs QTP - Chen 2001 vs QTP - Chen 2001 vs QTP - Chen 2003 vs QTP - Chen 2003 vs QTP - Guo 2003a vs QTP - Guo 2003b vs QTP - Guo 2008 vs QTP - Jiang 2006	6 (P < 0.00001) 0/101 101 ne), I (Quetiapine) 8 (P = 0.50) 14/107 1/30 5/45 9/73 5/30 5/40 52/97	1/100 100 7/114 0/32 2/44 4/75 0/30 0/43 6/94		100.0 % 18.0 % 1.4 % 5.4 % 10.6 % 1.7 % 1.7 % 21.4 %	0.33 [0.01, 8.01] 2.13 [0.89, 5.08] 3.19 [0.14, 75.49] 2.44 [0.50, 11.94] 2.31 [0.74, 7.18] 11.00 [0.64, 190.53] 11.80 [0.67, 206.88] 8.40 [3.79, 18.62]
Test for overall effect: Z = 7.84 4 dystonia vs QTP - Peuskens 1997 Subtotal (95% CI) Total events: 0 (Chlorpromazin Heterogeneity: not applicable Test for overall effect: Z = 0.64 5 myotonia vs QTP - Chen 2001 vs QTP - Chen 2001 vs QTP - Chen 2007 vs QTP - Chen 2003 vs QTP - Chen 2003 vs QTP - Guo 2003a vs QTP - Guo 2003b vs QTP - Guo 2008 vs QTP - Jiang 2006 vs QTP - Jin 2007	6 (P < 0.00001) 0/101 101 ne), I (Quetiapine) 8 (P = 0.50) 14/107 1/30 5/45 9/73 5/30 5/40 5/40 52/97 12/30	1/100 100 7/114 0/32 2/44 4/75 0/30 0/43 6/94 2/30		100.0 % 18.0 % 1.4 % 5.4 % 10.6 % 1.7 % 21.4 % 6.8 %	0.33 [0.01, 8.01] 2.13 [0.89, 5.08] 3.19 [0.14, 75.49] 2.44 [0.50, 11.94] 2.31 [0.74, 7.18] 11.00 [0.64, 190.53] 11.80 [0.67, 206.88] 8.40 [3.79, 18.62] 6.00 [1.47, 24.55]

0.001 0.01 0.1 1 10 100 1000

Chlorpromazine Quetiapine

(Continued ...)

Study or subgroup	Chlorpromazine	Quetiapine	Risk Ratio	Weight	(Continue Risk Ratio
	n/N	n/N	IV,Random,95% CI		IV,Random,95% C
vs QTP - Zhou 2004	9/39	3/40		9.0 %	3.08 [0.90, 10.53]
Subtotal (95% CI)	629	628	•	100.0 %	4.59 [3.18, 6.64]
Total events: 169 (Chlorpromaz					
Heterogeneity: $Tau^2 = 0.0$; Chi ² Test for overall effect: $Z = 8.11$		47); l ² =0.0%			
6 need additional medication for	, ,				
vs QTP - Peuskens 1997	15/101	10/101		100.0 %	1.50 [0.71, 3.18
Subtotal (95% CI)	101	101	•	100.0 %	1.50 [0.71, 3.18
Total events: 15 (Chlorpromazi					
Heterogeneity: not applicable					
Test for overall effect: $Z = 1.06$	(P = 0.29)				
7 torsion movement	5407	0/114		(70)	
vs QTP - Chen 2001	5/107	0/114	•	6.7 %	.7 [0.66, 209.3
vs QTP - Cheng 2003	2/45	0/44		6.1 %	4.89 [0.24, 99.08
vs QTP - Guo 2003a	14/73	0/75		7.1 %	29.78 [1.81, 490.26
vs QTP - Jiang 2006	12/97	3/94		36.4 %	3.88 [1.13, 13.30
vs QTP - Jin 2007	7/30	0/30		7.0 %	15.00 [0.89, 251.42
vs QTP - Mei 2007	5/49	1/47		12.4 %	4.80 [0.58, 39.53
vs QTP - Tian 2006	1/46	0/46		5.5 %	3.00 [0.13, 71.78
vs QTP - Wang 2005	4/57	1/48		11.9 %	3.37 [0.39, 29.13
vs QTP - Zhang 2006	7/33	0/28		7.0 %	12.79 [0.76, 214.54
Subtotal (95% CI)	537	526	•	100.0 %	5.81 [2.76, 12.23
Total events: 57 (Chlorpromazi Heterogeneity: Tau ² = 0.0; Chi ⁻ Test for overall effect: Z = 4.64 8 tremor	$^{2} = 3.14$, df = 8 (P = 0.93)); I ² =0.0%			
vs QTP - Chen 2001	24/107	9/114	-	20.4 %	2.84 [1.38, 5.83
vs QTP - Chen 2007	2/30	0/32		2.0 %	5.32 [0.27, 106.54
vs QTP - Cheng 2003	11/45	2/44		7.4 %	5.38 [1.26, 22.88
vs QTP - Guo 2003a	13/73	5/75		13.7 %	2.67 [1.00, 7.12
vs QTP - Guo 2003b	4/30	0/30	+	2.1 %	9.00 [0.51, 160.17
vs QTP - Guo 2008	0/43	6/40	·	2.2 %	0.07 [0.00, 1.23
vs QTP - Jiang 2006	11/97	7/94		15.3 %	1.52 [0.62, 3.76
vs QTP - Jin 2007	7/30	1/30		4.1 %	7.00 [0.92, 53.47
vs QTP - Mei 2007	7/49	4/47		10.6 %	1.68 [0.53, 5.36
vs QTP - Wang 2005	7/57	2/48	 	6.8 %	2.95 [0.64, 3.53

0.001 0.01 0.1 1 10 100 1000

Chlorpromazine Quetiapine

(Continued . . .)

Study or subgroup	Chlorpromazine	Quetiapine	Risk Ratio	Weight	(Continued) Risk Ratio
Study of Subgroup	n/N	n/N	IV,Random,95% Cl	v veigite	IV,Random,95% CI
vs QTP - Yang 2007	8/32	1/31		4.1 %	7.75 [1.03, 58.38]
vs QTP - Zhou 2004	5/39	1/40	+	3.8 %	5.13 [0.63, 41.93]
vs QTP - Zou 2006	15/43	2/43		7.7 %	7.50 [1.82, 30.83]
Subtotal (95% CI)	675	668	•	100.0 %	2.90 [1.89, 4.45]
Total events: 114 (Chlorproma	azine), 40 (Quetiapine)				
Heterogeneity: Tau ² = 0.10; C	$hi^2 = 14.41, df = 12 (P = 0)$	0.28); $ ^2 = 7\%$			
Test for overall effect: $Z = 4.89$	9 (P < 0.00001)				
Test for subgroup differences:	Chi ² = 42.50, df = 7 (P =	0.00), l ² =84%			

0.001 0.01 0.1 1 10 100 1000 Chlorpromazine Quetiapine

Analysis 3.24. Comparison 3 CHLORPROMAZINE versus QUETIAPINE, Outcome 24 Adverse effects: 9a. Metabolic - weight gain.

Review: Chlorpromazine versus atypical antipsychotic drugs for schizophrenia Comparison: 3 CHLORPROMAZINE versus QUETIAPINE Outcome: 24 Adverse effects: 9a. Metabolic - weight gain

Study or subgroup	Chlorpromazine	Quetiapine	Risk Ratio M-	Weight	Risk Ratio M-
	n/N	n/N	H,Random,95% Cl		H,Random,95% Cl
l weight gain					
vs QTP - Chen 2001	27/107	19/114	-	19.7 %	1.51 [0.90, 2.56]
vs QTP - Chen 2007	9/30	8/32	-	12.4 %	1.20 [0.53, 2.70]
vs QTP - Cheng 2003	10/45	6/44		10.4 %	1.63 [0.65, 4.10]
vs QTP - Guo 2003a	12/73	9/75		12.5 %	1.37 [0.61, 3.05]
vs QTP - Guo 2003b	9/30	1/30		2.9 %	9.00 [1.21, 66.70]
vs QTP - Guo 2007	1/26	0/26		1.2 %	3.00 [0.13, 70.42]
vs QTP - Guo 2008	3/40	4/43		5.3 %	0.81 [0.19, 3.38]
vs QTP - He 2003	5/20	3/20		6.3 %	1.67 [0.46, 6.06]
vs QTP - Ji 2004	2/30	2/30		3.2 %	1.00 [0.15, 6.64]
			0.01 0.1 1 10 100		
			chlorpromazine Favours quetiapine	2	
		ratours (i avoaro qaeaapin	-	

(Continued . . .)

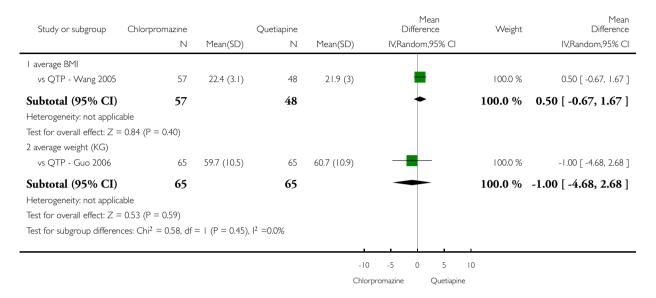
Study or subgroup	Chlorpromazine n/N	Quetiapine n/N	Risk Ratio M- H,Random,95% Cl	Weight	(Continued) Risk Ratio M- H,Random,95% Cl
vs QTP - Jiang 2008	5/30	0/30		1.5 %	.00 [0.64, 90.53]
vs QTP - Liu 2003	6/39	0/44		1.5 %	14.63 [0.85, 251.51]
vs QTP - Tian 2006	0/46	8/46	← →	1.5 %	0.06 [0.00, 0.99]
vs QTP - Wan 2002	5/30	4/30	_	6.9 %	1.25 [0.37, 4.21]
vs QTP - Yang 2007	2/32	1/31	<u> </u>	2.2 %	1.94 [0.18, 20.30]
vs QTP - Zou 2006	21/43	6/43		12.5 %	3.50 [1.57, 7.81]
Total (95% CI) Total events: 117 (Chlorpror Heterogeneity: Tau ² = 0.10;	, , , ,	638 0.21); I ² =22%	•	100.0 %	1.67 [1.17, 2.39]
Test for overall effect: $Z = 2$.	· /				
Test for subgroup differences	s: Not applicable				
			0.01 0.1 1 10 100		

Favours chlorpromazine Favours quetiapine

Analysis 3.25. Comparison 3 CHLORPROMAZINE versus QUETIAPINE, Outcome 25 Adverse effects: 9b. Metabolic - short term (up to 6 months).

Review: Chlorpromazine versus atypical antipsychotic drugs for schizophrenia Comparison: 3 CHLORPROMAZINE versus QUETIAPINE

Outcome: 25 Adverse effects: 9b. Metabolic - short term (up to 6 months)



Analysis 3.26. Comparison 3 CHLORPROMAZINE versus QUETIAPINE, Outcome 26 Adverse effects: 10. Various other - short term (up to 6 months).

Review: Chlorpromazine versus atypical antipsychotic drugs for schizophrenia Comparison: 3 CHLORPROMAZINE versus QUETIAPINE Outcome: 26 Adverse effects: 10. Various other - short term (up to 6 months)

Study or subgroup	Chlorpromazine	Quetiapine	Risk Ratio M-	Weight	Risk Ratio M-
	n/N	n/N	H,Random,95% Cl		H,Random,95%
I unspecified adverse effects					
vs QTP - Cai 2006	61/96	28/101	-	27.0 %	2.29 [1.62, 3.25]
vs QTP - Ji 2004	22/33	18/33	+	25.4 %	1.22 [0.82, 1.81]
vs QTP - Peuskens 1997	44/100	34/101	-	26.9 %	1.31 [0.92, 1.86]
vs QTP - Wang 2004	32/48	2/48	-	20.7 %	2.67 [1.57, 4.53]
Total (95% CI)	277	283	•	100.0 %	1.73 [1.19, 2.52]
Total events: 159 (Chlorproma	zine), 92 (Quetiapine)				
Heterogeneity: $Tau^2 = 0.10$; Ch	$hi^2 = 10.62, df = 3 (P = 0.0)$)); l ² =72%			
Test for overall effect: $Z = 2.88$	B (P = 0.0040)				
Test for subgroup differences: N	Not applicable				
		(0.01 0.1 1 10 100		
		Favours c	hlorpromazine Favours quetiapi	ne	

Analysis 3.27. Comparison 3 CHLORPROMAZINE versus QUETIAPINE, Outcome 27 Adverse effects: 11. Average endpoint score (TESS, high = poor) - skewed data.

Adverse effects: 11. Average en	dpoint score	(TESS, high = po	oor) - skewed data
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Study	Intervention	Mean	SD	Ν	
short term (up to 6 m	onths)				short term (up
vs QTP - Cai 2007	Chlorpromazine	3.0	2.2	46	
vs QTP - Cai 2007	Quetiapine	2.4	2.3	48	
vs QTP - Guo 2005	Chlorpromazine	4.2	3.0	40	
vs QTP - Guo 2005	Quetiapine	2.0	2.4	40	
vs QTP - Guo 2008	Chlorpromazine	2.8	2.2	40	
vs QTP - Guo 2008	Quetiapine	1.9	1.6	43	
vs QTP - Hu 2003	Chlorpromazine	5.33	3.94	22	

vs QTP - Hu 2003	Quetiapine	6.92	4.35	19	
vs QTP - Li 2003	Chlorpromazine	4.8	3.1	37	
vs QTP - Li 2003	Quetiapine	2.9	2.8	40	
vs QTP - Zhang 2002	Chlorpromazine	6.94	4.35	57	
vs QTP - Zhang 2002	Quetiapine	6.07	5.04	60	
vs QTP - Zhang 2008	Chlorpromazine	9.35	6.23	30	
vs QTP - Zhang 2008	Quetiapine	6.63	5.2	30	
medium term (7 to 12	months)			I	medium term (7
vs QTP - Li 2003	Chlorpromazine	4.2	3.0	37	
vs QTP - Li 2003	Quetiapine	2.1	2.3	40	

Adverse effects: 11. Average endpoint score (TESS, high = poor) - skewed data (Continued)

Analysis 3.28. Comparison 3 CHLORPROMAZINE versus QUETIAPINE, Outcome 28 Quality of life: 1. General - average endpoint score (GQOLI - 74, high = better).

Review: Chlorpromazine versus atypical antipsychotic drugs for schizophrenia Comparison: 3 CHLORPROMAZINE versus QUETIAPINE Outcome: 28 Quality of life: 1. General - average endpoint score (GQOLI - 74, high = better)

Study or subgroup	Chlorpromazine		Quetiapine			Mean rence	Weight	Mean Difference
	Ν	Mean(SD)	Ν	Mean(SD)	IV,Rando	m,95% Cl		IV,Random,95% CI
I short term (up to 6 m	onths)							
vs QTP - Ji 2004	29	60.49 (9.62)	30	66.98 (9.23)	+		100.0 %	-6.49 [-11.30, -1.68]
Subtotal (95% CI)	29		30		•		100.0 %	-6.49 [-11.30, -1.68]
Heterogeneity: not appli	cable							
Test for overall effect: Z	= 2.64 (P = 0.0082)							
Test for subgroup differe	nces: Not applicable							
						i		
				-	100 -50 0	50	100	
					Quetiapine	Chlorpror	nazine	

Analysis 3.29. Comparison 3 CHLORPROMAZINE versus QUETIAPINE, Outcome 29 Leaving the study early: 1a. Short term (up to 6 months).

Review: Chlorpromazine versus atypical antipsychotic drugs for schizophrenia Comparison: 3 CHLORPROMAZINE versus QUETIAPINE Outcome: 29 Leaving the study early: La Short term (up to 6 months)

Outcome: 29	Leaving the study early:	Ta. Short term	(up to 6 months)
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IV,Random,95% (Weight	Risk Ratio	Quetiapine	Chlorpromazine	Study or subgroup
		IV,Random,95% CI	n/N	n/N	
2725070 1755	4.3 %		2/114	7/107	due to adverse effect vs QTP - Chen 2001
3.73 [0.79, 17.55					•
4.89 [0.24, 99.08	1.2 %		0/44	2/45	vs QTP - Cheng 2003
5.00 [0.25, 101.18	1.2 %		0/43	2/43	vs QTP - Guo 2008
1.33 [0.32, 5.50	5.2 %		3/33	4/33	vs QTP - Ji 2004
1.03 [0.55, 1.92	27.0 %	+	16/94	17/97	vs QTP - Jiang 2006
2.04 [0.94, 4.43	17.4 %	-	9/196	18/192	vs QTP - NCT00882518
2.27 [0.72, 7.14	8.0 %		4/101	9/100	vs QTP - Peuskens 1997
2.00 [0.38, 10.41	3.8 %	_ 	2/48	4/48	vs QTP - Wang 2004
0.92 [0.45, 1.89	20.0 %	-	11/48	12/57	vs QTP - Wang 2005
1.44 [0.57, 3.66	12.0 %		7/119	10/118	vs QTP - Zhang 2003
1.43 [1.04, 1.98	100.0 %	•	840	840	Subtotal (95% CI)
1.60 [0.27, 9.38	17.4 %	_	2/114	3/107	vs QTP - Chen 2001
					2 due to inefficacy
3.00 [0.13, 71.65	5.4 %		0/43	1/43	vs QTP - Guo 2008
1.31 [0.56, 3.03	77.2 %	-	9/192	12/196	vs QTP - NCT00882518
1.42 [0.68, 2.96	100.0 %	•	349	346	ubtotal (95% CI)
			$ ^2 = 0.0\%$	0.27, df = 2 (P = 0.87);	bal events: 16 (Chlorpromazine) leterogeneity: Tau ² = 0.0; Chi ² = est for overall effect: $Z = 0.92$ (P due to any other reason
1.14 [0.49, 2.67	12.6 %	-	7/25	8/25	vs QTP - Cao 2005
-	2.6 % . %		7/25 3/44	8/25 0/45	vs QTP - Cao 2005
0.14 [0.01, 2.63	1.1 %		3/44	0/45	vs QTP - Cao 2005 vs QTP - Cheng 2003
0.14 [0.01, 2.63	1.1 % 7.6 %		3/44 5/35	0/45 6/36	vs QTP - Cao 2005 vs QTP - Cheng 2003 vs QTP - Guo 2003b
0.14 [0.01, 2.63	1.1 %		3/44	0/45	vs QTP - Cao 2005 vs QTP - Cheng 2003

Study or subgroup	Chlorpromazine n/N	Quetiapine n/N	Risk Ratio IV,Random,95% CI	Weight	(Continued) Risk Ratio IV,Random,95% Cl
vs QTP - Peng 2006	2/20	2/20		2.6 %	1.00 [0.16, 6.42]
vs QTP - Peuskens 1997	27/100	27/101	+	43.6 %	1.01 [0.64, 1.59]
vs QTP - Wang 2004	2/48	0/48		1.0 %	5.00 [0.25, 101.48]
vs QTP - Yang 2007	2/30	1/31		1.6 %	2.07 [0.20, 21.61]
vs QTP - Zhou 2003	2/20	2/20		2.6 %	1.00 [0.16, 6.42]
vs QTP - Zhou 2004	2/41	2/42		2.5 %	1.02 [0.15, 6.93]
vs QTP - Zou 2006	2/20	2/20		2.6 %	1.00 [0.16, 6.42]
Subtotal (95% CI)	609	614	•	100.0 %	1.04 [0.77, 1.41]
Heterogeneity: Tau ² = 0.0; Chi ² = Test for overall effect: Z = 0.27 (P 4 due to loss to follow-up vs QTP - Cai 2006		8); ² =0.0% 8/109		59.0 %	0.55 [0.17, 1.75]
vs QTP - Jiang 2006	3/97	5/94		41.0 %	0.58 [0.14, 2.36]
Subtotal (95% CI)	197	203	-	100.0 %	0.56 [0.23, 1.37]
Total events: 7 (Chlorpromazine), Heterogeneity: Tau ² = 0.0; Chi ² = Test for overall effect: $Z = 1.27$ (P Test for subgroup differences: Chi ²	0.00, df = 1 (P = 0.94) = 0.21)				

Chlorpromazine Quetiapine

Analysis 3.30. Comparison 3 CHLORPROMAZINE versus QUETIAPINE, Outcome 30 Leaving the study early: 1b. Medium term (7 to 12 months).

Review: Chlorpromazine versus atypical antipsychotic drugs for schizophrenia Comparison: 3 CHLORPROMAZINE versus QUETIAPINE Outcome: 30 Leaving the study early: 1b. Medium term (7 to 12 months)

Study or subgroup	Chlorpromazine n/N	Quetiapine n/N	Risk Ratio IV,Random,95% Cl	Weight	Risk Ratio IV,Random,95% CI
vs QTP - Li 2003	14/51	12/52		100.0 %	1.19 [0.61, 2.32]
Total (95% CI)	51	52	+	100.0 %	1.19 [0.61, 2.32]
Total events: 14 (Chlorpr	romazine), 12 (Quetiapine)				
Heterogeneity: not applie	cable				
Test for overall effect: Z =	= 0.51 (P = 0.61)				
Test for subgroup differer	nces: Not applicable				
			0.01 0.1 1 10 100)	
			Chlorpromazine Quetiapine		

ADDITIONAL TABLES

Table 1. Related Cochrane Reviews

Comparison	Reference
Chlorpromazine versus placebo	Adams 2014
Chlorpromazine versus haloperidol	Leucht 2008
Chlorpromazine doses	Liu 2009
Chlorpromazine cessation	Almerie 2007
Chlorpromazine for acute aggression	Ahmed 2010

APPENDICES

Appendix I. Previous searches

1.1 Search in 2013 (Protocol Step)

I.I.I Electronic searches

1.1.1.1 Cochrane Schizophrenia Group Trials Register

The Trials Search Co-ordinator will search the Cochrane Schizophrenia Group's Trials Register using the phrase:

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

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

1.1.2 Searching other resources

1.1.2.1 Reference searching

We will inspect references of all included studies for further relevant studies published in any language.

1.1.2.2 Personal contact

We will contact the first author of each included study for information regarding unpublished trials.

CONTRIBUTIONS OF AUTHORS

Kumar Saha developed the protocol.

Rashid Zaman developed the protocol.

Stephanie Sampson helped to develop the protocol, and wrote the review.

Li Bo performed data screening and extraction, and contributed to writing the review.

Sai Zhao performed data screening and data extraction.

Jun Xia did reliability checks and extracted data.

DECLARATIONS OF INTEREST

Kumar Saha has no known conflicts of interest. Rashid Zaman has no known conflicts of interest. Stephanie Sampson has no known conflicts of interest. Li Bo has no known conflicts of interest. Sai Zhao has no known conflicts of interest. Jun Xia has no known conflicts of interest.

SOURCES OF SUPPORT

Internal sources

• Nottinghamshire Healthcare NHS Trust, UK.

External sources

- National Institute for Health Research (NIHR), UK.
- Cochrane Collaboration Programme Grant 2011; Reference number: 10/4001/15
- National Natural Science Foundation of China, China.
- NSFC project number: 81303151
- Beijing Nova Program, China.
- Project numbers: xxjh2015A093 and Z1511000003150125

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

We adhered to the Cochrane protocol for data extraction and data management. However, due to the large number of results we obtained from the literature searches, we have presented comparisons with chlorpromazine with the specific name of the comparator drug instead of the planned, generic 'chlorpromazine versus atypical antipsychotics'. We have only included data for three drug comparisons and will include all other comparator atypical antipsychotics in future updates of this Cochrane review. We clarified and amended the anticholinergic outcomes to include hypersalivation and leaving the study data.

The adverse effects outcomes have been arranged into new categories that are now used by the Cochrane Schizophrenia Group.

INDEX TERMS

Medical Subject Headings (MeSH)

Antipsychotic Agents [*therapeutic use]; Benzodiazepines [therapeutic use]; Chlorpromazine [*therapeutic use]; Quetiapine Fumarate [therapeutic use]; Randomized Controlled Trials as Topic; Risperidone [therapeutic use]; Schizophrenia [*drug therapy]

MeSH check words

Adult; Humans