Fluphenazine decanoate (depot) and enanthate for schizophrenia (Review)

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[Intervention Review]

Fluphenazine decanoate (depot) and enanthate for schizophrenia

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ABSTRACT

Background

Intramuscular injections (depot preparations) offer an advantage over oral medication for treating schizophrenia by reducing poor compliance. The benefits gained by long-acting preparations, however, may be offset by a higher incidence of adverse effects.

Objectives

To assess the effects of fluphenazine decanoate and enanthate versus oral anti-psychotics and other depot neuroleptic preparations for individuals with schizophrenia in terms of clinical, social and economic outcomes.

Search methods

We searched the Cochrane Schizophrenia Group's Trials Register (February 2011 and October 16, 2013), which is based on regular searches of CINAHL, BIOSIS, AMED, EMBASE, PubMed, MEDLINE, PsycINFO, and registries of clinical trials.

Selection criteria

We considered all relevant randomised controlled trials (RCTs) focusing on people with schizophrenia comparing fluphenazine decanoate or enanthate with placebo or oral anti-psychotics or other depot preparations.

Data collection and analysis

We reliably selected, assessed the quality, and extracted data of the included studies. For dichotomous data, we estimated risk ratio (RR) with 95% confidence intervals (CI). Analysis was by intention-to-treat. We used the mean difference (MD) for normal continuous data. We excluded continuous data if loss to follow-up was greater than 50%. Tests of heterogeneity and for publication bias were undertaken. We used a fixed-effect model for all analyses unless there was high heterogeneity. For this update. we assessed risk of bias of included studies and used the GRADE (Grading of Recommendations Assessment, Development and Evaluation) approach to create a 'Summary of findings' table.

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Main results

This review now includes 73 randomised studies, with 4870 participants. Overall, the quality of the evidence is *low to very low*.

Compared with placebo, use of fluphenazine decanoate does not result in any significant differences in death, nor does it reduce relapse over six months to one year, but one longer-term study found that relapse was significantly reduced in the fluphenazine arm (n = 54, 1 RCT, RR 0.35, CI 0.19 to 0.64, *very low quality evidence*). A very similar number of people left the medium-term studies (six months to one year) early in the fluphenazine decanoate (24%) and placebo (19%) groups, however, a two-year study significantly favoured fluphenazine decanoate (n = 54, 1 RCT, RR 0.47, CI 0.23 to 0.96, *very low quality evidence*). No significant differences were found in mental state measured on the Brief Psychiatric Rating Scale (BPRS) or in extrapyramidal adverse effects, although these outcomes were only reported in one small study each. No study comparing fluphenazine decanoate with placebo reported clinically significant changes in global state or hospital admissions.

Fluphenazine decanoate does not reduce relapse more than oral neuroleptics in the medium term (n = 419, 6 RCTs, RR 1.46 CI 0.75 to 2.83, *very low quality evidence*). A small study found no difference in clinically significant changes in global state. No difference in the number of participants leaving the study early was found between fluphenazine decanoate (17%) and oral neuroleptics (18%), and no significant differences were found in mental state measured on the BPRS. Extrapyramidal adverse effects were significantly less for people receiving fluphenazine decanoate compared with oral neuroleptics (n = 259, 3 RCTs, RR 0.47 CI 0.24 to 0.91, *very low quality evidence*). No study comparing fluphenazine decanoate with oral neuroleptics reported death or hospital admissions.

No significant difference in relapse rates in the medium term between fluphenazine decanoate and fluphenazine enanthate was found (n = 49, 1 RCT, RR 2.43, CI 0.71 to 8.32, *very low quality evidence*), immediate- and short-term studies were also equivocal. One small study reported the number of participants leaving the study early (29% versus 12%) and mental state measured on the BPRS and found no significant difference for either outcome. No significant difference was found in extrapyramidal adverse effects between fluphenazine decanoate and fluphenazine enanthate. No study comparing fluphenazine decanoate with fluphenazine enanthate reported death, clinically significant changes in global state or hospital admissions.

Authors' conclusions

There are more data for fluphenazine decanoate than for the enanthate ester. Both are effective antipsychotic preparations. Fluphenazine decanoate produced fewer movement disorder effects than other oral antipsychotics but data were of low quality, and overall, adverse effect data were equivocal. In the context of trials, there is little advantage of these depots over oral medications in terms of compliance but this is unlikely to be applicable to everyday clinical practice.

PLAIN LANGUAGE SUMMARY

Depot fluphenazine decanoate and enanthate for schizophrenia

People with schizophrenia often hear voices or see things (hallucinations) and have strange beliefs (delusions). The main treatment for these symptoms of schizophrenia are antipsychotic drugs, which can be taken by mouth (tablet) or by an injection (depot). Fluphenazine was one of the first antipsychotic to be produced in depot form. The depot comes in two forms (decanoate and enanthate). Depot injections are often used for people who refuse or forget to take tablets (showing poor compliance or adherence with medication). Fluphenazine is an older antipsychotic drug that is very effective in the treatment of schizophrenia. However, when compared to newer antipsychotic drugs, fluphenazine may have serious side effects (such as involuntary shaking, tremors, muscle stiffness and the inability to sit still) and is known to lower people's mood.

This review aimed to investigate the effects of fluphenazine (decanoate and enanthate) for schizophrenia. Searches for relevant randomised controlled trials was run in February 2011 and October 16, 2013. Authors could include and extract data from 73 studies with a total of 4870 participants. There were more studies on fluphenazine decanoate than enanthate.The review authors rated the quality of the evidence in the included trials to be low or very low. A long-term result from only one trial indicated fluphenazine decanoate reduces the rate of relapse when compared with placebo ('dummy treatment'). Three studies found that fluphenazine decanoate produced fewer general movement disorders than oral antipsychotics. However, other results showed, overall, the effects and outcomes, including adverse effects for fluphenazine (decanoate and enanthate) are similar to other oral and depot antipsychotics. Important outcomes and information about use of services, going into hospital, satisfaction with care and costs were not reported in any study.

Depot injections may offer an advantage over tablets (oral medication) in terms of people taking their medication (complying and adhering to treatment). However, this needs to be balanced with the likelihood of serious side effects, such as involuntary shaking,

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muscle stiffness, the inability to sit still and lowering in people's mood. Results did not show any strong evidence that depot fluphenazine produced more adverse effects than other antipsychotics.

This should be addressed in future large scale and high quality studies.

This plain language summary has been written by a consumer Ben Gray from Rethink Mental Illness.

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SUMMARY OF FINDINGS FOR THE MAIN COMPARISON [Explanation]

FLUPHENAZINE DECANOATE compared with PLACEBO for schizophrenia

Patient or population: patients with schizophrenia
Settings: hospital and community
Intervention: FLUPHENAZINE DECANOATE
Comparison: PLACEBO

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	PLACEBO	FLUPHENAZINE DECANOATE				
Death Follow-up: 2 years	**0 per 1000**	**0 per 1000** (0 to 0)	**RR 5** (0.25 to 99.51)	54 (1 study)	⊕○○○ **very low**[1,2,3]	
Relapse Follow-up: medium term (6 months to 1 year)	**673 per 1000**	**418 per 1000** (162 to 1000)	**RR 0.62** (0.24 to 1.6)	196 (3 studies)	⊕○○○ **very low**[3,4,5,6]	
Clinically significant change in global state - not reported	See comment	See comment	Not estimable	-	See comment	No studies reported data for this outcome.
Hospital admission - not reported	See comment	See comment	Not estimable	-	See comment	No studies reported data for this outcome.
Leaving the study early Follow-up: medium term (6 months to 1 year)	**185 per 1000**	**241 per 1000** (143 to 406)	**RR 1.3** (0.77 to 2.19)	216 (4 studies)	⊕○○○ **very low**[3,4,6]	

Mental state BPRS Follow-up: 9 months		The mean mental state in the intervention groups was **2.03 lower** (4.51 lower to 0.45 higher)		16 (1 study)	⊕○○○ **very low**[3,6,7]
Extrapyramidal adverse effects - tardive dyskinesia Follow-up: 2 years	**852 per 1000**	**707 per 1000** (528 to 946)	**RR 0.83** (0.62 to 1.11)	54 (1 study)	⊕○○○ **very low**[1,2,3]

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

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

[1] Risk of bias: serious - This study had an unclear risk of bias for randomisation, allocation concealment and blinding.
[2] Imprecision: very serious - There were few participants and few events; the confidence intervals are wide.
[3] Publication bias: strongly suspected - Four studies or fewer reported data for this outcome.
[4] Risk of bias: serious - The studies had an unclear risk of bias for randomisation, allocation concealment and blinding of participants.
[5] Inconsistency: very serious - There is very high heterogeneity.
[6] Imprecision: serious - There are wide confidence intervals.
[7] Risk of bias: very serious - This study had a high risk of bias for incomplete outcome data, and an unclear risk of bias for randomisation, allocation concealment and blinding.

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BACKGROUND

Description of the condition

One in every 10,000 people per year are diagnosed with schizophrenia, with a lifetime prevalence of about 1% (Jablensky 1992). It often runs a chronic course with acute exacerbations and often partial remissions. The neuroleptic group of drugs is the mainstay treatment for this illness (Dencker 1980). These are generally regarded as highly effective, especially in controlling such symptoms as hallucinations and fixed false beliefs (delusions) (Kane 1986). They seem to reduce the risk of acute relapse.
Anti-psychotic drugs are usually given orally (Aaes-Jorgenson 1985), but compliance with medication given by this route may be difficult to quantify. Problems with treatment adherence are common throughout medicine (Haynes 1979). Those who suffer from long-term illness such as schizophrenia are less likely to take medication regularly if experiencing adverse effects (Kane 1998), or if they experience cognitive impairments (David 1994) and erosion of insight. The development of depot injections in the 1960s and initial clinical trials (Hirsch 1973b) gave rise to extensive use of depots as a means of long-term maintenance treatment.

Description of the intervention

Fluphenazine was one of the first oral antipsychotics to be produced in a depot form. Two forms of the depot, a decanoate (Modecate) and an enanthate (Moditen) are available. The decanoate is more commonly prescribed (Marder 1990) and lasts about four to six weeks in the body, while a single dose of the enanthate is shorter acting (one to three weeks). Evidence also suggests that the decanoate may produce slightly less adverse effects than its enanthate counterpart (Kurland 1970). However, in comparison with newer depot formulations fluphenazine decanoate has been reported to cause greater extrapyramidal adverse effects (Knights 1979) and to significantly lower mood (De Alarcon 1969a).

How the intervention might work

Depots mainly consist of an ester of the active drug held in an oily suspension. This is injected intramuscularly and is slowly released. Depots may be given every one to six weeks. Individuals may be maintained in the community with regular injections administered by community psychiatric nurses, sometimes in clinics set up for this purpose (Barnes 1994). The use of depots eradicates covert non-compliance.

Why it is important to do this review

A systematic review undertaken over a decade ago suggested that, for those with serious mental illness, stopping anti-psychotics resulted in 58% of people relapsing, whereas only 16% of those who were still on the drugs became acutely ill within a one-year period (Davis 1986). Evidence also points to the fact that experiencing a relapse of schizophrenia lowers a person's level of social functioning and quality of life (Curson 1985). Relapse prevention has also enormous financial implications. For example, within the UK, a Department of Health burden of disease analysis in 1996 indicated that schizophrenia accounted for 5.4% of all National Heath Service inpatient expenditure, placing it behind only learning disability and stroke in magnitude (DoH 1996).

OBJECTIVES

To assess the effects of fluphenazine decanoate and enanthate versus oral anti-psychotics and other depot neuroleptic preparations for individuals with schizophrenia in terms of clinical, social and economic outcomes.

METHODS

Criteria for considering studies for this review

Types of studies

All relevant randomised controlled trials. If a trial had been described as 'double blind' but implied randomisation, we would have included such trials in a sensitivity analysis (see Sensitivity analysis). If their inclusion did not result in a substantive difference, they would have remained in the analyses. If their inclusion did result in statistically significant differences, we would not have added the data from these lower quality studies to the results of the better trials, but presented such data within a subcategory.

We excluded quasi-randomised studies, such as those allocating by alternate days of the week. Where people were given additional treatments with fluphenazine decanoate or fluphenazine enanthate, we only included data if the adjunct treatment was evenly distributed between groups and it was only the fluphenazine decanoate or fluphenazine enanthate that was randomised.

Types of participants

Adults, however defined, with schizophrenia or related disorders, including schizophreniform disorder, schizoaffective disorder and delusional disorder, again, by any means of diagnosis.

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We are interested in making sure that information is as relevant to the current care of people with schizophrenia as possible so proposed to clearly highlight 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. Fluphenazine decanoate: any dose.
2. Fluphenazine enanthate: any dose.
3. Oral anti-psychotics (with the exception of fluphenazine hydrochloride): any dose.
4. Other depot preparations: any dose.
5. Placebo.

Types of outcome measures

Outcomes were grouped into immediate (zero to five weeks), short term (six weeks to five months), medium term (six months to one year) and longer term (over 12 months)

Primary outcomes

1. Death and all causes of mortality
2. Clinical global state
2.1 Relapse
2.2 Clinically significant change in global state - as defined by each of the studies
3. Leaving the study early
4. Service utilisation outcomes
4.1 Hospital admission

Secondary outcomes

1. Clinical global state
1.1 Mean score/change in global state
2. Behaviour*
3. Mental state
3.1 Clinically significant change in psychotic symptoms - as defined by each of the studies
3.2 Mean score/change in psychotic symptoms
3.3 Clinically significant change in positive symptoms - as defined by each of the studies
3.4 Mean score/change in positive symptoms
3.5 Clinically significant response in negative symptoms - as defined by each of the studies
3.6 Mean score/change in negative symptoms
4. Extrapyramidal adverse effects
4.1 Incidence of use of antiparkinson drugs
4.2 Clinically significant extrapyramidal adverse effects - as defined by each of the studies
4.3 Mean score/change in extrapyramidal adverse effects
5. Other adverse effects, general and specific
6. Service utilisation outcomes
6.1 Days in hospital
7. Economic outcomes
8. Quality of life/satisfaction with care for either recipients of care or carers
8.1 Significant change in quality of life/satisfaction - as defined by each of the studies
8.2 Mean score/change in quality of life/satisfaction.
9. 'Summary of findings' table
We used the GRADE approach to interpret findings (Schünemann 2008) and used GRADE profiler to import data from RevMan 5 (Review 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 selected the following main outcomes at medium-term follow-up for inclusion in the 'Summary of findings' table.

1. Death and all causes of mortality
2. Relapse
3. Clinically significant change in global state
4. Hospital admission
5. Leaving the study early
6. Mental state
7. Extrapyramidal adverse effects

* additional outcome

Search methods for identification of studies

Electronic searches

1. Cochrane Schizophrenia Group's Trials Register

The Trials Search Co-ordinator (TSC) searched the Cochrane Schizophrenia Group's Registry of Trials (February 2011 and October 16, 2013) using the following search strategies which have been developed based on literature review and consulting the authors of the review:
((*anaten* or *Cardilac* or *Cenilene* or *dapotum* or *Decafen* or *decazate* or *Decentan* or *enanthate* or *eutimox* or *Fludeca* or *flufen* or *flunanthate* or *fluphen* or *Idazoxan* or *Lyogen * or *lyoridin* or *Mirenil* or *modec* or *moditen* or *Omca* or *Oxyprothepin* or *Pacinol* or *Permitil* or *phenathiazine* or *piperazine* or *prolixin* or *Prolongatum* or *Rx 781094* or *sediten* or *selecten* or *Sevinol* or *sinqualone* or *siqualone* or *trancin*) and (*decanoat* or *depot* or *long?act* or *delayed?act*)):ti,ab,kw of REFERENCE or (*fluphenaz* and *depot*):sin of STUDY

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The Cochrane Schizophrenia Group's Registry of Trials is compiled by systematic searches of major resources (including AMED, BIOSIS, CINAHL, EMBASE, MEDLINE, PsycINFO, PubMed, and registries of clinical trials) and their monthly updates, handsearches, grey literature, and conference proceedings (see Group Module). There is no language, date, document type, or publication status limitations for inclusion of records into the register. For previous searches, see Appendix 1.

Searching other resources

1. Reference searching

We also inspected the references of all identified trials for more studies. We sought each of the included studies as a citation on the SCISEARCH database. Then we inspected reports of articles that had cited these studies in order to identify further trials.

2. Personal contact

We tried to contact the first author of each included study for information regarding unpublished trials. We contacted companies producing depots and made requests for reports of published and unpublished trials. Where authors responded, this is noted in the Characteristics of included studies.

Data collection and analysis

This is an update of the original review (David 2004). Methods used in data collection and analysis for this update are below, for previous methods please see Appendix 2.

Selection of studies

For the update screening, two members of the Enhance Reviews team (NM and RA) independently inspected citations from the 2011 and 2013 searches and identified relevant abstracts. A random 20% sample was independently re-inspected by a senior researcher in the team to ensure reliability. Where disputes arose, the full report was acquired for more detailed scrutiny. If citations met inclusion criteria, we obtained full reports of the papers for more detailed inspection. Again, a random 20% of reports were re-inspected by a senior researcher in the team 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

For this update, review author NM extracted data from included studies and RA checked the data. We extracted data presented only in graphs and figures whenever possible, but only included if two review authors had the same results. When further information was necessary, we contacted authors of studies in order to obtain missing data or for clarification. No studies were multi-centre; had there been, we would have extracted data relevant to each component centre separately where possible.

2. Management

2.1 Forms

We extracted data onto standard, simple forms.

2.2 Scale-derived data

We included continuous data from rating scales only if:
a. the psychometric properties of the measuring instrument have been described in a peer-reviewed journal (Marshall 2000); and
b. the measuring instrument has not been written or modified by one of the trialists for that particular trial.

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. On the other hand, calculation of change needs two assessments (baseline and endpoint), which can be difficult in unstable and difficult to measure conditions such as schizophrenia. We decided primarily to use endpoint data, and only use change data if the former were not available. We combined endpoint and change data in the analysis as we used mean differences (MD) rather than standardised mean differences throughout (Higgins 2011, Chapter 9.4.5.2).

2.4 Skewed data

Continuous data on clinical and social outcomes are often not normally distributed. To avoid the pitfall of applying parametric tests to non-parametric data, we aimed to apply the following standards to all data before inclusion: a) standard deviations and means are reported in the paper or obtainable from the authors; b) when a scale starts from the finite number zero, the standard deviation, when multiplied by two, is less than the mean (as otherwise the mean is unlikely to be an appropriate measure of the centre of the distribution (Altman 1996)); c) if a scale started from a positive value (such as the Positive and Negative Syndrome Scale (PANSS), Kay 1986), which can have values from 30 to 210), we modified the calculation described above to take the scale starting point into account. In these cases skew is present if 2 SD > (S-S min), where S is the mean score and S min is the minimum score. Endpoint scores on scales often have a finite start and end point and these rules can be applied. We entered skewed endpoint data from studies of fewer than 200 participants in 'other tables' within the data and analyses section rather than into a statistical analysis. Skewed data pose less of a problem when looking at mean if the

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sample size is large; we entered such data from studies with over 200 participants into syntheses.

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

2.5 Common measure

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

2.6 Conversion of continuous to binary

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

2.7 Direction of graphs

We entered data in such a way that the area to the left of the line of no effect indicated a favourable outcome for fluphenazine esters.

Assessment of risk of bias in included studies

For this 2013 update, the Enhanced Reviews team used the criteria described in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011) to assess trial quality. This new set of criteria is based on evidence of associations between overestimate of effect and high risk of bias of the article such as sequence generation, allocation concealment, blinding, incomplete outcome data and selective reporting.

We have noted the level of risk of bias in both the text of the review and in the Summary of findings for the main comparison, Summary of findings 2 and Summary of findings 3.

Measures of treatment effect

1. Binary data

For binary outcomes, we calculated a standard estimation of the risk ratio (RR) and its 95% confidence interval (CI). It has been shown that RR is more intuitive (Boissel 1999) than odds ratios and that odds ratios tend to be interpreted as RR by clinicians (Deeks 2000). The Number Needed to Treat/Harm (NNT/H) statistic with its confidence intervals is intuitively attractive to clinicians but is problematic both in its accurate calculation in meta-analyses and interpretation (Hutton 2009). Therefore, we did not present NNTs.

2. Continuous data

For continuous outcomes, we estimated mean difference (MD) between groups. We prefer not to calculate effect size measures (standardised mean difference SMD). However, if scales of very considerable similarity were used, we presumed there was a small difference in measurement, and we calculated effect size and transformed the effect back to the units of one or more of the specific instruments. Where trials reported mean data adjusted for baseline and standard error using ANCOVA, we entered this data using the generic inverse variance according to section 9.4.5.2 of the *Cochrane Handbook* (Higgins 2011).

Unit of analysis issues

1. Cluster trials

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

None of the trials we included were cluster trials. Had there been, where clustering was not accounted for in primary studies, we would have presented data in a table, with a (*) symbol to indicate the presence of a probable unit of analysis error. In subsequent versions of this review, we would seek to contact first authors of 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 had been incorporated into the analysis of primary studies, we would have presented these data as if from a non-cluster randomised study, but adjusted for the clustering effect.

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

If cluster studies have been appropriately analysed taking into account ICCs and relevant data documented in the report, synthesis with other studies would have been possible using the generic inverse variance technique.

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2. Cross-over trials

Some included studies used a cross-over design. 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 only used data of the first phase of cross-over studies.

3. Studies with multiple treatment groups

For the included studies with more than two treatment arms, we presented the additional treatment arms in comparisons. Where data were binary, we simply added these and combined them within the two-by-two table. Where data were continuous we combined data following the formula in section 7.7.3.8 (Combining groups) of the *Handbook* (Higgins 2011). Where the additional treatment arms were not relevant, we did not reproduce these data.

Dealing with missing data

1. Overall loss of credibility

At some degree of loss of follow-up, data must lose credibility (Xia 2009). We chose that, for any particular outcome, where more than 30% of those randomised were lost to follow-up by six months, or 50% of data by beyond that time be unaccounted for, we did not reproduce these data or use them within analyses.

2. Continuous

2.1 Attrition

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

2.2 Standard deviations

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

Assessment of heterogeneity

1. Clinical heterogeneity

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

3. Statistical heterogeneity

3.1 Visual inspection

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

3.2 Employing the I^2 statistic

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

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Assessment of reporting biases

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

Data synthesis

We understand that there is no closed argument for preference for use of fixed-effect or random-effects models. The random-effects method incorporates an assumption that the different studies are estimating different, yet related, intervention effects. This often seems to be true to us and the random-effects model takes into account differences between studies, even if there is no statistically significant heterogeneity. There is, however, a disadvantage to the random-effects model: it puts added weight onto small studies which often are the most biased ones. Depending on the direction of effect, these studies can either inflate or deflate the effect size. We chose the fixed-effect model for all analyses, unless there was high heterogeneity (see Assessment of heterogeneity), in which case we used the random-effects model. The reader is, however, able to choose to inspect the data using the random-effects model.

Subgroup analysis and investigation of heterogeneity

1. Subgroup analyses - only primary outcomes

1.1 Clinical state, stage or problem

We proposed to undertake this review and provide an overview of the effects of fluphenazine esters for people with schizophrenia in general. In addition, however, we tried to report data on subgroups of people in the same clinical state, stage and with similar problems. In order to do subgroup analyses, we needed to have at least six studies for an outcome.

Sensitivity analysis

We aimed to apply all sensitivity analyses to the primary outcomes of this review, again, if there were at least six studies with data for a particular outcome.

1. Implication of randomisation

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

2. Assumptions for lost binary data

If assumptions had to be made regarding people lost to follow-up and missing SDs data (see Dealing with missing data), we would have compared the findings on primary outcomes when we used our assumption compared with completer data only. We would have undertaken a sensitivity analysis to test 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 would have reported results and discussed them, but continued to employ our assumption.

3. Risk of bias

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

4. Imputed values

If we had included cluster trials, we also would have completed a sensitivity analysis to assess the effects of including data from trials if we needed to use imputed values for ICC in calculating the design effect in cluster randomised trials.

If we had noted substantial differences in the direction or precision of effect estimates in any of the sensitivity analyses listed above, we would not have pooled data from the excluded trials with the other trials contributing to the outcome, but would have presented them separately.

5. Fixed-effect and random-effects

We synthesised data using a fixed-effect model.

6. Dose

We tested the sensitivity of the primary outcomes as to whether high (250 mg) or low (25 mg) dose of fluphenazine decanoate was used or whether the trials used an intermediate/high (0.5 mg) or low (0.25 mg) dose of fluphenazine enanthate.

RESULTS

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Description of studies

Please see Characteristics of included studies, Characteristics of excluded studies and Characteristics of studies awaiting classification.

Results of the search

The original search yielded 982 citations using the search strategy. Two hundred and forty-eight citations were related to fluphenazine decanoate or enanthate but only 62 referred to controlled clinical trials (all published in journals). The review was also updated in May 2002, a further electronic search yielded 247 citations from which we obtained 124 articles for further inspection.

The 2013 update search identified 44 potential studies and after screening we added four new studies (Ju 2000; Kane 1978; Khazaie 2005; Shenoy 1981) to the included studies. Two previously included studies, Marder 1984 and Marder 1987, were found to include the same participants, and so were added as the same study. The total number of included studies is now 73 randomised controlled trials with a total of 90 reports.

For overall screening from the three searches see Figure 1.

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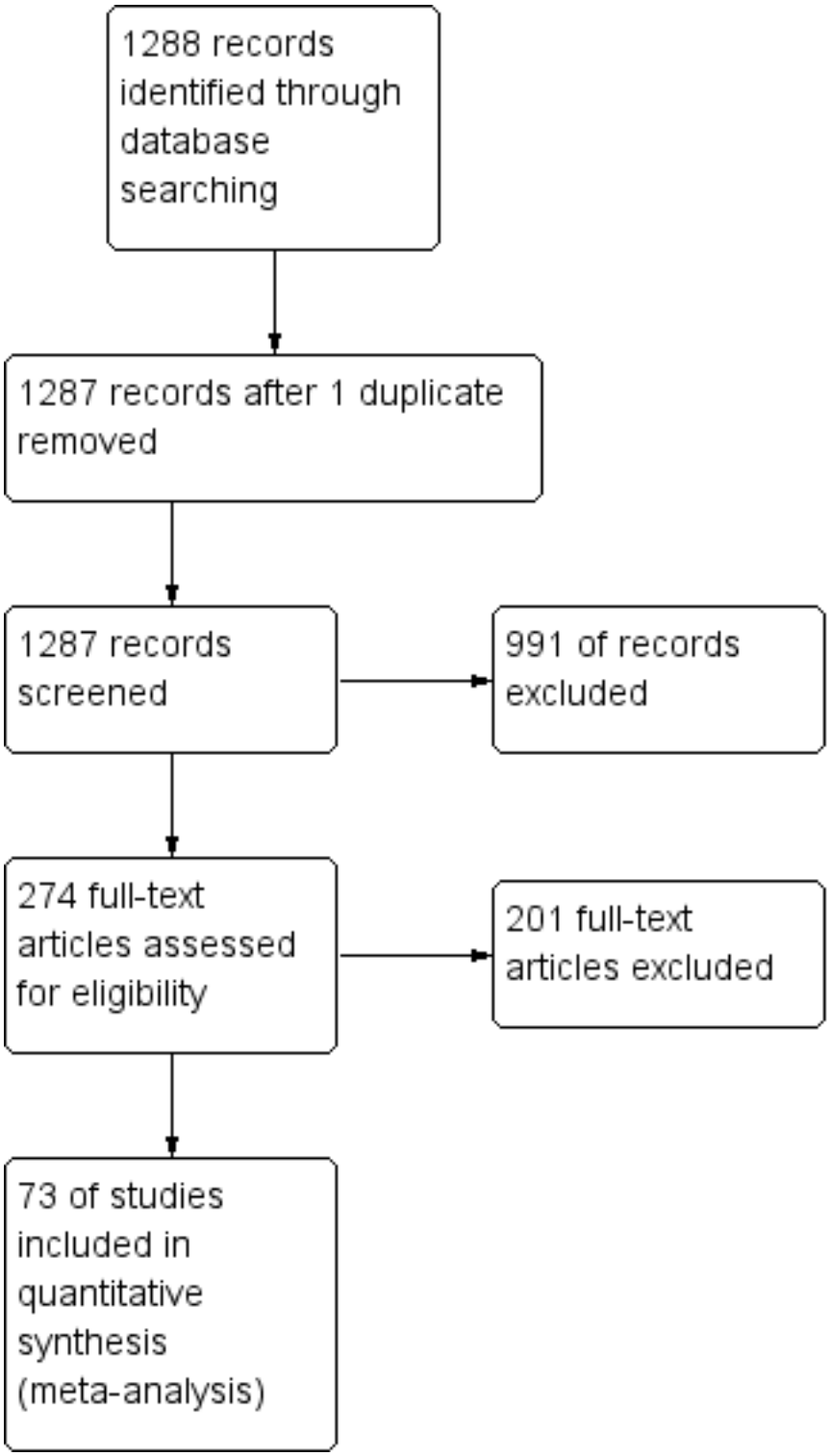
Figure 1. Study flow diagram.



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Included studies

1. Length of trials

The duration for all the studies ranged between two weeks (Kane 1978) to three years (Dencker 1973).

2. Participants

The diagnoses of all participants were schizophrenia or some other similar psychotic disorder. Most of the studies included people of both sexes, although seven studies (Albert 1980; Asarnow 1988; Kurland 1966; Marder 1987; McCreadie 1980; McCreadie 1982) included only men and 16 trials failed to mention the sex of participants. Ages ranged between 13 and 81 years, but most people were in the 18 to 65 age range. Most trial participants had long histories of schizophrenia, although many studies (n = 44) failed to mention the length of time people had been ill. Researchers frequently used operational criteria for diagnoses (RDC, Schneider's first rank symptoms, Hay & Forrest 1972 criteria, PSE, Kraepelinian, ICD -9, DSM-II/III, Bleuler's criteria, Feighner 1972 criteria, Chinese Classification of Mental Disorders and Huangshan council schizophrenia standard), although 31 (43%) trials did not specify which diagnostic criteria were used.

3. Setting

The trials were both community- and hospital-based. People in two studies (Schooler 1980; Wistedt 1984) were given the first two injections whilst in hospital and after which medication continued to be administered in the community. Both Dencker 1973 and Wistedt 1984 studied people initially in a hospital setting followed by a continuation in the community. Several studies involved people from both hospital and community settings (Dencker 1973; Donlon 1976; Kaneno 1991; Magnus 1979; Marder 1987; McCreadie 1980; Rifkin 1977; Schooler 1997; Simon 1978). A surprisingly large number (11) of studies did not mention the setting used (Albert 1980; Javed 1991; Kissling 1985; McKane 1987; Odejide 1982; Quitkin 1978; Russell 1982; Schneider 1981; Schlosberg 1978; Sharma 1991; Wistedt 1983). Thirty-one trials were conducted in North America and another 29 in Europe, 10 in Asia, one in Africa; and two did not report the country.

4. Study size

The largest study was by Schooler 1997 who randomised 313 people, whereas Altamura 1985 only included 11. The majority randomised between 30 and 60 people.

5. Interventions

Six of the included trials compared fluphenazine decanoate with placebo (Dotti 1979; Hirsch 1975; Jolley 1990; Odejide 1982; Rifkin 1977; Shenoy 1981) and one study compared fluphenazine enanthate with placebo (Van Praag 1970). Ten studies compared fluphenazine decanoate with enanthate (Altamura 1985; Asarnow 1988; Chouinard 1978; Chouinard 1982; Donlon 1976; Kane 1978; Keskiner 1971; Kurland 1966; MacCrimmon 1978; Van Praag 1973). Fourteen studies compared fluphenazine esters with oral antipsychotics. Thirty-five trials compared fluphenazine decanoate or enanthate with other depot formulations. There were 10 dosage studies - nine comparing fluphenazine decanoate and one comparing fluphenazine enanthate (Goldstein 1978). Of the 73 included trials, 66 used fluphenazine decanoate as an intervention.

6. Outcomes

6.1 Outcome reporting

Many of the trials presented their findings in graphs or using P values alone. Graphical presentation made it impossible to acquire raw data for synthesis. Requests for raw data from authors have so far failed with the exception of Pinto 1979 and Quitkin 1978. It was also common to use P values as a measure of association between intervention and outcomes instead of showing the strength of the association.

6.2 Missing outcomes

No study reported on hospital and service outcomes or commented on participants' overall satisfaction during or after the trial. Economic outcomes were not reviewed by any of the included studies.

6.1 Outcome scales

Scales that provided usable data are listed below. We listed data that were not usable in the Characteristics of included studies under outcomes, 'unable to use'.

6.1.1 Global functioning

a) Clinical Global Impression - CGI (Guy 1976)

This is a three-item rating instrument commonly used in schizophrenia studies. It enables clinicians to quantify the severity of illness and overall clinical improvement during therapy. A

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seven-point scoring system is usually used with low scores indicating decreased severity and/or greater recovery.
b) Global Assessment Scale - GAS (Endicott 1976)
This is an observer-rated scale for evaluating the overall functioning of an individual during a specified time period on a continuum from psychological or psychiatric sickness to health. Score ranges from zero to 100, where a higher score indicates better functioning.

6.1.2 Mental state

a) Brief Psychiatric Rating Scale - BPRS (Overall 1962)
The BPRS is an 18-item scale measuring positive symptoms, general psychopathology and affective symptoms. The original scale has 16 items, but a revised 18-item scale is commonly used. Scores can range from zero to 126. Each item is rated on a seven-point scale, with high scores indicating more severe symptoms.
b) Comprehensive Psychopathological Rating Scale - CPRS (Asberg 1978)
The scale is designed to measure psychopathology over time via a clinical interview. It contains 67 items, including one global rating and one item documenting the reliability of the interview. The majority of the items (40) are based upon reported symptoms. Assumed reliability of the rating is scored as zero (very poor), one (fair), two (good) or three (very good).
c) Krawiecka Scale (Krawiecka 1977)
This mental state scale encompasses both positive and negative symptoms of schizophrenia. It is used to evaluate the mental state and behaviour in chronic psychotic people with higher scores indicating greater severity. It is also known as the Manchester Scale.
d) Scale for the Assessment of Negative Symptoms - SANS (Andreasen 1983)
This scale allows a global rating of the following negative symptoms: alogia (impoverished thinking), affective blunting, avolition-apathy, anhedonia-asociality, and attention impairment. Assessments are made on a six-point scale from zero (not at all) to five (severe). Higher scores indicate more symptoms.
e) Scale for the Assessment of Positive Symptoms - SAPS (Andreasen 1984)
This six-point scale gives a global rating of positive symptoms such as delusions, hallucinations and disordered thinking. Higher scores indicate more symptoms.

6.1.3 Behaviour

a) Nurses Observational Scale of Inpatients Evaluation - NOSIE (Honigfeld 1962).
This is an 80-item scale with items rated on a five-point scale from zero (not present) to four (always present). Ratings are based on behaviour over the previous three days. The seven headings are social competence, social interest, personal neatness, co-operation, irritability, manifest psychosis and psychotic depression. The total score ranges from zero to 320 with high scores indicating a poor outcome.

6.1.4 Adverse effects

a) Abnormal Involuntary Movement Side Effects Scale - AIMS (Guy 1976)
This is a 12-item scale designed to record the occurrence of dyskinetic movements. Ten items of this scale have been used to assess tardive dyskinesia, a long-term drug-induced movement disorder. A five-point scoring system (from zero - none to four - severe) has been used to rate each of the 10 items. Using this scale in short-term treatment may be helpful in assessing some short-term abnormal movement disorders. A low score indicates low levels of dyskinetic movements.
b) Dosage Record and Treatment Emergent Symptoms Scale - DOTES (Guy 1976)
This adverse effect tool seems less of a scale, where the degree and severity of a symptom is recorded, and more of a checklist. The DOTES seems to record the presence or absence of a list of adverse effects.
c) Extrapyramidal Symptom Rating Scale - ESRS (Chouinard 1980)
This consists of a questionnaire relating to parkinsonian symptoms (nine items), a physician's examination for parkinsonism and dyskinetic movements (eight items), and a clinical global impression of tardive dyskinesia. High scores indicate severe levels of movement disorder.
d) Simpson and Angus Scale - SAS (Simpson 1970b)
The SAS is a 10-item scale, used to evaluate the presence and severity of drug-induced parkinsonian symptomatology. The ten items focus on rigidity rather than bradykinesia, and do not assess subjective rigidity or slowness. Items are rated for severity on a zero to four scale, with a scoring system of zero to four for each item. This scale is referred to as the RSESE in Ju 2000. A low score indicates low levels of parkinsonism.
e) UKU Side Effects Rating Scale - UKU-SERS (Lingjaerde 1987).
The UKU rates four major topics: psychological adverse effects (10 items), neurological adverse effects (eight items), autonomic adverse effects (11 items) and other adverse effects (19 items). Each item is defined by means of a four-point scale where zero means not present or doubtfully present. Scoring range zero to144.
f) Treatment Emergent Symptom Scale -TESS (Guy 1976)
This checklist assesses a variety of characteristics for each adverse event, including severity, relationship to the drug, temporal characteristics (timing after a dose, duration and pattern during the day), contributing factors, course, and action taken to counteract the effect. Symptoms can be listed a priori or can be recorded as observed by the investigator. High scores indicate worse symptoms.
g) Symptom Checklist 90 - SCL-90 (Derogatis 1977)

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This is a self-report scale of physical symptoms.
h) Maryland Psychiatric Research Center Involuntary Movement Scale (Cassady 1997)
The MPRC rates the severity of tardive dyskinesia. It gives a global rating of dyskinesia in 11 body areas and two ratings during gait. It is rated on an eight-point scale (zero to seven), with higher scores indicating worse symptoms.

6.1.5 Quality of life

a) Quality of life scale - QLS (Heinrich 1984)
This 21-item scale is based on a semi-structured interview providing information on symptoms and functioning during the preceding four weeks. There are seven severity steps (zero to six; six being adequately functioning and zero being deficient). Four item categories have been identified by factor analysis i) interpersonal relationships (seven items), ii) instrumental role (four items), iii) intrapsychic function (seven items) and iv) common place objects and activities. Higher scores indicate better quality of life.

Excluded studies

We excluded 201 studies, mainly because they were not randomised controlled trials (RCTs), or controlled clinical trials (CCTs), because neither fluphenazine decanoate nor fluphenazine enanthate were included in the interventions or because trialists did not report any usable data. In the latter case, we contacted authors requesting raw data but we have, in most cases, received no reply. Other reasons for exclusion were that the two drugs were not analysed (Crawford 1974; Wistedt 1983a) or clinical outcomes were not measured (Landmark 1994; Leff 1973; Marder 1990a; Marder 1991a; Stevens 1973).

Awaiting assessment

Six studies await assessment. del Giudice 1970; Jue 1996; Kabes 1984; Ravanic 1996 are reports for which we have citations but no papers. These are currently being sought. Two papers await translation (Angst 1973; Ushakov 1990a).

Ongoing studies

We have not identified any ongoing studies.

Risk of bias in included studies

See also 'Risk of bias' tables in Characteristics of included studies, and Figure 2 and Figure 3.

Figure 2. 'Risk of bias' graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.

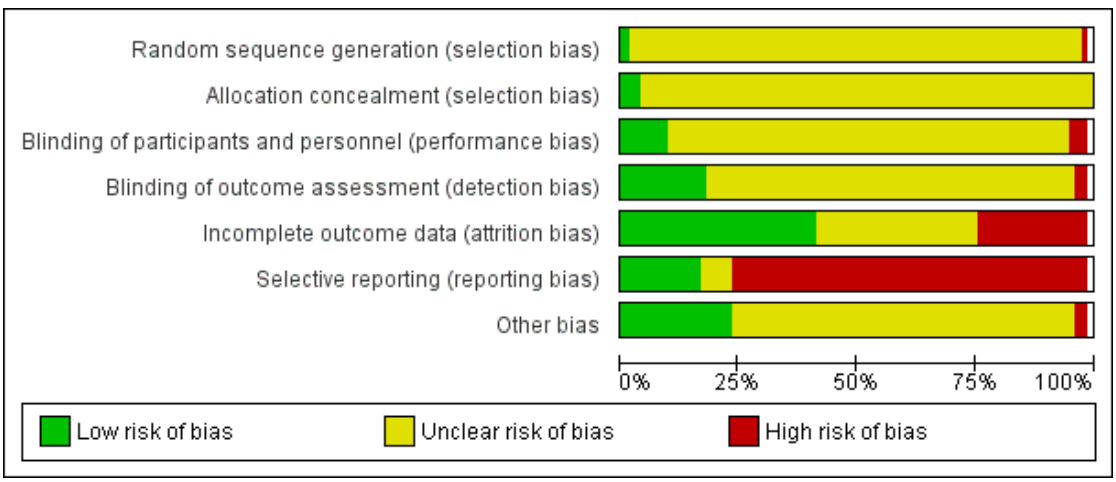

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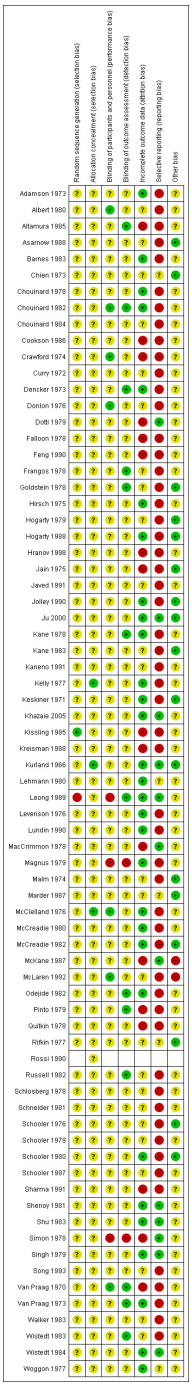
Figure 3. 'Risk of bias' summary: review authors' judgements about each risk of bias item for each included study.



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Since the last version of this review was published, the methods for assessing the risk of bias of studies has changed. All studies were re-assessed for risk of bias in the current version of this review. The risk of bias has not been fully assessed for two studies as they are not reported in English and we were not able to translate them (Kaneno 1991; Rossi 1990), although Kaneno 1991 had a section in English and the risk of bias has been completed based on this.

Allocation

All included studies were reported as randomised, but only five described the method of randomisation: Kissling 1985 used a coin-throwing method, Frangos 1978 a randomisation code, Magnus 1979 a pre-arranged prescribing list, and Wistedt 1984 a randomisation list. Leong 1989 described the method of randomisation as the next available study number in the numerical sequence. However only Kissling 1985 was rated as low risk, Leong 1989 was rated to be a high risk and the other studies were all rated as unclear risk of bias for sequence generation.

Three other studies did not report method of randomisation but did describe allocation concealment (Kelly 1977; Kurland 1966; McClelland 1976). In these three trials the allocation codes were known only to the hospital pharamcists or nurses involved in the trial, and were rated as low risk of bias; the remaining studies were rated as unclear risk of bias.

Blinding

Most studies reported using double-blind methodology, although the technique used was not described in the majority of these studies. Seven studies were rated low risk of bias for blinding of participants and personnel, and stated blindness was achieved through use of identical injections of medication (Albert 1980; Chouinard 1982; Crawford 1974; Donlon 1976; McClelland 1976; McLaren 1992; Van Praag 1970).

Only 14 studies described outcome assessors as being blinded to treatment and were rated low risk of bias (Altamura 1985; Chouinard 1982; Dencker 1973; Frangos 1978; Goldstein 1978; Kane 1978; Leong 1989; McClelland 1976; Odejide 1982; Pinto 1979; Russell 1982; Van Praag 1970; Van Praag 1973; Wistedt 1983). Magnus 1979 and Simon 1978 were open label trials and Leong 1989 described using a 'partially-blinded' method where only outcome assessors were blinded. The remaining studies were of unclear risk of bias as no information on blinding of outcome assessors was provided.

Incomplete outcome data

Twenty-nine studies were rated as low risk of bias for incomplete outcome data and 25 studies had an unclear risk of bias. Seventeen studies were rated as high risk of bias, for two of these it was due to more than 50% of losses to follow-up (Jain 1975; Kissling 1985), and only data for the outcome "Leaving the study early" was used for these studies.

Selective reporting

Only 12 studies were of low risk of bias with regard to selective reporting, and five were unclear. The remaining studies were of high risk of bias, mainly due to poor data reporting. Continuous data were particularly problematic as many studies presented findings without standard deviations or any other measure of variance, in graphs, in percentiles or by inexact P values. Furthermore, many pre-planned outcomes were not reported at all.

Other potential sources of bias

McKane 1987 and McLaren 1992 were subject to other biases as they were funded by the pharmaceutical industry. Eighteen studies were rated as low risk of bias for other potential sources of bias, and the remaining had an unclear risk of bias.

Effects of interventions

See: **Summary of findings for the main comparison** FLUPHENAZINE DECANOATE compared with PLACEBO for schizophrenia; **Summary of findings 2** FLUPHENAZINE DECANOATE compared with ORAL NEUROLEPTICS for schizophrenia; **Summary of findings 3** FLUPHENAZINE DECANAOTE compared to FLUPHENAZINE ENANTHATE for schizophrenia

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

COMPARISON 1: FLUPHENAZINE DECANOATE versus PLACEBO

1.1 Death

The only study reporting mortality was Jolley 1990 where two deaths occurred in the treatment group (fluphenazine decanoate) compared to none in the placebo group (n = 54, RR 5.00, CI 0.30 to 99.51). Nevertheless, the result was not statistically significant (Analysis 1.1).

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1.2 Global state

Heterogeneous data from three studies (Hirsch 1975; Odejide 1982; Rifkin 1977) found relapse rates to be equivocal over six months to one year for the fluphenazine decanoate group compared with people receiving placebo (n = 196, 3 RCTs, RR 0.62, CI 0.24 to 1.60). Shenoy 1981 reported no relapses in the short term at six weeks. Relapse rates for longer-term studies (Jolley 1990) at two years significantly favoured fluphenazine decanoate (n = 54, RR 0.35, CI 0.19 to 0.64) compared to placebo (Analysis 1.2). Furthermore, one short-term study of six weeks found no significant difference between treatment group when global state was measured on the Global Assessment Scale (GAS) (Analysis 1.3).

1.3 Leaving the study early

Four trials in which 216 people had been randomised to fluphenazine decanoate or placebo had, in total, 21% attrition (Analysis 1.4). No significant difference was found in people leaving the study early between groups (RR 1.30, CI 0,77 to 2.19). Shenoy 1981 reported short-term data at six weeks and also found no significant difference between treatment groups. Jolley 1990 reported longer-term data at two years for leaving the study early that significantly favoured depot fluphenazine compared to placebo (n = 54, RR 0.47, CI 0.23 to 0.96).

1.4 Mental state

Only one trial (Dotti 1979) reported general mental state on the Brief Psychiatric Rating Scale (BPRS), the results were equivocal (Analysis 1.5). The single study by Odejide 1982 reporting on depression showed equivocal results between fluphenazine decanoate and placebo (Analysis 1.6).

1.5 Adverse effects

Limited data were available. Jolley 1990 reported equivocal data for incidence of tardive dyskinesia (Analysis 1.7). Rifkin 1977 reported on toxicity (no further details reported), which was significantly higher in the depot fluphenazine group (n = 45 RR, 7.65, CI 1.04 to 56.26; Analysis 1.8).

COMPARISON 2: FLUPHENAZINE DECANOATE versus ORAL NEUROLEPTICS

2.1 Death

There were no reports of death in any of the studies comparing depot fluphenazine versus other oral neuroleptics.

2.2 Global state

Using the negative outcome, 'no clinically important global change' Adamson 1973 and Curry 1972 produced results favouring fluphenazine decanoate at 0 to 5 weeks (n = 74, 2 RCTs, RR 0.61 CI 0.46 to 0.81; Analysis 2.1). Song 1993 reported on outcomes at 6 months to one year, with equivocal findings (n = 102, RR 0.85, CI 0.56 to 1.27). Using the CGI scale, Shu 1983 also reported equivocal findings (n = 34, MD at 6 weeks -0.10 CI -2.79 to 2.59; Analysis 2.3). There was no significant difference between those taking fluphenazine decanoate and people on oral neuroleptics for relapse at 6 months to one year (n = 419, 6 RCTs, RR 1.46, CI 0.75 to 2.83); relapse data recorded at more than one year were also not significant (n = 216, 3 RCTs, RR 1.25 0.81 to 1.95; Analysis 2.2).

2.3 Leaving the study early

Ten trials reported no significant difference between the number of people who left the study early over six months to one year in either the fluphenazine decanoate group or the oral antipsychotic group (n = 937, RR 0.96, CI 0.73 to 1.25; Analysis 2.4). Studies by Curry 1972 (at 28 days), Shu 1983 (at six weeks) and Falloon 1978 and Simon 1978 (at more than one year) were also equivocal.

2.4 Behaviour

Simon 1978 found no difference in Nurses Observational Scale of Inpatients Evaluation (NOSIE) scale scores between groups (n = 120, MD -0.56, CI -6.92 to 5.80; Analysis 2.5). Barnes 1983 reported a significant difference for change in disturbed behaviour (n = 36); these data are skewed (Analysis 2.6).

2.5 Mental state

Only Simon 1978, reported on mental state (BPRS endpoint scores) and found no significant difference between groups (n = 120, MD -0.75, CI -5.75 to 4.25; Analysis 2.7). Schooler 1979 and Falloon 1978 reporting on depression found no significant difference between those receiving fluphenazine decanoate and oral neuroleptics (n = 214, RR six months to one year 0.89, CI 0.60 to 1.32; n = 44, RR more than one year 1.53,CI 0.91 to 2.57; Analysis 2.8).

2.6 Adverse effects

Three studies, McCreadie 1980, McCreadie 1982 and Schooler 1980, report homogenous data for general movement disorders (six months to one year), which significantly favoured fluphenazine decanoate compared to oral neuroleptics (n = 259, RR 0.47, CI 0.24 to 0.91; Analysis 2.9). The single longer-term study by Falloon 1978 found no significant difference for incidence of movement disorders (n = 44, RR 0.40, CI 0.12 to

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1.28). Rifkin 1977 reported on akathisia at one year. Akathisia was significantly lower in the oral fluphenazine group (n = 51, RR 20.54 CI 1.25 to 337.94; Analysis 2.10). Trials reported limited data for the outcome 'needing anticholinergic drugs' and all findings were equivocal (Analysis 2.11). McCreadie 1982 found tardive dyskinesia to be significantly less common for those allocated fluphenazine decanoate compared with people on pimozide (n = 28, RR medium term 0.62, CI 0.41 to 0.93; Analysis 2.12). The other study that reported on tardive dyskinesia was Simon 1978. Trialists did not find any difference between fluphenazine decanoate and oral neuroleptic (n = 120, RR at 18 months 0.16, CI 0.01 to 2.99). Shu 1983, using the Simpson and Angus Scale (SAS) reported no significant difference at six weeks between fluphenazine decanoate and penfluridol (n = 32, MD 1.30, CI 0.01 to 2.59; Analysis 2.14). Adamson 1973 (immediate), McCreadie 1982 and Schooler 1980 (medium term) reported general adverse effects. Outcomes are equivocal (Analysis 2.17). Falloon 1978 was the only longer-term study to report on tremor, with equivocal results for depot fluphenazine and pimozide (n = 44, RR 0.80, CI 0.26 to 2.45; Analysis 2.13). Schooler 1976 reports equivocal data for the adverse effect of blurred vision (Analysis 2.15). Rifkin 1977 also reported on toxicity (no further details), which was more frequent for the depot fluphenazine group (n = 51, RR 4.87, CI 1.14 to 20.72; Analysis 2.16).

COMPARISON 3: FLUPHENAZINE DECANOATE versus OTHER DEPOT NEUROLEPTICS

3.1 Death

McKane 1987 reported one death occurring in the treatment group (fluphenazine decanoate) compared to none in the haloperidol decanoate group (n = 38, RR 3.0, CI 0.13 to 69.31; Analysis 3.1). Nevertheless, the result was not statistically significant.

3.2 Global state

Eleven studies reported the outcome of 'relapse' at six months to one year. We found no statistically significant difference between the fluphenazine decanoate group and the other depot groups (n = 581, RR 0.82, CI 0.56 to 1.18). Longer studies (more than one year) also found no difference between interventions (n = 252, RR 1.22, CI 0.77 to 1.92). Wistedt 1984 did report relapse data at 20 weeks but, again, results were equivocal (Analysis 3.3). Outcomes for 'no clinically important global change' at six months to one year reported by Dencker 1973, Leong 1989 and Schlosberg 1978 were not significant for the fluphenazine decanoate and other depot neuroleptic groups (n = 187, RR 1.04, CI 0.96 to 1.12; Analysis 3.2); Ju 2000 also reported short-term data and also found no significant difference. Leong 1989 supported this result by reporting no significant differences in the number of people who became severely ill in the comparison of fluphenazine decanoate with other depot drugs (n = 60, RR 1.07, CI 0.94 to 1.23; Analysis 3.4).

Chouinard 1984 and Schlosberg 1978 report continuous data at six months to one year on clinical global impression. There is no clear advantage between fluphenazine decanoate and other depot neuroleptics (n = 90, MD -0.10, CI -0.41 to 0.21; Analysis 3.7). These findings were confirmed by Chouinard 1984 and Cookson 1986 who reported no significant difference in needing additional antipsychotics at six months to one year between the depot groups (n = 91, RR 0.53, CI 0.14 to 1.96; Analysis 3.5). Frangos 1978 also reported the outcome of 'not improved' (n = 50, RR at four months RR 2.50, CI 0.53 to 11.70) and Leong 1989, at seven months (n = 60, RR 0.75, CI 0.18 to 3.07) (Analysis 3.8). Finally, Wistedt 1984 reported non-significant data for clinical global impression at zero to five weeks. These data are skewed so are not displayed graphically (Analysis 3.6).

3.3 Leaving the study early

Fifteen included trials found no significant difference in the number of people who left the study early in either the fluphenazine decanoate group or the other depot group (n = 775, RR medium term 1.13, CI 0.89 to 1.44). Studies found no differences across any time period from the immediate to those lasting longer than one year (Analysis 3.9).

3.4 Behaviour

Simon 1978 supported this outcome by reporting no difference in NOSIE-30 scores between the groups (n = 118, MD - -5.21 -10.85 to 0.43; Analysis 3.10).

3.5 Mental state

We found short- and medium-term studies assessing mental state (BPRS endpoint scores) to significantly favour 'other depot neuroleptics' for the short term (n = 203, 2 RCTs MD 1.11, CI 0.86 to 1.36) and medium term (n = 162, 3 RCTs, MD 1.20, CI 1.10 to 1.30) (Analysis 3.11). Longer-term studies (McKane 1987, Simon 1978) did not show any differences for mental state in either intervention (n = 141, MD 0.85 CI -2.32 to 4.03; Analysis 3.11). Dichotomised medium-term BPRS data reported by Dencker 1973 found no significant difference between depot fluphenazine and pipothiazine palmitate (Analysis 3.12). The only study reporting on the outcome of depression was Dencker 1973 who found no significant difference between fluphenazine decanoate and pipothiazine palmitate (n = 67, RR medium term 1.02, CI 0.81 to 1.28; Analysis 3.13). Ju 2000 reported data for positive and negative symptoms on the Scale for the Assessment of Positive Symptom(SAPS) and SANS, respectively, from six weeks to five months, but these data are skewed so are not displayed graphically (Analysis 3.14).

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3.6 Adverse effects

The occurrence of dyskinetic movements in general was the same across short-, medium- and longer-term studies (Analysis 3.15). Feng 1990 reporting on a small, short-term study found no significant difference between fluphenazine decanoate and haloperidol decanoate (n = 30 RR 2.00, CI 0.43 to 9.32). Dencker 1973, Leong 1989 and Schlosberg 1978 (comparing fluphenazine decanoate with pipothiazide palmitate) and McLaren 1992 (comparing with bromperidol decanoate) found no significant difference in the occurrence of dyskinestic movements (n = 234, RR at six months to one year 1.08, CI 0.86 to 1.34). Longer-term studies also found no significant difference with movement disorders between fluphenazine decanoate and other depot neuroleptics. For the outcome of 'needing anticholinergic medication', eight studies, when synthesised, found in favour of other depots by one year (n = 448, RR 1.24 0.93 to 1.64). However, these data were heterogeneous and using the random-effects model (as per protocol), the result was not statistically significant (Analysis 3.16). For the same outcome, three longer-term studies were equivocal but significantly favoured the 'other depot neuroleptics' group when analysed with a fixed-effect model (n = 220, RR 1.28, CI 1.08 to 1.51). Outcomes such as dry mouth, tardive dyskinesia and parkinsonism were not significantly different between depot fluphenazine and other depot neuroleptics (Analysis 3.22; Analysis 3.18; Analysis 3.17, respectively). Tremor (short term, 2 RCTs and medium term, 3 RCTs) was not more common for people given the depot flupenthixol (Analysis 3.19). Ju 2000 reported data for movement disorders from six weeks to five months on the TESS and RSESE, but these data are skewed so are not displayed graphically (Analysis 3.20). When reporting blurred vision, the results of one medium term trial were not significant, but one longer-term study, Pinto 1979, did report significant results (P = 0.04) favouring flupenthixol decanoate (n = 64, RR 17.88, CI 1.08 to 294.82; Analysis 3.21). General adverse effects (short-term data) were reported by Frangos 1978 and Javed 1991 and favoured other depot neuroleptics (n = 88, RR 1.36, CI 1.07 to 1.74). However, medium-term data (n = 249, six months to one year) were equivocal (Analysis 3.23).

COMPARISON 4: FLUPHENAZINE DECANOATE - DOSAGE STUDIES (HIGH DOSE versus STANDARD DOSE)

4.1 Global state

McClelland 1976 and Kreisman 1988 reported no significant difference in relapse scores (medium term) between either depot group (n = 182, RR 2.11, CI 0.30 to 14.91; Analysis 4.1). Also, McClelland 1976 reported no significant difference in needing additional antipsychotics (six months to one year) between fluphenazine decanoate (high dose) group and the standard dosage groups (n = 50, 1 RCTs, RR 1.67, CI 0.45 to 6.24; Analysis 4.2). Outcomes for global improvement 'not improved' were reported by Lehmann 1980 (nurse and psychiatrist rated) at six months to one year (Analysis 4.3). Results for nurse rated outcomes significantly favoured the standard dosage group (n = 40, 1 RCT, RR 1.58, CI 1.09 to 2.30). However, results for psychiatrist rated were not significant for either dosage intervention at six months (n = 40, 1 RCT, RR 1.15, CI 0.77 to 1.74).

4.2 Leaving the study early

Lehmann 1980 and McClelland 1976 reported no difference in the number leaving the study (six months to one year) for either intervention (n = 90, 2 RCTs, RR 0.60, CI 0.15 to 2.36; Analysis 4.4).

4.3 Mental state

McClelland 1976 further reported no difference in BPRS endpoint score (n = 50, 1 RCT, MD -0.03, CI -5.79 to 5.73) for either the high or standard dosage group (Analysis 4.5).

4.4 Adverse effects

McClelland 1976 reported no difference between the groups for those needing anticholinergic medication (n = 50, RR 1.67, CI 0.45 to 6.24) at six months to one year, suggesting the incidence of adverse effects is comparable between the groups, as the use of anticholinergic drugs is considered to be a direct measure of the severity of adverse effects due to medication (Analysis 4.6).

COMPARISON 5: FLUPHENAZINE DECANOATE - DOSAGE STUDIES - (LOW DOSE versus STANDARD DOSE)

5.1 Global state

Relapse data, assessed over six months to one year were equivocal. Longer-term studies (more than one year) reported by Asarnow 1988, Hogarty 1988 and Marder 1987 were also equivocal (Analysis 5.1).

5.2 Leaving the study early

Asarnow 1988, Hogarty 1988, and Marder 1987 reported no difference in the number of people who left the study early in each dosage group after more than one year of medication (n = 172, RR 0.67, CI 0.33 to 1.36; Analysis 5.2).

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5.3 Mental state

The data obtained for mental state (e.g. BPRS score etc.) were skewed and therefore could not be included in the analyses.

5.4 Adverse effects

Marder 1987 reported that there was no significant difference in the number of people requiring additional anticholinergic drugs at six months to one year (n = 50, RR 2.55, CI 0.72 to 9.05). Kane 1983 supported this finding by reporting that the number of people with tardive dyskinesia (n = 126, RR 0.52, CI 0.10 to 2.72) at six months to one year, was not significantly different between the groups receiving low doses of fluphenazine decanoate and standard dosage fluphenazine. Kane 1983, however, did report a statistically significant (P = 0.03) difference at endpoint analysis with the Simpson Dyskinesia Scale (n = 126), which favoured low-dose fluphenazine decanoate, although data were skewed and therefore not graphically reported (Analysis 5.3).

COMPARISON 6: FLUPHENAZINE ENANTHATE versus PLACEBO

6.1 Adverse effects - at eight weeks

Only Van Praag 1973 reported for this comparison. This small trial reported no significant difference in the number of people needing anticholinergic drugs in the fluphenazine enanthate and placebo groups (n = 25, RR 9.69, CI 0.58 to 163.02; Analysis 6.1).

COMPARISON 7. FLUPHENAZINE ENANTHATE versus ORAL NEUROLEPTICS

7.1 Global state

Chien 1973 reported no significant difference in global change (immediate term, zero to five weeks) between fluphenazine enanthate and chlorpromazine (n = 31, RR 0.67, CI 0.27 to 1.66; Analysis 7.1).

7.2 Adverse effects

Reports of adverse effects, again from the same study and for the immediate term were all not significantly different (n = 31, RR movement disorders 2.34, CI 0.53 to 10.30; RR general adverse effects 2.81, CI 0.94 to 8.45; RR parkinsonism 6.56, CI 0.91 to 47.21; Analysis 7.2).

COMPARISON 8: FLUPHENAZINE ENANTHATE versus OTHER DEPOT NEUROLEPTICS

8.1 Global state

Albert 1980 and Chouinard 1978 reported no significant difference in needing additional antipsychotics (at six months to one year) for fluphenazine enanthate compared with other depot groups (n = 65, RR 0.50, CI 0.24 to 1.05; Analysis 8.1). Both Malm 1974, at six weeks to five months (n = 57, RR 2.38, CI 0.66 to 8.61) and Chouinard 1978, at six months to one year (n = 32, RR 0.33, CI 0.04 to 2.87) reported no statistically significant differences in relapse rates between the fluphenazine enanthate group and the other depot (pipothiazine palmitate) groups (Analysis 8.2).

8.2 Leaving the study early

Only Jain 1975 provided data for numbers leaving the study early (zero to five weeks). These data significantly favoured fluphenazine enanthate compared with the other depot neuroleptics - pipothiazine palmitate (n = 30, RR 0.09, CI 0.01 to 0.62). However, this outcome should be interpreted with caution given the limited number of participants. The number of people who left the study early by six weeks to five months, in the single study by Malm 1974 using fluspirilene as a control, was not significant (n = 57, RR 2.38, CI 0.66 to 8.61). Similarly, Chouinard 1978 found no difference between the fluphenazine enanthate group and the other depot neuroleptic group - pipothiazine palmitate at six months to one year (n = 32, RR 0.33, CI 0.04 to 2.87) (Analysis 8.3).

8.3 Mental state

Singh 1979 reported general BPRS scores and found a significant difference between the two groups favouring the other depot group (n = 30, MD 0.40, CI 0.34 to 0.46; Analysis 8.4). Specific scores on, for example, depression found no difference between the two groups (Singh 1979, n = 30, RR 7.00, CI 0.39 to 124.83; Analysis 8.5).

8.4 Adverse effects

Findings were equivocal for outcomes of 'movement disorders' (medium term: n = 63, 2 RCTs, RR 1.52, CI 0.75 to 3.07; Analysis 8.6), tardive dyskinesia (medium term: n = 32, 1 RCT, RR 0.89, CI 0.46 to 1.71; Analysis 8.8), tremor (medium term: n = 95, 3 RCTs, RR 1.24, CI 0.82 to 1.87; Analysis 8.9), blurred vision (medium term: n = 30, 1 RCT, RR 3.00, CI 0.13 to 68.26; Analysis 8.10) and dry mouth (medium term: n = 62, 2 RCTs, RR 0.80, CI 0.36 to 1.76; Analysis 8.11). Malm 1974 reported that those receiving fluspirilene required significantly less anticholinergic drugs at six weeks to five months than the fluphenazine enanthate group (n =

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57, RR 2.86, CI 1.16 to 7.06). The numbers of people needing additional anticholinergic drugs at six months to one year were found (Albert 1980; Chouinard 1978) to be equivocal (n = 65, RR 1.02, CI 0.76 to 1.35) for the fluphenazine enanthate and other depot neuroleptic groups (Analysis 8.7).

COMPARISON 9: FLUPHENAZINE ENANTHATE - DOSAGE STUDIES (LOW DOSE versus INTERMEDIATE/HIGH DOSE)

9.1 Global state

A single study by Goldstein 1978 reported the global outcome of relapse at six weeks to five months (Analysis 9.1). Trialists found statistically significant differences favouring the high-dosage fluphenazine enanthate group compared with low-dosage fluphenazine enanthate (n = 104, RR 9.35, CI 2.28 to 38.29). For every fourth person administered a low dose of fluphenazine decanoate, one would relapse. However, this result must be treated with caution as only one study is involved.

9.2 Leaving the study early

Goldstein 1978 found no significant difference in the number of people who left the study early (six weeks to five months) whilst receiving either high or low dosages of fluphenazine enanthate (n = 104, RR 3.12, CI 0.66 to 14.74; Analysis 9.2).

COMPARISON 10: FLUPHENAZINE DECANOATE versus FLUPHENAZINE ENANTHATE

10.1 Global state

Van Praag 1973 reported data for 'needing additional antipsychotic treatment' at zero to five weeks (Analysis 10.1). This trial found a significant difference between the fluphenazines (decanoate and enanthate) (n = 33, RR 0.39, CI 0.18 to 0.86). Chouinard 1982 was the only study to report the numbers of people requiring additional antipsychotic treatment at six months to one year and found no significant difference.
The number of people who relapsed whilst receiving medication at zero to five weeks was not significant for the two studies available (n = 44, 2 RCTs, RR 0.66, CI 0.18 to 2.43). Donlon 1976 reported no significant difference in relapse rates at six weeks to five months between the fluphenazine decanoate group and the fluphenazine enanthate group (n = 30, RR 2.29, CI 0.70 to 7.48). MacCrimmon 1978, reporting on relapse over the medium term (six months to one year) found no significant difference (n = 49, RR 2.43, CI 0.71 to 8.32) (Analysis 10.2).

10.2 Leaving the study early

The number of people leaving the study early (Analysis 10.3) at zero to five weeks was not significantly different between the fluphenazine decanoate and enanthate groups (n = 44, 2 RCTs, RR 0.66, CI 0.18 to 2.43). Short term outcomes (6 weeks to 5 months) were also not significantly different between the fluphenazine ester groups (n = 42, 2 RCTs, RR 2.29 CI 0.70 to 7.48). Medium-term data (six months to one year) were consistent with the results of the two shorter study periods, finding no difference in the number of people leaving the study early for the two fluphenazine ester groups (n = 49, 1 RCT, RR 2.43, CI 0.71 to 8.32).

10.3 Mental state

Only one study by MacCrimmon 1978 reported on mental state, using BPRS endpoint scores at one year. They found no significant difference between the fluphenazine esters (n = 39, MD 0.00, CI -3.93 to 3.93; (Analysis 10.4).

10.4 Adverse effects

The number of people in these studies reporting movement disorders for immediate (zero to five weeks) or short term (six weeks to five months) was not significantly different between the fluphenazine esters (Analysis 10.5). Reports of adverse effects (zero to five weeks), parkinsonism (six weeks to five months) and akathisia (zero to five weeks) were equivocal for fluphenazine decanoate and enanthate groups (Analysis 10.9; Analysis 10.7; Analysis 10.8, respectively).
The number of people needing anticholinergic drugs at zero to five weeks was found by Van Praag 1973 to be significantly lower for the fluphenazine decanoate group (n = 33, RR 0.29, CI 0.12 to 0.70). For longer-term studies (six weeks to five months and six months to one year) there were no significant differences in the number of people needing anticholinergic drugs (Analysis 10.6).

COMPARISON 11: FLUPHENAZINE DECANOATE EVERY TWO WEEKS versus EVERY SIX WEEKS

We found only one relevant trial (Khazaie 2005) that compared the use of fluphenazine decanoate every two weeks with every six weeks.

11.1 Global state

There was no significant difference between fluphenazine decanoate every two weeks and every six weeks in the number of participants relapsing (n = 37, RR 0.89, CI 0.55 to 1.44; Analysis 11.1).

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11.2 Leaving the study early

The number of participants leaving the study early also did not differ significantly between fluphenazine decanoate every two weeks and every six weeks (n = 37, RR 1.17, CI 0.46 to 2.98; Analysis 11.2).

11.3 Mental state

Total BPRS scores were not significantly different between fluphenazine decanoate every two weeks and every six weeks (n = 37, MD 2.72, CI -1.16 to 6.60, Analysis 11.3), nor was the BPRS sub-scale for thought disorder (n = 37, MD -0.39, CI -1.51 to 0.73; Analysis 11.3).

11.4 Adverse effects

There was no significant difference between fluphenazine decanoate every two weeks and every six weeks in parkinsonian symptoms (n = 37, MD 1.30, CI -0.03 to 2.63) and dyskinesia (n = 37, MD 2.40, CI -1.77 to 6.57) measured on the Maryland Psychiatric Research Center Involuntary Movement Scale (MPRC) scale (Analysis 11.4).

11.5 Quality of life

We did not find any difference between fluphenazine decanoate every two weeks and every six weeks in the quality of life of participants (n = 37, MD 1.42, CI -9.68 to 12.52, Analysis 11.5).

12. Subgroup analyses

The only primary outcome with enough studies (at least six) to warrant subgroup analysis was relapse from Comparison 2 and Comparison 3. However, studies either included chronic patients, a mix of chronic and acute, or did not report the stage of the illness, therefore, it was not possible to undertake any subgroup analyses.

13. Sensitivity analysis

The only primary outcome with enough studies (at least six) to warrant sensitivity analysis was relapse from Comparison 2 and Comparison 3.

13.1 Implication of randomisation

All trials were described as randomised in the review.

13.2 Assumptions for lost binary data

We did not make any assumptions about lost binary data.

13.3 Risk of bias

For relapse at medium term in Comparison 2 (Analysis 3.3), only Leong 1989 had a high risk of bias for randomisation. The results remained non-significant with the removal of this trial. For this outcome, all trials had a high risk of bias for selective reporting except, again, for Leong 1989 and results were unchanged.
For relapse at medium term in Comparison 3 (Analysis 2.2), all studies had unclear risk of bias for randomisation and all had a high or unclear risk of bias for selective reporting.

13.4 Imputed values

We did not have any cluster randomised trials and did not impute any data.

13.5 Dose

The mean daily dose of fluphenazine decanoate at endpoint ranged from 0.3 to 300 mg and for fluphenazine enanthate ranged from 2.35 to 387.5 mg. Two studies, Cookson 1986 and Curry 1972, did not specify the average dose. The way data were reported did not permit any more sensitivity analyses than those which have already been presented.

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ADDITIONAL SUMMARY OF FINDINGS [Explanation]

FLUPHENAZINE DECANOATE compared with ORAL NEUROLEPTICS for schizophrenia

Patient or population: patients with schizophrenia
Settings: hospital and community
Intervention: FLUPHENAZINE DECANOATE
Comparison: ORAL NEUROLEPTICS

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	ORAL NEUROLEPTICS	FLUPHENAZINE DECANOATE				
Death - not reported	See comment	See comment	Not estimable	-	See comment	No studies reported data for this outcome.
Relapse Follow-up: medium term (6 months to 1 year)	**423 per 1000**	**618 per 1000** (317 to 1000)	**RR 1.46** (0.75 to 2.83)	419 (6 studies)	⊕○○○ **very low**[1,2,3]	
No clinically important global change Follow-up: medium term (6 months to 1 year)	**519 per 1000**	**441 per 1000** (291 to 659)	**RR 0.85** (0.56 to 1.27)	102 (1 study)	⊕○○○ **very low**[3,4,5]	
Hospital admission - not reported	See comment	See comment	Not estimable	-	See comment	No studies reported data for this outcome.
Leaving the study early Follow-up: medium term (6 months to 1 year)	**184 per 1000**	**177 per 1000** (134 to 230)	**RR 0.96** (0.73 to 1.25)	937 (10 studies)	⊕⊕○○ **low**[3,6,7]	

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Mental state BPRS endpoint score Follow-up: (longer term - more than 1 year)		The mean mental state in the intervention groups was **0.75 lower** (5.75 lower to 4.25 higher)		120 (1 study)	⊕○○○ **very low**[3,5,8]	
Extrapyramidal adverse effects - general Follow-up: medium term (6 months to 1 year)	**137 per 1000**	**64 per 1000** (33 to 125)	**RR 0.47** (0.24 to 0.91)	259 (3 studies)	⊕○○○ **very low**[3,5,9]	Studies also reported equivocal results for akathisia, needing anti-cholinergic drugs, tardive dyskinesia, tremor, and symptoms on the Simpson Angus scale

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

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

[1] Risk of bias: serious - Studies had an unclear risk of bias for randomisation, allocation concealment and blinding. One study had a high risk of bias for incomplete outcome data.
[2] Inconsistency: serious - There is high heterogeneity.
[3] Imprecision: serious - There are wide confidence intervals.
[4] Risk of bias: serious - This study had an unclear risk of bias for randomisation, allocation concealment, blinding and incomplete outcome data.
[5] Publication bias: strongly suspected - Three studies or fewer reported data for this outcome.
[6] Risk of bias: serious - Studies had an unclear risk of bias for randomisation, allocation concealment and blinding, although one study had a low risk of bias for blinding of participants. One study had a high risk of bias for incomplete outcome data.
[7] Publication bias: undetected - It seems that larger trials have not been performed, see Figure 4.
[8] Risk of bias: very serious - This study had a high risk of bias for blinding as it is an open label study. It has an unclear risk of bias for randomisation and allocation concealment.

[9] Risk of bias: serious - Studies had an unclear risk of bias for randomisation, allocation concealment and blinding.

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FLUPHENAZINE DECANAOTE compared to FLUPHENAZINE ENANTHATE for schizophrenia

Patient or population: patients with schizophrenia
Settings: hospital and community
Intervention: FLUPHENAZINE DECANAOTE
Comparison: FLUPHENAZINE ENANTHATE

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	FLUPHENAZINE ENANTHATE	FLUPHENAZINE DECANAOTE				
Death - not reported	See comment	See comment	Not estimable	-	See comment	No studies reported data for this outcome.
Relapse Follow-up: medium term (6 months to 1 year)	**120 per 1000**	**292 per 1000** (85 to 998)	**RR 2.43** (0.71 to 8.32)	49 (1 study)	⊕○○○ **very low**[1,2,3]	
Clinically significant change in global state - not reported	See comment	See comment	Not estimable	-	See comment	No studies reported data for this outcome.
Hospital admission - not reported	See comment	See comment	Not estimable	-	See comment	No studies reported data for this outcome.
Leaving the study early Follow-up: medium term (6 months to 1 year)	**120 per 1000**	**292 per 1000** (85 to 998)	**RR 2.43** (0.71 to 8.32)	49 (1 study)	⊕○○○ **very low**[1,2,3]	

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Mental State BPRS Follow-up: medium term (6 months to 1 year)		The mean mental state in the intervention groups was **0 higher** (3.93 lower to 3.93 higher)		39 (1 study)	⊕○○○ **very low**[1,3,4]	
Extrapyramidal adverse effects - general Follow-up: short term (6 weeks to 5 months)	**538 per 1000**	**614 per 1000** (425 to 883)	**RR 1.14** (0.79 to 1.64)	49 (2 studies)	⊕○○○ **very low**[3,4,5]	Studies also reported equivocal results for Parkinsonism, akathisia and needing anticholinergic drugs

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

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

[1] Risk of bias: serious - This study had an unclear risk of bias for randomisation, allocation concealment and blinding.
[2] Imprecision: very serious - There were few participants and few events; the confidence intervals are wide.
[3] Publication bias: strongly suspected - Fewer than three studies reported data for this outcome.
[4] Imprecision: serious - There are wide confidence intervals.
[5] Risk of bias: serious - The studies had an unclear risk of bias for randomisation and blinding of outcome assessors. One was low risk of bias for allocation concealment and the other for blinding of participants.

DISCUSSION

Summary of main results

Seventy-three trials including 4870 participants were included in the review. The summary below reflects the outcomes chosen for Summary of findings for the main comparison, Summary of findings 2 and Summary of findings 3, and are considered the main findings of this review. Overall, the quality of the evidence was rated as low to very low.

1. Fluphenazine decanoate versus placebo

1.1 Death

Only one, small study (Jolley 1990) reported on death and no significant differences were observed.

1.2 Global state

1.2.1 Clinically significant change in global state

No studies reported data for this outcome.

1.2.2 Relapse

Very low quality evidence from three studies showed that medium-term relapse rates were not significantly lower in the fluphenazine decanoate group (43%) compared with placebo (67%). Only longer-term data from one small trial (Jolley 1990) significantly reduced relapse.

1.3 Hospital admission

No studies reported data for this outcome.

1.4 Leaving the study early

The numbers of people leaving the study early in the fluphenazine decanoate (24%) and placebo (19%) groups were very similar, however, the quality of the evidence was very low. This figure could be higher in clinical practice because rigorous adherence to protocols in these randomised studies may decrease attrition, although the opposite could also be true. Although adherence to protocol improves internal validity, it can potentially decrease the external validity and applicability of results. The single two-year study significantly favoured fluphenazine decanoate compared with placebo (Jolley 1990).

1.5 Mental state

One very small study (Dotti 1979) found no difference in mental state measured on the BPRS.

1.6 Extrapyramidal adverse effects

The occurrence of tardive dyskinesia (long term) was not significantly different, although the quality of the evidence is very low and data were again from a single small study (Jolley 1990).

2. Fluphenazine decanoate versus oral neuroleptics

2.1 Death

No studies reported data for this outcome.

2.2 Relapse

Very low quality evidence from six studies showed that medium-term rates of relapse were not significantly different in the fluphenazine decanoate group (49%) compared with oral neuroleptics (42%).

2.3 Clinically significant change in global state

One small study (Song 1993) found no difference in the number of participants showing a clinically significant change in global state.

2.4 Hospital admission

No studies reported data for this outcome.

2.5 Leaving the study early

Low-quality evidence showed no difference in the number of participants leaving the study early for fluphenazine decanoate (17%) versus oral neuroleptics (18%).

2.6 Mental state

Very low quality evidence from one study (Simon 1978) found no difference in mental state measured on the BPRS.

2.7 Extrapyramidal adverse effects

Three small studies showed that general extrapyramidal adverse effects were lower in the fluphenazine decanoate group (7%) compared to oral neuroleptics (14%). However, the quality of the evidence was judged to be very low, and there was no difference with longer-term data. The outcome of 'needing additional anticholinergic drug' was equivocal over short-, medium- and longer-term, suggesting oral neuroleptics and fluphenazine decanoate are similar in their ability to induce movement disorders. Also, tardive

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dyskinesia was significantly lower for the fluphenazine decanoate group during medium-term evaluation, but was not different to oral neuroleptics with longer-term data.

3. Fluphenazine decanoate versus other depot antipsychotics

3.1 Death

One study did report a death in fluphenazine decanoate treatment group, however, this did produce an effect with no significant differences between groups for death.

3.2 Global state

Eleven studies reported equivocal data fro the outcome of 'relapse' at six months to one year. Other global state outcomes such as significant clinical improvement, clinical global impression, needing additional antipsychotics and 'not improved' were also equivocal.

3.3 Leaving the study early

Fifteen included trials found people were no more likely to leave the study early if they were receiving fluphenazine decanoate or other depot antipsychotics.

3.4 Behaviour

Only one study reported equivocal data.

3.5 Mental state

Short- and medium-term studies assessing mental state (BPRS endpoint scores) to significantly favour 'other depot neuroleptics' for the short term and medium term. Long-term studies did not find such difference in mental state. One study reported on the outcome of depression; Dencker 1973, found no significant difference between fluphenazine decanoate and pipothiazine palmitate.

3.6 Adverse effects

The occurrence of dyskinetic movements in general was the same across short-, medium- and longer-term studies. Outcomes such as dry mouth, tardive dyskinesia and parkinsonism were not significantly different between depot fluphenazine and other depot neuroleptics. When reporting blurred vision, the results of one medium-term trial were not significant, but one longer-term study, Pinto 1979, did report significant results favouring flupenthixol decanoate. General adverse effects (short-term data) were reported by Frangos 1978 and Javed 1991 and favoured other depot neuroleptics. However, medium-term data were equivocal.

4. Fluphenazine decanoate versus fluphenazine enanthate

4.1 Death

No studies reported data for this outcome.

4.2 Relapse

Very low quality evidence from only one small study (MacCrimmon 1978) found no significant difference in the number of participants experiencing relapse in the medium term. Results were also equivocal for immediate- and short-term studies.

4.3 Clinically significant change in global state

No studies reported data for this outcome.

4.4 Hospital admission

No studies reported data for this outcome.

4.5 Leaving the study early

No difference in the number of participants leaving the study early was found between fluphenazine decanoate (29%) and fluphenazine enanthate (12%), but this is based on one small study (MacCrimmon 1978) and considered to be very low quality evidence.

4.6 Mental state

BPRS data were only available from one small trial (MacCrimmon 1978). This study reported identical scores for both of the fluphenazine depots groups.

4.7 Extrapyramidal adverse effects

Very low evidence from two very small studies showed that two preparations caused roughly equal incidences of general movement disorders. Results were also equivocal for parkinsonism, akathisia and needing additional anticholinergics in the short and immediate term.

Overall completeness and applicability of evidence

Trials were based mainly in the community, or combined both hospital and community settings. Ages ranged between 13 and 81 years, but most people were in the 18 to 65 age range. The duration of illness was long in most participants in the studies that reported this. Included trials were conducted around the world, although the majority (56) were based in North America and Europe and none were based in Australia or South America. There is a broad

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mixture of participants, settings and clinical applicability of the interventions which should increase generalisability.The dosages of fluphenazine decanoate and enanthate reflected current clinical practice. Outcomes were, however, limited. No trials reported data on service utilisation, hospital admission and economic outcomes. It is a shame that so few outcomes were included.

Quality of the evidence

The quality of the evidence is low to very low based on GRADE (Schünemann 2008). Although all studies were reported as randomised, only five reported the method of randomisation and another three the method of allocation concealment. For the majority of studies the method of blinding was not reported despite most stating that they were double blind. In 83% of studies, the risk of bias for selective reporting was rated as high; many preplanned outcomes were not reported and continuous data were often reported as mean without standard deviation, only as P values, or graphically. Poor presentation of data meant that a lot of potentially informative data were lost.

Potential biases in the review process

A thorough search strategy was used in this review. There may still be gaps in the search strategy such as unpublished data (grey literature), which are difficult to obtain. Futhermore, when assessing the risk of bias of studies previously included in this review, we were unable to assess the risk of bias for one study in Italian. However, this study did not contribute to any outcomes in the 'Summary of findings' tables and therefore the omission of this one study did not affect the overall quality judgement.
For most outcomes we are not able to tell if there was publication bias, as no more than 10 trials reported data for these, and a funnel plot could not be performed. For leaving the study early in the comparison of fluphenazine decanoate versus oral neuroleptics, there does appear to be publication bias, as the funnel plot indicates that larger trials have not been performed.

Agreements and disagreements with other studies or reviews

We do not know of any other systematic reviews on this topic.

AUTHORS' CONCLUSIONS

Implications for practice

1. For people with schizophrenia

When compared with either placebo or oral neuroleptics, fluphenazine decanoate does not appear to have a clinically important effect in terms of improving relapse rates based on medium-term (six months to one year) data. Longer-term data, however, do support the use of fluphenazine decanoate to reduce relapse when compared to placebo, but not when compared to oral neuroleptics. Relapse data for fluphenazine enanthate were limited and no data comparing it with placebo or oral neuroleptics were available. Fluphenazine depot preparations, especially the decanoate, seem equivalent to oral medications and may even cause less adverse effects.

2. For clinicians

The data on the effects of fluphenazine decanoate are clearer than for fluphenazine enanthate. Within the highly unusual setting of a randomised trial, the decanoate may have some advantages over the oral antipsychotics. In clinical life there may be greater advantages in terms of compliance. There are no data to support the claim that depots cause more adverse effects than oral preparations. There are also no data to support the use of high doses.

3. For managers or policy makers

Studies did not report data relating to service utilisation and care management. Outcomes relating to use of hospitals and services, satisfaction with care and economics were not reported in any study. This deficiency remains and should be addressed in real world randomised studies.

Implications for research

1. General

Trialists involved in future studies should implement the CONSORT statement (Moher 2001) to ensure that outcomes are more relevant. Inclusion of hospital and services outcomes, satisfaction with care and economic outcomes would provide valuable data for people with schizophrenia, clinicians and policy makers.

2. Specific

A recurring failure to report the exact methodology of allocation was evident throughout the included trials. Only five studies stated the randomisation process used; Kissling 1985 used a coin-throwing method, Frangos 1978 a randomisation code, Magnus 1979 a pre-arranged prescribing list, and Wistedt 1984 a randomisation list and Leong 1989 allocated to the next available study number. Allocation concealment is essential to ensure that selection bias is kept to a minimum.
Only 14 studies described outcome assessors as being blinded to treatment and were rated low risk of bias (Altamura 1985; Chouinard 1982; Dencker 1973; Frangos 1978; Goldstein 1978;

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Kane 1978; Leong 1989; McClelland 1976; Odejide 1982; Pinto 1979; Russell 1982; Van Praag 1970; Van Praag 1973; Wistedt 1983). Magnus 1979 and Simon 1978 were open label trials and Leong 1989 described using a 'partially-blinded' method where only outcome assessors were blinded. The remaining studies were of unclear risk of bias as no information on blinding of outcome assessors was provided. Although most studies were stated to be double blind, only 14 studies described outcome assessors as being blinded to treatment and were rated low risk of bias (Altamura 1985; Chouinard 1982; Dencker 1973; Frangos 1978; Goldstein 1978; Kane 1978; Leong 1989; McClelland 1976; Odejide 1982; Pinto 1979; Russell 1982; Van Praag 1970; Van Praag 1973; Wistedt 1983). This is an important strategy for avoiding performance and detection bias. Odejide 1982 included participants who were unaccounted for after randomisation was undertaken. This study did not specify from which groups this withdrawal had occurred. In 12 trials the number of people who left the study was not reported. It is important to know how many, and from which groups, people were withdrawn in order to evaluate exclusion bias. Studies included both community-based and hospitalised people but 16 failed to report the setting (Albert 1980; Feng 1990; Hranov 1998; Javed 1991; Kissling 1985; Kreisman 1988; Lehmann 1980; McKane 1987; Odejide 1982; Quitkin 1978; Rossi 1990; Russell 1982; Schlosberg 1978; Schneider 1981; Sharma 1991; Wistedt 1983). A few studies, all using fluphenazine decanoate as an intervention, involved people in hospital at the beginning of the trial but these people were later discharged into the community (Dencker 1973; Donlon 1976; Magnus 1979; Marder 1987; McCreadie 1980; Rifkin 1977; Schooler 1980; Schooler 1997; Simon 1978; Wistedt 1984). More community-based studies would be welcome.

This review highlights the need for good controlled clinical trials to address the effects of fluphenazine decanoate and fluphenazine enanthate and to assess their clinical suitability in certain situations. Despite the many studies that are in existence, we do think that more studies are required in each category but particularly in the case of fluphenazine enanthate where data were particularly few. We realise that such design needs a great deal of planning but suggest a simple outline in Table 1.

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* *Indicates the major publication for the study*

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CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Adamson 1973

Methods	Allocation: randomised. Blindness: double. Duration: 28 days. Design: cross-over x2. Country: UK.
Participants	Diagnosis: schizophrenia. N = 37 (in phase II). Age: 24-65 years. Sex: 22M, 15F. History: all in hospital for > 1 year. Setting: hospital.
Interventions	1. Fluphenazine decanoate: dose 12.5 mg/IM day one, 25 mg/IM day 7. N = 19. 2. Chloropromazine: dose 50-100 mg/bid. N = 18.
Outcomes	Behaviour: leaving the study early. Adverse effects: various side effects Unable to use - Mental state: BPRS (no data). Behaviour: WWBRS (no data).
Notes	No usable continuous data.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"Divided randomly", "matched for sex, mean age, mean weight and mean plasma chlorpromazine concentrations"
Allocation concealment (selection bias)	Unclear risk	Details of allocation concealment not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	"Double-blind", no further details reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	"Double-blind", no further details reported.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No losses to follow-up reported.

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Selective reporting (reporting bias)	High risk	Not all outcomes fully reported, no data reported for BPRS and WWBRS
Other bias	Unclear risk	Source of funding not reported.

Albert 1980

Methods	Allocation: randomised. Blindness: double. Duration: 39 weeks. Design: drug stabilisation period 2 months, treatment 3 months. Country: Canada.
Participants	Diagnosis: schizophrenia. N = 33. Age: approximate age mid 40s. Sex: all male. History: average duration spent in hospital 16-20 years. Setting: hospital.
Interventions	1. Fluphenazine enanthate: dose mean 50mg/IM/biweekly. N = 11. 2. Pipothiazine palmitate: dose mean 100mg/IM or 150 mg/IM*/monthly. N = 11
Outcomes	Global state: need for additional medication. Behaviour: leaving the study early. Adverse effects: Evaluation Scale. Unable to use - Global state: CGI (no SD). Mental state: BPRS (no SD). Adverse effects: NOSIE (no SD).
Notes	* 2 different dosage groups for PP. Authors contacted.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	"patients were randomly assigned". Method not reported.
Allocation concealment (selection bias)	Unclear risk	Details of allocation concealment not reported.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	"The identity of the medications was masked and the double blind character of the study preserved by inserting an identi-

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		cal placebo injection at two week intervals”
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	“The identity of the medications was masked and the double blind character of the study preserved by inserting an identical placebo injection at two week intervals”. Blinding of outcome assessment not specifically reported
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Number of patients randomised to each group have been reported. However, it is unclear if all participants completed the study
Selective reporting (reporting bias)	High risk	Standard deviations and information on Serious Adverse Events have not been reported
Other bias	Unclear risk	Source of funding not reported.

Altamura 1985

Methods	Allocation: randomised. Blindness: double. Duration: 2-3 week (2 periods). Design: parallel group. Country: United Kingdom.
Participants	Diagnosis: schizophrenia (PSE- DSM III). N = 11. Age: 35-60 years. Sex: 2M, 9F. History: duration illness < 2 yrs. Setting: community.
Interventions	1. Fluphenazine decanoate: dose 25 mg/IM every 3-4 weeks. N = 6. 2. Fluphenazine enanthate: dose 25 mg/IM every 3-4 weeks. N = 5
Outcomes	Behaviour: leaving the study early. Adverse effects: various side effects. Unable to use - Mental state: CPRS (no data). Physiological: (various measures, blood tests - non-clinical outcomes, data unusable). Cognitive: handwriting (non-clinical outcomes, data unusable)
Notes	No usable continuous data. Authors contacted.

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Altamura 1985 (*Continued*)

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	"The assignment of order of treatments was randomised". Method not reported
Allocation concealment (selection bias)	Unclear risk	Details of allocation concealment not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	An uninvolved person administered the doses and the ampules were not seen by the patients or rater. Other involved personnel might have been unblinded
Blinding of outcome assessment (detection bias) All outcomes	Low risk	An uninvolved person administered the doses and the ampules were not seen by the rater
Incomplete outcome data (attrition bias) All outcomes	High risk	4/11 participants left early. Reasons are not reported per intervention group. Losses to follow-up/missing data imbalanced in numbers across intervention groups. 2/5 vs 2/6. The study was terminated due to to high incidence of side effects
Selective reporting (reporting bias)	High risk	Results for "unwanted effects" not reported separately (akinesia, involuntary movement, autonomic disturbances and drowsiness) and only part of the rating scale was used. "only two scores on the four point rating scale were... used... absent and maximum...no attempt could be made to derive a figure representing a grading of effect". Although this is mainly a safety study, presence/absence of Serious Adverse Events not reported
Other bias	Unclear risk	Source of funding not reported.

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Asarnow 1988

Methods	Allocation: randomised. Blindness: double. Duration: 2 years. Design: dosage study. Country: United States.
Participants	Diagnosis: schizophrenia. N = 36. Age: 34-41 years. Sex: all male. History: stabilised for < 2 months, informed consent given. Setting: community.
Interventions	1. Fluphenazine decanoate: dose 25mg/IM (standard) biweekly. N = 14. 2. Fluphenazine decanoate: dose 5mg/IM (low) biweekly. N = 22
Outcomes	Behaviour: leaving the study early. Unable to use - Mental state: BPRS (no SD). Cognitive: information-processing skills (non-clinical outcomes, data unusable)
Notes	Very little usable data

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"randomly assigned". Method not reported.
Allocation concealment (selection bias)	Unclear risk	Details of allocation concealment not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	"double-blind". Blinding details not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	"double-blind". Blinding details not reported.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Reported data for drop-outs is unclear. "two patients in the GSLD and PSLD groups and one patient each in the GSSD and PSLD groups dropped out before completion..."

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Selective reporting (reporting bias)	High risk	Although the results for stated outcomes have been reported, the results are not presented as useful data (i.e. mean, SD). Also, not all expected outcomes were reported (e.g. presence/absence adverse events, serious adverse events)
Other bias	Low risk	The study seems to be free of other sources of bias.

Barnes 1983

Methods	Allocation: assigned to two groups by independent statistician. Blindness: double. Duration: 1 year. Design: parallel group. Country: United Kingdom.
Participants	Diagnosis: schizophrenia (PSE). N = 36. Age: mean ~ 49 years. Sex: 18M, 18F. History: not stated. Setting: community.
Interventions	1. Fluphenazine decanoate: dose 25 mg/IM biweekly. N = 19. 2. Pimozide: dose 8 mg biweekly. N = 17.
Outcomes	Behaviour: leaving the study early. Unable to use - Behaviour: SBAS (non-clinical outcomes, data unusable).
Notes	Analysis: last observation carried forward. No continuous outcomes measured.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	"Patients were assigned to two groups by an independent statistician, matched on the basis of age, sex and calculated weekly fluphenazine dose"
Allocation concealment (selection bias)	Unclear risk	Details of allocation concealment not reported.

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Barnes 1983 (*Continued*)

Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	"double blind...double dummy" Blinding details not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Blinding details not reported.
Incomplete outcome data (attrition bias) All outcomes	Low risk	In "the 1-year follow-up results of all patients who had begun the trial, including drop-outs, withdrawals and relapsers, were involved in the analysis...Unfortunately, the SBAS data were incomplete for one relapsed patient who was abroad from the time of relapse to the end of the trial."
Selective reporting (reporting bias)	High risk	Results for SBAS have been reported as percentages, only. Other expected outcomes (e.g. presence/absence of adverse events, serious adverse events have not been reported)
Other bias	Unclear risk	Source of funding has not been reported.

Chien 1973

Methods	Allocation: randomised. Blindness: single. Duration: 30 days. Design: parallel group. Country: USA.
Participants	Diagnosis: psychosis. N = 31. Age: 17-62 years, mean ~ 37 years. Sex: 24M, 22F. History: acutely psychotic, recently admitted. Setting: hospital.
Interventions	1. Fluphenazine enanthate: dose 12.5 -75 mg/IM, mean 28.5 mg/IM every 12 days. N = 16. 2. Chlorpromazine: dose mean 388 mg/day. N = 15.
Outcomes	Global state: need for additional medication. Behaviour: leaving the study early. Adverse effects: TESF. Unable to use - Behaviour: NOSIE (no data).

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Notes		
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	"randomly assigned". Method not reported.
Allocation concealment (selection bias)	Unclear risk	Details of allocation concealment not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Blinding of participants and personnel not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	"each patient was rated after 10 days of treatment on a seven-point scale of global improvement by an independent research psychiatrist who had no knowledge of the patient's medication". Blinding methods of nurses rating NOISE not reported
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Losses to follow-up not reported.
Selective reporting (reporting bias)	Unclear risk	Data for NOSIE not reported.
Other bias	Low risk	"supported in part by Public Health Service research grant MH-16128 from the National Institute of Mental Health."

Chouinard 1978

Methods	Allocation: randomised. Blindness: double. Duration: 9 months. Design: parallel group. Country: Canada.
Participants	Diagnosis: schizophrenia. N = 32. Age: 20-60 years. Sex: 16M, 16F. History: informed consent given. Setting: community.

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Interventions	1. Fluphenazine enanthate: dose 6.25-100 mg/IM biweekly. N = 16. 2. Pipothiazine palmitate: dose 25-100 mg/IM monthly. N = 16 Dose adjusted to therapeutic response.
Outcomes	Global state: CGI, need for additional medication. Mental state: BPRS. Behaviour: leaving the study early. Adverse effects: HRSD, EPS, TESF. Unable to use - Adverse effects: various effects (no SD). Physiological: various measures (non-clinical outcomes, data unusable)
Notes	Analysis: last observation carried forward.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Random allocation. Methods of randomisation not reported.
Allocation concealment (selection bias)	Unclear risk	Allocation concealment details not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	"Except for the nurse responsible for giving the injections, the procedure was double blind."
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Outcome blinding details not reported.
Incomplete outcome data (attrition bias) All outcomes	Low risk	4 patients did not complete the study. Reasons for dropping out have been described. Number of drop-outs was balanced between the groups. "Psychiatric evaluations of these four patients were made on the days they left the study and were used ...for the statistical analysis of the rating scale data."
Selective reporting (reporting bias)	High risk	Not all outcomes fully reported. The study reports most but not all expected outcomes (e.g.presence/absence serious adverse events)
Other bias	Unclear risk	Source of funding has not been reported.

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Chouinard 1982

Methods	Allocation: randomised. Blindness: double. Duration: 7 months, preceded by 1 month stabilisation period. Design: parallel group. Country: Canada.
Participants	Diagnosis: schizophrenia (DSM II). N = 50* Age: 24-65 years, median ~ 41 years. Sex: 27M, 21F. History: on FE for 1 month, able to give informed consent. Setting: community.
Interventions	1. Fluphenazine decanoate: dose 2.5-250 mg/IM, mean 27 mg/IM monthly. N = 24. 2. Fluphenazine enanthate: dose 2.5-325 mg/IM, mean ~ 35 mg/IM biweekly. N = 24 Dose adjusted to therapeutic response.
Outcomes	Global state: need for additional medication. Behaviour: leaving the study early. Additional medication. Unable to use - Mental state: BPRS (no SD). Adverse effects: TESF (no data); ESRS (authors own scale**).
Notes	Authors contacted. Results for FE & FD pooled. * 2 dropped out after randomisation/ moved & suicide. ** see Marshall et al 1998

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"randomly assigned". Method not reported.
Allocation concealment (selection bias)	Unclear risk	Details of allocation concealment not reported.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	"double-blind". "Both preparations were administered as identical suspensions in oil"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	"Assessment of psychiatric symptoms was based on clinical interviews conducted by the psychiatrist...under blind conditions"

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Chouinard 1982 (*Continued*)

Incomplete outcome data (attrition bias) All outcomes	Low risk	"Two patients did not complete the 28 week trial...One of these left the country after 12 weeks of treatment with fluphenazine decanoate; the other committed suicide after 22 weeks of treatment with fluphenazine enanthate"
Selective reporting (reporting bias)	High risk	Results reported incompletely for BPRS scores. Adverse events,other than EPS and TD not reported
Other bias	Unclear risk	Source of funding not reported.

Chouinard 1984

Methods	Allocation: randomised, stratified by sex & past frequency of depot administration. Blindness: double. Duration: 8 months. Design: parallel group. Country: Canada.
Participants	Diagnosis: schizophrenia (DSM III). N = 72. Age: 18-66 years, mean ~ 44 years. Sex: 36M, 36F. History: on depot >3 months; duration illness 3-38 years, mean 16 years, able to give informed consent. Setting: community.
Interventions	1. Fluphenazine decanoate: dose 2.5-300 mg/IM, mean 75 mg/IM every 2-4 weeks. N = 36. 2. Haloperidol decanoate: dose 15-900 mg/IM, mean 225 mg/IM every 2-4 weeks. N = 36
Outcomes	Global state: CGI, need for additional medication. Mental state: BPRS. Behaviour: leaving the study early. Unable to use - Adverse effects: ESRS (authors own scale*), TESF (no data). Physiological: various measures (non clinical outcomes, data unusable)
Notes	Statistics: last observation brought forward. *see Marshall et al 1998.

Risk of bias

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

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Chouinard 1984 (*Continued*)

Random sequence generation (selection bias)	Unclear risk	"randomly assigned". Method not reported.
Allocation concealment (selection bias)	Unclear risk	Details of allocation concealment not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	"double -blind". Blinding details not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Blinding details not reported.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Losses to follow-up have not been reported.
Selective reporting (reporting bias)	High risk	Most of the outcomes have been reported only as P < .05.
Other bias	Unclear risk	Source of funding has not been reported.

Cookson 1986

Methods	Allocation: randomised, separate randomisation sequences for males and females. Blindness: double. Duration: 8 months. Design: parallel group. Country: United Kingdom.
Participants	Diagnosis: schizophrenia implied. N = 19. Age: 26-60 years. Sex: 9M, 10F. History: 1 yr treatment with fluphenazine decanoate, overweight BMI 25+, physically fit, stable during previous year Setting: community.
Interventions	Fluphenazine decanoate: dose 26.4 mg/IM, every 2-6 weeks, average 3.6 months. N = 9. 2. Haloperidol decanoate: dose 22.2 mg/IM every 2-5 weeks, average 3.6 months. N = 10
Outcomes	Behaviour: leaving the study early. Unable to use - Mental state: CPRS, KGS (no data). Adverse effects: SAS, AIMS (no data). Physiological: various measures (non clinical outcomes, data unusable)

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Cookson 1986 (*Continued*)

Notes	Analysis: last observation carried forward.	
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	"...randomly assigned...Separate randomisation sequences were used for male and female patients." Method not reported
Allocation concealment (selection bias)	Unclear risk	Details of allocation concealment not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	"double-blind". Blinding details not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	"double-blind". Blinding details not reported.
Incomplete outcome data (attrition bias) All outcomes	High risk	Losses to follow-up are imbalanced. "Two patients- both on the haloperidol decanoate-dropped out". Also, prolactin levels not measured for all subjects i.e. "available for six patients on fluphenazine decanoate ...and eight on haloperidol decanoate."
Selective reporting (reporting bias)	High risk	Body weight and prolactin levels have been reported. However, results of clinical assessments not fully reported
Other bias	Unclear risk	Source of funding not reported.

Crawford 1974

Methods	Allocation: randomised. Blindness: double. Duration: 40 weeks. Design: parallel group. Country: United Kingdom (Scotland).
Participants	Diagnosis: schizophrenia (Forest & Hay 1971/72 criteria). N = 31. Age: 20-65 years. Sex: 9M, 22F. History: mean duration illness 1-27 years, mean ~ 14 years.

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	Setting: community.	
Interventions	1. Fluphenazine decanoate: (dosage not stated). N = 14. 2. Trifluoperazine hydrochloride (oral): (dosage not stated). N = 17	
Outcomes	Behaviour: leaving the study early. Unable to use - Mental state: BPRS (no data).	
Notes		

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	"randomly allocated". Method not reported.
Allocation concealment (selection bias)	Unclear risk	Details of allocation concealment not reported.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	"double-blind". "The preparations employed had identical appearances"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	"double-blind". Blinding details not reported.
Incomplete outcome data (attrition bias) All outcomes	High risk	2 participants, both from the trifluoperazine hydrochloride group, dropped out "within four weeks" of the study and were not included in the analysis. Withdrawal rate was 6/15 in the trifluoperazine hydrochloride group and 2/12 in the fluphenazine group
Selective reporting (reporting bias)	High risk	Not all outcome data was fully reported.
Other bias	Unclear risk	Source of funding not reported.

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Curry 1972

Methods	Allocation: randomised. Blindness: double. Duration: 28 days. Design: parallel group. Country: United Kingdom.
Participants	Diagnosis: schizophrenia. N = 37. Age: not stated. Sex: male and female. History: chronically ill. Setting: hospital.
Interventions	1. Fluphenazine decanoate: (dosage not stated). N = 19. 2. Chlorpromazine (oral): (dosage not stated). N = 18.
Outcomes	Behaviour: WWBRS. Leaving the study early. Unable to use - Mental state: BPRS (no SD).
Notes	Authors contacted.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"randomised". Method not reported.
Allocation concealment (selection bias)	Unclear risk	Details of allocation concealment not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	"double-blind". Blinding details not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	"double-blind". Blinding details not reported.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Losses to follow-up not reported.
Selective reporting (reporting bias)	High risk	Incomplete study results. Results not reported as mean (SD).
Other bias	Unclear risk	Source of funding not reported.

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Dencker 1973

Methods	Allocations: randomised. Blindness: double. Duration: 3 years. Design: 3 months adjustment, 1-3 months maintenance, 2-6 months maintenance, 2-year follow-up. Country: Sweden.
Participants	Diagnosis: schizophrenia. N = 67. Age: 18-65 years, mean ~ 41 years. Sex: 51M, 14F. History: duration illness > 5 years. Setting: 1 year in hospital, 2 years in community.
Interventions	1.Fluphenazine decanoate: dose 3.1-50mg/IM, mean 6.25 mg/IM monthly (mean monthly dose for 2-year continuation phase 27.8 mg/IM). N = 35. 2. Pipothiazine palmitate: dose 25-400 mg/IM, mean 50 mg/IM monthly (mean monthly dose for 2-year continuation phase 152.3 mg/IM). N = 32
Outcomes	Global state: need for additional medication. Behaviour: leaving the study early. Adverse effects: EPS, HRSD. Unable to use - Mental state: BPRS, S-Scale, HRSD (no SD). Cognitive: Handwriting test (non-clinical outcomes, data not usable). Social ability: ADL, work performance, SRE (non-clinical outcomes, data not usable). Adverse effects: EPS (no data).
Notes	Authors contacted.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Method of sequence generation not reported.
Allocation concealment (selection bias)	Unclear risk	Details of allocation concealment not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	"double blind". " the injections were given by a nurse, who was the only person who knew the code"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	"double blind". " the injections were given by a nurse, who was the only person who knew the code." "most of rating were made by one psychologist, and the rest by one of the psychiatrists"

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Incomplete outcome data (attrition bias) All outcomes	Low risk	Losses to follow-up balanced in numbers across intervention groups 9% vs 17%
Selective reporting (reporting bias)	High risk	Although all outcomes have been reported, data for most of the outcomes (BPRS, Hamilton depression scale, side effects rating scale, rating scale for extra-pyramidal side effect) cannot be used i.e. only mean reported (SD not reported)
Other bias	Unclear risk	Source of funding not reported

Donlon 1976

Methods	Allocation: randomised. Blindness: double. Duration: 2 months. Design: parallel group. Country: USA.
Participants	Diagnosis: schizophrenia. N = 40/41*. Age: 18-57 years, mean ~ 29 years. Sex: 12M, 18F. History: able to give informed consent. Setting: hospital & community.
Interventions	1. Fluphenazine decanoate: dose 75-500mg/IM, mean 296.4 mg/IM 2-3x week. N = 14. 2. Fluphenazine enanthate: dose 50-550 mg/IM, mean 387.5 mg/IM 2-3x week. N = 16
Outcomes	Global state: need for additional medication. Behaviour: leaving the study early. Adverse effects: EPS Rating Scale. Unable to use - Global state: CGI (no data). Mental state: BPRS (no data).
Notes	Data put in depot vs depot category in both FE & FD treatment groups *2 different N values in the paper.

Risk of bias

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

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Donlon 1976 (*Continued*)

Random sequence generation (selection bias)	Unclear risk	"assigned...on a random basis". Method not reported.
Allocation concealment (selection bias)	Unclear risk	Details of allocation concealment not reported.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	"double blind", "FE and FD were supplied in identical bottles"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	"double-blind". Blinding of outcome assessors not reported.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Losses to follow-up not reported. 41 participants randomised, but number in each group not reported. Allocation per group reported for 30 patients: "Eleven patients either voluntarily dropped out or were lost to follow-up prior to the end of 1 month. ..3 patients on FE terminated during the second month", other reasons for leaving early not reported
Selective reporting (reporting bias)	High risk	CGI and BPRS results incompletely reported (only P values).
Other bias	Unclear risk	Source of funding not reported.

Dotti 1979

Methods	Allocation: randomised. Blindness: double. Duration: 9 months. Design: parallel group. Country: Italy.
Participants	Diagnosis: schizophrenia. N = 20. Age: 19-32 years. Sex: all male. History: previous episodes of psychosis. Setting: community.
Interventions	1. Fluphenazine decanoate: dose 25-50 mg (frequency not stated). N = 10. 2. Placebo: (frequency not stated). N = 10.

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Dotti 1979 (*Continued*)

Outcomes	Behaviour: leaving the study early. Mental state: BPRS.	
Notes		

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	Medication was prepared in a pharmacy, but no details of allocation concealment reported
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	"Double blind", no details reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	"Double blind", no details reported.
Incomplete outcome data (attrition bias) All outcomes	High risk	Four participants left the study early, one from the fluphenazine group and three from the placebo group, reasons not reported
Selective reporting (reporting bias)	Low risk	All outcomes reported.
Other bias	Unclear risk	Source of funding not reported.

Falloon 1978

Methods	Allocation: randomised. Blindness: double. Duration: 20 months. Design: 2 trials - I & II. Country: United Kingdom.
Participants	Diagnosis: schizophrenia (Schneider). N = 44. Age: 17-60 years, mean ~ 39 years. Sex: 20M, 24F. History: stabilised prior to study entry. Setting: community.

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Interventions	1. Fluphenazine decanoate: dose mean 25 mg/IM/weekly, maximum 50 mg/ biweekly. N = 20. 2. Pimozide: dose mean 8 mg/IM/day, maximum 16 mg/day. N = 24 Flexible dosage.	
Outcomes	Global state: need for additional medication. Behaviour: leaving the study early. Adverse effects: checklist for SE's. Unable to use - Mental state: PSE (no data). Social ability: SPS (non-clinical outcome, data unusable).	
Notes		

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	"randomly allocated". Method not reported.
Allocation concealment (selection bias)	Unclear risk	Details of allocation concealment not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	"double- blind control conditions...active pimozide tablets +inert fluphenazine injections, or...active fluphenazine injections +inert pimozide tablets." Blinding of personnel unclear
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	"double- blind". Blinding of outcome assessor unclear.
Incomplete outcome data (attrition bias) All outcomes	High risk	Three patients (all from one group) were withdrawn, losses to follow-up are unbalanced
Selective reporting (reporting bias)	High risk	Incomplete reporting of data.
Other bias	Unclear risk	Sources of funding not reported.

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Feng 1990

Methods	Allocation: randomised. Blindness: double. Duration: 12 weeks. Design: parallel group. Country: China.
Participants	Diagnosis: schizophrenia (Huangshan council schizophrenia standard 1984). N = 30. Age: 27-54 years, mean ~ 41 years. Sex: 24M, 64F. History: all chronically ill > 5 years. Setting: not stated.
Interventions	1. Fluphenazine decanoate: dose 25 mg/mL fortnightly injections. N = 15. 2. Haloperidol decanoate: dose 25 mg/mL monthly injections. N = 15
Outcomes	Behaviour: leaving the study early. Adverse effects. Unable to use - Mental state: MIE (data unusable). Adverse effects: SAS (data unusable). Global state: CGI (not reported).
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"randomly assigned". Method not reported.
Allocation concealment (selection bias)	Unclear risk	Details of allocation concealment not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	"double blind...patients and doctors did not know what kind of medicine to be applied till end of treatment". Blinding details not reported
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	"double blind...patients and doctors did not know what kind of medicine to be applied till end of treatment". Blinding details not reported
Incomplete outcome data (attrition bias) All outcomes	High risk	Losses to follow-up unbalanced between groups: 3 (20%) in the haloperidol group and 1 (7%) in the fluphenazine group

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Selective reporting (reporting bias)	High risk	CGI outcome data not reported, no usable data for MIE and SAS
Other bias	Unclear risk	Source of funding not reported.

Frangos 1978

Methods	Allocation: randomised (randomisation code). Blindness: double. Duration: 16 weeks. Design: parallel group. Country: Greece.
Participants	Diagnosis: schizophrenia. N = 50. Age: 21-62 years, mean ~ 44 years. Sex: 25 M, 25 F. History: hospitalised for at least 2 years. Setting: hospital.
Interventions	1. Fluphenazine decanoate: dose 25-150 mg/IM, mean 76 mg/IM biweekly. N = 25. 2. Fluspirilene decanoate: dose 4-20 mg/IM, mean 12 mg/IM weekly. N = 25
Outcomes	Adverse effects: SE Rating Scale. Unable to use - Global state: CGI (no data). Mental state: BPRS (no SD). Behaviour: NOSIE (no SD).
Notes	Authors contacted.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	"randomly allocated", "according to a randomisation code".
Allocation concealment (selection bias)	Unclear risk	Details of allocation concealment not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	"all patients were treated with weekly injections; fluspirilene administered every week and fluphenazine decanoate every 2 weeks with placebo...in the between periods". Blinding details of personnel administering the injections not reported

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Blinding of outcome assessment (detection bias) All outcomes	Low risk	"randomisation code unknown to the investigators involved with the patient evaluation". "investigators concerned with drug administration were not involved in the patient evaluations"
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	No details reported, losses to follow-up not reported.
Selective reporting (reporting bias)	High risk	Data reported incompletely: only P values for BPRS, NOISE-30, and extrapyramidal symptoms. Adverse events reported, presence/absence of serious adverse events not reported
Other bias	Unclear risk	Source of funding has not been reported.

Goldstein 1978

Methods	Allocation: randomised. Blindness: single. Duration: 6 weeks. Design: 6 month follow-up (not controlled). Country: United States.
Participants	Diagnosis: schizophrenia. N = 104. Age: mean ~ 23 years. Sex: 45M, 37F. History: acutely ill, 1st or 2nd admission, able to give informed consent. Setting: community.
Interventions	1. Fluphenazine enanthate: dose (high) 1 mL/IM biweekly. N = 53. 2. Fluphenazine enanthate: dose (low) 0.25 mL /IM biweekly. N = 51
Outcomes	Behaviour: leaving the study early. Unable to use - Mental state: BPRS (no data). Family therapy: non-clinical outcome (data unusable).
Notes	Analysis: last observation carried forward.

Risk of bias

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

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Goldstein 1978 (*Continued*)

Random sequence generation (selection bias)	Unclear risk	"...patient was... assigned by a random method". Details of method not reported
Allocation concealment (selection bias)	Unclear risk	Details of allocation concealment not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	" single blind...the patient was blind to the dose level but the treating psychiatrist was not"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	"...all ratings of clinical behavior were carried out by raters blind to drug and family therapy status."
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	"...eight withdrew after release from the hospital... treatment refusers came from three groups; high dose therapy (two), low dose therapy (three), low dose no therapy (three)." None of the participants from high dose no therapy dropped out
Selective reporting (reporting bias)	High risk	Relapse reported. Data for BPRS not reported as mean SD, data for family therapy not reported
Other bias	Low risk	Supported by grants from National Institute for Mental Health

Hirsch 1975

Methods	Allocation: randomised. Blindness: double. Duration: 7 months. Design: parallel group. Country: Norway.
Participants	Diagnosis: schizophrenia. N = 81. Age: under 67 years. Sex: male & female. History: chronically ill. Seting: community.
Interventions	1. Fluphenazine decanoate: dose monthly average 25 mg/IM. N = 40. 2. Placebo. N = 41.

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Hirsch 1975 (*Continued*)

Outcomes	Global state: relapse. Behaviour: leaving the study early. Unable to use - Mental state: PSE (data unusable). Behaviour: SPS (data unusable).	
Notes	Unable to complete risk of bias table - PDF missing.	
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	"Randomly allocated by a research assistant", no further details reported
Allocation concealment (selection bias)	Unclear risk	Details of allocation concealment not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	"Double-blind", "A number of checks by questionnaires filled out by the doctors, nurses, and the patient's general practitioner confirmed that the double-blind procedure had been successful"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	"Double-blind", details of blinding of outcome assessors not reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	"One patient had [drugs from other sources], and he was excluded from the analysis"
Selective reporting (reporting bias)	High risk	Some outcomes were not fully reported: no data for PSE and SPS
Other bias	Unclear risk	Source of funding not reported.

Hogarty 1979

Methods	Allocation: randomised. Blindness: double. Duration: 2 years. Design: parallel study. Country: United States.
Participants	Diagnosis: schizophrenia. N = 105.

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	Age: 18-55 years, mean ~ 34 years. Sex: 46M, 54F. History: received no other psychotropic medication, able to give informed consent. Setting: community.
Interventions	1. Fluphenazine decanoate: dose 12.5-125 mg/IM, mean 25 mg/IM biweekly. N = 27. 2. Fluphenazine hydrochloride (oral): dose 2.5-40 mg/IM, mean 2.5 mg/IM daily. N = 25
Outcomes	Behaviour: leaving the study early. Unable to use - Mental state: BPRS (no SD). Behaviour: KAS (no data). Adverse effects: SSI, SEC, HSC, TESS (no data).
Notes	Last observation carried forward

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	"randomly assigned". Method not reported.
Allocation concealment (selection bias)	Unclear risk	Details of allocation concealment not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	"double-blind". Subjects blinded; "...providing each patient with an injection and tablets i.e. active injections of fluphenazine decanoate with inactive placebo tablets or placebo injections...with active...tablets. The active and placebo forms of the medication were identical in appearance. " Blinding of details of personnel not reported
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Blinding of details not reported.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Insufficient information: number of subjects allocated per group unclear; "...the analyses included only patients known to be receiving their injection... and who appeared for their prescribed oral medication, independent whether they... took their tablets or not."

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Selective reporting (reporting bias)	High risk	Outcomes not reported (SSI, HCI, KAS) or incompletely reported (BPRS)
Other bias	Low risk	"...supported by Psychopharmacology Research Branch, National Institute of Mental Health"

Hogarty 1988

Methods	Allocation: randomised, stratification by dose & household EE. Blindness: double. Duration: 2 years. Design: dosage study. Country: United States.
Participants	Diagnosis: schizophrenia, schizoaffective (RDC). N = 70. Age: mean 28 yrs, range 17-55 yrs. Sex: 40 M, 30 F. History: living at home, mean duration illness ~ 7 years, stabilised 6 months after discharge, able to give informed consent. Setting: community.
Interventions	1. Fluphenazine decanoate: standard dose mean 25 mg/IM biweekly. N = 33. 2. Fluphenazine decanoate: minimal dose mean 3.8 mg/IM biweekly. N = 37 Prescribed dose - no upper or lower limit.
Outcomes	Behaviour: leaving the study early. Unable to use - Mental state: BPRS, SCL-90 (no data). Adverse effects: MRQ (no data).
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	"random". Method not reported.
Allocation concealment (selection bias)	Unclear risk	Details of allocation concealment not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	"double-blind". "...injections were provided by two non blinded nurses who scrupulously concealed the information on

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		dose assignment from patients and the treating clinical research team. Blinding details not reported
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	”double-blind“. ”...injections were provided by two non blinded nurses who scrupulously concealed the information on dose assignment from patients and the treating clinical research team. Blinding details not reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	Drop-outs have been reported per group of intervention. Overall losses to follow-up data balanced across intervention groups: 14 (42%) drop-outs at standard dose and 16 (43%) drop-outs at minimal dose, with similar reasons for missing data. Dropouts for clinical reasons (relapse) also balanced
Selective reporting (reporting bias)	High risk	Outcome data (BPRS, MRQ, SCL-90, social performance) incompletely reported
Other bias	Low risk	Funded by a grant from the Schizophrenia Research Branch, National Institute of Mental Health

Hranov 1998

Methods	Allocation: randomised. Blindness: not described. Duration: 6 months. Design: parallel group. Country: not reported.
Participants	Diagnosis: schizophrenia (ICD-10). N = 41. Age: 21-55. mean ~ 41 years. Sex: 17M, 24F. History: not stated. Setting: not stated.
Interventions	1 Fluphenazine decanoate: dose 99.3 mg/IM/month. N = 21. 2. Haloperidol decanoate: dose 47.3 mg/month. N = 20.
Outcomes	Behaviour: leaving the study early. Unable to use - Global state: CGI (data unusable). Mental state: PANSS (data unusable).

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	Adverse effects: UKU (data unusable).	
Notes		

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	" randomised". Method not reported.
Allocation concealment (selection bias)	Unclear risk	Details of allocation concealment not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Blinding not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Blinding not reported.
Incomplete outcome data (attrition bias) All outcomes	High risk	6 (30%) participants in the fluphenazine group and 4 (19%) in the haloperidol group left the study early. Reasons for leaving early not reported
Selective reporting (reporting bias)	High risk	Outcome results reported incompletely.
Other bias	Unclear risk	Source of funding not reported.

Jain 1975

Methods	Allocation: randomised. Blindness: double. Duration: 20 weeks, preceded by 2-week washout. Design: parallel group. Country: Canada.
Participants	Diagnosis: schizophrenia. N = 30. Age: 24-61 years, mean ~ 49 years. Sex: 14F, 16M. History: hospitalised for under 1 year. Setting: hospital.
Interventions	1. Fluphenazine enanthate: dose 125 mg/IM biweekly. N = 15. 2. Pipothiazine palmitate: dose 250 mg/IM biweekly. N = 15.

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Jain 1975 (*Continued*)

Outcomes	Global state: CGI. Behaviour: leaving the study early. Adverse effects: TESS. Unable to use - Mental state: BPRS (no data).	
Notes	73% drop-out rate in the PP group, data not usable.	
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	"randomised". Method not reported.
Allocation concealment (selection bias)	Unclear risk	Details of allocation concealment not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	"double-blind". Blinding details not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	"double-blind". Blinding details not reported.
Incomplete outcome data (attrition bias) All outcomes	High risk	Losses to follow-up unbalanced between groups: 4 (27%) participants left the study early in the pipothiazine group and 1 (5%) in the fluphenazine group
Selective reporting (reporting bias)	High risk	Outcome data incompletely reported for BPRS.
Other bias	Low risk	Partially supported by Public Health Service Grant from the Department of Health, Education and Welfare, Washington D.C

Javed 1991

Methods	Allocation: randomised. Blindness: double. Duration: 12 weeks. Design: parallel group. Country: Pakistan.

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Participants	Diagnosis: schizophrenia (DSM III). N = 45. Age: mean ~ 50 years. Sex: 33M, 5F. History: stabilised for 6 months on neuroleptics, involved in rehabilitation, duration illness 13 years. Setting: not stated.
Interventions	1. Fluphenazine decanoate: dose 25 mg/IM biweekly. N = 20. 2. Flupenthixol decanoate: dose 40 mg/IM biweekly. N = 18.
Outcomes	:Behaviour: leaving the study early. Mental state: HRSD. Adverse effects: EPSE, SE checklist. Unable to use - Global state: CGI (no SD). Mental state: BPRS (no SD).
Notes	Authors contacted.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	"randomised". Method not reported.
Allocation concealment (selection bias)	Unclear risk	Details of allocation concealment not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	"double-blind". Blinding details not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	"double-blind". Blinding details not reported.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	7/45 patients dropped out of the study. 1/7 died and 6/7 "dropped out for reasons not related to the treatment...did not keep up their appointments." The number of drop-outs not reported across the intervention group
Selective reporting (reporting bias)	High risk	All outcomes reported as mean scores (without SD): CGI, BPRS, Hamilton, SAS, Side effects checklist (side effects not

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		described). Serious adverse events not reported
Other bias	Unclear risk	Source of funding not reported.

Jolley 1990

Methods	Allocation: randomised. Blindness: double. Duration: 2 years. Design: 2 year follow-up. Country: United KIngdom.
Participants	Diagnosis: schizophrenia (DSM III). N = 54. Age: not stated. Sex: not stated. History: stable patients in remission, who has been free of florid symptoms (delusions, hallucinations, bizarre behaviour and thought disorders) for at least 6 months. Setting: community.
Interventions	1. Fluphenazine decanoate: (dosage not reported). N = 27. 2. Placebo. (dosage not reported). N = 27.
Outcomes	Death. Behaviour: leaving the study early. Adverse effects: AIMS. Unable to use - Adverse effects: SAS (data unusable). Social ability: SAS (non clinical outcomes, data unusable).
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	"randomised". Method not reported.
Allocation concealment (selection bias)	Unclear risk	Details of allocation concealment not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	"double-blind". Blinding details not reported.

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Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	"double-blind". Blinding details not reported.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Losses to follow up balanced across the groups: 5 (19%) in the placebo group and 6 (22%) in the treatment group
Selective reporting (reporting bias)	High risk	Not all outcomes have been fully reported.
Other bias	Low risk	Supported by grants from The Department for Health and Social Security, North West Thames Regional Research Fund and the Priory hospital

Ju 2000

Methods	Allocation: Randomly assigned. Blindness: not mentioned. Duration: 12 weeks. Design: parallel. Country: China.
Participants	Diagnosis: schizophrenia (CCMD-2-R). N = 152. Age: mean ~ 31 years, range 18-45. Sex: 93M, 59F History: course of disease 2-6 years. Setting: hospital.
Interventions	1. Fluphenazine decanoate: start from 25 mg, controlled dose at range of 25-125 mg, given once for every 2 weeks. N = 49. 2. Pipothiazine palmitate: start from 25 mg, controlled dose at range of 25-125 mg, given once for every 4 weeks. N = 103
Outcomes	Global state: clinically important global change. Behaviour: leaving the study early. Mental state: BPRS, SANS, SAPS. Adverse effects: TESS, RSESE.
Notes	

Risk of bias

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

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Ju 2000 (*Continued*)

Random sequence generation (selection bias)	Unclear risk	Randomised, no further details reported.
Allocation concealment (selection bias)	Unclear risk	Details of allocation concealment not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not mentioned.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not mentioned.
Incomplete outcome data (attrition bias) All outcomes	Low risk	All the patients complete the 12-week treatment.
Selective reporting (reporting bias)	Low risk	All the outcomes were reported.
Other bias	Low risk	No other sources of bias.

Kane 1978

Methods	Allocation: randomised. Blindness: unclear. Duration: 2 weeks. Design: parallel. Country: United States.
Participants	Diagnosis: schizophrenia (criteria not reported). N = 49. Age: 13-37 years. Sex: 29M, 20F. History: Recently discharged schizophrenic patients stabilized on oral antipsychotic medication and procyclidine. Setting: community.
Interventions	1. Fluphenazine enanthate, 12.5mg and 2 mcg benztropine mesylate; IM. N = 12 2. Fluphenazine decanoate, 12.5 mg and 2 mcg benztropine mesylate; IM. N = 13 3. Fluphenazine enanthate, 18.75 mg IM. N = 14 4. Fluphenazine decanoate, 18.75 mg.; IM. N = 10
Outcomes	Adverse effects: SAS
Notes	11/23 patients receiving fluphenazine decanoate and 13/26 patients receiving fluphenazine enanthate also took oral antipsychotics. 3 patients in the fluphenazine enanthate and 2 in the fluphenazine decanoate group received imipramine and 1 patient in each group received lithium

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	The two fluphenazine decanoate and two fluphenazine enanthate groups were combined in the analysis as the doses are standard doses in each group	
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	"randomly assigned". Method not reported.
Allocation concealment (selection bias)	Unclear risk	Details of allocation concealment not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Blinding details of personnel and patients not reported.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	"An examination of extrapyramidal side effects was carried out ...by a physician blind to the type of injection received"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Losses to follow-up or missing data balanced across intervention groups, with similar reasons for missing data. "The data was incomplete in 11 patients (22%) due to noncompliance. 10 of these 11 patients missed the 2-week examination. There was no significant difference in compliance between the fluphenazine enanthate and fluphenazine decanoate groups"
Selective reporting (reporting bias)	High risk	The study reports only the primary outcome i.e. extrapyramidal symptoms. Other expected outcomes (e.g. relapse, hospital admission, non-EPS adverse events) have not been reported
Other bias	Unclear risk	Source of funding not reported.

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Kane 1983

Methods	Allocation: randomised. Blindness: double. Duration: 1 year. Design: dosage study. Country: United States.
Participants	Diagnosis: schizophrenia (RDC). N = 126. Age: 17-60 years, mean ~ 29 years. Sex: 63M, 37F. History: in state of remission, able to give informed consent. Setting: community.
Interventions	1. Fluphenazine decanoate (low dose): dose 1.25-5.0 mg/IM biweekly. N = 62. 2. Fluphenazine decanoate (standard dose): dose 12.5-50 mg/IM biweekly. N = 64
Outcomes	Behaviour: leaving the study early. Adverse effects: SDS, SAS. Unable to use - Global State: CGI (no data). Mental State: BPRS (no data). Behaviour: SAS-R (data unusable).
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"randomly assigned". Method not reported.
Allocation concealment (selection bias)	Unclear risk	Details of allocation concealment not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	"double-blind". Blinding details not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Blinding details not reported.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Losses to follow-up not reported.
Selective reporting (reporting bias)	High risk	Outcome data for BPRS and CGI not reported.

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Other bias	Low risk	"...supported, in part, by grants...from the National Institute of Mental Health"

Kaneno 1991

Methods	Allocation: randomised. Blindness: double. Duration: 6 months. Design: parallel group. County: Japan.
Participants	Diagnosis: schizophrenia. N = 259. Age: 20 - 65 years. Sex: 168M, 91F. History: not stated. Setting: hospital and community.
Interventions	1. Fluphenazine decanoate: dose 12-50 mg/ml/IM administered 6 times at 4-week intervals. N = 127. 2. Haloperidol: dose 3.0-12.1mg administered 6 times. N = 132
Outcomes	Suicide. Behaviour: leaving the study early. Unable to use - Mental state: BPRS, KORS (no SD). Adverse effects: OSR (no SD).
Notes	Article mostly written in Japanese, risk of bias assessed from the English section only

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Randomisation details not reported.
Allocation concealment (selection bias)	Unclear risk	Details of allocation concealment not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	"double blind".
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Blinding details not reported.

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Incomplete outcome data (attrition bias) All outcomes	Unclear risk	All participants (completed and terminated) were entered to the analysis. No missing data
Selective reporting (reporting bias)	High risk	Data not reported fully for mental state and adverse effects
Other bias	Unclear risk	The paper is in Japanese.

Kelly 1977

Methods	Allocation: randomised. Blindness: single. Duration: 9 months. Design: parallel group. Country: UK.
Participants	Diagnosis: schizophrenia (Schneider 1st Rank). N = 60. Age: 18 - 65 years, mean ~ 42 years. Sex: 18M, 35F. History: not stated. Setting: community. Excluded: epilepsy, ECT, brain damage, pregnancy, marked metal retardation or parkinsonism
Interventions	1. Fluphenazine decanoate: dose 1ml/IM every 3 weeks. N = 30. 2. Flupenthixol decanoate: dose 1ml/IM every 3 weeks. N = 30 Medication adjusted weeks 1-9, stable thereafter.
Outcomes	Leaving the study early. Global state: relapse. Unable to use - Mental state: BPRS (no SD). Adverse effects: EPS (no data).
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	"randomly allocated". Method not reported.
Allocation concealment (selection bias)	Low risk	"the key to the allocation [was] known only to the hospital pharmacist and to the nurse administering the injections"

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Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Insufficient information: patients may have blinded, nurses were unblinded. "...the key to the allocation [was] known only to the nurse administering the injections."
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Blinding details not reported.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Number and reasons for missing data balanced. 60 randomised, 53 completed patients. 6 patients relapsed (3 in each group and 1 became pregnant
Selective reporting (reporting bias)	High risk	No data reported for EPS, data not fully reported for BPRS.
Other bias	Unclear risk	Source of funding not reported.

Keskiner 1971

Methods	Allocation: randomised. Blindness: double. Duration: 8 weeks (4 weeks before cross-over). Design: cross-over. Country: United States.
Participants	Diagnosis: schizophrenia. N = 12. Age: 25 - 51 years, mean ~ 38 years. Sex: 3M, 9F. History: duration of illness 5-25 years (mean 14 years). Setting: hospital.
Interventions	1. Fluphenazine enanthate: dose 1 mg/kg body weight/IM single dose. N = 6. 2. Fluphenazine decanoate: dose 1 mg/kg body weight IM single dose. N = 6
Outcomes	Behaviour: leaving the study early. Unable to use - Global state: GES (data unusable). Mental state: BPRS (data unusable). Adverse effects: TESS (data unusable).
Notes	

Risk of bias

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Keskiner 1971 (*Continued*)

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"randomly separated". Method not reported.
Allocation concealment (selection bias)	Unclear risk	Details of allocation concealment not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	"double-blind". Blinding details not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	"double-blind". Blinding details not reported.
Incomplete outcome data (attrition bias) All outcomes	Low risk	All participants completed the study.
Selective reporting (reporting bias)	High risk	Reports reported incompletely.
Other bias	Low risk	"Supported, in part, by Psychiatric Research Foundation of Missouri and The Squibb Institute for Medical Research, new brunswick, NJ"

Khazaie 2005

Methods	Allocation: randomised. Blindness: double blind. Duration: 54 weeks. Design: parallel. Country: Iran.
Participants	Diagnosis: schizophrenia or schizoaffective disorder (DSM IV). N = 50. Age: mean ~ 34 years. Sex: 36M, 14F. History: duration of illness mean 12.0 years (SD = 6.6). Setting: community.
Interventions	1. Fluphenazine decanoate: 25 mg every 2 weeks. N = 25. 2. Fluphenazine decanoate: 25 mg every 6 weeks. N = 25. All patients, in both groups, received injections every two weeks; group 1 received fluphenazine at each time i.e. every two weeks and group 2 received placebo injections between each fluphenazine injection

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Outcomes	Mental state: BPRS. Clinical impression: CGI. Quality of life: Quality of life Scale. Extrapyramidal adverse effects: Maryland Psychiatric Research Center Involuntary Movement Scale Not used in review - General functioning: Level of Functioning Scale.	
Notes		

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	"randomly assigned". Method not reported.
Allocation concealment (selection bias)	Unclear risk	Details of allocation concealment not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	"double-blind". Blinding details not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	"double-blind". Blinding details not reported.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Losses to follow-up balanced in numbers across allocation groups: 7 participants from the 2-week group and 6 from the 6-week group. Reasons for drop-outs not reported per allocation group
Selective reporting (reporting bias)	Low risk	All outcome results have been reported.
Other bias	Unclear risk	Source of funding not reported.

Kissling 1985

Methods	Allocation: randomised (coin throwing). Blindness: double. Duration: 6 months. Design: parallel group. Country: Germany.

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Participants	Diagnosis: schizophrenia, schizoaffective psychosis (DSM III). N = 54. Age: FD - mean age 28 years, HD - mean age 35 years. Sex: 24M, 7F. History: on oral medication, required depot treatment for >6 months, able to give informed consent. Setting: not stated.
Interventions	1. Fluphenazine decanoate: dose mean 25 mg/IM biweekly. N = 22. 2. Haloperidol decanoate: dose mean 50 mg/IM monthly. N = 32
Outcomes	Behaviour: leaving the study early. Unable to use - Global state: need for additional anticholinergic medication (data unusable). Mental state: BPRS (data unusable). Adverse effects: EPMS, DOTES, STESS (data unusable). Physiological: serum levels (non clinical outcomes).
Notes	The drop-out rate after 6 months was FD-60%, HD- 30%.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	"random allocation (coin throwing)".
Allocation concealment (selection bias)	Unclear risk	Details of allocation concealment not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	"double-blind". Blinding details not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	"double-blind". Blinding details not reported.
Incomplete outcome data (attrition bias) All outcomes	High risk	Losses to follow-up/missing data imbalanced in numbers or reasons across intervention groups. 10 (30%) of participants in the haloperidol group left the study early and 13 (60%) in the fluphenazine group
Selective reporting (reporting bias)	High risk	All outcomes have been reported, however data presented is not usable

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Other bias	Unclear risk	Source of funding not reported.

Kreisman 1988

Methods	Allocation: randomised. Blindness: double. Duration: 1 year. Design: dosage study. Country: United States.
Participants	Diagnosis: schizophrenia (Research Diagnostic Criteria - Spitzer 1977). N = 132. Age: 17- 60 years. Sex: 91 M, 41 F. History: 'were in remission, at a stable clinical plateau'. Setting: community. Excluded: presumptive tardive dyskinesia, neurological disorders, serious substance abuse, mental retardation, physical illnesses, or requiring adjunctive medication except for antiparkinsonian agents and minor tranquillisers
Interventions	1. Fluphenazine decanoate (low dose): dose 1.25-5 mg/cc biweekly. N = 66. 2. Fluphenazine decanoate (high dose): dose 12.5-50 mg/cc biweekly. N = 66
Outcomes	Global state: relapse. Unable to use - Global state: GAS (data unusable). Mental state: BPRS (no SD). Behaviour: SAS II, PRS (no usable data).
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	"randomly assigned". Method not reported.
Allocation concealment (selection bias)	Unclear risk	Details of allocation concealment not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	"double-blind". Blinding details not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	"double-blind". Blinding details not reported.

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Incomplete outcome data (attrition bias) All outcomes	High risk	132 participants entered the study, the final sample was 51. Reasons for losses to follow-up not reported
Selective reporting (reporting bias)	High risk	Outcomes reported as P values.
Other bias	Unclear risk	Source of funding not reported

Kurland 1966

Methods	Allocation: randomised. Blindness: double. Duration: 24 weeks (first arm 12 weeks). Design: cross-over. Country: United States.
Participants	Diagnosis: schizophrenia. N = 19. Age: 23 - 53 years. Sex: all male. History: chronically ill. Setting: hospital.
Interventions	1. Fluphenazine decanoate: dose mean 25 mg/IM monthly. N = 9. 2. Fluphenazine enanthate: dose mean 22.8 mg/IM monthly. N = 10
Outcomes	Adverse effects. Unable to use - Physiological: weight measures, BP (non-clinical outcomes).
Notes	No continuous outcomes measured. Data put in depot vs depot category in both FE & FD treatment groups

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	"randomly assigned". Method not reported.
Allocation concealment (selection bias)	Low risk	"Medication was administered under a code number known only to the pharmacist."
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	"double-blind". Blinding details not reported.

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Kurland 1966 (*Continued*)

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	"double-blind". Blinding details not reported.
Incomplete outcome data (attrition bias) All outcomes	Low risk	All patients completed the study.
Selective reporting (reporting bias)	Low risk	All outcomes reported.
Other bias	Low risk	"grant-in aid from the Squibb Institute for Medical Research"

Lehmann 1980

Methods	Allocation: randomised. Blindness: double. Duration: 24 weeks. Desgin: dosage study. Country: Germany.
Participants	Diagnosis: schizophrenia (ICD 2951). N = 40. Age: 35 -38 years. Sex: 27M,13F. History: all patients chronically ill and resistant to standard doses of neuroleptics. Setting: not stated.
Interventions	1. Fluphenazine decanoate: dose 225 mg/day. N = 20. 2. Fluphenazine decanoate: dose 25 mg/day. N = 20.
Outcomes	Global state: GRS. Behaviour: leaving the study early. Unable to use - Mental state: EWL-K (no usable data).
Notes	Article in German.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Randomised, details not reported.
Allocation concealment (selection bias)	Unclear risk	Not reported.

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Lehmann 1980 (*Continued*)

Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	To assure the double-blindness, the patients whose doses were reduced were given placebo injections
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Double-blind, details not reported.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Forty patients were randomised and 39 patients were analysed after 24 weeks. There was one drop-out from the high-dosage group
Selective reporting (reporting bias)	Unclear risk	Unable to use data for EWL-K, other outcomes reported.
Other bias	Unclear risk	Source of funding not reported.

Leong 1989

Methods	Allocation: randomised. Blindness: partial. Duration: 28 weeks. Design: parallel group. Country: Singapore.
Participants	Diagnosis: schizophrenia (ICD-295). N = 60. Age: 18 - 65 years, mean ~ 38 years. Sex: 27M, 33F. History: able to give informed consent, patients in remission. Setting: community.
Interventions	1. Fluphenazine decanoate: dose 12.5-50 mg/IM monthly. N = 30. 2. Pipothiazine palmitate: dose 25-50 mg/IM monthly. N = 30. Flexible dose.
Outcomes	Global state: CGI, need for additional medication. Mental state: BPRS. Behaviour: leaving the study early. Adverse effects: various measures, EPS.
Notes	

Risk of bias

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

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Leong 1989 (*Continued*)

Random sequence generation (selection bias)	High risk	"randomised", "On admission, the patients were assigned the next available study number in numerical sequence and allocated to receive either pipothiazine palmitate or fluphenazine decanoate"
Allocation concealment (selection bias)	Unclear risk	Details of allocation concealment not reported.
Blinding of participants and personnel (performance bias) All outcomes	High risk	"The administration of the study medications was open to the person giving the injections..."
Blinding of outcome assessment (detection bias) All outcomes	Low risk	"...the patients' symptoms and side effects. ..were assessed by one of the investigators who had no knowledge of which study medication had been prescribed."
Incomplete outcome data (attrition bias) All outcomes	Low risk	All participants completed the trial.
Selective reporting (reporting bias)	Low risk	All outcomes reported.
Other bias	Unclear risk	Source of funding not reported.

Levenson 1976

Methods	Allocation: randomised. Blindness: double. Duration: 21 days. Design: 3 treatment groups. Country: United States.
Participants	Diagnosis: schizophrenia (Spitzerian criteria). N = 12. Age: 18 - 53 years, mean ~ 30 years. Sex: 4M, 8F. History: able to give informed consent. Setting: hospital.
Interventions	1. Fluphenazine decanoate: dose 2.5-7.5 mg/day. N 5. 2. Thiothixine: dose 5 -15 mg/day. N = 3. 3. Haloperidol: dose 2.5 -7.5mg/day. N = 4.
Outcomes	Behaviour: leaving the study early. Adverse effects. Unable to use -

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	Mental state: BPRS (no usable data).	
Notes		

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	"randomly assigned". Method not reported.
Allocation concealment (selection bias)	Unclear risk	Details of allocation concealment not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	"double-blind". Blinding details not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	"double-blind". Blinding details not reported.
Incomplete outcome data (attrition bias) All outcomes	Low risk	"Five patients received an administrative discharge from the study prior ton remission for reasons unrelated to their illness, to the medication they were receiving, or to any other pertinent study variable"
Selective reporting (reporting bias)	High risk	Clinical outcome (BPRS) reported incompletely.
Other bias	Unclear risk	Source of funding not reported.

Lundin 1990

Methods	Allocation: randomised. Blindness: double. Duration: 1 year (preceded by 6 month 'run-in' period). Design: parallel group. Country: Norway.
Participants	Diagnosis: schizophrenia (NIMH Collaborative Study/ DSM III). N = 58. Age: 18 -65 years. Sex: 46M, 12F. History: > 3 months satisfactory response on depot, duration illness 6 -< 24 months, able to give informed consent. Setting: community.

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Interventions	1. Fluphenazine decanoate: dose mean 34.8 mg/IM monthly. N = 30. 2. Flupenthixol decanoate: dose mean 54.7 mg/IM monthly. N = 28	
Outcomes	Behaviour: leaving the study early. Unable to use - Global state: TES (no data). Mental state: BPRS, CPRS (no data). Adverse effects: EPS, HRSD, CSE (no data). Social ability: KAS (non clinical outcome, data unusable).	
Notes	Authors contacted.	
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	"randomly allocated". Method not reported.
Allocation concealment (selection bias)	Unclear risk	Details of allocation concealment not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	"double-blind". Blinding details not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	"double-blind". Blinding details not reported.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Losses to follow-up / missing data balanced across intervention groups, with similar reasons for missing data
Selective reporting (reporting bias)	High risk	Results reported incompletely: BPRS, CPRS, CSE, SAS, HRSD, KAS
Other bias	Unclear risk	Source of funding not reported.

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MacCrimmon 1978

Methods	Allocation: randomised. Blindness: double. Duration: 1 year. Design: parallel group. Country: Canada.
Participants	Diagnosis: schizophrenia. N = 49. Age: 28-54 years, mean ~ 40 years. Sex: 16M, 23F. History: duration illness 1-21 years, mean ~ 12 years. Setting: community.
Interventions	1. Fluphenazine decanoate: dose 25-37.5/IM every 28 days. N = 24. 2. Fluphenazine enanthate: dose 25-37.5 mg/IM every 25 days. N = 25
Outcomes	Global state: need for additional medication. Mental state: BPRS. Behaviour: leaving the study early. Side effects: Bordeleau Scale.
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	"randomly assigned". Method not reported.
Allocation concealment (selection bias)	Unclear risk	Details of allocation concealment not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	"double-blind". Blinding details not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	"double-blind". Blinding details not reported.
Incomplete outcome data (attrition bias) All outcomes	High risk	Losses to follow-up/missing data imbalanced in numbers and reasons across intervention groups. Fluphenazine enanthate 3 (12%) and fluphenazine decaonate 7 (29%)
Selective reporting (reporting bias)	Low risk	Outcomes have been reported: BPRS, extrapyramidal symptoms, other adverse

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		events and serious adverse events
Other bias	Unclear risk	Source of funding not reported.

Magnus 1979

Methods	Allocation: randomised, prearranged prescribing list. Blindness: open. Duration: 6 months. Design: parallel group. Country: UK.
Participants	Diagnosis: schizophrenia. N = 50. Age: 'approximately equal in both groups'. Sex: male and female 'approximately equal in both groups' History: newly admitted to hospital (either first episode or relapse). Setting: community and hospital.
Interventions	1. Fluphenazine decanoate: every 2-3 weeks, dose range 50-100 mg/IM. N = 26. 2. Fluspirilene: weekly, dose range 6-12 mg/IM. N = 24. Indiviually adjusted doses.
Outcomes	Global state: need for additional medication. Behaviour: leaving the study early. Adverse effects. Unable to use - Mental state: BPRS (no SD) self and nurse's assessment (no data). Social ability: WWBRS (non-clinical outcomes, data unusable)
Notes	Authors contacted. Unable to complete risk of bias table - PDF missing.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	"Patients were allocated...according to a pre-arranged randomised prescribing list"
Allocation concealment (selection bias)	Unclear risk	Details of allocation concealment not reported.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open trial.

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Blinding of outcome assessment (detection bias) All outcomes	High risk	Open trial.
Incomplete outcome data (attrition bias) All outcomes	Low risk	"All but two (one in each group) completed six months treatment"
Selective reporting (reporting bias)	High risk	Not all outcomes reported: no SD reported for BPRS and no data for nurse's assessment
Other bias	Unclear risk	Smith Kline & French Laboratories provided statistical help.

Malm 1974

Methods	Allocation: randomised. Blindness: double. Duration: 8 weeks. Design: parallel group. Country: Sweden.
Participants	Diagnosis: schizophrenia. N = 62. Age: 18-65 years. Sex: 21M, 36F. History: duration illness 2-39 years, mean ~15 years. Setting: hospital.
Interventions	1. Fluphenazine enanthate: dose 7.5-50 mg/IM, mean 28.5 mg/IM biweekly. N = 26. 2. Fluspirilene: dose 1-14 mg/IM, mean 5.7 mg/IMweekly. N = 31
Outcomes	Global state: need for additional medication. Behaviour: leaving the study early. Unable to use - Mental state: S-Scale (no data). Behaviour: ADL (no data). Adverse effects: SE scale (no SD). Physiological: various measures (non-clinical outcomes, data unusable)
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	"allocated randomly". Method not reported.

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Malm 1974 (*Continued*)

Allocation concealment (selection bias)	Unclear risk	Details of allocation concealment not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	"double-blind". Patients blinded. Nurses administering the injections: not blinded to the study medications
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Blinding details not reported.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	62 participants were enrolled but number randomised to each group not reported. 5 participants were withdrawn during the first two months, intervention groups not reported
Selective reporting (reporting bias)	High risk	Outcomes incompletely reported: S-Scale, Side effects, Nurses' ratings (ADL)
Other bias	Low risk	"Supported, in part, by a grant from LEO Research Foundation, Helsingborg."

Marder 1987

Methods	Allocation: randomised. Blindness: double. Duration: 2 years. Design: dosage study. Country: United States.
Participants	Diagnosis: schizophrenia (DSM III). N = 66. Age: mean ~ 35 years. Sex: all male. History: drug free for a month, duration illness mean 24 months (5 mg), 170 months (25 mg). Setting: community and hospital.
Interventions	1. Fluphenazine decanoate (low dose): dose mean 5 mg/IM biweekly. N = 35. 2. Fluphenzazine decanoate (standard): dose mean 25 mg/IM biweekly. N = 31
Outcomes	Global state: relapse. Behaviour: leaving the study early. Adverse effects: need for additional medication. Unable to use - Mental state: BPRS (no data). Adverse effects: Hopkins SCL-90R, side-effects scale (no data)

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Notes		
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	"randomised". Method not reported.
Allocation concealment (selection bias)	Unclear risk	Details of allocation concealment not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Double-blind. Blinding details not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Double-blind. Blinding details not reported.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	2/35 and 6/31 participants left the study early during the first six months", reasons not reported
Selective reporting (reporting bias)	Unclear risk	Outcomes incompletely reported: SCL-90, SE Scale, IMEPS, Subjective EPS Rating Scale. P values for most outcomes and data at 1 month (SCL-90) and three months (side effects)
Other bias	Low risk	"...supported by Veterans Administration Medical Research and the UCLA Mental Mental Health Clinical Research Center for the Study of schizophrenia; and the national Institute of mental Health grant...E. R. Squibb and Sons...provided the low dose formulation of fluphenazine decanoate."

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McClelland 1976

Methods	Allocation: randomised. Blindness: double. Duration: 6 months (preceded by pretrial of 6 weeks). Design: dosage study. Country: UK.
Participants	Diagnosis: schizophrenia (Kraepelinian). N = 50. Age: 18-60 years. Sex: 22M, 28F. History: disabled, able to give informed consent, minimum hospital stay > 12 months. Setting: hospital.
Interventions	1. Fluphenazine decanoate (VHD): dose mean 250 mg/IM weekly. N = 25. 2. Fluphenazine decanoate (standard): dose mean 12.5 mg/IM weekly. N = 25
Outcomes	Global state: need for additional medication. Mental state: BPRS. Behaviour: leaving the study early. Adverse effects: EPS Scale. Unable to use - Behaviour: WWBRS (no data). Physiological measures: weight (non-clinical outcomes, data unusable)
Notes	Unable to complete risk of bias table - PDF missing.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"Random allocation", no further details reported.
Allocation concealment (selection bias)	Low risk	"Allocation to the experimental or control group was carried out by the hospital pharmacist"
Blinding of participants and personnel (performance bias) All outcomes	Low risk	"Double-blind design and entailed the 'double-dummy' technique." "The manufacturer prepared 10-ml ampules of fluphenazine decanoate, 25mg/ml and inactive preparation containing only sesame oil, as well as 0.5 ml ampules with 25 mg/ml of the drug and a sesame oil placebo". "All hospital personnel were 'blind"'.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	"Double-blind", blinding of outcome assessors not reported.

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Incomplete outcome data (attrition bias) All outcomes	Low risk	Two participants in the VHD group left the study early and three in the standard dose group
Selective reporting (reporting bias)	High risk	No data were reported for the WWBRS.
Other bias	Unclear risk	Source of funding not reported.

McCreadie 1980

Methods	Allocation: randomised. Blindness: double. Duration: 9 months. Design: parallel group. Country: United Kingdom (Scotland).
Participants	Diagnosis: schizophrenia (Feighner's Criteria). N = 35. Age: 19-70 years, mean 47-55 years. Sex: all male. History: on antipsychotics for mean 4 years, duration illness 18-26 years, able to give informed consent. Setting: hospital and community.
Interventions	1. Fluphenazine decanoate: dose mean 12.5 mg/IM, maximum 50 mg weekly. N = 18. 2. Pimozide: dose mean 8mg/IM, maximum 32 mg every 4 days/week. N = 16
Outcomes	Global state: relapse, need for additional medication. Adverse effects: Kraweicka scale. Unable to use - Mental state: Hamilton-Lorr scale (no data). Behaviour: Wing Ward Behaviour Scale (no data).
Notes	N differs in the paper and abstract.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	"randomly allocated". Method not reported.
Allocation concealment (selection bias)	Unclear risk	Details of allocation concealment not reported.

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Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	"double-blind". "To ensure double-blind conditions patients received active fluphenazine injections and placebo pimozide tablets, or placebo injections and active tablets." Participants blinded. Blinding details of personnel unclear
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	"double-blind". Blinding details of outcome assessors unclear
Incomplete outcome data (attrition bias) All outcomes	Low risk	Losses to follow-up and missing data balanced across intervention groups (4/16 vs 3/18), with similar reasons for missing data (relapse: 3/16 vs 3/18; 1 participant dropped out due to non-compliance with medication)
Selective reporting (reporting bias)	High risk	Hamiiton-Lorr, Wing and Griffiths scales' results not reported
Other bias	Unclear risk	Funding source not reported. Medication supplied by Janssen Pharmaceutical and Squibb

McCreadie 1982

Methods	Allocation: randomised. Blindness: double. Duration: 9 months. Design: parallel group. Country: United Kingdom (Scotland).
Participants	Diagnosis: schizophrenia (Feighner's criteria). N = 28. Age: 27-70 years, mean ~ 55 years. Sex: all male. History: duration illness >27 yrs. Setting: hospital.
Interventions	1. Fluphenazine decanoate: dose 2-25 mg/IM, mean 14 mg/IM biweekly. N = 15. 2. Pimozide: dose 10-60mg/IM, mean 40 mg/IM weekly. N = 13.
Outcomes	Mental state: Krawiecka sub-scales. Behaviour: leaving the study early. Adverse effects: parkinsonism, tardive dyskinesia. Unable to use - Mental state: HLS (no data).

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	Behaviour: WWBRS (no data).	
Notes	Authors contacted.	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	"randomly allocated". Method not reported
Allocation concealment (selection bias)	Unclear risk	Details of allocation concealment not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	"double-blind". "To ensure double blind conditions, patients received either active pimozide tablets and dummy fluphenazine injections or dummy tablets and active injections." Blinding details of personnel, unclear
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	"double-blind". Blinding details of outcome assessors, unclear
Incomplete outcome data (attrition bias) All outcomes	Low risk	Losses to follow-up balanced across intervention groups (38% vs 40%), with similar reasons (exacerbation, adverse events) for missing data
Selective reporting (reporting bias)	High risk	Hamilton-Lorr scale, Wing Ward Behaviour Scale results not reported
Other bias	Low risk	"...supported by a research grant from Dumfries and Galloway Health Board". Medication and other materials provided by Janssen Pharmaceutical and Squibb Limited

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McKane 1987

Methods	Allocation: randomised. Blindness: double. Duration: 48 weeks. (preceded by 12 weeks 'run in' period where additional medication allowed). Design: parallel group. Country: United Kingdom (Scotland).
Participants	Diagnosis: schizophrenia (Feighner (1972). N = 38. Age: 31-71 years, mean ~ 56 years. Sex: 22M, 16F. History: previously on antipsychotics, consent given by next of kin. Setting: hospital.
Interventions	1. Fluphenazine decanoate: dose mean 106 mg/IM/week, week 12 dose mean 105/IM monthly. N = 19. 2. Haloperidol decanoate: dose mean 127 mg/IM, week 12 dose mean 120 mg/IM monthly. N = 19
Outcomes	Global state: Global 5-point scale, need for additional medication. Behaviour: leaving the study early. Adverse effects: AIMS, SAS, Parkinsonism.
Notes	5 people unaccounted for in th FD group.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"randomly allocated". Method not reported
Allocation concealment (selection bias)	Unclear risk	Details of allocation concealment not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	"double-blind". Blinding details not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	"double-blind". Blinding details not reported.
Incomplete outcome data (attrition bias) All outcomes	High risk	Five patients left the study during the run-in period and 17 patients on haloperidol and 16 on fluphenazine entered the study proper. Losses to follow-up/missing data balanced in numbers 6/17 vs 4/16 but imbalanced in reasons (relapse 6/17 vs 1/

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		16; non-compliance: 0/17 vs 2/16; adverse events: 0/17 vs 1/16) across intervention groups
Selective reporting (reporting bias)	Low risk	Outcome results reported: Krawieka, Wing, SAS, AIMS.
Other bias	High risk	"Janssen Pharmaceutical...financial and other assistance".

McLaren 1992

Methods	Allocation: randomised. Blindness: double. Duration: 1 year. Design: parallel group. Country: United Kingdom.
Participants	Diagnosis: schizophrenia (ICD-9). N = 47. Age: 20-65 yrs. Sex: 27M, 20F. History: good physical health, received antipsychotics for at least 1 year previously, duration illness 18 years, able to give informed consent. Setting: community.
Interventions	1. Fluphenazine decanoate: dose 16-300 mg/IM/month, mean 103 mg/IM/month. N = 24. 2. Bromperidol decanoate: dose 67-400 mg/IM/month, mean 242 mg/IM/month. N = 23
Outcomes	Global state: relapse, need for additional medication. Behaviour: leaving the study early. Symptoms: NSRS. Unable to use - Mental state: KWS, MARDRS (no data). Social ability: MRSS (non clinical outcome, data unusable). Adverse effects: AIMS (data unusable), SAS (no data). Physiological measures: weight, blood samples (non-clinical outcomes, data unusable)
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	"randomly allocated". Method not reported.

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McLaren 1992 (*Continued*)

Allocation concealment (selection bias)	Unclear risk	Details of allocation concealment not reported.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	"double-blind" "identical ampoules".
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	"double-blind". Blinding details of outcome assessment not reported
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	"Two patients, both on fluphenazine decanoate withdrew consent". "Five patients, all in the bromperidol decanoate group were withdrawn from the study...following relapse", "One other patient, on bromperidol decanoate, was lost to follow-up during the sixth week of the study having deteriorated before contact was lost"
Selective reporting (reporting bias)	High risk	Data not reported or incomplete for the NSRS, Krawiecka-Goldberg scale, MARDRS, MRSS, SAS, AIMS
Other bias	High risk	financial support: Jannsen Pharmaceutical.

Odejide 1982

Methods	Allocation: randomised. Blindness: double. Duration: 12 months. Design: parallel group. Country: Nigeria.
Participants	Diagnosis: schizophrenia (ICD-9). N = 70. Age: not stated. Sex: not stated. History: treated with FD < 2 years, < 2 acute periods, able to give informed consent. Setting: community.
Interventions	1. Fluphenazine decanoate: dose 25 mg/IM every 4-8 weeks. N = 35. 2. Placebo. N = 35.
Outcomes	Global state: need for additional medication. Behaviour: leaving the study early. Adverse effects: AIMS. Unable to use -

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	Mental state: BPRS, PSE (no data).	
Notes	2 drop-outs unaccounted for in th FD group.	
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	"randomised". Method not reported.
Allocation concealment (selection bias)	Unclear risk	Details of allocation concealment not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	"double-blind". "patients were unaware of the contents of their injections". Blinding details of other personnel (e.g. nurses who administered the injections), not reported
Blinding of outcome assessment (detection bias) All outcomes	Low risk	"The psychiatrist who evaluated follow-up status, was blind to treatment status..."
Incomplete outcome data (attrition bias) All outcomes	Low risk	53/70 participants completed the study. Losses to follow-up or missing data balanced across intervention groups
Selective reporting (reporting bias)	High risk	Outcomes not reported (PSE) or incompletely reported (BPRS).
Other bias	Unclear risk	Source of funding not reported.

Pinto 1979

Methods	Allocation: randomised. Blindness: double. Duration: 18 months (preceded by 3 months 'run-in' period - medication unchanged). Design: parallel group. Country: United Kingdom.
Participants	Diagnosis: schizophrenia. N = 64. Age: not stated. Sex: not stated. History: receiving depot for at least 6 months, stable - no hospital admission for at least 3 months prior to trial. Setting: community.

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Interventions	1. Fluphenazine decanoate: dose mean 25 mg/IM every 3 weeks (initial dose 12.5 mg). N = 33. 2 Flupenthixol decanoate: dose mean 36.6 mg/IM every 3 weeks (initial dose 20 mg). N = 31	
Outcomes	Global state: need for additional medication. Adverse effects: EPSE. Leaving the study early. Unable to use - Mental state: BPRS (no SD).	
Notes	Authors contacted.	
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	"randomly allocated". Method not reported.
Allocation concealment (selection bias)	Unclear risk	Details of allocation concealment not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	"double-blind". Patients blinded, nurses unblinded. "injections were prepared and administered by nursing staff...neither the clinician nor the patients were aware of the treatment allocation
Blinding of outcome assessment (detection bias) All outcomes	Low risk	"...rating clinicians in ignorance of the allocation of patients to treatment groups"
Incomplete outcome data (attrition bias) All outcomes	High risk	Losses to follow-up/missing data imbalanced in numbers across intervention groups. "a total of eight patients all in the fluphenazine group, dropped-out of the trial..."
Selective reporting (reporting bias)	High risk	Outcome data incompletely reported (BPRS).
Other bias	Unclear risk	Source of funding not reported.

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Quitkin 1978

Methods	Allocation: randomised. Blindness: double. Duration: 1 year (six weeks prior to study entry, participants were stabilised on fluphenazine decanoate 0.5-2 mL/ 2 weeks. Design: parallel group. Country: United States.
Participants	Diagnosis: schizophrenia (RDC). N = 60. Age: 17-49 years. Sex: 41M,19F. History: < 2 psychotic episodes, able to give informed consent. Setting: community.
Interventions	1. Fluphenazine decanoate: dose 0.5-4 mL/IM biweekly. N = 29. 2. Penfluridol (oral): dose 20-160 mg/IM weekly. N = 27.
Outcomes	Global state: need for additional medication. Behaviour: leaving the study early. Unable to use - Global state: CGI (no data). Mental state: BPRS (no data). Adverse effects: KAS (no data). Social ability: SAS (non clinical outcome, data unusable).
Notes	Authors contacted.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	"random". Method not reported.
Allocation concealment (selection bias)	Unclear risk	Details of allocation concealment not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	"double-blind". Blinding details not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	"double-blind". Blinding details not reported.
Incomplete outcome data (attrition bias) All outcomes	High risk	"After 56 patients completed the study, the Food and Drug Administration suspended the use penfluridol", "these four patients whose failure to complete the study is un-

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		related to the clinical efficacy...will not be considered in further analysis" 35/56 participants completed the study; 4 from the penfluridol and 8 from the fluphenazine group left the study early
Selective reporting (reporting bias)	High risk	Outcome data not reported: BPRS, CGI, KASP, KASR.
Other bias	Unclear risk	Source of funding not reported.

Rifkin 1977

Methods	Allocation: randomised. Blindness: double. Duration: 1 year (psychotherapy given every 2 weeks for first 6 months, monthly thereafter). Design: 3 treatment groups. Country: United States.
Participants	Diagnosis: schizophrenia (Kraepelinian). N = 73. Age: 17-38 years, mean Sex: 50M, 23F. History: 16 participants acutely ill, stable while receiving FD/F HCL for 4 weeks, able to give informed consent. Setting: community.
Interventions	1.Fluphenazine decanoate: dose 0.5-2.0 mL/IM, mean 0.5 mL/IM biweekly. N = 23. 2. Fluphenazine hydrochloride (oral): dose 5-20 mg/IM, mean 5 mg/IM daily. N = 28. 3. Placebo. N = 22.
Outcomes	Behaviour: leaving the study early. Mental state: relapse. Adverse effects: toxicity. Unable to use - Global State: CGI (no data). Mental state: BPRS (patient evaluation, no data). Adverse effects: KAS (no data).
Notes	N differs in paper I for chronic patients compared to paper II. Continuous data reported in paper II but not usable- not separated into separate groups

Risk of bias

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

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Rifkin 1977 (*Continued*)

Random sequence generation (selection bias)	Unclear risk	"random". Method not reported.
Allocation concealment (selection bias)	Unclear risk	Details of allocation concealment not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	"double-blind". Patients blinded: "All patients received biweekly injections and daily pills-some being placebo." Blinding details of personnel not reported
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	"double-blind". Blinding details not reported.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Number of drop-outs are balanced across the intervention groups but reasons have not been reported
Selective reporting (reporting bias)	Unclear risk	Outcomes not fully reported.
Other bias	Low risk	"...supported by national Institute of Mental Health grant..."

Rossi 1990

Methods	Allocation: randomised. Blindness: double. Duration: 6 months. Design: parallel group. Country:
Participants	Diagnosis: schizophrenia (DSM III-R). N = 30. Age: 19-42 years, mean ~ 29 years. Sex: 18M, 13F. History: duration of illness (< 1 year n = 6), (1-6 years n = 20), (> 6 years n = 4). Setting: community.
Interventions	1. Fluphenazine decanoate: dose 25-50 mg/IM, mean 30 mg/IM monthly. N = 15. 2. Bromperidol decanoate: dose 50-100 mg/IM, mean 85 mg/IM monthly. N = 15
Outcomes	Behaviour: leaving the study early. Unable to use - Global state: CGI (no SD). Mental state: BPRS (no SD). Behaviour: CBS (no SD). Side effects: DOTES, TESS, EPSE (data unusable).

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Notes	Unable to complete 'Risk of bias' table - article in Italian	
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment (selection bias)	Unclear risk	B - Unclear

Russell 1982

Methods	Allocation: randomised. Blindness: double. Duration: 6 months. Design: parallel group. Country: United Kingdom.
Participants	Diagnosis: schizophrenia (ICD-9). N = 33. Age: mean ~ 36 years. Sex: 12M, 16F. History: duration illness 9 years, able to give informed consent. Setting: unclear.
Interventions	1. Fluphenazine decanoate: dose mean 12.5 mg/IM, maximum dose 25.5 mg/IM every 2-3 weeks. N = 13. 2. Fluspiriline decanoate: dose mean 3 mg/IM, maximum dose 10.94 mg/IM weekly. N = 20
Outcomes	Global state: need for additional medication. Behaviour: leaving the study early. Adverse effects: EPRS. Unable to use - Global state: CGI (no SD). Mental state: BPRS (no SD). Adverse effects: SAS (no data). Behaviour: MACC-BAS (no data).
Notes	Authors contacted.
Risk of bias	

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	"random allocation". Method not reported.

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Russell 1982 (*Continued*)

Allocation concealment (selection bias)	Unclear risk	Details of allocation concealment not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	"double-blind". Subjects blinded "...placebo injections being given. ..in the intervening weeks...". Blinding details of personnel not reported
Blinding of outcome assessment (detection bias) All outcomes	Low risk	"double-blind". "...a second psychiatrist rated each patient blind..."
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Two fluspirilene and three fluphenazine patients dropped out after one week", reasons not reported
Selective reporting (reporting bias)	High risk	BPRS and CGI incompletely reported (P values). SAS and MACC Behavior Adjustment Scale results not reported
Other bias	Unclear risk	"...supported by McNeil (Canada) laboratories.

Schlosberg 1978

Methods	Allocation: randomised. Blindness: double. Duration: 9 months (depot), 3 months (placebo)*. Design: parallel group. Country: Israel.
Participants	Diagnosis: schizophrenia. N = 75 (12 in placebo trial). Age: mean 42 years. Sex: not stated. History: duration illness mean ~ 17 years. Setting: not stated.
Interventions	1. Fluphenazine decanoate: dose 6.25-50 mg/IM monthly. N = 30. 2. Pipothiazine palmitate: dose 6.25-50 mg/IM monthly. N = 30
Outcomes	Leaving the study. Global Impression. Side effects. Unable to use - Mental state: BPRS (no SD). Behaviour: NOSIE (no SD).

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Schlosberg 1978 (*Continued*)

Notes	* Wash-out period 14 days.	
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	"randomly assigned". Method not reported.
Allocation concealment (selection bias)	Unclear risk	Details of allocation concealment not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	"double-blind". Patients blinded: "The drugs injected were pipotiazine palmitate, fluphenazine decanoate, and placebo...". Blinding details of personnel not reported
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	"double-blind". Blinding details not reported.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Number lost to follow-up not reported.
Selective reporting (reporting bias)	High risk	BPSD and NOISE results incompletely reported.
Other bias	Unclear risk	Source of funding not reported.

Schneider 1981

Methods	Allocation: randomised. Blindness: double. Duration: 1 year (preceded by 2 weeks washout). Design: parallel group. Country: United States.
Participants	Diagnosis: schizophrenia (DSM II). N = 59. Age: 21-65 years, mean ~ 45 years. Sex: 51M, 8F. History: duration illness mean ~ 21 years, able to give informed consent. Setting: hospital.
Interventions	1. Fluphenazine decanoate: dose 12.5-400 mg/IM every 2-5 weeks. N = 27. 2. Pipothiazine palmitate: dose 50-400 mg/IM every 2-5 weeks. N = 32

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Outcomes	Leaving the study early. Unable to use - Global state: CGI (no data). Physiological measures: blood samples (non-clinical outcome, data unusable)	
Notes	67% attrition rate in the treatment group, therefore the data are not usable	
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	"randomly assigned". Method not reported.
Allocation concealment (selection bias)	Unclear risk	Details of allocation concealment not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	"double-blind". Blinding details not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	"double-blind". Blinding details not reported.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Number of drop-outs not reported per allocation group. 59 patients were randomised, "a total of 34 patients remained in the study long enough to have at least 10 blood analyses"
Selective reporting (reporting bias)	High risk	Data not reported for CGI.
Other bias	Unclear risk	Source of funding not reported.

Schooler 1976

Methods	Allocation: randomised. Blindness: double. Duration: 1 year. Design: parallel group. Country: United States.
Participants	Diagnosis: schizophrenia (Schneiderian 1st rank). N = 197. Age: 18-55 years, mean ~ 30 years. Sex: 58M, 42F.

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	History: newly admitted from the community. Setting: community.
Interventions	1. Fluphenazine decanoate: dose 12.5-100 mg/IM, mean 34.7 mg/IM every 3 weeks. N = 102. 2. Fluphenazine (orally): dose max 60 mg, mean 25.2 mg/IM daily. N = 95
Outcomes	Leaving the study early. Additional medication. Side effects: TESS.
Notes	No continuous outcomes measured.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	"randomly assigned". Method not reported.
Allocation concealment (selection bias)	Unclear risk	Details of allocation concealment not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Patients blinded; blinding details of personnel not reported."...an injection of depot fluphenazine plus oral placebo or depot placebo plus oral fluphenazine. Both injections and pills...administered under double-blind conditions."
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	"double-blind". Blinding details not reported.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Insufficient information. Losses to follow-up not reported.
Selective reporting (reporting bias)	High risk	Incomplete data. "Treatment emergent symptoms were evaluated... by both a physician and a nurse...The data in this paper are the nurse's ratings"
Other bias	Low risk	"...supported by the National Institute of Mental Health grants..."

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Schooler 1979

Methods	Allocation: randomised. Blindness: double. Duration: 1 year. Design: parallel group. Country: USA.
Participants	Diagnosis: schizophrenia. N = 214*. Age: mean ~ 29 years. Sex: not stated. History: not stated. Setting: community.
Interventions	1. Fluphenazine decanoate: (dose and frequency not stated). N = 107. 2. Fluphenazine hydrochloride: (dose and frequency not stated). N = 107
Outcomes	Relapse. Unable to use - Mental state: BPRS (no SD). Side effects: SCL-9 (no SD).
Notes	*Maintenance phase

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"randomly assigned". Method not reported.
Allocation concealment (selection bias)	Unclear risk	Details of allocation concealment not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	"double blind". Blinding details not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	"double blind". Blinding details not reported.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Insufficient information. Losses to follow-up not reported.
Selective reporting (reporting bias)	High risk	BPRS and SCL-90 results incompletely reported.
Other bias	Unclear risk	Source of funding not reported.

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Schooler 1980

Methods	Allocation: randomised, stratified by sex. Blindness: double. Duration: 1 year. Design: parallel group. Country: United States.
Participants	Diagnosis: schizophrenia. N = 290*. Age: 18-55 years, mean ~ 29 years. Sex: 170M, 120F. History: able to give informed consent. Setting: initially in hospital for 7-9 weeks intensive treatment, followed by community
Interventions	1. Fluphenazine decanoate: dose 12.5-100 mg/IM, mean 34.2 mg/IM every 3 weeks. N = 143. 2. Fluphenazine hydrochloride (oral): dose 2.5-60 mg, mean 24.8mg daily. N = 147
Outcomes	Leaving the study early. Side effects: DOTES, SCL-90. Unable to use - Global state: CGI, Community Nursing Assessment (no data). Mental state: BPRS, HRSD (no data). Social ability: SAS (non clinical outcomes, data unusable).
Notes	Results for both FD & FHCL groups together. Authors contacted * 214 entered maintenance phase.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"stratified by sex, randomly assigned". Method not reported.
Allocation concealment (selection bias)	Unclear risk	Details of allocation concealment not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	"double-blind". "...either fluphenazine decanoate and oral placebo or fluphenazine hydrochloride and placebo injection." Patients blinded. Blinding details of personnel not reported
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	"double blind". Blinding details not reported.

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Schooler 1980 (*Continued*)

Incomplete outcome data (attrition bias) All outcomes	Low risk	290 participants were randomised to the "intensive phase" of the study lasting 7 to 9 weeks. "76 participants were removed from treatment during the intensive treatment phase. There were no significant differences between the two treatments in reasons for or number of these terminations" "214 (107 from each of the two treatment regimes) entered the one-year "maintenance phase" of the study". "Patients continued to receive study treatment for a maximum of one year or until termination for either treatment-related or administrative reasons". Survival analysis was performed in the study
Selective reporting (reporting bias)	High risk	Incomplete report of outcome data (BPRS, Hopkins Symptom Checklist-90, CGI), no data Hamilton Depression Scale. Full BPRS data (mean SD) not reported per allocation group
Other bias	Low risk	"...supported by the Nations Institute of Mental Health grants..."

Schooler 1997

Methods	Allocation: randomised. Blindness: double. Duration: 16-24 weeks. Design: dosage study. Country: United States.
Participants	Diagnosis: schizophrenia (DSM III). N = 313. Age: mean 29.6 years. Sex: 207M 106F. History: acutely ill. Setting: community and /or hospital.
Interventions	1. Fluphenazine decanoate (low dose): dose 2.5-10 mg biweekly. N = 106. 2. Fluphenazine decanoate (standard): dose 12.5-50 mg biweekly. N = 107
Outcomes	Rehospitalised. Unable to use - Global impression: CGI (no data). Mental state: BPRS, SANS (no data). Side effects: AIMS, EPS, Early Signs Questionnaire (no data).

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	Family therapy strategies: (non-clinical outcomes, data unusable)	
Notes	Authors contacted.	
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	"randomly assigned". Method not reported.
Allocation concealment (selection bias)	Unclear risk	Details of allocation concealment not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	"double-blind". Blinding details not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	"double-blind". Blinding details not reported.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Information on losses to follow-up not reported.
Selective reporting (reporting bias)	High risk	Outcomes not reported: BPRS, SANS, CGI, Neurological Rating Scale (extrapyramidal symptoms), Early Signs Questionnaire. Family treatment strategies outcomes incompletely reported
Other bias	Unclear risk	Source of funding unclear. "All double-blind medication supplies as well as open label fluphenazine decanoate and fluphenazine hydrochloride were provided courtesy of Bristol-Myers Squibb Company...". "multicentre clinical trial...in collaboration with the Division of Treatment and Clinical Research of the national Institute of Mental Health"

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Sharma 1991

Methods	Allocation: randomised. Blindness: double. Duration: 48 weeks. Design: parallel group. Country: UK.
Participants	Diagnosis: schizophrenia (DSM III). N = 59. Age: 30-81 years, mean ~ 52 years. Sex: 34M, 25F. History: duration illness 22 years, able to give informed consent. Setting: not stated.
Interventions	1. Fluphenazine decanoate: dose 100 mg/IM/monthly. N = 29. 2. Haloperidol decanoate: dose 100 mg/IM/monthly. N = 30.
Outcomes	Leaving the study early. Additional medication. Side effects: EPS Rating Scale, AIMS. Unable to use - Mental state: CPRS (data unusable). Physiological measures: weight (non-clinical outcomes, data unusable)
Notes	N and drop-out numbers for each group changes.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"randomly allocated". Method not reported.
Allocation concealment (selection bias)	Unclear risk	Details of allocation concealment not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	"double-blind". Blinding details not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	"double-blind". Blinding details not reported.
Incomplete outcome data (attrition bias) All outcomes	High risk	Losses to follow-up unbalanced in numbers (6/30 fluphenazine vs 10/29 haloperidol) and reasons (treatment failure "primary reason for withdrawal in one patient on fluphenazine and 5 patients on haloperidol")

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Selective reporting (reporting bias)	High risk	CPRS results reported incompletely.
Other bias	Unclear risk	Source of funding not reported.

Shenoy 1981

Methods	Allocation: randomised. Blindness: double. Duration: 6 weeks. Design: parallel group. Country: USA.
Participants	Diagnosis: schizophrenia (DSM III criteria). N = 31. Age: mean 37.4 (11.33) years, range 23-59. Sex: not reported. History: chronic ambulatory schizophrenia patients treated with fluphenazine decanoate for two years. Setting: outpatients.
Interventions	1. Placebo, every 3 weeks. N = 17 2. Fluphenazine decanoate (dose not reported), every 3 weeks. N = 14
Outcomes	Global state: relapse, GAS. Mental State: SADS. Unable to use - Adverse effects: AIMS (data not reported per treatment group)
Notes	Participants in group 1 were given placebo injections as a "drug holiday". At the end of the 6-week study they were returned to their routine active medication

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	"patients were randomly assigned". Method not reported.
Allocation concealment (selection bias)	Unclear risk	Details of allocation concealment not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	"double-blind". Blinding details not reported.

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Shenoy 1981 (*Continued*)

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	"double-blind". Blinding details not reported.
Incomplete outcome data (attrition bias) All outcomes	Low risk	None of the patients relapsed. 3 participants did not complete the trial: 2 in the active and 1 in the placebo group. All drop-out were due to "failure to meet appointments"
Selective reporting (reporting bias)	Low risk	All outcomes have been reported.
Other bias	Unclear risk	Source of funding has not been reported.

Shu 1983

Methods	Allocation: randomised. Blindness: double. Duration: 6 weeks. Design: parallel group. Country: China.
Participants	Diagnosis: schizophrenia. N = 34. Age: 15-48 years. Sex: all male. History: not stated. Setting: hospital.
Interventions	1. Fluphenazine decanoate: (dose and frequency not stated). N = 16. 2. Penflurdidol + placebo: (dose and frequency not stated). N = 18
Outcomes	Global state: CGI. Leaving the study early. Side effects: SAS.
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	"randomised". Method not reported.
Allocation concealment (selection bias)	Unclear risk	Details of allocation concealment not reported.

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Shu 1983 (*Continued*)

Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	"double-blind". Blinding details not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	"double-blind". Blinding details not reported.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Losses to follow-up balanced across intervention groups: 3 (18%) lost in the fluphenazine group and 2 (11%) in the penflurdidol group, with similar reasons for missing data (exacerbation)
Selective reporting (reporting bias)	Low risk	Outcome data have been reported: CGI, A standardized psychiatric Assessment Scale for Chronic psychiatric Patients, rating Scale for Extramidal Side Effects (Simpson G M)
Other bias	Unclear risk	Source of funding not reported.

Simon 1978

Methods	Allocation: randomised. Blindness: open. Duration: 18 months. Design: 3 treatment groups. Country: France.
Participants	Diagnosis: schizophrenia (French classification of mental illness). N = 181. Age: 21-45 years. Sex: 117M, 64F. History: duration illness 3-10 years. Setting: community and/or hospital.
Interventions	1. Fluphenazine decanoate: dose mean 88 mg/IM every 22 days. N = 57. 2. Pipothiazine decanoate: dose mean 90 mg/IM every 25 days. N = 61. 3. Standard oral neuroleptics: no further details. N = 63.
Outcomes	Leaving the study early. Global state: CGI. Mental state: BPRS, NOSIE. Additional medication. Side effects.
Notes	

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Simon 1978 (*Continued*)

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	"balanced randomization". Method not reported.
Allocation concealment (selection bias)	Unclear risk	Details of allocation concealment not reported.
Blinding of participants and personnel (performance bias) All outcomes	High risk	"open study"
Blinding of outcome assessment (detection bias) All outcomes	High risk	"open study"
Incomplete outcome data (attrition bias) All outcomes	High risk	39 participants left the study early, 14 in the fluphenazine group, 15 in the pipothiazine group and 10 in the standard neuroleptics group. Reasons were similar across groups. "The 18 dropouts due to independent causes and those lost to follow up were not considered in the analysis"
Selective reporting (reporting bias)	Low risk	All outcome data has been reported.
Other bias	Unclear risk	"...supported by a grant from the Fondation de L'Industrie pharmaceutique pour la recherche..."

Singh 1979

Methods	Allocation: randomised. Blindness: double. Duration: 44 weeks. Design: parallel group. Country: Canada.
Participants	Diagnosis: schizophrenia (DSM-II). N = 30. Age: 29-59 years, mean ~ 44 years. Sex: 24M, 6F. History: duration illness 3-32 years. Setting: community.

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Singh 1979 (*Continued*)

Interventions	1. Fluphenazine enanthate: dose 25-75 mg/IM, mean 44.2 mg/IM/monthly. N = 15. 2. Pipothiazine palmitate: dose 100-150 mg/IM, mean 125 mg/IM/monthly. N = 15	
Outcomes	Mental state: BPRS. Side effects. Unable to use - Physicological measures: (non-clinical outcomes, data unusable)	
Notes		

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	"randomly assigned". Method not reported.
Allocation concealment (selection bias)	Unclear risk	Details of allocation concealment not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	"double blind". Patients blinded; " ...test medications were administered blind...on alternate two weeks, patients in the pipotiazine group received an injection of sesame oil...". Blinding details of personnel not reported
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	"double blind". Blinding details not reported.
Incomplete outcome data (attrition bias) All outcomes	Low risk	All patients completed the study.
Selective reporting (reporting bias)	Low risk	Outcome data reported for BPRS and side effects.
Other bias	Unclear risk	Source of funding not reported.

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Song 1993

Methods	Allocation: randomised. Blindness: double. Duration: 6 months. Design: 3 treatment groups. Country: not reported.
Participants	Diagnosis: schizophrenia. N = 154. Age: not stated. Sex: not stated. History: chronic. Setting: hospital.
Interventions	1. Fluphenazine decanoate: (dose and frequency not stated). N = 50. 2. Pipothiazine palmitate (oral): (dose and frequency not stated). N = 52. 3. Pipothiazine palmate (oral, non-blinded): (dose and frequency not stated). N = 52
Outcomes	Leaving the study early. Mental state: BPRS*. Unable to use - Side effects: TESS (data unusable).
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"randomised". Method not reported.
Allocation concealment (selection bias)	Unclear risk	Details of allocation concealment not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	"double blindness in pipotiazine palmitate group and Fluphenazine Decanoate group, and one non-blindness pipotiazine palmitate group". Details not reported
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	"double blindness in pipotiazine palmitate group and Fluphenazine Decanoate group, and one non-blindness pipotiazine palmitate group". Details not reported
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Losses to follow-up not reported.
Selective reporting (reporting bias)	High risk	Outcome data for TESS not reported fully.

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Other bias	Unclear risk	Source of funding not reported.

Van Praag 1970

Methods	Allocation: randomised. Blindness: double. Duration: 8 weeks, follow-up 4 weeks. Design: parallel group. Country: The Netherlands.
Participants	Diagnosis: psychotic*. N = 25. Age: not stated. Sex: not stated History: chronic and acute. Setting: hospital.
Interventions	1. Fluphenazine enanthate: dose mean 25 mg/IM + oral placebo every 3 weeks. N = 13. 2. Fluphenazine oral + depot placebo: dose and frequency not reported. N = 12 All received concomitant orphenadrine (Disipal) 50 mg tds.
Outcomes	Additional medication. Unable to use - Side effects: EPS checklist (no data). Behaviour: Wing Scale - Scale A (no data), Scale B: (authors own scale **). Physiological measures: (non-clinical outcomes, data unusable)
Notes	* Group 1 were acutely ill. Group 2. were chronically ill. **Marshall 1998.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	"divided at random". Method not reported.
Allocation concealment (selection bias)	Unclear risk	Details of allocation concealment not reported.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	"One category received active fluphenazine orally and placebo injections; the other received oral placebos and injections of fluphenazine enanthate...The test drug and placebo were contained in identical capsules...Active fluid and placebo

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		fluid were indistinguishable...Strict double-blind conditions prevailed throughout the experiment."
Blinding of outcome assessment (detection bias) All outcomes	Low risk	"Strict double-blind conditions prevailed throughout the experiment."
Incomplete outcome data (attrition bias) All outcomes	High risk	Missing data imbalanced across intervention groups 8% (oral group) versus 25% (depot group): 2 participants in the depo category left the study early due to deterioration of symptoms, a further patient in the depot category left due to encephalitis. 1 participant in the oral category due to severe oligophrenia
Selective reporting (reporting bias)	High risk	Outcome data not fully reported.
Other bias	Unclear risk	Source of funding not reported.

Van Praag 1973

Methods	Allocation: randomised. Blindness: double. Duration: 4 weeks. Design: parallel group. Country: The Netherlands.
Participants	Diagnosis: acutely psychotic. N = 33. Age: 19-70 years, mean ~ 42 years. Sex: 19F, 11M. History: not stated. Setting: hospital.
Interventions	1. Fluphenazine decanoate: dose 25 mg/IM every 3 weeks. N = 15. 2. Fluphenazine enanthate: dose 25 mg/IM every 3 weeks. N = 18
Outcomes	Leaving the study early. Additional medication. Unable to use - Behaviour: Wing Scale - A & B (no data).
Notes	Data put in depot vs depot category in both FE & FD treatment groups
Risk of bias	

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Van Praag 1973 (*Continued*)

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"randomly divided". Method not reported.
Allocation concealment (selection bias)	Unclear risk	Details of allocation concealment not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	"The conditions of a double-blind test were ensured". Blinding details not reported
Blinding of outcome assessment (detection bias) All outcomes	Low risk	"The evaluators- physicians and nurses- were blind to the distribution of enanthate and decanoate..."
Incomplete outcome data (attrition bias) All outcomes	Low risk	Missing data balanced across intervention groups: 2 (14%) participants from the enanthate group and 1 (6%) from the decanoate group, with similar reasons for missing data
Selective reporting (reporting bias)	High risk	Outcome data not reported (Wing Scale A and Scale B)
Other bias	Unclear risk	Source of funding not reported

Walker 1983

Methods	Allocation: randomised. Blindness: double. Duration: 24 weeks (preceded by 12 week open trial). Design: parallel group. Country: United Kingdom.
Participants	Diagnosis: schizophrenia. N = 39. Age: 23-67 years, mean ~ 45 years. Sex: male and female. History: currently maintained on depot neuroleptics, at least one hospitalisation, duration illness 1-20 years. Setting: community.
Interventions	1.Fluphenazine decanoate: dose 12.5mg/weeks-37.5 mg/4 weeks, mean 24.8 mg/IM every 3-4 weeks. N = 20. 2. Clopenthixol decanoate: dose 200mg/4 weeks - 600 mg/2 weeks, mean 220 mg/IM every 3-4 weeks. N = 19

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Outcomes	Side effects: Side Effects Inventory. Unable to use - Global state: CGI, Krawiecka, Goldberg & Vaughan Rating Scale (no SD). Mental state: BPRS (no SD). Physiological measures: blood/liver tests, weight, BP (non-clinical outcomes, data unusable)	
Notes	Authors contacted. Analysis: last observation carried forward.	
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	"randomly allocated". Method not reported.
Allocation concealment (selection bias)	Unclear risk	Details of allocation concealment not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	"double-blind". Blinding details not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	"double-blind". Blinding details not reported.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Missed data per allocation group unclear. "Forty five patients entered the trial. Six patients failed to return following the first interview and so were discounted. One patient returned to her home country, and so failed to attend for the final assessment"
Selective reporting (reporting bias)	High risk	Outcome data incompletely reported (SD not reported): CGI, BPRS, Krawiecka, Goldberg & Vaughan Rating Scale
Other bias	Unclear risk	Source of funding not reported.

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Wistedt 1983

Methods	Allocation: randomised. Blindness: double. Duration: 2 years. Design: parallel group. Country: Sweden.
Participants	Diagnosis: schizophrenia (Bleuler's criteria). N = 32. Age: 26-67 years, mean ~ 41years. Sex: 15M, 17F. History: stabilised on depots, relapse in connection with withdrawal; duration illness mean ~ 14 years. Setting: not stated.
Interventions	1. Fluphenazine decanoate: dose mean 27mg/IM every 3 weeks. N = 15. 2. Flupenthixol decanoate: dose mean 31mg/IM every 3 weeks. N = 17
Outcomes	Leaving the study early. Side effects: SRSE, AIMS. Unable to use - Global state: CGI (no data). Mental state: CPRS (no data).
Notes	Authors contacted.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"allocated randomly". Method not reported.
Allocation concealment (selection bias)	Unclear risk	Details of allocation concealment not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	"double-blind". Blinding details not reported.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	"The injections were given by a nurse who did not participate in the assessment."
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Missing data balanced across intervention groups (27% fluphenazine group vs 40% flupenthixol group). Reasons for losses to follow-up not reported
Selective reporting (reporting bias)	High risk	Incomplete outcome data: CGI, CPRS.

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Other bias	Unclear risk	Source of funding not reported.

Wistedt 1984

Methods	Allocation: randomised. Blindness: double. Duration: 20 weeks. Design: parallel group. Country: Sweden.
Participants	Diagnosis: schizophrenia (RDC). N = 51. Age range: 21-63 years. Sex: 33M, 18F. History: 6 months treatment forseen, duration illness < 12 years, able to give informed consent. Setting: 4 weeks in hospital, thereafter in the community.
Interventions	1. Fluphenazine decanoate: dose mean 84 mg/IM/monthly. N = 26. 2. Haloperidol decanoate: dose mean 122 mg/IM/monthly. N = 25 Depot (FD/HD) dose range: 25-100 mg/injection, initially adjusted at 2nd injection (max. 300 mg)
Outcomes	Global State: CGI. Mental state: CPRS. Leaving the study early. Additional medication. Side effects: EPS, AIMS. Unable to use - Physiological measures: drug plasma levels, weight changes (non clinical outcomes, data unusable)
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	"allocated to the two groups according to a randomisation list...Patients were balanced in groups of six" Details not reported
Allocation concealment (selection bias)	Unclear risk	Details of allocation concealment not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	"Injections were give double-blind". Blinding details not reported

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Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Blinding details not reported.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Missing data balanced across intervention groups (15% fluphenazine vs 15% haloperidol), with similar reasons for missing data
Selective reporting (reporting bias)	Low risk	All primary outcomes reported: CPRS, CGI, EPS.
Other bias	Unclear risk	Source of funding not reported.

Woggon 1977

Methods	Allocation: randomised. Blindness: double. Duration: 6 months. Design: parallel group. Country: Germany.
Participants	Diagnosis: schizophrenia (ICD Nr). N = 61. Age: 21-79 years. Sex: 36M, 25F. History: 6 months treatment. Setting: community.
Interventions	1. Fluphenazine decanoate: dose 25-37.5 mg/IM every 3 weeks. N = 30. 2. Pipothiazine palmitate: dose 100 mg/IM every 4 weeks. N = 31
Outcomes	Leaving the study early. Unable to use - Side effects: (data unusable).
Notes	Article in German.

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 reported.

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Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	The tests were performed double-blind. The dosage of both drugs and the additional medications were prescribed by an investigator who himself did not take part in the ratings
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Double-blind, details not reported.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No losses to follow-up.
Selective reporting (reporting bias)	Unclear risk	Data for side effects not usable, other outcomes reported.
Other bias	Unclear risk	Source of funding not reported.

Diagnostic tools:
CCMD-2-R: Chinese Classification of Mental Disorders, Second Edition, Revised
DSM III - Diagnostic Statistical Manual, version 3
ICD-9 - International Classification of Diseases, version 9
RDC - Research Diagnostic Criteria
Rating scales
Global state:
CGI - Clinical Global Impression
GAS - Global Assessment Scale
GRS - Global Rating Scale
GES - Global Evaluation Scale
KWS - Krawiecka-Goldberg Scale
PRS - Patient Rejection Scale
TES - Therapeutic Effects Scale
Mental state:
BPRS - Brief Psychiatric Rating Scale
CPRS - Comprehensive Psychopathological Rating Scale
EWL-K - List of Attributes self rating scale.
HLS - Hamilton-Lorr Scale
HRSD - Hamilton Psychiatric Rating Scale for Depression

KGS -
KORS - Keio University's Simplified Rating Scale for Psychiatric Symptoms
KWS -
MIE - Mental Illness Evaluation
PANSS - Positive and Negative Syndrome Scale
PSE - Wing Ward Present State Examination
SANS - Scale for Assessment of Negative Symptoms
SAPS - Scale for Assessment of Positive Symptoms
S-Scale - The Symptom Scale

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Behaviour:
CBS - Current Behaviour Schedule
MACC-BAS - MACC Behaviour Adjustment Scale
PRS -
WWBRS - Wing Ward Behaviour Rating Scale
Symptom scales:
HSC - Hopkins Symptom Checklist
MRSS - Morningside Rehabilitation Rating Scale
NSRS - Negative Symptom Rating Scale
SSI - Springfield Symptom Index
SCL-90 - Symptom Checklist -90
Social behaviour:
ADL - Activities of Daily Living
KAS - Katz Adjustment Scale
SAS - Social Adjustment Scale
SRE - Schedule of Recent Events
SBAS - Social Behaviour Assement Schedule
SPS - Social Performance Schedule
Side effects
AIMS - Abnormal Involuntary Movement Side effects
Bordeleau Scale
CSE - Clinical Side Effects Scale
DOTES - Dosage Record & Treatment Emergent Symptom Scale
EPMS - Extrapyramidal Motor Side-effects
EPSS - Extrapyramidal Side-effects Symptoms
EPS -Extrapyramidal symptom scale
IMEPS - Involuntary Movement and EPS Scale
MARDRS- Montgomery-Asberg Depression Rating Scale
MRQ - Medication Response Questionnaire
NOSIE - Nurses Observation Scale for Inpatient Evaluation
OSR - Overall Safety Rating
RSESE - Rating Scale for Extrapyramidal Side Effects
SAS - Simpson and Angus Scale
SDS - Simpson Dyskinesia Scale
SRSE - Simpson Rating Scale for EPS
SEC -Side Effects Checklist
SCL-9 Side effects Check List 9
STESS - Total Score of Side Effects Self Rating
TESF - Treatment Emergent Symptom Form
TESS - Treatment Emergent Symptoms Scale
UKU - Side Effects Rating Scale
Miscellaneous:
bid - twice daily
BMI - body mass index
BP - Blood Pressure
EE - Expressed Emotion
IM - intramuscular
NIMH - National Institute of Mental Health

SD - standard deviation
tds - three times daily
VHD - Very High Dose

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Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Abuzzahab 1976a	Allocation: not randomised.
Abuzzahab 1976b	Allocation: double blind. Participants: people with schizophrenia. Interventions: oral fluphenazine versus pimozide.
Abuzzahab 1977	Allocation: not randomised.
Abuzzahab 1980	Allocation: double blind. Participants: people with psychopathology. Interventions: fluphenazine HCl versus pimozide.
Ahlfors 1971	Allocation: randomly selected. Participants: people with schizophrenia. Interventions: fluphenazine enanthate versus pipotiazine undecylenic ester. Outcomes: no data presented.
Ahlfors 1973	Allocation: randomised. Particpants: people with schizophrenia. Interventions: fluphenazine enanthate versus pipotiazine undecylenate. Outcomes: no usable data, authors contacted.
Altamura 1987	Allocation: not randomised.
Angst 1975	Allocation: double blind. Participants: people with schizophrenia. Interventions: fluphenazine decanoate versus fluspirilen versus penfluridol versus perphenazino enanthate versus pipothiazine palmitate. Outcomes: no usable data.
Arato 1979	Allocation: not randomised (retrospective study).
Astrup 1974	Allocation: not randomised.
Balon 1982	Allocation: double blind - cross-over study. Participants: people with schizophrenia. Interventions: depot fluphenazine decanoate versus hydroxyprotepine decanoate. Outcomes: no usable data.
Bankier 1968	Allocation: randomised. Participants: people with schizophrenia. Interventions: trifluoperazine versus placebo.

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Bao 1991	Allocation: randomised. Participants: people with schizophrenia. Interventions: flupenthixol decanoate versus chlorpromazine.
Barnes 2010	Allocation: randomised. Participants: people with schizophrenia. Interventions: first generation antipsychotics versus second generation (non-clozapine) antipsychotics
Barsa 1965	Allocation: double blind. Participants: not specified.
Bastie 1974	Allocation: not randomised.
Benassi 1968	Allocation: not randomised.
Berliner 1974	Allocation: not randomised.
Bilone 1988	Allocation: not randomised.
Bloch 2004	Allocation: randomised. Participants: people with schizophrenia. Interventions: lidocaine-prilocaine cream versus placebo to reduce pain injection site pain of depot antipsychotics
Boyer 1987	Allocation: randomised. Participants: people with schizophrenia. Interventions: amisulpride versus fluphenazine. Outcomes: no usable data (no SDs).
Brankovic 1998	Allocation: not randomised.
Breier 1987	Allocation: double blind. Participants: people with schizophrenia. Interventions: fluphenazine - withdrawal study.
Caranza 1973	Allocation: not randomised.
Carpenter 1992	Allocation: randomised. Participants: people with schizophrenia. Interventions: fluphenazine versus placebo versus diazepam. Outcomes: withdrawal study.
Carpenter 1993	Allocation: randomised. Participants: people with schizophrenia. Interventions: Fluphenazine decanoate 1 cc, every 2 weeks versus fluphenazine decanoate 1 cc, every 6 weeks. Outcome data: no usable data reported (conference proceeding)

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Carpenter 1999	Allocation: randomised. Participants: people with schizophrenia. Interventions: fluphenazine decanoate injection 2/52 versus 6/52 with oral fluphenazine prescribed as required
Casacchia 1989	Allocation: randomised. Participants: people with schizophrenia. Interventions: bromperidol decanoate versus fluphenazine decanoate. Outcomes: no usable data.
Castellini	Allocation: open - cross-over study.
Chacon 1972	Allocation: double blind - cross-over study.
Chacon 1973	Allocation: double blind. Participants: people with schizophrenia. Interventions: fluphenazine decanoate versus chloropromazine. Outcomes: no usable data, authors contacted.
Charalampous 1977	Allocation: random double-blind fashion. Participants: people with schizophrenia. Interventions: oral fluphenazine versus pentofluridol.
Chien 1974	Allocation: randomised. Participants: people with psychotic illnesses including schizophrenia. Interventions: fluphenazine enanthate versus different dosages of antiparkinson drugs (not antipsychotics)
Childers 1964	Allocation: randomised. Participants: people with schizophrenia. Interventions: electro convulsive therapy (ECT) versus oral fluphenazine versus chlorpromazine versus chlorpromazine with ECT
Chouinard 1970	Allocation: randomised. Participants: people with schizophrenia. Interventions: oral fluphenazine versus pimozide.
Chowdhury 1980	Allocation: randomised. Participants: people with schizophrenia. Interventions: fluphenazine decanoate versus flupenthixol decanoate. Outcomes: no usable data, authors contacted.
Clark 1971	Allocation: randomised. Participants: people with schizophrenia. Interventions: oral fluphenazine versus chlorpromazine versus thioridazine versus placebo
Cohen 1985	Allocation: not randomised.

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Cole 1967	Allocation: randomised. Participants: people with schizophrenia. Interventions: oral fluphenazine versus chlorpromazine versus acetophenazine
Cookson 1991	Allocation: double blind. Participants: people with schizophrenia. Interventions: haloperidol decanoate versus fluphenazine decanoate. Outcomes: no usable data.
Coufal 1981	Allocation: not randomised.
Curry 1979	Allocation: double blind - cross-over study.
Curson 1985	Allocation: randomised. Participants: people with schizophrenia. Interventions: fluphenazine decanoate and flupenthixol decanoate versus placebo, the data for the two antipsychotics (depot and oral) were analysed as one group
Curson 1986	Allocation: not randomised.
De Alarcon 1969	Allocation: not randomised - case reports.
De Buck 1973	Allocation: randomised. Participants: people with schizophrenia. Interventions: oral fluphenazine (dosage study).
Del Giudice 1975	Allocation: randomised. Participants: people with schizophrenia. Interventions: fluphenazine enanthate versus fluphenazine hydrochloride (orally). Outcomes: no usable data, no continuous outcomes measured.
Dencker 1978	Allocation: randomised. Participants: people with schizophrenia. Intervention: high - low doses of fluphenazine enanthate. Outcomes: no usable data.
Dencker 1981	Allocation: not randomised.
Dengler 1969	Allocation: not randomised.
DeWolfe 1971	Allocation: randomised Participants: people with schizophrenia. Interventions: fluphenazine enanthate versus thorazine-stelazine (orally). Outcomes: data not usable, drop-out rate 60% in 6-week trial
Donlon 1976 1	Allocation: randomised. Participants: people with schizophrenia. Interventions: fluphenazine decanoate versus fluphenazine enanthate. Outcomes: no usable data.

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Donlon 1977	Allocation: randomised. Participants: people with schizophrenia. Interventions: oral fluphenazine versus pimozide.
Donlon 1978	Allocation: quasi-randomised.
Doongaji 1988	Allocation: randomised. Participants: people with schizophrenia. Interventions: fluphenazine decanoate versus penfluridol. Outcomes: no usable data, authors contacted.
Dossenbach 1997	Allocation: randomised. Participants: people with schizophrenia. Interventions: oral fluphenazine versus olanzapine.
Downing 1963	Allocation: randomised. Participants: people with schizophrenia. Interventions: chlorpromazine versus fluphenazine versus thioridazine versus placebo. Outcomes: no usable data.
Emsley 1999	Allocation: randomised. Participants: people with schizophrenia. Interventions: quetiapine versus haloperidol with fluphenazine prescribed (4-week run-in phase)
Engelhardt 1973	Allocation: randomised. Participants: people with schizophrenia. Interventions: oral fluphenazine versus haloperidol versus placebo
Engstrand 1969	Allocation: not randomised.
Faltus 1974	Allocation: not randomised.
Faretra 1970	Allocation: randomised. Participants: people with schizophrenia. Interventions: oral fluphenazine versus haloperidol.
Ferenc 2000	Allocation: double blind. Participants: people with schizophrenia. Interventions: oral fluphenazine versus olanzapine.
Filip 1985	Allocation: randomised. Participants: people with schizophrenia. Interventions: fluphenazine decanoate versus oxyprothepin decanoate with cross over at 6 months. Outcomes: no usable data - results provided at 12 months without separating the treatments
Floru 1974	Allocation: not randomised.
Floru 1975	Allocation: not randomised.

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Giannelli 1990	Allocation: not randomised.
Gillis 1981	Allocation: randomised. Participants: people with schizophrenia. Interventions: no usable data.
Gitlin 1988	Allocation: randomised. Participants: people with schizophrenia. Interventions: fluphenazine decanoate versus placebo. Outcomes: no usable data (plasma study).
Gitlin 2001	Allocation: randomised cross-over trial. Participants: people with schizophrenia. Interventions: fluphenazine decanoate versus placebo. Outcomes: no usable data, no results reported for first phase of the study
Goff 2005	Allocation: randomised. Participants: people with schizophrenia. Interventions: d-cycloserine as add-on to conventional antipsychotics versus placebo add-on
Goldberg 1967	Allocation: randomised. Participants: people with schizophrenia. Interventions: chlorpromazine versus fluphenazine versus thioridazine. Outcomes: no usable data.
Goldberg 1968	Allocation: randomised. Participants: people with schizophrenia. Interventions: placebo versus thioridazine versus chlorpromazine versus fluphenazine. Outcomes: no usable data.
Goldberg 1970	Allocation: randomised. Participants: people with schizophrenia. Interventions: prolixin enanthate versus oral phenothiazines
Goldberg 1981	Allocation: randomised - withdrawal study.
Gopalakrishnan 2006	Allocation: randomised. Participants: people with schizophrenia. Interventions: sildenafil versus placebo.
Grosser 1970	Allocation: randomised. Participants: people with schizophrenia. Interventions: fluphenazine decanoate versus fluphenazine enanthate. Outcomes: no usable data.
Haider 1968	Allocation: randomised. Participants: people with schizophrenia. Interventions: fluphenazine enanthate versus fluphenazine (oral). Outcomes: no usable data.

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Hall 1968	Allocation: randomised. Participants: people with schizophrenia. Interventions: oral fluphenazine versus haloperidol.
Hamilton 1979	Allocation: randomised. Participants: people with schizophrenia. Interventions: fluphenazine decanoate versus flupenthixol decanoate. Outcomes: no usable data, no outcomes measured.
Hanlon 1965	Allocation: randomised. Participants: people with schizophrenia. Interventions: oral fluphenazine versus chlorpromazine, thioridazine, trifluoperazine, prochlorpromazine, perphenazine, thiopropazate and trifluperazine
Harper 1976	Allocation: double blind - cross-over study. Participants: people with schizophrenia. Interventions: chlorpromazine depot preparations versus fluphenazine. Outcomes: no usable data.
Haslam 1975	Allocation: randomised. Participants: people with schizophrenia. Interventions: fluphenazine decanoate versus flupenthixol decanoate. Outcomes: no usable data, data difficult to interpret.
Held 1970	Allocation: randomised. Participants: people with schizophrenia. Interventions: phenothiazines and placebo. Outcomes: no usable data.
Hirsch 1973	Allocation: randomised. Participants: people with schizophrenia. Interventions: fluphenazine decanoate and placebo, withdrawal study
Hirsch 1978	Allocation: double blind. Participants: people with schizophrenia. Interventions: fluphenazine versus flupenthixol. Outcomes: no usable data.
Hirsch 1989	Allocation: randomised. Participants: people with schizophrenia. Interventions: fluphenazine decanoate versus active injections with haloperidol prescribed as required
Hogarty 1995	Allocation: randomised. Participants: people with schizophrenia. Interventions: fluphenazine decanoate - low dose versus standard dose. Outcomes: fluphenazine decanoate measured against anxiolytics or antidepressants not antipsychotics
Holden 1970	Allocation: double blind - cross-over study.

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Holt 1984	Allocation: not randomised.
Hsu 1967	Allocation: randomised. Participants: people suffering from psychotic disorders, including schizophrenia. Interventions: fluphenazine enanthate versus placebo. Outcomes: no usable data.
Inderbitzen 1994	Allocation: not randomised.
Inderbitzin 1993	Allocation: randomised. Participants: people with schizophrenia. Interventions: reduced fluphenazine decanoate dose by 50% (10% per month for 5 months) versus at least 20 mg fluphenazine decanoate every four weeks. Outcome data: no usable data reported (conference proceeding)
Ionescu 1983	Allocation: not randomised.
Iqbal 1978	Allocation: not randomised.
Irwin 1986	Allocation: double blind. Participants: people with schizophrenia. Interventions: 5-HT versus placebo.
Itil 1970a	Allocation: not randomised.
Itil 1970b	Allocation: double blind - cross-over study.
Itil 1971	Allocation: double blind. Participants: people with schizophrenia. Interventions: fluphenazine hydrochloride. Outcomes: no usable data.
Itil 1978	Allocation: not randomised.
Jakovljevic 1999	Allocation: randomised. Participants: people with schizophrenia. Interventions: oral fluphenazine versus olanzapine.
James 1977	Allocation: randomised. Participants: people with schizophrenia. Interventions: fluphenazine decanoate versus penfluridol. Outcomes: no usable data (no SD).
Johnson 1975	Allocation: not randomised.
Jones 2006	Allocation: randomised. Participants: people with schizophrenia. Interventions: first generation antipsychotics versus second generation antipsychotics

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Kabes 1980a	Allocation: "divided randomly into 2 groups" - cross-over study. Participants: people with schizophrenia. Interventions: depot preparations plus fluphenazine, oxyprothepine/oxyprotepin. Outcomes: no usable data.
Kabes 1980b	Allocation: randomised. Participants: people with schizophrenia. Interventions: oxyprothepin decanoate versus fluphenazine decanoate - medication crossed over at 6 months. Outcomes: no usable data - results presented at 12 months without differentiating each treatment arm
Kabes 1981	Allocation: double blind - cross-over study. Participants: people with schizophrenia. Interventions: oxyprothepin decanoate versus fluphenazine decanoate. Outcomes: no usable data.
Kane 1979	Allocation: randomised. Participants: people with schizophrenia. Interventions: fluphenazine decanoate and placebo. Outcomes: withdrawal study.
Kane 1982	Allocation: randomised. Participants: people with acute first episode schizophrenia. Interventions: fluphenazine decanoate versus placebo. Outcomes: no usable data, authors contacted.
Kane 1983 b	Allocation: not randomised - review article.
Keith 2002	Allocation: randomised. Participants: people with schizophrenia. Interventions: Continuous low dose (2.5-10 mg) fluphenazine decanoate versus standard dose (12.5-50 mg) versus targeted dose (vehicle), delivered by injection every two weeks for two years. Outcome data: no usable data reported (conference proceeding)
Kelly 1999	Allocation: not randomised.
Kenway 1971	Allocation: randomised - cross-over study.
Keskiner 1968a	Allocation: not randomised.
Keskiner 1968b	Allocation: randomised. Participants: people with schizophrenia. Interventions: fluphenazine decanoate versus placebo. Outcomes: withdrawal study.
King 1979	Allocation: randomised. Participants: people with schizophrenia. Interventions: family therapy in conjunction with high- and low-dose phenothiazines

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Kinon 1993	Allocation: randomised. Participants: people with schizophrenia. Interventions: fluphenazine high dose versus fluphenazine low dose versus haloperidol. Outcomes: no usable data.
Kinross-Wright 1963	Allocation: not randomised.
Knights 1979	Allocation: not randomised.
Kong 1989	Allocation: not randomised.
Landmark 1994	Allocation: randomised. Participants: people with schizophrenia. Interventions: fluphenazine decanoate versus fluphenazine hydrochloride (oral). Outcomes: no usable data, no clinical outcomes reported.
Lapierre 1975	Allocation: randomised. Participants: people with schizophrenia. Interventions: fluphenazine versus pimozide. Outcomes: no usable data.
Lapierre 1976	Allocation: randomised. Participants: people with schizophrenia. Interventions: fluphenazine versus pimozide + half of each group received psychotherapy. Outcomes: no usable data.
Lapierre 1978	Allocation: randomised. Participants: people with schizophrenia. Interventions: oral fluphenazine versus penfluridol.
Lapierre 1983	Allocation: randomised. Participants: people with schizophrenia. Interventions: pipothiazine palmitate versus fluphenazine decanoate. Outcomes: no usable data.
Lasky 1962	Allocation: randomised. Participants: people with schizophrenia. Interventions: chlorpromazine versus thioridazine versus chlorprothixene versus triflupromazine. Outcomes: no usable data - drop outs > 50%.
Leff 1971	Allocation: randomised. Particpants: people with schizophrenia. Interventions: trifluperazine versus chlorpromazine.
Leff 1973	Allocation: randomised. Participants: people with schizophrenia. Interventions: maintenance therapy and life events.

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Levinson 1990	Allocation: randomised. Participants: people with schizophrenia. Interventions: fluphenazine 10, 20 mg/day for 24 days and fluphenazine 10, 20 and 30 mg/day for 28 days. Outcomes: no usable data.
Lewis 2003	Allocation: randomised. Participants: people with schizophrenia. Interventions: first generation antipsychotics versus second generation antipsychotics
Litman 1994	Allocation: double blind. Participants: people with schizophrenia. Interventions: fluphenazine versus benztropine (1st phase) and fluphenazine versus clozapine 92nd phase). Outcomes: no usable data.
Ljubin 2000	Allocation: randomised. Participants: people with schizophrenia. Interventions: oral fluphenazine versus olanzapine.
Mahmoud 2004	Allocation: randomised. Participants: people with schizophrenia. Interventions: risperidone versus conventional antipsychotics
Marder 1986	Allocation: randomised. Participants: people with schizophrenia. Interventions: fluphenazine decanoate (dosage study). Outcomes: no usable data.
Marder 1989	Allocation: randomised. Participants: people with schizophrenia. Interventions: fluphenazine decanoate versus fluphenazine (oral). Outcomes: no usable data, drug metabolism study - no clinical outcomes measured
Marder 1990a	Allocation: randomised. Participants: people with schizophrenia. Interventions: fluphenazine decanoate (dosage study). Outcomes: no usable data, authors contacted.
Marder 1991a	Allocation: randomised. Participants: people with schizophrenia. Interventions: fluphenazine decanoate (dosage study). Outcomes: no usable data, pharmacological study - no clinical outcomes reported
Marder 1991b	Allocattion: randomised. Participants: people with schizophrenia. Interventions: fluphenazine decanoate versus placebo. Outcomes: no usable data, trial of different measuring procedures

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Marder 1996	Allocation: randomised. Particpants: people with schizophrenia. Interventions: fluphenazine decanoate versus placebo. Outcomes: no usable data.
Marder 2002	Allocation: randomised. Particpants: people with schizophrenia. Interventions: low-dose fluphenazine decanoate versus medium dose fluphenazine decanoate versus high-dose fluphenazine decanoate. Outcomes: no usable data.
Martenyi 2000	Allocation: double blind. Participants: people with schizophrenia. Interventions: olanzapine versus fluphenazine. Outcomes: no usable data.
Martin 1972	Allocation: not randomised.
Mattes 1984	Allocation: double blind. Participants: people with schizophrenia. Interventions: lithium versus fluphenazine (oral and decanoate) versus placebo. Outcomes: no usable data.
McCreadie 1983	Allocation: not randomised.
McCreadie 1986	Allocation: double blind. Participants: people with schizophrenia. Interventions: haloperidol versus fluphenazine. Outcomes: no usable data.
Meco 1987	Allocation: not randomised but double blinded. Participants: people with schizophrenia. Interventions: fluphenazine decanoate versus haloperidol decanoate. Outcomes: no usable data, authors contacted.
Mimica 1998	Allocation: randomised. Participants: people with schizophrenia. Interventions: oral fluphenazine versus olanzapine.
Montejo 2010	Allocation: not randomised.
Morris 1970	Allocation: randomised - cross-over study.
National 1964	Allocation: “randomly assigned”. Participants: people with schizophrenia. Interventions: oral fluphenazine versus chlorpromazine versus thioridazine versus placebo

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Nestoros 1978	Allocation: “randomly assigned” Participants: people with schizophrenia. Interventions: oral fluphenazine versus butaclamol.
Owen 1993	Allocation: admitted sequentially - cross-over study.
Palma 1997	Allocation: randomised. Participants: people with schizophrenia. Interventions: flupenthixol decanoate versus other neuroleptics including fluphenazine decanoate. Outcomes: fluphenazine decanoate results not presented separately from the other neuroleptics
Pichot 1988	Allocation: randomised. Participants: people with schizophrenia. Interventions: oral fluphenazine versus amisulpride.
Pickar 1987	Allocation: review of studies.
Pickar 1992	Allocation: double blind - cross-over study.
Pickar 1994	Allocation: double blind - cross-over study.
Pollack 1964	Allocation: randomised. Partcipants: people with schizophrenia. Interventions: fluphenazine decanoate versus placebo. Outcomes: no usable data.
Preussler 1995	Allocation: randomised. Participants: people with schizophrenia. Interventions: clozapine versus fluphenazine. Outcomes: no usable data.
Preussler 1997	Allocation: randomised. Participants: people with schizophrenia. Interventions: clozapine versus fluphenazine. Outcomes: no usable data.
Quitkin 1975	Allocation: “randomly assigned”. Participants: people with schizophrenia. Interventions: oral fluphenazine (dosage study).
Quitkin 1977	Allocation: randomised. Participants: people with schizophrenia. Interventions: fluphenazine decanoate versus penfluridol. Outcomes: no usable data, preliminary report.
Ravaris 1965	Allocation: not randomised.

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Ravaris 1967	Allocation: randomised. Participants: people with schizophrenia. Interventions: fluphenazine enanthate versus fluphenazine (oral). Outcomes: no usable data.
Rifkin 1976	Allocation: randomised. Participants: people with schizophrenia. Interventions: fluphenazine decanoate versus fluphenazine (oral) versus placebo. Outcomes: no usable data.
Roose 1982	Allocation: not randomised.
Rossger 1997	Allocation: randomised. Participants: people with schizophrenia. Interventions: clozapine versus fluphenazine. Outcomes: no usable data.
Saxena 1996	Allocation: non-specific - authors contacted (conference abstract)
Schausberger 1999	Allocation: randomised. Participants: people with schizophrenia. Interventions: oral fluphenazine versus olanzapine.
Schipper 1971	Allocation: not randomised.
Schooler 1971	Allocation: randomised. Participants: people with schizophrenia. Interventions: acetophenazine maleate versus chlorpromazine versus fluphenazine hydrochloride. Outcomes: no usable data.
Schooler 1977	Allocation: not randomised - double blinded.
Schubert 1988	Allocation: randomised. Participants: people with schizophrenia. Interventions: fluphenazine versus haloperidol. Outcomes: no usable data.
Shafti 2009	Allocation: randomised. Participants: people with schizophrenia. Interventions: fluphenazine versus placebo as add-on to olanzapine
Simpson 1970	Allocation: randomised. Participants: people with schizophrenia. Interventions: fluphenazine. Outcomes: no usable data.
Siris 1990	Allocation: randomised. Participants: people with schizophrenia. Interventions: imipramine versus placebo as add-on to fluphenazine decanoate and benztropine

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Siris 1991	Allocation: randomised. Participants: people with schizophrenia. Interventions: imipramine versus placebo as add-on to fluphenazine decanoate and benztropine
Steingard 1994	Allocation: randomised. Participants: people with schizophrenia. Interventions: fluphenazine versus placebo. Outcomes: no usable data.
Stevens 1973	Allocation: randomised. Participants: people with schizophrenia. Interventions: fluphenazine decanoate versus placebo. Outcomes: no usable data.
Tegeler 1985	Allocation: randomised. Participants: people with schizophrenia. Interventions: fluphenazine decanoate versus clopenthixol decanoate. Outcomes: no usable data, authors contacted.
Tetreault 1969	Allocation: randomised. Participants: people with schizophrenia. Interventions: fluphenazine enanthate versus oral fluphenazine bichloralhydrate
Tran 1998	Allocation: randomised. Participants: people with schizophrenia. Interventions: olanzapine versus fluphenazine. Outcomes: no usable data.
Tsai 2004	Allocation: randomised. Participants: people with schizophrenia. Interventions: sarcosine versus placebo as add-on to antipsychotics
Tsai 2006	Allocation: randomised. Participants: people with schizophrenia. Interventions: D-alanine versus placebo as add-on to antipsychotics as add-on to antipsychotics
Turner 1966	Allocation: randomised. Participants: not described.
Turner 2004	Allocation: not randomised.
Ushakov 1990	Allocation: not randomised, case series.
van Putten 1986	Allocation: randomised. Participants: people with schizophrenia. Interventions: 1st report - haloperidol (dosage study), 2nd report - fluphenazine (dosage study). Outcomes: no usable data.

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van Putten 1991	Allocation: randomised. Participants: people with schizophrenia. Interventions: fluphenazine (dosage study). Outcomes: no usable data.
Verster 1998	Allocation: randomised. Participants: people with schizophrenia. Interventions: fluphenazine decanoate versus generic substitute
Vestre 1962	Allocation: randomised. Participants: people with schizophrenia. Interventions: oral fluphenazine versus triflupromazine versus phenobarbital
Viala 1988	Allocation: not randomised.
Villeneuve 1970	Allocation: not randomised.
Vinar 1970	Allocation: double blind. Participants: people with schizophrenia. Interventions: fluphenazine versus fluphenazine long-acting form. Outcomes: no usable data.
Weiden 1993	Allocation: randomised. Participants: people with schizophrenia. Interventions: fluphenazine decanoate (dosage study). Outcomes: no usable data, prescribing patterns study.
Wiles 1990	Allocation: double blind. Participants: people with schizophrenia. Interventions: haloperidol decanoate versus fluphenazine decanoate. Outcomes: no usable data, authors contacted.
Winter 1973	Allocation: randomised. Participants: people with schizophrenia. Interventions: fluphenazine decanoate versus fluspirilene decanoate. Outcomes: no usable data.
Wistedt 1981	Allocation: randomised. Participants: people with schizophrenia. Interventions: fluphenazine decanoate and flupenthixol decanoate versus placebo. Outcomes: no usable data, the two drug treatments are grouped as one group
Wistedt 1983a	Allocation: randomised. Participants: people with schizophrenia. Interventions: fluphenazine decanoate and flupenthixol decanoate versus placebo. Outcomes: no usable data - both drugs placed in one group.

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Wistedt 1983b	Allocation: randomised. Participants: people with schizophrenia. Interventions: discontinuation study.
Zapletalek 1981	Allocation: not randomised.

Characteristics of studies awaiting assessment *[ordered by study ID]*

Angst 1973

Methods	
Participants	
Interventions	
Outcomes	
Notes	Article in German

del Giudice 1970

Methods	
Participants	
Interventions	
Outcomes	
Notes	Missing PDF

Jue 1996

Methods	
Participants	
Interventions	
Outcomes	
Notes	Missing PDF

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Kabes 1984

Methods	
Participants	
Interventions	
Outcomes	
Notes	Missing PDF

Ravanic 1996

Methods	
Participants	
Interventions	
Outcomes	
Notes	Missing PDF

Ushakov 1990a

Methods	Unclear
Participants	People with schizophrenia
Interventions	1. Fluphenazine decanoate (moditen-depot) 2. haloperidol decanoate
Outcomes	Efficacy
Notes	Article in Russian

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DATA AND ANALYSES

Comparison 1. FLUPHENAZINE DECANOATE vs PLACEBO

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Death	1	54	Risk Ratio (M-H, Fixed, 95% CI)	5.0 [0.25, 99.51]
2 Global state: 1. Relapse	5		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 short term (6 weeks to 5 months)	1	31	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
2.2 medium term (6 months to 1 year)	3	196	Risk Ratio (M-H, Random, 95% CI)	0.62 [0.24, 1.60]
2.3 longer term (more than 1 year)	1	54	Risk Ratio (M-H, Random, 95% CI)	0.35 [0.19, 0.64]
3 Global state: 2. GAS (short term - 6 weeks to 5 months) (high score = worse)	1	28	Mean Difference (IV, Fixed, 95% CI)	3.61 [-4.41, 11.63]
4 Leaving the study early	6		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
4.1 short term (6 weeks to 5 months)	1	31	Risk Ratio (M-H, Fixed, 95% CI)	2.43 [0.24, 24.07]
4.2 medium term (6 months to 1 year)	4	216	Risk Ratio (M-H, Fixed, 95% CI)	1.30 [0.77, 2.19]
4.3 longer term (more than 1 year)	1	54	Risk Ratio (M-H, Fixed, 95% CI)	0.47 [0.23, 0.96]
5 Mental state: 1. BPRS (endpoint scores - high score = worse)	1	16	Mean Difference (IV, Fixed, 95% CI)	-2.03 [-4.51, 0.45]
6 Mental state: 2. Depression (medium term - 6 months to 1 year)	1	70	Risk Ratio (M-H, Fixed, 95% CI)	1.0 [0.45, 2.22]
7 Adverse effects: 1. Movement disorders - tardive dyskinesia (longer term - more than 1 year)	1	54	Risk Ratio (M-H, Fixed, 95% CI)	0.83 [0.62, 1.11]
8 Adverse effects: 2. Toxicity	1	45	Risk Ratio (M-H, Fixed, 95% CI)	7.65 [1.04, 56.26]

Comparison 2. FLUPHENAZINE DECANOATE vs ORAL NEUROLEPTICS

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Global state: 1. No clinically important global change	3		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
1.1 immediate (0 to 5 weeks)	2	74	Risk Ratio (M-H, Fixed, 95% CI)	0.61 [0.46, 0.81]
1.2 medium term (6 months to 1 year)	1	102	Risk Ratio (M-H, Fixed, 95% CI)	0.85 [0.56, 1.27]
2 Global state: 2. Relapse	9		Risk Ratio (M-H, Random, 95% CI)	Subtotals only

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2.1 medium term (6 months to 1 year)	6	419	Risk Ratio (M-H, Random, 95% CI)	1.46 [0.75, 2.83]
2.2 longer term (more than 1 year)	3	216	Risk Ratio (M-H, Random, 95% CI)	1.25 [0.81, 1.95]
3 Global state: 3. Clinical Global Impression (short term - 6 weeks to 5 months) (high score = worse)	1	34	Mean Difference (IV, Fixed, 95% CI)	-0.10 [-2.79, 2.59]
4 Leaving the study early	14		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
4.1 immediate (0-5 weeks)	1	37	Risk Ratio (M-H, Fixed, 95% CI)	0.32 [0.01, 7.30]
4.2 short term (6 weeks to 5 months)	1	34	Risk Ratio (M-H, Fixed, 95% CI)	1.69 [0.32, 8.85]
4.3 medium term (6 months to 1 year)	10	937	Risk Ratio (M-H, Fixed, 95% CI)	0.96 [0.73, 1.25]
4.4 longer term (more than 1 year)	2	164	Risk Ratio (M-H, Fixed, 95% CI)	1.20 [0.61, 2.36]
5 Behaviour: 1. NOSIE-30 - endpoint scores (high score = poor)	1	120	Mean Difference (IV, Fixed, 95% CI)	-0.56 [-6.92, 5.80]
6 Behaviour: 2. skewed data (endpoint scores)			Other data	No numeric data
7 Mental state: 1. BPRS - endpoint scores (longer term - more than 1 year) (high score = poor)	1	120	Mean Difference (IV, Fixed, 95% CI)	-0.75 [-5.75, 4.25]
8 Mental state: 2. Depression	2		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
8.1 medium term (6 months to 1 year)	1	214	Risk Ratio (M-H, Fixed, 95% CI)	0.89 [0.60, 1.32]
8.2 longer term (more than 1 year)	1	44	Risk Ratio (M-H, Fixed, 95% CI)	1.53 [0.91, 2.57]
9 Adverse effects: 1a. Movement disorders - general	4		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
9.1 medium term (6 months to 1 year)	3	259	Risk Ratio (M-H, Fixed, 95% CI)	0.47 [0.24, 0.91]
9.2 longer term (more than 1 year)	1	44	Risk Ratio (M-H, Fixed, 95% CI)	0.4 [0.12, 1.28]
10 Adverse effects: 1b. Movement disorders - akathisia	1	51	Risk Ratio (M-H, Fixed, 95% CI)	20.54 [1.25, 337.94]
11 Adverse effects: 1c. Movement disorders - needing anticholinergic drugs	4		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
11.1 immediate (0 to 5 weeks)	1	37	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
11.2 medium term (6 months to 1 year)	2	231	Risk Ratio (M-H, Random, 95% CI)	0.86 [0.21, 3.45]
11.3 longer term (more than 1 year)	1	120	Risk Ratio (M-H, Random, 95% CI)	1.04 [0.86, 1.25]
12 Adverse effects: 1d. Movement disorders - tardive dyskinesia	2		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
12.1 medium term (6 months to 1 year)	1	28	Risk Ratio (M-H, Fixed, 95% CI)	0.62 [0.41, 0.93]
12.2 longer term (more than 1 year)	1	120	Risk Ratio (M-H, Fixed, 95% CI)	0.16 [0.01, 2.99]

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13 Adverse effects: 1e. Movement disorders - tremor (longer term - more than 1 year)	1	44	Risk Ratio (M-H, Fixed, 95% CI)	0.8 [0.26, 2.45]
14 Adverse effects: 1f. Movement disorders - average score (Simpson & Angus, 0 to 5 weeks, high = poor)	1	32	Mean Difference (IV, Fixed, 95% CI)	1.3 [0.01, 2.59]
15 Adverse effects: 2. Blurred vision - medium term (6 months to 1 year)	1	197	Risk Ratio (M-H, Fixed, 95% CI)	1.34 [0.75, 2.38]
16 Adverse effects: 3. Toxicity - medium term (6 months to 1 year)	1	51	Risk Ratio (M-H, Fixed, 95% CI)	4.87 [1.14, 20.72]
17 Adverse effects: 4. General adverse effects	3		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
17.1 immediate (0 to 5 weeks)	1	37	Risk Ratio (M-H, Fixed, 95% CI)	4.75 [0.24, 92.65]
17.2 medium term (6 months to 1 year)	2	242	Risk Ratio (M-H, Fixed, 95% CI)	0.98 [0.70, 1.37]
18 SENSITIVITY ANALYSIS Global state: 2. Relapse	6		Risk Ratio (M-H, Random, 95% CI)	Subtotals only

Comparison 3. FLUPHENAZINE DECANOATE vs OTHER DEPOT NEUROLEPTICS

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Death	1	38	Risk Ratio (M-H, Fixed, 95% CI)	3.0 [0.13, 69.31]
2 Global state: 1. No clinically important global change	4	339	Risk Ratio (M-H, Fixed, 95% CI)	1.07 [0.97, 1.18]
2.1 short term (6 weeks to 5 months)	1	152	Risk Ratio (M-H, Fixed, 95% CI)	1.16 [0.89, 1.51]
2.2 medium term (6 months to 1 year)	3	187	Risk Ratio (M-H, Fixed, 95% CI)	1.04 [0.96, 1.12]
3 Global state: 2. Relapse	16		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
3.1 short term (6 weeks to 5 months)	1	51	Risk Ratio (M-H, Fixed, 95% CI)	0.96 [0.27, 3.43]
3.2 medium term (6 months to 1 year)	11	581	Risk Ratio (M-H, Fixed, 95% CI)	0.82 [0.56, 1.18]
3.3 longer term (more than 1 year)	4	252	Risk Ratio (M-H, Fixed, 95% CI)	1.22 [0.77, 1.92]
4 Global state: 3. Severly ill (medium term 6 months to 1 year)	1	60	Risk Ratio (M-H, Fixed, 95% CI)	1.07 [0.94, 1.23]
5 Global state: 4. Needing additional antipsychotic treatment (6 months to 1 year)	2	91	Risk Ratio (M-H, Fixed, 95% CI)	0.53 [0.14, 1.96]

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6 Global state: 5. Clinical Global Impression. (short term - 6 weeks to 5 months) (skewed data)			Other data	No numeric data
7 Global state: 6. Clinical Global Impression. (medium term - 6 months to 1 year)	2	90	Mean Difference (IV, Fixed, 95% CI)	-0.10 [-0.41, 0.21]
8 Global state: 7. Clinical Global Impression - not improved (high score = poor)	2		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
8.1 short term (6 weeks to 5 months)	1	50	Risk Ratio (M-H, Fixed, 95% CI)	2.5 [0.53, 11.70]
8.2 medium term (6 months to 1 year)	1	60	Risk Ratio (M-H, Fixed, 95% CI)	0.75 [0.18, 3.07]
9 Leaving the study early	23		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
9.1 immediate (0 to 5 weeks)	1	12	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
9.2 short term (6 weeks to 5 months)	3	233	Risk Ratio (M-H, Fixed, 95% CI)	0.76 [0.32, 1.84]
9.3 medium term (6 months to 1 year)	15	775	Risk Ratio (M-H, Fixed, 95% CI)	1.13 [0.89, 1.44]
9.4 By more than 1 year	5	319	Risk Ratio (M-H, Fixed, 95% CI)	0.89 [0.64, 1.23]
10 Behaviour: 1. NOSIE-30 - endpoint scores (high score = poor)	1	118	Mean Difference (IV, Fixed, 95% CI)	-5.21 [-10.85, 0.43]
11 Mental state: 1. BPRS (endpoint scores - high score = poor)	7		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
11.1 short term (6 weeks to 5 months)	2	203	Mean Difference (IV, Fixed, 95% CI)	1.11 [0.86, 1.36]
11.2 medium term (6 months to 1 year)	3	162	Mean Difference (IV, Fixed, 95% CI)	1.20 [1.10, 1.30]
11.3 longer term (more than one year)	2	141	Mean Difference (IV, Fixed, 95% CI)	0.85 [-2.32, 4.03]
12 Mental state: 2. BPRS (endpoint scores 6 months to 1 year - dichotomous data)	1	67	Risk Ratio (M-H, Fixed, 95% CI)	0.91 [0.59, 1.43]
13 Mental state: 3. Depression (6 months to 1 year)	1	67	Risk Ratio (M-H, Fixed, 95% CI)	1.02 [0.81, 1.28]
14 Mental state: 4. SAPS and SANS (endpoint scores - high score = poor) (skewed data)			Other data	No numeric data
14.1 SAPS			Other data	No numeric data
14.2 SANS			Other data	No numeric data
15 Adverse effects: 1a. Movement disorders - general	7	308	Risk Ratio (M-H, Fixed, 95% CI)	1.11 [0.91, 1.35]
15.1 immediate term (0 to 5 weeks)	1	12	Risk Ratio (M-H, Fixed, 95% CI)	0.93 [0.24, 3.68]
15.2 short term (6 weeks to 5 months)	1	30	Risk Ratio (M-H, Fixed, 95% CI)	2.0 [0.43, 9.32]
15.3 medium term (6 months to 1 year)	4	234	Risk Ratio (M-H, Fixed, 95% CI)	1.08 [0.86, 1.34]

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15.4 longer term (more than 1 year)	1	32	Risk Ratio (M-H, Fixed, 95% CI)	1.13 [0.76, 1.69]
16 Adverse effects: 1b. Movement disorders - needing anticholinergic drugs	12		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
16.1 short term (6 weeks to 5 months)	1	51	Risk Ratio (M-H, Random, 95% CI)	1.48 [0.96, 2.28]
16.2 medium term (6 months to 1 year)	8	448	Risk Ratio (M-H, Random, 95% CI)	1.24 [0.93, 1.64]
16.3 longer term (more than 1 year)	3	220	Risk Ratio (M-H, Random, 95% CI)	1.26 [0.86, 1.83]
17 Adverse effects: 1c. Movement disorders - parkinsonism	3	190	Risk Ratio (M-H, Fixed, 95% CI)	1.12 [0.47, 2.69]
17.1 immediate (0 to 5 weeks)	1	12	Risk Ratio (M-H, Fixed, 95% CI)	0.93 [0.24, 3.68]
17.2 medium term (6 months to 1 year)	1	60	Risk Ratio (M-H, Fixed, 95% CI)	1.25 [0.37, 4.21]
17.3 longer term (more than 1 year)	1	118	Risk Ratio (M-H, Fixed, 95% CI)	1.07 [0.07, 16.71]
18 Adverse effects: 1d. Movement disorders - tardive dyskinesia: longer term (more than 1 year)	2	150	Risk Ratio (M-H, Fixed, 95% CI)	0.62 [0.32, 1.23]
19 Adverse effects: 1e. Movement disorders - tremor	5		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
19.1 short term (6 weeks to 5 months)	2	80	Risk Ratio (M-H, Fixed, 95% CI)	1.36 [0.76, 2.46]
19.2 medium term (6 months to 1 year)	3	152	Risk Ratio (M-H, Fixed, 95% CI)	1.14 [0.73, 1.78]
20 Adverse effects: 1f. Movement disorders - endpoint scores (short term - 6 weeks to 5 months)			Other data	No numeric data
20.1 TESS (high = poor)			Other data	No numeric data
20.2 RSESE (high = poor)			Other data	No numeric data
21 Adverse effects: 2. Blurred vision	2		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
21.1 medium term (6 months to 1 year)	1	32	Risk Ratio (M-H, Fixed, 95% CI)	0.88 [0.44, 1.78]
21.2 longer term (more than 1 year)	1	64	Risk Ratio (M-H, Fixed, 95% CI)	17.88 [1.08, 294.82]
22 Adverse effects: 3. Dry mouth: longer term (more than 1 year)	1	32	Risk Ratio (M-H, Fixed, 95% CI)	0.72 [0.38, 1.37]
23 Adverse effects: 4. General adverse effects	7		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
23.1 short term (6 weeks to 5 months)	2	88	Risk Ratio (M-H, Fixed, 95% CI)	1.36 [1.07, 1.74]
23.2 medium term (6 months to 1 year)	5	249	Risk Ratio (M-H, Fixed, 95% CI)	1.04 [0.83, 1.32]
24 SENSITIVITY ANALYSIS Global state: 2. Relapse	11		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only

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24.1 medium term (6 months to 1 year)	11	581	Risk Ratio (M-H, Fixed, 95% CI)	0.82 [0.56, 1.18]

Comparison 4. FLUPHENAZINE DECANOATE - DOSAGE STUDIES - HIGH DOSE vs STANDARD

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Global state: 1. Relapse (medium term - 6 months to 1 year)	2	182	Risk Ratio (M-H, Random, 95% CI)	2.11 [0.30, 14.91]
2 Global state: 2. Needing additional antispsychotic treatment (medium term - 6 months to 1 year)	1	50	Risk Ratio (M-H, Fixed, 95% CI)	1.67 [0.45, 6.24]
3 Global state: 3. Not improved (medium term - 6 months to 1 year)	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
3.1 nurse rated	1	40	Risk Ratio (M-H, Fixed, 95% CI)	1.58 [1.09, 2.30]
3.2 psychiatrist rated	1	40	Risk Ratio (M-H, Fixed, 95% CI)	1.15 [0.77, 1.74]
4 Leaving the study early (medium term - 6 months to 1 year)	2	90	Risk Ratio (M-H, Fixed, 95% CI)	0.6 [0.15, 2.36]
5 Mental state: BPRS endpoint scores (medium term - 6 months to 1 year, high score = poor)	1	50	Mean Difference (IV, Fixed, 95% CI)	-0.03 [-5.79, 5.73]
6 Adverse effects: Movement disorders - needing anticholinergic drugs (medium term - 6 months to 1 year)	1	50	Risk Ratio (M-H, Fixed, 95% CI)	1.67 [0.45, 6.24]

Comparison 5. FLUPHENAZINE DECANOATE - DOSAGE STUDIES - LOW DOSE vs STANDARD

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Global state: Relapse	6		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
1.1 medium term (6 months to 1 year)	3	471	Risk Ratio (M-H, Random, 95% CI)	3.33 [0.77, 14.51]
1.2 longer term (more than 1 year)	3	172	Risk Ratio (M-H, Random, 95% CI)	0.84 [0.38, 1.89]
2 Leaving the study early	3		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
2.1 longer term (more than 1 year)	3	172	Risk Ratio (M-H, Fixed, 95% CI)	0.67 [0.33, 1.36]
3 Adverse effects: 1. Movement disorders (medium term - 6 months to 1 year)	2		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
3.1 Tardive dyskinesia	1	126	Risk Ratio (M-H, Fixed, 95% CI)	0.52 [0.10, 2.72]

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3.2 Needing anticholinergic drugs	1	50	Risk Ratio (M-H, Fixed, 95% CI)	2.55 [0.72, 9.05]
4 Adverse effects: 2. Continuous data - skewed data (endpoint scores, high = poor)			Other data	No numeric data

Comparison 6. FLUPHENAZINE ENANTHATE vs PLACEBO

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Adverse effects: Movement disorders - general	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
1.1 Needing anticholinergic drugs (short term - 6 weeks to 5 months)	1	25	Risk Ratio (M-H, Fixed, 95% CI)	9.69 [0.58, 163.02]

Comparison 7. FLUPHENAZINE ENANTHATE vs ORAL NEUROLEPTICS

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Global state: No clinically important global change (immediate - 0 to 5 weeks)	1	31	Risk Ratio (M-H, Fixed, 95% CI)	0.67 [0.27, 1.66]
2 Adverse effects: Movement disorders - general	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
2.1 movement disorders: immediate (0 to 5 weeks)	1	31	Risk Ratio (M-H, Fixed, 95% CI)	2.34 [0.53, 10.30]
2.2 side effects: immediate (0 to 5 weeks)	1	31	Risk Ratio (M-H, Fixed, 95% CI)	2.81 [0.94, 8.45]
2.3 parkinsonism: immediate (0 to 5 weeks)	1	31	Risk Ratio (M-H, Fixed, 95% CI)	6.56 [0.91, 47.21]

Comparison 8. FLUPHENAZINE ENANTHATE vs OTHER DEPOT NEUROLEPTICS

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Global state: 1. Needing additional antipsychotic treatment (6 months to 1 year)	2	65	Risk Ratio (M-H, Fixed, 95% CI)	0.5 [0.24, 1.05]
2 Global state: 2. Relapse	2		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only

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2.1 short term (6 weeks to 5 months)	1	57	Risk Ratio (M-H, Fixed, 95% CI)	2.38 [0.66, 8.61]
2.2 medium term (6 months to 1 year)	1	32	Risk Ratio (M-H, Fixed, 95% CI)	0.33 [0.04, 2.87]
3 Leaving the study early	3		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
3.1 immediate (0 to 5 weeks)	1	30	Risk Ratio (M-H, Fixed, 95% CI)	0.09 [0.01, 0.62]
3.2 short term (6 weeks to 5 months)	1	57	Risk Ratio (M-H, Fixed, 95% CI)	2.38 [0.66, 8.61]
3.3 medium term (6 months to 1 year)	1	32	Risk Ratio (M-H, Fixed, 95% CI)	0.33 [0.04, 2.87]
4 Mental state: 1. BPRS - endpoint scores (medium term - 6 months to 1 year) (high score = poor)	1	30	Mean Difference (IV, Fixed, 95% CI)	0.40 [0.34, 0.46]
5 Mental state: 2. Depression (medium term - 6 months to 1 year)	1	30	Risk Ratio (M-H, Fixed, 95% CI)	7.0 [0.39, 124.83]
6 Adverse effects: 1a. Movement disorders - general (medium term - 6 months to 1 year)	2	63	Risk Ratio (M-H, Fixed, 95% CI)	1.52 [0.75, 3.07]
7 Adverse effects: 1b. Movement disorders - needing additional anticholinergic drugs	3		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
7.1 short term (6 weeks to 5 months)	1	57	Risk Ratio (M-H, Fixed, 95% CI)	2.86 [1.16, 7.06]
7.2 medium term (6 months to 1 year)	2	65	Risk Ratio (M-H, Fixed, 95% CI)	1.02 [0.76, 1.35]
8 Adverse effects: 1c. Movement disorders - tardive dyskinesia: medium term (6 months to 1 year)	1	32	Risk Ratio (M-H, Fixed, 95% CI)	0.89 [0.46, 1.71]
9 Adverse effects: 1d. Movement disorders - tremor (medium term - 6 months to 1 year)	3	95	Risk Ratio (M-H, Fixed, 95% CI)	1.24 [0.82, 1.87]
10 Adverse effects: 2. Blurred vision (medium term - 6 months to 1 year)	1	30	Risk Ratio (M-H, Fixed, 95% CI)	3.0 [0.13, 68.26]
11 Adverse effects: 3. Dry mouth (medium term - 6 months to 1 year)	2	62	Risk Ratio (M-H, Fixed, 95% CI)	0.8 [0.36, 1.76]

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Comparison 9. FLUPHENAZINE ENANTHATE - DOSAGE STUDIES - LOW DOSE vs INTERMEDIATE/HIGH DOSE

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Global state: Relapse (short term - 6 weeks to 5 months)	1	104	Risk Ratio (M-H, Fixed, 95% CI)	9.35 [2.28, 38.29]
2 Leaving the study early (short term - 6 weeks to 5 months)	1	104	Risk Ratio (M-H, Fixed, 95% CI)	3.12 [0.66, 14.74]

Comparison 10. FLUPHENAZINE DECANAOTE vs FLUPHENAZINE ENANTHATE

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Global state: 1. Needing additional antipsychotic treatment	2		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
1.1 immediate (0 to 5 weeks)	1	33	Risk Ratio (M-H, Fixed, 95% CI)	0.39 [0.18, 0.86]
1.2 mediium term (6 months to 1 year)	1	48	Risk Ratio (M-H, Fixed, 95% CI)	1.0 [0.15, 6.53]
2 Global state: 2. Relapse	4		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
2.1 immediate (0 to 5 weeks)	2	44	Risk Ratio (M-H, Fixed, 95% CI)	0.66 [0.18, 2.43]
2.2 short term (6 weeks to 5 months)	1	30	Risk Ratio (M-H, Fixed, 95% CI)	2.29 [0.70, 7.48]
2.3 medium term (6 months to 1 year)	1	49	Risk Ratio (M-H, Fixed, 95% CI)	2.43 [0.71, 8.32]
3 Behavioiur: Leaving the study early	5		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
3.1 immediate (0 to 5 weeks)	2	44	Risk Ratio (M-H, Fixed, 95% CI)	0.66 [0.18, 2.43]
3.2 short term (6 weeks to 5 months)	2	42	Risk Ratio (M-H, Fixed, 95% CI)	2.29 [0.70, 7.48]
3.3 medium term (6 months to 1 year)	1	49	Risk Ratio (M-H, Fixed, 95% CI)	2.43 [0.71, 8.32]
4 Mental State: BPRS medium term (6 months to 1 year - high score = poor)	1	39	Mean Difference (IV, Fixed, 95% CI)	0.0 [-3.93, 3.93]
5 Adverse effects: 1a. Movement disorders - general	3		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
5.1 Immediate (0 to 5 weeks)	1	49	Risk Ratio (M-H, Fixed, 95% CI)	2.65 [0.82, 8.64]
5.2 short term (6 weeks to 5 months)	2	49	Risk Ratio (M-H, Fixed, 95% CI)	1.14 [0.79, 1.64]
6 Adverse effects: 1b. Movement disorders - needing anticholinergic drugs	4		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
6.1 immediate (0 to 5 weeks)	1	33	Risk Ratio (M-H, Fixed, 95% CI)	0.29 [0.12, 0.70]

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6.2 short term (6 weeks to 5 months)	1	30	Risk Ratio (M-H, Fixed, 95% CI)	0.99 [0.82, 1.20]
6.3 medium term (6 months to 1 year)	2	97	Risk Ratio (M-H, Fixed, 95% CI)	0.78 [0.57, 1.07]
7 Adverse effects: 1c. Movement disorders - parkinsonism (short term - 6 weeks to 5 months)	1	19	Risk Ratio (M-H, Fixed, 95% CI)	0.37 [0.02, 8.01]
8 Adverse effects: 1d. Movement disorders - akathisia (Immediate - 0 to 5 weeks)	1	49	Risk Ratio (M-H, Fixed, 95% CI)	6.19 [0.82, 46.62]
9 Adverse effects: 2. General adverse effects (immediate - 0 to 5 weeks)	1	11	Risk Ratio (M-H, Fixed, 95% CI)	0.08 [0.01, 1.14]

Comparison 11. FLUPHENAZINE DECANOATE - DOSAGE STUDIES - 2 WEEKS vs 6 WEEKS

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Global state: 1. Relapse (1 year)	1	37	Risk Ratio (M-H, Random, 95% CI)	0.89 [0.55, 1.44]
2 Leaving the study early (1 year)	1	50	Risk Ratio (M-H, Fixed, 95% CI)	1.17 [0.46, 2.98]
3 Mental state: 1. BPRS - endpoint scores (1 year) (high score = poor)	1		Mean Difference (Fixed, 95% CI)	Subtotals only
3.1 Total	1	37	Mean Difference (Fixed, 95% CI)	2.72 [-1.16, 6.60]
3.2 Thought disorder	1	37	Mean Difference (Fixed, 95% CI)	-0.39 [-1.51, 0.73]
4 Adverse effects: 1. Movement disorders - MPRC (1 year, high = poor)	1		Mean Difference (Fixed, 95% CI)	Subtotals only
4.1 Parkinsonian symptoms	1	37	Mean Difference (Fixed, 95% CI)	1.3 [-0.03, 2.63]
4.2 Dyskinesia	1	37	Mean Difference (Fixed, 95% CI)	2.4 [-1.77, 6.57]
5 Quality of life: Quality of life scale (1 year) (high score = good)	1	37	Mean Difference (Fixed, 95% CI)	1.42 [-9.68, 12.52]

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Analysis 1.1. Comparison 1 FLUPHENAZINE DECANOATE vs PLACEBO, Outcome 1 Death.

Review: Fluphenazine decanoate (depot) and enanthate for schizophrenia

Comparison: 1 FLUPHENAZINE DECANOATE vs PLACEBO

Outcome: 1 Death

Study or subgroup	FLUPHENAZINE DECANOATE n/N	PLACEBO n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Jolley 1990	2/27	0/27		100.0 %	5.00 [0.25, 99.51]
Total (95% CI)	**27**	**27**		**100.0 %**	**5.00 [0.25, 99.51]**

Total events: 2 (FLUPHENAZINE DECANOATE), 0 (PLACEBO)

Heterogeneity: not applicable

Test for overall effect: Z = 1.05 (P = 0.29)

Test for subgroup differences: Not applicable

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Analysis 1.2. Comparison 1 FLUPHENAZINE DECANOATE vs PLACEBO, Outcome 2 Global state: 1. Relapse.

Review: Fluphenazine decanoate (depot) and enanthate for schizophrenia

Comparison: 1 FLUPHENAZINE DECANOATE vs PLACEBO

Outcome: 2 Global state: 1. Relapse

Study or subgroup	FLUPHENAZINE DECANOATE n/N	PLACEBO n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
1 short term (6 weeks to 5 months)					
Shenoy 1981	0/14	0/17			Not estimable
Subtotal (95% CI)	**14**	**17**			**Not estimable**
Total events: 0 (FLUPHENAZINE DECANOATE), 0 (PLACEBO)					
Heterogeneity: not applicable					
Test for overall effect: not applicable					
2 medium term (6 months to 1 year)					
Hirsch 1975	7/40	28/41		30.6 %	0.26 [0.13, 0.52]
Odejide 1982	15/35	23/35		34.0 %	0.65 [0.42, 1.02]
Rifkin 1977	20/23	15/22		35.3 %	1.28 [0.92, 1.77]
Subtotal (95% CI)	**98**	**98**		**100.0 %**	**0.62 [0.24, 1.60]**
Total events: 42 (FLUPHENAZINE DECANOATE), 66 (PLACEBO)					
Heterogeneity: $Tau^2 = 0.63$; $Chi^2 = 24.16$, df = 2 (P<0.00001); $I^2 = 92\%$					
Test for overall effect: Z = 0.99 (P = 0.32)					
3 longer term (more than 1 year)					
Jolley 1990	8/27	23/27		100.0 %	0.35 [0.19, 0.64]
Subtotal (95% CI)	**27**	**27**		**100.0 %**	**0.35 [0.19, 0.64]**
Total events: 8 (FLUPHENAZINE DECANOATE), 23 (PLACEBO)					
Heterogeneity: not applicable					
Test for overall effect: Z = 3.44 (P = 0.00059)					

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Analysis 1.3. Comparison 1 FLUPHENAZINE DECANOATE vs PLACEBO, Outcome 3 Global state: 2. GAS (short term - 6 weeks to 5 months) (high score = worse).

Review: Fluphenazine decanoate (depot) and enanthate for schizophrenia

Comparison: 1 FLUPHENAZINE DECANOATE vs PLACEBO

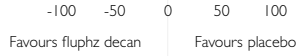
Outcome: 3 Global state: 2. GAS (short term - 6 weeks to 5 months) (high score = worse)

Study or subgroup	FLUPHENAZINE DECANOATE N	Mean(SD)	PLACEBO N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Shenoy 1981	12	67.17 (10.7041)	16	63.56 (10.72)		100.0 %	3.61 [-4.41, 11.63]
Total (95% CI)	**12**		**16**			**100.0 %**	**3.61 [-4.41, 11.63]**

Heterogeneity: not applicable

Test for overall effect: Z = 0.88 (P = 0.38)

Test for subgroup differences: Not applicable



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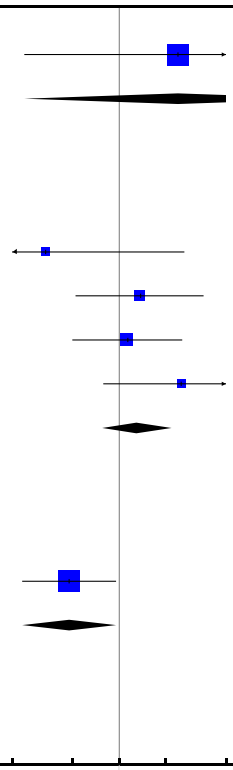
Analysis 1.4. Comparison 1 FLUPHENAZINE DECANOATE vs PLACEBO, Outcome 4 Leaving the study early.

Review: Fluphenazine decanoate (depot) and enanthate for schizophrenia

Comparison: 1 FLUPHENAZINE DECANOATE vs PLACEBO

Outcome: 4 Leaving the study early

Study or subgroup	FLUPHENAZINE DECANOATE n/N	PLACEBO n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
1 short term (6 weeks to 5 months)					
Shenoy 1981	2/14	1/17		100.0 %	2.43 [0.24, 24.07]
Subtotal (95% CI)	**14**	**17**		**100.0 %**	**2.43 [0.24, 24.07]**
Total events: 2 (FLUPHENAZINE DECANOATE), 1 (PLACEBO)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.76 (P = 0.45)					
2 medium term (6 months to 1 year)					
Dotti 1979	1/10	3/10		15.0 %	0.33 [0.04, 2.69]
Hirsch 1975	8/40	6/41		29.6 %	1.37 [0.52, 3.59]
Odejide 1982	9/35	8/35		40.0 %	1.13 [0.49, 2.58]
Rifkin 1977	8/23	3/22		15.3 %	2.55 [0.78, 8.39]
Subtotal (95% CI)	**108**	**108**		**100.0 %**	**1.30 [0.77, 2.19]**
Total events: 26 (FLUPHENAZINE DECANOATE), 20 (PLACEBO)					
Heterogeneity: Chi^2 = 2.99, df = 3 (P = 0.39); I^2 =0.0%					
Test for overall effect: Z = 0.97 (P = 0.33)					
3 longer term (more than 1 year)					
Jolley 1990	7/27	15/27		100.0 %	0.47 [0.23, 0.96]
Subtotal (95% CI)	**27**	**27**		**100.0 %**	**0.47 [0.23, 0.96]**
Total events: 7 (FLUPHENAZINE DECANOATE), 15 (PLACEBO)					
Heterogeneity: not applicable					
Test for overall effect: Z = 2.07 (P = 0.038)					



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Analysis 1.5. Comparison 1 FLUPHENAZINE DECANOATE vs PLACEBO, Outcome 5 Mental state: 1. BPRS (endpoint scores - high score = worse).

Review: Fluphenazine decanoate (depot) and enanthate for schizophrenia

Comparison: 1 FLUPHENAZINE DECANOATE vs PLACEBO

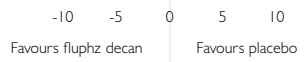
Outcome: 5 Mental state: 1. BPRS (endpoint scores - high score = worse)

Study or subgroup	FLUPHENAZINE DECANOATE N	Mean(SD)	PLACEBO N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Dotti 1979	9	21.11 (2.56)	7	23.14 (2.47)		100.0 %	-2.03 [-4.51, 0.45]
Total (95% CI)	**9**		**7**			**100.0 %**	**-2.03 [-4.51, 0.45]**

Heterogeneity: not applicable

Test for overall effect: Z = 1.60 (P = 0.11)

Test for subgroup differences: Not applicable



Analysis 1.6. Comparison 1 FLUPHENAZINE DECANOATE vs PLACEBO, Outcome 6 Mental state: 2. Depression (medium term - 6 months to 1 year).

Review: Fluphenazine decanoate (depot) and enanthate for schizophrenia

Comparison: 1 FLUPHENAZINE DECANOATE vs PLACEBO

Outcome: 6 Mental state: 2. Depression (medium term - 6 months to 1 year)

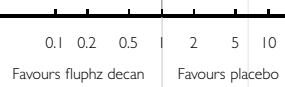
Study or subgroup	FLUPHENAZINE DECANOATE n/N	PLACEBO n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Odejide 1982	9/35	9/35		100.0 %	1.00 [0.45, 2.22]
Total (95% CI)	**35**	**35**		**100.0 %**	**1.00 [0.45, 2.22]**

Total events: 9 (FLUPHENAZINE DECANOATE), 9 (PLACEBO)

Heterogeneity: not applicable

Test for overall effect: Z = 0.0 (P = 1.0)

Test for subgroup differences: Not applicable



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Analysis 1.7. Comparison 1 FLUPHENAZINE DECANOATE vs PLACEBO, Outcome 7 Adverse effects: 1. Movement disorders - tardive dyskinesia (longer term - more than 1 year).

Review: Fluphenazine decanoate (depot) and enanthate for schizophrenia

Comparison: 1 FLUPHENAZINE DECANOATE vs PLACEBO

Outcome: 7 Adverse effects: 1. Movement disorders - tardive dyskinesia (longer term - more than 1 year)

Study or subgroup	FLUPHENAZINE DECANOATE n/N	PLACEBO n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Jolley 1990	19/27	23/27		100.0 %	0.83 [0.62, 1.11]
Total (95% CI)	**27**	**27**		**100.0 %**	**0.83 [0.62, 1.11]**

Total events: 19 (FLUPHENAZINE DECANOATE), 23 (PLACEBO)

Heterogeneity: not applicable

Test for overall effect: Z = 1.29 (P = 0.20)

Test for subgroup differences: Not applicable

Analysis 1.8. Comparison 1 FLUPHENAZINE DECANOATE vs PLACEBO, Outcome 8 Adverse effects: 2. Toxicity.

Review: Fluphenazine decanoate (depot) and enanthate for schizophrenia

Comparison: 1 FLUPHENAZINE DECANOATE vs PLACEBO

Outcome: 8 Adverse effects: 2. Toxicity

Study or subgroup	FLUPHENAZINE DECANOATE n/N	PLACEBO n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Rifkin 1977	8/23	1/22		100.0 %	7.65 [1.04, 56.26]
Total (95% CI)	**23**	**22**		**100.0 %**	**7.65 [1.04, 56.26]**

Total events: 8 (FLUPHENAZINE DECANOATE), 1 (PLACEBO)

Heterogeneity: not applicable

Test for overall effect: Z = 2.00 (P = 0.046)

Test for subgroup differences: Not applicable

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Analysis 2.1. Comparison 2 FLUPHENAZINE DECANOATE vs ORAL NEUROLEPTICS, Outcome 1 Global state: 1. No clinically important global change.

Review: Fluphenazine decanoate (depot) and enanthate for schizophrenia

Comparison: 2 FLUPHENAZINE DECANOATE vs ORAL NEUROLEPTICS

Outcome: 1 Global state: 1. No clinically important global change

Study or subgroup	FLUPHENAZINE DECANOATE n/N	ORAL NEU-ROLEPTICS n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
1 immediate (0 to 5 weeks)					
Adamson 1973	11/19	17/18		50.0 %	0.61 [0.41, 0.91]
Curry 1972	11/19	17/18		50.0 %	0.61 [0.41, 0.91]
Subtotal (95% CI)	**38**	**36**		**100.0 %**	**0.61 [0.46, 0.81]**
Total events: 22 (FLUPHENAZINE DECANOATE), 34 (ORAL NEUROLEPTICS)					
Heterogeneity: Chi^2 = 0.0, df = 1 (P = 1.00); I^2 =0.0%					
Test for overall effect: Z = 3.40 (P = 0.00069)					
2 medium term (6 months to 1 year)					
Song 1993	22/50	27/52		100.0 %	0.85 [0.56, 1.27]
Subtotal (95% CI)	**50**	**52**		**100.0 %**	**0.85 [0.56, 1.27]**
Total events: 22 (FLUPHENAZINE DECANOATE), 27 (ORAL NEUROLEPTICS)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.80 (P = 0.43)					

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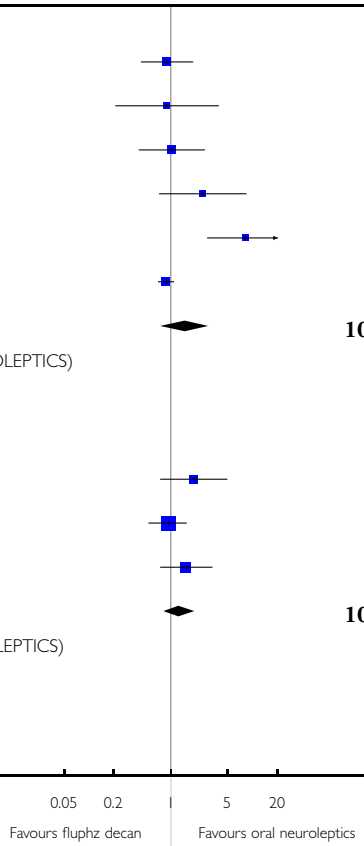
Analysis 2.2. Comparison 2 FLUPHENAZINE DECANOATE vs ORAL NEUROLEPTICS, Outcome 2 Global state: 2. Relapse.

Review: Fluphenazine decanoate (depot) and enanthate for schizophrenia

Comparison: 2 FLUPHENAZINE DECANOATE vs ORAL NEUROLEPTICS

Outcome: 2 Global state: 2. Relapse

Study or subgroup	FLUPHENAZINE DECANOATE n/N	ORAL NEU-ROLEPTICS n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
1 medium term (6 months to 1 year)					
Barnes 1983	8/19	8/17		19.2 %	0.89 [0.43, 1.86]
McCreadie 1980	3/18	3/16		11.3 %	0.89 [0.21, 3.80]
McCreadie 1982	6/15	5/13		16.8 %	1.04 [0.41, 2.62]
Quitkin 1978	8/29	3/27		13.5 %	2.48 [0.73, 8.40]
Rifkin 1977	20/23	3/28		15.0 %	8.12 [2.75, 23.92]
Schooler 1980	58/107	66/107		24.2 %	0.88 [0.70, 1.11]
Subtotal (95% CI)	**211**	**208**		**100.0 %**	**1.46 [0.75, 2.83]**
Total events: 103 (FLUPHENAZINE DECANOATE), 88 (ORAL NEUROLEPTICS)					
Heterogeneity: Tau^2 = 0.46; Chi^2 = 20.42, df = 5 (P = 0.001); I^2 =76%					
Test for overall effect: Z = 1.12 (P = 0.26)					
2 longer term (more than 1 year)					
Falloon 1978	8/20	5/24		19.6 %	1.92 [0.74, 4.95]
Hogarty 1979	13/27	13/25		49.4 %	0.93 [0.54, 1.59]
Simon 1978	14/57	10/63		31.0 %	1.55 [0.75, 3.20]
Subtotal (95% CI)	**104**	**112**		**100.0 %**	**1.25 [0.81, 1.95]**
Total events: 35 (FLUPHENAZINE DECANOATE), 28 (ORAL NEUROLEPTICS)					
Heterogeneity: Tau^2 = 0.03; Chi^2 = 2.38, df = 2 (P = 0.30); I^2 =16%					
Test for overall effect: Z = 1.00 (P = 0.32)					
Test for subgroup differences: Chi^2 = 0.14, df = 1 (P = 0.71), I^2 =0.0%					



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Analysis 2.3. Comparison 2 FLUPHENAZINE DECANOATE vs ORAL NEUROLEPTICS, Outcome 3 Global state: 3. Clinical Global Impression (short term - 6 weeks to 5 months) (high score = worse).

Review: Fluphenazine decanoate (depot) and enanthate for schizophrenia

Comparison: 2 FLUPHENAZINE DECANOATE vs ORAL NEUROLEPTICS

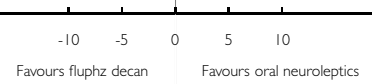
Outcome: 3 Global state: 3. Clinical Global Impression (short term - 6 weeks to 5 months) (high score = worse)

Study or subgroup	FLUPHENAZINE DECANOATE N	Mean(SD)	ORAL NEU-ROLEPTICS N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Shu 1983	16	5 (3.6)	18	5.1 (4.4)		100.0 %	-0.10 [-2.79, 2.59]
Total (95% CI)	**16**		**18**			**100.0 %**	**-0.10 [-2.79, 2.59]**

Heterogeneity: not applicable

Test for overall effect: Z = 0.07 (P = 0.94)

Test for subgroup differences: Not applicable



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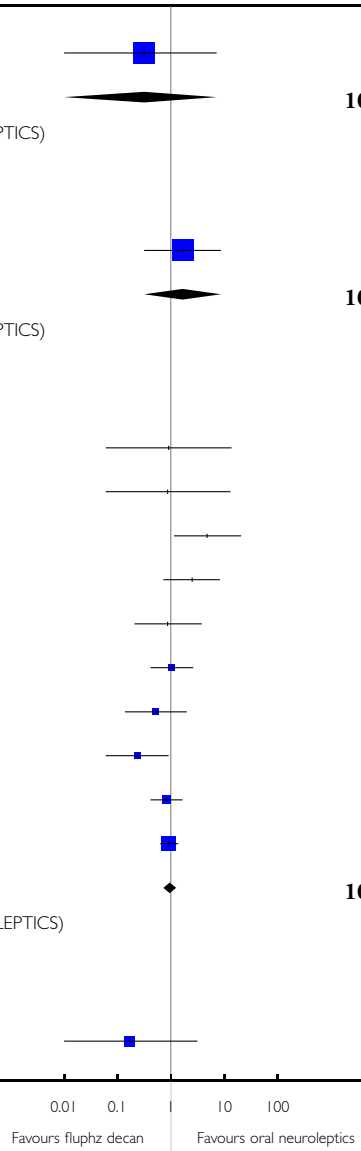
Analysis 2.4. Comparison 2 FLUPHENAZINE DECANOATE vs ORAL NEUROLEPTICS, Outcome 4 Leaving the study early.

Review: Fluphenazine decanoate (depot) and enanthate for schizophrenia

Comparison: 2 FLUPHENAZINE DECANOATE vs ORAL NEUROLEPTICS

Outcome: 4 Leaving the study early

Study or subgroup	FLUPHENAZINE DECANOATE n/N	ORAL NEU-ROLEPTICS n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
1 immediate (0-5 weeks)					
Curry 1972	0/19	1/18		100.0 %	0.32 [0.01, 7.30]
Subtotal (95% CI)	**19**	**18**		**100.0 %**	**0.32 [0.01, 7.30]**
Total events: 0 (FLUPHENAZINE DECANOATE), 1 (ORAL NEUROLEPTICS)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.72 (P = 0.47)					
2 short term (6 weeks to 5 months)					
Shu 1983	3/16	2/18		100.0 %	1.69 [0.32, 8.85]
Subtotal (95% CI)	**16**	**18**		**100.0 %**	**1.69 [0.32, 8.85]**
Total events: 3 (FLUPHENAZINE DECANOATE), 2 (ORAL NEUROLEPTICS)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.62 (P = 0.54)					
3 medium term (6 months to 1 year)					
Magnus 1979	1/26	1/24		1.2 %	0.92 [0.06, 13.95]
Barnes 1983	1/19	1/17		1.2 %	0.89 [0.06, 13.23]
Rifkin 1977	8/23	2/28		2.1 %	4.87 [1.14, 20.72]
Quitkin 1978	8/29	3/27		3.6 %	2.48 [0.73, 8.40]
McCreadie 1980	3/18	3/16		3.7 %	0.89 [0.21, 3.80]
McCreadie 1982	6/15	5/13		6.3 %	1.04 [0.41, 2.62]
Song 1993	3/50	6/52		6.9 %	0.52 [0.14, 1.97]
Crawford 1974	2/14	10/17		10.6 %	0.24 [0.06, 0.93]
Kaneno 1991	13/127	16/132		18.3 %	0.84 [0.42, 1.68]
Schooler 1980	36/143	40/147		46.1 %	0.93 [0.63, 1.36]
Subtotal (95% CI)	**464**	**473**		**100.0 %**	**0.96 [0.73, 1.25]**
Total events: 81 (FLUPHENAZINE DECANOATE), 87 (ORAL NEUROLEPTICS)					
Heterogeneity: Chi^2 = 12.21, df = 9 (P = 0.20); I^2 =26%					
Test for overall effect: Z = 0.33 (P = 0.74)					
4 longer term (more than 1 year)					
Falloon 1978	0/20	3/24		25.2 %	0.17 [0.01, 3.11]



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Study or subgroup	FLUPHENAZINE DECANOATE n/N	ORAL NEU-ROLEPTICS n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Simon 1978	14/57	10/63		74.8 %	1.55 [0.75, 3.20]
Subtotal (95% CI)	**77**	**87**		**100.0 %**	**1.20 [0.61, 2.36]**

Total events: 14 (FLUPHENAZINE DECANOATE), 13 (ORAL NEUROLEPTICS)

Heterogeneity: Chi^2 = 2.20, df = 1 (P = 0.14); I^2 =55%

Test for overall effect: Z = 0.53 (P = 0.60)

Analysis 2.5. Comparison 2 FLUPHENAZINE DECANOATE vs ORAL NEUROLEPTICS, Outcome 5 Behaviour: 1. NOSIE-30 - endpoint scores (high score = poor).

Review: Fluphenazine decanoate (depot) and enanthate for schizophrenia

Comparison: 2 FLUPHENAZINE DECANOATE vs ORAL NEUROLEPTICS

Outcome: 5 Behaviour: 1. NOSIE-30 - endpoint scores (high score = poor)

Study or subgroup	FLUPHENAZINE DECANOATE N	Mean(SD)	ORAL NEU-ROLEPTICS N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Simon 1978	57	152.25 (16.97)	63	152.81 (18.55)		100.0 %	-0.56 [-6.92, 5.80]
Total (95% CI)	**57**		**63**			**100.0 %**	**-0.56 [-6.92, 5.80]**

Heterogeneity: not applicable

Test for overall effect: Z = 0.17 (P = 0.86)

Test for subgroup differences: Not applicable

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Analysis 2.6. Comparison 2 FLUPHENAZINE DECANOATE vs ORAL NEUROLEPTICS, Outcome 6 Behaviour: 2. skewed data (endpoint scores).

Behaviour: 2. skewed data (endpoint scores)

Study	Intervention	mean	SD	N
Barnes 1983	Fluphenazine decanoate	5.7	4.1	19
Barnes 1983	Pimozide	4.2	5.5	17

Analysis 2.7. Comparison 2 FLUPHENAZINE DECANOATE vs ORAL NEUROLEPTICS, Outcome 7 Mental state: 1. BPRS - endpoint scores (longer term - more than 1 year) (high score = poor).

Review: Fluphenazine decanoate (depot) and enanthate for schizophrenia

Comparison: 2 FLUPHENAZINE DECANOATE vs ORAL NEUROLEPTICS

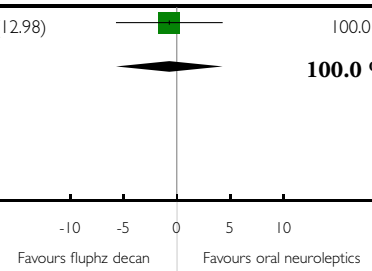
Outcome: 7 Mental state: 1. BPRS - endpoint scores (longer term - more than 1 year) (high score = poor)

Study or subgroup	FLUPHENAZINE DECANOATE N	Mean(SD)	ORAL NEU-ROLEPTICS N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Simon 1978	57	60.33 (14.8)	63	61.08 (12.98)		100.0 %	-0.75 [-5.75, 4.25]
Total (95% CI)	**57**		**63**			**100.0 %**	**-0.75 [-5.75, 4.25]**

Heterogeneity: not applicable

Test for overall effect: Z = 0.29 (P = 0.77)

Test for subgroup differences: Not applicable



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Analysis 2.8. Comparison 2 FLUPHENAZINE DECANOATE vs ORAL NEUROLEPTICS, Outcome 8 Mental state: 2. Depression.

Review: Fluphenazine decanoate (depot) and enanthate for schizophrenia

Comparison: 2 FLUPHENAZINE DECANOATE vs ORAL NEUROLEPTICS

Outcome: 8 Mental state: 2. Depression

Study or subgroup	FLUPHENAZINE DECANOATE n/N	ORAL NEU-ROLEPTICS n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
1 medium term (6 months to 1 year)					
Schooler 1979	32/107	36/107		100.0 %	0.89 [0.60, 1.32]
Subtotal (95% CI)	**107**	**107**		**100.0 %**	**0.89 [0.60, 1.32]**
Total events: 32 (FLUPHENAZINE DECANOATE), 36 (ORAL NEUROLEPTICS)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.59 (P = 0.56)					
2 longer term (more than 1 year)					
Falloon 1978	14/20	11/24		100.0 %	1.53 [0.91, 2.57]
Subtotal (95% CI)	**20**	**24**		**100.0 %**	**1.53 [0.91, 2.57]**
Total events: 14 (FLUPHENAZINE DECANOATE), 11 (ORAL NEUROLEPTICS)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.59 (P = 0.11)					

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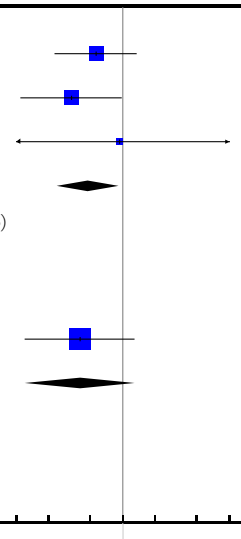
Analysis 2.9. Comparison 2 FLUPHENAZINE DECANOATE vs ORAL NEUROLEPTICS, Outcome 9 Adverse effects: 1a. Movement disorders - general.

Review: Fluphenazine decanoate (depot) and enanthate for schizophrenia

Comparison: 2 FLUPHENAZINE DECANOATE vs ORAL NEUROLEPTICS

Outcome: 9 Adverse effects: 1a. Movement disorders - general

Study or subgroup	FLUPHENAZINE DECANOATE n/N	ORAL NEU-ROLEPTICS n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
1 medium term (6 months to 1 year)					
McCreadie 1980	5/18	8/16		46.9 %	0.56 [0.23, 1.36]
McCreadie 1982	3/15	8/13		47.4 %	0.33 [0.11, 0.98]
Schooler 1979	1/102	1/95		5.7 %	0.93 [0.06, 14.68]
Subtotal (95% CI)	**135**	**124**		**100.0 %**	**0.47 [0.24, 0.91]**
Total events: 9 (FLUPHENAZINE DECANOATE), 17 (ORAL NEUROLEPTICS)					
Heterogeneity: Chi^2 = 0.80, df = 2 (P = 0.67); I^2 =0.0%					
Test for overall effect: Z = 2.23 (P = 0.026)					
2 longer term (more than 1 year)					
Falloon 1978	3/20	9/24		100.0 %	0.40 [0.12, 1.28]
Subtotal (95% CI)	**20**	**24**		**100.0 %**	**0.40 [0.12, 1.28]**
Total events: 3 (FLUPHENAZINE DECANOATE), 9 (ORAL NEUROLEPTICS)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.54 (P = 0.12)					



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Analysis 2.10. Comparison 2 FLUPHENAZINE DECANOATE vs ORAL NEUROLEPTICS, Outcome 10 Adverse effects: 1b. Movement disorders - akathisia.

Review: Fluphenazine decanoate (depot) and enanthate for schizophrenia

Comparison: 2 FLUPHENAZINE DECANOATE vs ORAL NEUROLEPTICS

Outcome: 10 Adverse effects: 1b. Movement disorders - akathisia

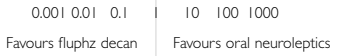
Study or subgroup	FLUPHENAZINE DECANOATE n/N	ORAL NEU-ROLEPTICS n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Rifkin 1977	8/23	0/28		100.0 %	20.54 [1.25, 337.94]
Total (95% CI)	**23**	**28**		**100.0 %**	**20.54 [1.25, 337.94]**

Total events: 8 (FLUPHENAZINE DECANOATE), 0 (ORAL NEUROLEPTICS)

Heterogeneity: not applicable

Test for overall effect: Z = 2.12 (P = 0.034)

Test for subgroup differences: Not applicable



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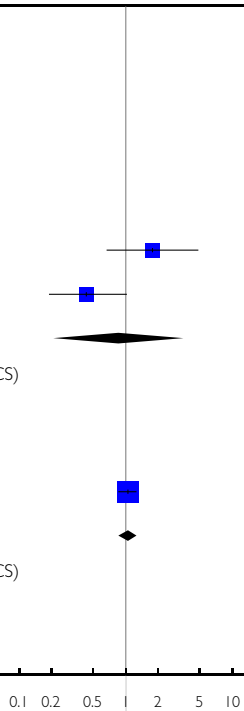
Analysis 2.11. Comparison 2 FLUPHENAZINE DECANOATE vs ORAL NEUROLEPTICS, Outcome 11 Adverse effects: 1c. Movement disorders - needing anticholinergic drugs.

Review: Fluphenazine decanoate (depot) and enanthate for schizophrenia

Comparison: 2 FLUPHENAZINE DECANOATE vs ORAL NEUROLEPTICS

Outcome: 11 Adverse effects: 1c. Movement disorders - needing anticholinergic drugs

Study or subgroup	FLUPHENAZINE DECANOATE n/N	ORAL NEU-ROLEPTICS n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
1 immediate (0 to 5 weeks)					
Adamson 1973	0/19	0/18			Not estimable
Subtotal (95% CI)	**19**	**18**			**Not estimable**
Total events: 0 (FLUPHENAZINE DECANOATE), 0 (ORAL NEUROLEPTICS)					
Heterogeneity: not applicable					
Test for overall effect: not applicable					
2 medium term (6 months to 1 year)					
McCreadie 1980	8/18	4/16		48.3 %	1.78 [0.66, 4.80]
Schooler 1980	7/102	15/95		51.7 %	0.43 [0.19, 1.02]
Subtotal (95% CI)	**120**	**111**		**100.0 %**	**0.86 [0.21, 3.45]**
Total events: 15 (FLUPHENAZINE DECANOATE), 19 (ORAL NEUROLEPTICS)					
Heterogeneity: $Tau^2 = 0.79$; $Chi^2 = 4.52$, df = 1 (P = 0.03); $I^2 = 78\%$					
Test for overall effect: Z = 0.22 (P = 0.83)					
3 longer term (more than 1 year)					
Simon 1978	46/57	49/63		100.0 %	1.04 [0.86, 1.25]
Subtotal (95% CI)	**57**	**63**		**100.0 %**	**1.04 [0.86, 1.25]**
Total events: 46 (FLUPHENAZINE DECANOATE), 49 (ORAL NEUROLEPTICS)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.39 (P = 0.69)					



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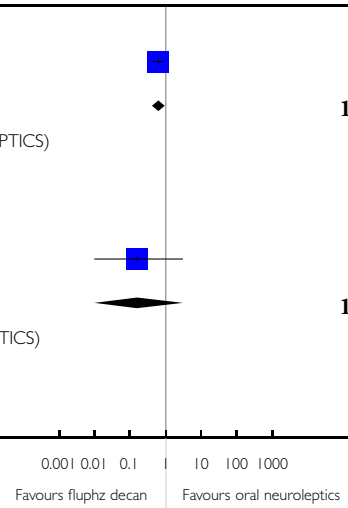
Analysis 2.12. Comparison 2 FLUPHENAZINE DECANOATE vs ORAL NEUROLEPTICS, Outcome 12 Adverse effects: 1d. Movement disorders - tardive dyskinesia.

Review: Fluphenazine decanoate (depot) and enanthate for schizophrenia

Comparison: 2 FLUPHENAZINE DECANOATE vs ORAL NEUROLEPTICS

Outcome: 12 Adverse effects: 1d. Movement disorders - tardive dyskinesia

Study or subgroup	FLUPHENAZINE DECANOATE n/N	ORAL NEU-ROLEPTICS n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
1 medium term (6 months to 1 year)					
McCreadie 1982	9/15	13/13		100.0 %	0.62 [0.41, 0.93]
Subtotal (95% CI)	**15**	**13**		**100.0 %**	**0.62 [0.41, 0.93]**
Total events: 9 (FLUPHENAZINE DECANOATE), 13 (ORAL NEUROLEPTICS)					
Heterogeneity: not applicable					
Test for overall effect: Z = 2.28 (P = 0.023)					
2 longer term (more than 1 year)					
Simon 1978	0/57	3/63		100.0 %	0.16 [0.01, 2.99]
Subtotal (95% CI)	**57**	**63**		**100.0 %**	**0.16 [0.01, 2.99]**
Total events: 0 (FLUPHENAZINE DECANOATE), 3 (ORAL NEUROLEPTICS)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.23 (P = 0.22)					



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Analysis 2.13. Comparison 2 FLUPHENAZINE DECANOATE vs ORAL NEUROLEPTICS, Outcome 13 Adverse effects: 1e. Movement disorders - tremor (longer term - more than 1 year).

Review: Fluphenazine decanoate (depot) and enanthate for schizophrenia

Comparison: 2 FLUPHENAZINE DECANOATE vs ORAL NEUROLEPTICS

Outcome: 13 Adverse effects: 1e. Movement disorders - tremor (longer term - more than 1 year)

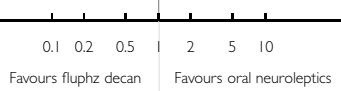
Study or subgroup	FLUPHENAZINE DECANOATE n/N	ORAL NEU-ROLEPTICS n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Falloon 1978	4/20	6/24		100.0 %	0.80 [0.26, 2.45]
Total (95% CI)	**20**	**24**		**100.0 %**	**0.80 [0.26, 2.45]**

Total events: 4 (FLUPHENAZINE DECANOATE), 6 (ORAL NEUROLEPTICS)

Heterogeneity: not applicable

Test for overall effect: Z = 0.39 (P = 0.70)

Test for subgroup differences: Not applicable



Analysis 2.14. Comparison 2 FLUPHENAZINE DECANOATE vs ORAL NEUROLEPTICS, Outcome 14 Adverse effects: 1f. Movement disorders - average score (Simpson & Angus, 0 to 5 weeks, high = poor).

Review: Fluphenazine decanoate (depot) and enanthate for schizophrenia

Comparison: 2 FLUPHENAZINE DECANOATE vs ORAL NEUROLEPTICS

Outcome: 14 Adverse effects: 1f. Movement disorders - average score (Simpson % Angus, 0 to 5 weeks, high = poor)

Study or subgroup	FLUPHENAZINE DECANOATE N	Mean(SD)	ORAL NEU-ROLEPTICS N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Shu 1983	16	2.6 (2)	16	1.3 (1.7)		100.0 %	1.30 [0.01, 2.59]
Total (95% CI)	**16**		**16**			**100.0 %**	**1.30 [0.01, 2.59]**

Heterogeneity: not applicable

Test for overall effect: Z = 1.98 (P = 0.048)

Test for subgroup differences: Not applicable

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Analysis 2.15. Comparison 2 FLUPHENAZINE DECANOATE vs ORAL NEUROLEPTICS, Outcome 15 Adverse effects: 2. Blurred vision - medium term (6 months to 1 year).

Review: Fluphenazine decanoate (depot) and enanthate for schizophrenia

Comparison: 2 FLUPHENAZINE DECANOATE vs ORAL NEUROLEPTICS

Outcome: 15 Adverse effects: 2. Blurred vision - medium term (6 months to 1 year)

Study or subgroup	FLUPHENAZINE DECANOATE n/N	ORAL NEU-ROLEPTICS n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Schooler 1980	23/102	16/95		100.0 %	1.34 [0.75, 2.38]
Total (95% CI)	**102**	**95**		**100.0 %**	**1.34 [0.75, 2.38]**

Total events: 23 (FLUPHENAZINE DECANOATE), 16 (ORAL NEUROLEPTICS)

Heterogeneity: not applicable

Test for overall effect: Z = 1.00 (P = 0.32)

Test for subgroup differences: Not applicable

Analysis 2.16. Comparison 2 FLUPHENAZINE DECANOATE vs ORAL NEUROLEPTICS, Outcome 16 Adverse effects: 3. Toxicity - medium term (6 months to 1 year).

Review: Fluphenazine decanoate (depot) and enanthate for schizophrenia

Comparison: 2 FLUPHENAZINE DECANOATE vs ORAL NEUROLEPTICS

Outcome: 16 Adverse effects: 3. Toxicity - medium term (6 months to 1 year)

Study or subgroup	FLUPHENAZINE DECANOATE n/N	ORAL NEU-ROLEPTICS n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Rifkin 1977	8/23	2/28		100.0 %	4.87 [1.14, 20.72]
Total (95% CI)	**23**	**28**		**100.0 %**	**4.87 [1.14, 20.72]**

Total events: 8 (FLUPHENAZINE DECANOATE), 2 (ORAL NEUROLEPTICS)

Heterogeneity: not applicable

Test for overall effect: Z = 2.14 (P = 0.032)

Test for subgroup differences: Not applicable

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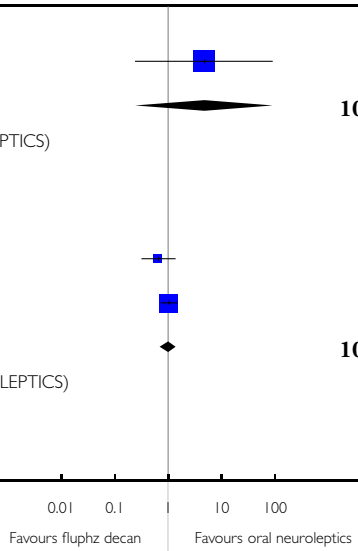
Analysis 2.17. Comparison 2 FLUPHENAZINE DECANOATE vs ORAL NEUROLEPTICS, Outcome 17 Adverse effects: 4. General adverse effects.

Review: Fluphenazine decanoate (depot) and enanthate for schizophrenia

Comparison: 2 FLUPHENAZINE DECANOATE vs ORAL NEUROLEPTICS

Outcome: 17 Adverse effects: 4. General adverse effects

Study or subgroup	FLUPHENAZINE DECANOATE n/N	ORAL NEU-ROLEPTICS n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
1 immediate (0 to 5 weeks)					
Adamson 1973	2/19	0/18		100.0 %	4.75 [0.24, 92.65]
Subtotal (95% CI)	**19**	**18**		**100.0 %**	**4.75 [0.24, 92.65]**
Total events: 2 (FLUPHENAZINE DECANOATE), 0 (ORAL NEUROLEPTICS)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.03 (P = 0.30)					
2 medium term (6 months to 1 year)					
McCreadie 1982	6/15	8/13		19.7 %	0.65 [0.31, 1.38]
Schooler 1980	37/107	35/107		80.3 %	1.06 [0.73, 1.54]
Subtotal (95% CI)	**122**	**120**		**100.0 %**	**0.98 [0.70, 1.37]**
Total events: 43 (FLUPHENAZINE DECANOATE), 43 (ORAL NEUROLEPTICS)					
Heterogeneity: Chi^2 = 1.29, df = 1 (P = 0.26); I^2 =22%					
Test for overall effect: Z = 0.14 (P = 0.89)					



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Analysis 2.18. Comparison 2 FLUPHENAZINE DECANOATE vs ORAL NEUROLEPTICS, Outcome 18 SENSITIVITY ANALYSIS Global state: 2. Relapse.

Review: Fluphenazine decanoate (depot) and enanthate for schizophrenia

Comparison: 2 FLUPHENAZINE DECANOATE vs ORAL NEUROLEPTICS

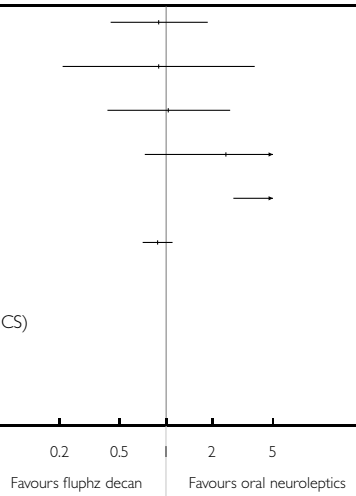
Outcome: 18 SENSITIVITY ANALYSIS Global state: 2. Relapse

Study or subgroup	FLUPHENAZINE DECANOATE n/N	ORAL NEU-ROLEPTICS n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Barnes 1983	8/19	8/17			0.89 [0.43, 1.86]
McCreadie 1980	3/18	3/16			0.89 [0.21, 3.80]
McCreadie 1982	6/15	5/13			1.04 [0.41, 2.62]
Quitkin 1978	8/29	3/27			2.48 [0.73, 8.40]
Rifkin 1977	20/23	3/28			8.12 [2.75, 23.92]
Schooler 1980	58/107	66/107			0.88 [0.70, 1.11]
Subtotal (95% CI)	**0**	**0**			**0.0 [0.0, 0.0]**

Total events: 103 (FLUPHENAZINE DECANOATE), 88 (ORAL NEUROLEPTICS)

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.0$, df = 0 (P<0.00001); $I^2 = 0.0\%$

Test for overall effect: Z = 0.0 (P < 0.00001)



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Analysis 3.1. Comparison 3 FLUPHENAZINE DECANOATE vs OTHER DEPOT NEUROLEPTICS, Outcome 1 Death.

Review: Fluphenazine decanoate (depot) and enanthate for schizophrenia

Comparison: 3 FLUPHENAZINE DECANOATE vs OTHER DEPOT NEUROLEPTICS

Outcome: 1 Death

Study or subgroup	FLUPHENAZINE DECANOATE n/N	OTHER DEPOT NEUROLEPTICS n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
McKane 1987	1/19	0/19		100.0 %	3.00 [0.13, 69.31]
Total (95% CI)	**19**	**19**		**100.0 %**	**3.00 [0.13, 69.31]**

Total events: 1 (FLUPHENAZINE DECANOATE), 0 (OTHER DEPOT NEUROLEPTICS)

Heterogeneity: not applicable

Test for overall effect: Z = 0.69 (P = 0.49)

Test for subgroup differences: Not applicable

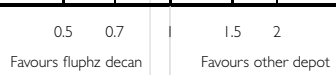
Analysis 3.2. Comparison 3 FLUPHENAZINE DECANOATE vs OTHER DEPOT NEUROLEPTICS, Outcome 2 Global state: 1. No clinically important global change.

Review: Fluphenazine decanoate (depot) and enanthate for schizophrenia

Comparison: 3 FLUPHENAZINE DECANOATE vs OTHER DEPOT NEUROLEPTICS

Outcome: 2 Global state: 1. No clinically important global change

Study or subgroup	FLUPHENAZINE DECANOATE n/N	OTHER DEPOT NEUROLEPTICS n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
1 short term (6 weeks to 5 months)					
Ju 2000	32/49	58/103		30.1 %	1.16 [0.89, 1.51]
Subtotal (95% CI)	**49**	**103**		**30.1 %**	**1.16 [0.89, 1.51]**
Total events: 32 (FLUPHENAZINE DECANOATE), 58 (OTHER DEPOT NEUROLEPTICS)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.09 (P = 0.27)					
2 medium term (6 months to 1 year)					
Dencker 1973	32/35	29/32		24.4 %	1.01 [0.87, 1.17]
Leong 1989	29/30	27/30		21.7 %	1.07 [0.94, 1.23]



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Study or subgroup	FLUPHENAZINE DECANOATE n/N	OTHER DEPOT NEUROLEPTICS n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Schlosberg 1978	30/30	29/30		23.8 %	1.03 [0.94, 1.13]
Subtotal (95% CI)	**95**	**92**		**69.9 %**	**1.04 [0.96, 1.12]**
Total events: 91 (FLUPHENAZINE DECANOATE), 85 (OTHER DEPOT NEUROLEPTICS)					
Heterogeneity: Chi^2 = 0.39, df = 2 (P = 0.82); I^2 =0.0%					
Test for overall effect: Z = 0.98 (P = 0.33)					
Total (95% CI)	**144**	**195**		**100.0 %**	**1.07 [0.97, 1.18]**
Total events: 123 (FLUPHENAZINE DECANOATE), 143 (OTHER DEPOT NEUROLEPTICS)					
Heterogeneity: Chi^2 = 1.67, df = 3 (P = 0.64); I^2 =0.0%					
Test for overall effect: Z = 1.44 (P = 0.15)					
Test for subgroup differences: Chi^2 = 0.62, df = 1 (P = 0.43), I^2 =0.0%					

Analysis 3.3. Comparison 3 FLUPHENAZINE DECANOATE vs OTHER DEPOT NEUROLEPTICS, Outcome 3 Global state: 2. Relapse.

Review: Fluphenazine decanoate (depot) and enanthate for schizophrenia

Comparison: 3 FLUPHENAZINE DECANOATE vs OTHER DEPOT NEUROLEPTICS

Outcome: 3 Global state: 2. Relapse

Study or subgroup	FLUPHENAZINE DECANOATE n/N	OTHER DEPOT NEUROLEPTICS n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
1 short term (6 weeks to 5 months)					
Wistedt 1984	4/26	4/25		100.0 %	0.96 [0.27, 3.43]
Subtotal (95% CI)	**26**	**25**		**100.0 %**	**0.96 [0.27, 3.43]**
Total events: 4 (FLUPHENAZINE DECANOATE), 4 (OTHER DEPOT NEUROLEPTICS)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.06 (P = 0.95)					
2 medium term (6 months to 1 year)					
Chouinard 1984	1/36	0/36		1.0 %	3.00 [0.13, 71.28]
Cookson 1986	0/9	2/10		4.9 %	0.22 [0.01, 4.05]
Dencker 1973	6/35	3/32		6.4 %	1.83 [0.50, 6.71]

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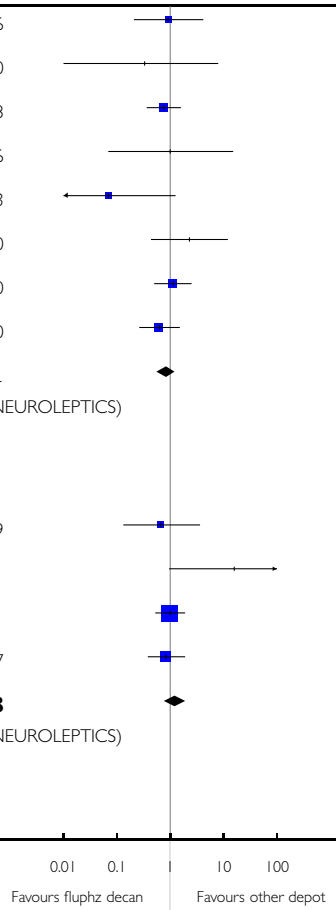
Study or subgroup	FLUPHENAZINE DECANOATE n/N	OTHER DEPOT NEUROLEPTICS n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Kelly 1977	3/28	3/26		6.3 %	0.93 [0.21, 4.20]
Leong 1989	0/30	1/30		3.1 %	0.33 [0.01, 7.87]
Lundin 1990	9/30	11/28		23.2 %	0.76 [0.37, 1.56]
Magnus 1979	1/26	1/26		2.0 %	1.00 [0.07, 15.15]
McLaren 1992	0/24	6/23		13.5 %	0.07 [0.00, 1.24]
Russell 1982	3/13	2/20		3.2 %	2.31 [0.44, 11.98]
Schlosberg 1978	9/30	8/30		16.3 %	1.13 [0.50, 2.52]
Sharma 1991	6/29	10/30		20.0 %	0.62 [0.26, 1.49]
Subtotal (95% CI)	**290**	**291**		**100.0 %**	**0.82 [0.56, 1.18]**
Total events: 38 (FLUPHENAZINE DECANOATE), 47 (OTHER DEPOT NEUROLEPTICS)					
Heterogeneity: Chi^2 = 8.59, df = 10 (P = 0.57); I^2 =0.0%					
Test for overall effect: Z = 1.07 (P = 0.28)					
3 longer term (more than 1 year)					
McKane 1987	2/19	3/19		11.8 %	0.67 [0.13, 3.55]
Pinto 1979	8/33	0/31		2.0 %	16.00 [0.96, 266.03]
Simon 1978	14/57	15/61		56.8 %	1.00 [0.53, 1.88]
Wistedt 1983	6/15	8/17		29.4 %	0.85 [0.38, 1.89]
Subtotal (95% CI)	**124**	**128**		**100.0 %**	**1.22 [0.77, 1.92]**
Total events: 30 (FLUPHENAZINE DECANOATE), 26 (OTHER DEPOT NEUROLEPTICS)					
Heterogeneity: Chi^2 = 4.89, df = 3 (P = 0.18); I^2 =39%					
Test for overall effect: Z = 0.85 (P = 0.39)					



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Analysis 3.4. Comparison 3 FLUPHENAZINE DECANOATE vs OTHER DEPOT NEUROLEPTICS, Outcome 4 Global state: 3. Severly ill (medium term 6 months to 1 year).

Review: Fluphenazine decanoate (depot) and enanthate for schizophrenia

Comparison: 3 FLUPHENAZINE DECANOATE vs OTHER DEPOT NEUROLEPTICS

Outcome: 4 Global state: 3. Severly ill (medium term 6 months to 1 year)

Study or subgroup	FLUPHENAZINE DECANOATE n/N	OTHER DEPOT NEUROLEPTICS n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Leong 1989	29/30	27/30		100.0 %	1.07 [0.94, 1.23]
Total (95% CI)	**30**	**30**		**100.0 %**	**1.07 [0.94, 1.23]**

Total events: 29 (FLUPHENAZINE DECANOATE), 27 (OTHER DEPOT NEUROLEPTICS)

Heterogeneity: not applicable

Test for overall effect: Z = 1.03 (P = 0.31)

Test for subgroup differences: Not applicable

Analysis 3.5. Comparison 3 FLUPHENAZINE DECANOATE vs OTHER DEPOT NEUROLEPTICS, Outcome 5 Global state: 4. Needing additional antipsychotic treatment (6 months to 1 year).

Review: Fluphenazine decanoate (depot) and enanthate for schizophrenia

Comparison: 3 FLUPHENAZINE DECANOATE vs OTHER DEPOT NEUROLEPTICS

Outcome: 5 Global state: 4. Needing additional antipsychotic treatment (6 months to 1 year)

Study or subgroup	FLUPHENAZINE DECANOATE n/N	OTHER DEPOT NEUROLEPTICS n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Chouinard 1984	2/36	2/36		34.5 %	1.00 [0.15, 6.72]
Cookson 1986	1/9	4/10		65.5 %	0.28 [0.04, 2.05]
Total (95% CI)	**45**	**46**		**100.0 %**	**0.53 [0.14, 1.96]**

Total events: 3 (FLUPHENAZINE DECANOATE), 6 (OTHER DEPOT NEUROLEPTICS)

Heterogeneity: Chi^2 = 0.83, df = 1 (P = 0.36); I^2 =0.0%

Test for overall effect: Z = 0.96 (P = 0.34)

Test for subgroup differences: Not applicable

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Analysis 3.6. Comparison 3 FLUPHENAZINE DECANOATE vs OTHER DEPOT NEUROLEPTICS, Outcome 6 Global state: 5. Clinical Global Impression. (short term - 6 weeks to 5 months) (skewed data).

Global state: 5. Clinical Global Impression. (short term - 6 weeks to 5 months) (skewed data)

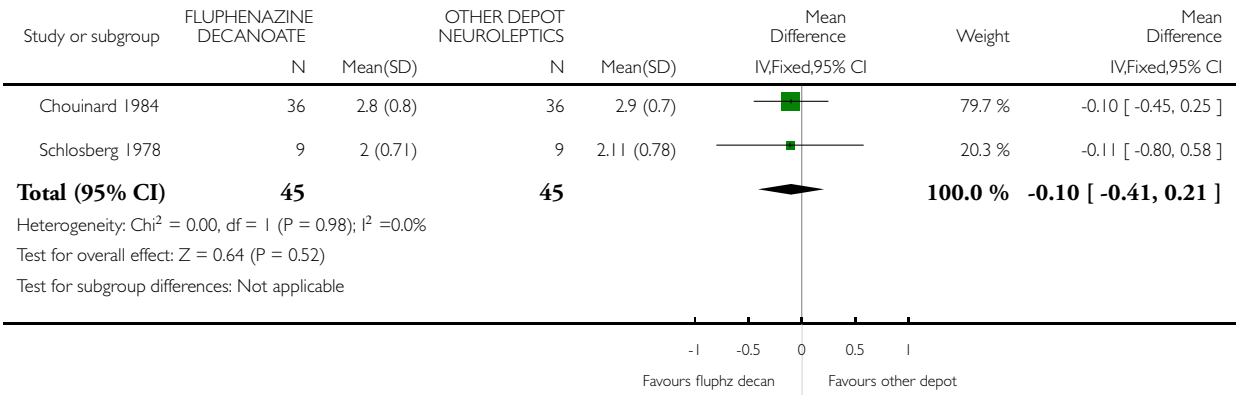
Study	Intervention	mean	SD	N
Wistedt 1984	Fluphenazine decanoate	2.9	2	26
Wistedt 1984	Pipothiazine	2.9	1.5	25

Analysis 3.7. Comparison 3 FLUPHENAZINE DECANOATE vs OTHER DEPOT NEUROLEPTICS, Outcome 7 Global state: 6. Clinical Global Impression. (medium term - 6 months to 1 year).

Review: Fluphenazine decanoate (depot) and enanthate for schizophrenia

Comparison: 3 FLUPHENAZINE DECANOATE vs OTHER DEPOT NEUROLEPTICS

Outcome: 7 Global state: 6. Clinical Global Impression. (medium term - 6 months to 1 year)



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Analysis 3.8. Comparison 3 FLUPHENAZINE DECANOATE vs OTHER DEPOT NEUROLEPTICS, Outcome 8 Global state: 7. Clinical Global Impression - not improved (high score = poor).

Review: Fluphenazine decanoate (depot) and enanthate for schizophrenia

Comparison: 3 FLUPHENAZINE DECANOATE vs OTHER DEPOT NEUROLEPTICS

Outcome: 8 Global state: 7. Clinical Global Impression - not improved (high score = poor)

Study or subgroup	FLUPHENAZINE DECANOATE n/N	OTHER DEPOT NEUROLEPTICS n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
1 short term (6 weeks to 5 months)					
Frangos 1978	5/25	2/25		100.0 %	2.50 [0.53, 11.70]
Subtotal (95% CI)	**25**	**25**		**100.0 %**	**2.50 [0.53, 11.70]**
Total events: 5 (FLUPHENAZINE DECANOATE), 2 (OTHER DEPOT NEUROLEPTICS)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.16 (P = 0.24)					
2 medium term (6 months to 1 year)					
Leong 1989	3/30	4/30		100.0 %	0.75 [0.18, 3.07]
Subtotal (95% CI)	**30**	**30**		**100.0 %**	**0.75 [0.18, 3.07]**
Total events: 3 (FLUPHENAZINE DECANOATE), 4 (OTHER DEPOT NEUROLEPTICS)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.40 (P = 0.69)					

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Analysis 3.9. Comparison 3 FLUPHENAZINE DECANOATE vs OTHER DEPOT NEUROLEPTICS, Outcome 9 Leaving the study early.

Review: Fluphenazine decanoate (depot) and enanthate for schizophrenia

Comparison: 3 FLUPHENAZINE DECANOATE vs OTHER DEPOT NEUROLEPTICS

Outcome: 9 Leaving the study early

Study or subgroup	FLUPHENAZINE DECANOATE n/N	OTHER DEPOT NEUROLEPTICS n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
1 immediate (0 to 5 weeks)					
Levenson 1976	0/5	0/7			Not estimable
Subtotal (95% CI)	**5**	**7**			**Not estimable**
Total events: 0 (FLUPHENAZINE DECANOATE), 0 (OTHER DEPOT NEUROLEPTICS)					
Heterogeneity: not applicable					
Test for overall effect: not applicable					
2 short term (6 weeks to 5 months)					
Feng 1990	3/15	5/15		55.1 %	0.60 [0.17, 2.07]
Ju 2000	0/49	0/103			Not estimable
Wistedt 1984	4/26	4/25		44.9 %	0.96 [0.27, 3.43]
Subtotal (95% CI)	**90**	**143**		**100.0 %**	**0.76 [0.32, 1.84]**
Total events: 7 (FLUPHENAZINE DECANOATE), 9 (OTHER DEPOT NEUROLEPTICS)					
Heterogeneity: Chi^2 = 0.27, df = 1 (P = 0.60); I^2 =0.0%					
Test for overall effect: Z = 0.60 (P = 0.55)					
3 medium term (6 months to 1 year)					
Chouinard 1984	1/32	0/32		0.6 %	3.00 [0.13, 71.00]
Cookson 1986	0/9	2/10		2.9 %	0.22 [0.01, 4.05]
Dencker 1973	6/35	3/32		3.9 %	1.83 [0.50, 6.71]
Hranov 1998	6/21	4/20		5.1 %	1.43 [0.47, 4.32]
Kelly 1977	3/30	3/30		3.7 %	1.00 [0.22, 4.56]
Kissling 1985	13/22	10/32		10.0 %	1.89 [1.02, 3.52]
Leong 1989	0/30	1/30		1.8 %	0.33 [0.01, 7.87]
Lundin 1990	9/30	11/28		14.0 %	0.76 [0.37, 1.56]
Magnus 1979	1/26	1/24		1.3 %	0.92 [0.06, 13.95]
Rossi 1990	2/15	3/15		3.7 %	0.67 [0.13, 3.44]
Russell 1982	3/13	2/20		1.9 %	2.31 [0.44, 11.98]
Schlosberg 1978	9/30	8/30		9.9 %	1.13 [0.50, 2.52]
Schneider 1981	18/27	16/32		18.1 %	1.33 [0.86, 2.06]

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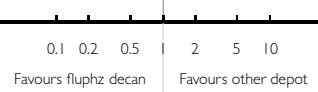
Study or subgroup	FLUPHENAZINE DECANOATE n/N	OTHER DEPOT NEUROLEPTICS n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Sharma 1991	6/29	10/30		12.1 %	0.62 [0.26, 1.49]
Woggon 1977	9/30	9/31		10.9 %	1.03 [0.48, 2.24]
Subtotal (95% CI)	**379**	**396**		**100.0 %**	**1.13 [0.89, 1.44]**
Total events: 86 (FLUPHENAZINE DECANOATE), 83 (OTHER DEPOT NEUROLEPTICS)					
Heterogeneity: Chi^2 = 10.22, df = 14 (P = 0.75); I^2 =0.0%					
Test for overall effect: Z = 0.98 (P = 0.33)					
4 By more than 1 year					
Dencker 1973	10/34	21/33		41.1 %	0.46 [0.26, 0.83]
McKane 1987	7/19	8/19		15.4 %	0.88 [0.40, 1.93]
Pinto 1979	8/33	0/31		1.0 %	16.00 [0.96, 266.03]
Simon 1978	14/57	15/61		28.0 %	1.00 [0.53, 1.88]
Wistedt 1983	6/15	8/17		14.5 %	0.85 [0.38, 1.89]
Subtotal (95% CI)	**158**	**161**		**100.0 %**	**0.89 [0.64, 1.23]**
Total events: 45 (FLUPHENAZINE DECANOATE), 52 (OTHER DEPOT NEUROLEPTICS)					
Heterogeneity: Chi^2 = 9.04, df = 4 (P = 0.06); I^2 =56%					
Test for overall effect: Z = 0.72 (P = 0.47)					



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Analysis 3.10. Comparison 3 FLUPHENAZINE DECANOATE vs OTHER DEPOT NEUROLEPTICS, Outcome 10 Behaviour: 1. NOSIE-30 - endpoint scores (high score = poor).

Review: Fluphenazine decanoate (depot) and enanthate for schizophrenia

Comparison: 3 FLUPHENAZINE DECANOATE vs OTHER DEPOT NEUROLEPTICS

Outcome: 10 Behaviour: 1. NOSIE-30 - endpoint scores (high score = poor)

Study or subgroup	FLUPHENAZINE DECANOATE N	Mean(SD)	OTHER DEPOT NEUROLEPTICS N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Simon 1978	57	152.25 (16.97)	61	157.46 (14.04)		100.0 %	-5.21 [-10.85, 0.43]
Total (95% CI)	**57**		**61**			**100.0 %**	**-5.21 [-10.85, 0.43]**

Heterogeneity: not applicable

Test for overall effect: Z = 1.81 (P = 0.070)

Test for subgroup differences: Not applicable

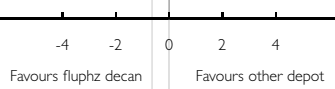
Analysis 3.11. Comparison 3 FLUPHENAZINE DECANOATE vs OTHER DEPOT NEUROLEPTICS, Outcome 11 Mental state: 1. BPRS (endpoint scores - high score = poor).

Review: Fluphenazine decanoate (depot) and enanthate for schizophrenia

Comparison: 3 FLUPHENAZINE DECANOATE vs OTHER DEPOT NEUROLEPTICS

Outcome: 11 Mental state: 1. BPRS (endpoint scores - high score = poor)

Study or subgroup	FLUPHENAZINE DECANOATE N	Mean(SD)	OTHER DEPOT NEUROLEPTICS N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
1 short term (6 weeks to 5 months)							
Ju 2000	49	28 (7)	103	26 (9)		0.9 %	2.00 [-0.62, 4.62]
Wistedt 1984	26	4.1 (0.4)	25	3 (0.5)		99.1 %	1.10 [0.85, 1.35]
Subtotal (95% CI)	**75**		**128**			**100.0 %**	**1.11 [0.86, 1.36]**
Heterogeneity: Chi^2 = 0.45, df = 1 (P = 0.50); I^2 =0.0%							
Test for overall effect: Z = 8.76 (P < 0.00001)							
2 medium term (6 months to 1 year)							
Chouinard 1984	36	24.5 (7.2)	36	25 (5.7)		0.1 %	-0.50 [-3.50, 2.50]
Leong 1989	30	2.8 (0.2)	30	1.6 (0.2)		99.9 %	1.20 [1.10, 1.30]



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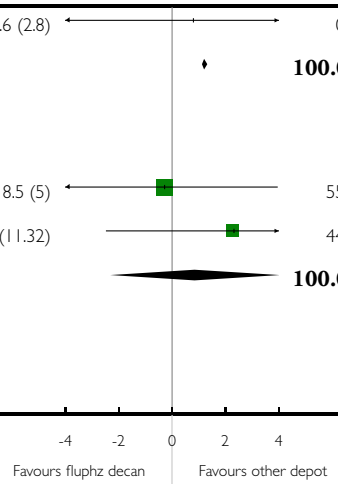
Study or subgroup	FLUPHENAZINE DECANOATE N	Mean(SD)	OTHER DEPOT NEUROLEPTICS N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Rossi 1990	15	38.4 (13.9)	15	37.6 (2.8)		0.0 %	0.80 [-6.38, 7.98]
Subtotal (95% CI)	**81**		**81**			**100.0 %**	**1.20 [1.10, 1.30]**
Heterogeneity: Chi^2 = 1.24, df = 2 (P = 0.54); I^2 =0.0%							
Test for overall effect: Z = 23.21 (P < 0.00001)							
3 longer term (more than one year)							
McKane 1987	12	8.2 (5.4)	11	8.5 (5)		55.8 %	-0.30 [-4.55, 3.95]
Simon 1978	57	60.33 (14.8)	61	58.02 (11.32)		44.2 %	2.31 [-2.47, 7.09]
Subtotal (95% CI)	**69**		**72**			**100.0 %**	**0.85 [-2.32, 4.03]**
Heterogeneity: Chi^2 = 0.64, df = 1 (P = 0.42); I^2 =0.0%							
Test for overall effect: Z = 0.53 (P = 0.60)							
Test for subgroup differences: Chi^2 = 0.48, df = 2 (P = 0.79), I^2 =0.0%							



Analysis 3.12. Comparison 3 FLUPHENAZINE DECANOATE vs OTHER DEPOT NEUROLEPTICS, Outcome 12 Mental state: 2. BPRS (endpoint scores 6 months to 1 year - dichotomous data).

Review: Fluphenazine decanoate (depot) and enanthate for schizophrenia

Comparison: 3 FLUPHENAZINE DECANOATE vs OTHER DEPOT NEUROLEPTICS

Outcome: 12 Mental state: 2. BPRS (endpoint scores 6 months to 1 year - dichotomous data)

Study or subgroup	FLUPHENAZINE DECANOATE n/N	OTHER DEPOT NEUROLEPTICS n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Dencker 1973	18/35	18/32		100.0 %	0.91 [0.59, 1.43]
Total (95% CI)	**35**	**32**		**100.0 %**	**0.91 [0.59, 1.43]**
Total events: 18 (FLUPHENAZINE DECANOATE), 18 (OTHER DEPOT NEUROLEPTICS)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.40 (P = 0.69)					
Test for subgroup differences: Not applicable					

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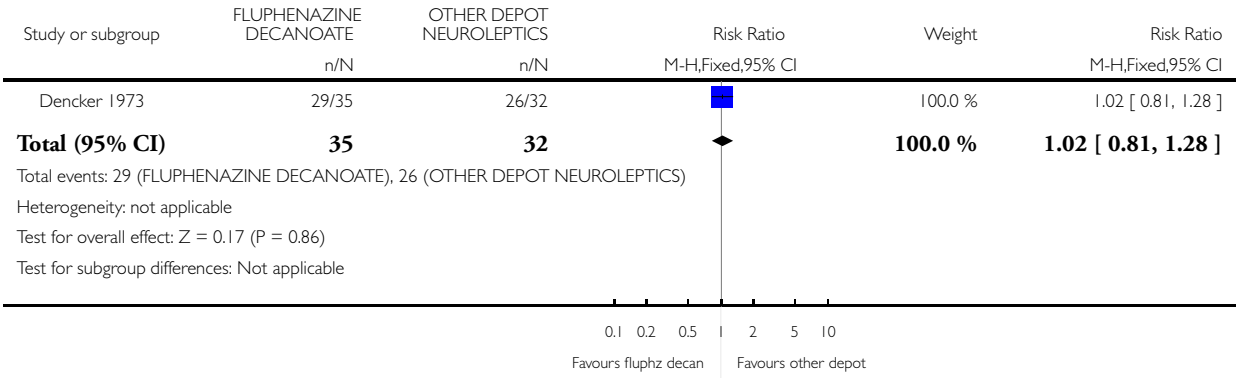
Analysis 3.13. Comparison 3 FLUPHENAZINE DECANOATE vs OTHER DEPOT NEUROLEPTICS, Outcome 13 Mental state: 3. Depression (6 months to 1 year).

Review: Fluphenazine decanoate (depot) and enanthate for schizophrenia

Comparison: 3 FLUPHENAZINE DECANOATE vs OTHER DEPOT NEUROLEPTICS

Outcome: 13 Mental state: 3. Depression (6 months to 1 year)



Analysis 3.14. Comparison 3 FLUPHENAZINE DECANOATE vs OTHER DEPOT NEUROLEPTICS, Outcome 14 Mental state: 4. SAPS and SANS (endpoint scores - high score = poor) (skewed data).

Mental state: 4. SAPS and SANS (endpoint scores - high score = poor) (skewed data)

Study	**Intervention**	**mean**	**SD**	**N**
SAPS				
Ju 2000	Fluphenazine decanoate	31.4	21.1	49
Ju 2000	Pipothiazine palmitate	20.1	23.1	103
SANS				
Ju 2000	Fluphenazine decanoate	14.6	11.4	49
Ju 2000	Pipothiazine palmitate	9.4	14.7	103

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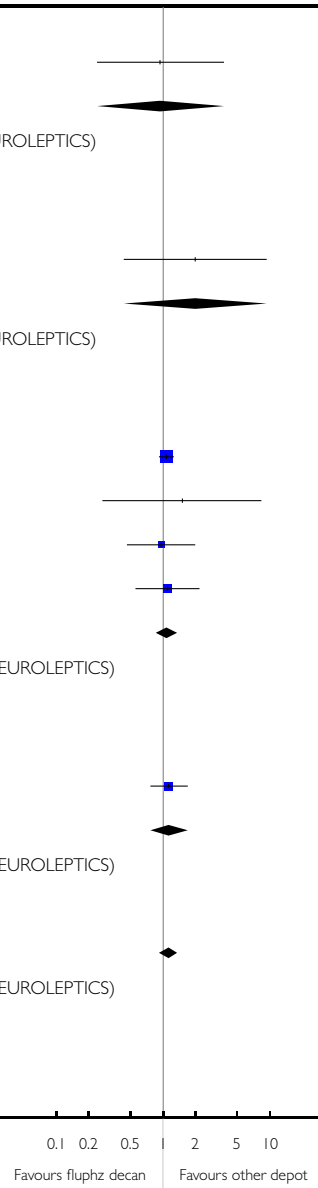
Analysis 3.15. Comparison 3 FLUPHENAZINE DECANOATE vs OTHER DEPOT NEUROLEPTICS, Outcome 15 Adverse effects: 1a. Movement disorders - general.

Review: Fluphenazine decanoate (depot) and enanthate for schizophrenia

Comparison: 3 FLUPHENAZINE DECANOATE vs OTHER DEPOT NEUROLEPTICS

Outcome: 15 Adverse effects: 1a. Movement disorders - general

Study or subgroup	FLUPHENAZINE DECANOATE n/N	OTHER DEPOT NEUROLEPTICS n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
1 immediate term (0 to 5 weeks)					
Levenson 1976	2/5	3/7		3.8 %	0.93 [0.24, 3.68]
Subtotal (95% CI)	**5**	**7**		**3.8 %**	**0.93 [0.24, 3.68]**
Total events: 2 (FLUPHENAZINE DECANOATE), 3 (OTHER DEPOT NEUROLEPTICS)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.10 (P = 0.92)					
2 short term (6 weeks to 5 months)					
Feng 1990	4/15	2/15		3.0 %	2.00 [0.43, 9.32]
Subtotal (95% CI)	**15**	**15**		**3.0 %**	**2.00 [0.43, 9.32]**
Total events: 4 (FLUPHENAZINE DECANOATE), 2 (OTHER DEPOT NEUROLEPTICS)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.88 (P = 0.38)					
3 medium term (6 months to 1 year)					
Dencker 1973	33/35	28/32		44.2 %	1.08 [0.92, 1.26]
Leong 1989	3/30	2/30		3.0 %	1.50 [0.27, 8.34]
McLaren 1992	9/24	9/23		13.9 %	0.96 [0.46, 1.98]
Schlosberg 1978	11/30	10/30		15.1 %	1.10 [0.55, 2.19]
Subtotal (95% CI)	**119**	**115**		**76.2 %**	**1.08 [0.86, 1.34]**
Total events: 56 (FLUPHENAZINE DECANOATE), 49 (OTHER DEPOT NEUROLEPTICS)					
Heterogeneity: Chi^2 = 0.25, df = 3 (P = 0.97); I^2 =0.0%					
Test for overall effect: Z = 0.66 (P = 0.51)					
4 longer term (more than 1 year)					
Wistedt 1983	12/15	12/17		17.0 %	1.13 [0.76, 1.69]
Subtotal (95% CI)	**15**	**17**		**17.0 %**	**1.13 [0.76, 1.69]**
Total events: 12 (FLUPHENAZINE DECANOATE), 12 (OTHER DEPOT NEUROLEPTICS)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.62 (P = 0.54)					
Total (95% CI)	**154**	**154**		**100.0 %**	**1.11 [0.91, 1.35]**
Total events: 74 (FLUPHENAZINE DECANOATE), 66 (OTHER DEPOT NEUROLEPTICS)					
Heterogeneity: Chi^2 = 1.05, df = 6 (P = 0.98); I^2 =0.0%					
Test for overall effect: Z = 1.03 (P = 0.30)					
Test for subgroup differences: Chi^2 = 0.69, df = 3 (P = 0.88), I^2 =0.0%					



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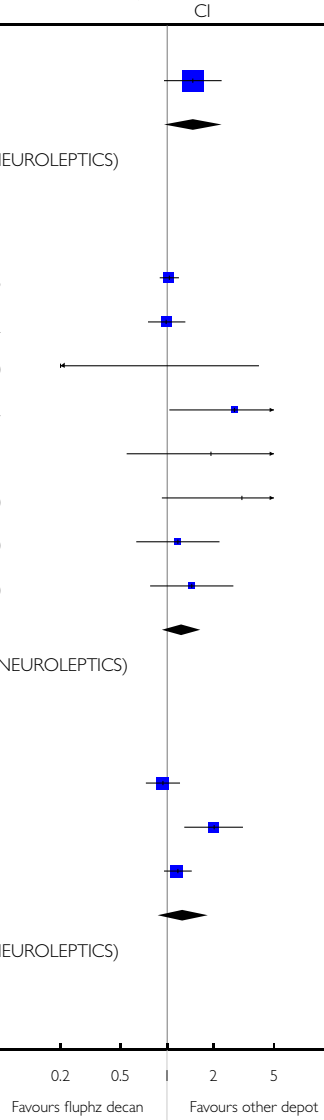
Analysis 3.16. Comparison 3 FLUPHENAZINE DECANOATE vs OTHER DEPOT NEUROLEPTICS, Outcome 16 Adverse effects: 1b. Movement disorders - needing anticholinergic drugs.

Review: Fluphenazine decanoate (depot) and enanthate for schizophrenia

Comparison: 3 FLUPHENAZINE DECANOATE vs OTHER DEPOT NEUROLEPTICS

Outcome: 16 Adverse effects: 1b. Movement disorders - needing anticholinergic drugs

Study or subgroup	FLUPHENAZINE DECANOATE n/N	OTHER DEPOT NEUROLEPTICS n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
1 short term (6 weeks to 5 months)					
Wistedt 1984	20/26	13/25		100.0 %	1.48 [0.96, 2.28]
Subtotal (95% CI)	**26**	**25**		**100.0 %**	**1.48 [0.96, 2.28]**
Total events: 20 (FLUPHENAZINE DECANOATE), 13 (OTHER DEPOT NEUROLEPTICS)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.78 (P = 0.075)					
2 medium term (6 months to 1 year)					
Chouinard 1984	33/36	32/36		31.6 %	1.03 [0.89, 1.20]
Dencker 1973	26/35	24/32		26.0 %	0.99 [0.75, 1.31]
Leong 1989	0/30	2/30		0.9 %	0.20 [0.01, 4.00]
Magnus 1979	12/26	4/24		6.7 %	2.77 [1.03, 7.42]
McLaren 1992	6/24	3/23		4.4 %	1.92 [0.54, 6.77]
Russell 1982	6/13	3/20		4.8 %	3.08 [0.93, 10.19]
Schlosberg 1978	13/30	11/30		12.9 %	1.18 [0.63, 2.20]
Sharma 1991	14/29	10/30		12.7 %	1.45 [0.77, 2.72]
Subtotal (95% CI)	**223**	**225**		**100.0 %**	**1.24 [0.93, 1.64]**
Total events: 110 (FLUPHENAZINE DECANOATE), 89 (OTHER DEPOT NEUROLEPTICS)					
Heterogeneity: Tau^2 = 0.06; Chi^2 = 14.24, df = 7 (P = 0.05); I^2 =51%					
Test for overall effect: Z = 1.47 (P = 0.14)					
3 longer term (more than 1 year)					
McKane 1987	16/19	17/19		35.7 %	0.94 [0.73, 1.21]
Pinto 1979	28/33	13/31		26.9 %	2.02 [1.30, 3.14]
Simon 1978	46/57	42/61		37.3 %	1.17 [0.95, 1.45]
Subtotal (95% CI)	**109**	**111**		**100.0 %**	**1.26 [0.86, 1.83]**
Total events: 90 (FLUPHENAZINE DECANOATE), 72 (OTHER DEPOT NEUROLEPTICS)					
Heterogeneity: Tau^2 = 0.09; Chi^2 = 10.67, df = 2 (P = 0.005); I^2 =81%					
Test for overall effect: Z = 1.18 (P = 0.24)					



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Analysis 3.17. Comparison 3 FLUPHENAZINE DECANOATE vs OTHER DEPOT NEUROLEPTICS, Outcome 17 Adverse effects: 1c. Movement disorders - parkinsonism.

Review: Fluphenazine decanoate (depot) and enanthate for schizophrenia

Comparison: 3 FLUPHENAZINE DECANOATE vs OTHER DEPOT NEUROLEPTICS

Outcome: 17 Adverse effects: 1c. Movement disorders - parkinsonism

Study or subgroup	FLUPHENAZINE DECANOATE n/N	OTHER DEPOT NEUROLEPTICS n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
1 immediate (0 to 5 weeks)					
Levenson 1976	2/5	3/7		33.5 %	0.93 [0.24, 3.68]
Subtotal (95% CI)	**5**	**7**		**33.5 %**	**0.93 [0.24, 3.68]**
Total events: 2 (FLUPHENAZINE DECANOATE), 3 (OTHER DEPOT NEUROLEPTICS)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.10 (P = 0.92)					
2 medium term (6 months to 1 year)					
Leong 1989	5/30	4/30		53.6 %	1.25 [0.37, 4.21]
Subtotal (95% CI)	**30**	**30**		**53.6 %**	**1.25 [0.37, 4.21]**
Total events: 5 (FLUPHENAZINE DECANOATE), 4 (OTHER DEPOT NEUROLEPTICS)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.36 (P = 0.72)					
3 longer term (more than 1 year)					
Simon 1978	1/57	1/61		12.9 %	1.07 [0.07, 16.71]
Subtotal (95% CI)	**57**	**61**		**12.9 %**	**1.07 [0.07, 16.71]**
Total events: 1 (FLUPHENAZINE DECANOATE), 1 (OTHER DEPOT NEUROLEPTICS)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.05 (P = 0.96)					
Total (95% CI)	**92**	**98**		**100.0 %**	**1.12 [0.47, 2.69]**
Total events: 8 (FLUPHENAZINE DECANOATE), 8 (OTHER DEPOT NEUROLEPTICS)					
Heterogeneity: Chi^2 = 0.10, df = 2 (P = 0.95); I^2 =0.0%					
Test for overall effect: Z = 0.25 (P = 0.80)					
Test for subgroup differences: Chi^2 = 0.10, df = 2 (P = 0.95), I^2 =0.0%					

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Analysis 3.18. Comparison 3 FLUPHENAZINE DECANOATE vs OTHER DEPOT NEUROLEPTICS, Outcome 18 Adverse effects: 1d. Movement disorders - tardive dyskinesia: longer term (more than 1 year).

Review: Fluphenazine decanoate (depot) and enanthate for schizophrenia

Comparison: 3 FLUPHENAZINE DECANOATE vs OTHER DEPOT NEUROLEPTICS

Outcome: 18 Adverse effects: 1d. Movement disorders - tardive dyskinesia: longer term (more than 1 year)

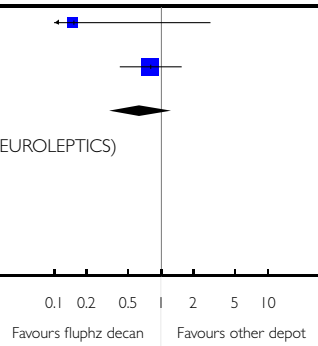
Study or subgroup	FLUPHENAZINE DECANOATE n/N	OTHER DEPOT NEUROLEPTICS n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Simon 1978	0/57	3/61		26.5 %	0.15 [0.01, 2.89]
Wistedt 1983	7/15	10/17		73.5 %	0.79 [0.41, 1.55]
Total (95% CI)	**72**	**78**		**100.0 %**	**0.62 [0.32, 1.23]**

Total events: 7 (FLUPHENAZINE DECANOATE), 13 (OTHER DEPOT NEUROLEPTICS)

Heterogeneity: Chi^2 = 1.37, df = 1 (P = 0.24); I^2 =27%

Test for overall effect: Z = 1.37 (P = 0.17)

Test for subgroup differences: Not applicable



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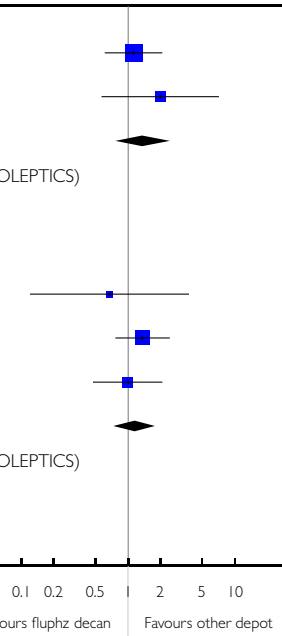
Analysis 3.19. Comparison 3 FLUPHENAZINE DECANOATE vs OTHER DEPOT NEUROLEPTICS, Outcome 19 Adverse effects: 1e. Movement disorders - tremor.

Review: Fluphenazine decanoate (depot) and enanthate for schizophrenia

Comparison: 3 FLUPHENAZINE DECANOATE vs OTHER DEPOT NEUROLEPTICS

Outcome: 19 Adverse effects: 1e. Movement disorders - tremor

Study or subgroup	FLUPHENAZINE DECANOATE n/N	OTHER DEPOT NEUROLEPTICS n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
1 short term (6 weeks to 5 months)					
Feng 1990	9/15	8/15		72.7 %	1.13 [0.60, 2.11]
Frangos 1978	6/25	3/25		27.3 %	2.00 [0.56, 7.12]
Subtotal (95% CI)	**40**	**40**		**100.0 %**	**1.36 [0.76, 2.46]**
Total events: 15 (FLUPHENAZINE DECANOATE), 11 (OTHER DEPOT NEUROLEPTICS)					
Heterogeneity: Chi^2 = 0.71, df = 1 (P = 0.40); I^2 =0.0%					
Test for overall effect: Z = 1.03 (P = 0.30)					
2 medium term (6 months to 1 year)					
Leong 1989	2/30	3/30		14.0 %	0.67 [0.12, 3.71]
Schlosberg 1978	15/30	11/30		51.2 %	1.36 [0.76, 2.46]
Wistedt 1983	7/15	8/17		34.9 %	0.99 [0.47, 2.08]
Subtotal (95% CI)	**75**	**77**		**100.0 %**	**1.14 [0.73, 1.78]**
Total events: 24 (FLUPHENAZINE DECANOATE), 22 (OTHER DEPOT NEUROLEPTICS)					
Heterogeneity: Chi^2 = 0.87, df = 2 (P = 0.65); I^2 =0.0%					
Test for overall effect: Z = 0.56 (P = 0.58)					



Analysis 3.20. Comparison 3 FLUPHENAZINE DECANOATE vs OTHER DEPOT NEUROLEPTICS, Outcome 20 Adverse effects: 1f. Movement disorders - endpoint scores (short term - 6 weeks to 5 months).

Adverse effects: 1f. Movement disorders - endpoint scores (short term - 6 weeks to 5 months)

Study	**Intervention**	**mean**	**SD**	**N**
TESS (high = poor)				
Ju 2000	Fluphenazine decanoate	10.2	8.1	49
Ju 2000	Pipothiazine palmitate	2.6	3.9	103
RSESE (high = poor)				
Ju 2000	Fluphenazine decanoate	7.5	7	49

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Ju 2000	Pipothiazine palmitate	1.0	2.1	103

Analysis 3.21. Comparison 3 FLUPHENAZINE DECANOATE vs OTHER DEPOT NEUROLEPTICS, Outcome 21 Adverse effects: 2. Blurred vision.

Review: Fluphenazine decanoate (depot) and enanthate for schizophrenia

Comparison: 3 FLUPHENAZINE DECANOATE vs OTHER DEPOT NEUROLEPTICS

Outcome: 21 Adverse effects: 2. Blurred vision

Study or subgroup	FLUPHENAZINE DECANOATE n/N	OTHER DEPOT NEUROLEPTICS n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
1 medium term (6 months to 1 year)					
Wistedt 1983	7/15	9/17		100.0 %	0.88 [0.44, 1.78]
Subtotal (95% CI)	**15**	**17**		**100.0 %**	**0.88 [0.44, 1.78]**
Total events: 7 (FLUPHENAZINE DECANOATE), 9 (OTHER DEPOT NEUROLEPTICS)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.35 (P = 0.72)					
2 longer term (more than 1 year)					
Pinto 1979	9/33	0/31		100.0 %	17.88 [1.08, 294.82]
Subtotal (95% CI)	**33**	**31**		**100.0 %**	**17.88 [1.08, 294.82]**
Total events: 9 (FLUPHENAZINE DECANOATE), 0 (OTHER DEPOT NEUROLEPTICS)					
Heterogeneity: not applicable					
Test for overall effect: Z = 2.02 (P = 0.044)					

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Analysis 3.22. Comparison 3 FLUPHENAZINE DECANOATE vs OTHER DEPOT NEUROLEPTICS, Outcome 22 Adverse effects: 3. Dry mouth: longer term (more than 1 year).

Review: Fluphenazine decanoate (depot) and enanthate for schizophrenia

Comparison: 3 FLUPHENAZINE DECANOATE vs OTHER DEPOT NEUROLEPTICS

Outcome: 22 Adverse effects: 3. Dry mouth: longer term (more than 1 year)

Study or subgroup	FLUPHENAZINE DECANOATE n/N	OTHER DEPOT NEUROLEPTICS n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Wistedt 1983	7/15	11/17		100.0 %	0.72 [0.38, 1.37]
Total (95% CI)	**15**	**17**		**100.0 %**	**0.72 [0.38, 1.37]**

Total events: 7 (FLUPHENAZINE DECANOATE), 11 (OTHER DEPOT NEUROLEPTICS)

Heterogeneity: not applicable

Test for overall effect: Z = 0.99 (P = 0.32)

Test for subgroup differences: Not applicable

Analysis 3.23. Comparison 3 FLUPHENAZINE DECANOATE vs OTHER DEPOT NEUROLEPTICS, Outcome 23 Adverse effects: 4. General adverse effects.

Review: Fluphenazine decanoate (depot) and enanthate for schizophrenia

Comparison: 3 FLUPHENAZINE DECANOATE vs OTHER DEPOT NEUROLEPTICS

Outcome: 23 Adverse effects: 4. General adverse effects

Study or subgroup	FLUPHENAZINE DECANOATE n/N	OTHER DEPOT NEUROLEPTICS n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
1 short term (6 weeks to 5 months)					
Frangos 1978	22/25	16/25		55.9 %	1.38 [0.99, 1.91]
Javed 1991	18/20	12/18		44.1 %	1.35 [0.94, 1.93]
Subtotal (95% CI)	**45**	**43**		**100.0 %**	**1.36 [1.07, 1.74]**

Total events: 40 (FLUPHENAZINE DECANOATE), 28 (OTHER DEPOT NEUROLEPTICS)

Heterogeneity: Chi^2 = 0.01, df = 1 (P = 0.94); I^2 =0.0%

Test for overall effect: Z = 2.52 (P = 0.012)

2 medium term (6 months to 1 year)					
Dencker 1973	29/35	25/32		44.6 %	1.06 [0.84, 1.34]

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Study or subgroup	FLUPHENAZINE DECANOATE n/N	OTHER DEPOT NEUROLEPTICS n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Leong 1989	6/30	2/30		3.4 %	3.00 [0.66, 13.69]
Magnus 1979	15/26	4/24		7.1 %	3.46 [1.33, 8.98]
Russell 1982	3/13	8/20		10.8 %	0.58 [0.19, 1.78]
Walker 1983	9/20	19/19		34.1 %	0.46 [0.29, 0.75]
Subtotal (95% CI)	**124**	**125**		**100.0 %**	**1.04 [0.83, 1.32]**

Total events: 62 (FLUPHENAZINE DECANOATE), 58 (OTHER DEPOT NEUROLEPTICS)

Heterogeneity: Chi^2 = 20.14, df = 4 (P = 0.00047); I^2 =80%

Test for overall effect: Z = 0.34 (P = 0.73)

Analysis 3.24. Comparison 3 FLUPHENAZINE DECANOATE vs OTHER DEPOT NEUROLEPTICS, Outcome 24 SENSITIVITY ANALYSIS Global state: 2. Relapse.

Review: Fluphenazine decanoate (depot) and enanthate for schizophrenia

Comparison: 3 FLUPHENAZINE DECANOATE vs OTHER DEPOT NEUROLEPTICS

Outcome: 24 SENSITIVITY ANALYSIS Global state: 2. Relapse

Study or subgroup	FLUPHENAZINE DECANOATE n/N	OTHER DEPOT NEUROLEPTICS n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
1 medium term (6 months to 1 year)					
Chouinard 1984	1/36	0/36		1.0 %	3.00 [0.13, 71.28]
Cookson 1986	0/9	2/10		4.9 %	0.22 [0.01, 4.05]
Dencker 1973	6/35	3/32		6.4 %	1.83 [0.50, 6.71]
Kelly 1977	3/28	3/26		6.3 %	0.93 [0.21, 4.20]
Leong 1989	0/30	1/30		3.1 %	0.33 [0.01, 7.87]
Lundin 1990	9/30	11/28		23.2 %	0.76 [0.37, 1.56]
Magnus 1979	1/26	1/26		2.0 %	1.00 [0.07, 15.15]
McLaren 1992	0/24	6/23		13.5 %	0.07 [0.00, 1.24]

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Study or subgroup	FLUPHENAZINE DECANOATE n/N	OTHER DEPOT NEUROLEPTICS n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Russell 1982	3/13	2/20		3.2 %	2.31 [0.44, 11.98]
Schlosberg 1978	9/30	8/30		16.3 %	1.13 [0.50, 2.52]
Sharma 1991	6/29	10/30		20.0 %	0.62 [0.26, 1.49]
Subtotal (95% CI)	**290**	**291**		**100.0 %**	**0.82 [0.56, 1.18]**

Total events: 38 (FLUPHENAZINE DECANOATE), 47 (OTHER DEPOT NEUROLEPTICS)

Heterogeneity: Chi^2 = 8.59, df = 10 (P = 0.57); I^2 =0.0%

Test for overall effect: Z = 1.07 (P = 0.28)

Analysis 4.1. Comparison 4 FLUPHENAZINE DECANOATE - DOSAGE STUDIES - HIGH DOSE vs STANDARD, Outcome 1 Global state: 1. Relapse (medium term - 6 months to 1 year).

Review: Fluphenazine decanoate (depot) and enanthate for schizophrenia

Comparison: 4 FLUPHENAZINE DECANOATE - DOSAGE STUDIES - HIGH DOSE vs STANDARD

Outcome: 1 Global state: 1. Relapse (medium term - 6 months to 1 year)

Study or subgroup	FLUPHZ DECAN HIGH DOSE n/N	FLUPHZ DECAN STANRD DOSE n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Kreisman 1988	30/66	6/66		57.2 %	5.00 [2.23, 11.21]
McClelland 1976	2/25	3/25		42.8 %	0.67 [0.12, 3.65]
Total (95% CI)	**91**	**91**		**100.0 %**	**2.11 [0.30, 14.91]**

Total events: 32 (FLUPHZ DECAN HIGH DOSE), 9 (FLUPHZ DECAN STANRD DOSE)

Heterogeneity: Tau^2 = 1.57; Chi^2 = 4.40, df = 1 (P = 0.04); I^2 =77%

Test for overall effect: Z = 0.75 (P = 0.45)

Test for subgroup differences: Not applicable

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Analysis 4.2. Comparison 4 FLUPHENAZINE DECANOATE - DOSAGE STUDIES - HIGH DOSE vs STANDARD, Outcome 2 Global state: 2. Needing additional antispsychotic treatment (medium term - 6 months to 1 year).

Review: Fluphenazine decanoate (depot) and enanthate for schizophrenia

Comparison: 4 FLUPHENAZINE DECANOATE - DOSAGE STUDIES - HIGH DOSE vs STANDARD

Outcome: 2 Global state: 2. Needing additional antispsychotic treatment (medium term - 6 months to 1 year)

Study or subgroup	FLUPHZ DECAN HIGH DOSE n/N	FLUPHZ DECAN STANRD DOSE n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
McClelland 1976	5/25	3/25		100.0 %	1.67 [0.45, 6.24]
Total (95% CI)	**25**	**25**		**100.0 %**	**1.67 [0.45, 6.24]**

Total events: 5 (FLUPHZ DECAN HIGH DOSE), 3 (FLUPHZ DECAN STANRD DOSE)

Heterogeneity: not applicable

Test for overall effect: Z = 0.76 (P = 0.45)

Test for subgroup differences: Not applicable

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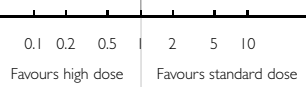
Analysis 4.3. Comparison 4 FLUPHENAZINE DECANOATE - DOSAGE STUDIES - HIGH DOSE vs STANDARD, Outcome 3 Global state: 3. Not improved (medium term - 6 months to 1 year).

Review: Fluphenazine decanoate (depot) and enanthate for schizophrenia

Comparison: 4 FLUPHENAZINE DECANOATE - DOSAGE STUDIES - HIGH DOSE vs STANDARD

Outcome: 3 Global state: 3. Not improved (medium term - 6 months to 1 year)

Study or subgroup	FLUPHZ DECAN HIGH DOSE n/N	FLUPHZ DECAN STANRD DOSE n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
1 nurse rated					
Lehmann 1980	19/20	12/20		100.0 %	1.58 [1.09, 2.30]
Subtotal (95% CI)	**20**	**20**		**100.0 %**	**1.58 [1.09, 2.30]**
Total events: 19 (FLUPHZ DECAN HIGH DOSE), 12 (FLUPHZ DECAN STANRD DOSE)					
Heterogeneity: not applicable					
Test for overall effect: Z = 2.42 (P = 0.015)					
2 psychiatrist rated					
Lehmann 1980	15/20	13/20		100.0 %	1.15 [0.77, 1.74]
Subtotal (95% CI)	**20**	**20**		**100.0 %**	**1.15 [0.77, 1.74]**
Total events: 15 (FLUPHZ DECAN HIGH DOSE), 13 (FLUPHZ DECAN STANRD DOSE)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.69 (P = 0.49)					



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Analysis 4.4. Comparison 4 FLUPHENAZINE DECANOATE - DOSAGE STUDIES - HIGH DOSE vs STANDARD, Outcome 4 Leaving the study early (medium term - 6 months to 1 year).

Review: Fluphenazine decanoate (depot) and enanthate for schizophrenia

Comparison: 4 FLUPHENAZINE DECANOATE - DOSAGE STUDIES - HIGH DOSE vs STANDARD

Outcome: 4 Leaving the study early (medium term - 6 months to 1 year)

Study or subgroup	FLUPHZ DECAN HIGH DOSE n/N	FLUPHZ DECAN STANRD DOSE n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Lehmann 1980	1/20	2/20		40.0 %	0.50 [0.05, 5.08]
McClelland 1976	2/25	3/25		60.0 %	0.67 [0.12, 3.65]
Total (95% CI)	**45**	**45**		**100.0 %**	**0.60 [0.15, 2.36]**

Total events: 3 (FLUPHZ DECAN HIGH DOSE), 5 (FLUPHZ DECAN STANRD DOSE)

Heterogeneity: $Chi^2 = 0.04$, df = 1 (P = 0.84); $I^2 = 0.0\%$

Test for overall effect: Z = 0.73 (P = 0.46)

Test for subgroup differences: Not applicable

Analysis 4.5. Comparison 4 FLUPHENAZINE DECANOATE - DOSAGE STUDIES - HIGH DOSE vs STANDARD, Outcome 5 Mental state: BPRS endpoint scores (medium term - 6 months to 1 year, high score = poor).

Review: Fluphenazine decanoate (depot) and enanthate for schizophrenia

Comparison: 4 FLUPHENAZINE DECANOATE - DOSAGE STUDIES - HIGH DOSE vs STANDARD

Outcome: 5 Mental state: BPRS endpoint scores (medium term - 6 months to 1 year, high score = poor)

Study or subgroup	FLUPHZ DECAN HIGH DOSE N	Mean(SD)	FLUPHZ DECAN STANRD DOSE N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
McClelland 1976	25	34.65 (11.48)	25	34.68 (9.19)		100.0 %	-0.03 [-5.79, 5.73]
Total (95% CI)	**25**		**25**			**100.0 %**	**-0.03 [-5.79, 5.73]**

Heterogeneity: not applicable

Test for overall effect: Z = 0.01 (P = 0.99)

Test for subgroup differences: Not applicable

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Analysis 4.6. Comparison 4 FLUPHENAZINE DECANOATE - DOSAGE STUDIES - HIGH DOSE vs STANDARD, Outcome 6 Adverse effects: Movement disorders - needing anticholinergic drugs (medium term - 6 months to 1 year).

Review: Fluphenazine decanoate (depot) and enanthate for schizophrenia

Comparison: 4 FLUPHENAZINE DECANOATE - DOSAGE STUDIES - HIGH DOSE vs STANDARD

Outcome: 6 Adverse effects: Movement disorders - needing anticholinergic drugs (medium term - 6 months to 1 year)

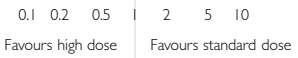
Study or subgroup	FLUPHZ DECAN HIGH DOSE n/N	FLUPHZ DECAN STANRD DOSE n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
McClelland 1976	5/25	3/25		100.0 %	1.67 [0.45, 6.24]
Total (95% CI)	**25**	**25**		**100.0 %**	**1.67 [0.45, 6.24]**

Total events: 5 (FLUPHZ DECAN HIGH DOSE), 3 (FLUPHZ DECAN STANRD DOSE)

Heterogeneity: not applicable

Test for overall effect: Z = 0.76 (P = 0.45)

Test for subgroup differences: Not applicable



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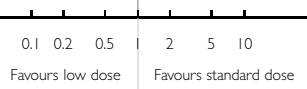
Analysis 5.1. Comparison 5 FLUPHENAZINE DECANOATE - DOSAGE STUDIES - LOW DOSE vs STANDARD, Outcome 1 Global state: Relapse.

Review: Fluphenazine decanoate (depot) and enanthate for schizophrenia

Comparison: 5 FLUPHENAZINE DECANOATE - DOSAGE STUDIES - LOW DOSE vs STANDARD

Outcome: 1 Global state: Relapse

Study or subgroup	FLUPHZ DECAN LOW DOSE n/N	FLUPHZ DECAN STANRD DOSE n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
1 medium term (6 months to 1 year)					
Kane 1983	26/62	3/64		30.5 %	8.95 [2.85, 28.05]
Kreisman 1988	30/66	6/66		33.5 %	5.00 [2.23, 11.21]
Schooler 1997	27/107	27/106		36.0 %	0.99 [0.62, 1.57]
Subtotal (95% CI)	**235**	**236**		**100.0 %**	**3.33 [0.77, 14.51]**
Total events: 83 (FLUPHZ DECAN LOW DOSE), 36 (FLUPHZ DECAN STANRD DOSE)					
Heterogeneity: Tau² = 1.51; Chi² = 21.86, df = 2 (P = 0.00002); I² =91%					
Test for overall effect: Z = 1.60 (P = 0.11)					
2 longer term (more than 1 year)					
Asarnow 1988	3/22	1/14		12.2 %	1.91 [0.22, 16.58]
Hogarty 1988	16/37	14/33		66.2 %	1.02 [0.59, 1.75]
Marder 1987	2/35	6/31		21.6 %	0.30 [0.06, 1.36]
Subtotal (95% CI)	**94**	**78**		**100.0 %**	**0.84 [0.38, 1.89]**
Total events: 21 (FLUPHZ DECAN LOW DOSE), 21 (FLUPHZ DECAN STANRD DOSE)					
Heterogeneity: Tau² = 0.18; Chi² = 2.78, df = 2 (P = 0.25); I² =28%					
Test for overall effect: Z = 0.42 (P = 0.68)					



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Analysis 5.2. Comparison 5 FLUPHENAZINE DECANOATE - DOSAGE STUDIES - LOW DOSE vs STANDARD, Outcome 2 Leaving the study early.

Review: Fluphenazine decanoate (depot) and enanthate for schizophrenia

Comparison: 5 FLUPHENAZINE DECANOATE - DOSAGE STUDIES - LOW DOSE vs STANDARD

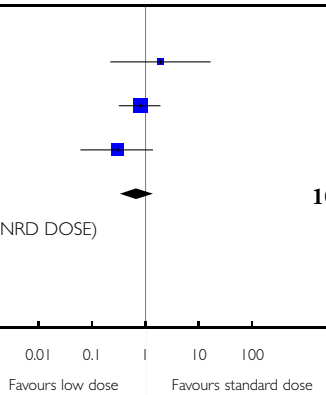
Outcome: 2 Leaving the study early

Study or subgroup	FLUPHZ DECAN LOW DOSE n/N	FLUPHZ DECAN STANRD DOSE n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
1 longer term (more than 1 year)					
Asarnow 1988	3/22	1/14		7.6 %	1.91 [0.22, 16.58]
Hogarty 1988	7/37	8/33		52.7 %	0.78 [0.32, 1.92]
Marder 1987	2/35	6/31		39.7 %	0.30 [0.06, 1.36]
Subtotal (95% CI)	**94**	**78**		**100.0 %**	**0.67 [0.33, 1.36]**

Total events: 12 (FLUPHZ DECAN LOW DOSE), 15 (FLUPHZ DECAN STANRD DOSE)

Heterogeneity: $Chi^2 = 2.12$, df = 2 (P = 0.35); $I^2 = 6\%$

Test for overall effect: Z = 1.10 (P = 0.27)



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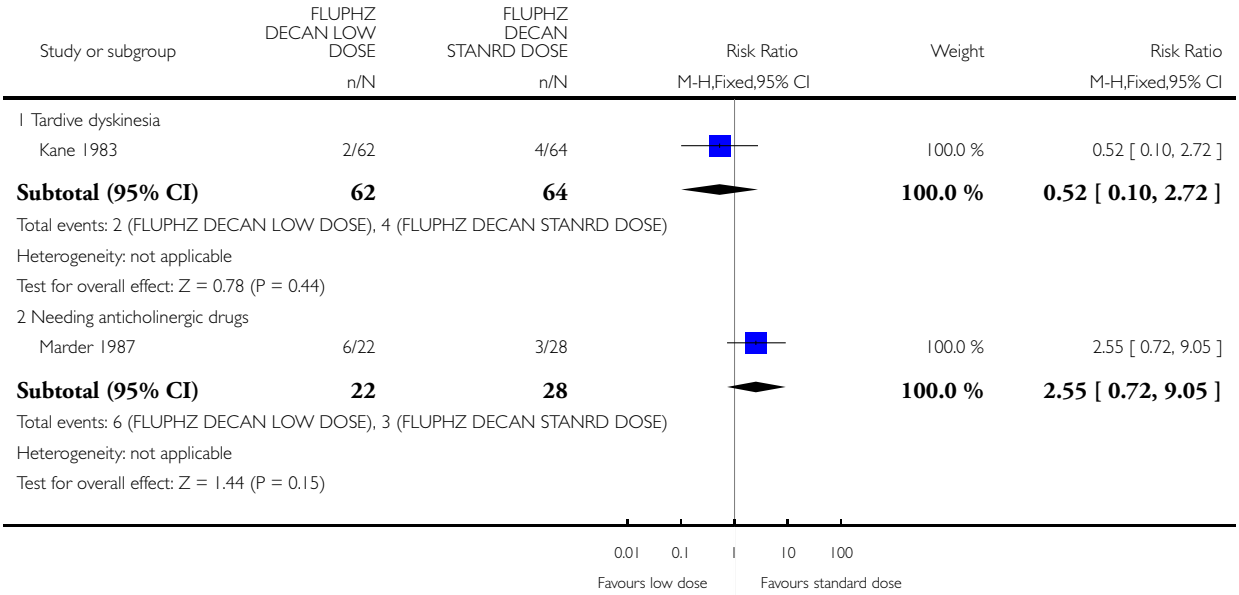
Analysis 5.3. Comparison 5 FLUPHENAZINE DECANOATE - DOSAGE STUDIES - LOW DOSE vs STANDARD, Outcome 3 Adverse effects: 1. Movement disorders (medium term - 6 months to 1 year).

Review: Fluphenazine decanoate (depot) and enanthate for schizophrenia

Comparison: 5 FLUPHENAZINE DECANOATE - DOSAGE STUDIES - LOW DOSE vs STANDARD

Outcome: 3 Adverse effects: 1. Movement disorders (medium term - 6 months to 1 year)



Analysis 5.4. Comparison 5 FLUPHENAZINE DECANOATE - DOSAGE STUDIES - LOW DOSE vs STANDARD, Outcome 4 Adverse effects: 2. Continuous data - skewed data (endpoint scores, high = poor).

Adverse effects: 2. Continuous data - skewed data (endpoint scores, high = poor)

Study	**Intervention**	**mean**	**SD**	**N**
Kane 1983	Fluphenazine decanoate (low dose)	0.52	1.00	62
Kane 1983	Fluphenazine decanoate (standard dose)	1.04	2.42	64

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Analysis 6.1. Comparison 6 FLUPHENAZINE ENANTHATE vs PLACEBO, Outcome 1 Adverse effects: Movement disorders - general.

Review: Fluphenazine decanoate (depot) and enanthate for schizophrenia

Comparison: 6 FLUPHENAZINE ENANTHATE vs PLACEBO

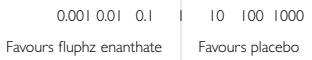
Outcome: 1 Adverse effects: Movement disorders - general

Study or subgroup	FLUPHENAZINE ENANTHATE n/N	PLACEBO n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
1 Needing anticholinergic drugs (short term - 6 weeks to 5 months)					
Van Praag 1970	4/12	0/13		100.0 %	9.69 [0.58, 163.02]
Subtotal (95% CI)	**12**	**13**		**100.0 %**	**9.69 [0.58, 163.02]**

Total events: 4 (FLUPHENAZINE ENANTHATE), 0 (PLACEBO)

Heterogeneity: not applicable

Test for overall effect: Z = 1.58 (P = 0.11)



Analysis 7.1. Comparison 7 FLUPHENAZINE ENANTHATE vs ORAL NEUROLEPTICS, Outcome 1 Global state: No clinically important global change (immediate - 0 to 5 weeks).

Review: Fluphenazine decanoate (depot) and enanthate for schizophrenia

Comparison: 7 FLUPHENAZINE ENANTHATE vs ORAL NEUROLEPTICS

Outcome: 1 Global state: No clinically important global change (immediate - 0 to 5 weeks)

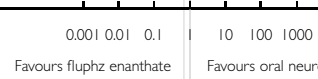
Study or subgroup	FLUPHENAZINE ENANTHATE n/N	ORAL NEU-ROLEPTICS n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Chien 1973	5/16	7/15		100.0 %	0.67 [0.27, 1.66]
Total (95% CI)	**16**	**15**		**100.0 %**	**0.67 [0.27, 1.66]**

Total events: 5 (FLUPHENAZINE ENANTHATE), 7 (ORAL NEUROLEPTICS)

Heterogeneity: not applicable

Test for overall effect: Z = 0.87 (P = 0.39)

Test for subgroup differences: Not applicable



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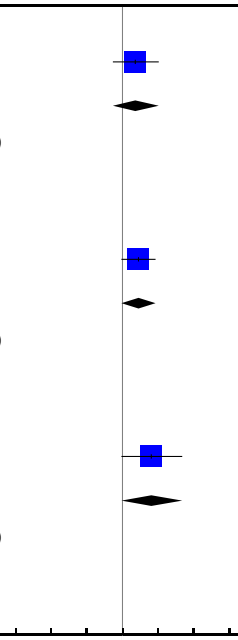
Analysis 7.2. Comparison 7 FLUPHENAZINE ENANTHATE vs ORAL NEUROLEPTICS, Outcome 2 Adverse effects: Movement disorders - general.

Review: Fluphenazine decanoate (depot) and enanthate for schizophrenia

Comparison: 7 FLUPHENAZINE ENANTHATE vs ORAL NEUROLEPTICS

Outcome: 2 Adverse effects: Movement disorders - general

Study or subgroup	FLUPHENAZINE ENANTHATE n/N	ORAL NEU-ROLEPTICS n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
1 movement disorders: immediate (0 to 5 weeks)					
Chien 1973	5/16	2/15		100.0 %	2.34 [0.53, 10.30]
Subtotal (95% CI)	**16**	**15**		**100.0 %**	**2.34 [0.53, 10.30]**
Total events: 5 (FLUPHENAZINE ENANTHATE), 2 (ORAL NEUROLEPTICS)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.13 (P = 0.26)					
2 side effects: immediate (0 to 5 weeks)					
Chien 1973	9/16	3/15		100.0 %	2.81 [0.94, 8.45]
Subtotal (95% CI)	**16**	**15**		**100.0 %**	**2.81 [0.94, 8.45]**
Total events: 9 (FLUPHENAZINE ENANTHATE), 3 (ORAL NEUROLEPTICS)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.84 (P = 0.066)					
3 parkinsonism: immediate (0 to 5 weeks)					
Chien 1973	7/16	1/15		100.0 %	6.56 [0.91, 47.21]
Subtotal (95% CI)	**16**	**15**		**100.0 %**	**6.56 [0.91, 47.21]**
Total events: 7 (FLUPHENAZINE ENANTHATE), 1 (ORAL NEUROLEPTICS)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.87 (P = 0.062)					



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Analysis 8.1. Comparison 8 FLUPHENAZINE ENANTHATE vs OTHER DEPOT NEUROLEPTICS, Outcome 1 Global state: 1. Needing additional antipsychotic treatment (6 months to 1 year).

Review: Fluphenazine decanoate (depot) and enanthate for schizophrenia

Comparison: 8 FLUPHENAZINE ENANTHATE vs OTHER DEPOT NEUROLEPTICS

Outcome: 1 Global state: 1. Needing additional antipsychotic treatment (6 months to 1 year)

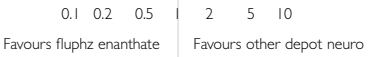
Study or subgroup	FLUPHENAZINE ENANTHATE n/N	OTHER DEPOT NEUROLEPTICS n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Albert 1980	4/11	13/22		59.1 %	0.62 [0.26, 1.45]
Chouinard 1978	2/16	6/16		40.9 %	0.33 [0.08, 1.41]
Total (95% CI)	**27**	**38**		**100.0 %**	**0.50 [0.24, 1.05]**

Total events: 6 (FLUPHENAZINE ENANTHATE), 19 (OTHER DEPOT NEUROLEPTICS)

Heterogeneity: $Chi^2 = 0.53$, df = 1 (P = 0.47); $I^2 = 0.0\%$

Test for overall effect: Z = 1.84 (P = 0.066)

Test for subgroup differences: Not applicable



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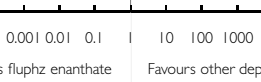
Analysis 8.2. Comparison 8 FLUPHENAZINE ENANTHATE vs OTHER DEPOT NEUROLEPTICS, Outcome 2 Global state: 2. Relapse.

Review: Fluphenazine decanoate (depot) and enanthate for schizophrenia

Comparison: 8 FLUPHENAZINE ENANTHATE vs OTHER DEPOT NEUROLEPTICS

Outcome: 2 Global state: 2. Relapse

Study or subgroup	FLUPHENAZINE ENANTHATE n/N	OTHER DEPOT NEUROLEPTICS n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
1 short term (6 weeks to 5 months)					
Malm 1974	6/26	3/31		100.0 %	2.38 [0.66, 8.61]
Subtotal (95% CI)	**26**	**31**		**100.0 %**	**2.38 [0.66, 8.61]**
Total events: 6 (FLUPHENAZINE ENANTHATE), 3 (OTHER DEPOT NEUROLEPTICS)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.33 (P = 0.18)					
2 medium term (6 months to 1 year)					
Chouinard 1978	1/16	3/16		100.0 %	0.33 [0.04, 2.87]
Subtotal (95% CI)	**16**	**16**		**100.0 %**	**0.33 [0.04, 2.87]**
Total events: 1 (FLUPHENAZINE ENANTHATE), 3 (OTHER DEPOT NEUROLEPTICS)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.00 (P = 0.32)					



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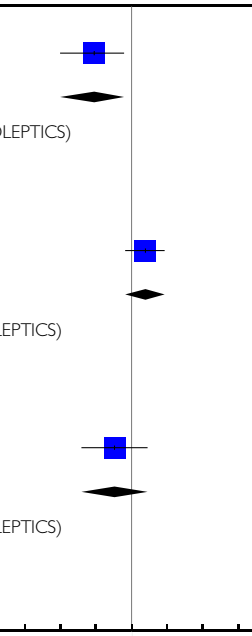
Analysis 8.3. Comparison 8 FLUPHENAZINE ENANTHATE vs OTHER DEPOT NEUROLEPTICS, Outcome 3 Leaving the study early.

Review: Fluphenazine decanoate (depot) and enanthate for schizophrenia

Comparison: 8 FLUPHENAZINE ENANTHATE vs OTHER DEPOT NEUROLEPTICS

Outcome: 3 Leaving the study early

Study or subgroup	FLUPHENAZINE ENANTHATE n/N	OTHER DEPOT NEUROLEPTICS n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
1 immediate (0 to 5 weeks)					
Jain 1975	1/15	11/15		100.0 %	0.09 [0.01, 0.62]
Subtotal (95% CI)	**15**	**15**		**100.0 %**	**0.09 [0.01, 0.62]**
Total events: 1 (FLUPHENAZINE ENANTHATE), 11 (OTHER DEPOT NEUROLEPTICS)					
Heterogeneity: not applicable					
Test for overall effect: Z = 2.45 (P = 0.014)					
2 short term (6 weeks to 5 months)					
Malm 1974	6/26	3/31		100.0 %	2.38 [0.66, 8.61]
Subtotal (95% CI)	**26**	**31**		**100.0 %**	**2.38 [0.66, 8.61]**
Total events: 6 (FLUPHENAZINE ENANTHATE), 3 (OTHER DEPOT NEUROLEPTICS)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.33 (P = 0.18)					
3 medium term (6 months to 1 year)					
Chouinard 1978	1/16	3/16		100.0 %	0.33 [0.04, 2.87]
Subtotal (95% CI)	**16**	**16**		**100.0 %**	**0.33 [0.04, 2.87]**
Total events: 1 (FLUPHENAZINE ENANTHATE), 3 (OTHER DEPOT NEUROLEPTICS)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.00 (P = 0.32)					



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Analysis 8.4. Comparison 8 FLUPHENAZINE ENANTHATE vs OTHER DEPOT NEUROLEPTICS, Outcome 4 Mental state: 1. BPRS - endpoint scores (medium term - 6 months to 1 year) (high score = poor).

Review: Fluphenazine decanoate (depot) and enanthate for schizophrenia

Comparison: 8 FLUPHENAZINE ENANTHATE vs OTHER DEPOT NEUROLEPTICS

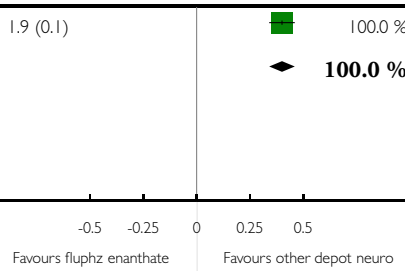
Outcome: 4 Mental state: 1. BPRS - endpoint scores (medium term - 6 months to 1 year) (high score = poor)

Study or subgroup	FLUPHENAZINE ENANTHATE N	Mean(SD)	OTHER DEPOT NEUROLEPTICS N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Singh 1979	15	2.3 (0.05)	15	1.9 (0.1)		100.0 %	0.40 [0.34, 0.46]
Total (95% CI)	**15**		**15**			**100.0 %**	**0.40 [0.34, 0.46]**

Heterogeneity: not applicable

Test for overall effect: Z = 13.86 (P < 0.00001)

Test for subgroup differences: Not applicable



Analysis 8.5. Comparison 8 FLUPHENAZINE ENANTHATE vs OTHER DEPOT NEUROLEPTICS, Outcome 5 Mental state: 2. Depression (medium term - 6 months to 1 year).

Review: Fluphenazine decanoate (depot) and enanthate for schizophrenia

Comparison: 8 FLUPHENAZINE ENANTHATE vs OTHER DEPOT NEUROLEPTICS

Outcome: 5 Mental state: 2. Depression (medium term - 6 months to 1 year)

Study or subgroup	FLUPHENAZINE ENANTHATE n/N	OTHER DEPOT NEUROLEPTICS n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Singh 1979	3/15	0/15		100.0 %	7.00 [0.39, 124.83]
Total (95% CI)	**15**	**15**		**100.0 %**	**7.00 [0.39, 124.83]**

Total events: 3 (FLUPHENAZINE ENANTHATE), 0 (OTHER DEPOT NEUROLEPTICS)

Heterogeneity: not applicable

Test for overall effect: Z = 1.32 (P = 0.19)

Test for subgroup differences: Not applicable

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Analysis 8.6. Comparison 8 FLUPHENAZINE ENANTHATE vs OTHER DEPOT NEUROLEPTICS, Outcome 6 Adverse effects: 1a. Movement disorders - general (medium term - 6 months to 1 year).

Review: Fluphenazine decanoate (depot) and enanthate for schizophrenia

Comparison: 8 FLUPHENAZINE ENANTHATE vs OTHER DEPOT NEUROLEPTICS

Outcome: 6 Adverse effects: 1a. Movement disorders - general (medium term - 6 months to 1 year)

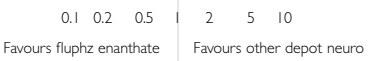
Study or subgroup	FLUPHENAZINE ENANTHATE n/N	OTHER DEPOT NEUROLEPTICS n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Albert 1980	0/11	1/22		14.6 %	0.64 [0.03, 14.52]
Singh 1979	10/15	6/15		85.4 %	1.67 [0.81, 3.41]
Total (95% CI)	**26**	**37**		**100.0 %**	**1.52 [0.75, 3.07]**

Total events: 10 (FLUPHENAZINE ENANTHATE), 7 (OTHER DEPOT NEUROLEPTICS)

Heterogeneity: $Chi^2 = 0.36$, df = 1 (P = 0.55); $I^2 = 0.0\%$

Test for overall effect: Z = 1.16 (P = 0.25)

Test for subgroup differences: Not applicable



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Analysis 8.7. Comparison 8 FLUPHENAZINE ENANTHATE vs OTHER DEPOT NEUROLEPTICS, Outcome 7 Adverse effects: 1b. Movement disorders - needing additional anticholinergic drugs.

Review: Fluphenazine decanoate (depot) and enanthate for schizophrenia

Comparison: 8 FLUPHENAZINE ENANTHATE vs OTHER DEPOT NEUROLEPTICS

Outcome: 7 Adverse effects: 1b. Movement disorders - needing additional anticholinergic drugs

Study or subgroup	FLUPHENAZINE ENANTHATE n/N	OTHER DEPOT NEUROLEPTICS n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
1 short term (6 weeks to 5 months)					
Malm 1974	12/26	5/31		100.0 %	2.86 [1.16, 7.06]
Subtotal (95% CI)	**26**	**31**		**100.0 %**	**2.86 [1.16, 7.06]**
Total events: 12 (FLUPHENAZINE ENANTHATE), 5 (OTHER DEPOT NEUROLEPTICS)					
Heterogeneity: not applicable					
Test for overall effect: Z = 2.28 (P = 0.023)					
2 medium term (6 months to 1 year)					
Albert 1980	0/11	3/22		14.2 %	0.27 [0.02, 4.88]
Chouinard 1978	16/16	14/16		85.8 %	1.14 [0.92, 1.41]
Subtotal (95% CI)	**27**	**38**		**100.0 %**	**1.02 [0.76, 1.35]**
Total events: 16 (FLUPHENAZINE ENANTHATE), 17 (OTHER DEPOT NEUROLEPTICS)					
Heterogeneity: Chi^2 = 1.89, df = 1 (P = 0.17); I^2 =47%					
Test for overall effect: Z = 0.10 (P = 0.92)					

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Analysis 8.8. Comparison 8 FLUPHENAZINE ENANTHATE vs OTHER DEPOT NEUROLEPTICS, Outcome 8 Adverse effects: 1c. Movement disorders - tardive dyskinesia: medium term (6 months to 1 year).

Review: Fluphenazine decanoate (depot) and enanthate for schizophrenia

Comparison: 8 FLUPHENAZINE ENANTHATE vs OTHER DEPOT NEUROLEPTICS

Outcome: 8 Adverse effects: 1c. Movement disorders - tardive dyskinesia: medium term (6 months to 1 year)

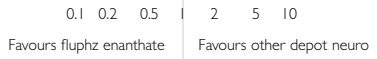
Study or subgroup	FLUPHENAZINE ENANTHATE n/N	OTHER DEPOT NEUROLEPTICS n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Chouinard 1978	8/16	9/16		100.0 %	0.89 [0.46, 1.71]
Total (95% CI)	**16**	**16**		**100.0 %**	**0.89 [0.46, 1.71]**

Total events: 8 (FLUPHENAZINE ENANTHATE), 9 (OTHER DEPOT NEUROLEPTICS)

Heterogeneity: not applicable

Test for overall effect: Z = 0.35 (P = 0.72)

Test for subgroup differences: Not applicable



Analysis 8.9. Comparison 8 FLUPHENAZINE ENANTHATE vs OTHER DEPOT NEUROLEPTICS, Outcome 9 Adverse effects: 1d. Movement disorders - tremor (medium term - 6 months to 1 year).

Review: Fluphenazine decanoate (depot) and enanthate for schizophrenia

Comparison: 8 FLUPHENAZINE ENANTHATE vs OTHER DEPOT NEUROLEPTICS

Outcome: 9 Adverse effects: 1d. Movement disorders - tremor (medium term - 6 months to 1 year)

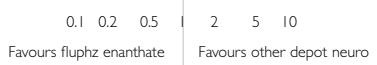
Study or subgroup	FLUPHENAZINE ENANTHATE n/N	OTHER DEPOT NEUROLEPTICS n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Albert 1980	5/11	10/22		32.3 %	1.00 [0.45, 2.21]
Chouinard 1978	9/16	8/16		38.7 %	1.13 [0.59, 2.16]
Singh 1979	10/15	6/15		29.0 %	1.67 [0.81, 3.41]
Total (95% CI)	**42**	**53**		**100.0 %**	**1.24 [0.82, 1.87]**

Total events: 24 (FLUPHENAZINE ENANTHATE), 24 (OTHER DEPOT NEUROLEPTICS)

Heterogeneity: Chi^2 = 1.02, df = 2 (P = 0.60); I^2 =0.0%

Test for overall effect: Z = 1.03 (P = 0.30)

Test for subgroup differences: Not applicable



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Analysis 8.10. Comparison 8 FLUPHENAZINE ENANTHATE vs OTHER DEPOT NEUROLEPTICS, Outcome 10 Adverse effects: 2. Blurred vision (medium term - 6 months to 1 year).

Review: Fluphenazine decanoate (depot) and enanthate for schizophrenia

Comparison: 8 FLUPHENAZINE ENANTHATE vs OTHER DEPOT NEUROLEPTICS

Outcome: 10 Adverse effects: 2. Blurred vision (medium term - 6 months to 1 year)

Study or subgroup	FLUPHENAZINE ENANTHATE n/N	OTHER DEPOT NEUROLEPTICS n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Singh 1979	1/15	0/15		100.0 %	3.00 [0.13, 68.26]
Total (95% CI)	**15**	**15**		**100.0 %**	**3.00 [0.13, 68.26]**

Total events: 1 (FLUPHENAZINE ENANTHATE), 0 (OTHER DEPOT NEUROLEPTICS)

Heterogeneity: not applicable

Test for overall effect: Z = 0.69 (P = 0.49)

Test for subgroup differences: Not applicable

Analysis 8.11. Comparison 8 FLUPHENAZINE ENANTHATE vs OTHER DEPOT NEUROLEPTICS, Outcome 11 Adverse effects: 3. Dry mouth (medium term - 6 months to 1 year).

Review: Fluphenazine decanoate (depot) and enanthate for schizophrenia

Comparison: 8 FLUPHENAZINE ENANTHATE vs OTHER DEPOT NEUROLEPTICS

Outcome: 11 Adverse effects: 3. Dry mouth (medium term - 6 months to 1 year)

Study or subgroup	FLUPHENAZINE ENANTHATE n/N	OTHER DEPOT NEUROLEPTICS n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Chouinard 1978	4/16	9/16		90.0 %	0.44 [0.17, 1.15]
Singh 1979	4/15	1/15		10.0 %	4.00 [0.50, 31.74]
Total (95% CI)	**31**	**31**		**100.0 %**	**0.80 [0.36, 1.76]**

Total events: 8 (FLUPHENAZINE ENANTHATE), 10 (OTHER DEPOT NEUROLEPTICS)

Heterogeneity: Chi^2 = 3.78, df = 1 (P = 0.05); I^2 =74%

Test for overall effect: Z = 0.55 (P = 0.58)

Test for subgroup differences: Not applicable

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Analysis 9.1. Comparison 9 FLUPHENAZINE ENANTHATE - DOSAGE STUDIES - LOW DOSE vs INTERMEDIATE/HIGH DOSE, Outcome 1 Global state: Relapse (short term - 6 weeks to 5 months).

Review: Fluphenazine decanoate (depot) and enanthate for schizophrenia

Comparison: 9 FLUPHENAZINE ENANTHATE - DOSAGE STUDIES - LOW DOSE vs INTERMEDIATE/HIGH DOSE

Outcome: 1 Global state: Relapse (short term - 6 weeks to 5 months)

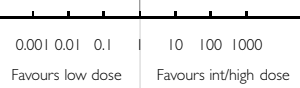
Study or subgroup	FLUPHZINE ENANTH LOW DOSE n/N	FLUPHZ ENAN INT/HIGH DOSE n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Goldstein 1978	18/51	2/53		100.0 %	9.35 [2.28, 38.29]
Total (95% CI)	**51**	**53**		**100.0 %**	**9.35 [2.28, 38.29]**

Total events: 18 (FLUPHZINE ENANTH LOW DOSE), 2 (FLUPHZ ENAN INT/HIGH DOSE)

Heterogeneity: not applicable

Test for overall effect: Z = 3.11 (P = 0.0019)

Test for subgroup differences: Not applicable



Analysis 9.2. Comparison 9 FLUPHENAZINE ENANTHATE - DOSAGE STUDIES - LOW DOSE vs INTERMEDIATE/HIGH DOSE, Outcome 2 Leaving the study early (short term - 6 weeks to 5 months).

Review: Fluphenazine decanoate (depot) and enanthate for schizophrenia

Comparison: 9 FLUPHENAZINE ENANTHATE - DOSAGE STUDIES - LOW DOSE vs INTERMEDIATE/HIGH DOSE

Outcome: 2 Leaving the study early (short term - 6 weeks to 5 months)

Study or subgroup	FLUPHZINE ENANTH LOW DOSE n/N	FLUPHZ ENAN INT/HIGH DOSE n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Goldstein 1978	6/51	2/53		100.0 %	3.12 [0.66, 14.74]
Total (95% CI)	**51**	**53**		**100.0 %**	**3.12 [0.66, 14.74]**

Total events: 6 (FLUPHZINE ENANTH LOW DOSE), 2 (FLUPHZ ENAN INT/HIGH DOSE)

Heterogeneity: not applicable

Test for overall effect: Z = 1.43 (P = 0.15)

Test for subgroup differences: Not applicable

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Analysis 10.1. Comparison 10 FLUPHENAZINE DECANAOTE vs FLUPHENAZINE ENANTHATE, Outcome 1 Global state: 1. Needing additional antipsychotic treatment.

Review: Fluphenazine decanoate (depot) and enanthate for schizophrenia

Comparison: 10 FLUPHENAZINE DECANAOTE vs FLUPHENAZINE ENANTHATE

Outcome: 1 Global state: 1. Needing additional antipsychotic treatment

Study or subgroup	FLUPHENAZINE DECANAOTE n/N	FLUPHENAZINE ENANTHATE n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
1 immediate (0 to 5 weeks)					
Van Praag 1973	5/17	12/16		100.0 %	0.39 [0.18, 0.86]
Subtotal (95% CI)	**17**	**16**		**100.0 %**	**0.39 [0.18, 0.86]**
Total events: 5 (FLUPHENAZINE DECANAOTE), 12 (FLUPHENAZINE ENANTHATE)					
Heterogeneity: not applicable					
Test for overall effect: Z = 2.33 (P = 0.020)					
2 mediium term (6 months to 1 year)					
Chouinard 1982	2/24	2/24		100.0 %	1.00 [0.15, 6.53]
Subtotal (95% CI)	**24**	**24**		**100.0 %**	**1.00 [0.15, 6.53]**
Total events: 2 (FLUPHENAZINE DECANAOTE), 2 (FLUPHENAZINE ENANTHATE)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.0 (P = 1.0)					

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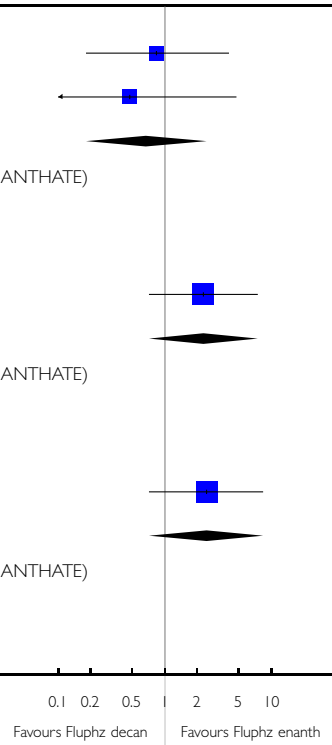
Analysis 10.2. Comparison 10 FLUPHENAZINE DECANAOTE vs FLUPHENAZINE ENANTHATE, Outcome 2 Global state: 2. Relapse.

Review: Fluphenazine decanoate (depot) and enanthate for schizophrenia

Comparison: 10 FLUPHENAZINE DECANAOTE vs FLUPHENAZINE ENANTHATE

Outcome: 2 Global state: 2. Relapse

Study or subgroup	FLUPHENAZINE DECANAOTE n/N	FLUPHENAZINE ENANTHATE n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
1 immediate (0 to 5 weeks)					
Altamura 1985	2/6	2/5		51.4 %	0.83 [0.18, 3.96]
Van Praag 1973	1/17	2/16		48.6 %	0.47 [0.05, 4.70]
Subtotal (95% CI)	**23**	**21**		**100.0 %**	**0.66 [0.18, 2.43]**
Total events: 3 (FLUPHENAZINE DECANAOTE), 4 (FLUPHENAZINE ENANTHATE)					
Heterogeneity: Chi^2 = 0.17, df = 1 (P = 0.68); I^2 =0.0%					
Test for overall effect: Z = 0.63 (P = 0.53)					
2 short term (6 weeks to 5 months)					
Donlon 1976	6/14	3/16		100.0 %	2.29 [0.70, 7.48]
Subtotal (95% CI)	**14**	**16**		**100.0 %**	**2.29 [0.70, 7.48]**
Total events: 6 (FLUPHENAZINE DECANAOTE), 3 (FLUPHENAZINE ENANTHATE)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.37 (P = 0.17)					
3 medium term (6 months to 1 year)					
MacCrimmon 1978	7/24	3/25		100.0 %	2.43 [0.71, 8.32]
Subtotal (95% CI)	**24**	**25**		**100.0 %**	**2.43 [0.71, 8.32]**
Total events: 7 (FLUPHENAZINE DECANAOTE), 3 (FLUPHENAZINE ENANTHATE)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.41 (P = 0.16)					



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Analysis 10.3. Comparison 10 FLUPHENAZINE DECANAOTE vs FLUPHENAZINE ENANTHATE, Outcome 3 Behavioiur: Leaving the study early.

Review: Fluphenazine decanoate (depot) and enanthate for schizophrenia

Comparison: 10 FLUPHENAZINE DECANAOTE vs FLUPHENAZINE ENANTHATE

Outcome: 3 Behavioiur: Leaving the study early

Study or subgroup	FLUPHENAZINE DECANAOTE n/N	FLUPHENAZINE ENANTHATE n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
1 immediate (0 to 5 weeks)					
Altamura 1985	2/6	2/5		51.4 %	0.83 [0.18, 3.96]
Van Praag 1973	1/17	2/16		48.6 %	0.47 [0.05, 4.70]
Subtotal (95% CI)	**23**	**21**		**100.0 %**	**0.66 [0.18, 2.43]**
Total events: 3 (FLUPHENAZINE DECANAOTE), 4 (FLUPHENAZINE ENANTHATE)					
Heterogeneity: Chi^2 = 0.17, df = 1 (P = 0.68); I^2 =0.0%					
Test for overall effect: Z = 0.63 (P = 0.53)					
2 short term (6 weeks to 5 months)					
Donlon 1976	6/14	3/16		100.0 %	2.29 [0.70, 7.48]
Keskiner 1971	0/6	0/6			Not estimable
Subtotal (95% CI)	**20**	**22**		**100.0 %**	**2.29 [0.70, 7.48]**
Total events: 6 (FLUPHENAZINE DECANAOTE), 3 (FLUPHENAZINE ENANTHATE)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.37 (P = 0.17)					
3 medium term (6 months to 1 year)					
MacCrimmon 1978	7/24	3/25		100.0 %	2.43 [0.71, 8.32]
Subtotal (95% CI)	**24**	**25**		**100.0 %**	**2.43 [0.71, 8.32]**
Total events: 7 (FLUPHENAZINE DECANAOTE), 3 (FLUPHENAZINE ENANTHATE)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.41 (P = 0.16)					

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Analysis 10.4. Comparison 10 FLUPHENAZINE DECANAOTE vs FLUPHENAZINE ENANTHATE, Outcome 4 Mental State: BPRS medium term (6 months to 1 year - high score = poor).

Review: Fluphenazine decanoate (depot) and enanthate for schizophrenia

Comparison: 10 FLUPHENAZINE DECANAOTE vs FLUPHENAZINE ENANTHATE

Outcome: 4 Mental State: BPRS medium term (6 months to 1 year - high score = poor)

Study or subgroup	FLUPHENAZINE DECANAOTE N	Mean(SD)	FLUPHENAZINE ENANTHATE N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
MacCrimmon 1978	17	26 (7)	22	26 (5)		100.0 %	0.0 [-3.93, 3.93]
Total (95% CI)	**17**		**22**			**100.0 %**	**0.0 [-3.93, 3.93]**

Heterogeneity: not applicable

Test for overall effect: Z = 0.0 (P = 1.0)

Test for subgroup differences: Not applicable

Analysis 10.5. Comparison 10 FLUPHENAZINE DECANAOTE vs FLUPHENAZINE ENANTHATE, Outcome 5 Adverse effects: 1a. Movement disorders - general.

Review: Fluphenazine decanoate (depot) and enanthate for schizophrenia

Comparison: 10 FLUPHENAZINE DECANAOTE vs FLUPHENAZINE ENANTHATE

Outcome: 5 Adverse effects: 1a. Movement disorders - general

Study or subgroup	FLUPHENAZINE DECANAOTE n/N	FLUPHENAZINE ENANTHATE n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
1 Immediate (0 to 5 weeks)					
Kane 1978 (1)	9/26	3/23		100.0 %	2.65 [0.82, 8.64]
Subtotal (95% CI)	**26**	**23**		**100.0 %**	**2.65 [0.82, 8.64]**
Total events: 9 (FLUPHENAZINE DECANAOTE), 3 (FLUPHENAZINE ENANTHATE)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.62 (P = 0.11)					
2 short term (6 weeks to 5 months)					
Donlon 1976	12/14	13/16		92.8 %	1.05 [0.77, 1.45]
Kurland 1966	2/9	1/10		7.2 %	2.22 [0.24, 20.57]
Subtotal (95% CI)	**23**	**26**		**100.0 %**	**1.14 [0.79, 1.64]**

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Study or subgroup	FLUPHENAZINE DECANAOTE n/N	FLUPHENAZINE ENANTHATE n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Total events: 14 (FLUPHENAZINE DECANAOTE), 14 (FLUPHENAZINE ENANTHATE)					
Heterogeneity: Chi^2 = 0.57, df = 1 (P = 0.45); I^2 =0.0%					
Test for overall effect: Z = 0.71 (P = 0.48)					
Test for subgroup differences: Chi^2 = 1.80, df = 1 (P = 0.18), I^2 =45%					

(1) 2 point increase on the Simpson Angus Scale

Analysis 10.6. Comparison 10 FLUPHENAZINE DECANAOTE vs FLUPHENAZINE ENANTHATE, Outcome 6 Adverse effects: 1b. Movement disorders - needing anticholinergic drugs.

Review: Fluphenazine decanoate (depot) and enanthate for schizophrenia

Comparison: 10 FLUPHENAZINE DECANAOTE vs FLUPHENAZINE ENANTHATE

Outcome: 6 Adverse effects: 1b. Movement disorders - needing anticholinergic drugs

Study or subgroup	FLUPHENAZINE DECANAOTE n/N	FLUPHENAZINE ENANTHATE n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
1 immediate (0 to 5 weeks)					
Van Praag 1973	4/17	13/16		100.0 %	0.29 [0.12, 0.70]
Subtotal (95% CI)	**17**	**16**		**100.0 %**	**0.29 [0.12, 0.70]**
Total events: 4 (FLUPHENAZINE DECANAOTE), 13 (FLUPHENAZINE ENANTHATE)					
Heterogeneity: not applicable					
Test for overall effect: Z = 2.73 (P = 0.0063)					
2 short term (6 weeks to 5 months)					
Donlon 1976	13/14	15/16		100.0 %	0.99 [0.82, 1.20]
Subtotal (95% CI)	**14**	**16**		**100.0 %**	**0.99 [0.82, 1.20]**
Total events: 13 (FLUPHENAZINE DECANAOTE), 15 (FLUPHENAZINE ENANTHATE)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.10 (P = 0.92)					
3 medium term (6 months to 1 year)					
Chouinard 1982	16/24	17/24		50.5 %	0.94 [0.64, 1.38]
MacCrimmon 1978	10/24	17/25		49.5 %	0.61 [0.36, 1.06]
Subtotal (95% CI)	**48**	**49**		**100.0 %**	**0.78 [0.57, 1.07]**

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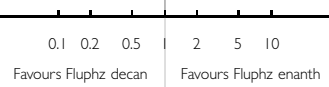
Study or subgroup	FLUPHENAZINE DECANAOTE n/N	FLUPHENAZINE ENANTHATE n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Total events: 26 (FLUPHENAZINE DECANAOTE), 34 (FLUPHENAZINE ENANTHATE)					
Heterogeneity: $Chi^2 = 1.69$, df = 1 (P = 0.19); $I^2 = 41\%$					
Test for overall effect: Z = 1.53 (P = 0.12)					



Analysis 10.7. Comparison 10 FLUPHENAZINE DECANAOTE vs FLUPHENAZINE ENANTHATE, Outcome 7 Adverse effects: 1c. Movement disorders - parkinsonism (short term - 6 weeks to 5 months).

Review: Fluphenazine decanoate (depot) and enanthate for schizophrenia

Comparison: 10 FLUPHENAZINE DECANAOTE vs FLUPHENAZINE ENANTHATE

Outcome: 7 Adverse effects: 1c. Movement disorders - parkinsonism (short term - 6 weeks to 5 months)

Study or subgroup	FLUPHENAZINE DECANAOTE n/N	FLUPHENAZINE ENANTHATE n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Kurland 1966	0/9	1/10		100.0 %	0.37 [0.02, 8.01]
Total (95% CI)	**9**	**10**		**100.0 %**	**0.37 [0.02, 8.01]**
Total events: 0 (FLUPHENAZINE DECANAOTE), 1 (FLUPHENAZINE ENANTHATE)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.64 (P = 0.52)					
Test for subgroup differences: Not applicable					

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Analysis 10.8. Comparison 10 FLUPHENAZINE DECANAOTE vs FLUPHENAZINE ENANTHATE, Outcome 8 Adverse effects: 1d. Movement disorders - akathisia (Immediate - 0 to 5 weeks).

Review: Fluphenazine decanoate (depot) and enanthate for schizophrenia

Comparison: 10 FLUPHENAZINE DECANAOTE vs FLUPHENAZINE ENANTHATE

Outcome: 8 Adverse effects: 1d. Movement disorders - akathisia (Immediate - 0 to 5 weeks)

Study or subgroup	FLUPHENAZINE DECANAOTE n/N	FLUPHENAZINE ENANTHATE n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Kane 1978	7/26	1/23		100.0 %	6.19 [0.82, 46.62]
Total (95% CI)	**26**	**23**		**100.0 %**	**6.19 [0.82, 46.62]**

Total events: 7 (FLUPHENAZINE DECANAOTE), 1 (FLUPHENAZINE ENANTHATE)

Heterogeneity: not applicable

Test for overall effect: Z = 1.77 (P = 0.077)

Test for subgroup differences: Not applicable

Analysis 10.9. Comparison 10 FLUPHENAZINE DECANAOTE vs FLUPHENAZINE ENANTHATE, Outcome 9 Adverse effects: 2. General adverse effects (immediate - 0 to 5 weeks).

Review: Fluphenazine decanoate (depot) and enanthate for schizophrenia

Comparison: 10 FLUPHENAZINE DECANAOTE vs FLUPHENAZINE ENANTHATE

Outcome: 9 Adverse effects: 2. General adverse effects (immediate - 0 to 5 weeks)

Study or subgroup	FLUPHENAZINE DECANAOTE n/N	FLUPHENAZINE ENANTHATE n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Altamura 1985	0/6	5/5		100.0 %	0.08 [0.01, 1.14]
Total (95% CI)	**6**	**5**		**100.0 %**	**0.08 [0.01, 1.14]**

Total events: 0 (FLUPHENAZINE DECANAOTE), 5 (FLUPHENAZINE ENANTHATE)

Heterogeneity: not applicable

Test for overall effect: Z = 1.87 (P = 0.062)

Test for subgroup differences: Not applicable

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Analysis 11.1. Comparison 11 FLUPHENAZINE DECANOATE - DOSAGE STUDIES - 2 WEEKS vs 6 WEEKS, Outcome 1 Global state: 1. Relapse (1 year).

Review: Fluphenazine decanoate (depot) and enanthate for schizophrenia

Comparison: 11 FLUPHENAZINE DECANOATE - DOSAGE STUDIES - 2 WEEKS vs 6 WEEKS

Outcome: 1 Global state: 1. Relapse (1 year)

Study or subgroup	FLUPHZ DECAN 2 WEEKS n/N	FLUPHZ DECAN 6 WEEKS n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Khazaie 2005	11/18	13/19		100.0 %	0.89 [0.55, 1.44]
Total (95% CI)	**18**	**19**		**100.0 %**	**0.89 [0.55, 1.44]**

Total events: 11 (FLUPHZ DECAN 2 WEEKS), 13 (FLUPHZ DECAN 6 WEEKS)

Heterogeneity: not applicable

Test for overall effect: Z = 0.46 (P = 0.64)

Test for subgroup differences: Not applicable

Analysis 11.2. Comparison 11 FLUPHENAZINE DECANOATE - DOSAGE STUDIES - 2 WEEKS vs 6 WEEKS, Outcome 2 Leaving the study early (1 year).

Review: Fluphenazine decanoate (depot) and enanthate for schizophrenia

Comparison: 11 FLUPHENAZINE DECANOATE - DOSAGE STUDIES - 2 WEEKS vs 6 WEEKS

Outcome: 2 Leaving the study early (1 year)

Study or subgroup	FLUPHZ DECAN 2 WEEKS n/N	FLUPHZ DECAN 6 WEEKS n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Khazaie 2005	7/25	6/25		100.0 %	1.17 [0.46, 2.98]
Total (95% CI)	**25**	**25**		**100.0 %**	**1.17 [0.46, 2.98]**

Total events: 7 (FLUPHZ DECAN 2 WEEKS), 6 (FLUPHZ DECAN 6 WEEKS)

Heterogeneity: not applicable

Test for overall effect: Z = 0.32 (P = 0.75)

Test for subgroup differences: Not applicable

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Analysis 11.3. Comparison 11 FLUPHENAZINE DECANOATE - DOSAGE STUDIES - 2 WEEKS vs 6 WEEKS, Outcome 3 Mental state: 1. BPRS - endpoint scores (1 year) (high score = poor).

Review: Fluphenazine decanoate (depot) and enanthate for schizophrenia

Comparison: 11 FLUPHENAZINE DECANOATE - DOSAGE STUDIES - 2 WEEKS vs 6 WEEKS

Outcome: 3 Mental state: 1. BPRS - endpoint scores (1 year) (high score = poor)

Study or subgroup	FLUPHZ DECAN 2 WEEKS N	FLUPHZ DECAN 6 WEEKS N	Mean Difference (SE)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
1 Total						
Khazaie 2005	18	19	2.72 (1.9799)		100.0 %	2.72 [-1.16, 6.60]
Subtotal (95% CI)	**18**	**19**			**100.0 %**	**2.72 [-1.16, 6.60]**
Heterogeneity: not applicable						
Test for overall effect: Z = 1.37 (P = 0.17)						
2 Thought disorder						
Khazaie 2005	18	19	-0.39 (0.5728)		100.0 %	-0.39 [-1.51, 0.73]
Subtotal (95% CI)	**18**	**19**			**100.0 %**	**-0.39 [-1.51, 0.73]**
Heterogeneity: not applicable						
Test for overall effect: Z = 0.68 (P = 0.50)						
Test for subgroup differences: Chi^2 = 2.28, df = 1 (P = 0.13), I^2 =56%						

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Analysis 11.4. Comparison 11 FLUPHENAZINE DECANOATE - DOSAGE STUDIES - 2 WEEKS vs 6 WEEKS, Outcome 4 Adverse effects: 1. Movement disorders - MPRC (1 year, high = poor).

Review: Fluphenazine decanoate (depot) and enanthate for schizophrenia

Comparison: 11 FLUPHENAZINE DECANOATE - DOSAGE STUDIES - 2 WEEKS vs 6 WEEKS

Outcome: 4 Adverse effects: 1. Movement disorders - MPRC (1 year, high = poor)

Study or subgroup	FLUPHZ DECAN 2 WEEKS N	FLUPHZ DECAN 6 WEEKS N	Mean Difference (SE)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
1 Parkinsonian symptoms						
Khazaie 2005	18	19	1.3 (0.6801)		100.0 %	1.30 [-0.03, 2.63]
Subtotal (95% CI)	**18**	**19**			**100.0 %**	**1.30 [-0.03, 2.63]**
Heterogeneity: not applicable						
Test for overall effect: Z = 1.91 (P = 0.056)						
2 Dyskinesia						
Khazaie 2005	18	19	2.4 (2.126)		100.0 %	2.40 [-1.77, 6.57]
Subtotal (95% CI)	**18**	**19**			**100.0 %**	**2.40 [-1.77, 6.57]**
Heterogeneity: not applicable						
Test for overall effect: Z = 1.13 (P = 0.26)						

Analysis 11.5. Comparison 11 FLUPHENAZINE DECANOATE - DOSAGE STUDIES - 2 WEEKS vs 6 WEEKS, Outcome 5 Quality of life: Quality of life scale (1 year) (high score = good).

Review: Fluphenazine decanoate (depot) and enanthate for schizophrenia

Comparison: 11 FLUPHENAZINE DECANOATE - DOSAGE STUDIES - 2 WEEKS vs 6 WEEKS

Outcome: 5 Quality of life: Quality of life scale (1 year) (high score = good)

Study or subgroup	FLUPHZ DECAN 2 WEEKS N	FLUPHZ DECAN 6 WEEKS N	Mean Difference (SE)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Khazaie 2005	18	19	1.42 (5.6639)		100.0 %	1.42 [-9.68, 12.52]
Total (95% CI)	**18**	**19**			**100.0 %**	**1.42 [-9.68, 12.52]**
Heterogeneity: not applicable						
Test for overall effect: Z = 0.25 (P = 0.80)						
Test for subgroup differences: Not applicable						

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ADDITIONAL TABLES

Table 1. Suggested design of future trials

Methods	Allocation: randomised - clearly described generation of sequence and concealment of allocation. Blindness: double - described and tested. Duration: 12 months minimum.
Participants	Diagnosis: schizophrenia (operational criteria). N = 300* Age: any. Gender: both. History: any.
Interventions	1. Fluphenazine decanoate/enanthate: clinically acceptable dose. N = 150 2. Oral antipsychotic: clinically acceptable dose. N = 150.
Outcomes	Death and all causes of mortality** Clinical global state - relapse**; clinically significant change in global state**; leaving the study early** Service utilisation outcomes - hospital admission**, time in hospital. Adverse effects: extrapyramidal adverse effects**, other adverse effects. Economic outcomes.
Notes	* The number of participants needed to gain sufficient power to highlight about a 10% difference between groups for primary outcome depends on the primary outcome used and the prevalence/magnitude of this outcome. N = 300 is approximately the size of study to detect a 10% difference in improvement with 80% certainty ** Primary outcome

APPENDICES

Appendix 1. Previous search strategies

1. We updated previous searches in May 2002 using the Cochrane Schizophrenia Group's Register search phrase:
[fluphen* or *fluphen* or *modec* or *moditen* or *eutimox* or *flufen* or *prolixin* or *siqualone* or *anaten* or *dapotum* or *decazate* or *lyoridin* in title, abstract, index terms of [REFERENCE] or [(fluphenaz* AND depot*) in interventions of STUDY]
2. Details of previous electronic searches.
2.1 Electronic searching
Relevant randomised trials were identified by searching several electronic databases (the Cochrane Schizophrenia Group's Register of Trials, the Cochrane Library, Biological Abstracts, EMBASE, MEDLINE, PsycLIT and SCISEARCH).
2.2 We searched the Cochrane Schizophrenia Group's Register (1998) using the phrase:
(FLUPHEN* and DECANOATE or ENANTHATE) or ((DEPOT* or (LONG and ACTING) or (DELAY* and ACTION)) and (FLUPHEN* or MODEC* or MODITEN* or EUTIMOX* or FLUFEN* or PROLIXIN* or SIQUALONE* or ANATEN* or DAPOTUM* or DECAZATE* or LYORIDIN*) or (#44=2 and #44=230) or #44=549)

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2.3 We searched the COCHRANE LIBRARY (Issue 2, 1998) using the Cochrane Schizophrenia Group's phrase for schizophrenia (see Group search strategy) combined with the phrase:
(FLUPHEN* and DECANOATE or ENANTHATE) or ((DEPOT* or (LONG and ACTING) or (DELAY* and ACTION)) and (FLUPHEN* or MODEC* or MODITEN* or EUTIMOX* or FLUFEN* or PROLIXIN* or SIQUALONE* or ANATEN* or DAPOTUM* or DECAZATE* or LYORIDIN*)) or (FLUPHEN* ME and DELAYED-ACTION-PREPARATIONS* ME))]
2.4 We searched BIOLOGICAL ABSTRACTS (January 1982 to June 1998 - current disc issue) using the Cochrane Schizophrenia Group's phrase for randomised controlled trials and schizophrenia (see Group search strategy) combined with the phrase:
[and (FLUPHENAZINE near1 DECANOATE or ENANTHATE) or ((DEPOT* or (LONG near4 ACTING) or (DELAY* near2 ACTION)) near (FLUPHENAZINE or MODEC* or MODITEN* or EUTIMOX* or FLUFEN* or PROLIXIN* or SIQUALONE* or ANATEN* or DAPOTUM* or DECAZOTE* or LYONRIDIN*)]
2.5 EMBASE (January 1980 to June 1998 - current disc issue): we searched this database using the Cochrane Schizophrenia Group's phrase for randomised controlled trials and schizophrenia (see Group search strategy) combined with the phrase:
(FLUPHEN* near1 DECANOATE or ENANTHATE) or ((DEPOT* or (LONG near4 ACTING) or (DELAY* near2 ACTION)) near (FLUPHEN* or MODITEN* or MODEC* or FLUFEN* or EUTIMOX* or PROLIXIN* or SIQUALONE* or ANATEN* or DAPOTUM* or DECAZATE* or LYORIDIN*) or "FLUPHENAZINE-DECANOATE"/ all subheadings]
2.6 We searched MEDLINE (January 1966 to June 1998 - current disc issue) using the Cochrane Schizophrenia Group's phrase for randomised controlled trials and schizophrenia (see Group search strategy) combined with the phrase:
(FLUPHEN* near1 DECANOATE or ENANTHATE) or ((DEPOT* or (LONG near4 ACTING) or (DELAY* near2 ACTION)) near (FLUPHEN* or MODEC* or MODITEN* or EUTIMOX* or FLUFEN* or PROLIXIN* or SEQUALONE* or ANATEN* or DAPOTUM* or DECAZATE* or LYORIDIN*) or ("FLUPHENAZINE"/ all subheadings and explode "DELAYED-ACTION-PREPARATIONS"/ all subheadings))]
2.7 We searched PsycLIT (January 1974 to June 1998 - current disc issue) using the Cochrane Schizophrenia Group's phrase for randomised controlled trials and schizophrenia (see Group search strategy) combined with the phrase:
(FLUPHEN* near1 DECANOATE or ENANTHATE) or ((DEPOT* or (LONG near4 ACTING) or (DELAY* near2 ACTION)) near (FLUPHEN* or MODEC* or MODITEN* or EUTIMOX* or FLUFEN* or PROLIXIN* or SIQUALONE* or ANATEN* or DAPOTUM* or DECAZATE* or LYORIDIN)

Appendix 2. Previous methods: data collection and analyses

1. Study selection

In the original review, all the studies we identified were inspected by the principal reviewer (SQ). A randomly selected sample of 10% of all reports was re-inspected by AD in order to ensure selection was reliable. Where disagreement occurred, we resolved this by discussion, where there was still doubt, we acquired the full article for further inspection. Once we had obtained the full articles, SQ and AD independently decided whether they met the review criteria. We resolved disagreement by discussion and when this was not possible sought further information. We added these trials to the list of those awaiting assessment pending acquisition of further information. For the updated version of this review, JR inspected and data extracted all studies.

2. Assessment of methodological quality

We allocated trials to three quality categories, as described in The Cochrane Collaboration Handbook (Alderson 2004). Again, we resolved disputes by discussion. When this was not possible and further information was necessary to clarify which category to allocate a trial to, we did not enter data and allocated the trial to the list of those awaiting assessment. We included only trials in Category A or B in the review.

3. Data collection

In the first version of this review SQ and AD independently extracted data from selected trials. JR did this for the updated version. Again, we resolved disputes by discussion. When this was not possible and further information was necessary to resolve the dilemma, we did not enter data and added this outcome of the trial to the list of those awaiting assessment.

4. Data synthesis

4.1 Incomplete data.

Where more than 30% of those randomised were lost to follow-up by six months, or 50% by beyond that time, we felt data to be too prone to bias and did not used these outcomes.

4.2 Dichotomous - yes/no - data.

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4.2.1 Statistics: For binary outcomes, for example, 'admitted' or 'not admitted', we estimated a Relative Risk with 95% confidence interval. Where possible, we calculated the number needed to treat statistic (NNT) taking into account the event rate in the control group.
4.2.2 Intention-to-treat: We present data on a 'once-randomised-always-analyse' basis. Those who were lost to follow-up are all assumed to have the negative outcome, with the exception of death, which was coded separately. For example, for the outcome of relapse, we considered those who were lost to follow-up all to have relapsed.
4.2.3 Data reporting
4.3 Continuous - scale - data
4.3.1 Normal data: Mental health continuous data 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: i. standard deviations and means had to be reported in the paper or had to be obtainable from the authors; ii. when a continuous outcome started from a finite number (such as 0), the standard deviation, when multiplied by 2, had to be less than the mean (as otherwise the mean is unlikely to be an appropriate measure of the centre of the distribution - Altman 1996). We did not enter data not meeting the second standard into the RevMan calculator (which assumes a normal distribution). However, data not meeting these standards can be reported in the 'Other data types' of the results section if they have been analysed with appropriate non-parametric tests. If continuous data were recording change, where the finite parameters of the measure were unclear, the reviewers decided whether the data were usable or not.
4.3.2 Rating scales: A wide range of instruments is available to measure mental health outcomes. These instruments vary in quality and many are not valid, or are ad hoc. For outcome instruments some minimum standards have to be set. They could be that: i. the psychometric properties of the instrument should have been described in a peer-reviewed journal; ii. not written or modified by one of the trialists; iii. the instrument should either be: (a) a self report, or (b) completed by an independent rater or relative (not the therapist); and iv. the instrument should be a global assessment of an area of functioning (Marshall 1998).
4.3.3 Endpoint versus change data: where possible we presented endpoint data and if both endpoint and change data were available for the same outcomes then we only reported the former in this review.
4.3.4 Cluster trials
Studies increasingly employ 'cluster randomisation' (such as randomisation by clinician or practice) but analysis and pooling of clustered data poses problems. Firstly, authors often fail to account for intra class correlation in clustered studies, leading to a 'unit of analysis' error (Divine 1992) whereby P values are spuriously low, confidence intervals unduly narrow and statistical significance overestimated. This causes type I errors (Bland 1997; Gulliford 1999).
Where clustering was not accounted for in primary studies, we presented data in a table, with a (*) symbol to indicate the presence of a probable unit of analysis error. In subsequent versions of this review we will seek to contact first authors of studies to obtain intra-class correlation co-efficients of their clustered data and to adjust for this using accepted methods (Gulliford 1999). If clustering had been incorporated into the analysis of primary studies, we would have presented these data as if from a non-cluster randomised study, but would have adjusted for the clustering effect.
We have sought statistical advice and have been advised that the binary data as presented in a report should be divided by a 'design effect'. This is calculated using the mean number of participants per cluster (m) and the intraclass correlation coefficient (ICC) [Design effect = 1+(m-1)*ICC] (Donner 2002). If the ICC was not reported it was assumed to be 0.1 (Ukoumunne 1999).

5. Heterogeneity

Firstly, we considered all the included studies within any comparison to judge clinical heterogeneity. We then used visual inspection of graphs to investigate the possibility of statistical heterogeneity. This was supplemented using, primarily, the I-squared statistic. This provides an estimate of the percentage of variability due to heterogeneity rather than chance alone. Where the I-squared estimate was greater than or equal to 75%, we interpreted this as indicating the presence of high levels of heterogeneity (Higgins 2003). If inconsistency was high, we did not summate these data, but presented them separately and investigated reasons for heterogeneity. Data were presented using a fixed-effect model for homogeneous data and a random-effects model for heterogeneous data.

6. Tables and figures

Where possible we entered data into RevMan in such a way that the area to the left of the line of no effect indicated a favourable outcome for the fluphenazine esters.

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WHAT'S NEW

Last assessed as up-to-date: 1 December 2013.

Date	Event	Description
1 May 2014	New citation required but conclusions have not changed	Additional data from three new trials have been added to the review, no change to overall conclusions of review
4 December 2013	New search has been performed	Results from 2013 search added to the review. Method sections amended to include new Cochrane methodology

HISTORY

Protocol first published: Issue 2, 1996

Review first published: Issue 4, 1997

Date	Event	Description
25 January 2011	Amended	byline corrected
30 October 2008	Amended	Converted to new review format.

CONTRIBUTIONS OF AUTHORS

Seema Quraishi - prepared protocol, undertook searches, selected and acquired studies, extracted data, summated data, produced report (2002, 2011).

Maurice Eisenbruch - prepared the protocol, undertook searches, selected and acquired studies, extracted data, summated data, produced reports (2002, 2011).

Anthony David - acquired funding, helped prepare protocol, select studies, extract data, and produce the report (2002, 2011).

Clive Adams - acquired funding, helped prepare protocol, undertook searches, selected and acquired studies, extracted and summated data, produce the reports and prepared the updated review (2002, 2011, 2013).

John Rathbone - selected and acquired studies, extracted and summated data and prepared the updated review (2002, 2011).

Enhance Reviews - Nicola Maayan and Rosie Asher screened studies, extracted data for two new studies, assessed the risk of bias for all included studies, prepared 'Summary of findings' tables and prepared the updated review (2013).

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DECLARATIONS OF INTEREST

The authors have declared no conflicts of interest.

Enhance Reviews: is a company that carries out systematic reviews mostly for the public sector, it currently does not provide services for the pharmaceutical industry.

SOURCES OF SUPPORT

Internal sources

- No sources of support supplied

External sources

- NHS-ROCD Health Technology Assessment Programme., UK.

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

We have updated our methods since publication of the protocol to reflect advances in Cochrane methodology.

INDEX TERMS

Medical Subject Headings (MeSH)

Antipsychotic Agents [*therapeutic use]; Delayed-Action Preparations [therapeutic use]; Fluphenazine [*analogs & derivatives; therapeutic use]; Randomized Controlled Trials as Topic; Schizophrenia [*drug therapy]

MeSH check words

Humans

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