UNIVERSITY of York

This is a repository copy of *Chlorpromazine versus atypical antipsychotic drugs for schizophrenia*.

White Rose Research Online URL for this paper:
https://eprints.whiterose.ac.uk/134711/

Version: Published Version

Article:
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

Reuse
Items deposited in White Rose Research Online are protected by copyright, with all rights reserved unless indicated otherwise. They may be downloaded and/or printed for private study, or other acts as permitted by national copyright laws. The publisher or other rights holders may allow further reproduction and re-use of the full text version. This is indicated by the licence information on the White Rose Research Online record for the item.

Takedown
If you consider content in White Rose Research Online to be in breach of UK law, please notify us by emailing eprints@whiterose.ac.uk including the URL of the record and the reason for the withdrawal request.

White Rose university consortium
Universities of Leeds, Sheffield & York

eprints@whiterose.ac.uk
https://eprints.whiterose.ac.uk/

Cochrane Library

Cochrane Database of Systematic Reviews

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.

www.cochranelibrary.com

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

WILEY

TABLE OF CONTENTS

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

[Intervention Review]

Chlorpromazine versus atypical antipsychotic drugs for schizophrenia

Kumar B Saha[1], Li Bo[2], Sai Zhao[3], Jun Xia[4], Stephanie Sampson[5], Rashid U Zaman[6]

[1]Addiction Psychiatry, Leeds and York Partnerships NHS Foundation Trust, Leeds, UK. [2]China Academy of Chinese Medical Sciences, Xiyuan Hospital, Beijing, China. [3]Systematic Review Solutions Ltd, Tianjin, China. [4]Cochrane Schizophrenia Group, The University of Nottingham, Nottingham, UK. [5]The University of Nottingham, Nottingham, UK. [6]Health Portfolio, Oxford Policy Management, Oxford, UK

Contact address: Li Bo, China Academy of Chinese Medical Sciences, Xiyuan Hospital, 1 Xi Yuan Cao Chang, Haidian District, Beijing, 100091, China. dr.libo@vip.163.com, bv1013@hotmail.com.

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.

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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.

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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.

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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/.

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

SUMMARY OF FINDINGS FOR THE MAIN COMPARISON [Explanation]

Chlorpromazine versus olanzapine for schizophrenia

Patient or population: people with schizophrenia
Settings: inpatient and outpatient
Intervention: chlorpromazine
Comparison: olanzapine

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	Number of participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Olanzapine	Chlorpromazine				
No significant clinical response: short term (up to 6 months) Follow-up: 6 to 12 weeks	**Low**[1]		**RR 2.34** (1.37 to 3.99)	204 (3 studies)	⊕⊕◯◯ **low**[2,3]	-
	700 per 1000	**1000 per 1000** (959 to 1000)				
	High[1]					
	190 per 1000	**445 per 1000** (260 to 758)				
Relapse: long term (over 12 months) Follow-up: mean 2 years	**Study population**		**RR 1.5** (0.46 to 4.86)	70 (1 study)	⊕◯◯◯ **very low**[3,4]	-
	114 per 1000	**171 per 1000** (53 to 555)				
	Moderate					
	114 per 1000	**171 per 1000** (52 to 554)				

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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 intervention 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 observed extrapyramidal symptoms - short term (up to 6 months) Follow-up: mean 8 weeks	**Low**		**RR 34.47** (4.79 to 248.3)	298 (2 studies)	⊕○○○ **very low**[2,3,8]	-
	10 per 1000	**345 per 1000** (48 to 1000)				
	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 intervention 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]	-

	159 per 1000	**268 per 1000** (71 to 1000)		
	Moderate[11]			
	229 per 1000	**387 per 1000** (103 to 1000)		

*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.

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[1]Control risk: the control risks are representative of the control group risks of the study population.
[2]Risk of bias: rated serious - most included studies had unclear risk of bias in terms of allocation and blinding, hence selection and detection bias are likely to be present. Two studies also had high risk of reporting bias.
[3]Publication bias: strongly suspected - we identified only small trial(s) from China for this outcome. Publication bias is highly suspected.
[4]Imprecision: serious - only one small trial with unclear risk of selection and detection bias contributed data to this outcome. The result was imprecise with few event and a wide CI.
[5]Inconsistency: serious - unexplained heterogeneity present, suggesting different magnitude of effect.
[6]Indirectness: serious - binary outcome assessing mental state is unavailable. We, therefore, employed BPRS score as an alternative indicator.
[7]Imprecision: serious - a relatively wide CI around the point of estimate of effect. Sample size is smaller than the optimal information size.
[8]Imprecision: serious - although significant difference was observed between groups, the CI was wide (95% CI 4.97 to 248.3).
[9]Indirectness: serious - binary outcome for quality of life is unavailable. We, thus, used outcome from QOL- physical health subscale as an alternative indicator.
[10]Imprecision: serious - although significant difference was observed between group, the total sample size is smaller than the optimal information size.
[11]Control risk: the control risks in the study population are very close to the moderate risk observed here. Thus we adopted it to represent the control risk.

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

[12]Risk 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.
[13]Imprecision: serious - estimate of effect was not significant and the total sample size is smaller than the desired optimal information size.

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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,

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

comparisons with new generation drugs, which are coming off-patent 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

1. 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.

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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.

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

- 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

1. 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

1. 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

1. 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.

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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 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

1. Binary data—

For binary outcomes we calculated a standard estimation of the risk ratio (RR) and its 95% confidence interval (CI). It has been shown that RR is more intuitive (Boissel 1999) than odds ratios (ORs) and that ORs tend to be interpreted as RRs by clinicians (Deeks 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.

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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

1. 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 intra-class 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

1. 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.

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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

1. Clinical heterogeneity

We considered all included studies initially, without seeing comparison data, to judge clinical heterogeneity. We simply inspected all studies for clearly outlying people or situations which we had not predicted would arise 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 I^2 statistic

We investigated heterogeneity between studies by considering the I^2 statistic alongside the Chi^2 test P value. The I^2 statistic provides an estimate of the percentage of inconsistency thought to be due to chance (Higgins 2003). The importance of the observed I^2 statistic value depends on: i. magnitude and direction of effects; and ii. strength of evidence for heterogeneity (e.g. P value from the Chi^2 test, or a CI for I^2 statistic). We interpreted an I^2 statistic estimate $\geq$ around 50% accompanied by a statistically significant Chi^2 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

1. 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

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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

1. 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

1. 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 fixed-effect model to evaluate whether this altered the significance of the results.

RESULTS

Description of studies

Results of the search

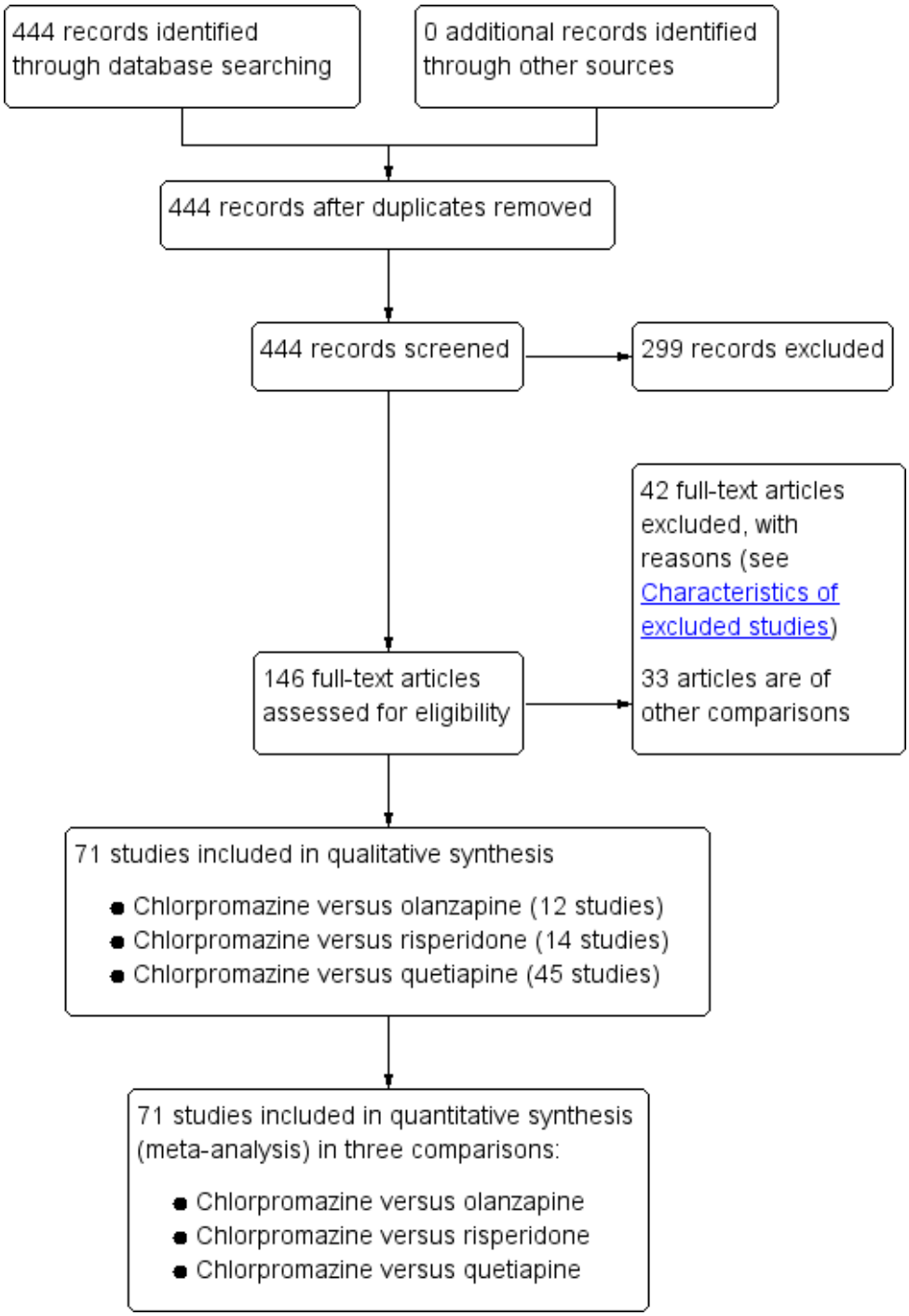
We identified 444 references following our literature search, of which we excluded 298 after screening by title/abstract. For this

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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.

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Figure 1. Study flow diagram.



Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Included studies

1. 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 well-reported 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.

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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 18-item 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 7-point 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.

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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 well-reported 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.

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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 18-item 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).

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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 well-reported 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 peer-reviewed 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 18-item 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.

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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

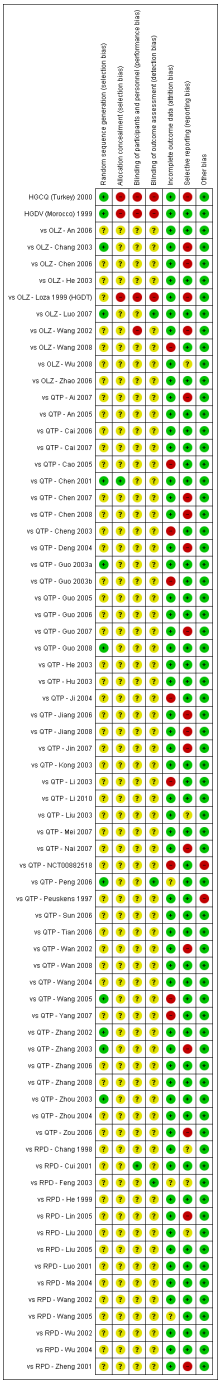
We excluded 42 studies; for details please consult the Characteristics of excluded studies section,

Risk of bias in included studies

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

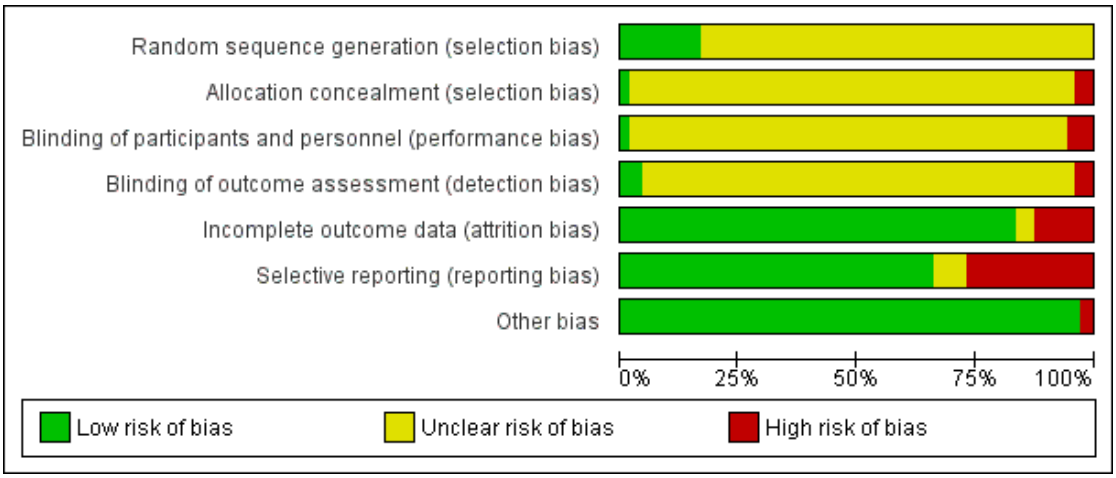
Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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



Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Figure 3. 'Risk of bias' graph: review authors' judgements about each 'Risk of bias' item presented as percentages across all included studies.



Allocation

1. Chlorpromazine versus olanzapine

Only four included studies provided adequate information regarding randomisation, which included methods such as a computer-generated 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

1. 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 -

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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

1. 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

1. 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

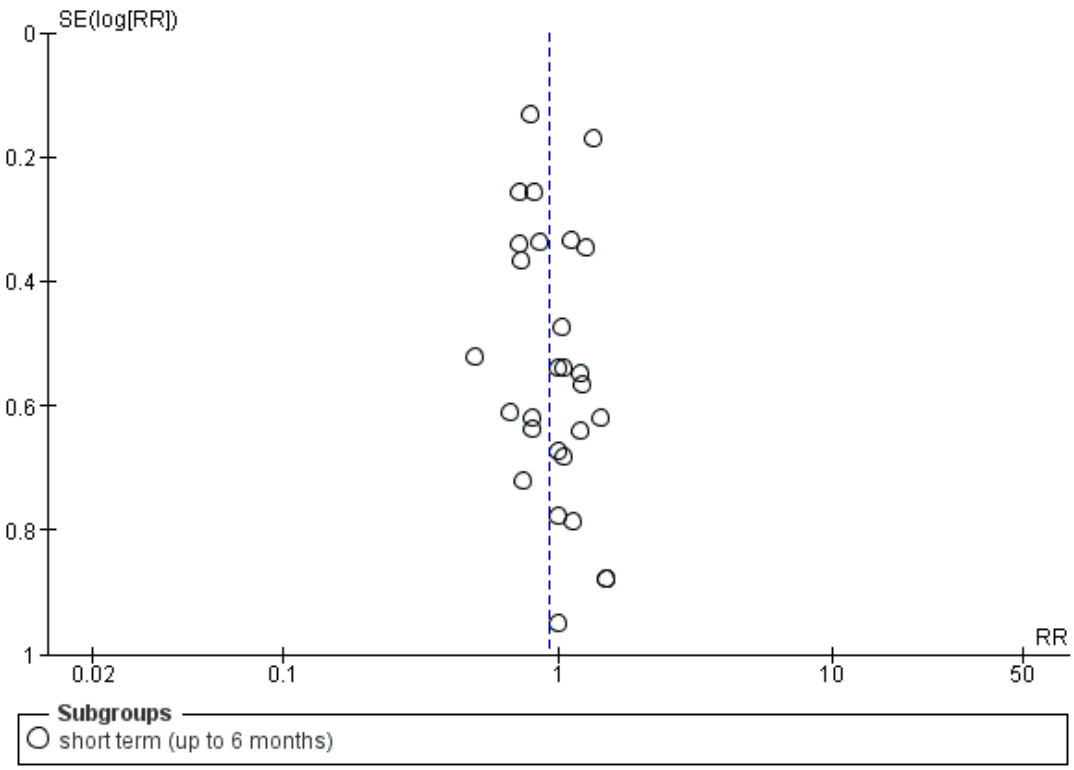
We rated two studies as at 'high' risk of bias for selective reporting due to pre-specified outcomes in each study not being fully reported or partially reported (vs RPD - Lin 2005; vs RPD - Zheng 2001). Two studies were rated as at 'unclear' risk of bias as it was not explicit whether all outcomes were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

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Figure 4. Funnel plot of comparison: 3 Chlorpromazine vs Quetiapine, outcome: 3.1 Clinical response: no significant clinical response.



Other potential sources of bias

1. 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 1: CHLORPROMAZINE versus OLANZAPINE

1.1 Clinical response: 1. No significant clinical response

1.1.1 short term - up to 6 months

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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)

1.2 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: 1. 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).

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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).

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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).

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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

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).

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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: 1a. 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).

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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: 1. 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: 1a. 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%).

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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: 1b. 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: 1. 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).

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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 ≤ 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).

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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%).

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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.

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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.

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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: 1a. 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: 1b. 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).

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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: 1c. 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: 1e. 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: 1. 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).

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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).

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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).

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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 (GQOL1 - 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: 1a. 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

1. 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.

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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 long-term 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.

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

ADDITIONAL SUMMARY OF FINDINGS [*Explanation*]

Chlorpromazine versus risperidone for schizophrenia

Patient or population: people with schizophrenia
Settings: inpatient and outpatient
Intervention: chlorpromazine
Comparison: risperidone

Outcomes	Illustrative comparative 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** (0.53 to 1.34)	475 (7 studies)	⊕⊕◯◯ **low**[2,3]	-
	60 per 1000	**50 per 1000** (32 to 80)				
	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) Follow-up: 6 to 12 weeks		The mean mental state: short term (up to 6 months) in the intervention groups was **0.9 higher** (3.49 lower to 5.28 higher)		247 (4 studies)	⊕◯◯◯ **very low**[2,4,5,6,7]	-

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Adverse effects: any observed extrapyramidal symptoms - short term (up to 6 months) Follow-up: 8 to 12 weeks	**Low**[1]		**RR 1.7** (0.85 to 3.4)	235 (3 studies)	⊕○○○ **very low**[2,6,7]	-
	130 per 1000	**221 per 1000** (111 to 442)				
	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 intervention groups was **14.2 lower** (20.5 to 7.9 lower)		100 (1 study)	⊕○○○ **very low**[7,8,9,10]	-
Leaving the study early due to adverse effects - short term (up to 6 months) Follow-up: mean 8 weeks	**Study population**		**RR 0.21** (0.01 to 4.11)	41 (1 study)	⊕○○○ **very low**[7,10]	-
	95 per 1000	**20 per 1000** (1 to 391)				
	Moderate					
	95 per 1000	**20 per 1000** (1 to 390)				

*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.

GRADE Working Group grades of evidence
High quality: further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: we are very uncertain about the estimate.

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

[2]Risk 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.
[3]Publication bias: strongly suspected - only Chinese studies with relatively small sample size were identified. Publication bias is highly likely.
[4]Inconsistency: serious - unexplained heterogeneity present, suggesting different magnitude of effect.
[5]Indirectness: serious - binary outcome assessing mental state is unavailable. We, therefore, employed BPRS score as an alternative indicator.
[6]Imprecision: 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.
[7]Publication bias: strongly suspected - only one study with unclear risk of selection and detection bias available for this outcome.
[8]Indirectness: serious - binary outcome for quality of life was not available. Therefore, we adopted QOL score as an indicator.
[9]Imprecision: serious - estimate of effect was significant with tight CI, but the study sample size is smaller than the optimal information size.
[10]Imprecision: serious - estimate of effect was not significant and with relatively wide CI. Sample size was smaller than the optimal information size.

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Chlorpromazine versus quetiapine for schizophrenia

Patient or population: people with schizophrenia
Settings: inpatient and outpatient
Intervention: chlorpromazine
Comparison: quetiapine

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	Number of participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Quetiapine	Chlorpromazine				
No significant clinical response: short term (up to 6 months) Follow-up: 4 to 16 weeks	**Low**[1]		**RR 0.93** (0.81 to 1.06)	3241 (28 studies)	⊕⊕⊕◯ **moderate**[2]	-
	70 per 1000	**65 per 1000** (57 to 74)				
	Moderate[1]					
	128 per 1000	**119 per 1000** (104 to 136)				
	High[1]					
	360 per 1000	**335 per 1000** (292 to 382)				
Mental state: short term (up to 6 months) BPRS endpoint scale score (high = poor) Follow-up: 6 to 12 weeks		The mean mental state: short term (up to 6 months) in the intervention groups was **0.18 lower** (1.23 lower to 0.88 higher)		548 (6 studies)	⊕◯◯◯ **very low**[2,3,4,5]	-

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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 intervention groups was **6.49 lower** (11.3 to 1.68 lower)		59 (1 study)	⊕○○○ **very low**[6,7,8,9]	-
Adverse effects: any observed extrapyramidal symptoms - short term (up to 6 months) Follow-up: 6 to 8 weeks	**Study population**		**RR 8.03** (4.78 to 13.51)	644 (8 studies)	⊕⊕○○ **low**[2,5]	-
	36 per 1000	**293 per 1000** (174 to 493)				
	Moderate					
	0 per 1000	**0 per 1000** (0 to 0)				
	High					
	80 per 1000	**642 per 1000** (382 to 1000)				
Leaving the study early due to any reason short term (up to 6 months) Follow-up: 6 to 16 weeks	**Moderate**[1]		**RR 1.04** (0.77 to 1.41)	1223 (12 studies)	⊕⊕⊕○ **moderate**[2]	-
	93 per 1000	**97 per 1000** (72 to 131)				
	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.

GRADE Working Group grades of evidence
High quality: further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: we are very uncertain about the estimate.

[1]Control risk: are representative of those observed in the study population.
[2]Risk 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.
[3]Indirectness: serious - binary outcome on mental state is not available. Thus we employed BPRS rating as an indicator.
[4]Imprecision: 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.
[5]Publication bias: strongly suspected - only Chinese trials with small sample size were identified for this outcome.
[6]Risk 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.
[7]Indirectness: serious - there was no binary measurement available on quality of life. Therefore, we used GQOLI-74 as an alternative indicator.
[8]Imprecision: serious - sample size was smaller than the optimal information size.
[9]Publication bias: strongly suspected - we only identified a Chinese trial with a small sample size with positive findings for this outcome.

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

DISCUSSION

Summary of main results

1. 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.

1.4 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.

1.5 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.

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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

1. 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.

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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

1. 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."

REFERENCES

References to studies included in this review

HGCQ (Turkey) 2000 ***{unpublished data only}***

Dossenbach M. Sleep quality and early morning wakefulness of schizophrenic patients treated with olanzapine compared to chlorpromazine. *European Neuropsychopharmacology* 2000;**10**(Supplement 3):S328–9.

Eli Lilly, Company. Study F1D-VI-HGCQ olanzapine versus chlorpromazine in Turkey. Unpublished document internal to Eli-Lilly 2000:1–560.

Kostakoglu E, Alptekin K, Kivicik BB, Martenyi F, Tunca Z, Gogus A, et al. Sleep quality and early morning wakefulness of schizophrenia patients treated with olanzapine compared to chlorpromazine [Errata]. *European Neuropsychopharmacology* 2001;**11**(Suppl 3):S369.

Mraz K, Gogus A, Tunca Z, Martenyi F, Dossenbach M. Olanzapine versus chlorpromazine in Turkey. Schizophrenia Research (Abstracts of the Winter Workshop on Schizophrenia; February 5-11, 2000; Davos, Switzerland). 2000.

HGDV (Morocco) 1999 ***{unpublished data only}***

Eli Lilly, Company. Study HGDV olanzapine (versus chlorpromazine in Morocco). Unpublished document internal to Eli-Lilly and Company 2001:1–512.

* HGDV/Morocco. Data supplied to the Cochrane Schizophrenia Group. Data on file 1999.

vs OLZ - An 2006 ***{published data only}***

An BF, Li Y, Wang CH. Olanzapine on effect of executive dysfunction in schizophrenia. *Journal of Clinical Psychiatry* 2006;**16**(3):144–5.

vs OLZ - Chang 2003 ***{published data only}***

Chang FW, Wang CH, Zhao Z. Clinical effects of olanzapine vs chlorpromazine in treating positive symptoms of schizophrenia. *Chinese Journal of New Drugs and Clinical Remedies* 2003;**22**(6):357–9.

vs OLZ - Chen 2006 ***{published data only}***

Chen F. Olanzapine and chlorpromazine in the treatment of schizophrenia. *Journal of Clinical Psychiatric Medicine* 2006; **16**:303–4.

vs OLZ - He 2003 ***{published data only}***

He J, An Q. A comparative trial of olanzapine versus chlorpromazine in the treatment of schizophrenia. *Shandong Mental Health Archive* 2003;**16**:78–80.

vs OLZ - Loza 1999 (HGDT) ***{published and unpublished data}***

Eli Lilly, Company. HGDT olanzapine versus chlorpromazine in Egypt. Unpublished document internal to Eli Lilly and Company 2001:1–513.

Loza N, El-Dosoky AM, Okasha TA, Khalil AH, Hasan NM, Dossenbach M, et al. Olanzapine compared to chlorpromazine in acute schizophrenia. *European Neuropsychopharmacology* 1999;**9**(Suppl 5):S291.

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

vs OLZ - Luo 2007 *{published data only}*
Luo C, Yang JW, Ren JP. Comparative study of the effect of olanzapine on serum lipid in schizophrenia. *Journal of Clinical Psychiatric Medicine* 2007;**17**:401–2.

vs OLZ - Wang 2002 *{published data only}*
Wang CH, Zhao Z, Li Y, Pan M, Liu X. Evaluation of proximal therapeutic effect and distal social function restoration of olanzapine on schizophrenia patients. *Zhongguo lin chuang kang fu [Chinese Journal of Clinical Rehabilitation]* 2002;**6**(17):2664–5.

vs OLZ - Wang 2008 *{published data only}*
Wang Q, Li L, Wang T. A comparative study of olanzapine in treatment of schizophrenia. *Journal of Psychiatry* 2008; **21**:373–5.

vs OLZ - Wu 2008 *{published data only}*
Wu Y, Lu WH, Yi ZH, Wang J, Song BF, Shi DQ, et al. Controlled study of olanzapine versus chlorpromazine for the quality of life of patients with schizophrenia. *Sichuan Mental Health Journal* 2008;**21**(1):8–11.

vs OLZ - Zhao 2006 *{published data only}*
Zhao Z, Yan F, Feng Y. A comparative study on olanzapine and chlorpromazine in the treatment of schizophrenia. *China Journal of Health Psychology* 2006;**14**:41–2.

vs QTP - Ai 2007 *{published data only}*
Ai L. A comparative study of efficacy and safety of seroquel versus chlorpromazine in the treatment of schizophrenia. *Heilongjiang Medical Journal* 2007;**31**(4):285.

vs QTP - An 2005 *{published data only}*
An QH, Hu KY, Meng XL. A comparison of intelligence disorders and memory disorders in the first-onset schizophrenia treated with quetiapine and chlorpromazine. *Chinese Journal of Behavioral Medical Science* 2005;**14**(1): 62–3.

vs QTP - Cai 2006 *{published data only}*
Cai DM. Clinical comparative study of quetiapine and chlorpromazine in the treatment of schizophrenia. *Medical Journal of Chinese People's Health* 2006;**18**(4):281–2.

vs QTP - Cai 2007 *{published data only}*
Cai Q, Wang Z, Lin Y, Zhang X. Quetiapine and chlorpromazine in the treatment of schizophrenia: a random, controlled trial. *Shanghai Archives of Psychiatry* 2007;**19**(1):12–4.

vs QTP - Cao 2005 *{published data only}*
Cao D, Xie SP, Chen QB, Yuan YG, Fang Q. Characteristics of the sexual disturbance caused by chlorpromazine, risperidone, quetiapine and olanzapine and their associations with the changes of blood glucose and blood lipids in male patients with schizophrenia. *Chinese Journal of Clinical Rehabilitation [Zhongguo Lin Chuang Kang Fu]* 2005;**9**(36): 63–8.

vs QTP - Chen 2001 *{published data only}*
* Chen J, Zhao J, Li L. Multi-center, double blind control study of domestic manufactured quetiapine on schizophrenia. *Chinese Journal of Psychiatry* 2001;**34**(4): 193–6.
Zhao JP, Chen JD, Chen YG, Shu L, Ma C. A double-blind and double-dummy comparative study of quetiapine and chlorpromazine in the treatment of schizophrenia. *Chinese New Drugs Journal* 2002;**11**(2):149–51.

vs QTP - Chen 2007 *{published data only}*
Chen F, Chen Y, Zhou B, Cheng F, Liu Y, Zho XW, et al. Quetiapine treatment in schizophrenia curative effect and quality of life. *Journal of Clinical Psychiatry [Linchuang Jingshen Yixue Zazhi]* 2007;**17**(5):319–20.

vs QTP - Chen 2008 *{published data only}*
Chen S. Quetiapine and chlorpromazine in the treatment of schizophrenia. *Medical Journal of Chinese People's Health* 2008;**20**(7):660.

vs QTP - Cheng 2003 *{published data only}*
Cheng XF. Control observation of quetiapine vs chlorpromazine in schizophrenia. *Journal of Clinical Psychosomatic Diseases* 2003;**9**(2):78–80.

vs QTP - Deng 2004 *{published data only}*
Deng YF, Liu CY, Liu ZR, Zhang W.

利培酮合用氯硝西泮治疗精神分裂症急性期兴奋状态疗效观察.

中国实用内科杂志 2004;**24**:496–7.

vs QTP - Guo 2003a *{published data only}*
Guo BY, Wang YB. Control studies on efficacy of quetiapine vs chlorpromazine in first - episode schizophrenics. *Journal of Clinical Psychosomatic Diseases* 2003;**9**(2):75–7.

vs QTP - Guo 2003b *{published data only}*
Guo P, Guo H, Yang C. A comparative study on the effects of quetiapine and chlorpromazine upon the life quality of patients with schizophrenia. *Nervous Diseases and Mental Hygiene* 2003;**3**(6):454–5.

vs QTP - Guo 2005 *{published data only}*
Guo HR, Song SY. Domestic quetiapine and chlorpromazine in the treatment of schizophrenia in controlled clinical studies. *Modern Journal of Integrated Traditional Chinese and Western Medicine* 2005;**14**:443–4.

vs QTP - Guo 2006 *{published data only}*
Guo XF, Zhao JP, Chen JD, Zhang ZC. The effect of chlorpromazine and quetiapine on serum lipid and glucose. *Journal of Clinical Psychiatry* 2006;**16**(5):257–9.

vs QTP - Guo 2007 *{published data only}*
Guo J, Cao C, Wu D. Effect of quetiapine and chlorpromazine on cognitive function in first-episode schizophrenic. *Chinese Journal of Health Psychology* 2007;**15** (7):583–4.

vs QTP - Guo 2008 *{published data only}*
Guo Z, Liu J, Yang J. Efficacy quetiapine in the treatment of schizophrenic patients and effect on the quality of life. *Chinese Journal of Health Psychology* 2008;**16**(5):544–6.

vs QTP - He 2003 *{published data only}*
He YD, Zhao CM, Shao AL, Chen YN. A comparative study of quetiapine and chlorpromazine in the treatment of

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

patients with schizophrenia. *Herald of Medicine* 2003;**22** (10):680–2.

vs QTP - Hu 2003 ***{published data only}***
Hu JM, Li Yi, Li Tao, Wang HM, Liu XH, Huo KJ. The effects of antipsychotics on serum prolactin in the first-episode schizophrenia patients. *West China Journal of Pharmaceutical Sciences* 2003;**18**(6):467–9.

vs QTP - Ji 2004 ***{published data only}***
Ji J, Ou W. Comparative study between the quality of life and its curative effect in schizophrenic patients treated with quetiapine or chlorpromazine. *Sichuan Mental Health* 2004; **17**(2):73–5.

vs QTP - Jiang 2006 ***{published data only}***
Jiang KD, Bai YL, Peng DH, Tang MQ, Fan JX, Ma JS. A random and controlled study of quetiapine and chlorpromazine in patients with schizophrenia. *Journal of Clinical Psychiatry [Linchuang Jingshen Yixue Zazhi]* 2006; **16**(6):352–3.

vs QTP - Jiang 2008 ***{published data only}***
Jiang GQ, Luo J. A controlled study of quetiapine and chlorpromazine for schizophrenia. *Chongqing Journal of Medicine* 2008;**37**(16):1835–6.

vs QTP - Jin 2007 ***{published data only}***
Jin S, Liu S, Sang W, Zhao M. Seroquel and chlorpromazine in treatment of schizophrenia: a random, controlled trial. *China Pharmaceuticals* 2007;**16**(19):56–7.

vs QTP - Kong 2003 ***{published data only}***
Kong DL, Zhang SQ, Shu MQ. Effects of quetiapine and chlorpromazine on serum prolactin of schizophrenics. *Journal of Clinical Psychosomatic Diseases* 2003;**9**(4):200–1.

vs QTP - Li 2003 ***{published data only}***
Li M, Hu F, Wang S. A study of quetiapine and chlorpromazine on the effects and quality of life in the treatment of schizophrenia. *Shandong Archives of Psychiatry* 2003;**16**(3):135–7.

vs QTP - Li 2010 ***{published data only}***
Li YQ, Zhuang JH. Quetiapine and chlorpromazine in the treatment of schizophrenia with depression. *Journal of Qiqi ha-er Medical College* 2010;**31**(3):395.

vs QTP - Liu 2003 ***{published data only}***
Liu SF, Qin X. Quetiapine for late onset schizophrenia. *Shandong Archive of Psychiatry* 2003;**16**(3):164.

vs QTP - Mei 2007 ***{published data only}***
Mei AC. Comparison of efficacy and safety of quetiapine and chlorpromazine in the treatment of schizophrenia. *Medical Journal of Chinese People's Health* 2007;**19**(17): 723–4.

vs QTP - Nai 2007 ***{published data only}***
Nai X, Hu X, Qiu S. Effect of quetiapine on cognition function of patients with first episode schizophrenia. *Journal of Medical Forum* 2007;**28**(2):38–9.

vs QTP - NCT00882518 ***{published data only}***
NCT00882518. Efficacy and safety of quetiapine fumarate in the treatment of schizophrenic patients. http://www.clinicaltrials.gov (accessed 28 February 2012).

vs QTP - Peng 2006 ***{published data only}***
Peng ZG, Zhou JX, Kuang WH, Li J, Huang MS. A randomized double - blind controlled study on the efficacy of quetiapine and chlorpromazine in treatment of schizophrenia. *West China Journal of Pharmaceutical Sciences* 2006;**21**(6):606–8.

vs QTP - Peuskens 1997 ***{published data only}***
Peuskens J, Link CGG. A comparison of quetiapine and chlorpromazine in the treatment of schizophrenia. *Acta Psychiatrica Scandinavica* 1997;**96**(4):265–73.

vs QTP - Sun 2006 ***{published data only}***
Sun XD, Zhou SB, Li ZM, Han ZF. Effect of cognitive function in first-episode schizophrenia treated with quetiapine. *Journal of Clinical Psychiatry* 2006;**16**(2):94–5.

vs QTP - Tian 2006 ***{published data only}***
Tian H, He Q, Du L, Wu R, Hui S, Zheng Q, et al. Comparative study on the effect of seroquel and chlorpromazine on schizophrenia. *China Pharmacy* 2006; **17**(9):682–3.

vs QTP - Wan 2002 ***{published data only}***
Wan C, Lan SZ, Zhu XJ, Liao B, Wan J. A double blind controlled study of quetiapine and chlorpromazine for schizophrenia. *Journal of Yichun University* 2002;**24**(2): 55–6.

vs QTP - Wan 2008 ***{published data only}***
Wan ZY, Mei HB. A controlled study of quetiapine and chlorpromazine for schizophrenia. *Medical Journal of Chinese People's Health* 2008;**20**(11):1151–3.

vs QTP - Wang 2004 ***{published data only}***
Wang XL, Jiang F, Li T. Comparison of efficacy and safety of quetiapine and larctigal in the treatment of schizophrenia. *Chinese Journal of Behavioral Medical Science* 2004;**13**(3): 288–90.

vs QTP - Wang 2005 ***{published data only}***
Wang H, Peng D, Bai Y. Efficacy of quetiapine in the treatment of female patients with schizophrenia. *Shanghai Archives of Psychiatry* 2005;**17**(2):83–6.

vs QTP - Yang 2007 ***{published data only}***
Yang L, Yuan YG. Quetiapine and chlorpromazine in the treatment of people with schizophrenia. *Medical Journal of Chinese People's Health* 2007;**19**(12):1050–1.

vs QTP - Zhang 2002 ***{published data only}***
Zhang S, Li Y, Xu J. A double-blind study of domestic quetiapine and chlorpromazine in the treatment of schizophrenia. *Shandong Archives of Psychiatry* 2002;**15**(3): 149–51.

vs QTP - Zhang 2003 ***{published data only}***
Zhang HY, Wang X, Liu C, Shu L, Li H, Gu N, et al. A comparison study on efficacy and safety of quetiapine and chlorpromazine in the treatment of schizophrenia. *Chinese Journal of Clinical Pharmacology* 2003;**19**(3):163–6.

vs QTP - Zhang 2006 ***{published data only}***
Ma J. Quetiapine and chlorpromazine in the treatment of first-episode schizophrenia controlled clinical studies.

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Chinese Clinical Practical Medicine 2007; Vol. 1, issue 2: 51–2.

Ma J. Quetiapine and chlorpromazine in the treatment of first-episode schizophrenia controlled clinical studies. *Journal of Qiqihar Medical College [Qiqihar Yixueyuan Xuebao]* 2007;**28**(9):1038–9.

* Zhang W, Ma JG, Xu FL. Comparison study on treatment of primary schizophrenia with quetiapine and chlorpromazine. *Heilongjiang Nursing Journal [Modern Nursing]* 2006;**30**(2):81–2.

vs QTP - Zhang 2008 ***{published data only}***

Zhang J. A controlled study of quetiapine and chlorpromazine for schizophrenia. *Neurological Disorders and Mental Health* 2008;**8**(2):149–50.

vs QTP - Zhou 2003 ***{published data only}***

Zhou J, Li J, Kuang W. Comparison between quetiapine and chlorpromazine in cognitive function of schizophrenic patients. *Chinese Mental Health Journal* 2003;**17**(10): 699–701.

vs QTP - Zhou 2004 ***{published data only}***

Zhou SB, Sun XD, Li YM. A comparative study on quetiapine and chlorpromazine in the treatment of schizophrenia. *Medical Journal of Chinese People's Health* 2004;**16**(11):657–9.

vs QTP - Zou 2006 ***{published data only}***

Zou X, Zhou Y, Zhang W. Study on quetiapine and chlorpromazine in treatment of schizophrenia. *China Pharmaceuticals* 2006;**15**(12):51–2.

vs RPD - Chang 1998 ***{published data only}***

Chang SL, Wang GH. Clinical observation of risperidone and chlorpromazine in the treatment of schizophrenia. Anhui Medical and Pharmaceutical Journal 1998; Vol. 2: 25–6.

vs RPD - Cui 2001 ***{published data only}***

Cui L. Risperidone and chlorpromazine in the treatment of schizophrenia, double-blind, controlled study, and serum prolactin efficacy. *Hebei Archive of Psychiatry* 2001;**14**: 205–8.

vs RPD - Feng 2003 ***{published data only}***

Feng YX, Sun F. A comparative study on the effects of risperidone and chlorpromazine upon the life quality of patients with schizophrenia. *Health Psychology Journal* 2003; **11**:117–8.

vs RPD - He 1999 ***{published data only}***

He M, Feng Y, Chen R. A controlled comparative study on risperidone and chlorpromazine in treatment of schizophrenia. *Chinese New Drugs Journal* 1999;**8**:185–7.

vs RPD - Lin 2005 ***{published data only}***

Lin WX. Risperidone and chlorpromazine in the treatment of clinical controlled study of 70 patients with schizophrenia. *Modern Chinese Practical Medicine Journal* 2005;**4**:27–8.

vs RPD - Liu 2000 ***{published data only}***

Liu Y, Huang X, Xie L. A comparative study of risperidone and chlorpromazine in the treatment of the negative symptoms of schizophrenia. *Journal of Medicine and Pharmacy* 2000;**19**:323–4.

vs RPD - Liu 2005 ***{published data only}***

Liu GR, Zhang YH. Risperidone and chlorpromazine on schizophrenia blood pressure, heart rate. *Occupation and Health* 2005;**21**:443–5.

vs RPD - Luo 2001 ***{published data only}***

Luo X, Jiang K, Gu N, Yang X, Zhu S. Comparison of effects and factors between risperidone and chlorpromazine on schizophrenia. *Chinese Journal of New Drugs and Clinical Remedies* 2001;**20**:264–6.

vs RPD - Ma 2004 ***{published data only}***

Ma Z H, Liu A Y, Zhou C M, Zhang Z. A comparative study of risperidone and chlorpromazine in the treatment of schizophrenia. *Medical Journal of Chinese People Health* 2004;**16**:202–4.

vs RPD - Wang 2002 ***{published data only}***

Wang Q, Jia C. Controlled study of risperidone and chlorpromazine in the treatment of schizophrenia. *Health Psychology Journal* 2002;**10**:226–8.

vs RPD - Wang 2005 ***{published data only}***

Wang X, Hu X, Yang J. Effect of chlorpromazine and risperidone on cognitive function of the patients with first episode schizophrenia. *Chinese Journal of Health Psychology* 2005;**13**:342–4.

vs RPD - Wu 2002 ***{published data only}***

Wu S, Xing G. A comparative trial on the efficacy of risperidone vs chlorpromazine in chronic schizophrenia. *Health Psychology Journal* 2002;**10**:364–5.

vs RPD - Wu 2004 ***{published data only}***

Wu Y, Lu W, Yi Z. A comparative study of risperidone and chlorpromazine on quality of life in patients with schizophrenia. *Shandong Archive of Psychiatry* 2004;**17**: 137–40.

vs RPD - Zheng 2001 ***{published data only}***

Zheng ZS, Huang JM, Yu XY. Efficacy of risperidone and chlorpromazine in the treatment of schizophrenia. *Chinese Hospital Pharmacy Journal* 2001;**21**:99–100.

References to studies excluded from this review

Appelberg 2004 ***{published data only}***

Appelberg B, Sintonen H, Tuisku K, Joffe G. Is it worthwhile to change clinically stable schizophrenic outpatients with mild to moderate residual symptoms and/or side effects from conventional to atypical antipsychotics? - a randomised study with olanzapine. Proceedings of the 12th Biennial Winter Workshop on Schizophrenia; 2004 Feb 7-13; Davos, Switzerland. 2004.

Appelberg B, Tuisku K, Joffe G. Is it worth while changing clinically stable schizophrenic out-patients with mild to moderate residual symptoms and/or side effects from conventional to atypical antipsychotics? A prospective, randomised study with olanzapine. *European Psychiatry* 2004;**19**(8):516–8.

Appelberg B, Tuisku K, Joffe G. Is it worthwhile changing clinically stable schizophrenic out-patients with mild to moderate residual symptoms and/or side effects from

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

conventional to atypical antipsychotics?. *Schizophrenia Research* 2004;**67**(1):140–1.
Joffe G, Sintonen H, Appelberg B. Shift from first generation antipsychotics to olanzapine may improve health-related quality of life of stable but residually symptomatic schizophrenic outpatients: a prospective, randomized study. *International Journal of Technology Assessment in Health Care* 2008;**24**(4):399–402.

Beuzen 1998 (HGCF) ***{published and unpublished data}***
Beasley CM, Beuzen JN, Birkett MA. [Olanzapine versus clozapine: an international double–blind study in the treatment of patients with treatment–resistent schizophrenia]. New Clinical Drug Evaluation Unit (NCDEU) Meeting; 1999 June 12-15; Boca Raton, FL, USA. 1999.
Beasley CM, Beuzen JN, Birkett MA. Olanzapine versus clozapine: an international double-blind study in the treatment of patients with treatment-resistent schizophrenia. American College of Neuropsychopharmacology Annual Meeting. Hawaii, 1998.
Beasley CM, Beuzen JN, Birkett MA. Olanzapine versus clozapine: an international double-blind study in the treatment of patients with treatment-resistent schizophrenia. American Psychiatric Association Meeting; 1999 January 31 - February 2; Washington, DC, USA. 1999.
Beasley CM, Beuzen JN, Birkett MA. Olanzapine versus clozapine: an international double-blind study in the treatment of patients with treatment-resistent schizophrenia. World Psychiatric Association; 1999 August 6-11; Hamburg, Germany. 1999.
* Beuzen JN, Birkett M, Kiesler G, Wood A. Olanzapine versus clozapine in resistant schizophrenic patients - results of an international double-blind randomised clinical trial. Proceedings of XXIst Collegium Internationale Neuro-psychopharmacologicum; 1998 July 12-16; Glasgow, UK. 1998.
Beuzen JN, Birkett MA, Kiesler GM. An investigation of subgroup effects in a study of olanzapine versus clozapine in the treatment of resistant schizophrenic patients. *European Neuropsychopharmacology* 1998;**8**(Suppl 2):S226–7.
David SR, Meehan KM, Sutton VK, Taylor CC. Treatment of negative symptoms with olanzapine in comparison with other novel antipsychotic agents. *International Journal of Neuropsychopharmacology* 2000;**3**(Suppl 1):S140.
Dossenbach M, Bitter I, Slabber M, Pretorius J, Bartko GY, Banics Z, et al. Olanzapine versus clozapine in patients nonresponsive or intolerant to standard acceptable treatment for schizophrenia. 153rd Annual Meeting of the American Psychiatric Association; 2000 May 13-18; Chicago, USA. 2000.
Dossenbach M, Bitter I, Slabber M, Pretorius J, Bartko GY, Banics Z, et al. Olanzapine versus clozapine in patients nonresponsive or intolerant to standard acceptable treatment for schizophrenia. 155th Annual Meeting of the American Psychiatric Association; 2002 May 18-23; Philadelphia, PA, USA. 2002.
Dossenbach M, Slabber M, Martenyi F, Bartko G, Bitter I. Olanzapine vs. clozapine in patients non responsive or intolerant to standard acceptable treatment of schizophrenia. 11th World Congress of Psychiatry; 1999 Aug 6-11; Hamburg, Germany. 1999:148.
Jean-Noel B, Wood AJ, Kiesler GM, Birkett M, Tollefson GD. Olanzapine vs. clozapine: an international double blind study in the treatment of resistant schizophrenia. 11th World Congress of Psychiatry; 1999 Aug 6-11; Hamburg, Germany. 1999:143.
Tollefson GD, Birkett MA, Kiesler GM, Wood AJ, Lilly Resistant Schizophrenia Study Group. Double-blind comparison of olanzapine versus clozapine in schizophrenic patients clinically eligible for treatment with clozapine. *Biological Psychiatry* 2001;**49**(1):52–63.

Bouchard 1998 ***{published data only}***
Bouchard RH. A comparative longitudinal study of risperidone versus classic neuroleptic drugs in the treatment of schizophrenia: 24 months observation. *Journal of Clinical Psychopharmacology* 2002;**28**:31–2.
Bouchard RH, Demers MF, Merette E, Pourcher E. Classical neuroleptics (CNLP) vs risperidone (RIS) interim 12 months efficacy analysis of a long-term, naturalistic study in schizophrenia. 21st Congress of the Collegium Internationale Neuro-Psychopharmacologicum (CINP); 1998 Jul 12-16; Glassgow, UK. 1998.
Bouchard RH, Merette C, Demers MF, Roy-Gagnon MH. Risperidone versus classical neuroleptics: preliminary results of a prospective naturalistic one year study. 151st Annual Meeting of the American Psychiatric Association; 1998 May 30-Jun 4; Toronto. Toronto, Canada, 1998:180.
Bouchard RH, Mérette C, Pourcher E, Demers MF, Villeneuve J, Roy Gagnon MH, et al. Longitudinal comparative study of risperidone and conventional neuroleptics for treating patients with schizophrenia. The Quebec Schizophrenia Study Group. *Journal of Clinical Psychopharmacology* 2000;**20**(3):295–304.
Bouchard RH, Pourcher E, Merette C, Demers MF, Villeneuve J, Roy Gagnon MH, et al. One-year follow-up of schizophrenic patients treated with risperidone or classical neuroleptics: a prospective, randomized, multicentred open-study. 11th Congress of the European College of Neuropsychoharmacology; 1998 Oct 31- Nov 4; Paris, France. 1998.
Bouchard RH, Pourcher E, Merette C, Demers MF, Villeneuve J, Roy MA, et al. Risperidone advantages in chronic schizophrenic patients: a 1-year effectiveness study. *Schizophrenia Research* 1999;**36**(1-3):271.

Chen 2001 ***{published data only}***
Chen GY, Li B, Li C. Clinical observation on schizophrenic patients treated with risperidone. *Journal of Clinical Psychiatry* 2001;**11**:325–8.

Conley 1998 ***{published data only}***
Conley R, Gounaris C. Demographic differences in olanzapine responders with therapy-refractory schizophrenia. Schizophrenia Research the VIth International Congress on Schizophrenia Research;1997

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

April 12-16; Colorado Springs, CO. 1997; Vol. 24 Suppl: 189.
* Conley RR, Tamminga CA, Bartko JJ, Richardson C, Peszke M, Lingle J, et al. Olanzapine compared with chlorpromazine in treatment-resistant schizophrenia. *American Journal of Psychiatry* 1998;**155**(7):914–20.
Conley RR, Tamminga CA, Beasley C. Olanzapine vs chlorpromazine in therapy-refractory schizophrenia. Schizophrenia Research, The VIth International Congress on Schizophrenia Research; 1997 April 12-16; Colorado Springs, CO. 1997; Vol. 24 Suppl:189.
Conley RR, Tamminga CA, Beasley C. Olanzapine vs. chlorpromazine in treatment-resistant schizophrenia. *Biological Psychiatry* 1997;**41**:1S–120S.
Conley RR, Tamminga CA, Beasley C, Maryland Study Group. Olanzapine vs. chlorpromazine in treatment-resistant schizophrenia. *Biological Psychiatry* 1997;**41**:73S.
Kelly DL, Conley RR, Tamminga CA. Differential olanzapine plasma concentrations by sex in a fixed-dose study. *Schizophrenia Research* 1999;**40**(2):101–4. [CSG NO. 4333]
Richardson C, Conley R. Olanzapine response in schizophrenic subjects with neuroleptic resistant disorganization. Schizophrenia Research, The VIth International Congress on Schizophrenia Research; 1997 April 12-16; Colorado Springs, CO. 1997; Vol. 24 Suppl: 191.

Czekalla 2001 ***{published data only}***
Czekalla J, Beasley CM Jr, Dellva MA, Berg PH, Grundy S. Analysis of the QTc interval during olanzapine treatment of patients with schizophrenia and related psychosis. *Journal of Clinical Psychiatry* 2001;**62**(3):191–8.

de Jesus Mari 2004 ***{published data only}***
de Jesus Mari J, Lima MS, Costa AN, Alexandrino N, Rodrigues-Filho S, de Oliveira IR, et al. The prevalence of tardive dyskinesia after a nine month naturalistic randomized trial comparing olanzapine with conventional treatment for schizophrenia and related disorders. *European Archives of Psychiatry and Clinical Neuroscience* 2004;**254**(6): 356–61.

Edgell 1998 ***{published data only}***
David SR, Meehan KM, Sutton VK, Taylor CC. Treatment of negative symptoms with olanzapine in comparison with other novel antipsychotic agents. *International Journal of Neuropsychopharmacology* 2000;**3**(Suppl 1):S140.
* Edgell ET, Andersen SW, Grainger D, Wang J. Resource use and quality of life of olanzapine compared with risperidone: results from an international randomized clinical trial. XXIst Collegium Internationale Neuro-psychopharmacologicum; 1998, July 12-16; Glasgow, UK. 1998.

Feng 2001 ***{published data only}***
Feng CX, Huang SX, Yang HZ. A comparative trial on the efficacy of risperidone vs chlorpromazine in treatment-resistant schizophrenia. *Shandong Archive of Psychiatry* 2001;**14**:95–6.

Hu 2005 ***{published data only}***
Hu TS. Comparative analysis of the positive symptoms of schizophrenia treated with risperidone. *Chinese Journal of Behavioral Medical Science* 2005;**14**:428.

Huang 2000a ***{published data only}***
Huang SX, Feng CX, Chen JY, Liu DQ. Risperidone vs chlorpromazine in treating schizophrenia: a randomized double-blind study. *Chinese Journal of New Drugs and Clinical Remedies* 2000;**19**:396–8.

Huang 2000b ***{published data only}***
Huang YH, Luo BM. Risperidone and chlorpromazine, clozapine drug-control study. *Chinese Journal of New Drugs and Clinical Remedies* 2000;**8**:210–1.

Kostakoglu 2001 ***{published data only}***
Kostakoglu E, Alptekin K, Kivircik BB, Dossenbach M, Tunca Z, Gogus A. Olanzapine vs. chlorpromazine- 6 weeks treatment of acute schizophrenia. *Journal of European College of Neuropsychopharmacology* 2001;**11**:S369.

Li 2007 ***{published data only}***
Li Z. Initial searching for the early influence and interfere about the regulating function of the blood-glucose affected by chlorpromazine and risperidal. *Journal of Health and Well Being* 2007;**4**:18–20.

Pappas 1997 ***{published data only}***
Pappas D, Konitsiotis S, Liakos A. Risperidone in the treatment of acute schizophrenic episodes. *European Neuropsychopharmacology* 1997;**7**:S206.

Qu 2006 ***{published data only}***
Qu ZW, Chen MD, Gu JQ, Fu WZ, Wang T, Gu LM, et al. Metabolism of the blood-glucose that affected by chlorpromazine or risperidone treatment. *Journal of Clinical Psychiatric Medicine [Linchuang Jingshen Yixue Zazhi]* 2006; **16**:68–70.

Shi 2007 ***{published data only}***
Shi Y, Wang Y, Li R. Effects of risperidone on NEF of eye movements in the first-episode schizophrenia. *Journal of Clinical Psychosomatic Diseases* 2007;**13**:487–9.

Su 2002 ***{published data only}***
Su YQ. Effects of low dosage risperdal to treat the first attack of schizophrenia. *Youjiang Medical Journal* 2002;**30**:380–1.

Tian 2005 ***{published data only}***
Tian R. Risperidone combined with chlorpromazine in the treatment of insomnia clinical observation of patients with schizophrenia. *Journal of Clinical Psychosomatic Diseases* 2005;**11**:151–2.

vs QTP - Arvanitis 1996 ***{published data only}***
Arvanitis LA, Miller BG. An atypical antipsychotic: results from a multiple fixed dose, placebo-controlled study. *European Neuropsychopharmacology* 1996;**6**:148.

vs QTP - AstraZeneca 2000 ***{published data only}***
AstraZeneca. A multicentre, double-blind, randomised trial to compare the effects of seroquel and chlorpromazine in patients with treatment-resistant schizophrenia (5077IL/ 0054 TRESS). http://www.clinicalstudyresults.org/ (accessed 28 February 2012).

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

vs QTP - AstraZeneca 2005 *{published data only}*
AstraZeneca. A multicenter, double-blind, randomized, comparison of quetiapine (seroquel®) and chlorpromazine in the treatment of subjects with treatment-resistant schizophrenia. http://www.clinicalstudyresults.org/ (accessed 28 February 2012).

vs QTP - Bai 2006 *{published data only}*
Bai H. Quetiapine and chlorpromazine in the treatment of schizophrenia. *Medical Journal of Chinese People's Health* 2006;**18**:1028–9.

vs QTP - Cai 2008 *{published data only}*
Cai J, Ji L, Liu X. Clinical effects comparison of quetiapine and chlorpromazine hydrochloride in treatment of female schizophrenia. *China Pharmaceuticals* 2008;**17**(21):52–3.

vs QTP - Du 2004 *{published data only}*
Du QX, Yu CF, Zhong W. A clinical comparative analysis of quetiapine and chlorpromazine in treatment of schizophrenia. *Medical Journal of Chinese People's Health* 2004;**16**(7):398–9.

vs QTP - Jiang 2004 *{published data only}*
Jiang K. Quetiapine vs chlorpromazine for schizophrenia - a multi-centre, randomized controlled clinical trial. Proceedings of the 1st Chinese National Conference of Psycho-Neuroscience; 2004 Unknown Dates; Changsha, China. Changsha, China, 2004:106.

vs QTP - Li 2005 *{published data only}*
Li YQ. Comparative analysis of side effects of quetiapine and chlorpromazine in the treatment of schizophrenia. *Practical Clinical Medicine* 2005;**6**:26–7.

vs QTP - Ma 2004 *{published data only}*
Ma ZW, Li MX, Shi YZ, Wang LH. Quetiapine (35 patients) vs chlorpromazine (34 patients) in treatment of schizophrenia. *Chinese Journal of New Drugs and Clinical Remedies* 2004;**23**(5):273–5.

vs QTP - Ning 2008 *{published data only}*
Ning Z, Liu S, Jin S. A comparison of cognitive function in first episode schizophrenia treated with seroquel or chlorpromazine. *Chinese Journal of Health Psychology* 2008; **16**(2):138–40.

vs QTP - Tang 2004 *{published data only}*
Tang Y. Quetiapine and chlorpromazine in the treatment of schizophrenia observed. *Chinese Modern Medicine* 2004;**3** (11):14.

vs QTP - Tang 2008 *{published data only}*
Tang CG, Wang RC. Comparison of efficacy and safety of quetiapine and chlorpromazine in the treatment of schizophrenia. *Medical Journal of Chinese People's Health* 2008;**20**(9):917–8.

vs QTP - Wang 2007 *{published data only}*
Wang Y, Li G, Xue JW, Li T. A comparative study of effects of quetiapine and chlorpromazine on the brain blood stream dynamics in the treatment of schizophrenia. *Linchuang Jingshen Yixue Zazhi* 2007;**17**(4):255–6.

vs QTP - Zhang 2007 *{published data only}*
Zhang L. A comparative study of quetiapine and chlorpromazine in the treatment of schizophrenia. *Chinese Modern Medicine and Pharmacy* 2007;**9**(2):97–8.

vs QTP - Zhong 2005 *{published data only}*
Zhong CL, Cui YH. Comparative study of influence of quetiapine on life quality in schizophrenic patients. *Journal of Clinical Psychological Medicine* 2005;**15**(2):103–5.

Wang 1998 *{published data only}*
Wang L, Song J, Su G. Random comparing research on the treatment of schizophrenia by risperidone and chlorpromazine. *Tianjin Pharmacy* 1998;**10**:57–60.

Wang 2004 *{published data only}*
Wang LG, Liu Y, Wan H. A comparative trial of the efficacy on olanzapine and chlorpromazine in treatment-resistant schizophrenia. *Heath Psychology Journal* 2004;**12**:203–4.

Wang 2006 *{published data only}*
Wang T. Study on influence of the short - term therapy by chlorpromazine or risperidal on 2hPG. *Journal of Qiqihar Medical College [Qiqihar Yixueyuan Xuebao]* 2006;**27**: 1417–8.

Xiong 2004 *{published data only}*
Xiong Y. Comparison study of childhood schizophrenia treated with risperidone and chlorpromazine. *Guizhou Medical Journal* 2004;**28**:697–8.

Yu 2001 *{published data only}*
Yu J, Chai M, Chen J. A comparison of cognitive function in schizophrenia treated with risperidone and chlorpromazine. *Journal of Clinical Psychological Medicine* 2001;**11**:265–6.

Yuan 2006 *{published data only}*
Yuan J, Qu WZ. The first use of chlorpromazine and risperidone on glucose metabolism in patients with schizophrenia. *Sichuan Mental Health* 2006;**19**:197–9.

Zou 2005 *{published data only}*
Zou QL, Fan JH, Chen SQ. A comparative trial on the efficacy of risperidone vs chlorpromazine in the treatment of chronic schizophrenia. *Medical Journal of Chinese People's Health* 2005;**17**:153–4.

Additional references

Adams 2005
Adams CE, Rathbone J, Thornley B, Clarke M, Borrill J, Wahlbeck K, et al. Chlorpromazine for schizophrenia: a Cochrane systematic review of 50 years of randomised controlled trials. *BMC Medicine* 2005;**3**:15. [DOI: 10.1186/1741-7015-3-15]

Adams 2006
Adams CE, Tharyan P, Coutinho ES, Stroup TS. The schizophrenia drug-treatment paradox: pharmacological treatment based on best possible evidence may be hardest to practise in high-income countries. *British Journal of Psychiatry* 2006;**189**:391–2. [PUBMED: 17077426]

Adams 2014
Adams CE, Awad G, Rathbone J, Thornley B. Chlorpromazine versus placebo for schizophrenia. *Cochrane*

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Database of Systematic Reviews 2014, Issue 1. [DOI: 10.1002/14651858.CD000284.pub3]

Ahmed 2010
Ahmed U, Jones H, Adams CE. Chlorpromazine for psychosis induced aggression or agitation. *Cochrane Database of Systematic Reviews* 2010, Issue 4. [DOI: 10.1002/14651858.CD007445.pub2]

Almerie 2007
Almerie MQ, Alkhateeb H, Essali A, Matar HE, Rezk E. Cessation of medication for people with schizophrenia already stable on chlorpromazine. *Cochrane Database of Systematic Reviews* 2007, Issue 1. [DOI: 10.1002/14651858.CD006329]

Altman 1996
Altman DG, Bland JM. Detecting skewness from summary information. *BMJ* 1996;**313**(7066):1200.

Andreasen 1982
Andreasen NC. Negative symptoms in schizophrenia. Definition and reliability. *Archives of General Psychiatry* 1982;**39**(7):784–8.

Andreasen 1984
Andreasen NC. *Scale for the Assessment of Positive Symptoms (SANS)*. Iowa City: University of Iowa, 1984.

Anon 2010
Anon. Scientific fraud: action needed in China. *Lancet* 2010;**375**(9709):94.

Arana 2000
Arana GW. An overview of side effects caused by typical antipsychotics. *Journal of Clinical Psychiatry* 2000;**61**(Suppl 8):5–11.

Bian 2008
Bian Q, Kato T, Monji A, Hashioka S, Mizoguchi Y, Horikawa H, et al. The effect of atypical antipsychotic drugs, perospirone, ziprasidone and quetiapine on microglial activation induced by interferon-gamma. *Progress in Neuro-Psychopharmacology and Biological Psychiatry* 2008; **32**(1):42–8.

Bland 1978
Bland RC, Parker JH, Orn H. Prognosis in schizophrenia. Prognostic predictors and outcome. *Archives of General Psychiatry* 1978;**35**(1):72–7. [DOI: 10.1001/archpsyc.1978.01770250074007]

Bland 1997
Bland JM, Kerry SM. Statistics notes. Trials randomised in clusters. *BMJ* 1997;**315**(7108):600.

Boissel 1999
Boissel JP, Cucherat M, Li W, Chatellier G, Gueyffier F, Buyse M, et al. The problem of therapeutic efficacy indices. 3. Comparison of the indices and their use [Apercu sur la problematique des indices d'efficacite therapeutique, 3: comparaison des indices et utilisation. Groupe d'etude des indices d'efficacite]. *Therapie* 1999;**54**(4):405–11. [PUBMED: 10667106]

Caccia 2010
Caccia S, Pasina L, Nobili A. New atypical antipsychotic drugs for schizophrenia: iloperidone. *Drug Design, Development and Therapy* 2010;**4**:33-48.

Chen 2002
Chen YF. Chinese classification of mental disorders (CCMD-3): towards integration in international classification. *Psychopathology* 2002;**35**(2-3):171–5.

Chouinard 1980
Chouinard G, Ross-Chouinard A, Annable L, Jones B. Extrapyramidal Symptom Rating Scale (abstract). *Canadian Journal of Neurogical Sciences* 1980;**7**:233.

Cincotta 2010
Cincotta SL, Rodefer JS. Emerging role of sertindole in the management of schizophrenia. *Neuropsychiatric Disease and Treatment* 2010;**7**:429–41.

Deeks 2000
Deeks J. Issues in the selection for meta-analyses of binary data. Proceedings of the 8th International Cochrane Colloquium; 2000 Oct 25-28; Cape Town. Cape Town: The Cochrane Collaboration, 2000.

Deeks 2011
Deeks JJ, Higgins JPT, Altman DG, on behalf of the Cochrane Statistical Methods Group. Chapter 9: Analysing data and undertaking meta-analyses. In: Higgins JPT, Green S (editors). Cochrane Handbook of Systematic Reviews of Interventions. Version 5.1.0 [updated March 2011]. The Cochrane Collaboration, 2011. Available from www.cochrane-handbook.org 2011.

Delay 1952
Delay J, Deniker P. The treatment of psychosis in a derivative of the neuroleptic hibernotherapie method [Le traitement des psychoses par une méthode neuroleptique dérivée de l'hibernothérapie]. In: Ossa PC editor(s). *CR Congrès des Médicins Aliénistes et Neurologistes de France et des Pays de Langue Française*. Paris: Masson, 1952:479.

Divine 1992
Divine GW, Brown JT, Frazier LM. The unit of analysis error in studies about physicians' patient care behavior. *Journal of General Internal Medicine* 1992;**7**(6):623–9.

Donner 2002
Donner A, Klar N. Issues in the meta-analysis of cluster randomized trials. *Statistics in Medicine* 2002;**21**(19): 2971–80.

DSM-IV 1994
American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 4th Edition. Washington DC: American Psychiatric Association, 1994.

DSM-IV-TR 2000
American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 4th Edition. Washington DC: American Psychiatric Association, 2000.

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Egger 1997
Egger M, Davey Smith G, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. *BMJ* 1997;**315**(7109):629–34.

Elbourne 2002
Elbourne D, Altman DG, Higgins JPT, Curtina F, Worthingtond HV, Vaile A. Meta-analyses involving cross-over trials: methodological issues. *International Journal of Epidemiology* 2002;**31**(1):140–9.

Flanagan 1982
Flanagan JC. Measurement of the quality of life: Current state of the art. *Archives of Physical Medicine and Rehabilitation* 1982;**63**(2):56–9.

Furukawa 2006
Furukawa TA, Barbui C, Cipriani A, Brambilla P, Watanabe N. Imputing missing standard deviations in meta-analyses can provide accurate results. *Journal of Clinical Epidemiology* 2006;**59**(1):7–10.

Gulliford 1999
Gulliford MC, Ukoumunne OC, Chinn S. Components of variance and intraclass correlations for the design of community-based surveys and intervention studies: data from the Health Survey for England 1994. *American Journal of Epidemiology* 1999;**149**(9):876–83.

Guy 1976
Guy W. *ECDEU Assessment Manual for Psychopharmacology*. Rockville, MD: National Institute of Mental Health. DHEW Publication NO (ADM), 1976:124–585.

Hamilton 1960
Hamilton M. A rating scale for depression. *Journal of Neurology, Neurosurgery and Psychiatry* 1960;**23**:56–62.

Higgins 2003
Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. *BMJ* 2003;**327** (7414):557–60.

Higgins 2011
Higgins JPT, Green S (editors). Cochrane Handbook for Systematic Reviews of Interventions. Version 5.1.0 [updated March 2011]. The Cochrane Collaboration, 2011. Available from www.cochrane-handbook.org.

Higgins 2011a
Higgins JPT, Deeks JJ. Chapter 7: Selecting studies and collecting data. In: Higgins JPT, Green S (editors). Cochrane Handbook of Systematic Reviews of Interventions. Version 5.1.0 [updated March 2011]. The Cochrane Collaboration, 2011. Available from www.cochrane-handbook.org 2011.

Higgins 2011b
Higgins JPT, Deeks JJ, Altman DG, on behalf of the Cochrane Statistical Methods Group. Chapter 16: Special topics in statistics. In: Higgins JPT, Green S (editors). Cochrane Handbook of Systematic Reviews of Interventions. Version 5.1.0 [updated March 2011]. The Cochrane Collaboration, 2011. Available from www.cochrane-handbook.org 2011.

Honigfeld 1965
Honigfeld G, Klett CJ. The nurses' observation scale for inpatient evaluation: a new scale for measuring improvement in chronic schizophrenia. *Journal of Clinical Psychology* 1965;**21**:65–71.

Hutton 2009
Hutton JL. Number needed to treat and number needed to harm are not the best way to report and assess the results of randomised clinical trials. *British Journal of Haematology* 2009;**146**(1):27–30.

ICD-10 1992
World Health Organization. F-20. *The ICD-10 Classification of Mental and Behavioural Disorders*. Geneva: Divison of Mental Health, WHO, 1992:86–109.

ICH E3 1995
ICH Expert Working Group. ICH harmonised tripartite guideline: structure and content of clinical study reports. International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use 30 November 1995.

Janssen 1988
Janssen PA, Niemegeers CJ, Awouters F, Schellekens KH, Megens AA, Meert TF. Pharmacology of risperidone (R 64 766), a new antipsychotic with serotonin-S2 and dopamine-D2 antagonistic properties. *Journal of Pharmacology and Experimental Therapeutics* 1988;**244**(2):685–93.

Kay 1986
Kay SR, Opler LA, Fiszbein A. *Positive and Negative Syndrome Scale (PANSS) Manual*. North Tonawanda, NY: Multi-Health Systems, 1986.

Kay 1987
Kay SR, Fiszbein A, Opler LA. The positive and negative syndrome scale (PANSS) for schizophrenia. *Schizophrenia Bulletin* 1987;**13**(2):261–76.

Kinon 1996
Kinon B J, Lieberman JA. Mechanisms of action of atypical antipsychotic drugs: a critical analysis. *Psychopharmacology* 1996;**124**(1-2):2–34. [DOI: 10.1007/BF02245602]

Kraeplin 1919
Kraeplin E. *Dementia Praecox and Paraphrenia*. Edinburgh: E&S Livingstone, 1919.

Laborit 1951
Laborit H, Huguenard P. Artificial hibernation by physical and pharmacodynamic means [L'hibernation artificielle par moyens pharmacodynamiques et physiques]. *Presse Médicale* 1951;**59**:1329.

Leucht 2005a
Leucht S, Kane JM, Kissling W, Hamann J, Etschel E, Engel R. Clinical implications of Brief Psychiatric Rating Scale scores. *British Journal of Psychiatry* 2005;**187**:366–71. [PUBMED: 16199797]

Leucht 2005b
Leucht S, Kane JM, Kissling W, Hamann J, Etschel E, Engel RR. What does the PANSS mean?. *Schizophrenia Research* 2005;**79**(2-3):231–8. [PUBMED: 15982856]

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Leucht 2007
Leucht S, Engel RR, Bäuml J, Davis JM. Is the superior efficacy of new generation antipsychotic drugs an artifact of LOCF?. *Schizophrenia Bulletin* 2007;**33**(1):183–91. [PUBMED: 16905632]

Leucht 2008
Leucht C, Kitzmantel M, Chua L, Kane J, Leucht S. Haloperidol versus chlorpromazine for schizophrenia. *Cochrane Database of Systematic Reviews* 2008, Issue 1. [DOI: 10.1002/14651858.CD004278.pub2]

Leucht 2009
Leucht S, Corves C, Arbter D, Engel RR, Li C, Davis JM. Second-generation versus first-generation antipsychotic drugs for schizophrenia: a meta-analysis. *Lancet* 2009;**373** (9657):31–41.

Liu 2009
Liu X, De Haan S. Chlorpromazine dose for people with schizophrenia. *Cochrane Database of Systematic Reviews* 2009, Issue 2. [DOI: 10.1002/14651858.CD007778]

Maier 1988
Maier W, Buller R, Philipp M, Heuser I. The Hamilton Anxiety Scale: reliability, validity and sensitivity to change in anxiety and depressive disorders. *Journal of Affective Disorders* 1988;**14**(1):61–8. [DOI: 10.1016/0165-0327 (88)90072-9]

Marshall 2000
Marshall M, Lockwood A, Bradley C, Adams C, Joy C, Fenton M. Unpublished rating scales: a major source of bias in randomised controlled trials of treatments for schizophrenia. *British Journal of Psychiatry* 2000;**176**: 249–52.

Mathews 2007
Mathews M, Muzina DJ. Atypical antipsychotics: new drugs, new challenges. *Cleveland Clinic Journal of Medicine* 2007;**74**(8):597–606.

McGrath 2008
McGrath J, Saha S, Chant D, Welham J. Schizophrenia: a concise overview of incidence, prevalence, and mortality. *Epidemiologic Reviews* 2008;**30**:67–76. [DOI: 10.1093/ epirev/mxn001]

Meltzer 1989
Meltzer HY. Clinical studies on the mechanism of action of clozapine: the dopamine-serotonin hypothesis of schizophrenia. *Psychopharmacology* 1989;**99 Suppl**:S18–27. [DOI: 10.1007/BF00442554]

Monchi 2001
Monchi O, Petrides M, Petre V, Worsley K, Dagher A. Wisconsin Card Sorting revisited: distinct neural circuits participating in different stages of the task identified by event-related functional magnetic resonance imaging. *The Journal of Neuroscience* 2001;**21**(19):7733–41.

Montgomery 1979
Montgomery SA, Asberg M. A new depression scale designed to be sensitive to change. *British Journal of Psychiatry* 1979;**134**:382–9.

Nadal 2001
Nadal R. Pharmacology of the atypical antipsychotic remoxipride, a dopamine D2 receptor antagonist. *CNS Drug Reviews* 2001;**7**(3):265–82.

Odejide 1982
Odejide AO, Ban TA. Psychotropic drug prescription pattern in a developing country (Nigeria). The need for an essential psychotherapeutic drug list. *International Pharmacopsychiatry* 1982;**17**(3):163–9.

Overall 1962
Overall JE, Gorham DR. The brief psychiatric rating scale. *Psychological Reports* 1962;**10**:799–812.

Parrott 1980
Parrott AC, Hindmarch I. The Leeds Sleep Evaluation Questionnaire in psychopharmacological Investigations - a review. *Psychopharmacology* 1980;**71**(2):173–9.

Risbood 2012
Risbood V, Lee JR, Roche-Desilets J, Fuller MA. Lurasidone: an atypical antipsychotic for schizophrenia. *Annals of Pharmacotherapy* 2012;**46**(7-8):1033–46.

Rossi 2006
Rossi A, Daneluzzo E, Tomassini A, Struglia F, Cavallaro F, Smeraldi E, et al. The effect of verbalization strategy on wisconsin card sorting test performance in schizophrenic patients receiving classical or atypical antipsychotics. *BMC Psychiatry* 2006;**6**:3.

Rzewuska 1988
Rzewuska M. Sulpiride: the best known atypical, safe neuroleptic drug. Review of literature. *Psychiatria Polska* 1998;**32**(5):655–66. [PUBMED: 9921002]

Saha 2005
Saha S, Chant D, Welham J, McGrath J. A systematic review of the prevalence of schizophrenia. *PLoS Medicine* 2005;**2**(5):e141. [DOI: 10.1371/journal.pmed.0020141]

Schünemann 2008
Schünemann HJ, Oxman AD, Vist GE, Higgins JPT, Deeks JJ, Glasziou P, et al. Chapter 12: Interpreting results and drawing conclusions. In: Higgins JPT, Green S editor(s). *Cochrane Handbook for Systematic Reviews of Interventions*. Chichester: The Cochrane Collaboration, 2008:359–83.

Smith 2010
Smith TLL, Carter CW. Asenapine: a novel atypical antipsychotic agent for schizophrenia and bipolar I disorder. *Journal of Pharmacy Technology* 2010;**26**:352–61.

Sterne 2011
Sterne JAC, Egger M, Moher D, on behalf of the Cochrane Bias Methods Group. Chapter 10: Addressing reporting biases. In: Higgins JPT, Green S (editors). Cochrane Handbook of Systematic Reviews of Interventions. Version 5.1.0 [updated March 2011]. The Cochrane Collaboration, 2011. Available from www.cochrane-handbook.org 2011.

Sullivan 1993
Sullivan M, Karlsson J, Bengtsson C, Furunes B, Lapidus L, Lissner L. The Göteborg Quality of Life Instrument - a psychometric evaluation of assessments of symptoms

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

and well-being among the women in a general population. *Scandinavian Journal of Primary Health Care* 1993;**11**(4): 267–75.

Takahashi 1999

Takahashi N, Terao T, Oga T, Okada M. Comparison of risperidone and mosapramine addition to neuroleptic treatment in chronic schizophrenia. *Neuropsychobiology* 1999;**39**(2):81–5.

Toren 1995

Toren P, Samuel E, Weizman R, Golomb A, Eldar S, Laor N. Emergence of transient compulsive symptoms during treatment with clothiapine. *Journal of the American Academy of Child & Adolescent Psychiatry* 1995;**34**(11):1469–72. [DOI: 10.1097/00004583-199511000-00013]

Turner 2007

Turner T. Chlorpromazine: unlocking psychosis. *BMJ (Clinical research ed.)* 2007;**334 Suppl 1**:s7. [PUBMED: 17204765]

Ukoumunne 1999

Ukoumunne OC, Gulliford MC, Chinn S, Sterne JAC, Burney PGJ. Methods for evaluating area-wide and organisation-based intervention in health and health care: a systematic review. *Health Technology Assessment* 1999;**3**(5): iii–92.

WHO 2011

World Health Organization. *WHO model list of essential medicines*. 17th Edition. Geneva: World Health Organization, March 2011.

WMS-IV 2009

Wechsler D, Holdnack JA, Drozdick LW. *Wechsler Memory Scale - Fourth Edition (WMS-IV)*. San Antonio: Pearson, 2009.

Wu 2006

Wu T, Li Y, Liu G, Bian Z, Li J, Zhang J, et al. Investigation of authenticity of 'claimed' randomized controlled trials (RCTs) and quality assessment of RCT reports published in China. Proceedings of the 14th Cochrane Colloquium; 2006 October 23-26; Dublin. Dublin, 2006.

Xia 2009

Xia J, Adams CE, Bhagat N, Bhagat V, Bhoopathi P, El-Sayeh H, et al. Loss to outcomes stakeholder survey: the LOSS study. *Psychiatric Bulletin* 2009;**33**(7):254–7.

Yorston 2000

Yorston G, Pinney A. Chlorpromazine equivalents and percentage of British National Formulary maximum recommended dose in patients receiving high-dose antipsychotics. *Psychiatric Bulletin* 2000;**24**(4):130–2.

Zhang 1999

Zhang W, Bymaster FPP. The in vivo effects of olanzapine and other antipsychotic agents on receptor occupancy and antagonism of dopamine D1, D2, D3, 5HT2A and muscarinic receptors. *Psychopharmacology* 1999;**141**(3): 267–78. [DOI: 10.1007/s002130050834]

* *Indicates the major publication for the study*

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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	1. Chlorpromazine: dose range 200 to 800 mg/day. N = 10. 2. 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 ***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"

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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 detection 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

Methods	Allocation: randomised, computer-generated, blocks for each investigator, 2:1, olanzapine to chlorpromazine. Blindness: open-label, medication kits issued. Duration: 6 weeks (preceded by washout phase; extension for responders). Design: single centre Morocco.
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
Interventions	1. Olanzapine: dose range 5 to 20 mg/day. N = 27. 2. Chlorpromazine: dose range 200 to 800 mg/day. N = 13.
Outcomes	Leaving study early. Mental state: BPRS, PANSS, MADRS, HAMA. Global state: CGI. Adverse events: ESRS, COSTART list, weight gain.
Notes	

Risk of bias		***Risk of bias***
Bias	**Authors' judgement**	**Support for judgement**

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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 study...personnel 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 detection 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 $\geq$ 60, length of illness less than 5 years, without organic diseases, without history of drug or alcohol dependence, clear of any antipsychotic medication for at least 1 month prior to hospital admission, able to complete cognitive test and consent to participation to the study
Interventions	1. Olanzapine: dose range 10.3 ± 4.2 mg/d. N = 35. 2. Chlorpromazine: dose range 240 ± 53 mg/d. N = 35.

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

vs OLZ - An 2006 (*Continued*)

Outcomes	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 olanzapine and chlorpromazine group respectively. The drop out is unlikely to have had any impact on the outcomes measured, except 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.

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

vs OLZ - Chang 2003 (*Continued*)

	Sex: male and female. Length of illness: 4 to 5 years. Inclusion criteria: not reported.
Interventions	1. Olanzapine: 5 to 20 mg/day. N = 32. 2. 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 ≤ 29%.

Risk of bias ***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.

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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	1. Chlorpromazine: 200 to 800 mg/day. N = 44. 2. 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.

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

vs OLZ - He 2003

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	1. Chlorpromazine: 100 to 600 mg/day. N = 40. 2. Olanzapine: 5 to 30 mg/day. N = 42.
Outcomes	Mental state: PANSS endpoint scale score, subscale scores. Adverse events.
Notes	

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

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

vs OLZ - Loza 1999 (HGDT)

Methods	Allocation: randomised, computer-generated, blocks for each investigator, 2:1, olanzapine 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	1. Olanzapine: dose range 5 to 20 mg/day. N = 27. 2. 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 ***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 site...the bottles were labelled 'Olanzapine' or 'Chlorpromazine' in addition to the study number"

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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 Effect 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 antipsychotic medications in combination Exclusion criteria: simple obesity, hypertension, hypothyroidism, severe heart, liver or renal disease
Interventions	1. Chlorpromazine: 50 to 400 mg/day. N = 20. 2. 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**

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

vs OLZ - Luo 2007 (*Continued*)

Random sequence generation (selection bias)	Low risk	Randomised with computer generated random 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 reported 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	1. Chlorpromazine: 25 to 600 mg/day. N = 28. 2. 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

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

vs OLZ - Wang 2002 (*Continued*)

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	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 reported 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	1. Chlorpromazine: 200 to 700 mg/day. N = 119. 2. Olanzapine: 5 to 15 mg/day. N = 118.

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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 ± SD', but we suspect they are 'mean ± 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 respectively. 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 appear 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.

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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	1. Chlorpromazine: 50 to 600 mg/day. N = 50. 2. 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 ***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 appear to be reported.
Other bias	Low risk	None obvious.

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

vs OLZ - Zhao 2006

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 lactating women, learning disability
Interventions	1. Chlorpromazine: 50 to 600 mg/day. N = 29. 2. 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.

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

vs QTP - Ai 2007

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	1. Chlorpromazine: 400 to 550 mg/day. N = 42. 2. Quetiapine: 400 to 750 mg/day. N = 43.
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.

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

vs QTP - An 2005

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 ± 5.4 years. Sex*: male = 45, female = 12. Length of illness: 0.8 ± 0.6 years. Inclusion criteria: first episode schizophrenia (CCMD-2-R), did not receive systematic treatment prior to admission, PANSS ≥ 60, length of illness less than 2 years, laboratory tests normal Exclusion criteria: patients with physical or organic diseases
Interventions	1. 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. 2. 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 participants but didn't receive any reply

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	All patients completed the trial.

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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

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	1. Chlorpromazine: chlorpromazine was titrated to a treatment dosage (decided by the doctor). N = 96, no further details were provided. 2. 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 ***Risk of bias***

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

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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 conducted
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 $\geq$ 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	1. Chlorpromazine: chlorpromazine was titrated from a dosage of 100 mg/d to a maximum dosage of 700 mg/d, frequency. N = 46. 2. 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:

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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	1. Chlorpromazine: dosage not stated. N = 25. 2. Quetiapine: dosage not stated. N = 25.

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

vs QTP - Cao 2005 (*Continued*)

Outcomes	Leaving the study early. Unable to use: Adverse effects - continuous data was reported, but the scale used was unclear. Sexual arousal, and other sexual related outcomes that were measured using an invalidated scale
Notes	Only male participants were included in the 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

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

vs QTP - Chen 2001 (*Continued*)

	current study
Interventions	1. Quetiapine: 200 to 800 mg/day. N = 114. 2. 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 ***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 experimental 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.

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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	1. Chlorpromazine: 360.3 ± 82.5 mg/day. N = 30. 2. 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.

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

vs QTP - Chen 2008

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	1. Chlorpromazine: titrated over a 1 week period from 100 mg/d to 400 to 600 mg/d. N = 30. 2. 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.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported.
Incomplete outcome data (attrition bias) All outcomes	Low risk	All patients completed the trial.
Selective reporting (reporting bias)	High risk	TESS were not fully reported.

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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 ± 10.3 years; chlorpromazine group:34.8 ± 10.5 years. Sex: quetiapine group: male 20, female 24; chlorpromazine group: male 22, female 23. Length of illness: quetiapine group: 6.4 ± 5.8 years; chlorpromazine group: 6.4 ± 5.7 years Inclusion criteria: PANSS score ≥ 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 ± 150 mg/d and 250 ± 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 ± 250 mg/d and 260 ± 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	*Numbers of participants in these two studies were not clearly stated in the paper. We assumed that each arm had the same number of participants as when randomised

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.

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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 quetiapine group because of advanced condition; 2 cases left the study early in the chlorpromazine 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: 1. Schizophrenia, CCMD-2. 2. BPRS score $\geq$ 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

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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 ≥ 60, length of illness < 1 year, not receiving long-acting antipsychotic drugs. Exclusion: severe physical illness, drug/alcohol dependent.
Interventions	1. Chlorpromazine: 600 ± 50 mg/day. N = 73. 2. Quetiapine: 450 ± 25 mg/day. N = 75.

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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 ***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

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

vs QTP - Guo 2003b (*Continued*)

Interventions	1. Quetiapine: titration period :1 to 2 weeks, average dosage: 300.72 ± 101.25 mg/d. N = 35. 2. 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 quetiapine group, 6 patients left the study early in the chlorpromazine group, without any reason reported. No ITT analysis was applied
Selective reporting (reporting bias)	Low risk	All the outcomes were well reported
Other bias	Low risk	None obvious.

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

vs QTP - Guo 2005

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.

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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 impairments
Interventions	1. Chlorpromazine: chlorpromazine titrated over a 2-week period from 50 mg/d to 200 to 800 mg/d. N = 65. 2. 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 ***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.

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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, pregnant/lactating women
Interventions	1. Chlorpromazine: 300 to 500 mg/day. N = 26. 2. 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 ***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.

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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 receiving 2 or more antipsychotic drugs, patients taking antipsychotic drugs 1 week before randomisation
Interventions	1. Chlorpromazine: < 1000 mg. N = 40. 2. 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%.

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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 table.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	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	1. Chlorpromazine: 468 ± 39 mg/day. N = 20. 2. 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.

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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	1. Chlorpromazine: 350 ± 67.8 mg/d. N = 19. 2. 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	

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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	1. Chlorpromazine: average dosage, 507 ± 27.8 mg/d. N = 33. 2. 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.

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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 quetiapine 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

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

vs QTP - Jiang 2006 (*Continued*)

Interventions	1. Chlorpromazine: 100 to 600 mg/d. N = 97. 2. 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 ***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 agitation, 10 because of abnormal liver function, 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.

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

vs QTP - Jiang 2008

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 ≥ 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	1. Chlorpromazine: 300 to 800 mg/d. N = 30. 2. 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.

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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	1. Chlorpromazine: 200 to 600 mg/day. N = 30. 2. 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 ***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.

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

vs QTP - Kong 2003

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, without cardiac, liver, kidney or endocrine diseases. Exclusion: lactating/pregnant women.
Interventions	1. Chlorpromazine: 200 to 400 mg/d. N = 15. 2. 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.

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

vs QTP - Li 2003

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 $\geq$ 60. Exclusion: severe physical illness, drug/alcohol dependent, pregnant/lactating women
Interventions	1. Chlorpromazine: 503 ± 134 mg/day. N = 51. 2. 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.
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 quetiapine group; 14 patients left the study early in chlorpromazine group. The reasons for dropout were either lack of efficacy or adverse effects. ITT was not used
Selective reporting (reporting bias)	Low risk	We did not find any evidence of selective reporting.

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

vs QTP - Li 2003 (*Continued*)

Other bias	Low risk	None obvious.

vs QTP - Li 2010

Methods	Allocation: randomised, no further detail. Blinding: not reported. Duration: 6 weeks. Setting: inpatients, China.
Participants	Diagnosis: schizophrenia (CCMD-3). N = 64. Sex: male = 37 and female = 27. Age: mean ~ 27.9 years, SD ~ 7.22 years. Length of illness: mean 32 months, SD 22 months. Inclusion: schizophrenia, CCMD-3. Exclusion: not reported.
Interventions	1. Chlorpromazine: 550 ± 12.5 mg/day. N = 32. 2. Quetiapine: 500 ± 17.5 mg/day. N = 32.
Outcomes	Leave the study early. Mental state: HAMD scores.
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	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.

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

vs QTP - Li 2010 (*Continued*)

Other bias	Low risk	None obvious.

vs QTP - Liu 2003

Methods	Allocation: randomised, no further detail. Blinding: not reported. Duration: 6 weeks. Setting: inpatients, China.
Participants	Diagnosis: schizophrenia (CCMD-2-R). N = 83. Sex: male = 45 and female = 38. Age: mean ~ 64.3 years, SD ~ 2.8 years. Length of illness: mean ~ 3.98 months, SD ~ 2.57 months. Inclusion: primary schizophrenia, CCMD-2-R; age ≥ 60 years, PANSS ≥ 60. Exclusion: not reported.
Interventions	1. Quetiapine: titrated upwards from initial dosage of 50 mg/d to 200 to 350 mg/day. N = 44. 2. Chlorpromazine: titrated upwards from initial dosage of 50 mg/d to 200 to 350 mg/day. N = 39.
Outcomes	Clinical response: no clinical improvement*. Mental state: PANSS scores. Adverse effects: TESS scores. Effects on physiology: laboratory findings, blood test and liver function
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 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.

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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 ≥ 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, pregnant or breastfeeding women
Interventions	1. Chlorpromazine: 425 ± 106 mg/day. N = 49. 2. 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 ***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.

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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	1. Chlorpromazine: 100 to 450 mg/day. N = 60. 2. 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 ***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.

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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	1. 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. 2. 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

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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 ***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	High risk	Thirty-eight patients in the quetiapine group and 44 patients in the chlorpromazine 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 extended-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

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

vs QTP - Peng 2006 (*Continued*)

	Length of illness: mean ~ 28.5 years, SD ~ 6.45years Exclusion: not stated.
Interventions	1. Chlorpromazine: 473.61 ± 107.26 mg/day. N = 20. 2. 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.

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

vs QTP - Peuskens 1997 (*Continued*)

	Length of illness: BPRS ≧ 27, at least 3 on 2 or more of the BPRS positive symptom items 'conceptual disorganisation', 'suspiciousness', hallucinatory behaviour' and 'unusual thought content'; CGI-S ≧ 4 Inclusion: 1. Acute exacerbation of chronic schizophrenia, or schizophreniform disorder (DSM-IV). 2. A total score of at least 27 on the 18 items of BPRS. 3. A score of at least 3 on 2 or more of the BPRS positive symptom items' conceptual. disorganisation' , 'suspiciousness' , 'hallucinatory behaviour ' , and ' unusual thought content'. 4. A score of at least four on the CGI severity of illness item. Exclusion: 1. Medical condition or laboratory abnormality that might confound the trial results or put the patient at risk. 2. Receiving long-acting depot medication. 3. Participated in another investigational drug trial during the 4 weeks prior to randomisation. 4. Significant alcohol or other drug abuse within the previous 12 months.
Interventions	1. Chlorpromazine: mean 384 mg/day; maximum 750 mg/day. N = 100. 2. Quetiapine: mean 407 mg/day; maximum 750 mg/day (but not > 500 mg/day for more than 14 days). N = 101.
Outcomes	Clinical response: no clinical improvement*. Global state: Need of additional antipsychotic drugs. Leave the study early. Adverse effects: extrapyramidal side effects (AIMS, BAS, SAS), haematology, liver function test, thyroid function tests, ECGs, need for medication to reduce EPS Uable to use: CGI (no SD), PANSS (no raw data), BPRS (no SD).
Notes	*No clinical improvement: decreased rate of BPRS score ≤ 50%

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.

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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 discontinuation 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	1. Chlorpromazine: mean ~ 485 mg/d, SD ~ 132 mg/d. N = 36. 2. 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.

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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	1. Chlorpromazine: 420 ± 67.2 mg/day. N = 46. 2. 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 ***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.

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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

Methods	Allocation: randomised, no further information. Blinding: double-blind. Duration: 6 weeks. Setting: inpatients, China.
Participants	Diagnosis: schizophrenia (CCMD-2-R). N = 60. Sex: not reported. Age: 18 to 60 years. Length of illness: not reported. Inclusion: first episode schizophrenia, PANSS $\geq$ 60. Exclusion: organic diseases, severe physical illness, alcohol or drug abuse, pregnant or breastfeeding women
Interventions	1. Chlorpromazine: 300 to 750 mg/d. N = 30. 2. Quetiapine: 300 to 750 mg/d. N = 30. No other antipsychotic drugs were used during treatment course, but Antan or benzodiazepine were used when necessary
Outcomes	Clinical response: no clinical improvement*. Mental state: PANSS scores (total, positive, negative and general pathological) Adverse effect: TESS.
Notes	*No clinical improvement: decreased rate of PANSS score $\leq$ 29% or symptoms deterioration

Risk of bias ***Risk of bias***

Bias	**Authors' judgement**	**Support for judgement**

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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 $\geq$ 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	1. Chlorpromazine: 300 to 800 mg/d. N = 30. 2. Quetiapine: 300 to 800 mg/d. N = 30. No other antipsychotic drugs were used during treatment course, but Antan or benzodiazepine 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

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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 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	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	1. Chlorpromazine: 300 to 750 mg/day. N = 48. 2. 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*

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

vs QTP - Wang 2004 (*Continued*)

	Adverse effects.
Notes	*PANSS 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 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	1. Chlorpromazine: 100 to 600 mg/day. N = 57. 2. Quetiapine: 400 to 750 mg/day. N = 48.

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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 ***Risk of bias***

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Randomisation, randomised by the random 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 analysis: 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.

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

vs QTP - Yang 2007

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	1. 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. 2. 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

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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	1. Chlorpromazine: 300 mg to 550 mg/day. N = 57. 2. 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 ***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.

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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

Methods	Allocation: randomised using computer generated random number. Blinding: double-blinded, no further details provided. Duration: 1 week wash out period, plus 6 weeks of intervention, followed by 1 week of reduced dose of medication to help patients to withdraw from the interventions. Setting: inpatients, multicentre, China.
Participants	Diagnosis: schizophrenia (CCMD-2-R). N = 237. Sex: male = 121 and female = 99. Age: mean ~ 32.27 years, SD ~ 11.33 years. Length of illness: mean ~ 7.0 years, SD ~ 7.3 years. Inclusion: BPRS score $\geq$ 36. Exclusion: 1. Patients with neurological, heart, liver, renal or other severe physical illnesses. 2. Pregnant or lactating women. 3. Alcohol or drug dependent patients. 4. Patients who received quetiapine or chlorpromazine 4 weeks prior to the study. 5. Patients with allergy of quetiapine and chlorpromazine. 6. Patients who participated in other clinical drug trials within the last 30 days of 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. Effects on physiology: pulse, blood pressure, laboratory findings
Notes	*Decreased rate of PANSS score < 30%.

Risk of bias ***Risk of bias***

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Randomised using computer-generated random number.

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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	1. Chlorpromazine: mean ~ 404.55 mg/d, SD ~ 66.42 mg/d. N = 33. 2. 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***

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

vs QTP - Zhang 2006 (*Continued*)

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 - 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	1. Chlorpromazine: titration period: 2 weeks, from 75 mg/d to a treatment dosage of 350 to 550 mg/d. N = 30. 2. 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%.

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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	1. Chlorpromazine: dosage not stated. N = 20. 2. 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*

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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 $\geq$ 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	1. Chlorpromazine: 200 to 600 mg/d. N = 41. 2. Quetiapine: 300 to 400 mg/d. N = 42.

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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 ***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 effect 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.

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

vs QTP - Zou 2006 (*Continued*)

	Exclusion: severe physical illness, drug/alcohol dependent, pregnant/lactating women, allergic to experimental drugs
Interventions	1. Quetiapine: 483.1 ± 25.5 mg/day. N = 43. 2. 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 ***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.

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

vs RPD - Chang 1998 (*Continued*)

	Length of illness: mean ~ 12 years, SD ~ 7 years. Inclusion criteria: without organic diseases.
Interventions	1. Chlorpromazine: dose range 0.6g/d, N = 20. 2. Risperidone: dose range 1 to 6mg/d, N = 38.
Outcomes	Clinical response: no significant clinical response. Adverse effects.
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 measure, as we were unable to obtain its protocol
Other bias	Low risk	None obvious.

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.

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

vs RPD - Cui 2001 (*Continued*)

	Length of illness: in risperidone group mean ~ 69 months, SD ~ 82 months; in chlorpromazine 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	1. Chlorpromazine: 426.67 ± 81.38 mg/day. N = 30. 2. 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 ***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 chlorpromazine were placed into capsules of equal size and same colour, dispensed by pharmacist. 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.

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

vs RPD - Feng 2003

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	1. Chlorpromazine: 355.79 ± 82.45 mg/day. N = 33. 2. 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.

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

vs RPD - Feng 2003 (*Continued*)

Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Three and 2 people dropped out of chlorpromazine and risperidone groups respectively. Trial authors did not report the reason for drop out. It's unclear if these participants 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	1. Chlorpromazine: 100 to 600 mg/day. N = 20. 2. 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 ***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.

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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.

vs RPD - Lin 2005

Methods	Allocation: randomised, no further information. Blindness: not reported. Duration: 8 weeks trial. Design: parallel group. Setting: inpatients, China.
Participants	Diagnosis: first episode schizophrenia (CCMD-3). N = 70. Age: mean ~ 32 years, SD ~ 14 years. Sex: male and female. Length of illness: chlorpromazine group 25.19 ± 42.54 months; risperidone group 32. 59 ± 45.80 months. Inclusion criteria: first episode schizophrenia, without receiving oral antipsychotic drugs one week prior to trial, or depot antipsychotic one month prior to trial, PANSS > 60 Exclusion criteria: severe organic or heart, liver, renal disease, pregnant or lactating women, or abnormal ECG
Interventions	1. Chlorpromazine: 100 to 450 mg/day. N = 35. 2. Risperidone: 1 to 4 mg/day. N = 35.
Outcomes	Clinical response: no significant clinical response*. Mental state: PANSS. Adverse effects.
Notes	*Paper did not describe the criteria of 'no significant clinical response'

Risk of bias	***Risk of bias***

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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 traumatic head injury
Interventions	1. Chlorpromazine: 500 to 700 mg/day. N = 15. 2. Risperidone: 3 to 4.5 mg/day. N = 17.
Outcomes	Mental state: SANS. Unable to use: Mental state: unvalidated SANS subscale scores.
Notes	

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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 judgement.
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	1. Chlorpromazine: 50 to 450 mg/day. N = 50. 2. Risperidone: 1 to 4 mg/day. N = 50.
Outcomes	Adverse effects. Blood pressure. Unable to use: Adverse effects: TESS subscale score.

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

vs RPD - Liu 2005 (*Continued*)

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	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	1. Chlorpromazine: 100 to 700 mg/day. N = 52. 2. Risperidone: 1 to 7 mg/day. N = 55.
Outcomes	Clinical response: no significant clinical response*. Mental state: PANSS

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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	1. Chlorpromazine: average dose 475 mg/day. N = 39. 2. Risperidone: 1 to 9 mg/day. N = 39.

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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 ***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.

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

vs RPD - Wang 2002 (*Continued*)

Interventions	1. Chlorpromazine: 400 mg/day. N = 20. 2. Risperidone: 4 mg/day. N = 19.** 3. 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 ***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 risperidone (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.

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

vs RPD - Wang 2005

Methods	Allocation: randomised, no further information. Blindness: not reported. Duration: 8 weeks trial. Design: parallel group. Setting: inpatients, China.
Participants	Diagnosis: first episode schizophrenia (CCMD-3). 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.
Interventions	1. Chlorpromazine: 25 to 450 mg/day. N = 50. 2. 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.

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

vs RPD - Wu 2002

Methods	Allocation: randomised, no further information. Blindness: not reported. Duration: 12 weeks trial. Design: parallel group. Setting: inpatients, China.
Participants	Diagnosis: chronic schizophrenia (CCMD-2-R). 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 impairment.
Interventions	1. Chlorpromazine: 400 to 600 mg/day. N = 35. 2. Risperidone: 4 to 6 mg/day. N = 35.
Outcomes	Clinical response: no significant clinical response*. Adverse effects.
Notes	*The paper did not report on how this is determined.

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.

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

vs RPD - Wu 2004

Methods	Allocation: randomised, no further information. Blindness: not reported. Duration: 3 months. Design: parallel group. Setting: inpatients, China.
Participants	Diagnosis: schizophrenia (CCMD-3). N = 100. Age: 18 to 43 years. Sex: male and female. Length of illness: 3 months to 7.2 years. Inclusion criteria: PANSS > 60, give informed consent to participate Exclusion criteria: severe organic or heart, liver, renal disease, drug or alcohol dependent
Interventions	1. Chlorpromazine: 300 to 600 mg/day. N = 50. 2. Risperidone: 3 to 6 mg/day. N = 50.
Outcomes	Mental state: PANSS. Quality of life: QOL. 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	Low risk	No incomplete outcome data.
Selective reporting (reporting bias)	Low risk	All measured outcomes are reported.
Other bias	Low risk	None obvious.

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

vs RPD - Zheng 2001

Methods	Allocation: randomised, no further information. Blindness: not reported. 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, liver, renal disease
Interventions	1. Chlorpromazine: 100 to 600 mg/day. N = 25. 2. Risperidone: 5 to 6 mg/day. N = 26.
Outcomes	Clinical response: no significant clinical response*. Adverse effects.
Notes	*BPRS score decreased rate < 50% is regarded 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 (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	BPRS, SAPS, SANS, NORS, TESS are all tested, but none were reported
Other bias	Low risk	None obvious.

Abbreviations: AIMS = Abnormal Involuntary Movement Scale

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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 chlorpromazine)
Beuzen 1998 (HGCF)	Allocation: randomised. Participants: treatment-resistant schizophrenia.

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

(*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 admission 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

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

(*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

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

(*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

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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]

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

6 Mental state: 3. Average endpoint score (various scales, high = poor) - skewed data			Other data	No numeric 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 subscale			Other data	No numeric data
6.5 PANSS positive symptom subscale			Other data	No numeric data
7 Service involvement: 1. Re-hospitalisation	1		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
7.1 long term (over 12 months)	1	70	Risk Ratio (M-H, Random, 95% CI)	1.5 [0.46, 4.86]
8 Functioning: 1. Executive function - average endpoint score (WCST, high = poor)	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
8.1 short term (up to 6 months)	1	53	Mean Difference (IV, Random, 95% CI)	10.96 [1.01, 20.91]
9 Adverse effects: 1. Anticholinergic - short term (up to 6 months)	6		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
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. Cardiovascular - short term (up to 6 months)	6		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
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 nervous system - short term (up to 6 months)	5		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
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. Gastrointestinal - short term (up to 6 months)	6		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
12.1 appetite loss	2	180	Risk Ratio (M-H, Random, 95% CI)	11.01 [2.82, 42.94]
12.2 constipation	6	622	Risk Ratio (M-H, Random, 95% CI)	4.29 [2.61, 7.05]
12.3 diarrhoea	1	80	Risk Ratio (M-H, Random, 95% CI)	5.0 [0.25, 100.97]
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 - short term (up to 6 months)	3	266	Risk Ratio (M-H, Random, 95% CI)	4.46 [1.16, 17.22]

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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 - short term (up to 6 months)	3		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
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 - weight gain - short term (up to 6 months)	5	536	Risk Ratio (M-H, Random, 95% CI)	0.70 [0.25, 1.96]
16 Adverse effects: 7b. Metabolic - weight gain - continuous measures	4		Mean Difference (IV, Random, 95% CI)	Subtotals only
16.1 short term (up to 6 months)	4	160	Mean Difference (IV, Random, 95% CI)	-5.11 [-9.15, -1.07]
16.2 medium term (7 to 12 months)	1	50	Mean Difference (IV, Random, 95% CI)	0.59 [-11.87, 13.05]
17 Adverse effects: 7c. Metabolic - other - continuous measures	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
17.1 cholesterol (TC) - short term (up to 6 months)	1	50	Mean Difference (IV, Random, 95% CI)	-0.40 [-1.02, 0.22]
17.2 high-density lipoprotein (HDL) - short term (up to 6 months)	1	50	Mean Difference (IV, Random, 95% CI)	0.05 [-0.12, 0.22]
17.3 low-density lipoprotein (LDL) - short term (up to 6 months)	1	50	Mean Difference (IV, Random, 95% CI)	-0.01 [-0.31, 0.29]
17.4 low-density lipoprotein (LDL) - medium term (7 to 12 months)	1	50	Mean Difference (IV, Random, 95% CI)	0.06 [-0.41, 0.53]
18 Adverse effects: 7d. Metabolic - other - average endpoint scores - skewed data			Other data	No numeric data
18.1 cholesterol (TC) - medium term (7 to 12 months)			Other data	No numeric data
18.2 high-density lipoprotein (HDL) - short term (up to 6 months)			Other data	No numeric data
18.3 triglyceride (TG) - short term (up to 6 months)			Other data	No numeric data
18.4 triglyceride (TG) - medium term (7 to 12 months)			Other data	No numeric data
19 Adverse effects: 8a. Movement disorders - extrapyramidal symptoms - short term (up to 6 months)	4		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
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]

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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]
25.3 GQOLI - psychological health	1	61	Mean Difference (IV, Random, 95% CI)	-22.60 [-25.94, -19.26]
25.4 GQOLI - social function	1	61	Mean Difference (IV, Random, 95% CI)	-18.20 [-20.51, -15.89]
26 Quality of life: 1b. Average endpoint score (QoL, high = better) - skewed data			Other data	No numeric data
26.1 short term (up to 6 months)			Other data	No numeric data
27 Leaving the study early - short term (up to 6 months)	4		Risk Ratio (M-H, Random, 95% CI)	Subtotals only

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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 hostile-suspiciousness subscale	2	130	Mean Difference (IV, Random, 95% CI)	0.89 [-1.41, 3.18]
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

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

5.3 PANSS general pathology subscale			Other data	No numeric data
5.4 PANSS negative symptom subscale			Other data	No numeric data
5.5 PANSS positive symptom subscale			Other data	No numeric data
5.6 SAPS total			Other data	No numeric data
6 Mental state: 2. Average change score - decreased rate (various scales, high = poor) - short term (up to 6 months)	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
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 endpoint score (WCST subscales, high = good) - short term (up to 6 months)	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
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. Anticholinergic - short term (up to 6 months)	10		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
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. Cardiovascular - short term (up to 6 months)	13		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
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. Cardiovascular - continuous measures - short term (up to 6 months)	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
10.1 cardiac rate (upright position)	1	100	Mean Difference (IV, Random, 95% CI)	3.90 [-1.57, 9.37]
10.2 cardiac rate (horizontal position)	1	100	Mean Difference (IV, Random, 95% CI)	7.42 [3.47, 11.37]
10.3 contractive blood pressure (upright position)	1	100	Mean Difference (IV, Random, 95% CI)	-1.06 [-2.20, 0.08]

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

10.4 contractive blood pressure (horizontal position)	1	100	Mean Difference (IV, Random, 95% CI)	1.38 [0.61, 2.15]
10.5 diastolic blood pressure (upright position)	1	100	Mean Difference (IV, Random, 95% CI)	-0.53 [-1.29, 0.23]
10.6 diastolic blood pressure (horizontal position)	1	100	Mean Difference (IV, Random, 95% CI)	0.39 [-0.18, 0.96]
11 Adverse effects: 3. Central nervous system - short term (up to 6 months)	6	1191	Odds Ratio (M-H, Random, 95% CI)	1.96 [0.92, 4.22]
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. Gastrointestinal - short term (up to 6 months)	9		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
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 - short term (up to 6 months)	3	266	Risk Ratio (M-H, Random, 95% CI)	4.46 [1.16, 17.22]
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 - short term (up to 6 months)	3	307	Risk Ratio (M-H, Random, 95% CI)	1.30 [0.17, 10.09]
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 - weight gain	4	302	Risk Ratio (M-H, Random, 95% CI)	1.36 [0.52, 3.59]
15.1 short term (up to 6 months)	4	302	Risk Ratio (M-H, Random, 95% CI)	1.36 [0.52, 3.59]
16 Adverse effects: 8. Movement disorders - short term (up to 6 months)	8		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
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 endpoint score (TESS) - skewed data			Other data	No numeric data
17.1 short term (up to 6 months)			Other data	No numeric data
18 Adverse effects: 10. Various other - short term (up to 6 months)	2		Risk Ratio (M-H, Random, 95% CI)	Subtotals only

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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]

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

6.3 BPRS activation subscale	1	60	Mean Difference (IV, Random, 95% CI)	0.22 [-0.26, 0.70]
6.4 BPRS hostile-suspiciousness subscale	1	60	Mean Difference (IV, Random, 95% CI)	-0.09 [-1.15, 0.97]
6.5 BPRS thinking disorder subscale	1	60	Mean Difference (IV, Random, 95% CI)	-0.15 [-1.39, 1.09]
6.6 BPRS withdraw-retardation subscale	1	60	Mean Difference (IV, Random, 95% CI)	-0.10 [-0.76, 0.56]
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 symptoms	17	1361	Mean Difference (IV, Random, 95% CI)	1.05 [0.13, 1.98]
6.10 PANSS general pathology	18	1530	Mean Difference (IV, Random, 95% CI)	-1.11 [-3.06, 0.84]
6.11 HAMD total	1	63	Mean Difference (IV, Random, 95% CI)	7.4 [5.13, 9.67]
7 Mental state: 1b. Average endpoint scores (various scales, high = poor) - medium term (6 to 12 months)	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
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 symptoms	1	77	Mean Difference (IV, Random, 95% CI)	2.70 [0.44, 4.96]
8 Mental state: 1c. Average endpoint scores (various scales, high = poor) -skewed data			Other data	No numeric data
8.1 PANSS total - short term (up to 6 months)			Other data	No numeric data
8.2 PANSS positive symptoms - short term (up to 6 months)			Other data	No numeric data
8.3 PANSS negative symptoms - short term (up to 6 months)			Other data	No numeric data
8.4 PANSS general pathology - short term (up to 6 months			Other data	No numeric data
9 Mental state: 1d. Average change score (various scales, high = poor) - short term (up to 6 months)	2		Mean Difference (IV, Random, 95% CI)	Subtotals only
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 symptoms	1	384	Mean Difference (IV, Random, 95% CI)	0.80 [0.70, 0.90]
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 decreased rate of BPRS/PANSS (%) - short term (up to 6 months)	7		Mean Difference (IV, Random, 95% CI)	Subtotals only
10.1 BPRS	1	197	Mean Difference (IV, Random, 95% CI)	-0.80 [-4.86, 3.26]
10.2 PANSS	6	782	Mean Difference (IV, Random, 95% CI)	-1.96 [-7.20, 3.28]

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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. Anticholinergic - short term (up to 6 months)	22		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
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. Cardiovascular - short term (up to 6 months)	22		Risk Ratio (IV, Random, 95% CI)	Subtotals only
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 nervous system - short term (up to 6 months)	21		Risk Ratio (IV, Random, 95% CI)	Subtotals only
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. Gastrointestinal - short term (up to 6 months)	22		Risk Ratio (IV, Random, 95% CI)	Subtotals only
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 - various - short term (up to 6 months)	4		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
17.1 gynaecomastia, galactorrhoea	1	83	Risk Ratio (M-H, Random, 95% CI)	5.37 [0.27, 108.47]
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]

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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)	1	30	Mean Difference (IV, Random, 95% CI)	24.62 [17.76, 31.48]
19 Adverse effects: 5c. Endocrine - skewed data - short term (up to 6 months)			Other data	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]

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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. Medium term (7 to 12 months)	1	103	Risk Ratio (IV, Random, 95% CI)	1.19 [0.61, 2.32]

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

Review: Chlorpromazine versus atypical antipsychotic drugs for schizophrenia

Comparison: 1 CHLORPROMAZINE versus OLANZAPINE

Outcome: 1 Clinical response: 1. No significant clinical response

Study or subgroup	Chlorpromazine n/N	Olanzapine n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
1 short term - up to 6 months					
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 (Chlorpromazine), 15 (Olanzapine)					
Heterogeneity: Tau^2 = 0.0; Chi^2 = 0.82, df = 2 (P = 0.66); I^2 =0.0%					
Test for overall effect: Z = 3.11 (P = 0.0019)					
2 long term - over 12 months					
vs OLZ - An 2006	11/35	6/35		27.1 %	1.83 [0.76, 4.41]

(*Continued* . . .)

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

(. . . *Continued*)

Study or subgroup	Chlorpromazine n/N	Olanzapine n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Subtotal (95% CI)	**35**	**35**		**27.1 %**	**1.83 [0.76, 4.41]**
Total events: 11 (Chlorpromazine), 6 (Olanzapine)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.35 (P = 0.18)					
Total (95% CI)	**134**	**140**		**100.0 %**	**2.19 [1.39, 3.45]**
Total events: 42 (Chlorpromazine), 21 (Olanzapine)					
Heterogeneity: Tau^2 = 0.0; Chi^2 = 1.03, df = 3 (P = 0.79); I^2 =0.0%					
Test for overall effect: Z = 3.36 (P = 0.00077)					
Test for subgroup differences: Chi^2 = 0.21, df = 1 (P = 0.64), I^2 =0.0%					

Analysis 1.2. Comparison 1 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: 1 CHLORPROMAZINE versus OLANZAPINE

Outcome: 2 Clinical response: 2. Average endpoint score (CGI, high = poor) - 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% 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 (HGDT)	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; Chi^2 = 3.90, df = 2 (P = 0.14); I^2 =49%							
Test for overall effect: Z = 3.17 (P = 0.0015)							
Test for subgroup differences: Not applicable							

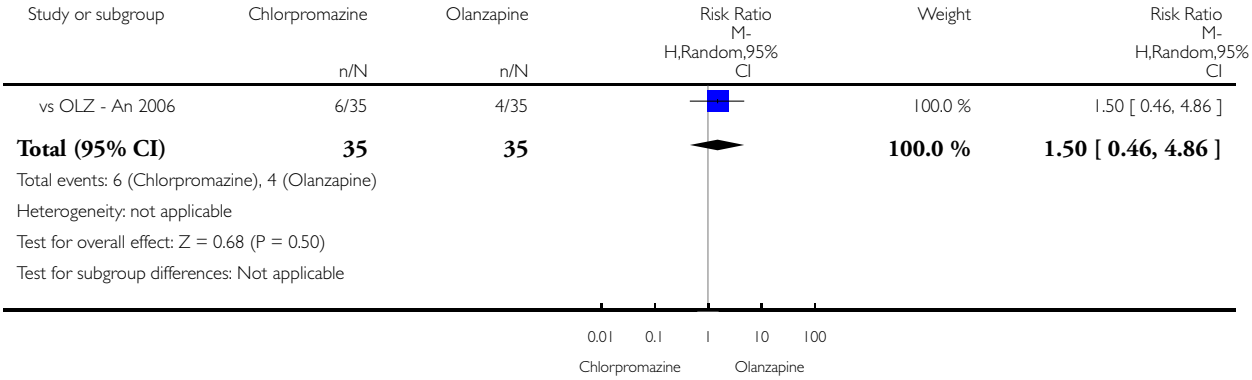
Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Analysis 1.3. Comparison 1 CHLORPROMAZINE versus OLANZAPINE, Outcome 3 Clinical response: 3. Relapse - long term (over 12 months).

Review: Chlorpromazine versus atypical antipsychotic drugs for schizophrenia

Comparison: 1 CHLORPROMAZINE versus OLANZAPINE

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



Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Analysis 1.4. Comparison 1 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: 1 CHLORPROMAZINE versus OLANZAPINE

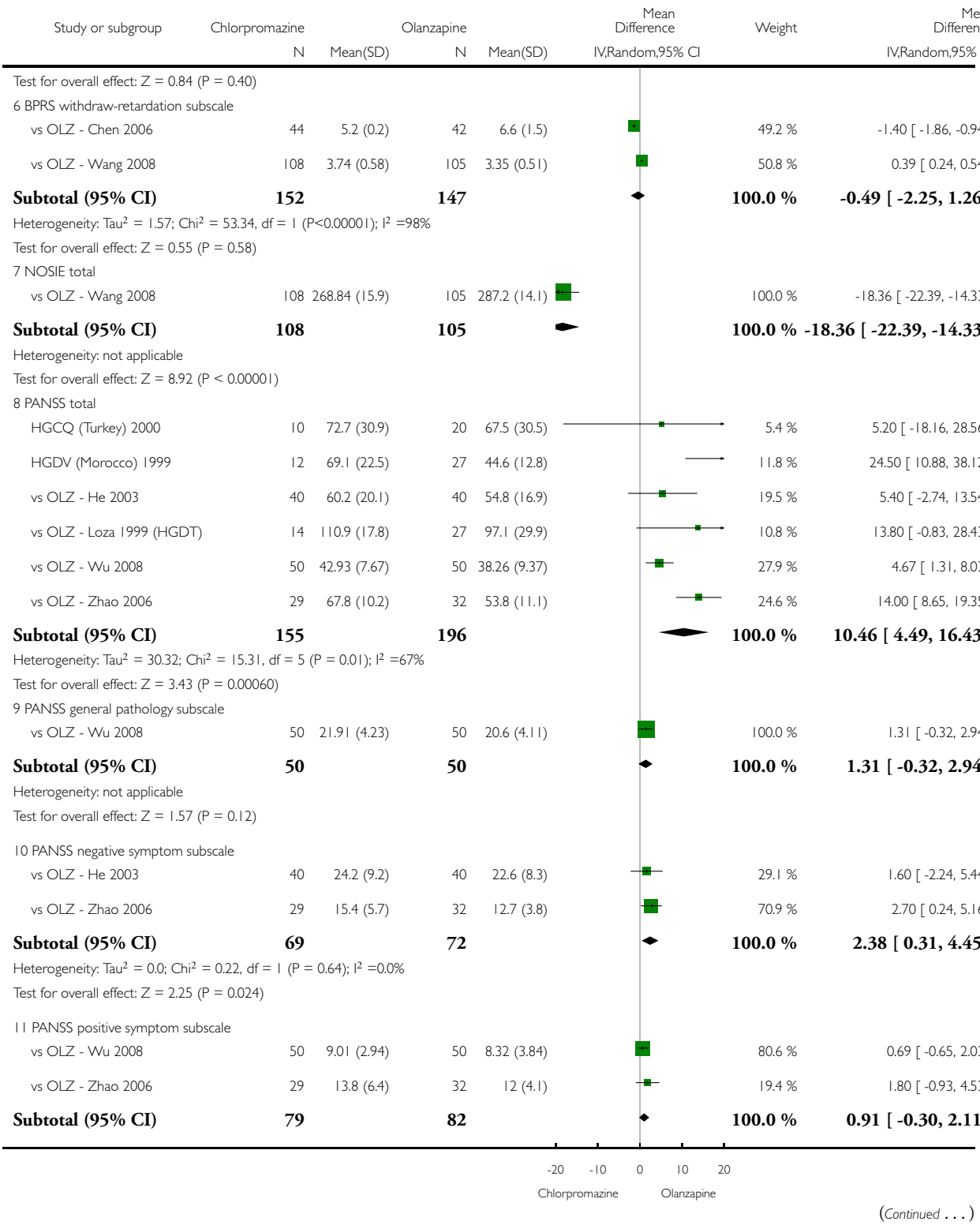
Outcome: 4 Mental state: 1. Average endpoint score (various scales, high = poor) - short term (up to 6 months)

Study or subgroup	Chlorpromazine N	Chlorpromazine Mean(SD)	Olanzapine N	Olanzapine Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
1 BPRS total							
vs OLZ - Chang 2003	27	27 (4)	31	22 (3)		30.9 %	5.00 [3.16, 6.84]
vs OLZ - Chen 2006	44	24.8 (6.4)	42	29.4 (11.3)		24.7 %	-4.60 [-8.51, -0.69]
vs OLZ - Loza 1999 (HGDT)	14	44 (11.2)	27	35.4 (16)		12.8 %	8.60 [0.18, 17.02]
vs OLZ - Wang 2002	28	27.1 (3.4)	32	21.7 (2.5)		31.6 %	5.40 [3.87, 6.93]
Subtotal (95% CI)	**113**		**132**			**100.0 %**	**3.21 [-0.62, 7.05]**
Heterogeneity: Tau^2 = 11.52; Chi^2 = 23.38, df = 3 (P = 0.00003); I^2 =87%							
Test for overall effect: Z = 1.64 (P = 0.10)							
2 BPRS activation subscale							
vs OLZ - Chen 2006	44	5.3 (0.8)	42	4.9 (1.8)		11.1 %	0.40 [-0.19, 0.99]
vs OLZ - Wang 2008	108	4.15 (0.95)	105	3.67 (0.57)		88.9 %	0.48 [0.27, 0.69]
Subtotal (95% CI)	**152**		**147**			**100.0 %**	**0.47 [0.27, 0.67]**
Heterogeneity: Tau^2 = 0.0; Chi^2 = 0.06, df = 1 (P = 0.80); I^2 =0.0%							
Test for overall effect: Z = 4.67 (P < 0.00001)							
3 BPRS anxiety-depression subscale							
vs OLZ - Wang 2008	108	7.17 (0.76)	105	5.6 (0.79)		100.0 %	1.57 [1.36, 1.78]
Subtotal (95% CI)	**108**		**105**			**100.0 %**	**1.57 [1.36, 1.78]**
Heterogeneity: not applicable							
Test for overall effect: Z = 14.77 (P < 0.00001)							
4 BPRS hostile-suspiciousness subscale							
vs OLZ - Chen 2006	44	4.6 (0.9)	42	5.8 (2.4)		47.7 %	-1.20 [-1.97, -0.43]
vs OLZ - Wang 2008	108	5.02 (1.34)	105	4.52 (0.78)		52.3 %	0.50 [0.21, 0.79]
Subtotal (95% CI)	**152**		**147**			**100.0 %**	**-0.31 [-1.98, 1.35]**
Heterogeneity: Tau^2 = 1.36; Chi^2 = 16.24, df = 1 (P = 0.00006); I^2 =94%							
Test for overall effect: Z = 0.37 (P = 0.71)							
5 BPRS thinking disorder subscale							
vs OLZ - Chen 2006	44	5.1 (0.9)	42	6.9 (2.8)		47.3 %	-1.80 [-2.69, -0.91]
vs OLZ - Wang 2008	108	4.84 (0.59)	105	4.74 (0.99)		52.7 %	0.10 [-0.12, 0.32]
Subtotal (95% CI)	**152**		**147**			**100.0 %**	**-0.80 [-2.66, 1.06]**
Heterogeneity: Tau^2 = 1.70; Chi^2 = 16.59, df = 1 (P = 0.00005); I^2 =94%							

(*Continued* . . .)

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

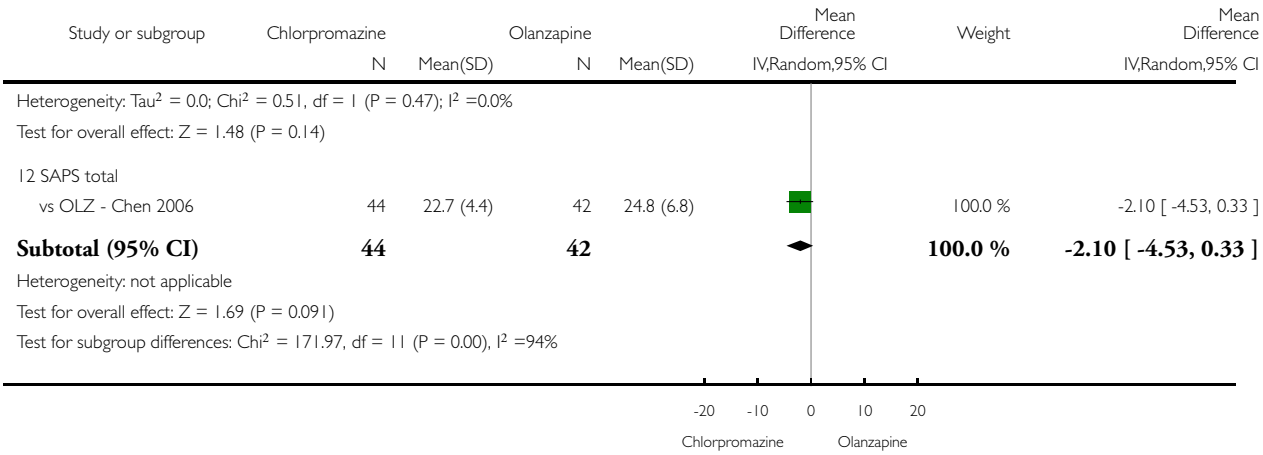
(. . . *Continued*)



(*Continued* . . .)

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

(. . . *Continued*)

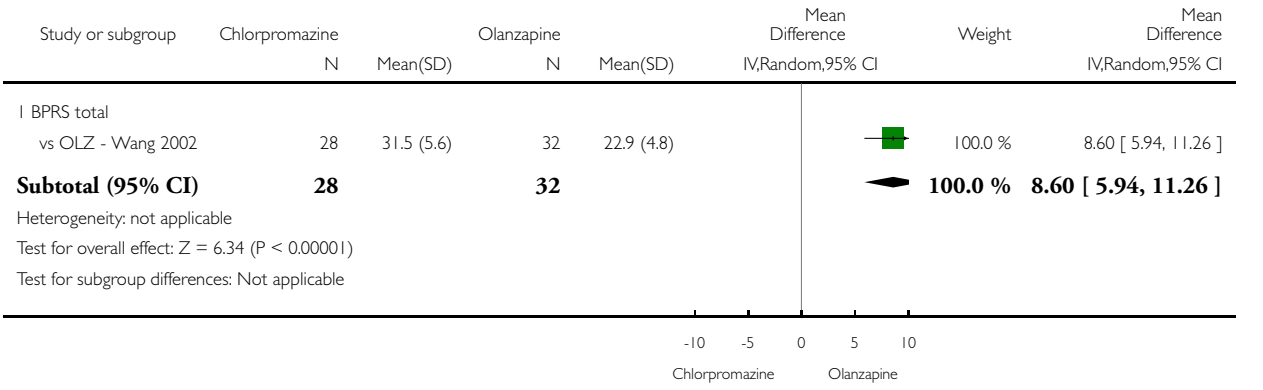


Analysis 1.5. Comparison 1 CHLORPROMAZINE versus OLANZAPINE, Outcome 5 Mental state: 2. Average endpoint score (BPRS, high = poor) - medium term (7 to 12 months).

Review: Chlorpromazine versus atypical antipsychotic drugs for schizophrenia

Comparison: 1 CHLORPROMAZINE versus OLANZAPINE

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



Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Analysis 1.6. Comparison 1 CHLORPROMAZINE versus OLANZAPINE, Outcome 6 Mental state: 3. Average endpoint score (various scales, high = poor) - skewed data.

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 symptom 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 symptom subscale					**PANSS positive**
vs OLZ - He 2003	Chlorpromazine	11.7	6.2	40	
vs OLZ - He 2003	Olanzapine	10.2	4.9	40	

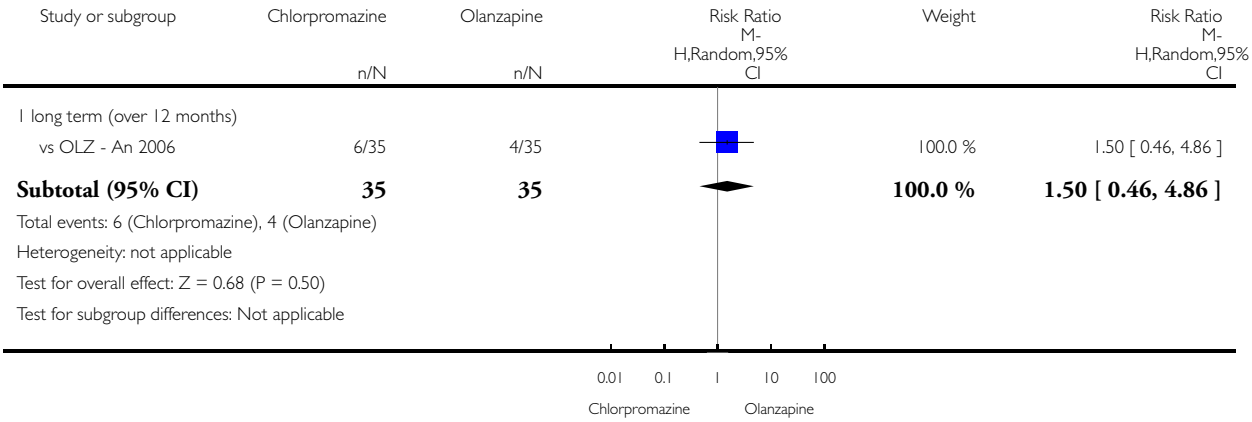
Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Analysis 1.7. Comparison 1 CHLORPROMAZINE versus OLANZAPINE, Outcome 7 Service involvement: 1. Re-hospitalisation.

Review: Chlorpromazine versus atypical antipsychotic drugs for schizophrenia

Comparison: 1 CHLORPROMAZINE versus OLANZAPINE

Outcome: 7 Service involvement: 1. Re-hospitalisation

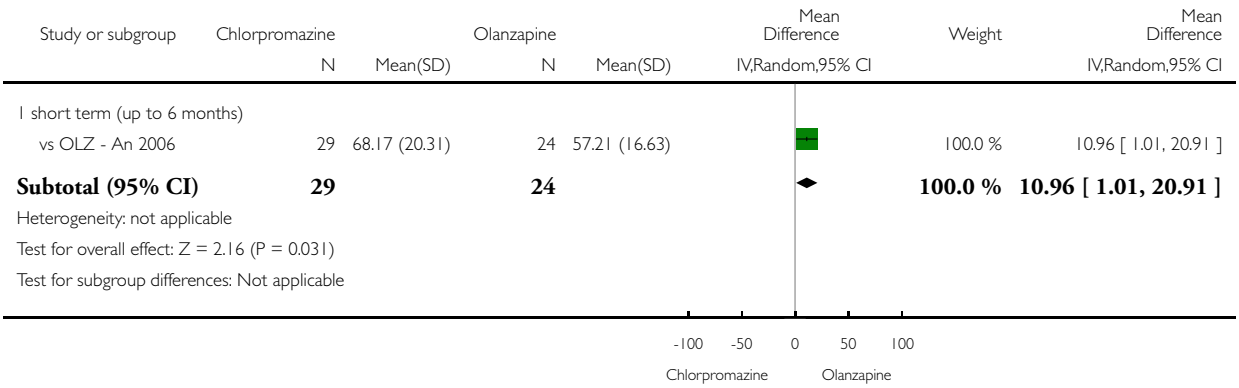


Analysis 1.8. Comparison 1 CHLORPROMAZINE versus OLANZAPINE, Outcome 8 Functioning: 1. Executive function - average endpoint score (WCST, high = poor).

Review: Chlorpromazine versus atypical antipsychotic drugs for schizophrenia

Comparison: 1 CHLORPROMAZINE versus OLANZAPINE

Outcome: 8 Functioning: 1. Executive function - average endpoint score (WCST, high = poor)



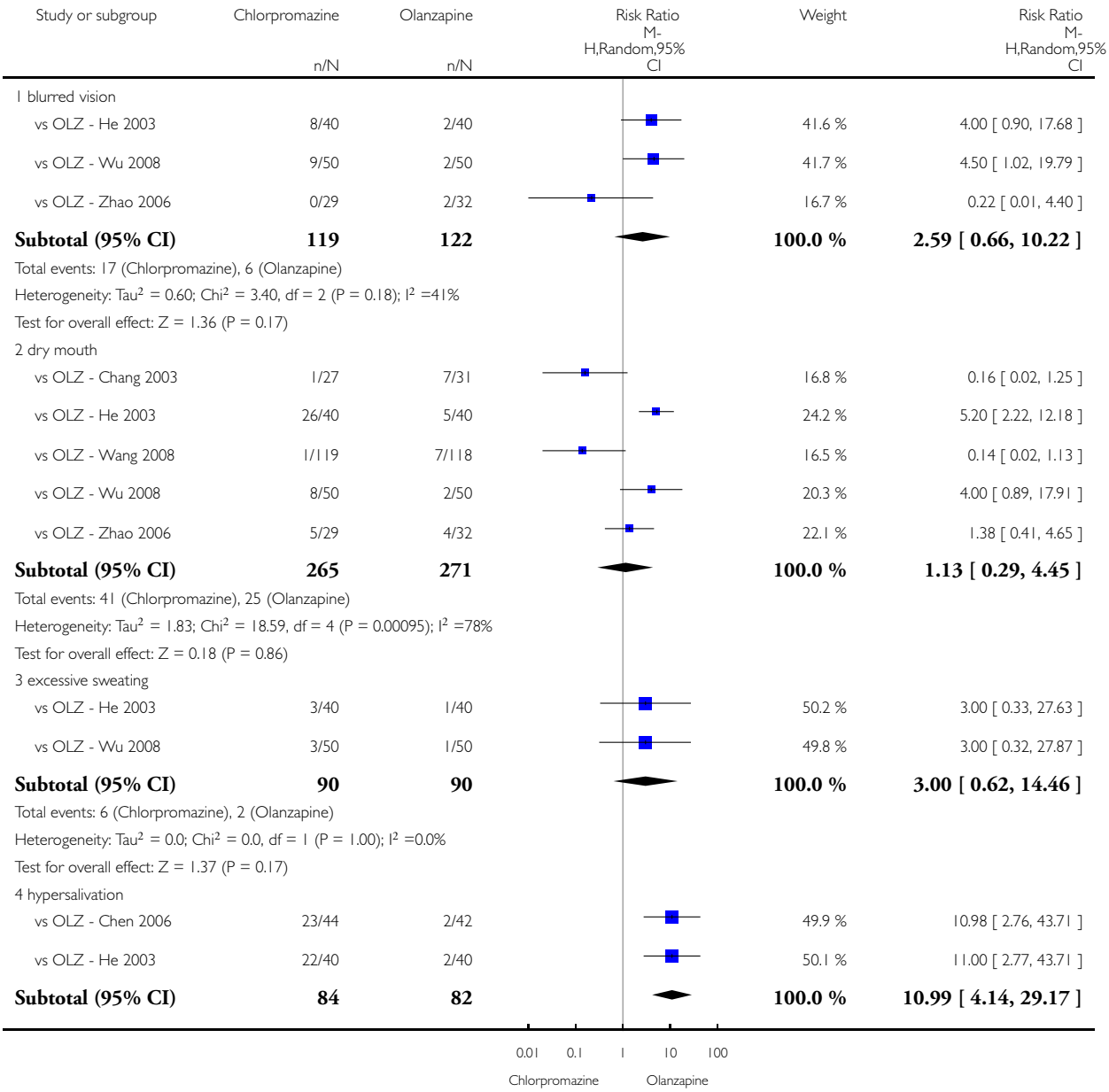
Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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

Review: Chlorpromazine versus atypical antipsychotic drugs for schizophrenia

Comparison: 1 CHLORPROMAZINE versus OLANZAPINE

Outcome: 9 Adverse effects: 1. Anticholinergic - short term (up to 6 months)

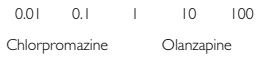


(*Continued* . . .)

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

(. . . *Continued*)

Study or subgroup	Chlorpromazine n/N	Olanzapine n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Total events: 45 (Chlorpromazine), 4 (Olanzapine)					
Heterogeneity: Tau^2 = 0.0; Chi^2 = 0.00, df = 1 (P = 1.00); I^2 =0.0%					
Test for overall effect: Z = 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 (Chlorpromazine), 4 (Olanzapine)					
Heterogeneity: not applicable					
Test for overall effect: Z = 2.06 (P = 0.039)					
Test for subgroup differences: Chi^2 = 8.13, df = 4 (P = 0.09), I^2 =51%					



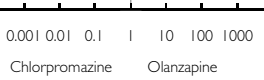
Analysis 1.10. Comparison 1 CHLORPROMAZINE versus OLANZAPINE, Outcome 10 Adverse effects: 2. Cardiovascular - short term (up to 6 months).

Review: Chlorpromazine versus atypical antipsychotic drugs for schizophrenia

Comparison: 1 CHLORPROMAZINE versus OLANZAPINE

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

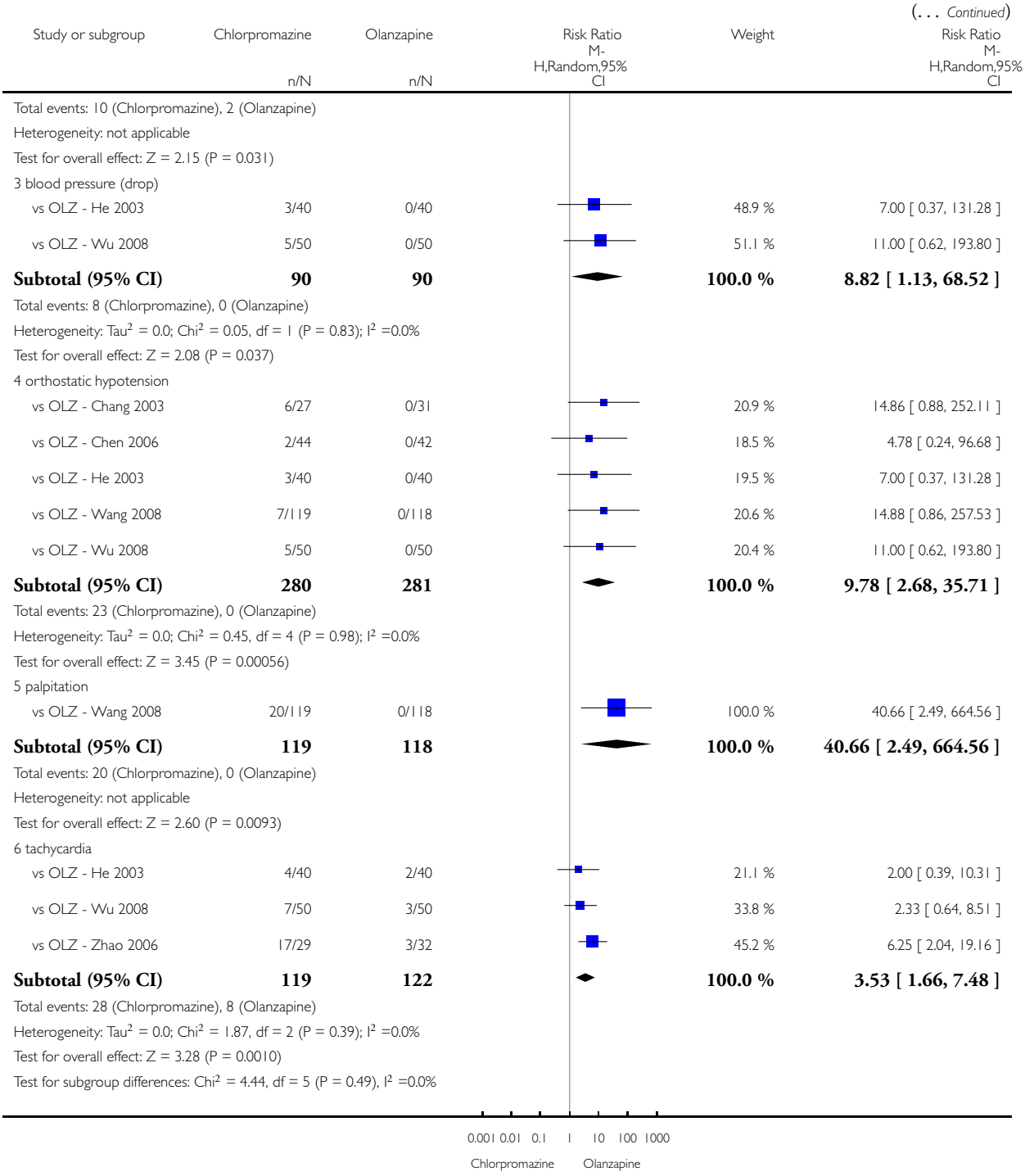
Study or subgroup	Chlorpromazine n/N	Olanzapine n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
1 abnormal ECG					
vs OLZ - He 2003	2/40	0/40		35.5 %	5.00 [0.25, 100.97]
vs OLZ - Wu 2008	3/50	1/50		64.5 %	3.00 [0.32, 27.87]
Subtotal (95% CI)	**90**	**90**		**100.0 %**	**3.60 [0.60, 21.55]**
Total events: 5 (Chlorpromazine), 1 (Olanzapine)					
Heterogeneity: Tau^2 = 0.0; Chi^2 = 0.07, df = 1 (P = 0.79); I^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]**



(*Continued* . . .)

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

(. . . *Continued*)



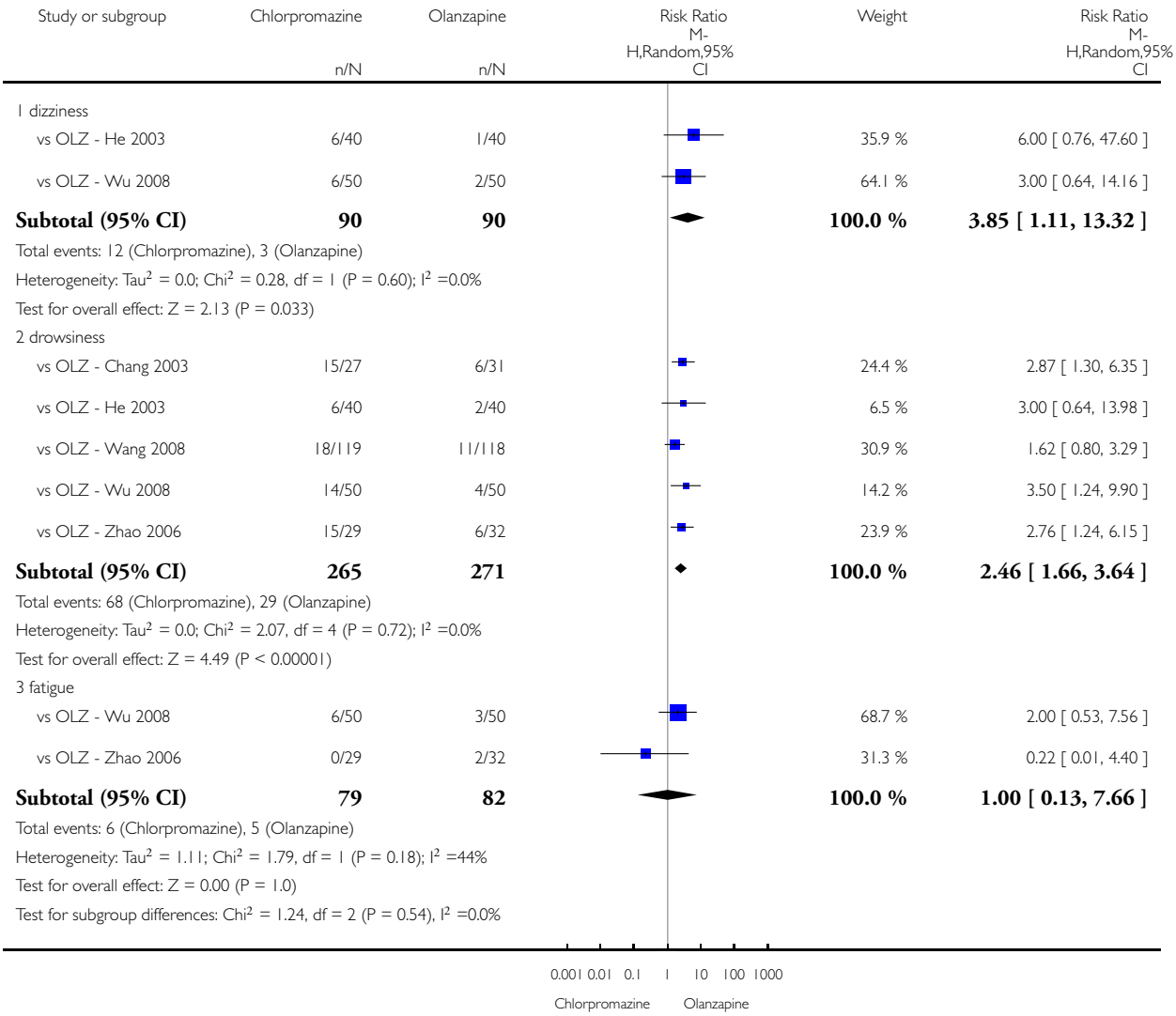
Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Analysis 1.11. Comparison 1 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: 1 CHLORPROMAZINE versus OLANZAPINE

Outcome: 11 Adverse effects: 3. Central nervous system - short term (up to 6 months)



Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

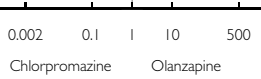
Analysis 1.12. Comparison 1 CHLORPROMAZINE versus OLANZAPINE, Outcome 12 Adverse effects: 4. Gastrointestinal - short term (up to 6 months).

Review: Chlorpromazine versus atypical antipsychotic drugs for schizophrenia

Comparison: 1 CHLORPROMAZINE versus OLANZAPINE

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

Study or subgroup	Chlorpromazine n/N	Olanzapine n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
1 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]**
Total events: 56 (Chlorpromazine), 5 (Olanzapine)					
Heterogeneity: Tau^2 = 0.48; Chi^2 = 1.78, df = 1 (P = 0.18); I^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]
vs OLZ - He 2003	16/40	5/40		30.3 %	3.20 [1.30, 7.90]
vs OLZ - Wang 2008	14/119	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 %	13.24 [1.83, 95.63]
Subtotal (95% CI)	**309**	**313**		**100.0 %**	**4.29 [2.61, 7.05]**
Total events: 82 (Chlorpromazine), 17 (Olanzapine)					
Heterogeneity: Tau^2 = 0.0; Chi^2 = 4.83, df = 5 (P = 0.44); I^2 =0.0%					
Test for overall effect: Z = 5.74 (P < 0.00001)					
3 diarrhoea					
vs OLZ - He 2003	2/40	0/40		100.0 %	5.00 [0.25, 100.97]
Subtotal (95% CI)	**40**	**40**		**100.0 %**	**5.00 [0.25, 100.97]**
Total events: 2 (Chlorpromazine), 0 (Olanzapine)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.05 (P = 0.29)					
4 dysphagia					
vs OLZ - Wu 2008	1/50	0/50		100.0 %	3.00 [0.13, 71.92]
Subtotal (95% CI)	**50**	**50**		**100.0 %**	**3.00 [0.13, 71.92]**
Total events: 1 (Chlorpromazine), 0 (Olanzapine)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.68 (P = 0.50)					
5 nausea/vomiting					

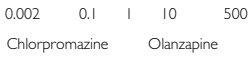


(*Continued* . . .)

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

(. . . *Continued*)

Study or subgroup	Chlorpromazine n/N	Olanzapine n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
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 (Chlorpromazine), 4 (Olanzapine)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.29$, df = 1 (P = 0.59); $I^2 = 0.0\%$					
Test for overall effect: Z = 0.63 (P = 0.53)					
Test for subgroup differences: $Chi^2 = 4.63$, df = 4 (P = 0.33), $I^2 = 14\%$					



Analysis 1.13. Comparison 1 CHLORPROMAZINE versus OLANZAPINE, Outcome 13 Adverse effects: 5. Haematology - short term (up to 6 months).

Review: Chlorpromazine versus atypical antipsychotic drugs for schizophrenia

Comparison: 1 CHLORPROMAZINE versus OLANZAPINE

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

Study or subgroup	Chlorpromazine n/N	Olanzapine n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
1 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**		**78.8 %**	**4.00 [0.87, 18.31]**
Total events: 8 (Chlorpromazine), 2 (Olanzapine)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.0$, df = 1 (P = 1.00); $I^2 = 0.0\%$					
Test for overall effect: Z = 1.79 (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 (Chlorpromazine), 0 (Olanzapine)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.27 (P = 0.20)					

(*Continued* . . .)

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

(. . . *Continued*)

Study or subgroup	Chlorpromazine n/N	Olanzapine n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Total (95% CI)	**134**	**132**		**100.0 %**	**4.46 [1.16, 17.22]**
Total events: 11 (Chlorpromazine), 2 (Olanzapine)					
Heterogeneity: Tau^2 = 0.0; Chi^2 = 0.09, df = 2 (P = 0.95); I^2 =0.0%					
Test for overall effect: Z = 2.17 (P = 0.030)					
Test for subgroup differences: Chi^2 = 0.09, df = 1 (P = 0.76), I^2 =0.0%					

Analysis 1.14. Comparison 1 CHLORPROMAZINE versus OLANZAPINE, Outcome 14 Adverse effects: 6. Hepatitic - short term (up to 6 months).

Review: Chlorpromazine versus atypical antipsychotic drugs for schizophrenia

Comparison: 1 CHLORPROMAZINE versus OLANZAPINE

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

Study or subgroup	Chlorpromazine n/N	Olanzapine n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
1 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 (Chlorpromazine), 0 (Olanzapine)					
Heterogeneity: not applicable					
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 (Chlorpromazine), 7 (Olanzapine)					
Heterogeneity: Tau^2 = 11.69; Chi^2 = 6.56, df = 1 (P = 0.01); I^2 =85%					
Test for overall effect: Z = 0.05 (P = 0.96)					
Test for subgroup differences: Chi^2 = 0.33, df = 1 (P = 0.57), I^2 =0.0%					

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Analysis 1.15. Comparison 1 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: 1 CHLORPROMAZINE versus OLANZAPINE

Outcome: 15 Adverse effects: 7a. Metabolic - weight gain - short term (up to 6 months)

Study or subgroup	Chlorpromazine n/N	Olanzapine n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% 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, 11.22]
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 (Chlorpromazine), 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: Not applicable

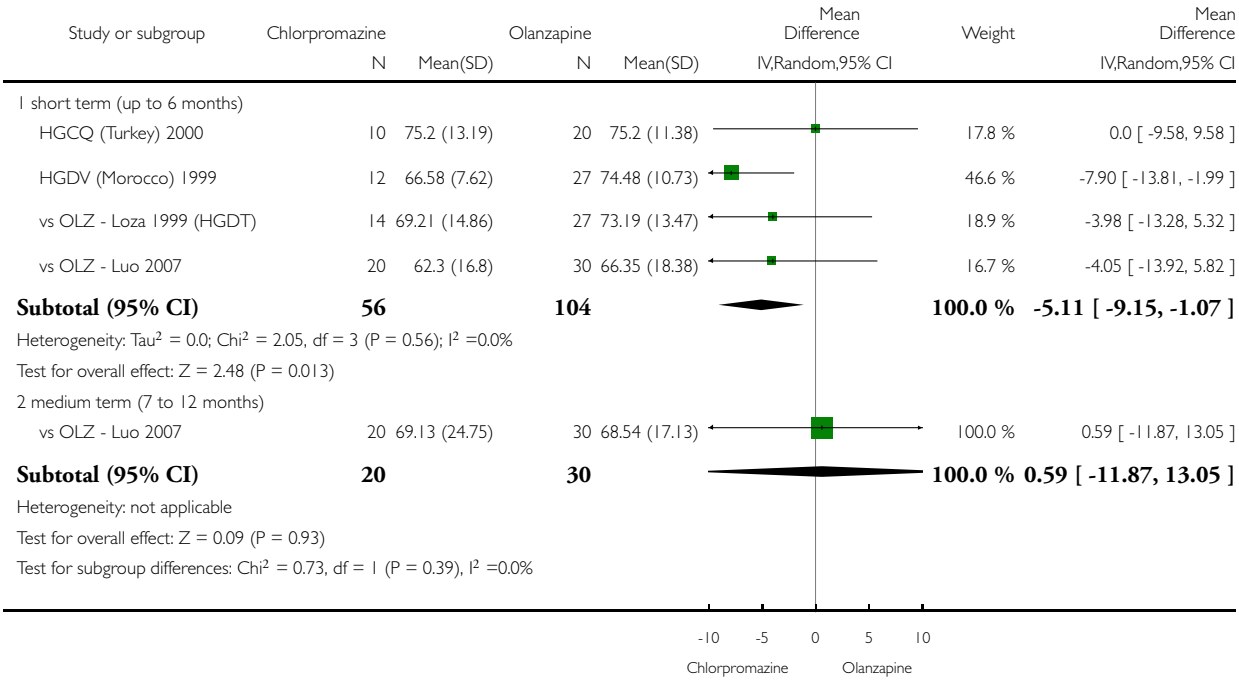
Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Analysis 1.16. Comparison 1 CHLORPROMAZINE versus OLANZAPINE, Outcome 16 Adverse effects: 7b. Metabolic - weight gain - continuous measures.

Review: Chlorpromazine versus atypical antipsychotic drugs for schizophrenia

Comparison: 1 CHLORPROMAZINE versus OLANZAPINE

Outcome: 16 Adverse effects: 7b. Metabolic - weight gain - continuous measures



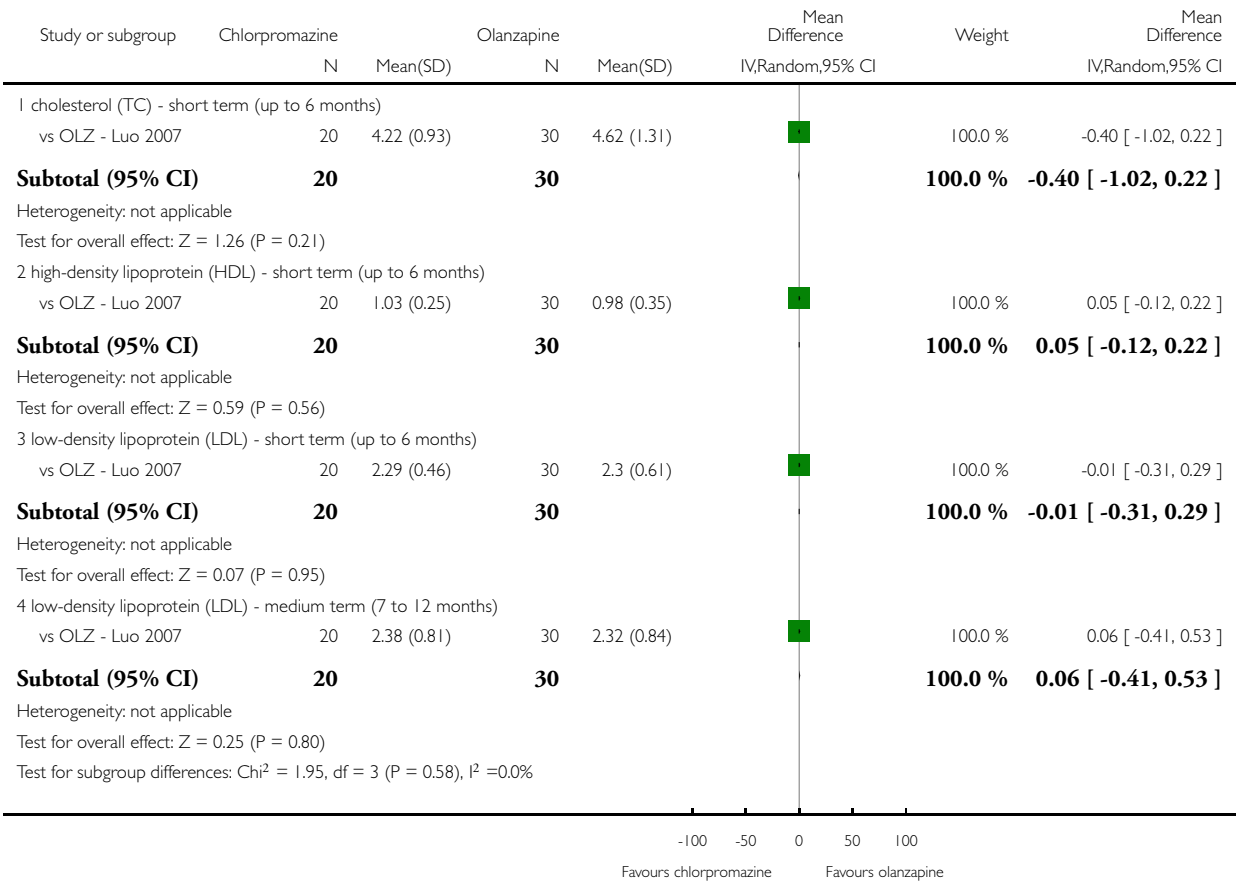
Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Analysis 1.17. Comparison 1 CHLORPROMAZINE versus OLANZAPINE, Outcome 17 Adverse effects: 7c. Metabolic - other - continuous measures.

Review: Chlorpromazine versus atypical antipsychotic drugs for schizophrenia

Comparison: 1 CHLORPROMAZINE versus OLANZAPINE

Outcome: 17 Adverse effects: 7c. Metabolic - other - continuous measures



Analysis 1.18. Comparison 1 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	N	
cholesterol (TC) - medium term (7 to 12 months)					**cholesterol (TC**
vs OLZ - Luo 2007	Chlorpromazine	4.5	2.21	20	
vs OLZ - Luo 2007	Olanzapine	4.52	2.73	30	

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Adverse effects: 7d. Metabolic - other - average endpoint scores - skewed data (*Continued*)

high-density lipoprotein (HDL) - short term (up to 6 months)					**high-density lip**
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)					**triglyceride (TG**
vs OLZ - Luo 2007	Chlorpromazine	1.44	1.07	20	
vs OLZ - Luo 2007	Olanzapine	2.13	2.07	30	
triglyceride (TG) - medium term (7 to 12 months)					**triglyceride (TG**
vs OLZ - Luo 2007	Chlorpromazine	2.26	2.04	20	
vs OLZ - Luo 2007	Olanzapine	2.32	2.14	30	

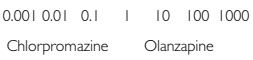
Analysis 1.19. Comparison 1 CHLORPROMAZINE versus OLANZAPINE, Outcome 19 Adverse effects: 8a. Movement disorders - extrapyramidal symptoms - short term (up to 6 months).

Review: Chlorpromazine versus atypical antipsychotic drugs for schizophrenia

Comparison: 1 CHLORPROMAZINE versus OLANZAPINE

Outcome: 19 Adverse effects: 8a. Movement disorders - extrapyramidal symptoms - short term (up to 6 months)

Study or subgroup	Chlorpromazine n/N	Olanzapine n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
1 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 (Chlorpromazine), 8 (Olanzapine)					
Heterogeneity: Tau^2 = 1.67; Chi^2 = 5.51, df = 2 (P = 0.06); I^2 =64%					
Test for overall effect: Z = 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]

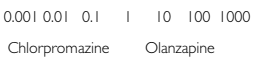


(*Continued* . . .)

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

(. . . *Continued*)

Study or subgroup	Chlorpromazine n/N	Olanzapine n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
vs OLZ - Zhao 2006	9/29	0/32		49.7 %	20.90 [1.27, 343.87]
Subtotal (95% CI)	**148**	**150**		**100.0 %**	**34.47 [4.79, 248.30]**
Total events: 37 (Chlorpromazine), 0 (Olanzapine)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.26$, df = 1 (P = 0.61); $I^2 = 0.0\%$					
Test for overall effect: Z = 3.51 (P = 0.00044)					
3 muscle stiffness					
vs OLZ - He 2003	1/40	0/40		45.0 %	3.00 [0.13, 71.51]
vs OLZ - Wu 2008	5/50	0/50		55.0 %	11.00 [0.62, 193.80]
Subtotal (95% CI)	**90**	**90**		**100.0 %**	**6.13 [0.73, 51.45]**
Total events: 6 (Chlorpromazine), 0 (Olanzapine)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.37$, df = 1 (P = 0.54); $I^2 = 0.0\%$					
Test for overall effect: Z = 1.67 (P = 0.095)					
4 tremor					
vs OLZ - He 2003	2/40	0/40		48.1 %	5.00 [0.25, 100.97]
vs OLZ - Wu 2008	4/50	0/50		51.9 %	9.00 [0.50, 162.89]
Subtotal (95% CI)	**90**	**90**		**100.0 %**	**6.78 [0.84, 54.57]**
Total events: 6 (Chlorpromazine), 0 (Olanzapine)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.08$, df = 1 (P = 0.78); $I^2 = 0.0\%$					
Test for overall effect: Z = 1.80 (P = 0.072)					
Test for subgroup differences: $Chi^2 = 4.49$, df = 3 (P = 0.21), $I^2 = 33\%$					



Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

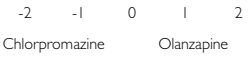
Analysis 1.20. Comparison 1 CHLORPROMAZINE versus OLANZAPINE, Outcome 20 Adverse effects: 8b. Movement disorders - extrapyramidal symptoms - average endpoint score (ESRS, high = poor).

Review: Chlorpromazine versus atypical antipsychotic drugs for schizophrenia

Comparison: 1 CHLORPROMAZINE versus OLANZAPINE

Outcome: 20 Adverse effects: 8b. Movement disorders - extrapyramidal symptoms - average endpoint score (ESRS, high = poor)

Study or subgroup	Chlorpromazine N	Mean(SD)	Olanzapine N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
1 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 (P = 0.020)							
Test for subgroup differences: Not applicable							



Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Analysis 1.21. Comparison 1 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: 1 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 N	Mean(SD)	Olanzapine N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
1 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 applicable							
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 applicable							
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 applicable							
Test for overall effect: Z = 1.63 (P = 0.10)							
Test for subgroup differences: Chi^2 = 1.22, df = 2 (P = 0.54), I^2 =0.0%							

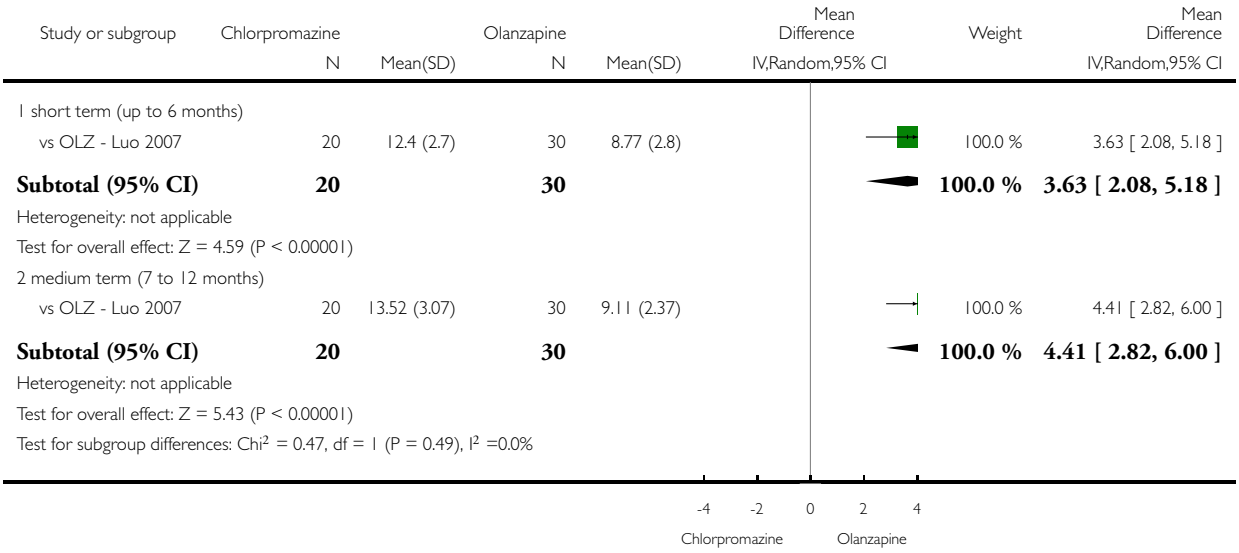
Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Analysis 1.22. Comparison 1 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: 1 CHLORPROMAZINE versus OLANZAPINE

Outcome: 22 Adverse effects: 9b. Various other - sleep - average length of sleep (hour/day)



Analysis 1.23. Comparison 1 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	N	
short term (up to 6 months)					**short term (up**
HGCQ (Turkey) 2000	Chlorpromazine	55.1	28.3	10	
HGCQ (Turkey) 2000	Olanzapine	55.9	18.8	20	

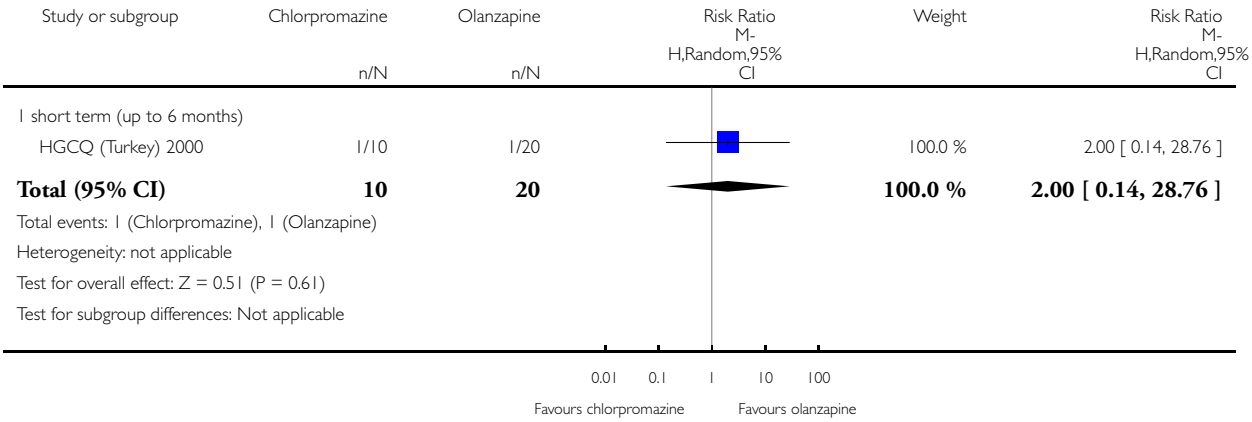
Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Analysis 1.24. Comparison 1 CHLORPROMAZINE versus OLANZAPINE, Outcome 24 Adverse effects: 9b. Various other - rash.

Review: Chlorpromazine versus atypical antipsychotic drugs for schizophrenia

Comparison: 1 CHLORPROMAZINE versus OLANZAPINE

Outcome: 24 Adverse effects: 9b. Various other - rash



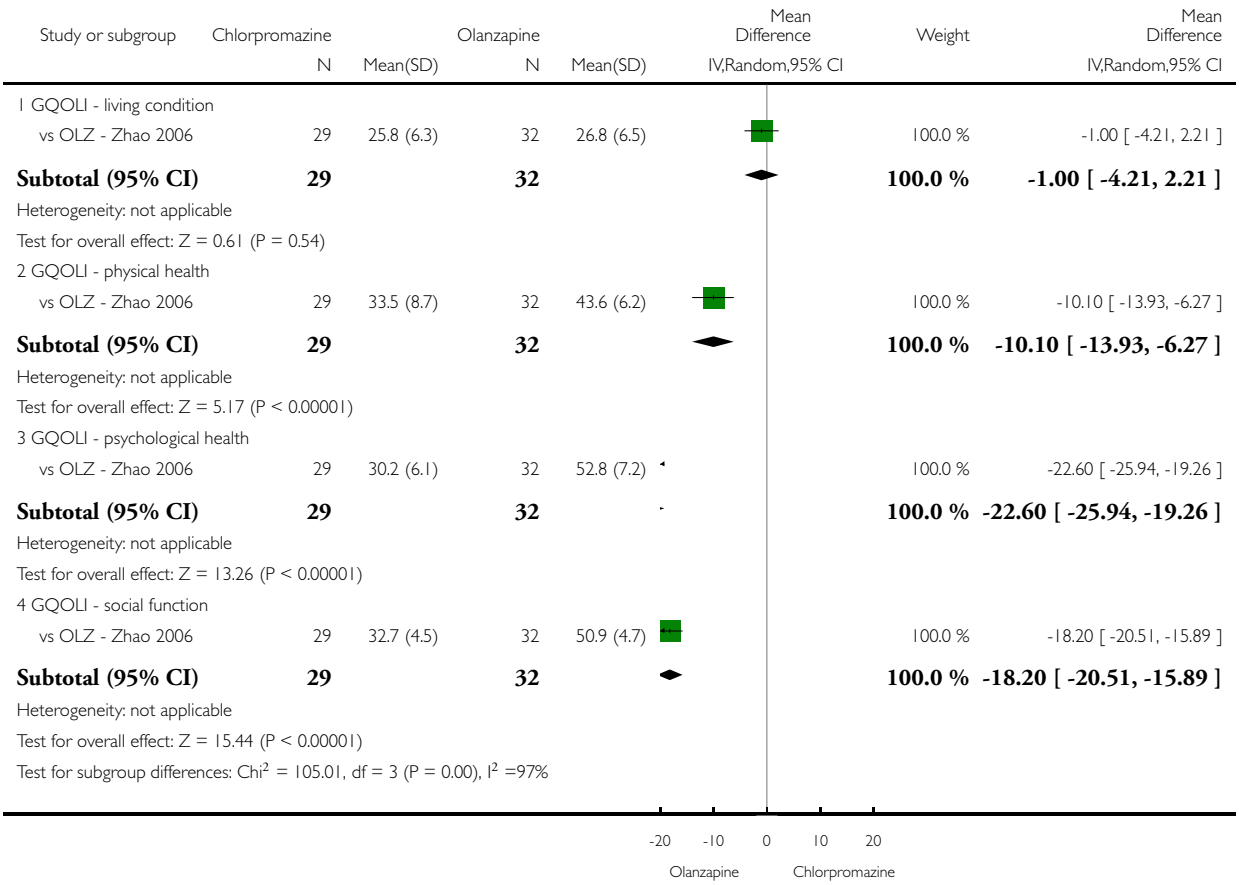
Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Analysis 1.25. Comparison 1 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: 1 CHLORPROMAZINE versus OLANZAPINE

Outcome: 25 Quality of life: 1a. Average endpoint scores (various scales, high = better) - short term (up to 6 months)



Analysis 1.26. Comparison 1 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	N	
short term (up to 6 months)					**short term (up**
vs OLZ - Loza 1999 (HGDT)	Chlorpromazine	47.7	26.6	14	

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

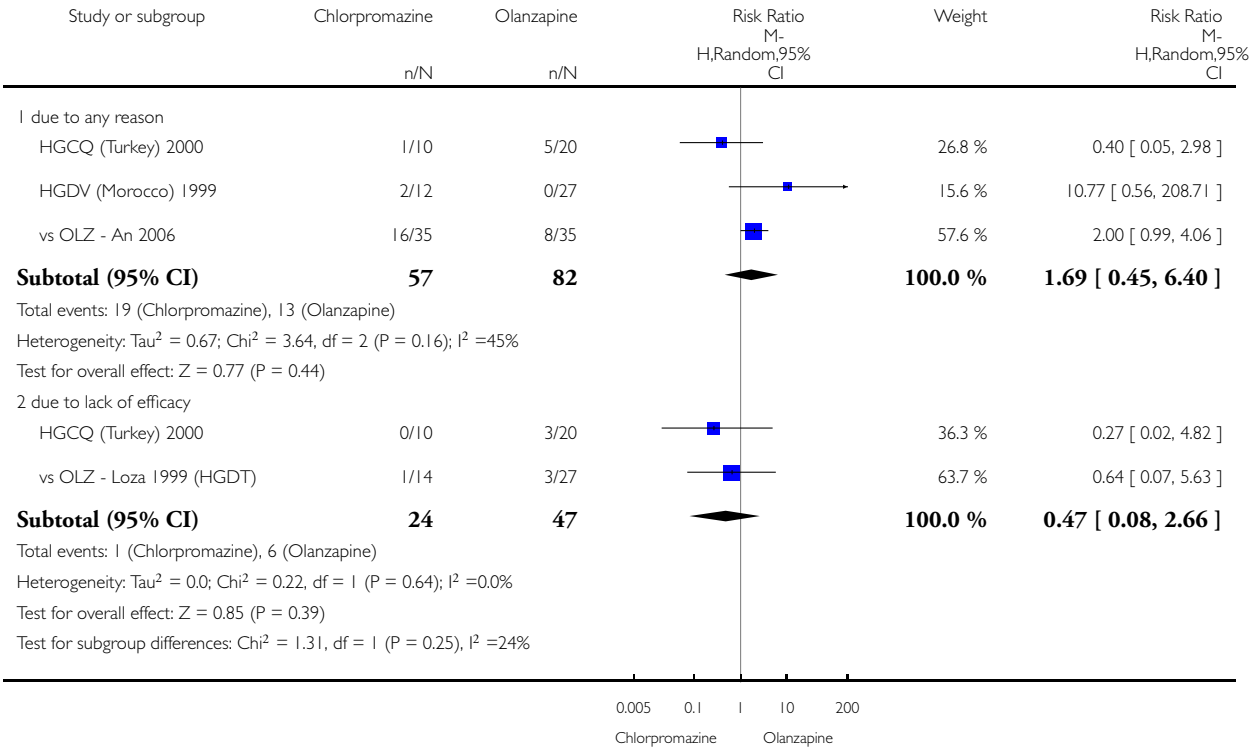
vs OLZ - Loza 1999 (HGDT)	Olanzapine	56.6	31.3	27

Analysis 1.27. Comparison 1 CHLORPROMAZINE versus OLANZAPINE, Outcome 27 Leaving the study early - short term (up to 6 months).

Review: Chlorpromazine versus atypical antipsychotic drugs for schizophrenia

Comparison: 1 CHLORPROMAZINE versus OLANZAPINE

Outcome: 27 Leaving the study early - short term (up to 6 months)



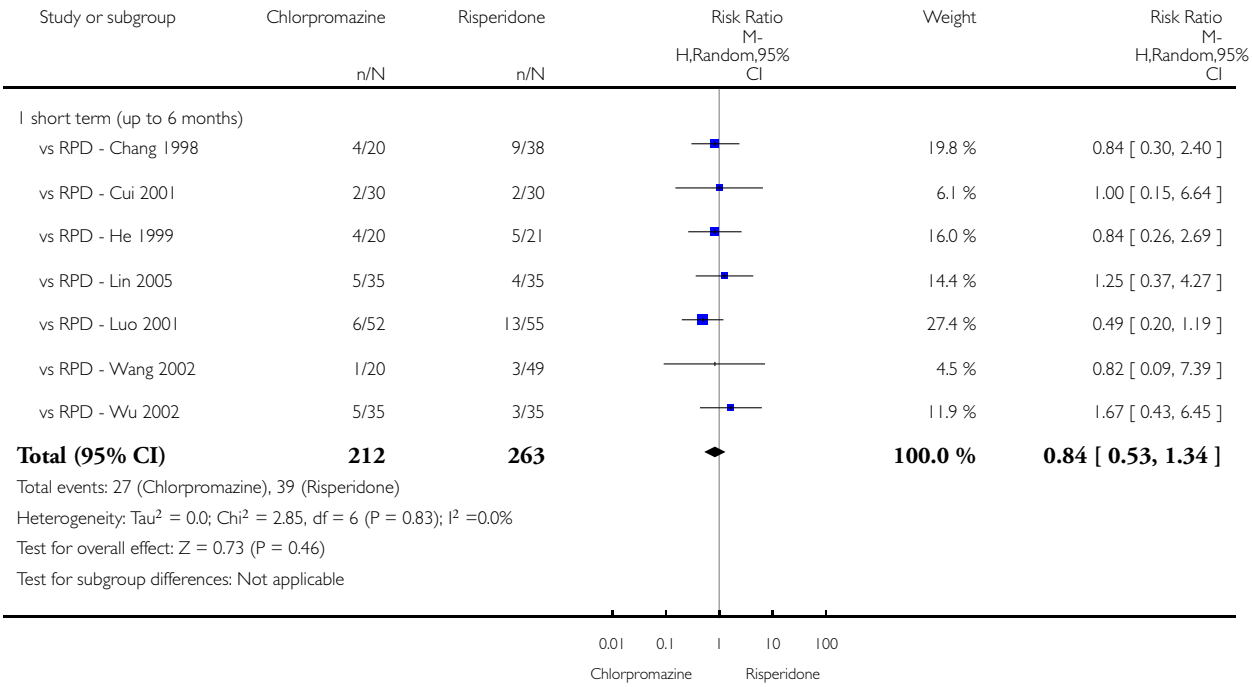
Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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: 1 Clinical response: 1. No significant clinical response



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	N
short term (up to 6 months)				**short term (up**
vs RPD - Ma 2004	Chlorpromazine	2.4	3.7	39
vs RPD - Ma 2004	Risperidone	1.8	6.6	39

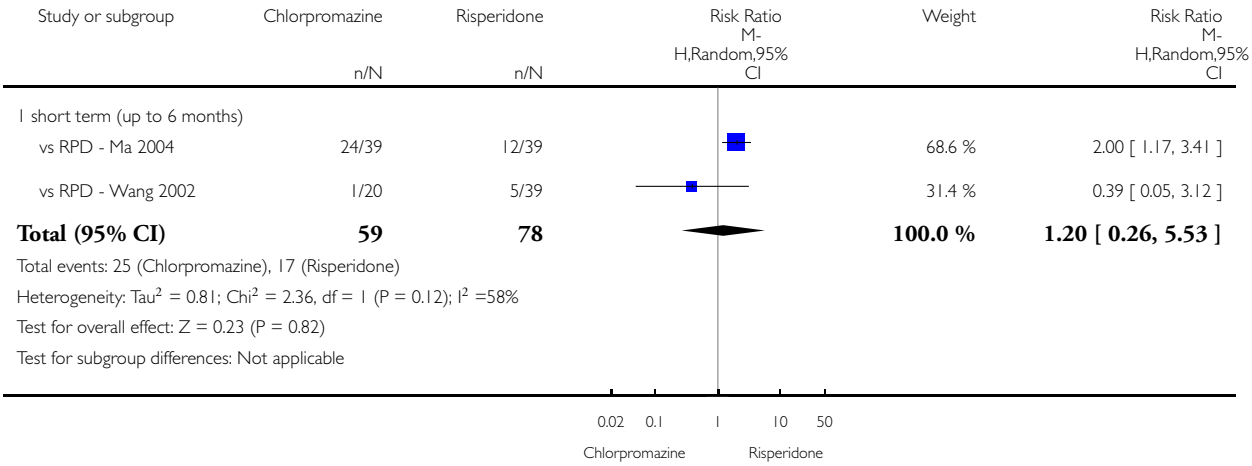
Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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



Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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: 1a. 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% CI	Weight	Mean Difference IV,Random,95% CI
1 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]
Subtotal (95% CI)	**124**		**123**			**100.0 %**	**0.90 [-3.49, 5.28]**
Heterogeneity: Tau^2 = 15.73; Chi^2 = 14.61, df = 3 (P = 0.002); I^2 =79%							
Test for overall effect: Z = 0.40 (P = 0.69)							
2 BPRS activation subscale							
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]
Subtotal (95% CI)	**65**		**65**			**100.0 %**	**0.41 [-0.81, 1.63]**
Heterogeneity: Tau^2 = 0.60; Chi^2 = 4.41, df = 1 (P = 0.04); I^2 =77%							
Test for overall effect: Z = 0.66 (P = 0.51)							
3 BPRS anxiety-depression subscale							
vs RPD - Cui 2001	30	4.5 (0.96)	30	5.27 (1.95)		48.9 %	-0.77 [-1.55, 0.01]
vs RPD - Wu 2002	35	5.17 (1.68)	35	4.26 (0.73)		51.1 %	0.91 [0.30, 1.52]
Subtotal (95% CI)	**65**		**65**			**100.0 %**	**0.09 [-1.56, 1.73]**
Heterogeneity: Tau^2 = 1.28; Chi^2 = 11.14, df = 1 (P = 0.00084); I^2 =91%							
Test for overall effect: Z = 0.11 (P = 0.92)							
4 BPRS hostile-suspiciousness subscale							
vs RPD - Cui 2001	30	4.5 (1.96)	30	4.8 (1.97)		49.3 %	-0.30 [-1.29, 0.69]
vs RPD - Wu 2002	35	5.98 (1.96)	35	3.94 (1.63)		50.7 %	2.04 [1.20, 2.88]
Subtotal (95% CI)	**65**		**65**			**100.0 %**	**0.89 [-1.41, 3.18]**
Heterogeneity: Tau^2 = 2.52; Chi^2 = 12.36, df = 1 (P = 0.00044); I^2 =92%							
Test for overall effect: Z = 0.76 (P = 0.45)							
5 NORS total							
vs RPD - He 1999	20	28.9 (7.8)	19	27.1 (5.9)		100.0 %	1.80 [-2.53, 6.13]
Subtotal (95% CI)	**20**		**19**			**100.0 %**	**1.80 [-2.53, 6.13]**
Heterogeneity: not applicable							
Test for overall effect: Z = 0.82 (P = 0.41)							

(*Continued . . .*)

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

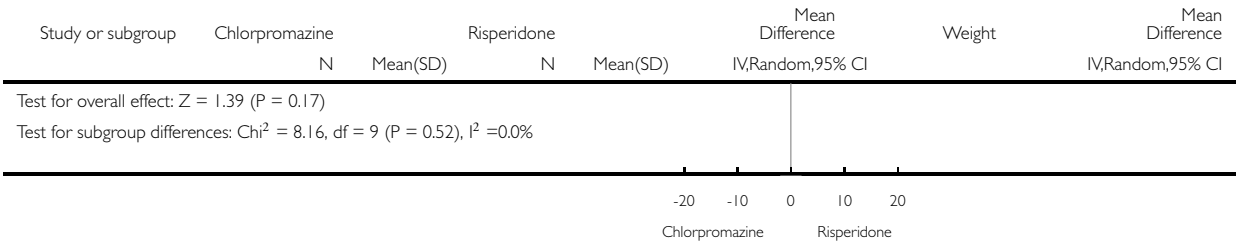
(. . . *Continued*)

Study or subgroup	Chlorpromazine N	Mean(SD)	Risperidone N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
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: Tau² = 8.80; Chi² = 8.70, df = 4 (P = 0.07); I² =54%							
Test for overall effect: Z = 1.05 (P = 0.29)							
7 PANSS positive symptom 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]
Subtotal (95% CI)	**167**		**170**			**100.0 %**	**0.03 [-1.67, 1.74]**
Heterogeneity: Tau² = 2.18; Chi² = 11.12, df = 3 (P = 0.01); I² =73%							
Test for overall effect: Z = 0.04 (P = 0.97)							
8 PANSS negative symptom subscale							
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)	**115**		**115**			**100.0 %**	**3.16 [-1.57, 7.89]**
Heterogeneity: Tau² = 16.56; Chi² = 40.11, df = 2 (P<0.00001); I² =95%							
Test for overall effect: Z = 1.31 (P = 0.19)							
9 PANSS general pathology subscale							
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)	**132**		**135**			**100.0 %**	**-0.85 [-2.15, 0.46]**
Heterogeneity: Tau² = 0.0; Chi² = 0.10, df = 2 (P = 0.95); I² =0.0%							
Test for overall effect: Z = 1.27 (P = 0.20)							
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**		**36**			**100.0 %**	**10.89 [-4.49, 26.27]**
Heterogeneity: Tau² = 114.12; Chi² = 13.51, df = 1 (P = 0.00024); I² =93%							

(*Continued* . . .)

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

(. . . *Continued*)



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**	**N**	
BPRS thinking disorder subscale					**BPRS thinking**
vs RPD - Wu 2002	Chlorpromazine	7.96	4.25	35	
vs RPD - Wu 2002	Risperidone	5.13	1.89	35	
BPRS withdraw-retardation 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 pathology 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 symptom 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	

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

vs RPD - Luo 2001	Risperidone	14	8	55	
PANSS positive symptom subscale					**PANSS positive**
vs RPD - Cui 2001	Chlorpromazine	11.67	13.6	30	
vs RPD - Cui 2001	Risperidone	11.6	4.67	30	
SAPS total					**SAPS total**
vs RPD - He 1999	Chlorpromazine	12.7	5.9	20	
vs RPD - He 1999	Risperidone	13.9	7.8	19	

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 N	Mean(SD)	Risperidone N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
1 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 applicable							
Test for overall effect: Z = 1.86 (P = 0.063)							
2 PANSS negative subscale							
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 applicable							
Test for overall effect: Z = 1.77 (P = 0.076)							
3 PANSS positive subscale							
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 applicable							
Test for overall effect: Z = 0.47 (P = 0.64)							
Test for subgroup differences: Chi^2 = 0.72, df = 2 (P = 0.70), I^2 =0.0%							

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

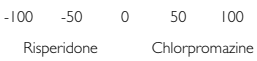
Analysis 2.7. Comparison 2 CHLORPROMAZINE versus RISPERIDONE, Outcome 7 Functioning: 1. Average endpoint score (WCST subscales, high = good) - short term (up to 6 months).

Review: Chlorpromazine versus atypical antipsychotic drugs for schizophrenia

Comparison: 2 CHLORPROMAZINE versus RISPERIDONE

Outcome: 7 Functioning: 1. Average endpoint score (WCST subscales, high = good) - short term (up to 6 months)

Study or subgroup	Chlorpromazine N	Mean(SD)	Risperidone N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
1 WCST-IQ							
vs RPD - Wang 2005	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 applicable							
Test for overall effect: Z = 3.15 (P = 0.0016)							
2 WCST-MQ							
vs RPD - Wang 2005	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 applicable							
Test for overall effect: Z = 4.16 (P = 0.000032)							
Test for subgroup differences: Chi² = 1.96, df = 1 (P = 0.16), I² =49%							



Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

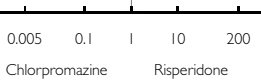
Analysis 2.8. Comparison 2 CHLORPROMAZINE versus RISPERIDONE, Outcome 8 Adverse effects: 1. Anticholinergic - short term (up to 6 months).

Review: Chlorpromazine versus atypical antipsychotic drugs for schizophrenia

Comparison: 2 CHLORPROMAZINE versus RISPERIDONE

Outcome: 8 Adverse effects: 1. Anticholinergic - short term (up to 6 months)

Study or subgroup	Chlorpromazine n/N	Risperidone n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
1 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]**
Total events: 38 (Chlorpromazine), 15 (Risperidone)					
Heterogeneity: Tau^2 = 0.03; Chi^2 = 4.25, df = 4 (P = 0.37); I^2 =6%					
Test for overall effect: Z = 2.86 (P = 0.0043)					
2 dry mouth					
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, 12.18]
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, 17.91]
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)	**415**	**437**		**100.0 %**	**2.00 [0.88, 4.51]**
Total events: 109 (Chlorpromazine), 43 (Risperidone)					
Heterogeneity: Tau^2 = 1.00; Chi^2 = 28.49, df = 8 (P = 0.00039); I^2 =72%					
Test for overall effect: Z = 1.66 (P = 0.096)					
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]
Subtotal (95% CI)	**90**	**90**		**100.0 %**	**3.00 [0.62, 14.46]**

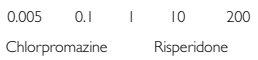


(*Continued . . .*)

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

(. . . *Continued*)

Study or subgroup	Chlorpromazine n/N	Risperidone n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Total events: 6 (Chlorpromazine), 2 (Risperidone)					
Heterogeneity: Tau^2 = 0.0; Chi^2 = 0.0, df = 1 (P = 1.00); I^2 =0.0%					
Test for overall effect: Z = 1.37 (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 %	11.00 [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 (Chlorpromazine), 5 (Risperidone)					
Heterogeneity: Tau^2 = 0.0; Chi^2 = 0.93, df = 4 (P = 0.92); I^2 =0.0%					
Test for overall effect: Z = 5.13 (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 (Chlorpromazine), 4 (Risperidone)					
Heterogeneity: not applicable					
Test for overall effect: Z = 2.06 (P = 0.039)					
Test for subgroup differences: Chi^2 = 7.66, df = 4 (P = 0.10), I^2 =48%					



Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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 n/N	Risperidone n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
1 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 (Chlorpromazine), 6 (Risperidone)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.20$, df = 2 (P = 0.90); $I^2 = 0.0\%$					
Test for overall effect: Z = 1.87 (P = 0.062)					
2 apathism					
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]**
Total events: 25 (Chlorpromazine), 4 (Risperidone)					
Heterogeneity: not applicable					
Test for overall effect: Z = 3.67 (P = 0.00025)					
3 blood pressure drop					
vs OLZ - He 2003	3/40	0/40		15.5 %	7.00 [0.37, 131.28]
vs OLZ - Wu 2008	5/50	0/50		16.1 %	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)	**125**	**125**		**100.0 %**	**8.25 [2.61, 26.12]**
Total events: 24 (Chlorpromazine), 2 (Risperidone)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.05$, df = 2 (P = 0.97); $I^2 = 0.0\%$					
Test for overall effect: Z = 3.59 (P = 0.00033)					
4 bradycardia					
vs RPD - Wu 2004	1/50	2/50		100.0 %	0.50 [0.05, 5.34]
Subtotal (95% CI)	**50**	**50**		**100.0 %**	**0.50 [0.05, 5.34]**
Total events: 1 (Chlorpromazine), 2 (Risperidone)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.57 (P = 0.57)					
5 orthostatic hypotension					
vs OLZ - Chang 2003	6/27	0/31		10.6 %	14.86 [0.88, 252.11]
vs OLZ - Chen 2006	2/44	0/42		9.4 %	4.78 [0.24, 96.68]

(*Continued . . .*)

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

(. . . *Continued*)

Study or subgroup	Chlorpromazine n/N	Risperidone n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% 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 (Chlorpromazine), 3 (Risperidone)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 1.17$, df = 4 (P = 0.88); $I^2 = 0.0\%$					
Test for overall effect: Z = 3.71 (P = 0.00021)					
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]**
Total events: 20 (Chlorpromazine), 0 (Risperidone)					
Heterogeneity: not applicable					
Test for overall effect: Z = 2.60 (P = 0.0093)					
7 sinus tachycardia					
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 (Chlorpromazine), 1 (Risperidone)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.02 (P = 0.31)					
8 tachycardia					
vs OLZ - He 2003	4/40	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 %	13.00 [0.76, 222.31]
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 (Chlorpromazine), 19 (Risperidone)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 3.82$, df = 6 (P = 0.70); $I^2 = 0.0\%$					
Test for overall effect: Z = 4.00 (P = 0.000063)					
Test for subgroup differences: $Chi^2 = 12.09$, df = 7 (P = 0.10), $I^2 = 42\%$					

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

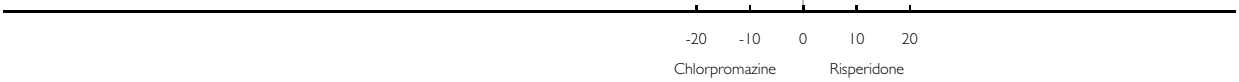
Analysis 2.10. Comparison 2 CHLORPROMAZINE versus RISPERIDONE, Outcome 10 Adverse effects: 2b. Cardiovascular - continuous measures - short term (up to 6 months).

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 N	Mean(SD)	Risperidone N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
1 cardiac rate (upright position)							
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 applicable							
Test for overall effect: Z = 1.40 (P = 0.16)							
2 cardiac rate (horizontal position)							
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 applicable							
Test for overall effect: Z = 3.68 (P = 0.00023)							
3 contractive blood pressure (upright position)							
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 applicable							
Test for overall effect: Z = 1.83 (P = 0.068)							
4 contractive blood pressure (horizontal position)							
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 applicable							
Test for overall effect: Z = 3.50 (P = 0.00046)							
5 diastolic blood pressure (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 applicable							
Test for overall effect: Z = 1.37 (P = 0.17)							
6 diastolic blood pressure (horizontal position)							
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 applicable							
Test for overall effect: Z = 1.35 (P = 0.18)							
Test for subgroup differences: Chi^2 = 31.88, df = 5 (P = 0.00), I^2 =84%							



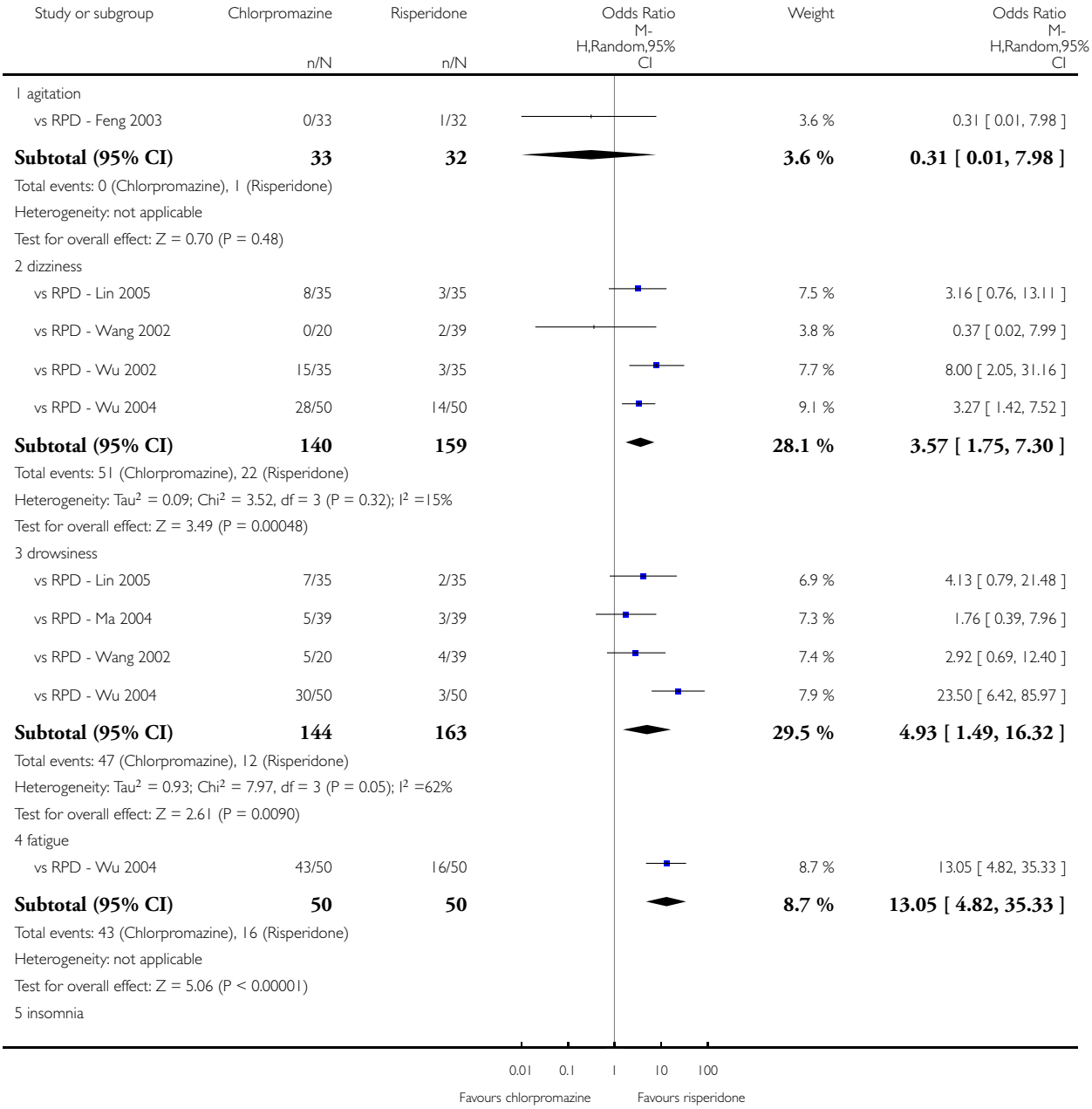
Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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

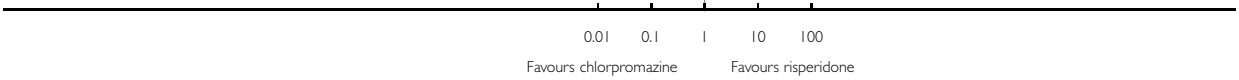


(*Continued . . .*)

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

(. . . *Continued*)

Study or subgroup	Chlorpromazine n/N	Risperidone n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
vs RPD - Feng 2003	0/33	8/32		4.1 %	0.04 [0.00, 0.78]
vs RPD - Lin 2005	1/35	3/35		5.3 %	0.31 [0.03, 3.17]
vs RPD - Ma 2004	2/39	1/39		5.0 %	2.05 [0.18, 23.63]
vs RPD - Wang 2002	0/20	6/39		4.1 %	0.13 [0.01, 2.35]
vs RPD - Wu 2002	2/35	6/35		6.8 %	0.29 [0.05, 1.57]
Subtotal (95% CI)	**162**	**180**		**25.2 %**	**0.29 [0.10, 0.90]**
Total events: 5 (Chlorpromazine), 24 (Risperidone)					
Heterogeneity: $Tau^2 = 0.22$; $Chi^2 = 4.59$, df = 4 (P = 0.33); $I^2 = 13\%$					
Test for overall effect: Z = 2.15 (P = 0.032)					
6 reduced activity					
vs RPD - Ma 2004	2/39	1/39		5.0 %	2.05 [0.18, 23.63]
Subtotal (95% CI)	**39**	**39**		**5.0 %**	**2.05 [0.18, 23.63]**
Total events: 2 (Chlorpromazine), 1 (Risperidone)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.58 (P = 0.56)					
Total (95% CI)	**568**	**623**		**100.0 %**	**1.96 [0.92, 4.22]**
Total events: 148 (Chlorpromazine), 76 (Risperidone)					
Heterogeneity: $Tau^2 = 1.49$; $Chi^2 = 49.19$, df = 15 (P = 0.00002); $I^2 = 70\%$					
Test for overall effect: Z = 1.73 (P = 0.083)					
Test for subgroup differences: $Chi^2 = 27.83$, df = 5 (P = 0.00), $I^2 = 82\%$					



Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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)

Study or subgroup	Chlorpromazine n/N	Risperidone n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
1 constipation					
vs OLZ - Chang 2003	12/27	1/31		3.6 %	13.78 [1.91, 99.16]
vs OLZ - Chen 2006	10/44	4/42		10.9 %	2.39 [0.81, 7.02]
vs OLZ - He 2003	16/40	5/40		14.9 %	3.20 [1.30, 7.90]
vs OLZ - Wang 2008	14/119	2/118		6.3 %	6.94 [1.61, 29.87]
vs OLZ - Wu 2008	18/50	4/50		12.3 %	4.50 [1.64, 12.36]
vs RPD - Ma 2004	2/39	2/39		3.8 %	1.00 [0.15, 6.75]
vs RPD - Wang 2002	0/20	3/39		1.7 %	0.27 [0.01, 5.02]
vs RPD - Wu 2002	10/35	3/35		9.0 %	3.33 [1.00, 11.09]
vs RPD - Wu 2004	35/50	14/50		37.7 %	2.50 [1.55, 4.04]
Subtotal (95% CI)	**424**	**444**		**100.0 %**	**3.00 [2.05, 4.39]**
Total events: 117 (Chlorpromazine), 38 (Risperidone)					
Heterogeneity: $Tau^2 = 0.04$; $Chi^2 = 9.01$, df = 8 (P = 0.34); $I^2 = 11\%$					
Test for overall effect: Z = 5.68 (P < 0.00001)					
2 diarrhoea					
vs OLZ - He 2003	2/40	0/40		100.0 %	5.00 [0.25, 100.97]
Subtotal (95% CI)	**40**	**40**		**100.0 %**	**5.00 [0.25, 100.97]**
Total events: 2 (Chlorpromazine), 0 (Risperidone)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.05 (P = 0.29)					
3 dysphagia					
vs RPD - Wu 2004	11/50	3/50		100.0 %	3.67 [1.09, 12.36]
Subtotal (95% CI)	**50**	**50**		**100.0 %**	**3.67 [1.09, 12.36]**
Total events: 11 (Chlorpromazine), 3 (Risperidone)					
Heterogeneity: not applicable					
Test for overall effect: Z = 2.10 (P = 0.036)					
4 loss of appetite					
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]**

(*Continued . . .*)

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

(. . . *Continued*)

Study or subgroup	Chlorpromazine n/N	Risperidone n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Total events: 56 (Chlorpromazine), 5 (Risperidone)					
Heterogeneity: Tau^2 = 0.48; Chi^2 = 1.78, df = 1 (P = 0.18); I^2 =44%					
Test for overall effect: Z = 3.45 (P = 0.00055)					
5 nausea/vomiting					
vs OLZ - He 2003	4/40	2/40		24.7 %	2.00 [0.39, 10.31]
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 (Chlorpromazine), 14 (Risperidone)					
Heterogeneity: Tau^2 = 0.0; Chi^2 = 2.95, df = 3 (P = 0.40); I^2 =0.0%					
Test for overall effect: Z = 0.40 (P = 0.69)					
Test for subgroup differences: Chi^2 = 12.58, df = 4 (P = 0.01), I^2 =68%					

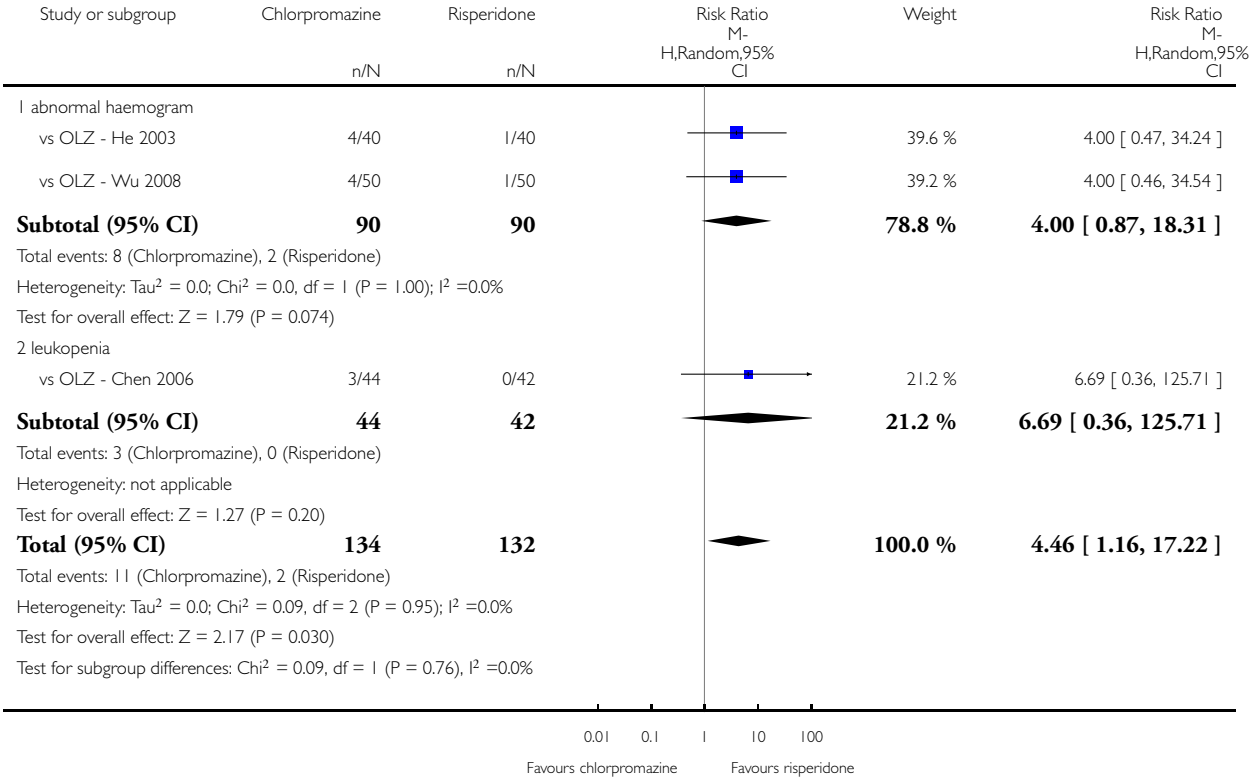
Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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)



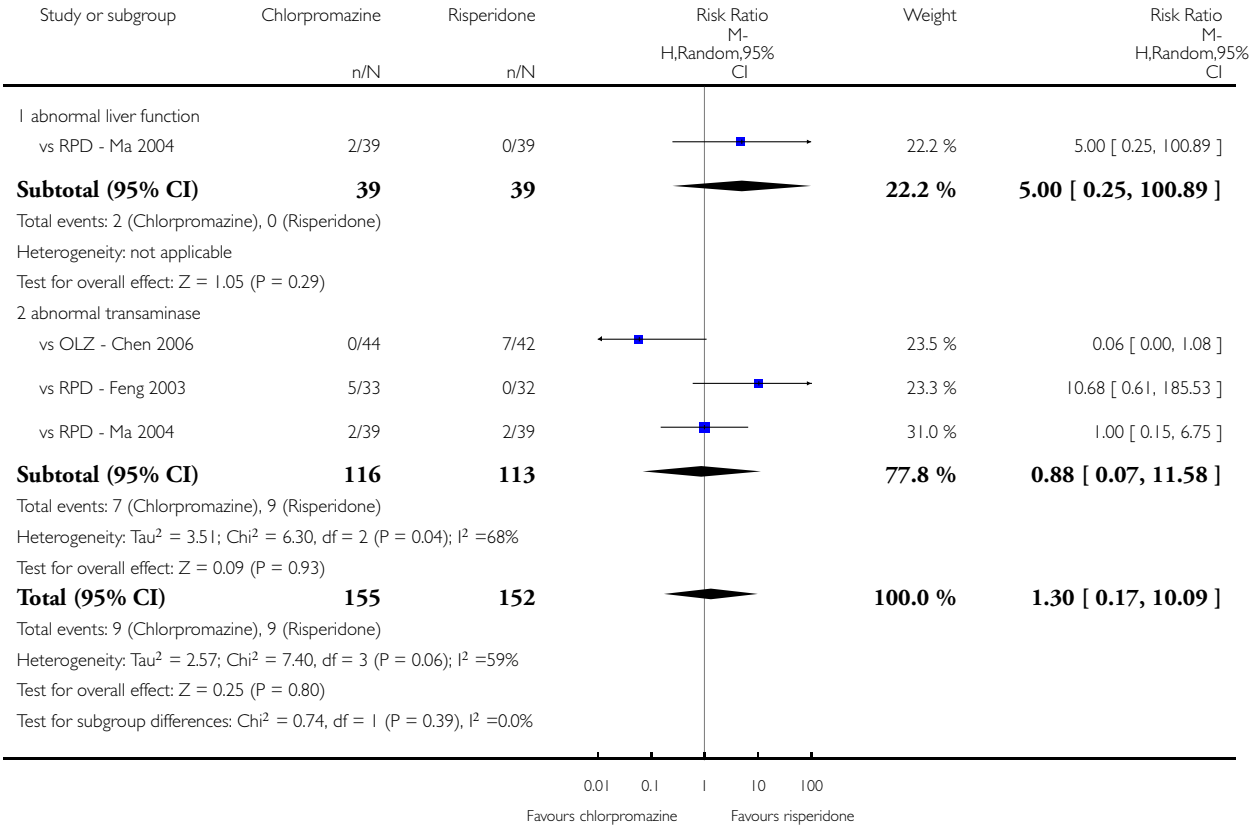
Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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)



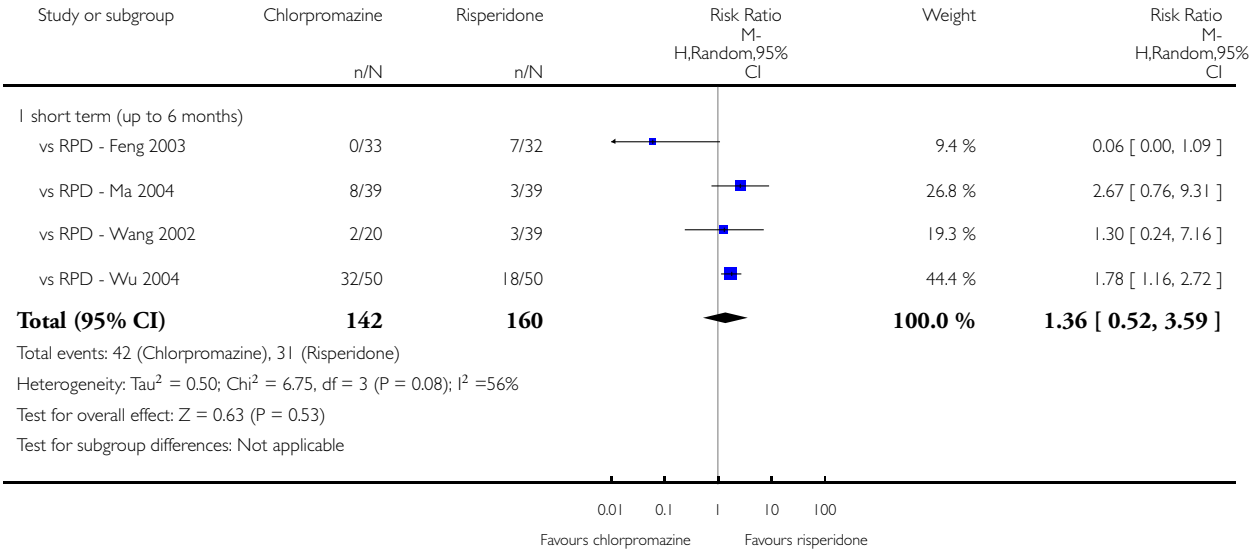
Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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



Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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

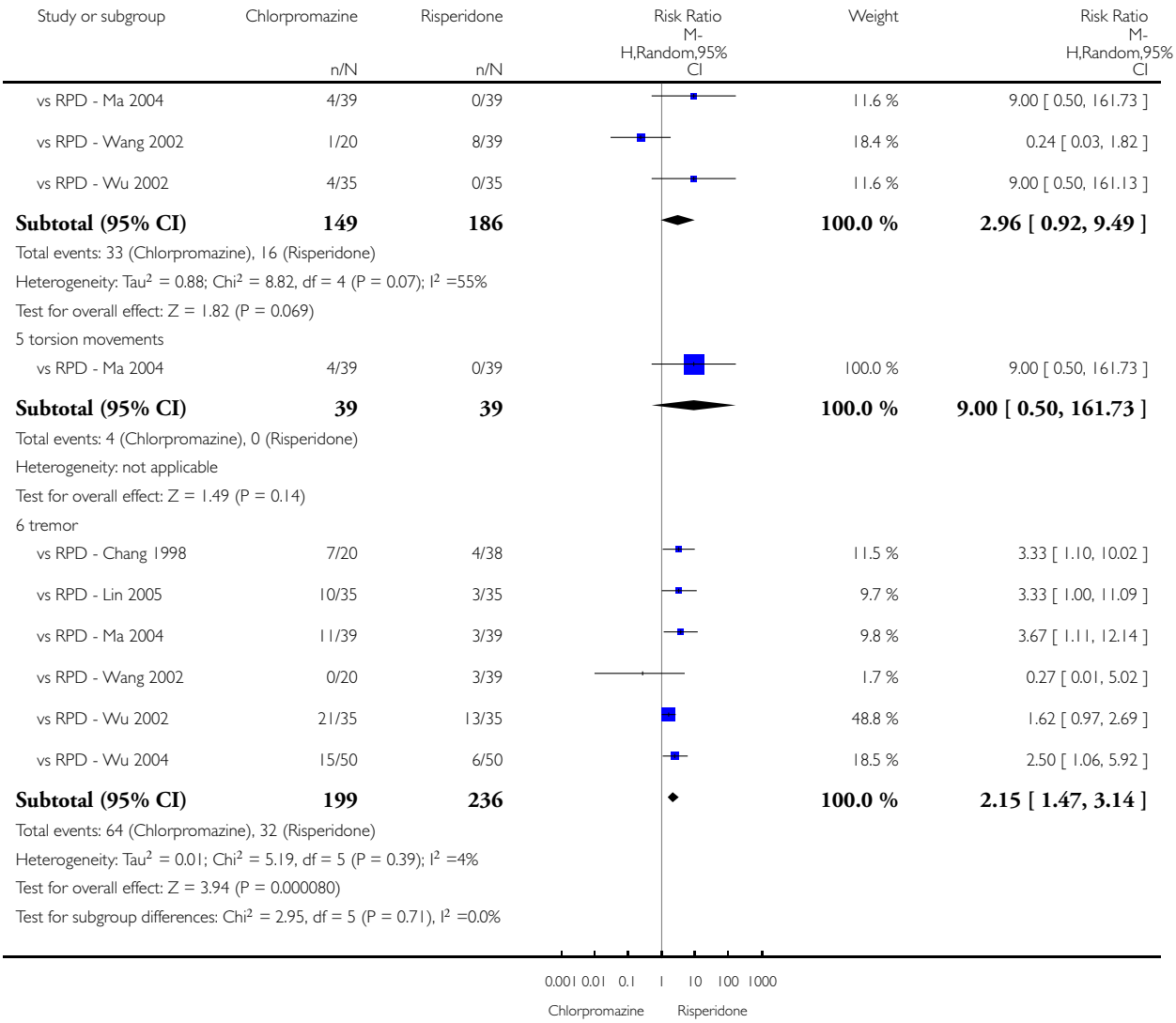
Outcome: 16 Adverse effects: 8. Movement disorders - short term (up to 6 months)

Study or subgroup	Chlorpromazine n/N	Risperidone n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
1 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]**
Total events: 62 (Chlorpromazine), 30 (Risperidone)					
Heterogeneity: $Tau^2 = 0.08$; $Chi^2 = 6.36$, df = 5 (P = 0.27); $I^2 = 21\%$					
Test for overall effect: Z = 3.48 (P = 0.00051)					
2 any EPS symptoms					
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)	**118**	**117**		**100.0 %**	**1.70 [0.85, 3.40]**
Total events: 46 (Chlorpromazine), 27 (Risperidone)					
Heterogeneity: $Tau^2 = 0.18$; $Chi^2 = 4.33$, df = 2 (P = 0.11); $I^2 = 54\%$					
Test for overall effect: Z = 1.49 (P = 0.13)					
3 dystonia					
vs RPD - Chang 1998	6/20	4/38		18.3 %	2.85 [0.91, 8.94]
vs RPD - Wu 2002	11/35	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)	**105**	**123**		**100.0 %**	**1.61 [0.97, 2.66]**
Total events: 32 (Chlorpromazine), 22 (Risperidone)					
Heterogeneity: $Tau^2 = 0.02$; $Chi^2 = 2.20$, df = 2 (P = 0.33); $I^2 = 9\%$					
Test for overall effect: Z = 1.85 (P = 0.064)					
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 . . .*)

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

(. . . *Continued*)



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	N	
short term (up to 6 months)					**short term (up**
vs RPD - Cui 2001	Chlorpromazine	3.23	2.87	30	

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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

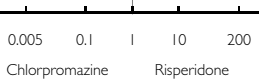
Analysis 2.18. Comparison 2 CHLORPROMAZINE versus RISPERIDONE, Outcome 18 Adverse effects: 10. Various other - short term (up to 6 months).

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 n/N	Risperidone n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
1 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 (Chlorpromazine), 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 (Chlorpromazine), 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 (Chlorpromazine), 11 (Risperidone)					
Heterogeneity: not applicable					
Test for overall effect: Z = 3.17 (P = 0.0015)					

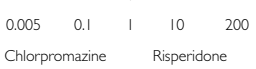


(*Continued* . . .)

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

(. . . *Continued*)

Study or subgroup	Chlorpromazine n/N	Risperidone n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
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 (Chlorpromazine), 24 (Risperidone)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.78 (P = 0.075)					
Test for subgroup differences: Chi^2 = 4.01, df = 3 (P = 0.26), I^2 =25%					



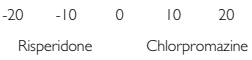
Analysis 2.19. Comparison 2 CHLORPROMAZINE versus RISPERIDONE, Outcome 19 Quality of life: 1. Average endpoint score (QOL, high = good).

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 N	Mean(SD)	Risperidone N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
1 short term (up to 6 months)							
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 applicable							
Test for overall effect: Z = 4.42 (P < 0.00001)							
Test for subgroup differences: Not applicable							



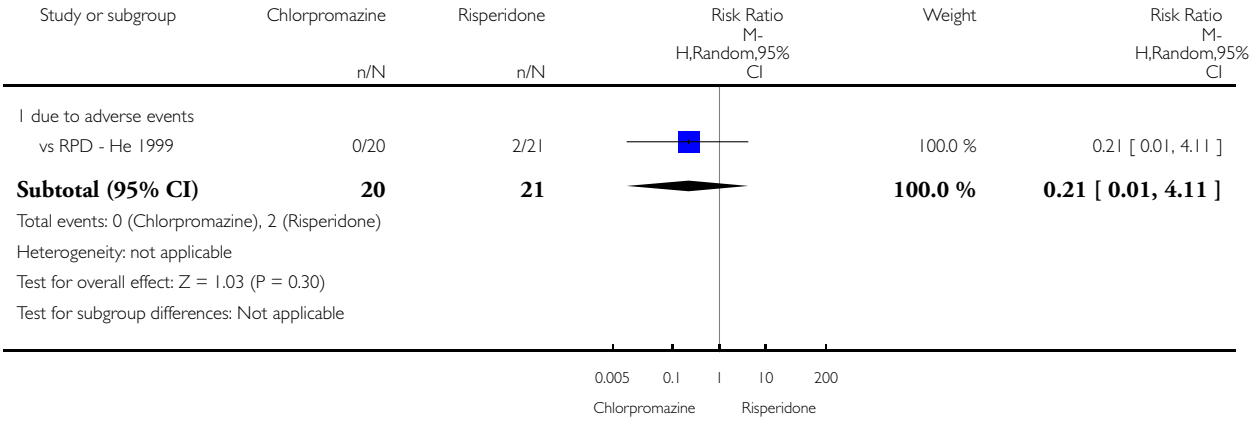
Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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)



Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

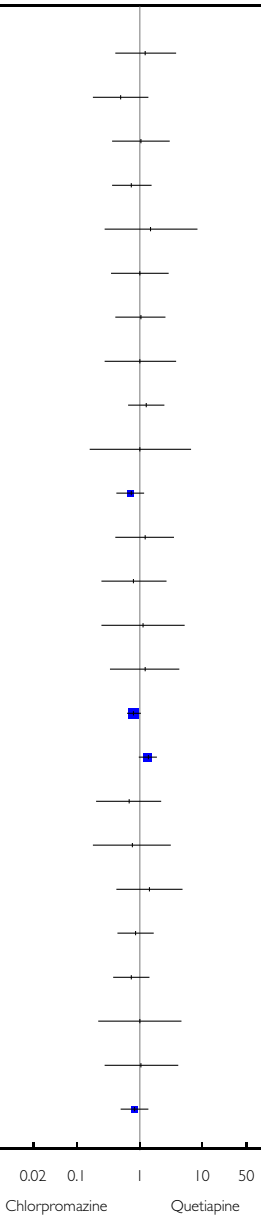
Analysis 3.1. Comparison 3 CHLORPROMAZINE versus QUETIAPINE, Outcome 1 Clinical response: 1. No significant clinical response.

Review: Chlorpromazine versus atypical antipsychotic drugs for schizophrenia

Comparison: 3 CHLORPROMAZINE versus QUETIAPINE

Outcome: 1 Clinical response: 1. No significant clinical response

Study or subgroup	Chlorpromazine n/N	Quetiapine n/N	Risk Ratio IV,Random,95% CI	Weight	Risk Ratio IV,Random,95% CI
1 short term (up to 6 months)					
vs QTP - Ai 2007	6/42	5/43		1.5 %	1.23 [0.41, 3.72]
vs QTP - Cai 2006	5/100	11/109		1.7 %	0.50 [0.18, 1.38]
vs QTP - Cai 2007	6/46	6/48		1.6 %	1.04 [0.36, 3.00]
vs QTP - Chen 2001	11/107	16/114		3.5 %	0.73 [0.36, 1.51]
vs QTP - Chen 2008	3/30	2/30		0.6 %	1.50 [0.27, 8.34]
vs QTP - Deng 2004	6/45	6/45		1.6 %	1.00 [0.35, 2.87]
vs QTP - Guo 2003a	8/73	8/75		2.1 %	1.03 [0.41, 2.59]
vs QTP - Guo 2005	4/40	4/40		1.0 %	1.00 [0.27, 3.72]
vs QTP - Guo 2008	13/40	11/43		3.9 %	1.27 [0.65, 2.50]
vs QTP - He 2003	2/20	2/20		0.5 %	1.00 [0.16, 6.42]
vs QTP - Jiang 2006	20/97	27/94		7.1 %	0.72 [0.43, 1.19]
vs QTP - Jiang 2008	6/30	5/30		1.6 %	1.20 [0.41, 3.51]
vs QTP - Jin 2007	4/30	5/30		1.2 %	0.80 [0.24, 2.69]
vs QTP - Liu 2003	3/39	3/44		0.8 %	1.13 [0.24, 5.27]
vs QTP - Mei 2007	5/49	4/47		1.2 %	1.20 [0.34, 4.19]
vs QTP - NCT00882518	64/190	82/194		27.0 %	0.80 [0.62, 1.03]
vs QTP - Peuskens 1997	48/100	36/101		16.4 %	1.35 [0.97, 1.88]
vs QTP - Tian 2006	4/46	6/46		1.3 %	0.67 [0.20, 2.21]
vs QTP - Wan 2002	3/30	4/30		0.9 %	0.75 [0.18, 3.07]
vs QTP - Wan 2008	5/28	4/32		1.2 %	1.43 [0.42, 4.81]
vs QTP - Wang 2004	12/48	14/48		4.2 %	0.86 [0.44, 1.66]
vs QTP - Wang 2005	12/57	14/48		4.0 %	0.72 [0.37, 1.41]
vs QTP - Yang 2007	3/30	3/30		0.8 %	1.00 [0.22, 4.56]
vs QTP - Zhang 2002	4/57	4/60		1.0 %	1.05 [0.28, 4.01]
vs QTP - Zhang 2003	22/118	27/119		7.2 %	0.82 [0.50, 1.36]



(*Continued* . . .)

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

(. . . *Continued*)

Study or subgroup	Chlorpromazine n/N	Quetiapine n/N	Risk Ratio IV,Random,95% CI	Weight	Risk Ratio IV,Random,95% CI
vs QTP - Zhang 2008	3/30	2/30		0.6 %	1.50 [0.27, 8.34]
vs QTP - Zhou 2004	13/41	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]**

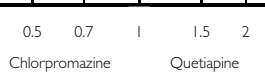
Total events: 299 (Chlorpromazine), 328 (Quetiapine)
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 13.40$, df = 27 (P = 0.99); $I^2 = 0.0\%$
Test for overall effect: Z = 1.05 (P = 0.29)
Test for subgroup differences: Not applicable

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: 1. Need of additional benzodiazepines/benzhexol

Study or subgroup	Chlorpromazine n/N	Quetiapine n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
1 short term (up to 6 months)					
vs QTP - Cheng 2003	33/45	21/44		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 (Chlorpromazine), 61 (Quetiapine)
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.55$, df = 1 (P = 0.46); $I^2 = 0.0\%$
Test for overall effect: Z = 2.76 (P = 0.0057)
Test for subgroup differences: Not applicable



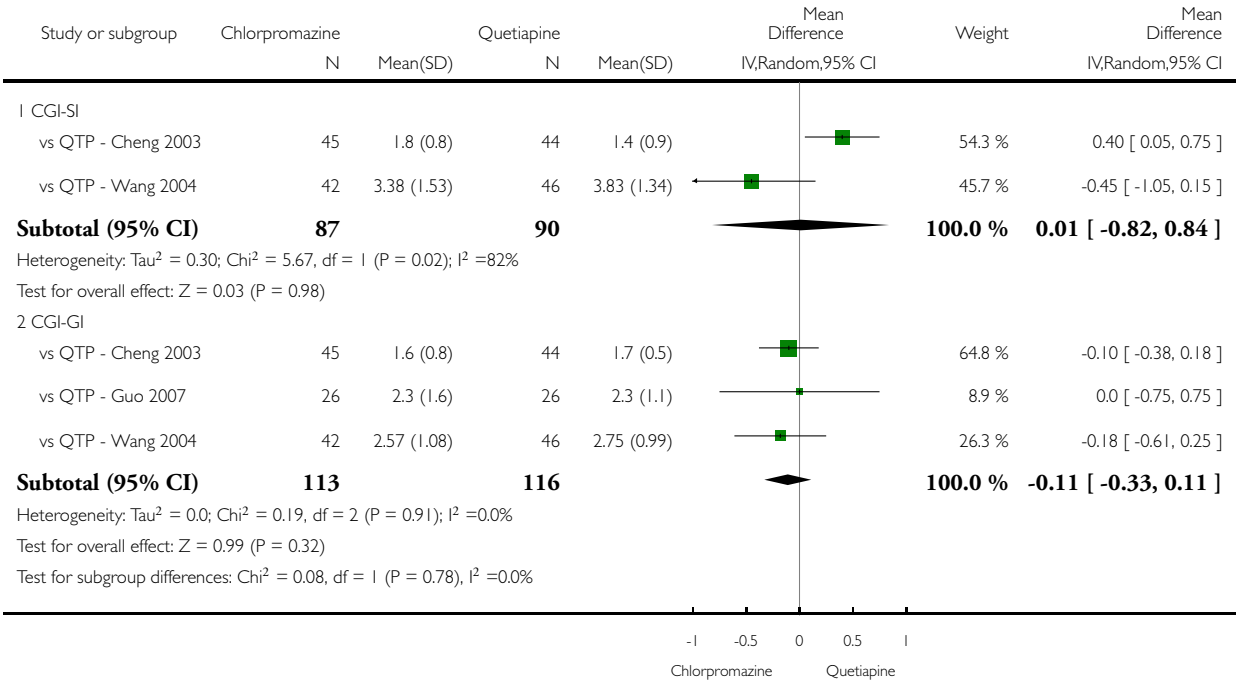
Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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)



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	N
short term (up to 6 months)				**short term (up t**
vs QTP - Guo 2007	Chlorpromazine	1.5	1.7	26
vs QTP - Guo 2007	Quetiapine	1.6	1.3	26

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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 N	Mean(SD)	Quetiapine N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
1 short term (up to 6 months)							
vs QTP - NCT00882518	190	-2.1 (0.11)	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 applicable							
Test for overall effect: Z = 25.55 (P < 0.00001)							
Test for subgroup differences: Not applicable							

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

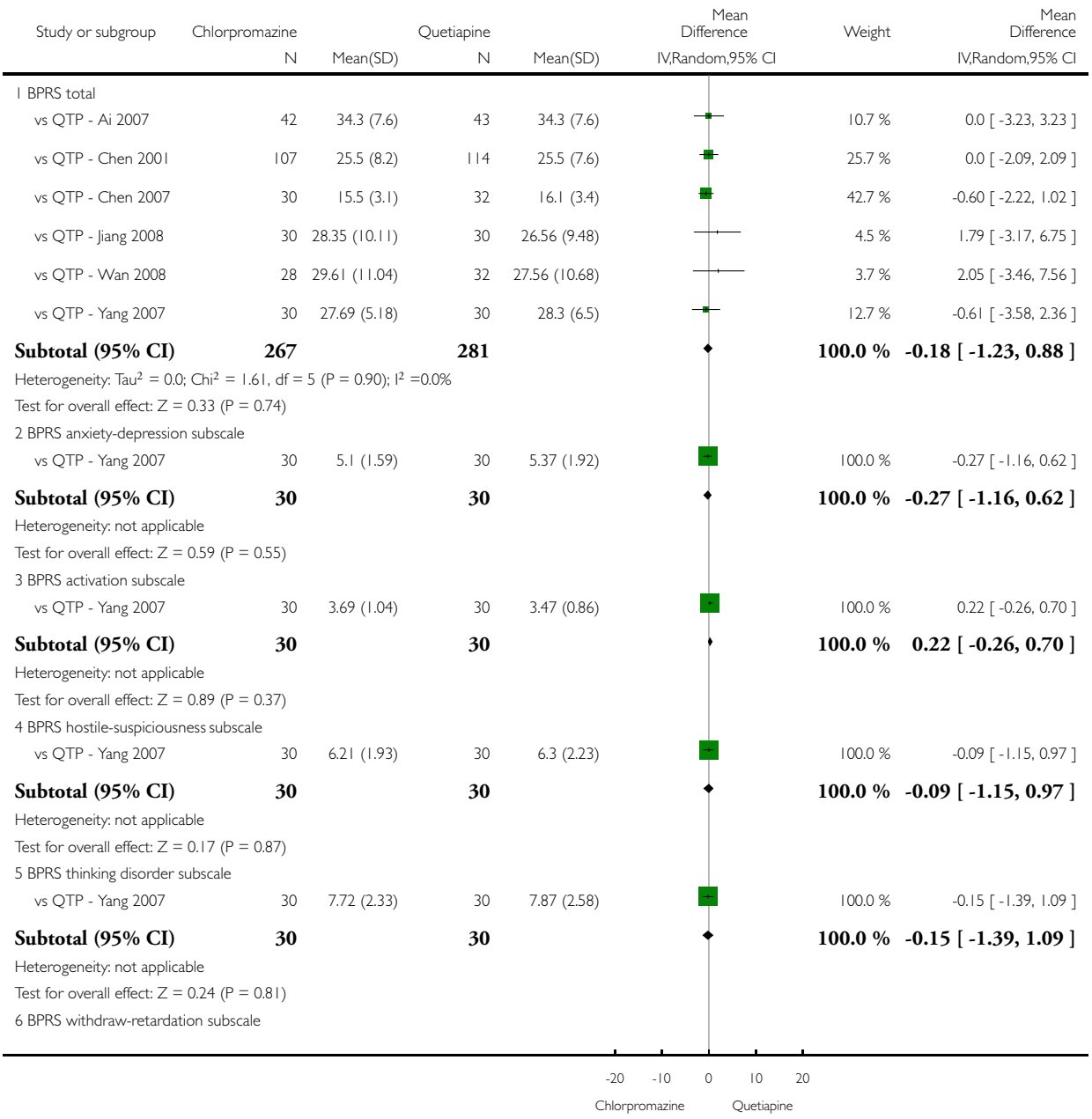
Analysis 3.6. Comparison 3 CHLORPROMAZINE versus QUETIAPINE, Outcome 6 Mental state: 1a. Average endpoint scores (various scales, high = poor) - short term (up to 6 months).

Review: Chlorpromazine versus atypical antipsychotic drugs for schizophrenia

Comparison: 3 CHLORPROMAZINE versus QUETIAPINE

Outcome: 6 Mental state: 1a. Average endpoint scores (various scales, high = poor) - short term (up to 6 months)

Study or subgroup	Chlorpromazine N	Mean(SD)	Quetiapine N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
1 BPRS total							
vs QTP - Ai 2007	42	34.3 (7.6)	43	34.3 (7.6)		10.7 %	0.0 [-3.23, 3.23]
vs QTP - Chen 2001	107	25.5 (8.2)	114	25.5 (7.6)		25.7 %	0.0 [-2.09, 2.09]
vs QTP - Chen 2007	30	15.5 (3.1)	32	16.1 (3.4)		42.7 %	-0.60 [-2.22, 1.02]
vs QTP - Jiang 2008	30	28.35 (10.11)	30	26.56 (9.48)		4.5 %	1.79 [-3.17, 6.75]
vs QTP - Wan 2008	28	29.61 (11.04)	32	27.56 (10.68)		3.7 %	2.05 [-3.46, 7.56]
vs QTP - Yang 2007	30	27.69 (5.18)	30	28.3 (6.5)		12.7 %	-0.61 [-3.58, 2.36]
Subtotal (95% CI)	**267**		**281**			**100.0 %**	**-0.18 [-1.23, 0.88]**
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 1.61$, df = 5 (P = 0.90); $I^2 = 0.0\%$							
Test for overall effect: Z = 0.33 (P = 0.74)							
2 BPRS anxiety-depression subscale							
vs QTP - Yang 2007	30	5.1 (1.59)	30	5.37 (1.92)		100.0 %	-0.27 [-1.16, 0.62]
Subtotal (95% CI)	**30**		**30**			**100.0 %**	**-0.27 [-1.16, 0.62]**
Heterogeneity: not applicable							
Test for overall effect: Z = 0.59 (P = 0.55)							
3 BPRS activation subscale							
vs QTP - Yang 2007	30	3.69 (1.04)	30	3.47 (0.86)		100.0 %	0.22 [-0.26, 0.70]
Subtotal (95% CI)	**30**		**30**			**100.0 %**	**0.22 [-0.26, 0.70]**
Heterogeneity: not applicable							
Test for overall effect: Z = 0.89 (P = 0.37)							
4 BPRS hostile-suspiciousness subscale							
vs QTP - Yang 2007	30	6.21 (1.93)	30	6.3 (2.23)		100.0 %	-0.09 [-1.15, 0.97]
Subtotal (95% CI)	**30**		**30**			**100.0 %**	**-0.09 [-1.15, 0.97]**
Heterogeneity: not applicable							
Test for overall effect: Z = 0.17 (P = 0.87)							
5 BPRS thinking disorder subscale							
vs QTP - Yang 2007	30	7.72 (2.33)	30	7.87 (2.58)		100.0 %	-0.15 [-1.39, 1.09]
Subtotal (95% CI)	**30**		**30**			**100.0 %**	**-0.15 [-1.39, 1.09]**
Heterogeneity: not applicable							
Test for overall effect: Z = 0.24 (P = 0.81)							
6 BPRS withdraw-retardation subscale							



(*Continued* . . .)

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

(. . . *Continued*)

Study or subgroup	Chlorpromazine N	Mean(SD)	Quetiapine N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
vs QTP - Yang 2007	30	5.07 (1.5)	30	5.17 (1.05)		100.0 %	-0.10 [-0.76, 0.56]
Subtotal (95% CI)	**30**		**30**			**100.0 %**	**-0.10 [-0.76, 0.56]**
Heterogeneity: not applicable							
Test for overall effect: Z = 0.30 (P = 0.76)							
7 PANSS total							
vs QTP - An 2005	30	57.68 (11.11)	30	55.67 (11)		4.2 %	2.01 [-3.58, 7.60]
vs QTP - Cai 2007	46	24.8 (8.3)	48	45.7 (13.8)		4.5 %	-20.90 [-25.48, -16.32]
vs QTP - Chen 2001	107	48.1 (15.2)	114	48.5 (14.8)		4.8 %	-0.40 [-4.36, 3.56]
vs QTP - Chen 2007	30	34.6 (10.7)	32	34.1 (10.2)		4.3 %	0.50 [-4.71, 5.71]
vs QTP - Chen 2008	30	42.8 (4.8)	30	44.3 (4.1)		5.3 %	-1.50 [-3.76, 0.76]
vs QTP - Cheng 2003	45	48.2 (15.1)	44	48 (15.2)		3.9 %	0.20 [-6.10, 6.50]
vs QTP - Guo 2003a	73	46.72 (17.12)	75	47.32 (17.212)		4.2 %	-0.60 [-6.13, 4.93]
vs QTP - Guo 2003b	30	48.66 (8.9)	30	45.42 (8.8)		4.6 %	3.24 [-1.24, 7.72]
vs QTP - Guo 2005	40	48.1 (15.2)	40	48.6 (13.8)		3.9 %	-0.50 [-6.86, 5.86]
vs QTP - Guo 2007	26	43.9 (12.3)	26	44.7 (12.2)		3.8 %	-0.80 [-7.46, 5.86]
vs QTP - Guo 2008	40	52.6 (16.4)	43	42.3 (17)		3.6 %	10.30 [3.11, 17.49]
vs QTP - He 2003	20	50 (12.9)	20	43.1 (10.2)		3.6 %	6.90 [-0.31, 14.11]
vs QTP - Ji 2004	29	34.63 (10.7)	30	34.05 (10.17)		4.3 %	0.58 [-4.75, 5.91]
vs QTP - Jiang 2008	30	39.24 (10.36)	30	37.21 (11.48)		4.2 %	2.03 [-3.50, 7.56]
vs QTP - Liu 2003	39	40.2 (13.9)	44	41.4 (14.4)		4.0 %	-1.20 [-7.29, 4.89]
vs QTP - Mei 2007	49	52.9 (18.3)	47	53.2 (23.6)		3.1 %	-0.30 [-8.77, 8.17]
vs QTP - Sun 2006	36	47.55 (10.63)	35	46.67 (11.4)		4.3 %	0.88 [-4.25, 6.01]
vs QTP - Tian 2006	46	47.6 (17.7)	46	45.2 (19.2)		3.4 %	2.40 [-5.15, 9.95]
vs QTP - Wan 2002	30	48 (14.3)	30	54.2 (14.4)		3.5 %	-6.20 [-13.46, 1.06]
vs QTP - Wan 2008	28	40.13 (18.24)	32	38.57 (12.56)		3.3 %	1.56 [-6.48, 9.60]
vs QTP - Wang 2004	42	58.67 (20.93)	46	61.63 (23.73)		2.9 %	-2.96 [-12.29, 6.37]
vs QTP - Wang 2005	57	53.1 (18.5)	48	53.7 (23.8)		3.2 %	-0.60 [-8.87, 7.67]
vs QTP - Zhang 2006	33	49.9 (7.02)	28	47.1 (7.06)		4.9 %	2.80 [-0.75, 6.35]
vs QTP - Zhou 2004	39	53.15 (9.84)	40	51.47 (10.62)		4.6 %	1.68 [-2.83, 6.19]
vs QTP - Zou 2006	43	49.9 (14.7)	43	47.8 (15.4)		3.9 %	2.10 [-4.26, 8.46]
Subtotal (95% CI)	**1018**		**1031**			**100.0 %**	**-0.05 [-2.30, 2.19]**
Heterogeneity: Tau^2 = 23.45; Chi^2 = 102.88, df = 24 (P<0.00001); I^2 =77%							
Test for overall effect: Z = 0.05 (P = 0.96)							

-20 -10 0 10 20

Chlorpromazine Quetiapine

(*Continued* . . .)

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

(. . . *Continued*)

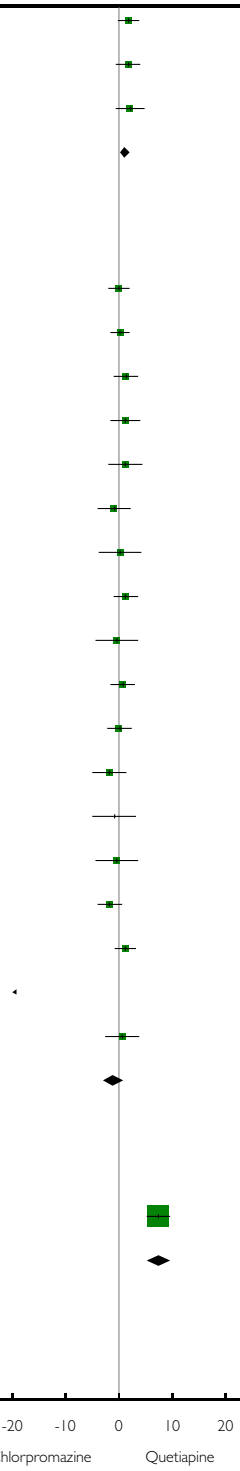
Study or subgroup	Chlorpromazine N	Mean(SD)	Quetiapine N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
8 PANSS positive symptoms							
vs QTP - An 2005	30	11.48 (4.45)	30	10.46 (4.89)		4.3 %	1.02 [-1.35, 3.39]
vs QTP - Chen 2001	107	11.4 (5.4)	114	11.2 (4.9)		13.1 %	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	11.1 (4.8)	44	11 (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)		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	11.7 (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]
Subtotal (95% CI)	**543**		**559**			**100.0 %**	**0.39 [-0.11, 0.88]**
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 9.93$, df = 12 (P = 0.62); $I^2 = 0.0\%$							
Test for overall effect: Z = 1.54 (P = 0.12)							
9 PANSS negative symptoms							
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)	114	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	13.7 (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	13.2 (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	12.1 (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]
vs QTP - Wang 2005	57	12.6 (6.3)	48	11.9 (6.1)		5.6 %	0.70 [-1.68, 3.08]

(*Continued* . . .)

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

(. . . *Continued*)

Study or subgroup	Chlorpromazine N	Mean(SD)	Quetiapine N	Mean(SD)	Mean Difference IV,Random,95% CI	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	13.78 (5.11)		5.7 %	1.77 [-0.51, 4.05]
vs QTP - Zou 2006	43	13.6 (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; Chi^2 = 54.37, df = 16 (P<0.00001); I^2 =71%							
Test for overall effect: Z = 2.23 (P = 0.026)							
10 PANSS general pathology							
vs QTP - An 2005	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)	**765**		**765**			**100.0 %**	**-1.11 [-3.06, 0.84]**
Heterogeneity: Tau^2 = 15.51; Chi^2 = 160.66, df = 17 (P<0.00001); I^2 =89%							
Test for overall effect: Z = 1.11 (P = 0.27)							
11 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)	**31**		**32**			**100.0 %**	**7.40 [5.13, 9.67]**
Heterogeneity: not applicable							
Test for overall effect: Z = 6.38 (P < 0.00001)							
Test for subgroup differences: Chi^2 = 46.97, df = 10 (P = 0.00), I^2 =79%							



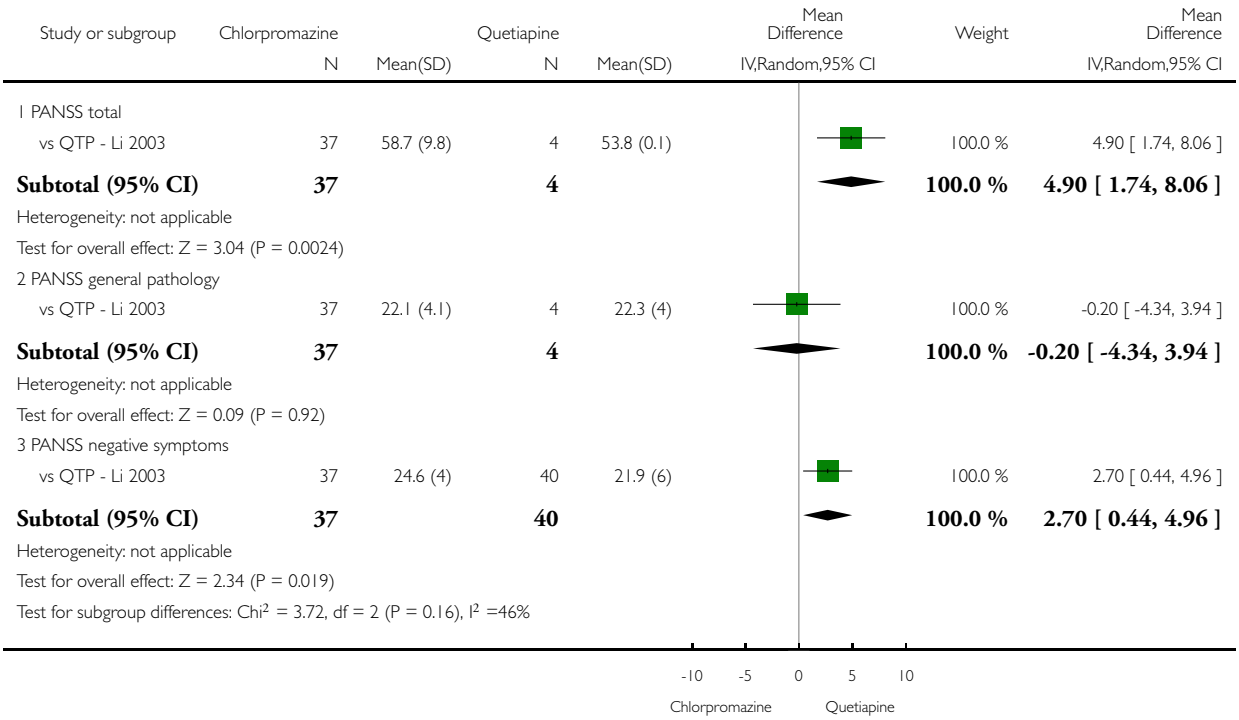
Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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: 1b. Average endpoint scores (various scales, high = poor) - medium term (6 to 12 months)



Analysis 3.8. Comparison 3 CHLORPROMAZINE versus QUETIAPINE, Outcome 8 Mental state: 1c. 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	N
PANSS total - short term (up to 6 months)				**PANSS total - s**

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Mental state: 1c. Average endpoint scores (various scales, high = poor) -skewed data (*Continued*)

vs QTP - Zhang 2002	Chlorpromazine	28.39	16.57	57
vs QTP - Zhang 2002	Quetiapine	9.27	16.36	60
PANSS positive symptoms - short term (up to 6 months)				**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

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Mental state: 1c. Average endpoint scores (various scales, high = poor) -skewed data (*Continued*)

PANSS negative symptoms - short term (up to 6 months)					**PANSS negative**
vs QTP - Guo 2003a	Chlorpromazine	12.3	7.1	73	
vs QTP - Guo 2003a	Quetiapine	12.9	6.9	75	
vs QTP - Mei 2007	Chlorpromazine	12.4	6.1	49	
vs QTP - Mei 2007	Quetiapine	11.7	5.9	47	
vs QTP - Wang 2004	Chlorpromazine	18.14	9.38	42	
vs QTP - Wang 2004	Quetiapine	18.63	9.3	46	
vs QTP - Zhang 2002	Chlorpromazine	15.88	4.11	57	
vs QTP - Zhang 2002	Quetiapine	10.87	6.19	60	
PANSS general pathology - short term (up to 6 months					**PANSS general**
vs QTP - Guo 2008	Chlorpromazine	20.1	10.9	40	
vs QTP - Guo 2008	Quetiapine	19.2	11.4	43	

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Analysis 3.9. Comparison 3 CHLORPROMAZINE versus QUETIAPINE, Outcome 9 Mental state: 1d. 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: 1d. Average change score (various scales, high = poor) - short term (up to 6 months)

Study or subgroup	Chlorpromazine N	Mean(SD)	Quetiapine N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
1 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: $Tau^2 = 0.0$; $Chi^2 = 0.24$, df = 1 (P = 0.63); $I^2 = 0.0\%$							
Test for overall effect: Z = 15.75 (P < 0.00001)							
2 PANSS positive symptoms							
vs QTP - NCT00882518	194	-9.9 (0.53)	190	-11.1 (0.51)		100.0 %	1.20 [1.10, 1.30]
Subtotal (95% CI)	**194**		**190**			**100.0 %**	**1.20 [1.10, 1.30]**
Heterogeneity: not applicable							
Test for overall effect: Z = 22.61 (P < 0.00001)							
3 PANSS negative symptoms							
vs QTP - NCT00882518	194	-5.9 (0.5)	190	-6.7 (0.48)		100.0 %	0.80 [0.70, 0.90]
Subtotal (95% CI)	**194**		**190**			**100.0 %**	**0.80 [0.70, 0.90]**
Heterogeneity: not applicable							
Test for overall effect: Z = 16.00 (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							
Test for overall effect: Z = 13.51 (P < 0.00001)							
Test for subgroup differences: $Chi^2 = 493.44$, df = 3 (P = 0.00), $I^2 = 99\%$							

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

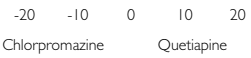
Analysis 3.10. Comparison 3 CHLORPROMAZINE versus QUETIAPINE, Outcome 10 Mental state: 1e. Average score decreased rate of BPRS/PANSS (%) - short term (up to 6 months).

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)

Study or subgroup	Chlorpromazine N	Mean(SD)	Quetiapine N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
1 BPRS							
vs QTP - Cai 2006	96	49.4 (13.1)	101	50.2 (15.9)		100.0 %	-0.80 [-4.86, 3.26]
Subtotal (95% CI)	**96**		**101**			**100.0 %**	**-0.80 [-4.86, 3.26]**
Heterogeneity: not applicable							
Test for overall effect: Z = 0.39 (P = 0.70)							
2 PANSS							
vs QTP - Cai 2007	46	67 (20)	48	83 (22)		14.8 %	-16.00 [-24.49, -7.51]
vs QTP - Chen 2001	94	66.4 (26.3)	105	65.9 (27.8)		16.2 %	0.50 [-7.02, 8.02]
vs QTP - Guo 2003a	73	64.9 (25.3)	75	64.7 (26.5)		15.0 %	0.20 [-8.15, 8.55]
vs QTP - Jin 2007	30	50.24 (6.93)	30	48.07 (6.11)		22.2 %	2.17 [-1.14, 5.48]
vs QTP - Zhang 2003	108	59.23 (33.61)	112	54.7 (33.83)		14.3 %	4.53 [-4.38, 13.44]
vs QTP - Zhang 2006	33	48.06 (13.2)	28	52.75 (13.1)		17.5 %	-4.69 [-11.31, 1.93]
Subtotal (95% CI)	**384**		**398**			**100.0 %**	**-1.96 [-7.20, 3.28]**
Heterogeneity: Tau^2 = 29.41; Chi^2 = 18.14, df = 5 (P = 0.003); I^2 =72%							
Test for overall effect: Z = 0.73 (P = 0.46)							
Test for subgroup differences: Chi^2 = 0.12, df = 1 (P = 0.73), I^2 =0.0%							



Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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 N	Mean(SD)	Quetiapine N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
1 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 applicable							
Test for overall effect: Z = 3.50 (P = 0.00046)							
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 applicable							
Test for overall effect: Z = 4.94 (P < 0.00001)							
Test for subgroup differences: Chi^2 = 2.64, df = 1 (P = 0.10), I^2 =62%							

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

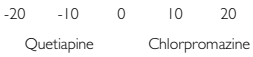
Analysis 3.12. Comparison 3 CHLORPROMAZINE versus QUETIAPINE, Outcome 12 Cognitive function: 1. Average endpoint score (various scales, high = better) - short term (up to 6 months).

Review: Chlorpromazine versus atypical antipsychotic drugs for schizophrenia

Comparison: 3 CHLORPROMAZINE versus QUETIAPINE

Outcome: 12 Cognitive function: 1. Average endpoint score (various scales, high = better) - short term (up to 6 months)

Study or subgroup	Chlorpromazine N	Mean(SD)	Quetiapine N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
1 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 %	11.64 [1.38, 21.90]
Subtotal (95% CI)	**62**		**61**			**100.0 %**	**8.92 [0.40, 17.43]**
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.87$, df = 1 (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 applicable							
Test for overall effect: Z = 2.24 (P = 0.025)							
Test for subgroup differences: $Chi^2 = 9.18$, df = 1 (P = 0.00), $I^2 = 89\%$							



Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

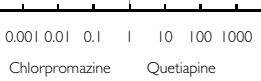
Analysis 3.13. Comparison 3 CHLORPROMAZINE versus QUETIAPINE, Outcome 13 Adverse effects: 1. Anticholinergic - short term (up to 6 months).

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)

Study or subgroup	Chlorpromazine n/N	Quetiapine n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
1 blurred vision					
vs QTP - Cai 2006	15/96	6/101		16.5 %	2.63 [1.06, 6.50]
vs QTP - Chen 2001	14/107	2/114		6.4 %	7.46 [1.74, 32.05]
vs QTP - Chen 2007	7/30	2/32		6.1 %	3.73 [0.84, 16.57]
vs QTP - Cheng 2003	6/45	1/44		3.1 %	5.87 [0.74, 46.76]
vs QTP - Guo 2003a	9/73	1/75		3.2 %	9.25 [1.20, 71.16]
vs QTP - Guo 2003b	3/20	2/30		4.7 %	2.25 [0.41, 12.28]
vs QTP - Guo 2008	2/40	0/43		1.5 %	5.37 [0.27, 108.47]
vs QTP - He 2003	3/20	0/20		1.6 %	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	4/30	0/30		1.6 %	9.00 [0.51, 160.17]
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]
vs QTP - Tian 2006	7/46	0/46		1.7 %	15.00 [0.88, 255.20]
vs QTP - Wan 2008	6/28	0/32		1.7 %	14.79 [0.87, 251.39]
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 QTP - Zhou 2004	10/39	2/40		6.4 %	5.13 [1.20, 21.92]
vs QTP - Zou 2006	20/43	3/43		10.5 %	6.67 [2.14, 20.79]
Subtotal (95% CI)	**883**	**897**		**100.0 %**	**5.00 [3.46, 7.22]**
Total events: 173 (Chlorpromazine), 30 (Quetiapine)					
Heterogeneity: Tau^2 = 0.0; Chi^2 = 7.79, df = 17 (P = 0.97); I^2 =0.0%					
Test for overall effect: Z = 8.58 (P < 0.00001)					
2 dry mouth					
vs QTP - Cai 2006	21/96	18/101		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	0/30	4/32		1.8 %	0.12 [0.01, 2.11]



(*Continued* . . .)

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

(. . . *Continued*)

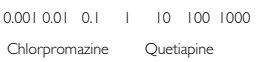
Study or subgroup	Chlorpromazine n/N	Quetiapine n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
vs QTP - Cheng 2003	7/45	3/44		6.0 %	2.28 [0.63, 8.26]
vs QTP - Guo 2003a	9/73	4/75		6.8 %	2.31 [0.74, 7.18]
vs QTP - Guo 2008	3/40	1/43		2.8 %	3.23 [0.35, 29.75]
vs QTP - He 2003	4/20	4/20		6.2 %	1.00 [0.29, 3.45]
vs QTP - Ji 2004	6/30	0/30		1.9 %	13.00 [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		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]**
Total events: 191 (Chlorpromazine), 73 (Quetiapine)					
Heterogeneity: Tau^2 = 0.33; Chi^2 = 32.99, df = 17 (P = 0.01); I^2 =48%					
Test for overall effect: Z = 4.00 (P = 0.000064)					
3 excessive sweating					
vs QTP - Chen 2007	3/30	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)	**80**	**82**		**100.0 %**	**3.91 [0.84, 18.19]**
Total events: 7 (Chlorpromazine), 1 (Quetiapine)					
Heterogeneity: Tau^2 = 0.0; Chi^2 = 0.22, df = 2 (P = 0.90); I^2 =0.0%					
Test for overall effect: Z = 1.74 (P = 0.082)					
4 hypersalivation					
vs QTP - Chen 2001	5/107	1/114		5.3 %	5.33 [0.63, 44.86]
vs QTP - Chen 2007	23/30	2/32		13.0 %	12.27 [3.16, 47.62]
vs QTP - Cheng 2003	2/45	1/44		4.3 %	1.96 [0.18, 20.80]
vs QTP - Guo 2003a	7/73	0/75		3.0 %	15.41 [0.90, 264.93]
vs QTP - He 2003	1/20	0/20		2.4 %	3.00 [0.13, 69.52]
vs QTP - Jiang 2006	22/97	7/94		37.3 %	3.05 [1.37, 6.79]

(*Continued* . . .)

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

(. . . *Continued*)

Study or subgroup	Chlorpromazine n/N	Quetiapine n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
vs QTP - Mei 2007	10/49	3/47		15.9 %	3.20 [0.94, 10.90]
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	1/31		3.2 %	0.97 [0.06, 14.82]
Subtotal (95% CI)	**568**	**567**		**100.0 %**	**3.85 [2.36, 6.28]**
Total events: 82 (Chlorpromazine), 17 (Quetiapine)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 6.08$, df = 10 (P = 0.81); $I^2 = 0.0\%$					
Test for overall effect: Z = 5.39 (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 (Chlorpromazine), 46 (Quetiapine)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 2.58$, df = 7 (P = 0.92); $I^2 = 0.0\%$					
Test for overall effect: Z = 1.68 (P = 0.093)					
Test for subgroup differences: $Chi^2 = 50.82$, df = 4 (P = 0.00), $I^2 = 92\%$					



Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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)

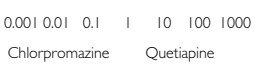
Study or subgroup	Chlorpromazine n/N	Quetiapine n/N	Risk Ratio IV,Random,95% CI	Weight	Risk Ratio IV,Random,95% CI
1 abnormal ECG					
vs QTP - Chen 2007	6/30	0/32		3.0 %	13.84 [0.81, 235.53]
vs QTP - Cheng 2003	6/45	3/44		13.8 %	1.96 [0.52, 7.34]
vs QTP - Deng 2004	13/45	9/45		43.7 %	1.44 [0.69, 3.04]
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]**
Total events: 45 (Chlorpromazine), 21 (Quetiapine)					
Heterogeneity: Tau^2 = 0.0; Chi^2 = 4.68, df = 6 (P = 0.59); I^2 =0.0%					
Test for overall effect: Z = 2.39 (P = 0.017)					
2 blood pressure drop					
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 (Chlorpromazine), 59 (Quetiapine)					
Heterogeneity: Tau^2 = 0.29; Chi^2 = 13.18, df = 7 (P = 0.07); I^2 =47%					
Test for overall effect: Z = 0.09 (P = 0.93)					
3 orthostatic hypotension					
vs QTP - Chen 2007	2/30	0/32		7.0 %	5.32 [0.27, 106.54]
vs QTP - Guo 2007	0/26	1/26		6.3 %	0.33 [0.01, 7.82]
vs QTP - Liu 2003	8/39	0/44		7.7 %	19.13 [1.14, 320.92]

(*Continued* . . .)

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

(. . . *Continued*)

Study or subgroup	Chlorpromazine n/N	Quetiapine n/N	Risk Ratio IV,Random,95% CI	Weight	Risk Ratio IV,Random,95% CI
vs QTP - Peuskens 1997	18/100	5/101		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), 13 (Quetiapine)					
Heterogeneity: Tau^2 = 0.31; Chi^2 = 8.02, df = 6 (P = 0.24); I^2 =25%					
Test for overall effect: Z = 2.26 (P = 0.024)					
4 tachycardia					
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, 4.41]
vs QTP - Guo 2003a	9/73	8/75		7.0 %	1.16 [0.47, 2.83]
vs QTP - Guo 2008	2/40	3/43		2.0 %	0.72 [0.13, 4.07]
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, 10.11]
vs QTP - Jiang 2008	7/30	3/30		3.7 %	2.33 [0.67, 8.18]
vs QTP - Liu 2003	12/39	4/44		5.2 %	3.38 [1.19, 9.64]
vs QTP - Tian 2006	18/46	2/46		3.0 %	9.00 [2.21, 36.59]
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)	**863**	**889**		**100.0 %**	**1.70 [1.33, 2.18]**
Total events: 172 (Chlorpromazine), 99 (Quetiapine)					
Heterogeneity: Tau^2 = 0.02; Chi^2 = 17.24, df = 16 (P = 0.37); I^2 =7%					
Test for overall effect: Z = 4.22 (P = 0.000025)					
Test for subgroup differences: Chi^2 = 4.31, df = 3 (P = 0.23), I^2 =30%					



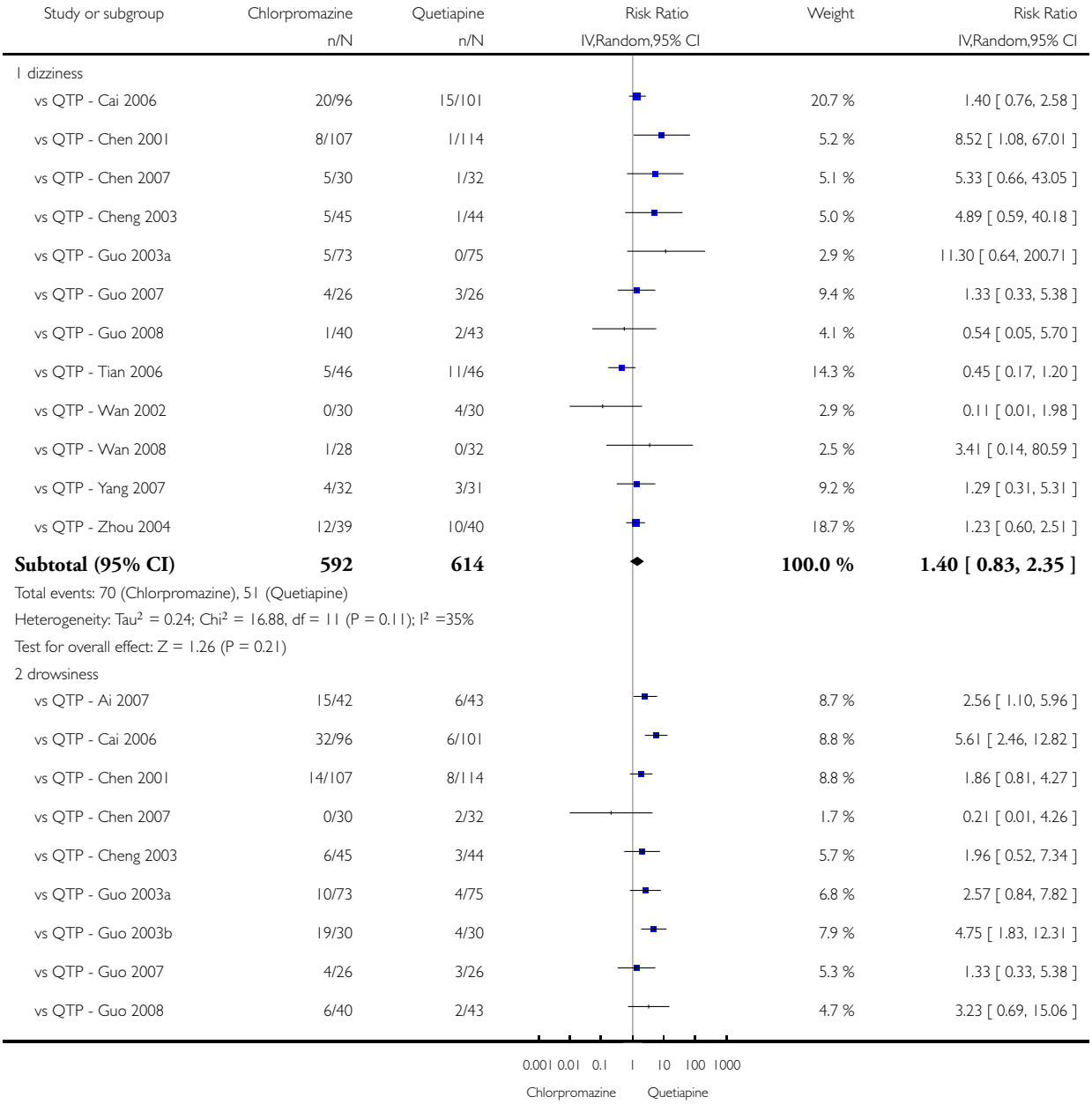
Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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)

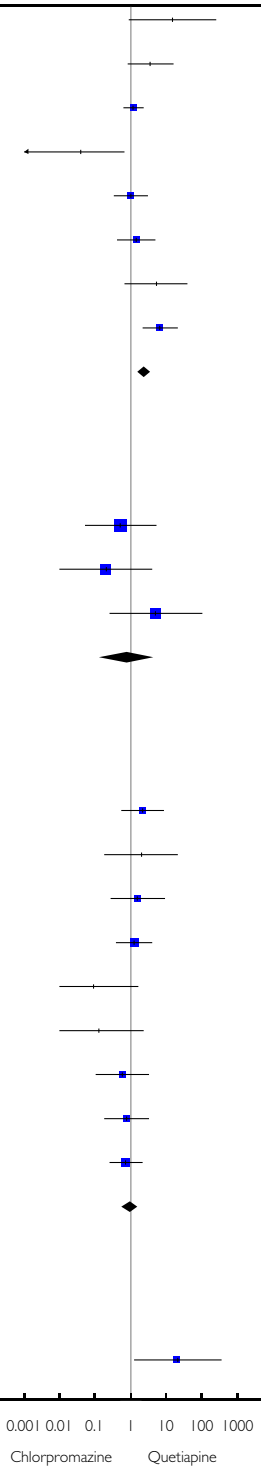


(*Continued . . .*)

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

(. . . *Continued*)

Study or subgroup	Chlorpromazine n/N	Quetiapine n/N	Risk Ratio IV,Random,95% CI	Weight	Risk Ratio 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	14/101		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 (Chlorpromazine), 79 (Quetiapine)					
Heterogeneity: Tau^2 = 0.33; Chi^2 = 31.15, df = 16 (P = 0.01); I^2 =49%					
Test for overall effect: Z = 3.92 (P = 0.000090)					
3 headache					
vs QTP - He 2003	1/20	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]
Subtotal (95% CI)	**96**	**96**		**100.0 %**	**0.74 [0.13, 4.18]**
Total events: 3 (Chlorpromazine), 4 (Quetiapine)					
Heterogeneity: Tau^2 = 0.40; Chi^2 = 2.40, df = 2 (P = 0.30); I^2 =17%					
Test for overall effect: Z = 0.34 (P = 0.74)					
4 insomnia					
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 (Chlorpromazine), 33 (Quetiapine)					
Heterogeneity: Tau^2 = 0.0; Chi^2 = 7.40, df = 8 (P = 0.49); I^2 =0.0%					
Test for overall effect: Z = 0.33 (P = 0.74)					
5 reduced activity					
vs QTP - Chen 2001	9/107	0/114		11.0 %	20.23 [1.19, 343.40]

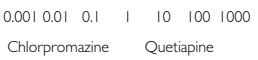


(*Continued* . . .)

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

(. . . *Continued*)

Study or subgroup	Chlorpromazine n/N	Quetiapine n/N	Risk Ratio IV,Random,95% CI	Weight	Risk Ratio IV,Random,95% CI
vs QTP - Cheng 2003	4/45	0/44		10.5 %	8.80 [0.49, 158.85]
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, 113.72]
vs QTP - Yang 2007	3/32	0/31		10.3 %	6.79 [0.36, 126.24]
vs QTP - Zhang 2006	10/33	0/28		11.3 %	17.91 [1.10, 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 (Chlorpromazine), 2 (Quetiapine)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 2.56$, df = 7 (P = 0.92); $I^2 = 0.0\%$					
Test for overall effect: Z = 4.29 (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 (Chlorpromazine), 1 (Quetiapine)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.69 (P = 0.49)					
Test for subgroup differences: $Chi^2 = 20.04$, df = 5 (P = 0.00), $I^2 = 75\%$					



Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

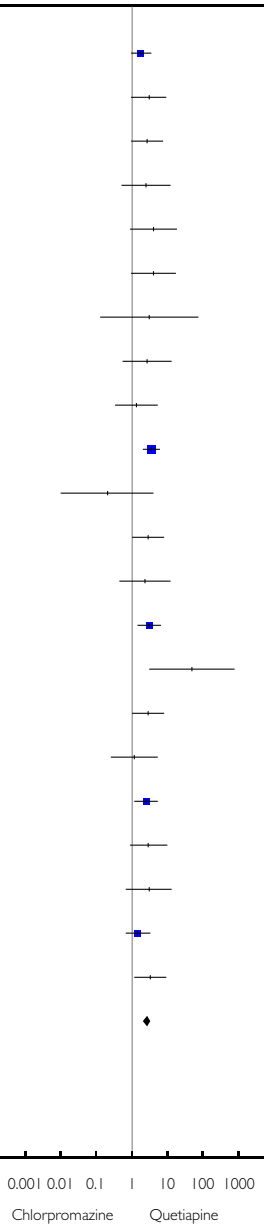
Analysis 3.16. Comparison 3 CHLORPROMAZINE versus QUETIAPINE, Outcome 16 Adverse effects: 4. Gastrointestinal - short term (up to 6 months).

Review: Chlorpromazine versus atypical antipsychotic drugs for schizophrenia

Comparison: 3 CHLORPROMAZINE versus QUETIAPINE

Outcome: 16 Adverse effects: 4. Gastrointestinal - short term (up to 6 months)

Study or subgroup	Chlorpromazine n/N	Quetiapine n/N	Risk Ratio IV,Random,95% CI	Weight	Risk Ratio IV,Random,95% CI
1 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 %	4.11 [0.90, 18.71]
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		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		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 (Chlorpromazine), 90 (Quetiapine)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 15.01$, df = 21 (P = 0.82); $I^2 = 0.0\%$					
Test for overall effect: Z = 8.18 (P < 0.00001)					



(*Continued* . . .)

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

(. . . *Continued*)

Study or subgroup	Chlorpromazine n/N	Quetiapine n/N	Risk Ratio IV,Random,95% CI	Weight	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)	**30**	**32**		**100.0 %**	**5.32 [0.27, 106.54]**
Total events: 2 (Chlorpromazine), 0 (Quetiapine)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.09 (P = 0.27)					
3 loss of appetite					
vs QTP - Chen 2001	4/107	1/114		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)	**232**	**240**		**100.0 %**	**2.52 [0.82, 7.72]**
Total events: 33 (Chlorpromazine), 9 (Quetiapine)					
Heterogeneity: Tau^2 = 0.68; Chi^2 = 7.06, df = 4 (P = 0.13); I^2 =43%					
Test for overall effect: Z = 1.62 (P = 0.10)					
4 nausea/vomiting					
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)	**402**	**417**		**100.0 %**	**1.23 [0.58, 2.63]**
Total events: 15 (Chlorpromazine), 12 (Quetiapine)					
Heterogeneity: Tau^2 = 0.0; Chi^2 = 3.04, df = 8 (P = 0.93); I^2 =0.0%					
Test for overall effect: Z = 0.54 (P = 0.59)					
Test for subgroup differences: Chi^2 = 3.55, df = 3 (P = 0.31), I^2 =15%					

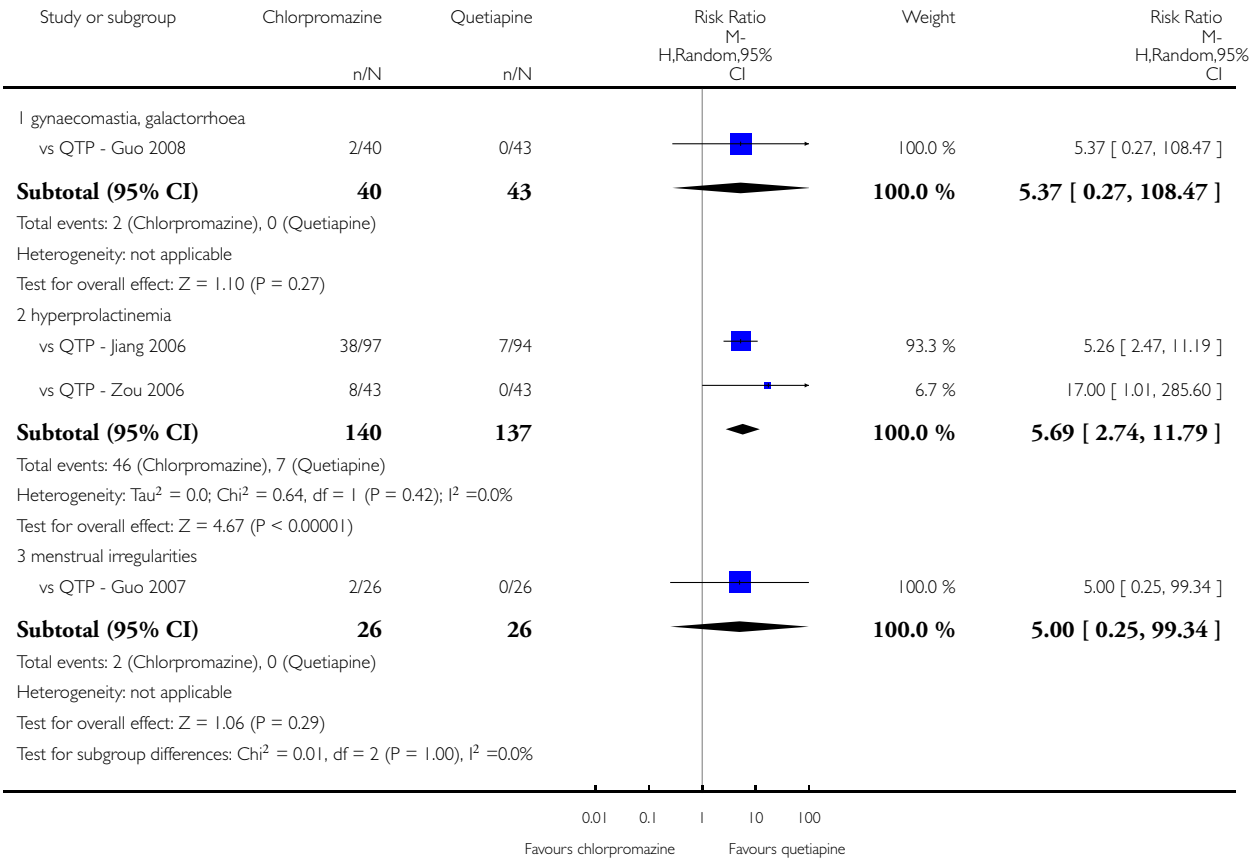
Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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)



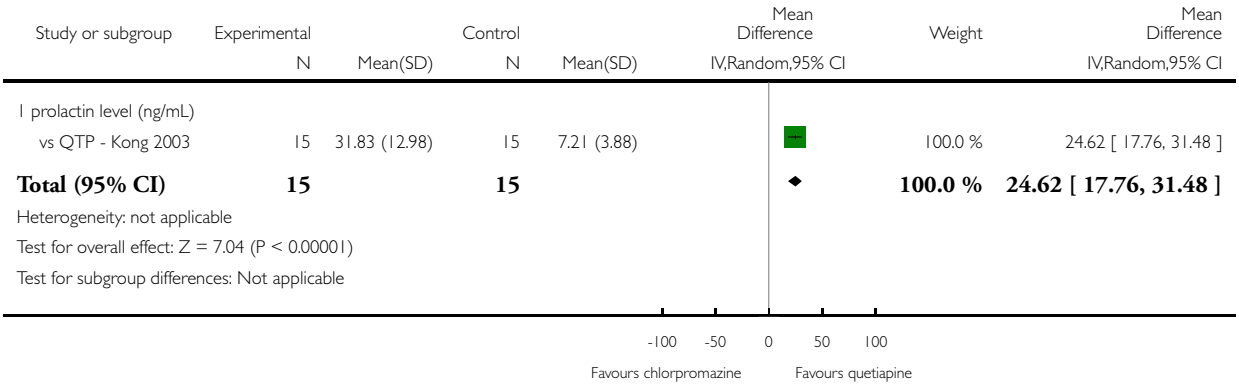
Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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)



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	N
average prolactin level (ng/mL)				**average prolacti**
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

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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 n/N	Quetiapine n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
1 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]**
Total events: 30 (Chlorpromazine), 19 (Quetiapine)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 5.85$, df = 7 (P = 0.56); $I^2 = 0.0\%$					
Test for overall effect: Z = 1.66 (P = 0.097)					
2 decreased white blood cell count					
vs QTP - Deng 2004	6/45	5/45		60.8 %	1.20 [0.39, 3.65]
vs QTP - He 2003	1/20	0/20		7.6 %	3.00 [0.13, 69.52]
vs QTP - Wan 2002	0/30	1/30		7.5 %	0.33 [0.01, 7.87]
vs QTP - Zhang 2003	2/118	3/119		24.0 %	0.67 [0.11, 3.95]
Subtotal (95% CI)	**213**	**214**		**100.0 %**	**1.02 [0.43, 2.42]**
Total events: 9 (Chlorpromazine), 9 (Quetiapine)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 1.23$, df = 3 (P = 0.75); $I^2 = 0.0\%$					
Test for overall effect: Z = 0.04 (P = 0.97)					
3 increased white blood cell count					
vs QTP - Zhou 2004	4/39	2/40		100.0 %	2.05 [0.40, 10.56]
Subtotal (95% CI)	**39**	**40**		**100.0 %**	**2.05 [0.40, 10.56]**
Total events: 4 (Chlorpromazine), 2 (Quetiapine)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.86 (P = 0.39)					
Test for subgroup differences: $Chi^2 = 0.96$, df = 2 (P = 0.62), $I^2 = 0.0\%$					

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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% CI	Weight	Mean Difference IV,Random,95% CI
1 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)	**65**		**65**			**100.0 %**	**0.10 [-0.18, 0.38]**
Heterogeneity: not applicable							
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)	**65**		**65**			**100.0 %**	**0.0 [-0.28, 0.28]**
Heterogeneity: not applicable							
Test for overall effect: Z = 0.0 (P = 1.0)							
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)	**65**		**65**			**100.0 %**	**0.20 [-0.11, 0.51]**
Heterogeneity: not applicable							
Test for overall effect: Z = 1.27 (P = 0.21)							
Test for subgroup differences: Chi^2 = 0.90, df = 2 (P = 0.64), I^2 =0.0%							

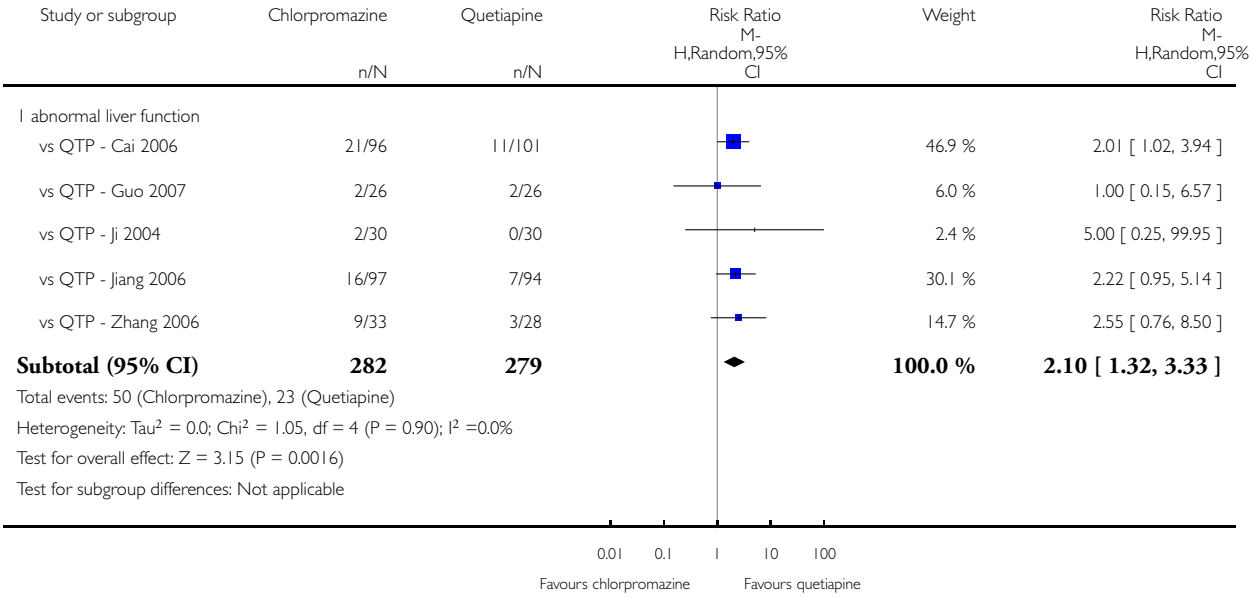
Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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)



Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

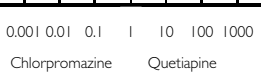
Analysis 3.23. Comparison 3 CHLORPROMAZINE versus QUETIAPINE, Outcome 23 Adverse effects: 8. Movement disorders - short term (up to 6 months).

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)

Study or subgroup	Chlorpromazine n/N	Quetiapine n/N	Risk Ratio IV,Random,95% CI	Weight	Risk Ratio IV,Random,95% CI
1 agitation					
vs QTP - He 2003	1/20	4/20		21.2 %	0.25 [0.03, 2.05]
vs QTP - Ji 2004	2/30	1/30		17.0 %	2.00 [0.19, 20.90]
vs QTP - Tian 2006	0/46	2/46		10.3 %	0.20 [0.01, 4.05]
vs QTP - Wan 2002	2/30	6/30		40.6 %	0.33 [0.07, 1.52]
vs QTP - Zhang 2006	0/33	3/28		11.0 %	0.12 [0.01, 2.26]
Subtotal (95% CI)	**159**	**154**		**100.0 %**	**0.36 [0.14, 0.95]**
Total events: 5 (Chlorpromazine), 16 (Quetiapine)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 2.85$, df = 4 (P = 0.58); $I^2 = 0.0\%$					
Test for overall effect: Z = 2.06 (P = 0.039)					
2 akathisia					
vs QTP - Chen 2001	17/107	3/114		10.2 %	6.04 [1.82, 20.02]
vs QTP - Chen 2007	7/30	0/32		1.8 %	15.97 [0.95, 268.00]
vs QTP - Cheng 2003	10/45	2/44		6.8 %	4.89 [1.14, 21.06]
vs QTP - Guo 2003a	9/73	1/75		3.5 %	9.25 [1.20, 71.16]
vs QTP - Guo 2003b	7/30	1/30		3.5 %	7.00 [0.92, 53.47]
vs QTP - Guo 2008	3/40	0/43		1.7 %	7.51 [0.40, 141.04]
vs QTP - Ji 2004	4/30	2/30		5.6 %	2.00 [0.40, 10.11]
vs QTP - Jiang 2006	10/97	5/94		13.6 %	1.94 [0.69, 5.46]
vs QTP - Jin 2007	7/30	1/30		3.5 %	7.00 [0.92, 53.47]
vs QTP - Mei 2007	4/49	2/47		5.4 %	1.92 [0.37, 9.98]
vs QTP - Peuskens 1997	6/101	4/100		9.6 %	1.49 [0.43, 5.10]
vs QTP - Tian 2006	16/46	1/46		3.7 %	16.00 [2.21, 115.71]
vs QTP - Wang 2005	3/57	1/48		2.9 %	2.53 [0.27, 23.50]
vs QTP - Yang 2007	6/32	0/31		1.8 %	12.61 [0.74, 214.70]
vs QTP - Zhang 2006	9/33	1/28		3.6 %	7.64 [1.03, 56.63]
vs QTP - Zhou 2004	10/39	5/40		15.2 %	2.05 [0.77, 5.46]

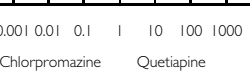


(*Continued . . .*)

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

(. . . *Continued*)

Study or subgroup	Chlorpromazine n/N	Quetiapine n/N	Risk Ratio IV,Random,95% CI	Weight	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 (Chlorpromazine), 31 (Quetiapine)					
Heterogeneity: Tau^2 = 0.0; Chi^2 = 14.71, df = 16 (P = 0.55); I^2 =0.0%					
Test for overall effect: Z = 6.76 (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 %	11.00 [1.51, 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]**
Total events: 141 (Chlorpromazine), 12 (Quetiapine)					
Heterogeneity: Tau^2 = 0.0; Chi^2 = 5.04, df = 7 (P = 0.66); I^2 =0.0%					
Test for overall effect: Z = 7.86 (P < 0.00001)					
4 dystonia					
vs QTP - Peuskens 1997	0/101	1/100		100.0 %	0.33 [0.01, 8.01]
Subtotal (95% CI)	**101**	**100**		**100.0 %**	**0.33 [0.01, 8.01]**
Total events: 0 (Chlorpromazine), 1 (Quetiapine)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.68 (P = 0.50)					
5 myotonia					
vs QTP - Chen 2001	14/107	7/114		18.0 %	2.13 [0.89, 5.08]
vs QTP - Chen 2007	1/30	0/32		1.4 %	3.19 [0.14, 75.49]
vs QTP - Cheng 2003	5/45	2/44		5.4 %	2.44 [0.50, 11.94]
vs QTP - Guo 2003a	9/73	4/75		10.6 %	2.31 [0.74, 7.18]
vs QTP - Guo 2003b	5/30	0/30		1.7 %	11.00 [0.64, 190.53]
vs QTP - Guo 2008	5/40	0/43		1.7 %	11.80 [0.67, 206.88]
vs QTP - Jiang 2006	52/97	6/94		21.4 %	8.40 [3.79, 18.62]
vs QTP - Jin 2007	12/30	2/30		6.8 %	6.00 [1.47, 24.55]
vs QTP - Mei 2007	27/49	3/47		10.7 %	8.63 [2.81, 26.56]
vs QTP - Wang 2005	27/57	3/48		10.6 %	7.58 [2.45, 23.45]
vs QTP - Yang 2007	3/32	1/31		2.8 %	2.91 [0.32, 26.46]

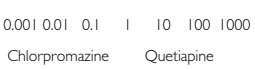


(*Continued* . . .)

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

(. . . *Continued*)

Study or subgroup	Chlorpromazine n/N	Quetiapine n/N	Risk Ratio IV,Random,95% CI	Weight	Risk Ratio IV,Random,95% CI
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 (Chlorpromazine), 31 (Quetiapine)					
Heterogeneity: Tau^2 = 0.0; Chi^2 = 10.74, df = 11 (P = 0.47); I^2 =0.0%					
Test for overall effect: Z = 8.11 (P < 0.00001)					
6 need additional medication for EPS symptoms					
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 (Chlorpromazine), 10 (Quetiapine)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.06 (P = 0.29)					
7 torsion movement					
vs QTP - Chen 2001	5/107	0/114		6.7 %	11.71 [0.66, 209.31]
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 (Chlorpromazine), 5 (Quetiapine)					
Heterogeneity: Tau^2 = 0.0; Chi^2 = 3.14, df = 8 (P = 0.93); I^2 =0.0%					
Test for overall effect: Z = 4.64 (P < 0.00001)					
8 tremor					
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, 13.53]

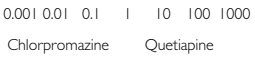


(*Continued* . . .)

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

(. . . *Continued*)

Study or subgroup	Chlorpromazine n/N	Quetiapine n/N	Risk Ratio IV,Random,95% CI	Weight	Risk Ratio 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 (Chlorpromazine), 40 (Quetiapine)					
Heterogeneity: $Tau^2 = 0.10$; $Chi^2 = 14.41$, df = 12 (P = 0.28); $I^2 = 17\%$					
Test for overall effect: Z = 4.89 (P < 0.00001)					
Test for subgroup differences: $Chi^2 = 42.50$, df = 7 (P = 0.00), $I^2 = 84\%$					



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 n/N	Quetiapine n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
1 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]

(*Continued* . . .)

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

(. . . *Continued*)

Study or subgroup	Chlorpromazine n/N	Quetiapine n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
vs QTP - Jiang 2008	5/30	0/30		1.5 %	11.00 [0.64, 190.53]
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		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)	**621**	**638**		**100.0 %**	**1.67 [1.17, 2.39]**

Total events: 117 (Chlorpromazine), 71 (Quetiapine)

Heterogeneity: $Tau^2 = 0.10$; $Chi^2 = 17.94$, df = 14 (P = 0.21); $I^2 = 22\%$

Test for overall effect: Z = 2.81 (P = 0.0049)

Test for subgroup differences: Not applicable

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

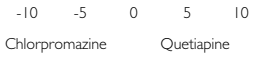
Analysis 3.25. Comparison 3 CHLORPROMAZINE versus QUETIAPINE, Outcome 25 Adverse effects: 9b. Metabolic - short term (up to 6 months).

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)

Study or subgroup	Chlorpromazine N	Mean(SD)	Quetiapine N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
1 average BMI							
vs QTP - Wang 2005	57	22.4 (3.1)	48	21.9 (3)		100.0 %	0.50 [-0.67, 1.67]
Subtotal (95% CI)	**57**		**48**			**100.0 %**	**0.50 [-0.67, 1.67]**
Heterogeneity: not applicable							
Test for overall effect: Z = 0.84 (P = 0.40)							
2 average weight (KG)							
vs QTP - Guo 2006	65	59.7 (10.5)	65	60.7 (10.9)		100.0 %	-1.00 [-4.68, 2.68]
Subtotal (95% CI)	**65**		**65**			**100.0 %**	**-1.00 [-4.68, 2.68]**
Heterogeneity: not applicable							
Test for overall effect: Z = 0.53 (P = 0.59)							
Test for subgroup differences: Chi^2 = 0.58, df = 1 (P = 0.45), I^2 =0.0%							



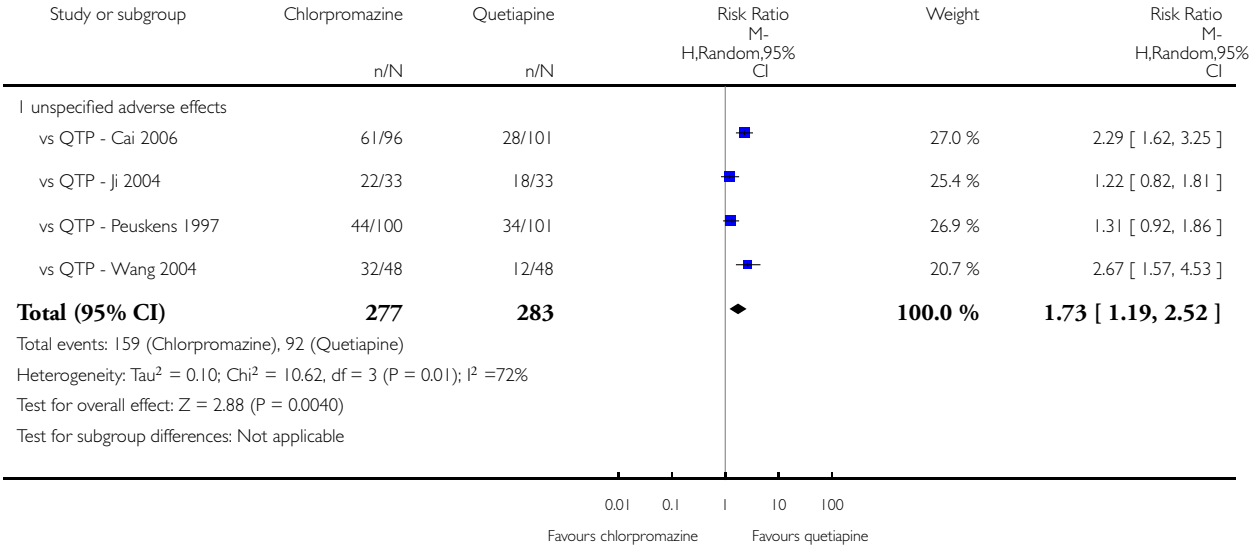
Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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)



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 endpoint score (TESS, high = poor) - skewed data

Study	Intervention	Mean	SD	N	
short term (up to 6 months)					**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	

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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

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)				**medium term (7**
vs QTP - Li 2003	Chlorpromazine	4.2	3.0	37
vs QTP - Li 2003	Quetiapine	2.1	2.3	40

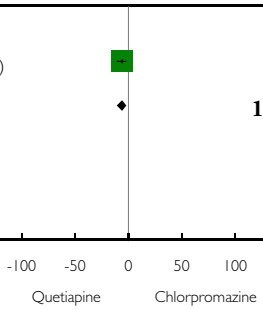
Analysis 3.28. Comparison 3 CHLORPROMAZINE versus QUETIAPINE, Outcome 28 Quality of life: 1. General - average endpoint score (GQOL1 - 74, high = better).

Review: Chlorpromazine versus atypical antipsychotic drugs for schizophrenia

Comparison: 3 CHLORPROMAZINE versus QUETIAPINE

Outcome: 28 Quality of life: 1. General - average endpoint score (GQOL1 - 74, high = better)

Study or subgroup	Chlorpromazine N	Mean(SD)	Quetiapine N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
1 short term (up to 6 months)							
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 applicable							
Test for overall effect: Z = 2.64 (P = 0.0082)							
Test for subgroup differences: Not applicable							



Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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: 1a. Short term (up to 6 months)

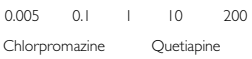
Study or subgroup	Chlorpromazine n/N	Quetiapine n/N	Risk Ratio IV,Random,95% CI	Weight	Risk Ratio IV,Random,95% CI
1 due to adverse effect					
vs QTP - Chen 2001	7/107	2/114		4.3 %	3.73 [0.79, 17.55]
vs QTP - Cheng 2003	2/45	0/44		1.2 %	4.89 [0.24, 99.08]
vs QTP - Guo 2008	2/43	0/43		1.2 %	5.00 [0.25, 101.18]
vs QTP - Ji 2004	4/33	3/33		5.2 %	1.33 [0.32, 5.50]
vs QTP - Jiang 2006	17/97	16/94		27.0 %	1.03 [0.55, 1.92]
vs QTP - NCT00882518	18/192	9/196		17.4 %	2.04 [0.94, 4.43]
vs QTP - Peuskens 1997	9/100	4/101		8.0 %	2.27 [0.72, 7.14]
vs QTP - Wang 2004	4/48	2/48		3.8 %	2.00 [0.38, 10.41]
vs QTP - Wang 2005	12/57	11/48		20.0 %	0.92 [0.45, 1.89]
vs QTP - Zhang 2003	10/118	7/119		12.0 %	1.44 [0.57, 3.66]
Subtotal (95% CI)	**840**	**840**		**100.0 %**	**1.43 [1.04, 1.98]**
Total events: 85 (Chlorpromazine), 54 (Quetiapine)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 6.90$, df = 9 (P = 0.65); $I^2 = 0.0\%$					
Test for overall effect: Z = 2.18 (P = 0.029)					
2 due to inefficacy					
vs QTP - Chen 2001	3/107	2/114		17.4 %	1.60 [0.27, 9.38]
vs QTP - Guo 2008	1/43	0/43		5.4 %	3.00 [0.13, 71.65]
vs QTP - NCT00882518	12/196	9/192		77.2 %	1.31 [0.56, 3.03]
Subtotal (95% CI)	**346**	**349**		**100.0 %**	**1.42 [0.68, 2.96]**
Total events: 16 (Chlorpromazine), 11 (Quetiapine)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.27$, df = 2 (P = 0.87); $I^2 = 0.0\%$					
Test for overall effect: Z = 0.92 (P = 0.36)					
3 due to any other reason					
vs QTP - Cao 2005	8/25	7/25		12.6 %	1.14 [0.49, 2.67]
vs QTP - Cheng 2003	0/45	3/44		1.1 %	0.14 [0.01, 2.63]
vs QTP - Guo 2003b	6/36	5/35		7.6 %	1.17 [0.39, 3.48]
vs QTP - Li 2010	1/32	0/32		0.9 %	3.00 [0.13, 71.00]
vs QTP - NCT00882518	16/192	17/196		21.3 %	0.96 [0.50, 1.85]

(*Continued* . . .)

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

(. . . *Continued*)

Study or subgroup	Chlorpromazine n/N	Quetiapine n/N	Risk Ratio IV,Random,95% CI	Weight	Risk Ratio IV,Random,95% CI
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]**
Total events: 70 (Chlorpromazine), 68 (Quetiapine)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 3.77$, df = 11 (P = 0.98); $I^2 = 0.0\%$					
Test for overall effect: Z = 0.27 (P = 0.78)					
4 due to loss to follow-up					
vs QTP - Cai 2006	4/100	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), 13 (Quetiapine)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.00$, df = 1 (P = 0.94); $I^2 = 0.0\%$					
Test for overall effect: Z = 1.27 (P = 0.21)					
Test for subgroup differences: $Chi^2 = 4.91$, df = 3 (P = 0.18), $I^2 = 39\%$					



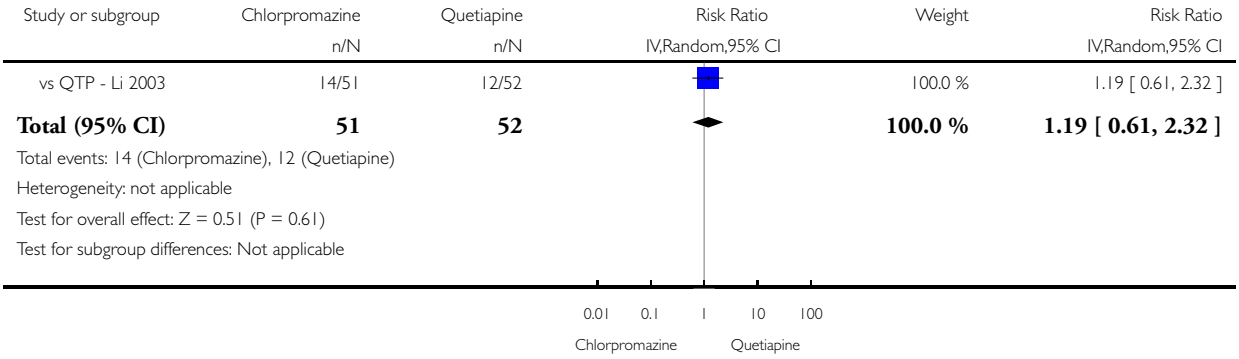
Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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)



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

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

APPENDICES

Appendix 1. Previous searches

1.1 Search in 2013 (Protocol Step)

1.1.1 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.

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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]

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

MeSH check words

Adult; Humans

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.