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Depot fluphenazine decanoate and enanthate for schizophrenia (Review)

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TABLE OF CONTENTS

[Intervention Review]

Depot fluphenazine decanoate 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 investigate the clinical effects of fluphenazine decanoate and enanthate.

Search methods

For this update we searched the Cochrane Schizophrenia Group's Register (May 2002).

Selection criteria

We considered all relevant randomised clinical controlled trials 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, quality rated and data extracted studies. For dichotomous data we estimated relative risk (RR) with 95% confidence intervals (CI), and, where possible, the number needed to treat/harm (NNT/H). Analysis was by intention-to-treat. We used the weighted mean difference (WMD) for normal continuous data. Tests of heterogeneity and for publication bias were undertaken.

Main results

This review now includes 70 randomised studies. Compared with placebo, fluphenazine decanoate did not reduce relapse over 6 months to 1 year, but one longer term study found that relapse was significantly reduced in the fluphenazine arm (n=54, RR 0.35, CI 0.2 to 0.6, NNT 2 CI 2 to 4). Fluphenazine decanoate does not reduce relapse more than oral neuroleptics (n=419, 6 RCTs, RR relapse 26-52 weeks 1.46 CI 0.8 to 2.8) or other depot antipsychotics (n=581, 11 RCTs, RR relapse 26-52 weeks 0.82 CI 0.6 to 1.2). Relapse rates over 6 months to 1 year were not significantly different between standard dosage of fluphenazine decanoate over a low dose group (n=523, 4 RCTs, RR 2.09 CI 0.6 to 7.1). Movement disorders were significantly less for people receiving fluphenazine decanoate compared with oral neuroleptics (n=259, 3 RCTs, RR 0.47 CI 0.2 to 0.9, NNT 14 CI 10 to 82).

For fluphenazine enanthate there were limited data but no clear difference in global change (0 to 5 weeks) when compared with oral neuroleptics (n=31, 1 RCTs, RR 0.67 CI 0.3 to 1.7), and in relapse rates over 6-26 weeks between fluphenazine enanthate and other depots. Compared with placebo, giving the enanthate caused no more people to need need anticholinergic drugs (n=25, 1 RCT, RR 9.69 CI 0.6 to 163.0) and movement disorders, tardive dyskinesia, tremor, blurred vision and dry mouth were equally prevalent when enanthate was compared with other depot neuroleptics.

Authors' conclusions

There are more data for fluphenazine decanoate than for the enanthate ester. Both are effective antipsychotic preparations. 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

For the November 2004 update we extended the scope of the review to include any comparison relevant to these common depot treatments. We subsequently looked for randomised controlled trials to determine the effects of depot fluphenazine decanoate and enanthate for schizophrenia when compared with placebo, other oral antipsychotics, other depot antipsychotics and studies comparing the depot fluphenazine esters. We included results of 70 trials. Fluphenazine decanoate reduces the rate of relapse when compared to placebo. Outcomes for fluphenazine decanoate and enanthate are similar to those of other oral and depot neuroleptics.

BACKGROUND

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. 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).

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. 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 1 to 6 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.

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 4-6 weeks in the body while a single dose of the enanthate is shorter acting (1-3 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).

OBJECTIVES

To assess the effects of flupehazine 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. We included trials described as 'double-blind' if it was implied that the study was randomised and the demographic details regarding participants in each group were similar. We excluded quasi-randomised studies, such as those allocating by using alternate days of the week.

Types of participants

People with schizophrenia or other similar psychotic disorders, irrespective of mode of diagnosis, age, ethnicity and sex. We did include studies describing participants as suffering from "serious mental illnesses" and did not giving a particular diagnostic grouping. The exception to this rule was when the majority of those randomised clearly did not have a functional non-affective psychotic illness.

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.

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

Types of outcome measures

Outcomes were grouped into immediate (0-5 weeks), short term (6 weeks-5 months), medium term (6 months-1 year) and longer term (over 12 months)

Primary outcomes

1. Death and all causes of mortality

2. Clinical global response

2.1 Relapse

2.2 Clinically significant change in global state - as defined by each of the studies

3. Service utilisation outcomes
3.1 Hospital admission.

Secondary outcomes

1. Clinical global response
1.1 Mean score/change in global state
1.2 Leaving the study early

2. Mental state
2.1 Clinically significant change in psychotic symptoms - as defined by each of the studies
2.2 Mean score/change in psychotic symptoms
2.3 Clinically significant change in positive symptoms - as defined by each of the studies

2.4 Mean score/change in positive symptoms
2.5 Clinically significant response in negative symptoms - as defined by each of the studies
2.6 Mean score/change in negative symptoms

3. Extrapyramidal adverse effects
3.1 Incidence of use of antiparkinson drugs
3.2 Clinically significant extrapyramidal adverse effects - as defined by each of the studies
3.3 Mean score/change in extrapyramidal adverse effects

4. Other adverse effects, general and specific

5. Service utilisation outcomes
5.1 Days in hospital

6. Economic outcomes

7. Quality of life/satisfaction with care for either recipients of care or carers
7.1 Significant change in quality of life/satisfaction - as defined by each of the studies
7.2 Mean score/change in quality of life/satisfaction.

Search methods for identification of studies

Electronic searches

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 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)

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)

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.

Data collection and analysis

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 6 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.
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.

RESULTS

Description of studies

See Excluded and Included studies table.

1. Excluded studies
We excluded one hundred and eighty one studies, mainly because they were not randomised controlled trials (RCTs), or controlled clinical trials (CCTs), or 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 1990, Marder 1991a, Stevens 1973).

2. Awaiting assessment
Five 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. One paper awaits translation (Engstrand 1969).

3. Ongoing studies
We have identified no ongoing studies.

4. Included studies
We included 70 randomised controlled trials with a total of 89 reports.

4.1 Length of trials
The duration for all the studies ranged between 2-3 weeks (Altamura 1985) to 3 years (Dencker 1973).

4.2 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 1984, Marder 1987, McCreadie 1980, McCreadie 1982) included only men and fourteen trials failed to mention the sex of participants. Ages ranged between 13 and 81 years.

4.3 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 (12) of studies did not mention the setting used (Albert 1980, Javed 1991, Kissling 1985, Marder 1984, McKane 1987, Odejide 1982, Quitkin 1978, Russell 1982, Schneider 1981, Schlosberg 1978, Sharma 1991, Wistedt 1983).

4.4 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.

4.5 Interventions
Five of the included trials compared fluphenazine decanoate with placebo (Dotti 1979, Hirsch 1975, Jolley 1990, Odejide 1982, Rifkin 1977) and one study compared fluphenazine enthanate with placebo (Van Praag 1970). Eight studies compared fluphenazine decanoate with enanthate (Altamura 1985, Asarnow 1988, Chouinard 1982, Donlon 1976, Keskiner 1971, Kurland 1966, MacCrimmon 1978, Van Praag 1973). Fourteen studies compared fluphenazine esters with oral antipsychotics. Thirty-four trials compared fluphenazine decanoate or enanthate with other depot formulations. There were eight dosage studies - eight comparing fluphenazine decanoate and one comparing fluphenazine enanthate (Goldstein 1978).

Seven studies (Altamura 1985, Chouinard 1978, Chouinard 1982, Donlon 1976, Kurland 1966, MacCrimmon 1978, Van Praag 1973) compared the fluphenazine esters, decanoate and enanthate and a further eight studies compared different doses of the decanoate ester (Asarnow 1988, Hogarty 1988, Kane 1983, Kelly 1977, Marder 1984, Marder 1987, McClelland 1976) or enanthate (Goldstein 1978). The rest of the trials compared fluphenazine decanoate or enanthate with other depot formulations. Of the 70 included trials, 63 of the studies used fluphenazine decanoate as an intervention.

4.6 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.

4.6.1 Outcome scales
Scales that provided usable data are listed below. We listed data that were not usable in the 'included studies table' under outcomes, 'unable to use'.

4.6.1.1 Global functioning
4.6.1.1.1 Clinical Global Impression - CGI (Guy 1976)
This is a three item rating instrument commonly used in schizophrenia studies. It enables clinicians to quantify severity of illness and overall clinical improvement during therapy. A seven-point scoring system is usually used with low scores indicating decreased severity and/or greater recovery.

4.6.1.2 Mental state
4.6.1.2.1 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 0-126. Each item is rated on a seven-point scale, with high scores indicating more severe symptoms.

4.6.1.2.2 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).

4.6.1.2.3 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.

4.6.1.3 Behaviour
4.6.1.3.1 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, cooperation, irritability, manifest psychosis and psychotic depression. The total score ranges from 0-320 with high scores indicating a poor outcome.

4.6.1.4 Adverse effects
4.6.1.4.1 Abnormal Involuntary Movement Side Effects Scale - AIMS (Guy 1976)
This is a twelve-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 0 - none to 4 - severe) has been used to rate each of the ten 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.

4.6.1.4.2 Dosage Record and Treatment Emergent Symptoms Scale - DOTES (Guy 1976a)
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.

4.6.1.4.3 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.

4.6.1.4.4 Simpson and Angus Scale (Simpson 1970b)
This SAS is a ten 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 0-4 scale, with a scoring system of 0-4 for each item. A low score indicates low levels of parkinsonism

4.6.1.4.5 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 0-144.

4.6.1.4.6 Treatment Emergent Symptom Scale -TESS (Guy 1976a)
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.

4.6.1.4.7 Symptom Checklist 90 - SCL-90 (Derogatis 1977)
This is a self-report scale of physical symptoms.

Risk of bias in included studies

1. Randomisation
Trialists described all included studies as randomised. Frangos 1978, Kissling 1985, Magnus 1979 and Wistedt 1984 were the only included studies that specified the process by which they undertook the allocation (code, coin throwing, pre-arranged prescribing list and randomisation list).

2. Blindness
Sixty six studies reported using double blind methodology, although the technique used was not described in any of them. Chien 1973, Hranov 1998. Goldstein 1978 used a single blind method and Leong 1989 described using a 'partially-blinded' method, although they gave no further details. No studies indicated that blind evaluation had been tested at outcome.

3. Loss to follow up
Sixty three studies accounted for all participants at completion of the study. Drop out rates were less than 25% on average for the four largest outcomes, i.e., fluphenazine decanoate versus placebo (17%), fluphenazine decanoate versus oral antipsychotics, (18%), fluphenazine decanoate versus other depot antipsychotics (23%), and fluphenazine enanthate versus other depot antipsychotics (21%).

Falloon 1978, Leong 1989 and Cookson 1986 reported no people on fluphenazine decanoate leaving the study early when compared with either oral or depot neuroleptics. In the latter study, last observations were carried forward and entered into the analysis. Kane 1979 and Pinto 1979 reported that no people left the control group (the former study compared fluphenazine decanoate with placebo and the latter study compared fluphenazine decanoate with another depot, flupenthixol decanoate). DeWolfe 1971 also reported no people having left the control group; in this case fluphenazine enanthate was compared to a thorazine -stelazine regimen (given orally). Kissling 1985 reported a 60% (13/22) drop out rate in the fluphenazine decanoate group and a 30% (10/32) drop out rate in the comparison haloperidol decanoate group after six months. This made all other results reported in the study unusable and these were not included in the analysis. DeWolfe 1971 reported a high drop out rate in the fluphenazine enanthate group (6/10) in a period of six weeks and therefore according to the protocol, all further results reported were not usable. Another two studies had high drop out rates, the first compared (Dencker 1978) fluphenazine decanoate with pipothiazine palmitate with a drop out rate of 63% in the control group and the other (Jain 1975) reported a 73% drop out rate in the control group. In both cases data are not usable and we did not enter them into the analysis.

4. Unbalanced groups
Several studies had very unbalanced groups. Dencker 1973 reported a drop out rate of 10 in the fluphenazine decanoate group compared to 21 in the other depot group. Reasons for withdrawal were adverse effects, shifts to other medications, two patients moved to another place and another refused to continue medication while on

fluphenazine decanoate. Asarnow 1988 also used fluphenazine decanoate as an intervention and reported unbalanced groups in the fluphenazine decanoate dosage study which observed low (n=22) and standard doses (n=14).

Effects of interventions

1. 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). We updated the review in May 2002. A further electronic search yielded 247 citations from which we obtained 124 articles for further inspection. We found 12 studies new to this review so there now are 70 randomised controlled trials in the included studies table and 180 in the excluded studies table. Six studies await assessment, five have so far been unobtainable and one awaits translation.

2. COMPARISON 1: FLUPHENAZINE DECANOATE versus PLACEBO

2.1 Death
The only instance of mortality came from Jolley 1990 where two deaths were reported in the treatment group (fluphenazine decanoate) compared to none occurring in the placebo group (n=54, RR 5.0 CI 0.3 to 99.5). Nevertheless the result was not statistically significant.

2.2 Global state
Heterogeneous data from three studies (Hirsch 1975, Odejide 1982, Rifkin 1977) found relapse rates to be equivocal over 6 months to 1 year for the fluphenazine decanoate group compared with people receiving placebo (n=196, 3 RCTs, RR 0.62 CI 0.2 to 1.6). Relapse rates for longer-term studies (Jolley 1990) at two years significantly favoured fluphenazine decanoate (n=54, RR 0.35, CI 0.2 to 0.6, NNT 2 CI 2 to 4) to placebo.

2.3 Behaviour
Four trials in which 216 people had been randomised to fluphenazine decanoate or placebo had, in total, 21% attrition. No significant difference was found in people leaving the study early between groups (RR 1.30 CI 0.8 to 2.2). Jolley 1990 reported longer-term data at two years for leaving the study early that significantly favoured depot fluphenazine to placebo (n=54, RR 0.47, CI 0.2 to 1.0, NNT 4 CI 3 to 46).

2.4 Mental state
The single study by Odejide 1982 reporting on depression showed equivocal results between fluphenazine decanoate and placebo.

2.5 Adverse effects
Limited data were available. Jolley 1990 reported equivocal data for incidence of tardive dyskinesia. 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, NNH 4 CI 2 to 551.

3. COMPARISON 2: FLUPHENAZINE DECANOATE versus ORAL NEUROLEPTICS

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

3.2 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 0.5 to 0.8, NNT 3 CI 2 to 6). Song 1993 reported on outcomes at 6 months to one year, with equivocal findings (n=102, RR 0.85, CI 0.6 to 1.3). Using the CGI scale, Shu 1983 also reported equivocal findings (n=34, MD at 6 weeks -0.10 CI -2.8 to 2.6). 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 0.8 to 2.8). Relapse data recorded at more than one year were also not significant (n=216, 3 RCTs, RR 1.30, CI 0.9 to 2.0).

3.3 Behaviour
Ten trials reported no significant different difference between the number of people who left the study early over 6 month to 1 year in either the fluphenazine decanoate group or the oral antipsychotic group (n=937, RR 0.96 CI 0.7 to 1.3). Studies by Curry 1972 (at 28 days), Shu 1983 (at 6 weeks) and Falloon 1978 and Simon 1978 (at more than 1 year) were also equivocal. This is further supported by Simon 1978, who found no difference in NOSIE scale scores between groups (n=120, MD -0.56 CI -6.9 to 5.8). Barnes 1983, reported on significant difference for change in disturbed behaviour (n=36). These data are skewed.

3.4 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 -5.8 to 4.3). Schooler 1979 and Falloon 1978 reporting on depression found no significant difference between those receiving fluphenazine decanoate and oral neuroleptics (n=214, RR 6 months to 1 year 0.89 CI 0.6 to 1.3; n=44, RR more than 1 year 1.53 CI 0.9 to 2.6).

3.5 Adverse effects
Three studies, McCreadie 1980, McCreadie 1982 and Schooler 1980, report homogenous data for general movement disorders (6 months to 1 year), which significantly favoured fluphenazine decanoate to oral neuroleptics (n=259, RR 0.47 CI 0.2 to 0.9, NNT 14 CI 10 to 82). The single longer-term study by Falloon 1978 found no significant difference for incidence of movement disorders (n=44, RR 0.40 CI 0.1 to 1.3). Rifkin 1977 reported on akathisia at one year. Akathisia was significantly lower in the oral fluphenazine group (n=51, RR 20.54 CI 1.3 to 338). Trials reported limited data for the outcome 'needing anticholinergic drugs' and all findings were equivocal. 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 0.60 CI 0.4 to 0.9). The other study to report 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 0.0 to 3.0). Shu 1983, using the Simpson & Angus Scale reported no significant difference at six weeks between fluphenazine decanoate and penfluridol (n=32, MD 1.30 CI 0.01 to 2.6). Adamson 1973 (immediate), McCreadie 1982 and Schooler 1980 (medium term) reported general adverse effects. Outcomes are equivocal. 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 0.3 to 2.5). Schooler 1976 reports equivocal data for the adverse effect of blurred vision. Rifkin 1977 also reported on toxicity (no further details) which was more frequent

for the depot fluphenazine group (n=51, RR 4.87 RR 1.1 to 20.7, NNH 4 CI 2 to 101).

4. COMPARISON 3: FLUPHENAZINE DECANOATE versus OTHER DEPOT NEUROLEPTICS

4.1 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 0.1 to 69.3). Nevertheless the result was not statistically significant.

4.2 Global state
Eleven studies report the outcome of 'relapse' at 6 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 0.6 to 1.2). Longer studies (more than one year) also found no difference between interventions (n=252, RR 1.22 CI 0.8 to 1.9). Wistedt 1984 did report relapse data at 20 weeks but, again, results were equivocal. Outcomes for 'no clinically important global change' at 6 months to 1 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 1.0 to 1.1). 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 0.9 to 1.2).

Chouinard 1984 and Schlosberg 1978 report continuous data at 6 months to 1 year on clinical global impression. There is no clear advantage between fluphenazine decanoate and other depot neuroleptics (n=90, WMD -0.10 CI -0.4 to 0.2). These findings were confirmed by Chouinard 1984 and Cookson 1986 who reported no significant difference in needing additional antipsychotics at 6 months to 1 year between the depot groups (n=91, RR 0.53 CI 0.1 to 2). Frangos 1978 also reported the outcome of 'not improved' (n=50, RR at 4 months RR 2.50 CI 0.5 to 11.7) and Leong 1989, at 7 months (n=60, RR 0.75 CI 0.2 to 3.1). Finally Wistedt 1984 reported non-significant data for clinical global impression at zero to 5 weeks. These data are skewed so are not displayed graphically.

4.3 Behaviour
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 0.9 to 1.4). Studies found no differences across any time period from the immediate to those lasting longer than one year. Simon 1978 supported this outcome by reporting no difference in NOSIE-30 scores between the groups (n=118, MD -0.56 CI -6.92 to 5.8).

4.4 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=51, 1 RCT MD 1.10 CI 0.9 to 1.4) and medium term (n=162, 3 RCTs, WMD 1.20 CI 1.1 to 1.3). Longer-term studies (McKane 1987, Simon 1978) did not show any differences for mental state in either intervention (n=141, WMD 0.85 CI -2.3 to 4.0). Dichotomised medium term BPRS data reported by Dencker 1973 found no significant difference between depot fluphenazine and pipothiazine palmitate. 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 0.8 to 1.3).

4.5 Adverse effects
The occurrence of dyskinetic movements in general was the same across short, medium and longer-term studies. Feng 1990 reporting on a small, short-term study found no significant difference between fluphenazine decanoate and haloperidol decanoate (n=30 RR 2.0 CI 0.4 to 9.3). 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 6 months to 1 year 1.08 CI 0.9 to 1.4). 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 1.22 CI 1.0 to 1.5 NNT 12 CI 6 to 84). However these data were heterogeneous and using the random effects model (as per protocol) the result was not statisitcally significant. For the same outcome, three longer-term studies were equivocal but significantly favoured the 'other depot neuroleptics' group when analysed with a fixed effects model (n=220, RR 1.28 CI 1.1 to 1.5, NNT 6 CI 4 to 20). Outcomes such as dry mouth, tardive dyskinesia and parkinsonism were not significantly different between depot fluphenazine and other depot neuroleptics. Tremor (short term, 2 RCTs and medium term, 3 RCTs) was not more common for people given the depot flupenthixol. 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=65, RR 17.88 CI 1.1 to 294.8, NNT 4 CI -8.3 to -2.4). 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 1.1 to 1.7). However, medium term data (n=249, 6 months to 1 year) were equivocal.

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

5.1 Global state
McClelland 1976 and Kreisman 1988 reported no significant difference in relapse scores (medium term) between either depot group (n=184, RR 2.11, CI 0.3 to 14.9). Also,
McClelland 1976 reported no significant difference in needing additional antipsychotics (6 months to 1 year) between fluphenazine decanoate (high dose) group and the standard dosage groups (n=50, 1 RCTs, RR 1.67 CI 0.5 to 6.2). Outcomes for global improvement 'not improved' were reported by Lehmann 1980 (nurse and psychiatrist rated) at 6 months to one year. Results for nurse rated outcomes significantly favoured the standard dosage group (n=40, 1 RCT, RR 1.58 CI 1.1 to 2.3). However, results for psychiatrist rated were not significant for either dosage intervention at 6 months (n=40, 1 RCT, RR 1.15 CI 0.8 to 1.7).

5.2 Behaviour
Lehmann 1980 and McClelland 1976 reported no difference in the number leaving the study (6 months to 1 year) for either intervention (n=90, 2 RCTs, RR 0.60 CI 0.2 to 2.4).

5.3 Mental state
McClelland 1976 further reports no difference in BPRS endpoint score (n=50, 1 RCT, MD -0.03 CI -5.8 to 5.7) for either high or standard dosage group.

5.4 Adverse effects
McClelland 1976 reported no difference between the groups for those needing anticholinergic medication (n=50, RR 1.67 CI 0.5 to 6.2) 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.

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

6.1 Global state
Relapse data, assessed over six months to one year were equivocal. Longer term studies (more than 1 year) reported by Asarnow 1988, Hogarty 1988 and Marder 1987 were also equivocal.

6.2 Behaviour
Marder 1984 reported no significant difference in those leaving the study early (6 months to 1 year) after receiving either low or standard dose fluphenazine decanoate (n=50, RR 0.31 CI 0.1 to 1.5). Asarnow 1988, Hogarty 1988, and Marder 1987 also report 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 0.3 to 1.4).

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

6.4 Adverse effects
Marder 1984 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 0.7 to 9.1). Kane 1983 supported this finding by reporting that the number of people with tardive dyskinesia (n=126, RR 0.52 CI 0.1 to 2.7) 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 endpont analysis with the Simpson Dyskinesia Scale (n=126), which favoured low dose fluphenazine decanoate, although data was skewed and therefore not graphically reported.

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.

7. COMPARISON 6: FLUPHENAZINE ENANTHATE versus PLACEBO

7.1 Adverse effects - at 8 weeks
Only Van Praag 1973 reports 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 0.6 to 163.0).

8. COMPARISON 7. FLUPHENAZINE ENANTHATE versus ORAL NEUROLEPTICS

8.1 Global state
Chien 1973 reported no significant difference in global change (immediate term- 0 to 5 weeks) between fluphenazine enanthate and chlorpromazine (n=31, RR 0.67 CI 0.3 to 1.7).

8.2 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 0.5 to 10.3; RR general adverse effects 2.81 CI 0.9 to 8.5; RR parkinsonism 6.56, CI 0.9 to 47.2).

9. COMPARISON 8: FLUPHENAZINE ENANTHATE versus OTHER DEPOT NEUROLEPTICS

9.1 Global state
Albert 1980 and Chouinard 1978 reported no significant difference in needing additional antipsychotics (at 6 months to one year) for fluphenazine enanthate compared with other depot groups (n=65, RR 0.50 CI 0.2 to 1.1). Both Malm 1974, at 6 weeks to 5 months (n=57, RR 2.38 CI 0.7 to 8.6) and Chouinard 1978, at 6 months to 1 year (n=32, RR 0.33 CI 0.0 to 2.9) reported no statistically significant differences in relapse rates between the fluphenazine enanthate group and the other depot (pipothiazine palmitate) groups.

9.2 Behaviour
Only Jain 1975 provided data for numbers leaving the study early (0 to 5 weeks). These data significantly favoured fluphenazine enanthate compared with the other depot neuroleptics - pipothiazine palmitate (n=30, RR 0.09, CI 0.0 to 0.6). However, this outcome should be interpreted with caution given the limited number of participants. The number of people who left the study early by 6 weeks to 5 months, in the single study by Malm 1974 using fluspirilene as a control, was not significant (n=57, RR 2.38 CI 0.7 to 8.6). Similarly, Chouinard 1978 found no difference between the fluphenazine enanthate group and the other depot neuroleptic group - pipothiazine palmitate at 6 months to 1 year (n=32, RR 0.33 CI 0.0 to 2.9).

9.3 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 0.3 to 0.5). Specific scores on, for example, depression found no difference between the two groups (Singh 1979, n=30, RR 7.00 CI 0.4 to 124.8).

9.4 Adverse effects
Findings were equivocal for outcomes of 'movement disorders' (medium term - n=63, 2 RCTs, RR 1.52 CI 0.8 to 3.1), tardive dyskinesia (medium term- n=32, 1 RCT, RR 0.89 CI 0.5 to 1.7), tremor (medium term- n=95, 3 RCTs, RR 1.24 CI 0.8 to 1.9), blurred vision (medium term- n=30, 1 RCT, RR 3.00 CI 0.1 to 68.3) and dry mouth (medium term- n=62, 2 RCTs, RR 0.80 CI 0.4 to 1.8). Malm 1974 reported that those receiving fluspirilene required significantly less anticholinergic drugs at 6 weeks to 5 months than the fluphenazine enanthate group (n=57, RR 2.86 CI 1.2 to 7.1). The numbers of people needing additional anticholinergic drugs at 6 months to one year were found (Albert 1980 and Chouinard 1978) to be equivocal (n=65, RR 1.02 CI 0.8 to 1.3) for the fluphenenazine enanthate and other depot neuroleptic groups.

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

10.1 Global state
A single study by Goldstein 1978 reported the global outcome of relapse at six weeks to five months. Trialists found statistically significant differences favouring the high dosage fluphenazine enanthate group compared with low dosage fluphenazine enanthate (n=104, RR 9.35 CI 2.3 to 38.3). For every forth person administered a low

dose of fluphenazine decanoate one would relapse (NNT 4 CI 2 to 21). However this result must be treated with caution as only one study is involved.

10.2 Behaviour
Goldstein 1978 found no significant difference in the number of people who left the study early (6 weeks to 5 months) whilst receiving either high or low dosages of fluphenazine enanthate (n=103, RR 3.12 CI 0.7 to 14.7).

11. COMPARISON 10: FLUPHENAZINE DECANOATE versus FLUPHENAZINE ENANTHATE

11.1 Global state
Van Praag 1973 reported data for 'needing additional antipsychotic treatment' at zero to 5 weeks. This trial found a significant difference between the fluphenazines (decanoate and enanthate) (n=33, RR 0.39 CI 0.2 to 0.9 NNT 3 CI 2 to 10). Chouinard 1982 was the only study to report the numbers of people requiring additional antipsychotic treatment at 6 months to 1 year and found no significant difference.

The number of people who relapsed whilst receiving medication at zero to 5 weeks was not significant for the two studies available (n=44, 2 RCTs, RR 0.66 CI 0.2 to 2.4). Donlon 1976 reported no significant difference in relapse rates at 6 weeks to 5 months between the fluphenazine decanoate group and the fluphenazine enanthate group (n=30, RR 2.29 CI 0.7 to 7.5). MacCrimmon 1978, reporting on relapse over the medium term (6 months to 1 year) found no significant difference (n=39, RR 2.43 CI 0.7 to 8.3).

11.2 Behaviour
The number of people leaving the study early at zero to 5 weeks was not significantly different between the fluphenazine decanoate and enanthate groups (n=44, 2 RCTs, RR 0.66 CI 0.2 to 2.4). 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 0.7 to 7.5). Medium term data (6 months to 1 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 0.7 to 8.3).

11.3 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 -3.9 to 3.9).

11.4 Adverse effects
The number of people in these studies reporting movement disorders for short term (6 weeks to 5 months) was not significantly different between the fluphenazine esters (n=49, 2 RCTs, RR 1.14 CI 0.8 to 1.6). Reports of adverse effects (0 to 5 weeks) and parkinsonism (6 weeks to 5 months) were equivocal for fluphenazine decanoate and enanthate groups.

The number of people needing anticholinergic drugs at zero to 5 weeks was found by Van Praag 1973 to be significantly lower for the fluphenazine decanoate group (n=33, RR 0.29 CI 0.1 to 0.7, NNT 2 CI 2 to 5). For longer term studies (6 weeks to 5 months and 6 months to 1 year) there were no significant differences in the number of people needing anticholinergic drugs.

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 trialists in any of the included studies.

DISCUSSION

1. General
Since the review was first published we have identified 1229 citations and included 70 studies. These 70 trials included 4638 people. Most studies were small, involving less than 60 people (n=49), although ten randomised over 100 (range 105-290). The age range was wide (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=41) failed to mention the length of time people had been ill. Researchers frequently used operational criteria for diagnoses (DSM III, II, RDC, Schneider's 1st rank symptoms, Hay & Forrest 1972 criteria, PSE, Kraepelinian, ICD -9, DSM-II/III, Bleuler's criteria, Feighner 1972 criteria and Huangshan council schizophrenia standard), although 30 (43%) trials did not specify which diagnostic criteria were used. Trials were based mainly in the community, or combined both hospital and community settings. The dosages of fluphenazine decanoate and enanthate reflected current clinical practice. Outcomes were, however, limited. No trials reported data on quality of life, service utilisation, hospital admission and economic outcomes. This broad mixture of participants, settings, clinical applicability of the interventions should increase generalisability. It is a shame that so few outcomes were included.

2. Quality of reporting
The quality of reporting was poor in the majority of studies, with only eight studies describing how randomisation was conducted. All studies were classified as category B (unclear allocation concealment) with a moderate risk of overestimating the estimate of effect.

3. COMPARISON: ALL INVOLVING FLUPHENAZINE DECANOATE
3.1 Global state
Relapse rates (medium term - 6 months to 1 year) were not significantly lower in the fluphenazine decanoate group compared with placebo. Only longer term data (more than one year) significantly reduced relapse. The benefits of giving antipsychotic drugs as a maintenance treatment in the medium term for schizophrenia are unclear when compared to placebo. The results are only significant when a fixed effects model is used for this heterogeneous group of data. For the outcome of relapse, fluphenazine decanoate did not seem to hold any advantage over the oral preparation or other depots, at least in the context of randomised trials. The impression that depot preparations offer an advantage to oral antipsychotics in terms of fewer demands on resources such as fewer hospitalisations is neither supported nor refuted by these trial-derived data. Equivocal relapse data were also reported for the dosage studies.

3.2 Behaviour
The numbers of people leaving the study early (6 months to 1 year) in the fluphenazine decanoate (24%) and placebo (19%) groups were very similar. 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 (NNT 4)(Jolley 1990).

Similar drop out rates occurred in fluphenazine decanoate (17%) versus oral neuroleptics (18%). Higher proportions of people left the study early when fluphenazine decanoate (24%) was compared with other depot neuroleptics (22%), but again the differences were not statistically significant. The dosage studies (6 months to 1 year) generally had even lower rates of drop out, high dose fluphenazine decanoate (6%) vs standard dose (11%), and low dose (22%) vs standard dose (7%). Again there was no significant difference between groups. Randomised studies imply that fluphenazine decanoate does not seem to offer additional benefits to prevent drop out compared with oral and other depot neuroleptics, or even placebo.

Simon 1978 reported scale derived behavioural data (NOSIE) for the comparisons fluphenazine decanoate versus oral neuroleptics and other depot neuroleptics. Both sets of data were equivocal.

3.3 Mental state
When fluphenazine decanoate was compared with oral neuroleptics, researchers found no differences for BPRS endpoint data (more than one year). Short and medium term BPRS data, however, significantly favoured 'other depot neuroleptics', although these findings were all based on small studies and are not totally convincing.

Depression scores (medium term and more than one year) were equivocal for fluphenazine decanoate when compared to placebo and oral and other depot neuroleptics, suggesting certain mental states may not be improved with antipsychotic medication. As only Odejide 1982 reported this outcome, larger studies, particularly with placebo comparators, are needed to confirm these initial findings.

3.4 Adverse affects
The occurrence of tardive dyskinesia (long term) was not significantly lower for placebo, although data were again from a single small study.

For oral neuroleptic comparisons, general movement disorders were significantly lower for fluphenazine decanoate over the medium term, but this advantage was not found in longer-term studies. 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 dyskinesia was significantly lower for the fluphenazine decanote group during medium term evaluation, but was not different to oral neuroleptics with longer-term data. For comparisons with other depot neuroleptics, general movement disorders and tardive dyskinesia were found equally commonly to fluphenazine decanoate. Needing anticholinergic drugs was equivocal for short term studies (fixed effects model); herterogeneous data from medium and longer-term studies also did not favour either depot fluphenazine or other depot neuroleptics. McClelland 1976 reported no difference in the requirement for anticholinergic medication between high dose fluphenazine decanoate and standard dose groups. Kane 1983 also reported no difference in the incidence of tardive dyskinesia between low and standard dosage groups. Fluphenazine in the decanoate form is considered by some to have more of a propensity to movement disorders than oral antipsychotics. The results from the randomised trials did not support this.

Studies reporting general adverse effects at 6-26 weeks significantly favoured the other depot group to fluphenazine decanoate. However, those treated with fluphenazine decanoate versus other depot antipsychotics at 6 months to 1 year reported no difference between the depots.

3.5 General
Fluphenazine is one of the older depots on the market and has been less favourably compared to the newer depots. The latter have been said to produce less adverse effects and improve the mental state. However, only six studies are involved and only three other depots have been used (haloperidol decanoate, pipothiazine palmitate and bromperidol). Such claims against fluphenazine decanoate seem more to do with marketing and less associated with evidence.

4. COMPARISON: ALL INVOLVING FLUPHENAZINE ENANTHATE
4.1 Global state
Relapse rates were similar for people given either fluphenazine enanthate or other depot neuroleptics. Data sets were small (Malm 1974, Chouinard 1978) and larger studies would be necessary to determine if fluphenazine enanthate reduces relapse more than other depot antipsychotics. Significantly less people relapsed when they were given intermediate/high dose fluphenazine enanthate compared to those receiving low dose (Goldstein 1978).

Chien 1973 was the only study to report data for 'no clinically important global change' (immediate term) with equivocal results between fluphenazine enanthate and oral neuroleptics. In the comparison with other depot antipsychotics, medium term data for 'needing additional antipsychotic treatment' were equivocal. Both outcomes were derived from small numbers of people and, if this preparation continues to be used, larger studies are needed to determine effects of the enanthate ester.

4.2 Behaviour
Van Praag 1970 compared fluphenazine enanthate with placebo but the authors failed to report how many people left the study early or relapsed during the trial. Jain 1975, however, reported that numbers of people leaving the study early (immediate term) were significantly higher in those given 'other depot neuroleptics', but numbers were very small (n=30).

4.3 Mental state
Only medium term BPRS data were available from Singh 1979. These significantly favoured the 'other depot neuroleptics' group (pipothiazine palmitate). Although the outcome was highly significant no firm conclusion can be made on such a small sample size (n=30). Singh 1979 also reported depression outcomes. These showed no advantage for either preparation.

4.4 Adverse affects
For fluphenazine enathate compared with placebo, data on general movement disorders and parkinsonism were equivocal over the immediate term, although, again, these are limited (n=31). General adverse effects may have been lower in the placebo group. In the comparison with other depots, rates of general movement disorders, tardive dyskinesia, tremor, blurred vision and dry mouth were all found to be similar. Again data were all extracted from small studies. One short term outcome, reported by Malm 1974, 'needing additional anticholinergics' was significantly lower for the other depot neuroleptics group, but this was not replicated by Albert 1980 and Chouinard 1978 over the medium term.

5. COMPARISON: ALL INVOLVING FLUPHENAZINE DECANOATE VERSUS FLUPHENAZINE ENANTHATE

5.1 Global state

Relapse data for immediate, short and medium term were all equivocal from these small studies (maximum n=49). Needing additional antipsychotic treatment (immediate term) significantly favoured the decanoate form although this came from a single study randomising just 33 people. Medium term data (n=49) were equivocal.

5.2 Behaviour

In terms of leaving the study early over the immediate, short and medium term, the two preparations were equally acceptable. Unfortunately the numbers randomised for these outcomes were small (maximum n=49).

5.3 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.

5.4 Adverse affects

The two preparations caused roughly equal incidences of general movement disorders, parkinsonism and general adverse effects. The only statistically significant outcome was that fewer people in the decanoate group required additional anticholinergics (immediate term) but this was not replicated in the short and medium term studies.

In clinical practice, many people with schizophrenia are first prescribed an antipsychotic with less potent parkinsonian adverse effects or are adequately treated with occasional antiparkinsonian medications. The studies we reviewed neither refute nor support the use of these routine therapeutic options.

6. Sensitivity analyses

The mean daily dose of fluphenazine decanoate at endpoint ranged from 0.3mg-300mg and for fluphenazine enanthate ranged from 2.35-387.5mg. 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.

AUTHORS' CONCLUSIONS

Implications for practice

1. For people with schizophrenia

Compared with placebo, fluphenazine decanoate does not appear to have a clinically important effect in terms of improving relapse rates based on medium term (6 months to 1 year) data. One longer term study, however, does support the use of fluphenazine decanoate to reduce relapse. 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 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 four 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. Allocation concealment is essential to ensure that selection bias is kept to a minimum. Seven studies failed to implement double blind evaluation of the outcomes (Chien 1973, Goldstein 1978, Hranov 1998, Kane 1978, Kelly 1977, Leong 1989, Simon 1978). 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 sixteen 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 17 failed to report the setting (Albert 1980, Feng 1990, Hranov 1998, Javed 1991, Kissling 1985, Kreisman 1988, Lehmann 1980, Marder 1984, 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. More studies are required in each category but particularly in the case of fluphenazine enanthate where data were particularly few.

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

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

Adamson 1973

Methods	Allocation: randomised. Blindness: double. Duration: 28 days. Design: crossover x2.
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 12.5mg/IM day one, 25mg/IM day 7. N=19. 2. Chloropromazine: dose 50-100mg/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 usuable continuous data.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Albert 1980

Methods	Allocation: randomised. Blindness: double. Duration: 39 weeks. Design: drug stabilisation period 2 months, treatment 3 months.
Participants	Diagnosis: schizophrenia. N=33. Age: approximate age mid 40s.

Albert 1980 *(Continued)*

	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 additonal 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
Allocation concealment?	Unclear risk	B - Unclear

Altamura 1985

Methods	Allocation: randomised. Blindness: double. Duration: 2-3 week (2 periods). Design: parallel group.
Participants	Diagnosis: schizophrenia (PSE- DSM III). N=11. Age: 35-60 years. Sex: 2M, 9F. History: duration illness <2yrs. Setting: community.
Interventions	1. Fluphenazine decanoate: dose 25mg/IM every 3-4 weeks. N=6. 2. Fluphenazine enanthate: dose 25mg/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-clincal outcomes, data unusuable). Cognitive: handwriting (non-clinical outcomes, data unusable).
Notes	No usable continuous data. Authors contacted.

Risk of bias

Bias	Authors' judgement	Support for judgement

Altamura 1985 *(Continued)*

Allocation concealment?	Unclear risk	B - Unclear

Asarnow 1988

Methods	Allocation: randomised. Blindness: double. Duration: 2 years. Design: dosage study.
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**
Allocation concealment?	Unclear risk	B - Unclear

Barnes 1983

Methods	Allocation: assigned to two groups by independent statistician. Blindness: double. Duration: 1 year. Design: parallel group.
Participants	Diagnosis: schizophrenia (PSE). N=36. Age: mean ˜ 49 years. Sex: 18M, 18F. History: no stated. Setting: community.
Interventions	1. Fluphenazine decanoate: dose 25mg/IM biweekly. N=19. 2. Pimozide: dose 8mg biweekly. N=17.
Outcomes	Behaviour: leaving the study early. Unable to use - Behaviour: SBAS (non-clinical outcomes, data unusable).

Barnes 1983 *(Continued)*

Notes	Analysis: last obeservation carried forward. No continuous outcomes measured.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Chien 1973

Methods	Allocation: randomised. Blindness: single. Duration: 30 days. Design: parallel group.
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 -75mg/IM, mean 28.5 mg/IM every 12 days. N=16. 2. Chlorpromazine: dose mean 388mg/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).
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Chouinard 1978

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

Chouinard 1978 *(Continued)*

	Setting: community.
Interventions	1. Fluphenazine enanthate: dose 6.25-100mg/IM biweekly. N=16. 2. Pipothiazine palmitate: dose 25-100mg/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
Allocation concealment?	Unclear risk	B - Unclear

Chouinard 1982

Methods	Allocation: randomised. Blindness: double. Duration: 7 months, preceeded by 1 month stabilisation period. Design: parallel group.
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 2.5-250mg/IM, mean 27mg/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

Chouinard 1982 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Chouinard 1984

Methods	Allocation: randomised, stratified by sex & past frequency of depot adminstration. Blindness: double. Duration: 8 months. Design: parallel group.
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 2.5-300mg/IM, mean 75mg/IM every 2-4 weeks. N=36. 2. Haloperidol decanoate: dose 15-900mg/IM, mean 225mg/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
Allocation concealment?	Unclear risk	B - Unclear

Cookson 1986

Methods	Allocation: randomised, seperate randomisation sequences for males and females. Blindness: double. Duration: 8 months. Design: parallel group.
Participants	Diagnosis: schizophrenia implied. N=19. Age: 26-60 years. Sex: 9M, 10F. History: 1yr treatment with fluphenazine decanoate, overweight BMI 25+, physically fit, stable during previous year

Cookson 1986 *(Continued)*

	Setting: community.
Interventions	Fluphenazine decanoate: dose 26.4mg/IM, every 2-6 weeks, average 3.6 months. N=9. 2. Haloperidol decanaote: dose 22.2mg/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).
Notes	Analysis: last observation carried forward.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Crawford 1974

Methods	Allocation: randomised. Blindness: double. Duration: 40 weeks. Design: parallel group.
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. 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
Allocation concealment?	Unclear risk	B - Unclear

Curry 1972

Methods	Allocation: randomised. Blindness: double.

Curry 1972 *(Continued)*

	Duration: 28 days. Design: parallel group.
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
Allocation concealment?	Unclear risk	B - Unclear

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.
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 6.25mg/IM monthly (mean monthly dose for 2 year continuation phase 27.8 mg/IM). N=35. 2. Pipothiazine palmitate: dose 25-400mg/IM, mean 50mg/IM monthly (mean monthly dose for 2 year continuation phase 152.3mg/IM). N=32.
Outcomes	Global state: need for additional medication. Behaviour: leaving the study early. Adverse effetcs: EPS, HRSD. Unable to use - Mental state: BPRS, S-Scale, HRSD (no SD). Cognitive: Handwriting test (non-clincal outcomes, data not usable). Social ability: ADL, work performance, SRE (non-clincal outcomes, data not usable). Adverse effects: EPS (no data).
Notes	Authors contacted.

Dencker 1973 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Donlon 1976

Methods	Allocation: randomised. Blindness: double. Duration: 2 months. Design: parallel group.
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 296.4mg/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 cetagory in both FE & FD treatment groups. *2 different N values in the paper.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Dotti 1979

Methods	Allocation: randomised. Blindness: double. Duration: 9 months. Design: parallel group.
Participants	Diagnosis: schizophrenia. N=20. Age: 19-32 years. Sex: all male. History: previous episodes of psychosis. Setting: community.

Dotti 1979 *(Continued)*

Interventions	1. Fluphenazine decanoate: dose 25-50mg (frequency not stated). N=10. 2. Placebo: (frequency not stated). N=10.
Outcomes	Behaviour: leaving the study early. Unable to use - Mental state: BPRS (data unusable).
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Falloon 1978

Methods	Allocation: randomised. Blindness: double. Duration: 20 months. Design: 2 trials - I & II.
Participants	Diagnosis: schizophrenia (Schneider). N=44. Age: 17-60 years, mean ~ 39 years. Sex: 20M, 24F. History: stabilised prior to study entry. Setting: community.
Interventions	1. Fluphenazine decanoate: dose mean 25mg/IM/weekly, maximum 50mg/ biweekly. N=20. 2. Pimozide: dose mean 8mg/IM/day, maximum 16 mg/day. N=24. Flexible dosage.
Outcomes	Global state: need for addtional 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
Allocation concealment?	Unclear risk	B - Unclear

Feng 1990

Methods	Allocation: randomised.

Feng 1990 *(Continued)*

	Blindness: double. Duration: 12 weeks. Design: parallel group.
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 25mg/ml fortnightly injections. N=15. 2. Haloperidol decanoate: dose 25mg/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).
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Frangos 1978

Methods	Allocation: randomised (randomisation code). Blindness: double. Duration: 16 weeks. Design: parallel group.
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 decanaote: dose 25-150mg/IM, mean 76mg/IM biweekly. N=25. 2. Fluspirilene decanaote: dose 4-20mg/IM, mean 12mg/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

Frangos 1978 *(Continued)*

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Goldstein 1978

Methods	Allocation: randomised. Blindness: single. Duration: 6 weeks. Design: 6 month follow-up (not controlled).
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) 1ml/IM biweekly. N=53. 2. Fluphenazine enanthate: dose (low) 0.25ml/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	last observation carried forward.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Hirsch 1975

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

Hirsch 1975 *(Continued)*

	Unable to use - Mental state: PSE (data unusable). Behaviour: SPS (data unusable).
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Hogarty 1979

Methods	Allocation: randomised. Blindness: double. Duration: 2 years. Design: parallel study.
Participants	Diagnosis: schizophrenia. N=105. 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 12.5-125mg/IM, mean 25 mg/IM biweekly. N=27. 2. Fluphenazine hydrocloride (oral): dose 2.5-40mg/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
Allocation concealment?	Unclear risk	B - Unclear

Hogarty 1988

Methods	Allocation: randomised, stratification by dose & household EE. Blindness: double. Duration: 2 years. Design: dosage study.
Participants	Diagnosis: schizophrenia, schizoaffective (RDC). N=70. Age: mean 28 yrs, range 17-55 yrs.

Hogarty 1988 *(Continued)*

	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 25mg/IM biweekly. N=33. 2. Fluphenazine decanoate: minimal dose mean 3.8mg/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
Allocation concealment?	Unclear risk	B - Unclear

Hranov 1998

Methods	Allocation: randomised. Blindness: not described. Duration: 6 months. Design: parallel group.
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 99.3mg/IM/month. N=21. 2. Haloperidol decanoate: dose 47.3mg/month. N=20.
Outcomes	Behaviour: leaving the study early. Unable to use - Global state: CGI (data unusable). Mental state: PANSS (data unusable). Adverse effects: UKU (data unusable).
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Jain 1975

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

Javed 1991

Methods	Allocation: randomised. Blindness: double. Duration: 12 weeks. Design: parallel group.
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 25mg/IM biweekly. N=20. 2. Flupenthixol decanoate: dose 40mg/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).

Javed 1991 *(Continued)*

Notes	Authors contacted.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Jolley 1990

Methods	Allocation: randomised. Blindness: double. Duration: 2 years. Design: 2 year follow up.
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
Allocation concealment?	Unclear risk	B - Unclear

Kane 1983

Methods	Allocation: randomised. Blindness: double. Duration: 1 year. Design: dosage study.
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.

Kane 1983 *(Continued)*

	Setting: community.
Interventions	1. Fluphenazine decanoate (low dose): dose 1.25-5.0mg/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
Allocation concealment?	Unclear risk	B - Unclear

Kaneno 1991

Methods	Allocation: randomised. Blindness: double. Duration: 6 months. Design: parallel group.
Participants	Diagnosis: schizophrenia. N=259. Age: 20 - 65 years. Sex: 168M, 91F. History: not stated. Setting: hospital and community.
Interventions	1. Fluphenazine decanoate: dose 12-50mg/ml/IM adminstered 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: ORS (no SD).
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Kelly 1977

Methods	Allocation: randomised. Blindness: single. Duration: 9 months. Design: parallel group.
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
Allocation concealment?	Unclear risk	B - Unclear

Keskiner 1971

Methods	Allocation: randomised. Blindness: double. Duration: 8 weeks (4 weeks before cross over). Design: cross-over.
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).

Keskiner 1971 *(Continued)*

Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Kissling 1985

Methods	Allocation: randomised (coin throwing). Blindness: double. Duration: 6 months. Design: parallel group.
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 25mg/IM biweekly. N=22. 2. Haloperidol decanoate: dose mean 50 mg/IMmonthly. N=32.
Outcomes	Behaviour: leaving the study early. Unable to use - Global state: need for additional anticholinergic medication (data unusable). Mental state: BPRS (data unusuable). 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
Allocation concealment?	Unclear risk	B - Unclear

Kreisman 1988

Methods	Allocation: randomised. Blindness: double. Duration: 1 year. Design: dosage study.
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.

Kreisman 1988 *(Continued)*

	Excluded: presumptive tardive dyskinesia, neurological disorders, serious substance abuse, mental retardation, physical illnesses, or requiring adjunctive medication except for antiparkinsonian agents and minor tranquilizers.
Interventions	1. Fluphenazine decanoate (low dose): dose 1.25-5mg/cc biweekly. N=66. 2. Fluphenazine decanoate (high dose): dose 12.5-50mg/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
Allocation concealment?	Unclear risk	B - Unclear

Kurland 1966

Methods	Allocation: randomised. Blindness: double. Duration: 24 weeks (first arm 12 weeks). Design: cross-over.
Participants	Diagnosis: schizophrenia. N=19. Age: 23 - 53 years. Sex: all male. History: chronically ill. Setting: hospital.
Interventions	1. Fluphenazine decanoate: dose mean 25mg/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, data unusable).
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
Allocation concealment?	Unclear risk	B - Unclear

Lehmann 1980

Methods	Allocation: randomised. Blindness: double. Duration: 24 weeks. Desgin: dosage study.
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	

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Leong 1989

Methods	Allocation: randomised. Blindness: partial. Duration: 28 weeks. Design: parallel group.
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 12.5-50mg/IM monthly. N=30. 2. Pipothiazine palmitate: dose 25-50mg/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

Leong 1989 *(Continued)*

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Levenson 1976

Methods	Allocation: randomised. Blindness: double. Duration: 21 days. Design: 3 treatment groups.
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 2.5-7.5mg/day. N=5. 2. Thiothixine: dose 5 -15mg/day. N=3. 3. Haloperidol: dose 2.5 -7.5mg/day. N=4.
Outcomes	Behaviour: leaving the study early. Adverse effects. Unable to use - Mental state: BPRS (no usable data).
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Lundin 1990

Methods	Allocation: randomised. Blindness: double. Duration: 1 year (preceeded by 6 month 'run-in' period). Design: parallel group.
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.
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.

Lundin 1990 *(Continued)*

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
Allocation concealment?	Unclear risk	B - Unclear

MacCrimmon 1978

Methods	Allocation: randomised. Blindness: double. Duration: 1 year. Design: parallel group.
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
Allocation concealment?	Unclear risk	B - Unclear

Magnus 1979

Methods	Allocation: randomised, prearranged prescribing list. Blindness: open. Duration: 6 months. Design: parallel group.
Participants	Diagnosis: schizophrenia.

Magnus 1979 *(Continued)*

	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.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Malm 1974

Methods	Allocation: randomised. Blindness: double. Duration: 8 weeks. Design: parallel group.
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 7.5-50mg/IM, mean 28.5 mg/IM biweekly. N=26. 2. Fluspirilene: dose 1-14 mg/IM, mean 5.7mg/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

Malm 1974 *(Continued)*

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Marder 1984

Methods	Allocation: randomised. Blindness: double. Duration: 1 year. Design: dosage study.
Participants	Diagnosis: schizophrenia. N=50. Age: mean ˜ 36 years. Sex: all male. History: duration illness mean ˜ 10 years, able to give informed consent , stabilised on FD <2 months. Setting: community.
Interventions	1. Fluphenazine decanoate (low dose): dose 5-10mg/IM, mean 5mg/IM biweekly. N=28. 2. Fluphenazine decanoate (standard): dose 25-50mg/IM, mean 25mg/IM biweekly. N=22.
Outcomes	Global state: need for additional medication. Behaviour: leaving the study early. Unable to use - Mental state: BPRS (no data). Adverse effects: SCL-90, SE Scale, IMEPS, Subjective EPS Rating Scale (no data).
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Marder 1987

Methods	Allocation: randomised. Blindness: double. Duration: 2 years. Design: dosage study.
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 (5mg), 170 months (25mg). Setting: community and hospital.
Interventions	1. Fluphenazine decanoate (low dose): dose mean 5mg/IM biweekly. N=35. 2. Fluphenzazine decanoate (standard): dose mean 25 mg/IM biweekly. N=31.
Outcomes	Behaviour: leaving the study early.

Marder 1987 *(Continued)*

	Unable to use - Mental state: BPRS (no data). Adverse effects: Hopkins SCL-90R, side effects scale (no data).
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

McClelland 1976

Methods	Allocation: randomised. Blindness: double. Duration: 6 months (preceeded by pretrial of 6 weeks). Design: dosage study.
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 (very high dose): 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	

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

McCreadie 1980

Methods	Allocation: randomised. Blindness: double. Duration: 9 months. Design: parallel group.
Participants	Diagnosis: schizophrenia (Feighner's Criteria).

McCreadie 1980 *(Continued)*

	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 12.5mg/IM, maximum 50mg weekly. N=18. 2. Pimozide: dose mean 8mg/IM, maximum 32mg 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
Allocation concealment?	Unclear risk	B - Unclear

McCreadie 1982

Methods	Allocation: randomised. Blindness: double. Duration: 9 months. Design: parallel group.
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 2-25mg/IM, mean 14mg/IM biweekly. N=15. 2. Pimozide: dose 10-60mg/IM, mean 40mg/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). Behaviour: WWBRS (no data).
Notes	Authors contacted.

Risk of bias

Bias	Authors' judgement	Support for judgement

McCreadie 1982 *(Continued)*

Allocation concealment?	Unclear risk	B - Unclear

McKane 1987

Methods	Allocation: randomised. Blindness: double. Duration: 48 weeks. (preceeded by 12 weeks 'run in' period where additional medication allowed). Design: parallel group.
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 106mg/IM/week, week 12 dose mean 105/IM monthly. N=19. 2. Haloperidol decanoate: dose mean 127mg/IM, week 12 dose mean 120 mg/IM monthly. N=19.
Outcomes	Global state: Global 5-point scale, need for additional medicaiton. 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**
Allocation concealment?	Unclear risk	B - Unclear

McLaren 1992

Methods	Allocation: randomised. Blindness: double. Duration: 1 year. Design: parallel group.
Participants	Diagnosis: schizophrenia (ICD-9). N=47. Age: 20-65 yrs. Sex: 27M, 20F. History: good physical health, recieved 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 103mg/IM/month. N=24. 2. Bromperidol decanaote: dose 67-400 mg/IM/month, mean 242mg/IM/month. N=23.
Outcomes	Global state: relapse, need for additional medication. Behaviour: leaving the study early. Symptoms: NSRS. Unable to use -

McLaren 1992 *(Continued)*

	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
Allocation concealment?	Unclear risk	B - Unclear

Odejide 1982

Methods	Allocation: randomised. Blindness: double. Duration: 12 months. Design: parallel group.
Participants	Diagnosis: schizophrenia (ICD-9). N=70. Age: not stated. Sex: not stated. History: treated with FD <2years, <2 acute periods, able to give informed consent. Setting: community.
Interventions	1. Fluphenazine decanoate: dose 25mg/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 - 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
Allocation concealment?	Unclear risk	B - Unclear

Pinto 1979

Methods	Allocation: randomised. Blindness: double. Duration: 18 months (preceeded by 3 months 'run-in' period - medication unchanged). Design: parallel group.
Participants	Diagnosis: schizophrenia. N=64.

Pinto 1979 *(Continued)*

	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.
Interventions	1. Fluphenazine decanoate: dose mean 25mg/IM every 3 weeks (initial dose 12.5 mg). N=33. 2 Flupenthixol decanoate: dose mean 36.6mg/IM every 3 weeks (initial dose 20 mg). N=31.
Outcomes	Global state: need for additonal 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
Allocation concealment?	Unclear risk	B - Unclear

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.
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

Quitkin 1978 *(Continued)*

Allocation concealment?	Unclear risk	B - Unclear

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.
Participants	Diagnosis: schizophrenia (Kraepelinian). N=73. Age: 17-38 years, mean Sex: 50M, 23F. History: 16 participants acutely ill, stable while recieving FD/F HCL for 4 weeks, able to give informed consent. Setting: community.
Interventions	1.Fluphenazine decanoate: dose 0.5-2.0ml/IM, mean 0.5ml/IM biweekly. N=23. 2. Fluphenazine hydrochloride (oral): dose 5-20mg/IM, mean 5mg/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. Continious data reported in paper II but not usable- not seperated into seperate groups.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment?	Unclear risk	B - Unclear

Rossi 1990

Methods	Allocation: randomised. Blindness: double. Duration: 6 months. Design: parallel group.
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 25-50mg/IM, mean 30mg/IM monthly. N=15.

Rossi 1990 *(Continued)*

	2. Bromperidol decanoate: dose 50-100 mg/IM, mean 85mg/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).
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Russell 1982

Methods	Allocation: randomised. Blindness: double. Duration: 6 months. Design: parallel group.
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 3mg/IM, maximum dose 10.94 mg/IM weekly. N=20.
Outcomes	Global state: need for addtional 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
Allocation concealment?	Unclear risk	B - Unclear

Schlosberg 1978

Methods	Allocation: randomised. Blindness: double. Duration: 9 months (depot), 3 months (placebo)*. Design: parallel group.
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 6.25-50mg/IM monthly. N=30. 2. Pipothiazine palmitate: dose 6.25-50mg/IM monthly. N=30.
Outcomes	Leaving the study. Global Impression. Side effects. Unable to use - Mental state: BPRS (no SD). Behaviour: NOSIE (no SD).
Notes	* Wash-out period 14 days.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Schneider 1981

Methods	Allocation: randomised. Blindness: double. Duration: 1 year (preceeded by 2 weeks washout). Design: parallel group.
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 decanaoate: dose 12.5-400mg/IM every 2-5 weeks. N=27. 2. Pipothiazine palmitate: dose 50-400 mg/IM every 2-5 weeks. N=32.
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.

Schneider 1981 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Schooler 1976

Methods	Allocation: randomised. Blindness: double. Duration: 1 year. Design: parallel group.
Participants	Diagnosis: schizophrenia (Schneiderian 1st rank). N=197. Age: 18-55 years, mean ~ 30 years. Sex: 58M, 42F. History: newly admitted from the community. Setting: community.
Interventions	1. Fluphenazine decanoate: dose 12.5-100mg/IM, mean 34.7mg/IM every 3 weeks. N=102. 2. Fluphenazine (orally): dose max 60mg, mean25.2 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
Allocation concealment?	Unclear risk	B - Unclear

Schooler 1979

Methods	Allocation: randomised. Blindness: double. Duration: 1 year. Design: parallel group.
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.

Schooler 1979 *(Continued)*

	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
Allocation concealment?	Unclear risk	B - Unclear

Schooler 1980

Methods	Allocation: randomised, stratified by sex. Blindness: double. Duration: 1 year. Design: parallel group.
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 12.5-100mg/IM, mean 34.2mg/IM every 3 weeks. N=143. 2. Fluphenazine hydrochloride (oral): dose 2.5-60mg, 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
Allocation concealment?	Unclear risk	B - Unclear

Schooler 1997

Methods	Allocation: randomised. Blindness: double. Duration: 16-24 weeks. Design: dosage study.

Schooler 1997 *(Continued)*

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 2.5-10mg 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). Family therapy strategies: (non-clinical outcomes, data unusable).
Notes	Authors contacted.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Sharma 1991

Methods	Allocation: randomised. Blindness: double. Duration: 48 weeks. Design: parallel group.
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 100mg/IM/monthly. N=29. 2. Haloperidol decanoate: dose 100mg/IM/monthly. N=30.
Outcomes	Leaving the study early. Additional medication. Side effects: EPS Rating Scale, AIMS. Unable to 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

Sharma 1991 *(Continued)*

Allocation concealment?	Unclear risk	B - Unclear

Shu 1983

Methods	Allocation: randomised. Blindness: double. Duration: 6 weeks. Design: parallel group.
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**
Allocation concealment?	Unclear risk	B - Unclear

Simon 1978

Methods	Allocation: randomised. Blindness: open. Duration: 18 months. Design: 3 treatment groups.
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 88mg/IM every 22 days. N=57. 2. Pipothiazine decanoate: dose mean 90mg/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.

Simon 1978 *(Continued)*

	Side effects.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Singh 1979

Methods	Allocation: randomised. Blindness: double. Duration: 44 weeks. Design: parallel group.
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.
Interventions	1. Fluphenazine enanthate: dose 25-75mg/IM, mean 44.2mg/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
Allocation concealment?	Unclear risk	B - Unclear

Song 1993

Methods	Allocation: randomised. Blindness: double. Duration: 6 months. Design: 3 treatment groups.
Participants	Diagnosis: schizophrenia. N=154. Age: not stated. Sex: not stated. History: chronic. Setting: hospital.

Song 1993 *(Continued)*

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
Allocation concealment?	Unclear risk	B - Unclear

Van Praag 1970

Methods	Allocation: randomised. Blindness: double. Duration: 8 weeks, follow up 4 weeks. Design: parallel group.
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 concomittant 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
Allocation concealment?	Unclear risk	B - Unclear

Van Praag 1973

Methods	Allocation: randomised. Blindness: double. Duration: 4 weeks. Design: parallel group.
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 25mg/IM every 3 weeks. N=15. 2. Fluphenazine enanthate: dose 25mg/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

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Walker 1983

Methods	Allocation: randomised. Blindness: double. Duration: 24 weeks (preceeded by 12 week open trial). Design: parallel group.
Participants	Diagnosis: schziophrenia. 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.
Outcomes	Side effects: Side Effects Inventory. Unable to use - Global state: CGI, Krawiecka, Goldberg & Vaughan Rating Scale (no SD). Mental state: BPRS (no SD).

Walker 1983 *(Continued)*

	Physiological measures: blood/liver tests, weight, BP (non-clincal outcomes, data unusable).
Notes	Authors contacted. Analysis: last oservation carried forward.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Wistedt 1983

Methods	Allocation: randomised. Blindness: double. Duration: 2 years. Design: parallel group.
Participants	Diagnosis: schizophrenia (Bleuler's criteria). N=32. Age: 26-67 years, mean ~ 41years. Sex: 15M, 17F. History: stabalised on depots, relapse in connection with withdrawl; 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
Allocation concealment?	Unclear risk	B - Unclear

Wistedt 1984

Methods	Allocation: randomised. Blindness: double. Duration: 20 weeks. Design: parallel group.
Participants	Diagnosis: schizophrenia (RDC). N=51. Age range: 21-63 years. Sex: 33M, 18F.

Wistedt 1984 *(Continued)*

	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 decanaote: dose mean 84mg/IM/monthly. N=26. 2. Haloperidol decanoate: dose mean 122mg/IM/monthly. N=25. Depot (FD/HD) dose range: 25-100 mg/injection, initially adjusted at 2nd injection (max. 300mg).
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
Allocation concealment?	Unclear risk	B - Unclear

Woggon 1977

Methods	Allocation: randomised. Blindness: double. Duration: 6 months. Design: parallel group.
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 25-37.5mg/IM every 3 weeks. N=30. 2. Pipothiazine palmitate: dose 100mg/IM every 4 weeks. N=31.
Outcomes	Leaving the study early. Unable to use - Side effects: (data unusable).
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Diagnostic tools:

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
GVRS - Goldberg & Vaughan Rating 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
IMPS - Inpatient Multidimensional Psychiatric Scale
KORS - Keio University's Simplified Rating Scale for Psychiatric Symptoms
MIE - Mental Illness Evaluation
PSE - Wing Ward Present State Examination
SANS - Scale for Assessment of Negative Symptoms
S-Scale - The Symptom Scale
Behaviour:
CBS - Current Behaviour Schedule
MACC-BAS - MACC Behaviour Adjustment Scale
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
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:
BP - Blood Pressure.
EE - Expressed Emotion
NIMH - National Institute of Mental Health
PER-C - Periodic Evaluation Record - Community Version
VHD - Very High Dose

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.
Bao 1991	Allocation: randomised. Participants: people with schizophrenia.

Study	Reason for exclusion
	Interventions: flupenthixol decanoate versus chlorpromazine.
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.
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 - withdrawl study.
Caranza 1973	Allocation: not randomised.
Carpenter 1992	Allocation: randomised. Participants: people with schizophrenia. Interventions: fluphenazine versus placebo versus diazepam. Outcomes: withdrawl study.
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.
Castellani	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.

Study	Reason for exclusion
	Interventions: fluphenzine enanthate versus different dosages of antiparkinson drugs (not antipsychotics).
Childers 1964	Allocation: randomised. Participants: people with schizophrenia. Interventions: electro convulsive therapy 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.
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 continous outcomes measured.
Dencker 1978	Allocation: randomised. Participants: people with schizophrenia. Intervention: high - low doses of fluphenazine enanthate.

Study	Reason for exclusion
	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 6wk trial.
Donlon 1976 1	Allocation: randomised. Participants: people with schizophrenia. Interventions: fluphenazine decanaoate versus fluphenazine enanthate. Outcomes: no usable data.
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.
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.

Study	Reason for exclusion
	Outcomes: no usable data - results provided at 12 months without seperating the treatments.
Floru 1975	Allocation: not randomised.
Gianelli 1990	Allocation: not randomised.
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).
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 ethanate versus oral phenothiazines.
Goldberg 1981	Allocation: randomised - withdrawl study.
Grosser 1970	Allocation: randomised. Participants: people with schizophrenia. Interventions: fluphenazine decanaoate 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.
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.

Study	Reason for exclusion
	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, withdrawl 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.
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.
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	Reason for exclusion
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.
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: withdrawl study.
Kane 1982	Allocation: randomised. Participants: people with acute first episode schizohphrenia. Interventions: fluphenazine decanoate versus placebo. Outcomes: no usable data, authors contacted.
Kane 1983 b	Allocation: not randomised - review article.
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: withdrawl study.

Study	Reason for exclusion
King 1979	Allocation: randomised. Participants: people with schizophrenia. Interventions: family therapy in conjunction with high and low dose phenothiazines.
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.
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.

Study	Reason for exclusion
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.
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 1990	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.
Marder 1996	Allocation: randomised. Particpants: people with schizophrenia. Interventions: fluphenazine decanoate versus placebo. 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.

Study	Reason for exclusion
	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.
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.
Nestoros 1978	Allocation: "randomly assigned" Participants: people with schizophrenia. Interventions: oral fluphenazine versus butaclamol.
Owen 1993	Allocation: admitted seqentially - 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 seperately 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).

Study	Reason for exclusion
Quitkin 1977	Allocation: randomised. Participants: people with schizophrenia. Interventions: fluphenazine decanoate versus penfluridol. Outcomes: no usable data, preliminary report.
Ravaris 1965	Allocation: not randomised.
Ravaris 1967	Allocation: randomised. Participants: people with schizphrenia. 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.
Simpson 1970	Allocation: randomised. Participants: people with schizophrenia. Interventions: fluphenazine. Outcomes: no usable data.
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.

Study	Reason for exclusion
	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.
Turner 1966	Allocation: randomised. Participants: not described.
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.
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.

Study	Reason for exclusion
Winter 1973	Allocation: randomised. Participants: people with schizophrenia. Interventions: fluphenazine decanoate versus fluspirilene decanaote. Outcomes: no usable data.
Wistedt 1981	Allocation: randomised. Participants: people with schizophrenia. Interventions: fluphenazine decanoate & 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 & flupenthixol decanoate versus placebo. Outcomes: no usable data - both drugs placed in 1 group.
Wistedt 1983b	Allocation: randomised. Participants: people with schizophrenia. Interventions: discontinuation study.
Zapletalek 1981	Allocation: not randomised.

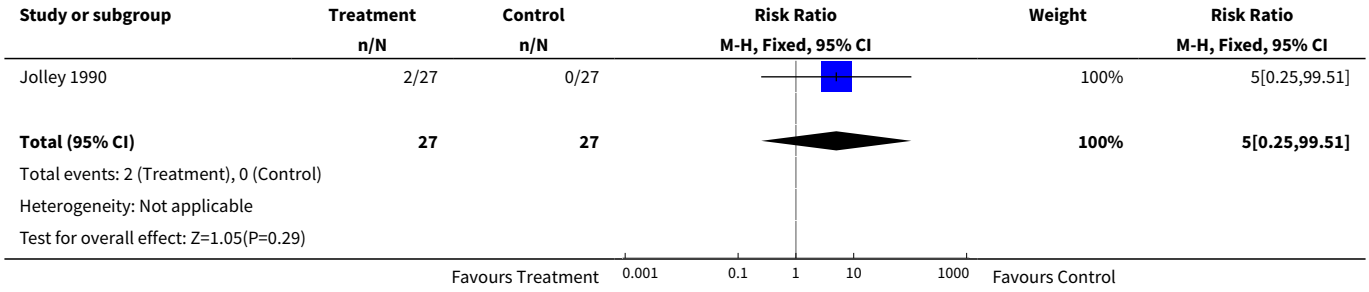
DATA AND ANALYSES

Comparison 1. FLUPHENAZINE DECANOATE vs PLACEBO

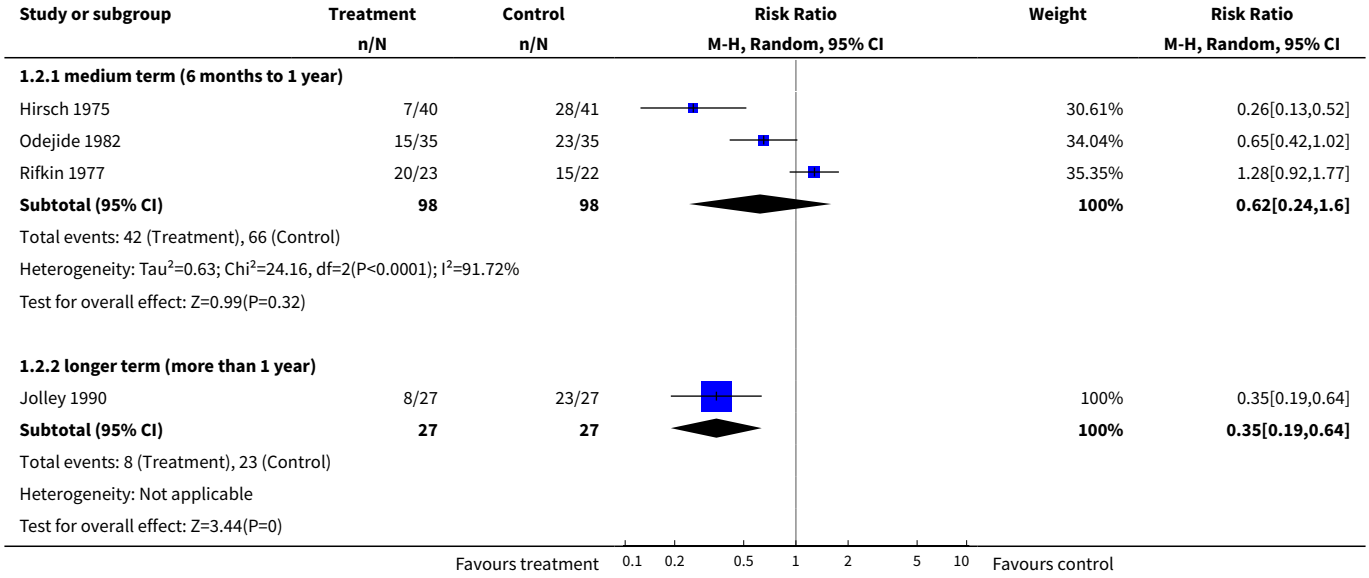
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Death	1	54	Risk Ratio (M-H, Fixed, 95% CI)	5.0 [0.25, 99.51]
2 Global state: Relapse	4		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 medium term (6 months to 1 year)	3	196	Risk Ratio (M-H, Random, 95% CI)	0.62 [0.24, 1.60]
2.2 longer term (more than 1 year)	1	54	Risk Ratio (M-H, Random, 95% CI)	0.35 [0.19, 0.64]
3 Behaviour: Leaving the study early	5		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
3.1 medium term (6 months to 1 year)	4	216	Risk Ratio (M-H, Fixed, 95% CI)	1.30 [0.77, 2.19]
3.2 longer term (more than 1 year)	1	54	Risk Ratio (M-H, Fixed, 95% CI)	0.47 [0.23, 0.96]
4 Mental state: Depression (medium term - 6 months to 1 year)	1	70	Risk Ratio (M-H, Fixed, 95% CI)	1.0 [0.45, 2.22]
5 Adverse effects: 1. Movement disorders - tardive dyskinesia (longer term - more than 1 year)	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
6 Adverse effects: 2. Toxicity	1	45	Risk Ratio (M-H, Fixed, 95% CI)	7.65 [1.04, 56.26]

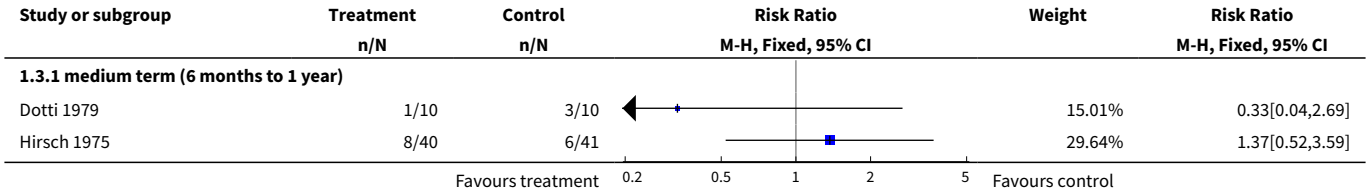
Analysis 1.1. Comparison 1 FLUPHENAZINE DECANOATE vs PLACEBO, Outcome 1 Death.

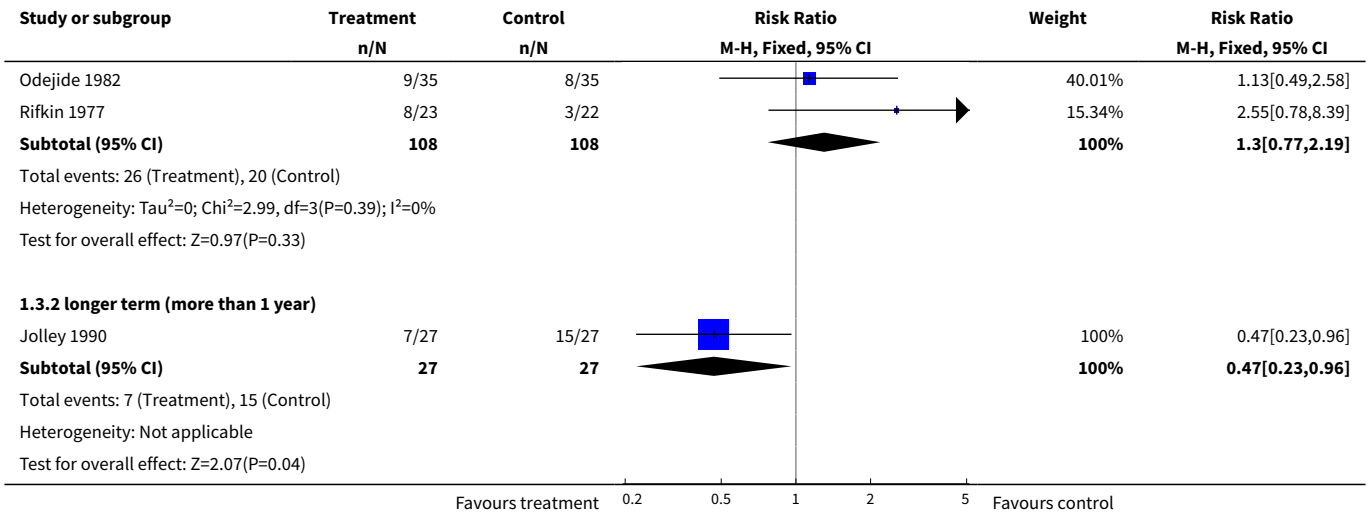


Analysis 1.2. Comparison 1 FLUPHENAZINE DECANOATE vs PLACEBO, Outcome 2 Global state: Relapse.

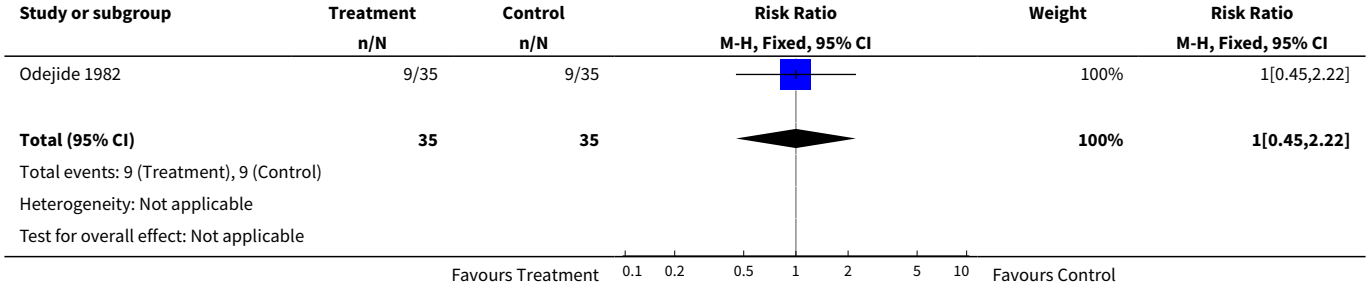


Analysis 1.3. Comparison 1 FLUPHENAZINE DECANOATE vs PLACEBO, Outcome 3 Behaviour: Leaving the study early.

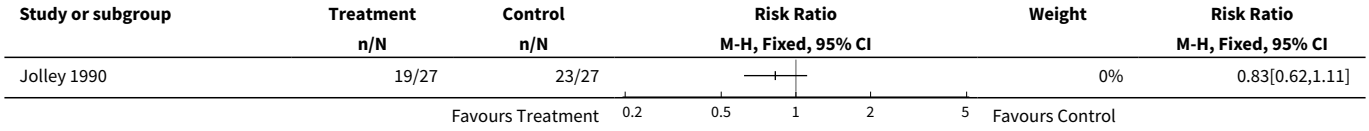




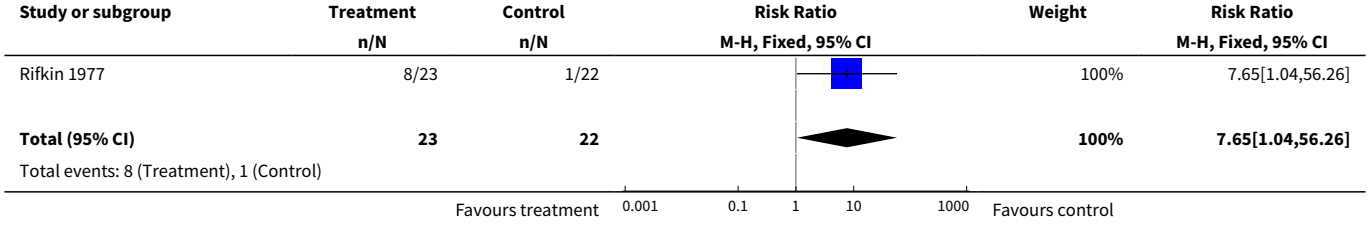
Analysis 1.4. Comparison 1 FLUPHENAZINE DECANOATE vs PLACEBO, Outcome 4 Mental state: Depression (medium term - 6 months to 1 year).

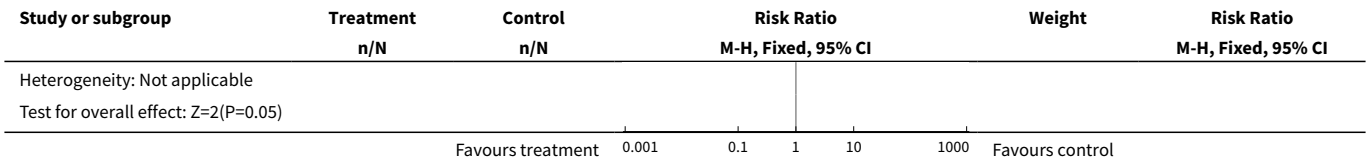


Analysis 1.5. Comparison 1 FLUPHENAZINE DECANOATE vs PLACEBO, Outcome 5 Adverse effects: 1. Movement disorders - tardive dyskinesia (longer term - more than 1 year).



Analysis 1.6. Comparison 1 FLUPHENAZINE DECANOATE vs PLACEBO, Outcome 6 Adverse effects: 2. Toxicity.



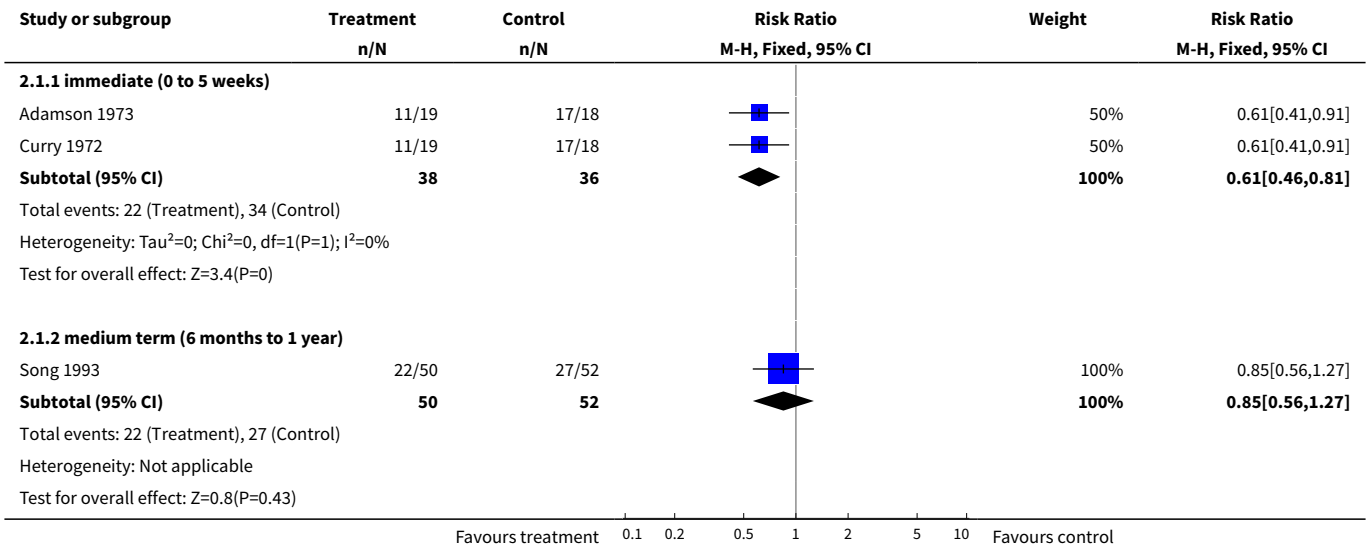


Comparison 2. FLUPHENAZINE DECANOATE vs ORAL NEUROLEPTICS

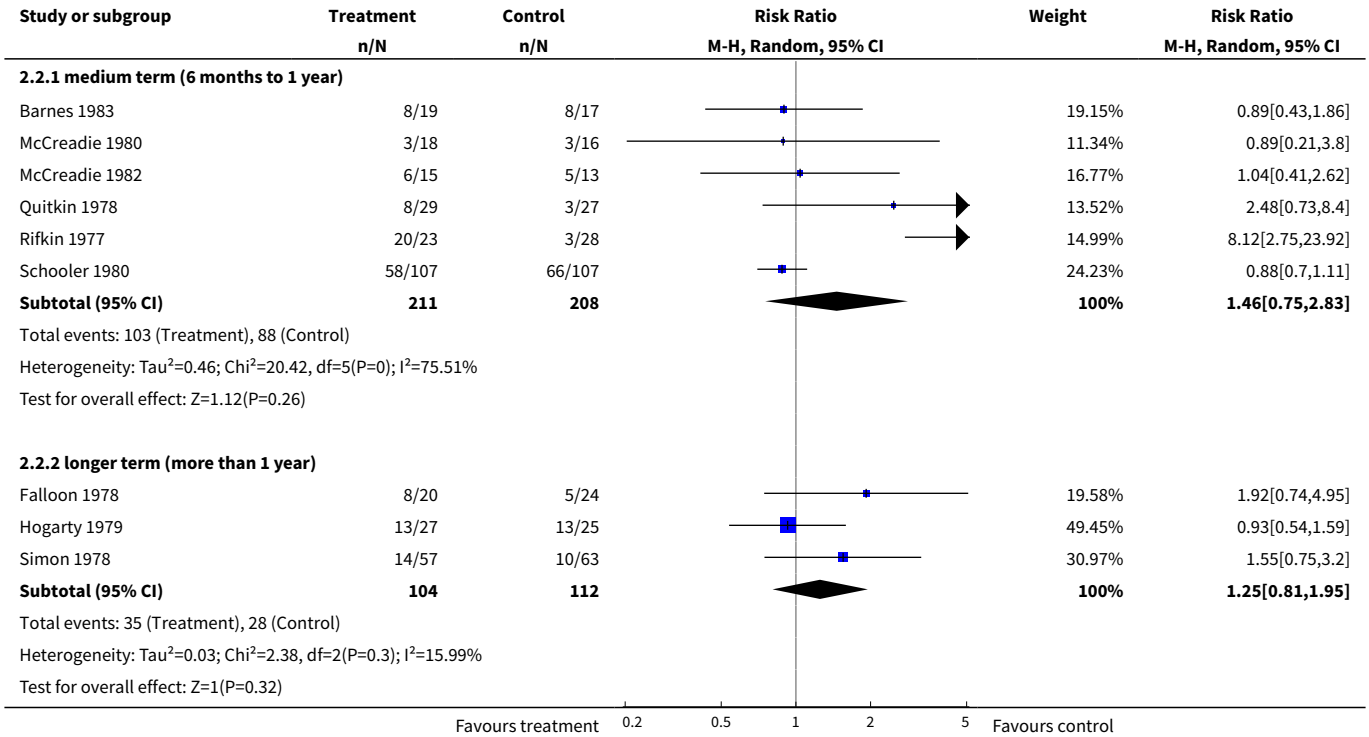
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Global state: 1. No clinically important global change	3		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
1.1 immediate (0 to 5 weeks)	2	74	Risk Ratio (M-H, Fixed, 95% CI)	0.61 [0.46, 0.81]
1.2 medium term (6 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
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 Behaviour: 1. 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: 2. NOSIE-30 - endpoint scores (high score=poor)	1	120	Mean Difference (IV, Fixed, 95% CI)	-0.56 [-6.92, 5.80]
6 Behaviour: 3. 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, Random, 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]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
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]
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]

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



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



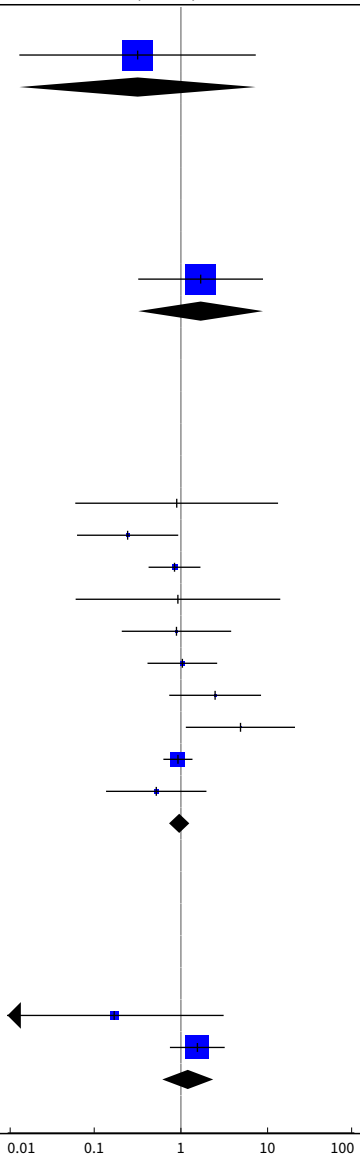
Analysis 2.3. Comparison 2 FLUPHENAZINE DECANOATE vs ORAL NEUROLEPTICS, Outcome 3 Global state: 3. Clinical Global Impression (short term - 6 weeks to 5 months) (high score=worse).

Study or subgroup	Treatment N	Treatment Mean(SD)	Control N	Control Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
Shu 1983	16	5 (3.6)	18	5.1 (4.4)		100%	-0.1[-2.79,2.59]
Total ***	**16**		**18**			**100%**	**-0.1[-2.79,2.59]**
Heterogeneity: Not applicable							
Test for overall effect: Z=0.07(P=0.94)							

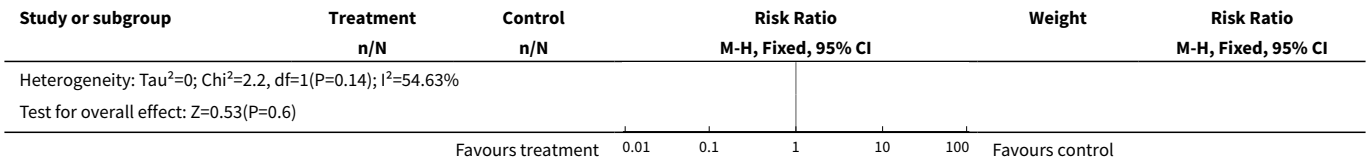
Favours treatment — Favours control

Analysis 2.4. Comparison 2 FLUPHENAZINE DECANOATE vs ORAL NEUROLEPTICS, Outcome 4 Behaviour: 1. Leaving the study early.

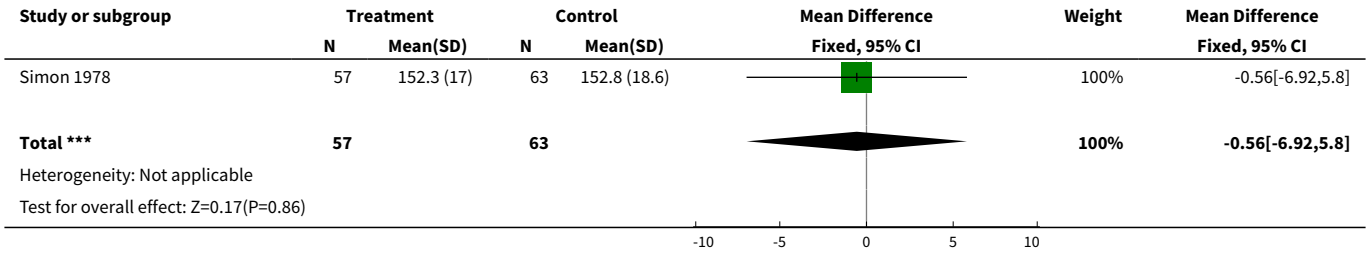
Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
2.4.1 immediate (0-5 weeks)					
Curry 1972	0/19	1/18		100%	0.32[0.01,7.3]
Subtotal (95% CI)	**19**	**18**		**100%**	**0.32[0.01,7.3]**
Total events: 0 (Treatment), 1 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.72(P=0.47)					
2.4.2 short term (6 weeks to 5 months)					
Shu 1983	3/16	2/18		100%	1.69[0.32,8.85]
Subtotal (95% CI)	**16**	**18**		**100%**	**1.69[0.32,8.85]**
Total events: 3 (Treatment), 2 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.62(P=0.54)					
2.4.3 medium term (6 months to 1 year)					
Barnes 1983	1/19	1/17		1.23%	0.89[0.06,13.23]
Crawford 1974	2/14	10/17		10.55%	0.24[0.06,0.93]
Kaneno 1991	13/127	16/132		18.33%	0.84[0.42,1.68]
Magnus 1979	1/26	1/24		1.22%	0.92[0.06,13.95]
McCreadie 1980	3/18	3/16		3.71%	0.89[0.21,3.8]
McCreadie 1982	6/15	5/13		6.26%	1.04[0.41,2.62]
Quitkin 1978	8/29	3/27		3.63%	2.48[0.73,8.4]
Rifkin 1977	8/23	2/28		2.11%	4.87[1.14,20.72]
Schooler 1980	36/143	40/147		46.09%	0.93[0.63,1.36]
Song 1993	3/50	6/52		6.87%	0.52[0.14,1.97]
Subtotal (95% CI)	**464**	**473**		**100%**	**0.96[0.73,1.25]**
Total events: 81 (Treatment), 87 (Control)					
Heterogeneity: Tau^2=0; Chi^2=12.21, df=9(P=0.2); I^2=26.28%					
Test for overall effect: Z=0.33(P=0.74)					
2.4.4 longer term (more than 1 year)					
Falloon 1978	0/20	3/24		25.17%	0.17[0.01,3.11]
Simon 1978	14/57	10/63		74.83%	1.55[0.75,3.2]
Subtotal (95% CI)	**77**	**87**		**100%**	**1.2[0.61,2.36]**
Total events: 14 (Treatment), 13 (Control)					



Favours treatment — Favours control



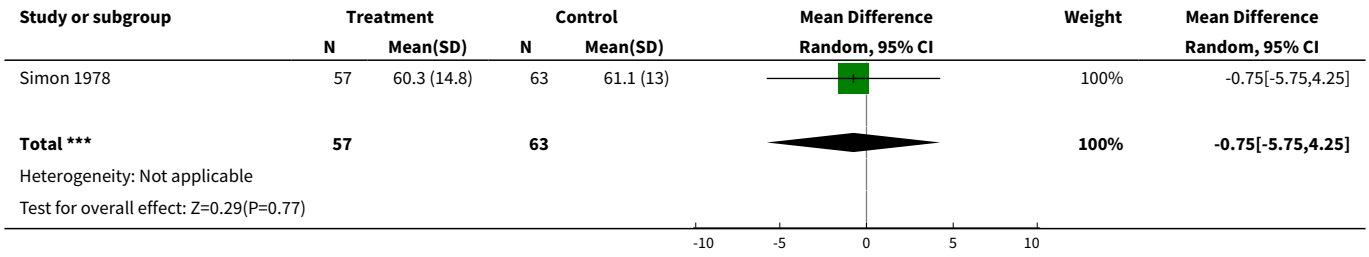
Analysis 2.5. Comparison 2 FLUPHENAZINE DECANOATE vs ORAL NEUROLEPTICS, Outcome 5 Behaviour: 2. NOSIE-30 - endpoint scores (high score=poor).



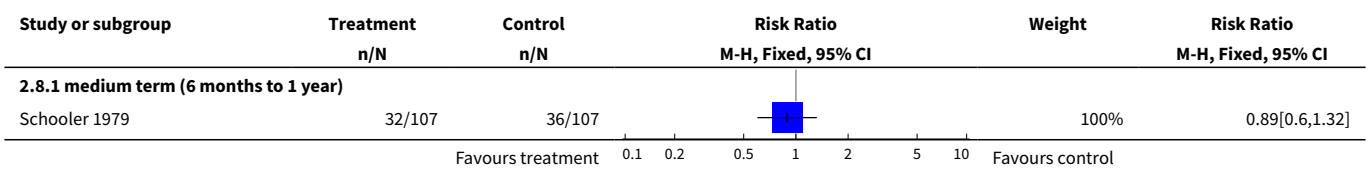
Analysis 2.6. Comparison 2 FLUPHENAZINE DECANOATE vs ORAL NEUROLEPTICS, Outcome 6 Behaviour: 3. skewed data (endpoint scores).

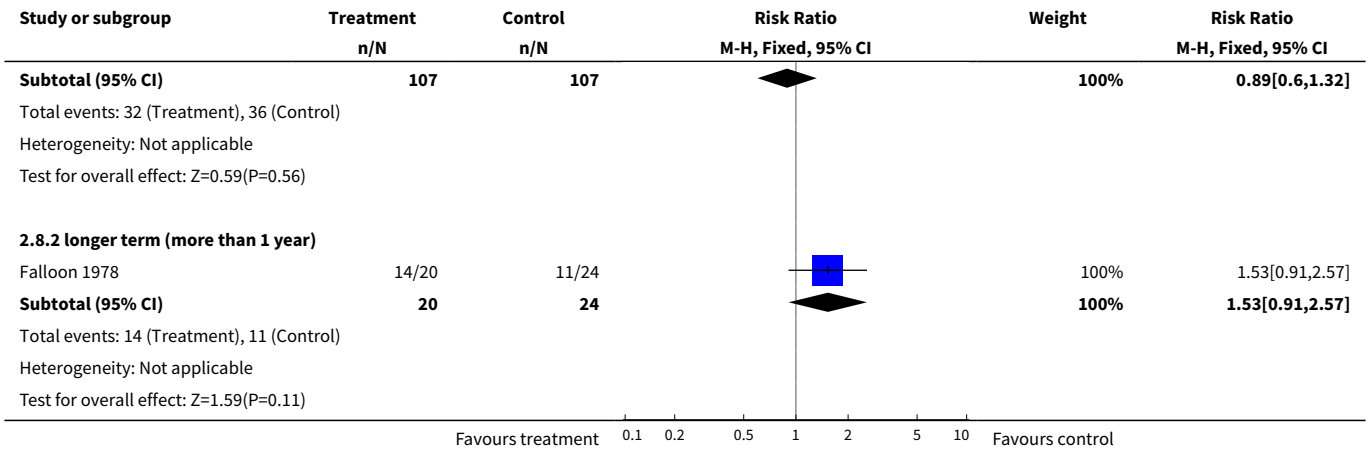
Behaviour: 3. skewed data (endpoint scores)				
Study	**Intervention**	**mean**	**SD**	**N**
Barnes 1983	Fluphenazine decanaote	5.7	4.1	19
Barnes 1983	Pimozide	4.2	5.5	17

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).

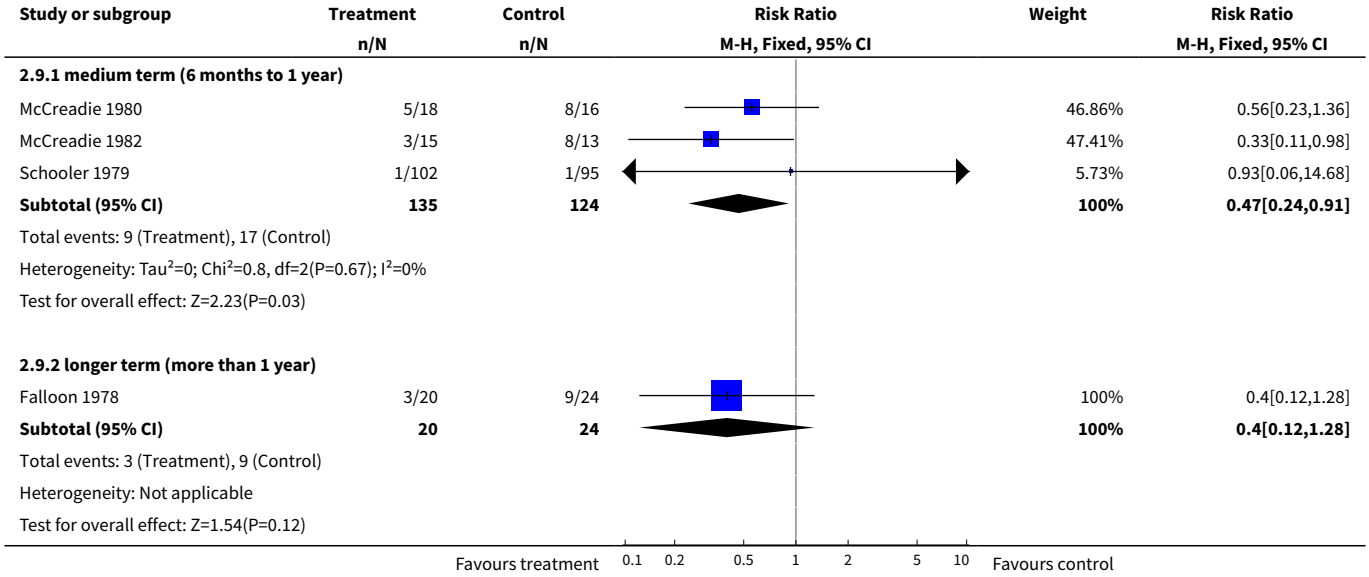


Analysis 2.8. Comparison 2 FLUPHENAZINE DECANOATE vs ORAL NEUROLEPTICS, Outcome 8 Mental state: 2. Depression.

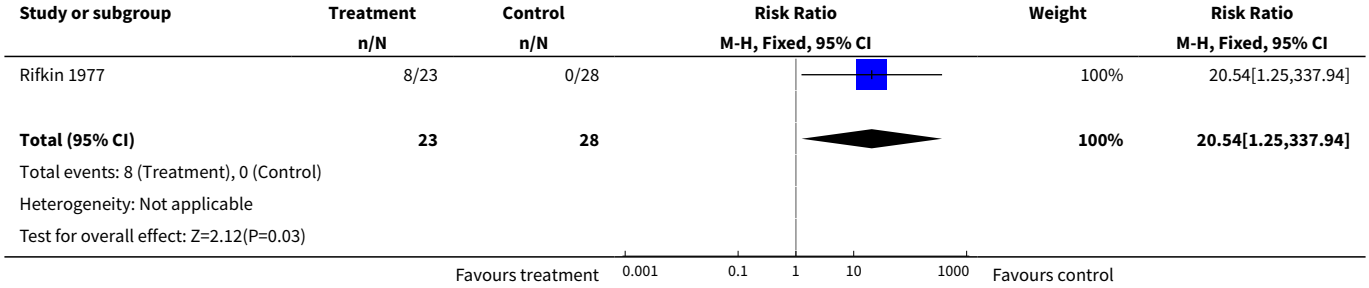




Analysis 2.9. Comparison 2 FLUPHENAZINE DECANOATE vs ORAL NEUROLEPTICS, Outcome 9 Adverse effects: 1a. Movement disorders - general.



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

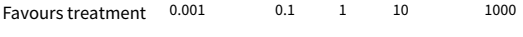


Analysis 2.11. Comparison 2 FLUPHENAZINE DECANOATE vs ORAL NEUROLEPTICS, Outcome 11 Adverse effects: 1c. Movement disorders - needing anticholinergic drugs.

Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
2.11.1 immediate (0 to 5 weeks)					
Adamson 1973	0/19	0/18			Not estimable
Subtotal (95% CI)	**19**	**18**			**Not estimable**
Total events: 0 (Treatment), 0 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
2.11.2 medium term (6 months to 1 year)					
McCreadie 1980	8/18	4/16		48.32%	1.78[0.66,4.8]
Schooler 1980	7/102	15/95		51.68%	0.43[0.19,1.02]
Subtotal (95% CI)	**120**	**111**		**100%**	**0.86[0.21,3.45]**
Total events: 15 (Treatment), 19 (Control)					
Heterogeneity: Tau^2=0.79; Chi^2=4.52, df=1(P=0.03); I^2=77.88%					
Test for overall effect: Z=0.22(P=0.83)					
2.11.3 longer term (more than 1 year)					
Simon 1978	46/57	49/63		100%	1.04[0.86,1.25]
Subtotal (95% CI)	**57**	**63**		**100%**	**1.04[0.86,1.25]**
Total events: 46 (Treatment), 49 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.39(P=0.69)					

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

Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
2.12.1 medium term (6 months to 1 year)					
McCreadie 1982	9/15	13/13		100%	0.62[0.41,0.93]
Subtotal (95% CI)	**15**	**13**		**100%**	**0.62[0.41,0.93]**
Total events: 9 (Treatment), 13 (Control)					
Heterogeneity: Tau^2=0; Chi^2=0, df=0(P<0.0001); I^2=100%					
Test for overall effect: Z=2.28(P=0.02)					
2.12.2 longer term (more than 1 year)					
Simon 1978	0/57	3/63		100%	0.16[0.01,2.99]
Subtotal (95% CI)	**57**	**63**		**100%**	**0.16[0.01,2.99]**
Total events: 0 (Treatment), 3 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=1.23(P=0.22)					

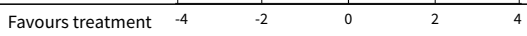


Analysis 2.13. Comparison 2 FLUPHENAZINE DECANOATE vs ORAL NEUROLEPTICS, Outcome 13 Adverse effects: 1e. Movement disorders - tremor (longer term - more than 1 year).

Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Falloon 1978	4/20	6/24		100%	0.8[0.26,2.45]
Total (95% CI)	**20**	**24**		**100%**	**0.8[0.26,2.45]**
Total events: 4 (Treatment), 6 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.39(P=0.7)					

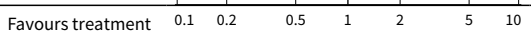
Analysis 2.14. Comparison 2 FLUPHENAZINE DECANOATE vs ORAL NEUROLEPTICS, Outcome 14 Adverse effects: 1f. Movement disorders - average score (Simpson & Angus, 0 to 5 weeks, high = poor).

Study or subgroup	Treatment N	Treatment Mean(SD)	Control N	Control Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
Shu 1983	16	2.6 (2)	16	1.3 (1.7)		100%	1.3[0.01,2.59]
Total ***	**16**		**16**			**100%**	**1.3[0.01,2.59]**
Heterogeneity: Not applicable							
Test for overall effect: Z=1.98(P=0.05)							



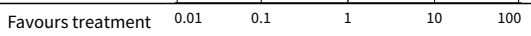
Analysis 2.15. Comparison 2 FLUPHENAZINE DECANOATE vs ORAL NEUROLEPTICS, Outcome 15 Adverse effects: 2. Blurred vision - medium term (6 months to 1 year).

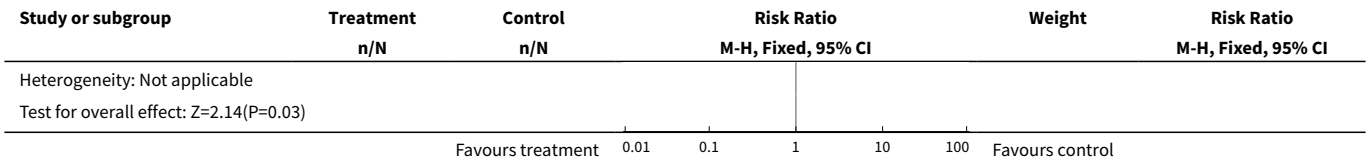
Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Schooler 1980	23/102	16/95		100%	1.34[0.75,2.38]
Total (95% CI)	**102**	**95**		**100%**	**1.34[0.75,2.38]**
Total events: 23 (Treatment), 16 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=1(P=0.32)					



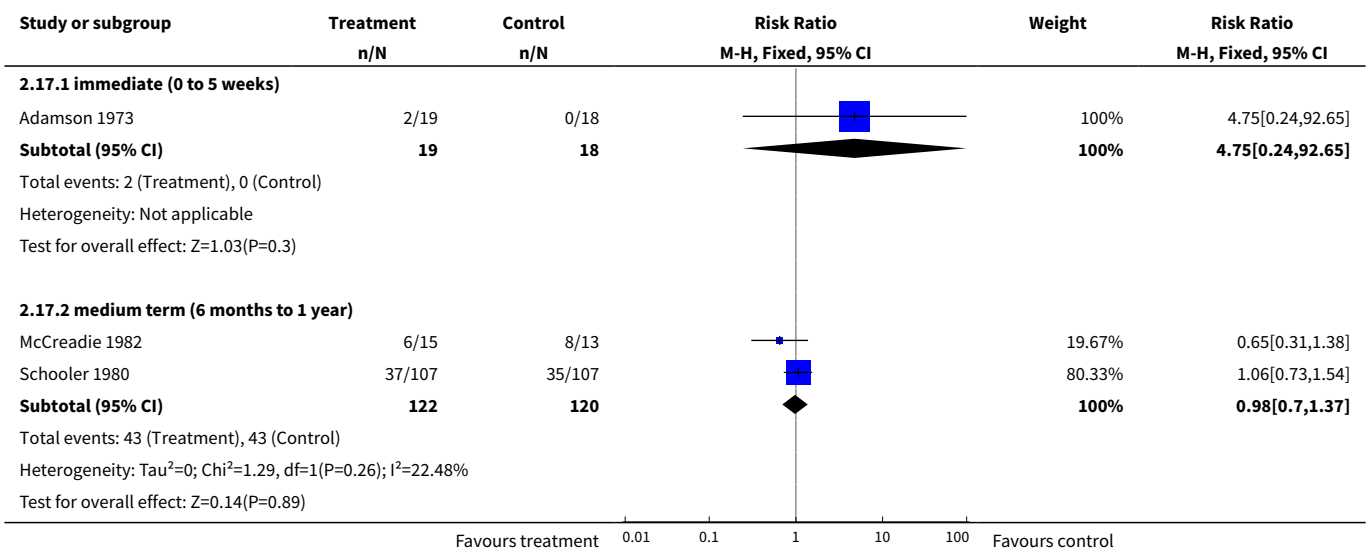
Analysis 2.16. Comparison 2 FLUPHENAZINE DECANOATE vs ORAL NEUROLEPTICS, Outcome 16 Adverse effects: 3. Toxicity - medium term (6 months to 1 year).

Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Rifkin 1977	8/23	2/28		100%	4.87[1.14,20.72]
Total (95% CI)	**23**	**28**		**100%**	**4.87[1.14,20.72]**
Total events: 8 (Treatment), 2 (Control)					





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



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 (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]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
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]
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 Behaviour: 1. Leaving the study early	22		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)	2	81	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: 2. 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)	6		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
11.1 short term (6 weeks to 5 months)	1	51	Mean Difference (IV, Fixed, 95% CI)	1.10 [0.85, 1.35]
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 Adverse effects: 1a. Movement disorders - general	7	308	Risk Ratio (M-H, Fixed, 95% CI)	1.11 [0.91, 1.35]
14.1 immediate term (0 to 5 weeks)	1	12	Risk Ratio (M-H, Fixed, 95% CI)	0.93 [0.24, 3.68]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
14.2 short term (6 weeks to 5 months)	1	30	Risk Ratio (M-H, Fixed, 95% CI)	2.0 [0.43, 9.32]
14.3 medium term (6 months to 1 year)	4	234	Risk Ratio (M-H, Fixed, 95% CI)	1.08 [0.86, 1.34]
14.4 longer term (more than 1 year)	1	32	Risk Ratio (M-H, Fixed, 95% CI)	1.13 [0.76, 1.69]
15 Adverse effects: 1b. Movement disorders - needing anticholinergic drugs	12		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
15.1 short term (6 weeks to 5 months)	1	51	Risk Ratio (M-H, Random, 95% CI)	1.48 [0.96, 2.28]
15.2 medium term (6 months to 1 year)	8	448	Risk Ratio (M-H, Random, 95% CI)	1.24 [0.93, 1.64]
15.3 longer term (more than 1 year)	3	220	Risk Ratio (M-H, Random, 95% CI)	1.26 [0.86, 1.83]
16 Adverse effects: 1c. Movement disorders - parkinsonism	3	190	Risk Ratio (M-H, Fixed, 95% CI)	1.12 [0.47, 2.69]
16.1 immediate (0 to 5 weeks)	1	12	Risk Ratio (M-H, Fixed, 95% CI)	0.93 [0.24, 3.68]
16.2 medium term (6 months to 1 year)	1	60	Risk Ratio (M-H, Fixed, 95% CI)	1.25 [0.37, 4.21]
16.3 longer term (more than 1 year)	1	118	Risk Ratio (M-H, Fixed, 95% CI)	1.07 [0.07, 16.71]
17 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]
18 Adverse effects: 1e. Movement disorders - tremor	5		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
18.1 short term (6 weeks to 5 months)	2	80	Risk Ratio (M-H, Fixed, 95% CI)	1.36 [0.76, 2.46]
18.2 medium term (6 months to 1 year)	3	152	Risk Ratio (M-H, Fixed, 95% CI)	1.14 [0.73, 1.78]
19 Adverse effects: 2. Blurred vision	2		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
19.1 medium term (6 months to 1 year)	1	32	Risk Ratio (M-H, Fixed, 95% CI)	0.88 [0.44, 1.78]
19.2 longer term (more than 1 year)	1	64	Risk Ratio (M-H, Fixed, 95% CI)	17.88 [1.08, 294.82]
20 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]
21 Adverse effects: 4. General adverse effects	7		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
21.1 short term (6 weeks to 5 months)	2	88	Risk Ratio (M-H, Fixed, 95% CI)	1.36 [1.07, 1.74]
21.2 medium term (6 months to 1 year)	5	249	Risk Ratio (M-H, Fixed, 95% CI)	1.04 [0.83, 1.32]

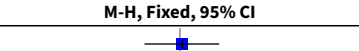
Analysis 3.1. Comparison 3 FLUPHENAZINE DECANOATE vs OTHER DEPOT NEUROLEPTICS, Outcome 1 Death.

Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
McKane 1987	1/19	0/19		100%	3[0.13,69.31]
Total (95% CI)	**19**	**19**		**100%**	**3[0.13,69.31]**
Total events: 1 (Treatment), 0 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.69(P=0.49)					

Favours Treatment — Favours Control

Analysis 3.2. Comparison 3 FLUPHENAZINE DECANOATE vs OTHER DEPOT NEUROLEPTICS, Outcome 2 Global state: 1. No clinically important global change (medium term - 6 months to 1 year).

Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Dencker 1973	32/35	29/32		34.91%	1.01[0.87,1.17]
Leong 1989	29/30	27/30		31.11%	1.07[0.94,1.23]
Schlosberg 1978	30/30	29/30		33.99%	1.03[0.94,1.13]
Total (95% CI)	**95**	**92**		**100%**	**1.04[0.96,1.12]**
Total events: 91 (Treatment), 85 (Control)					
Heterogeneity: Tau^2=0; Chi^2=0.39, df=2(P=0.82); I^2=0%					
Test for overall effect: Z=0.98(P=0.33)					

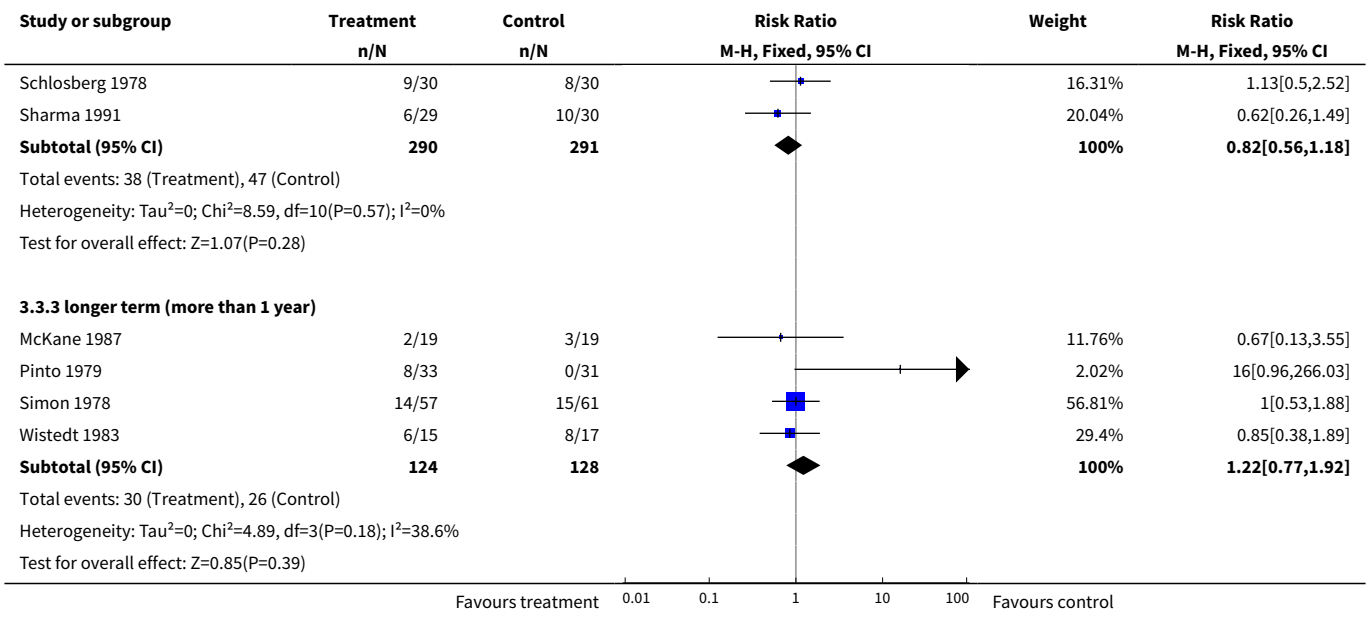


Favours Treatment — Favours Control

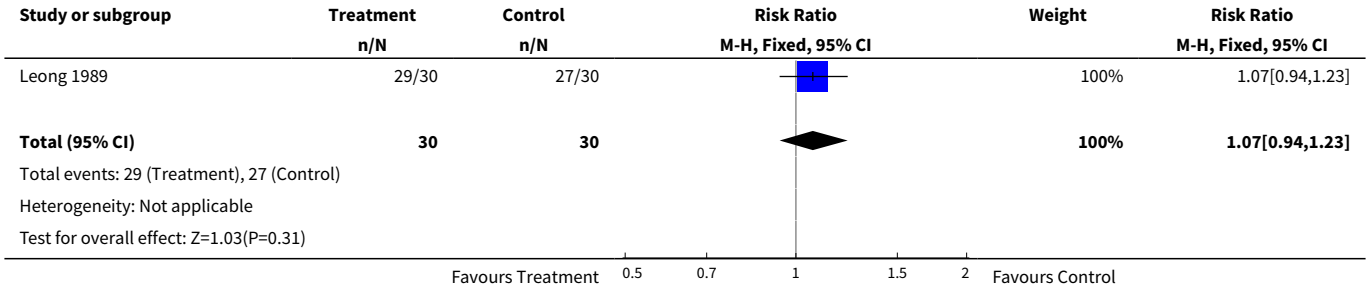
Analysis 3.3. Comparison 3 FLUPHENAZINE DECANOATE vs OTHER DEPOT NEUROLEPTICS, Outcome 3 Global state: 2. Relapse.

Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
3.3.1 short term (6 weeks to 5 months)					
Wistedt 1984	4/26	4/25		100%	0.96[0.27,3.43]
Subtotal (95% CI)	**26**	**25**		**100%**	**0.96[0.27,3.43]**
Total events: 4 (Treatment), 4 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.06(P=0.95)					
3.3.2 medium term (6 months to 1 year)					
Chouinard 1984	1/36	0/36		1.02%	3[0.13,71.28]
Cookson 1986	0/9	2/10		4.85%	0.22[0.01,4.05]
Dencker 1973	6/35	3/32		6.39%	1.83[0.5,6.71]
Kelly 1977	3/28	3/26		6.34%	0.93[0.21,4.2]
Leong 1989	0/30	1/30		3.06%	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		2.04%	1[0.07,15.15]
McLaren 1992	0/24	6/23		13.52%	0.07[0,1.24]
Russell 1982	3/13	2/20		3.21%	2.31[0.44,11.98]

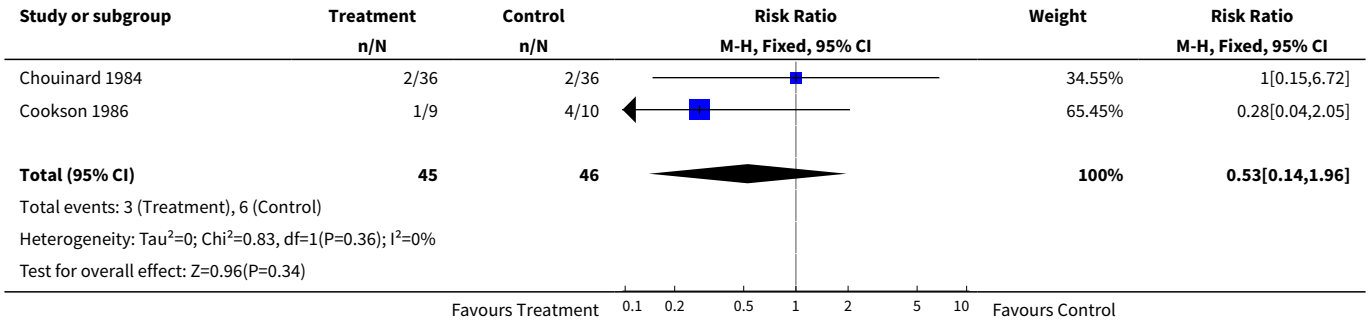
Favours treatment — Favours control



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).



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).



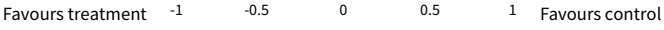
Analysis 3.6. Comparison 3 FLUPHENAZINE DECANOATE vs OTHER DEPOT NEUROLEPTICS, Outcome 6 Global state: 5. Clinical Global Impression. (short term - 6 weeks to 5 months) (skewed data).

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

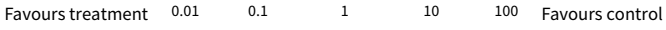
Analysis 3.7. Comparison 3 FLUPHENAZINE DECANOATE vs OTHER DEPOT NEUROLEPTICS, Outcome 7 Global state: 6. Clinical Global Impression. (medium term - 6 months to 1 year).

Study or subgroup	Treatment N	Treatment Mean(SD)	Control N	Control Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
Chouinard 1984	36	2.8 (0.8)	36	2.9 (0.7)		79.75%	-0.1[-0.45,0.25]
Schlosberg 1978	9	2 (0.7)	9	2.1 (0.8)		20.25%	-0.11[-0.8,0.58]
Total ***	**45**		**45**			**100%**	**-0.1[-0.41,0.21]**
Heterogeneity: Tau²=0; Chi²=0, df=1(P=0.98); I²=0%							
Test for overall effect: Z=0.64(P=0.52)							



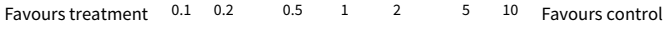
Analysis 3.8. Comparison 3 FLUPHENAZINE DECANOATE vs OTHER DEPOT NEUROLEPTICS, Outcome 8 Global state: 7. Clinical Global Impression - not improved (high score=poor).

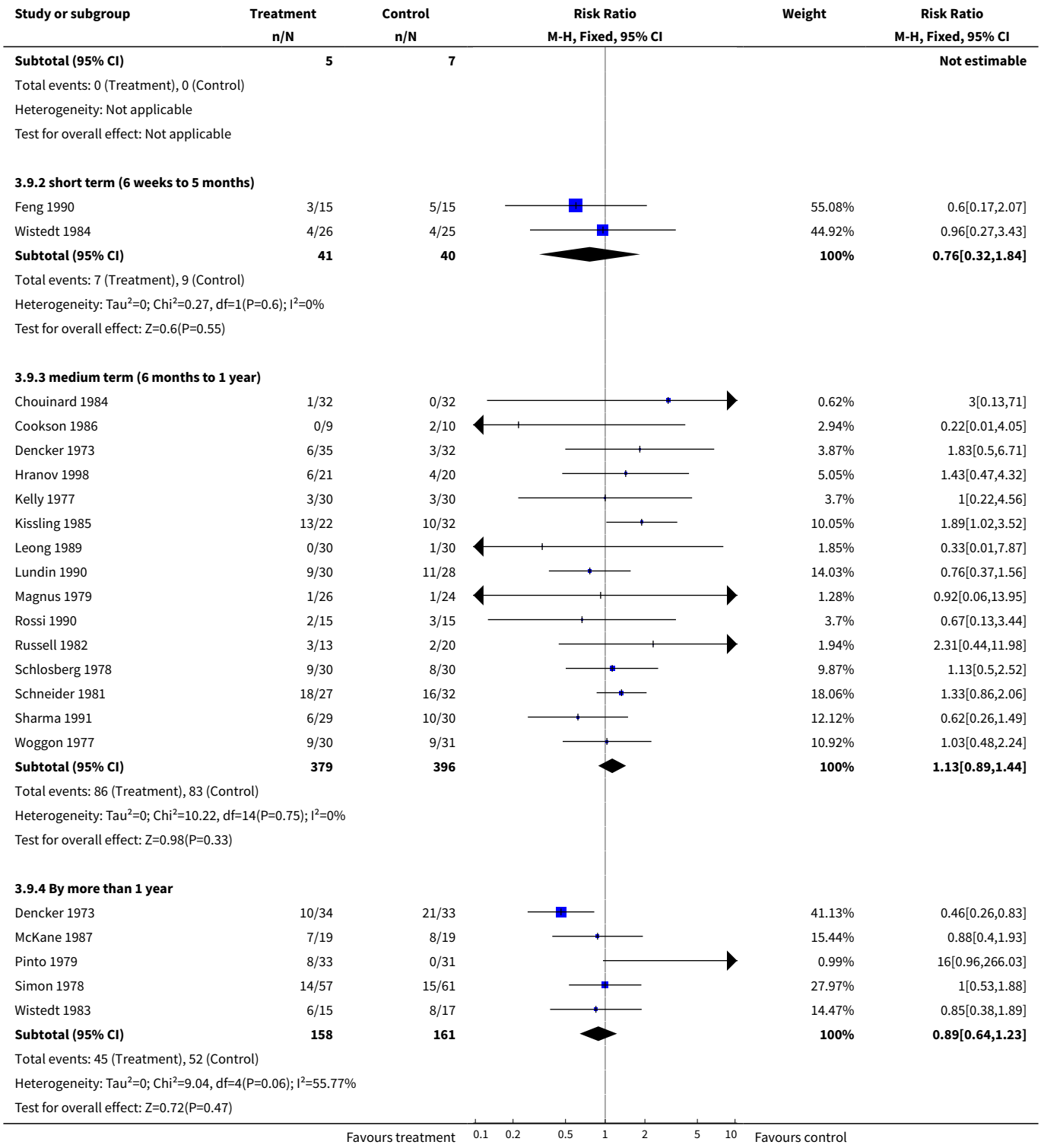
Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
3.8.1 short term (6 weeks to 5 months)					
Frangos 1978	5/25	2/25		100%	2.5[0.53,11.7]
Subtotal (95% CI)	**25**	**25**		**100%**	**2.5[0.53,11.7]**
Total events: 5 (Treatment), 2 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=1.16(P=0.24)					
3.8.2 medium term (6 months to 1 year)					
Leong 1989	3/30	4/30		100%	0.75[0.18,3.07]
Subtotal (95% CI)	**30**	**30**		**100%**	**0.75[0.18,3.07]**
Total events: 3 (Treatment), 4 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.4(P=0.69)					



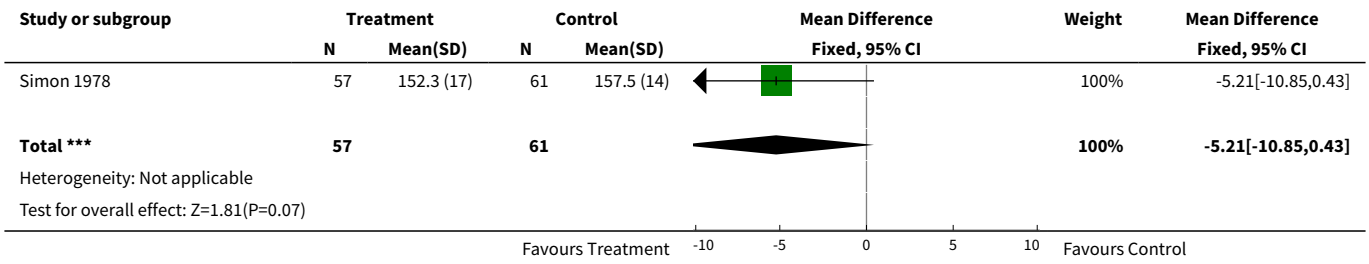
Analysis 3.9. Comparison 3 FLUPHENAZINE DECANOATE vs OTHER DEPOT NEUROLEPTICS, Outcome 9 Behaviour: 1. Leaving the study early.

Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
3.9.1 immediate (0 to 5 weeks)					
Levenson 1976	0/5	0/7			Not estimable

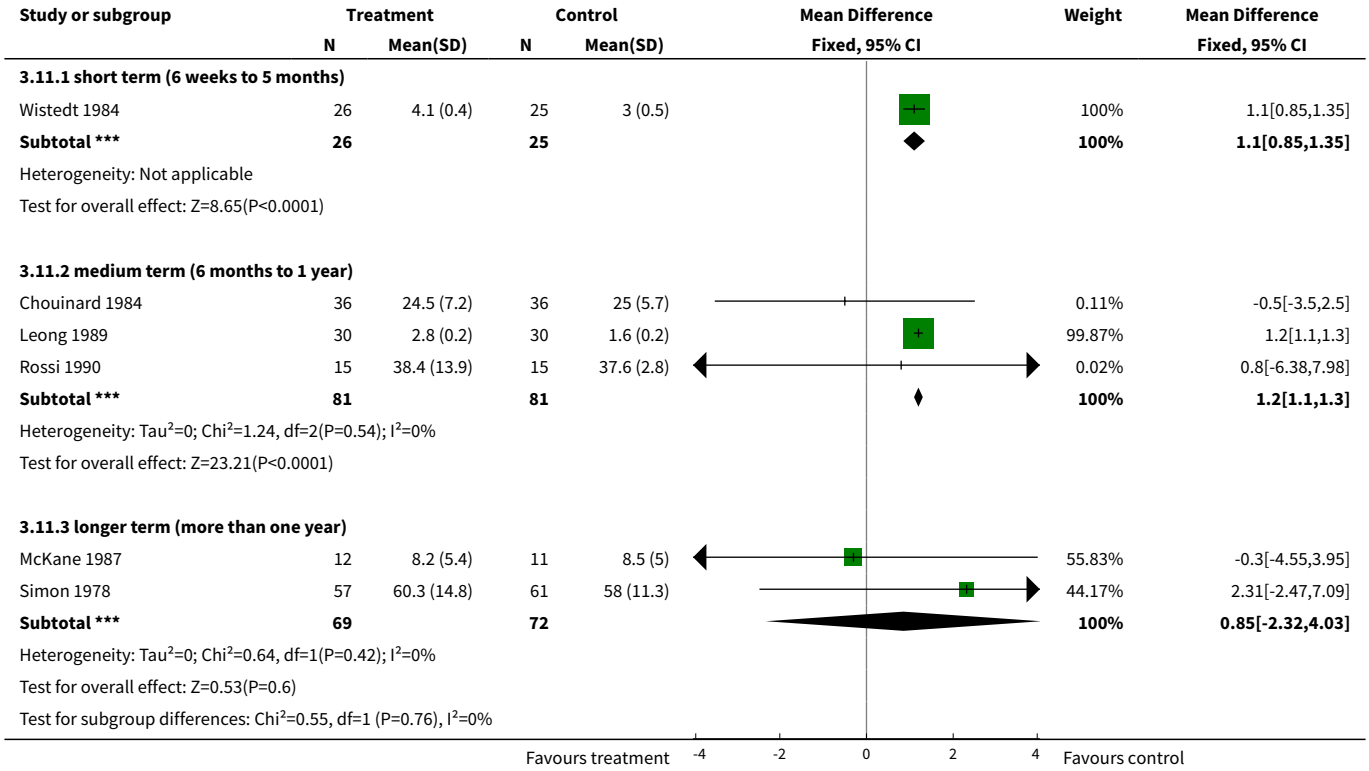




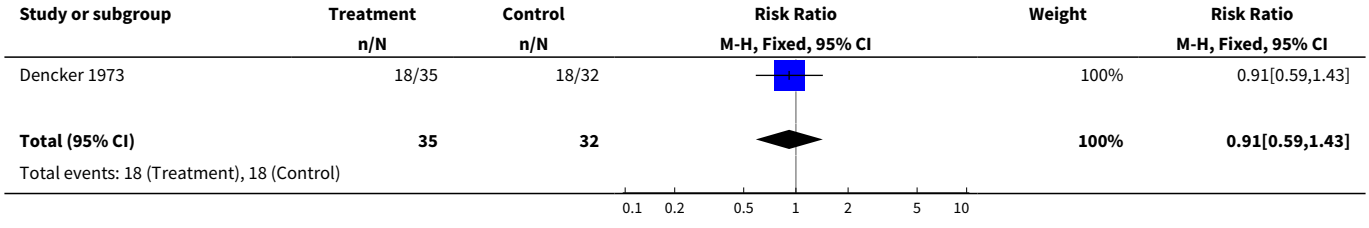
Analysis 3.10. Comparison 3 FLUPHENAZINE DECANOATE vs OTHER DEPOT NEUROLEPTICS, Outcome 10 Behaviour: 2. NOSIE-30 - endpoint scores (high score=poor).

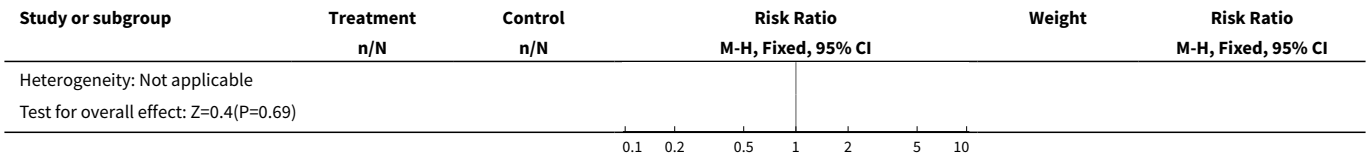


Analysis 3.11. Comparison 3 FLUPHENAZINE DECANOATE vs OTHER DEPOT NEUROLEPTICS, Outcome 11 Mental state: 1. BPRS (endpoint scores - high score=poor).

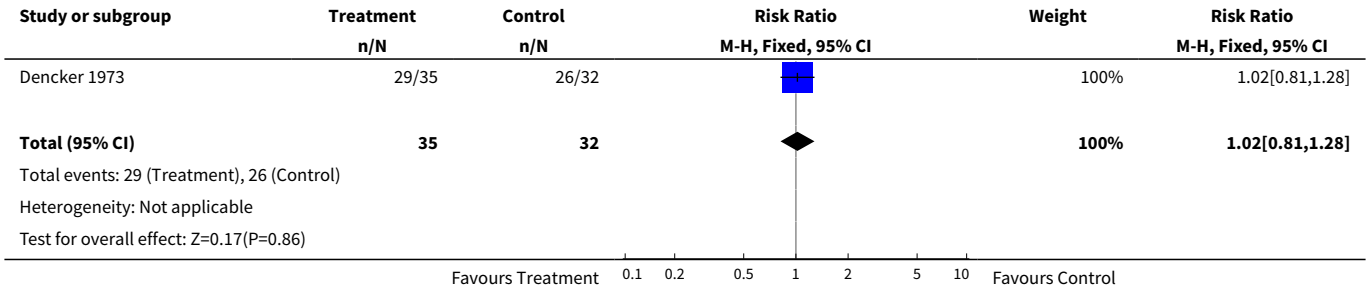


Analysis 3.12. Comparison 3 FLUPHENAZINE DECANOATE vs OTHER DEPOT NEUROLEPTICS, Outcome 12 Mental state: 2. BPRS (endpoint scores 6 months to 1 year - dichotomous data).

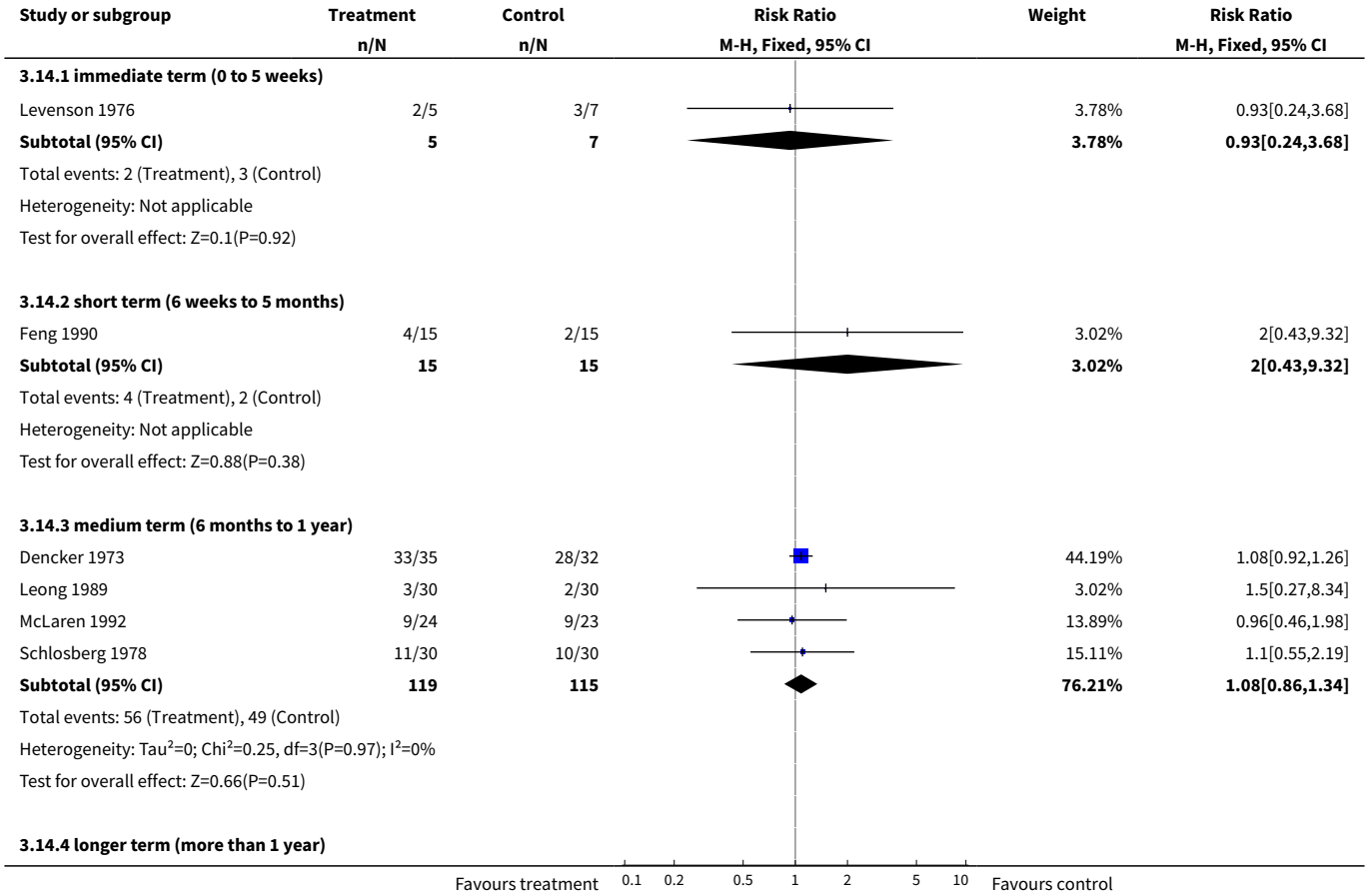


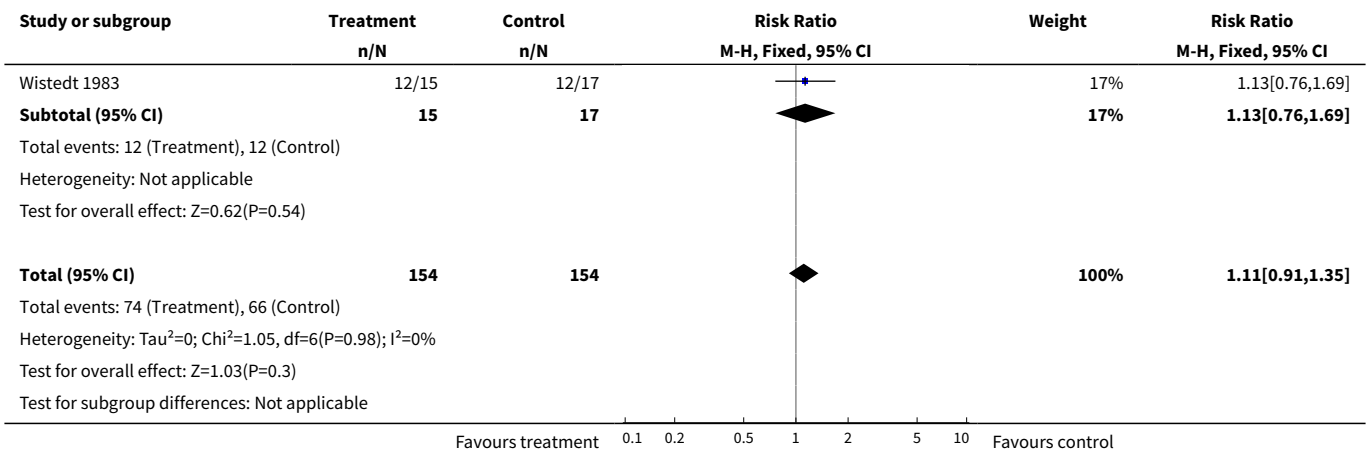


Analysis 3.13. Comparison 3 FLUPHENAZINE DECANOATE vs OTHER DEPOT NEUROLEPTICS, Outcome 13 Mental state: 3. Depression (6 months to 1 year).

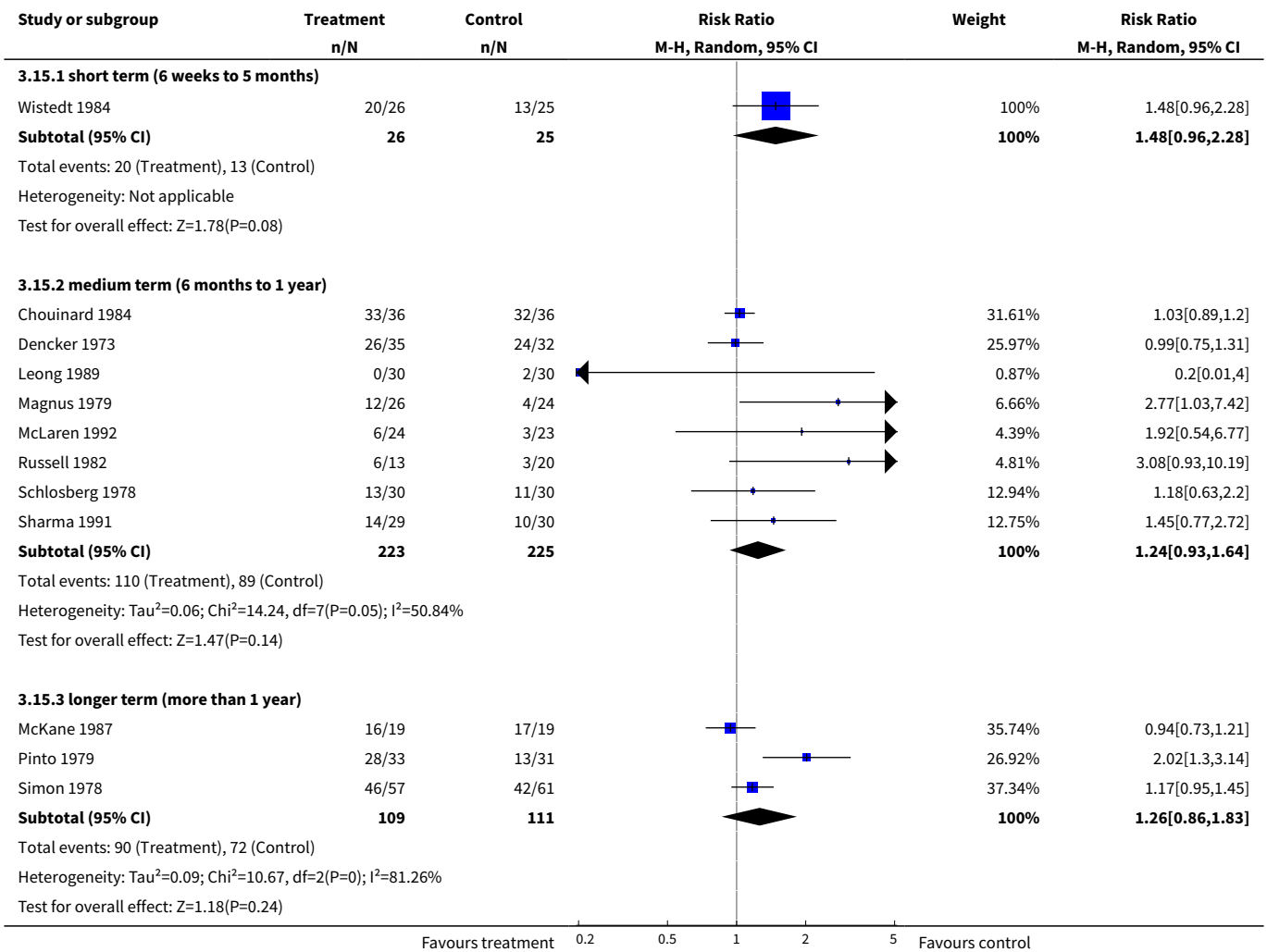


Analysis 3.14. Comparison 3 FLUPHENAZINE DECANOATE vs OTHER DEPOT NEUROLEPTICS, Outcome 14 Adverse effects: 1a. Movement disorders - general.

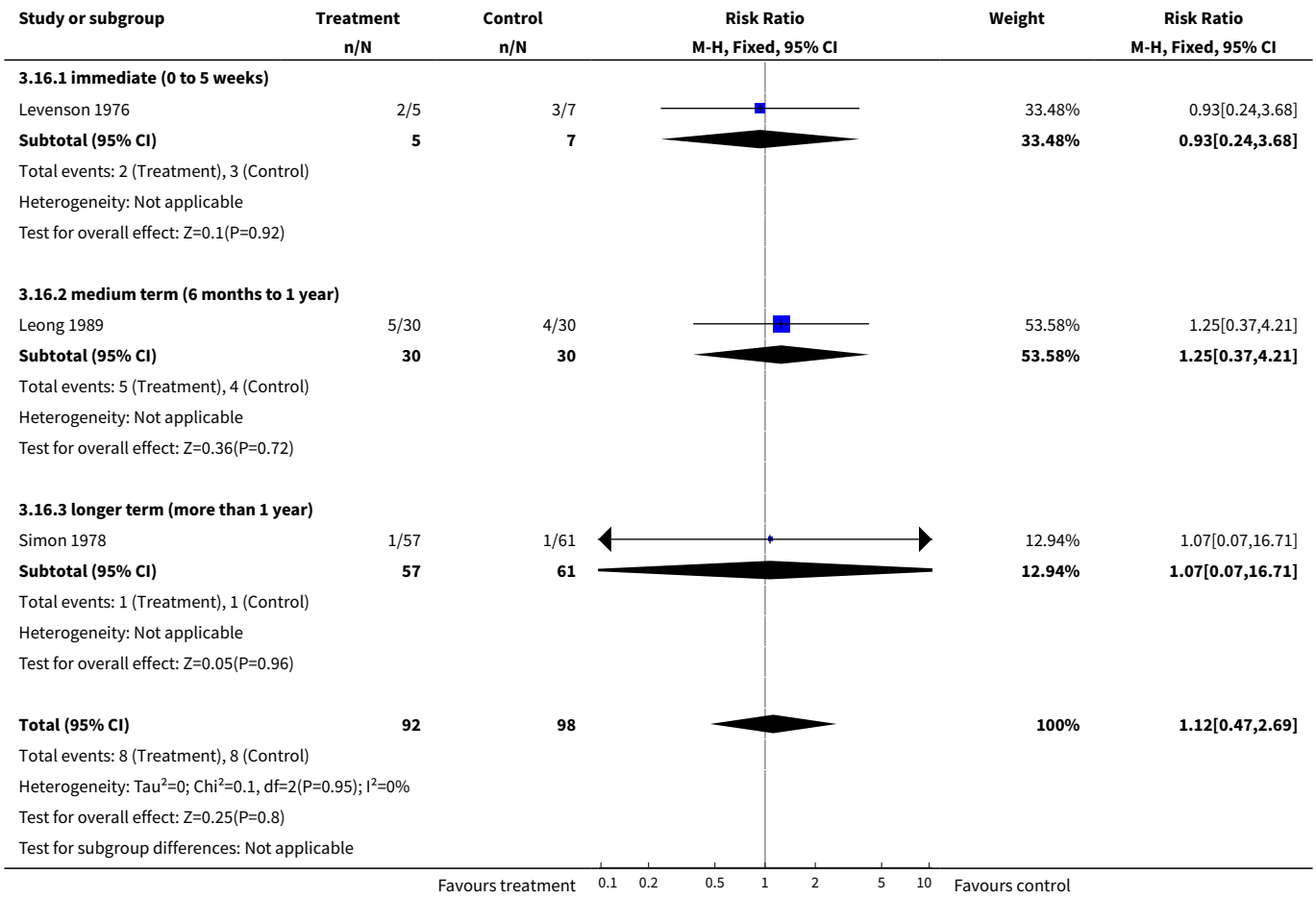




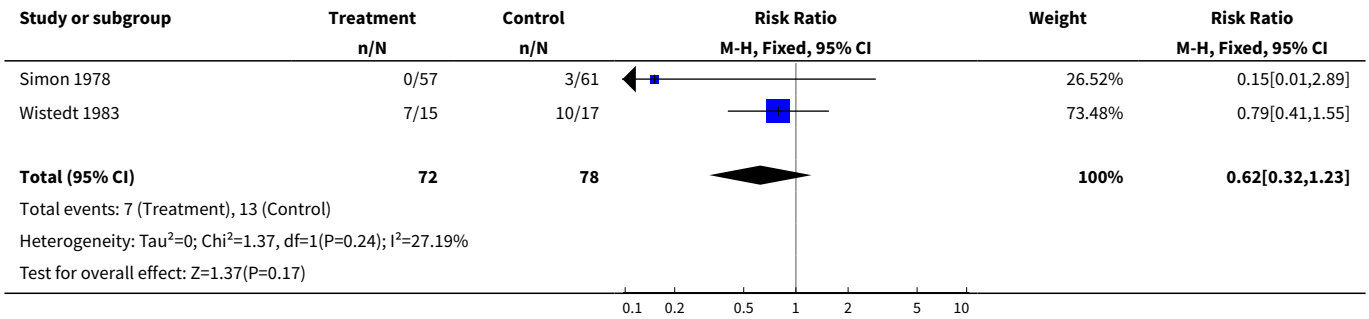
Analysis 3.15. Comparison 3 FLUPHENAZINE DECANOATE vs OTHER DEPOT NEUROLEPTICS, Outcome 15 Adverse effects: 1b. Movement disorders - needing anticholinergic drugs.



Analysis 3.16. Comparison 3 FLUPHENAZINE DECANOATE vs OTHER DEPOT NEUROLEPTICS, Outcome 16 Adverse effects: 1c. Movement disorders - parkinsonism.

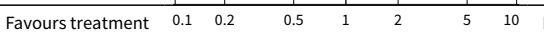


Analysis 3.17. Comparison 3 FLUPHENAZINE DECANOATE vs OTHER DEPOT NEUROLEPTICS, Outcome 17 Adverse effects: 1d. Movement disorders - tardive dyskinesia: longer term (more than 1 year).



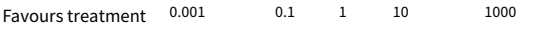
Analysis 3.18. Comparison 3 FLUPHENAZINE DECANOATE vs OTHER DEPOT NEUROLEPTICS, Outcome 18 Adverse effects: 1e. Movement disorders - tremor.

Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
3.18.1 short term (6 weeks to 5 months)					
Feng 1990	9/15	8/15		72.73%	1.13[0.6,2.11]
Frangos 1978	6/25	3/25		27.27%	2[0.56,7.12]
Subtotal (95% CI)	**40**	**40**		**100%**	**1.36[0.76,2.46]**
Total events: 15 (Treatment), 11 (Control)					
Heterogeneity: Tau^2=0; Chi^2=0.71, df=1(P=0.4); I^2=0%					
Test for overall effect: Z=1.03(P=0.3)					
3.18.2 medium term (6 months to 1 year)					
Leong 1989	2/30	3/30		13.95%	0.67[0.12,3.71]
Schlosberg 1978	15/30	11/30		51.16%	1.36[0.76,2.46]
Wistedt 1983	7/15	8/17		34.88%	0.99[0.47,2.08]
Subtotal (95% CI)	**75**	**77**		**100%**	**1.14[0.73,1.78]**
Total events: 24 (Treatment), 22 (Control)					
Heterogeneity: Tau^2=0; Chi^2=0.87, df=2(P=0.65); I^2=0%					
Test for overall effect: Z=0.56(P=0.58)					



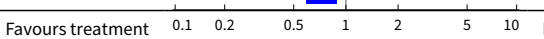
Analysis 3.19. Comparison 3 FLUPHENAZINE DECANOATE vs OTHER DEPOT NEUROLEPTICS, Outcome 19 Adverse effects: 2. Blurred vision.

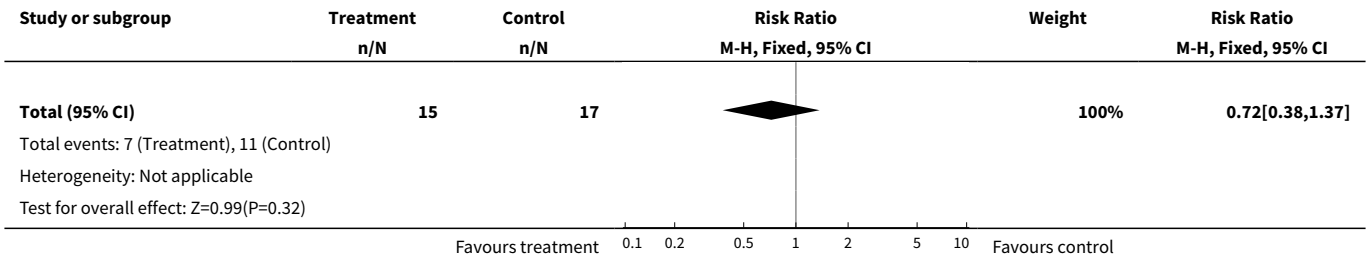
Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
3.19.1 medium term (6 months to 1 year)					
Wistedt 1983	7/15	9/17		100%	0.88[0.44,1.78]
Subtotal (95% CI)	**15**	**17**		**100%**	**0.88[0.44,1.78]**
Total events: 7 (Treatment), 9 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.35(P=0.72)					
3.19.2 longer term (more than 1 year)					
Pinto 1979	9/33	0/31		100%	17.88[1.08,294.82]
Subtotal (95% CI)	**33**	**31**		**100%**	**17.88[1.08,294.82]**
Total events: 9 (Treatment), 0 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=2.02(P=0.04)					



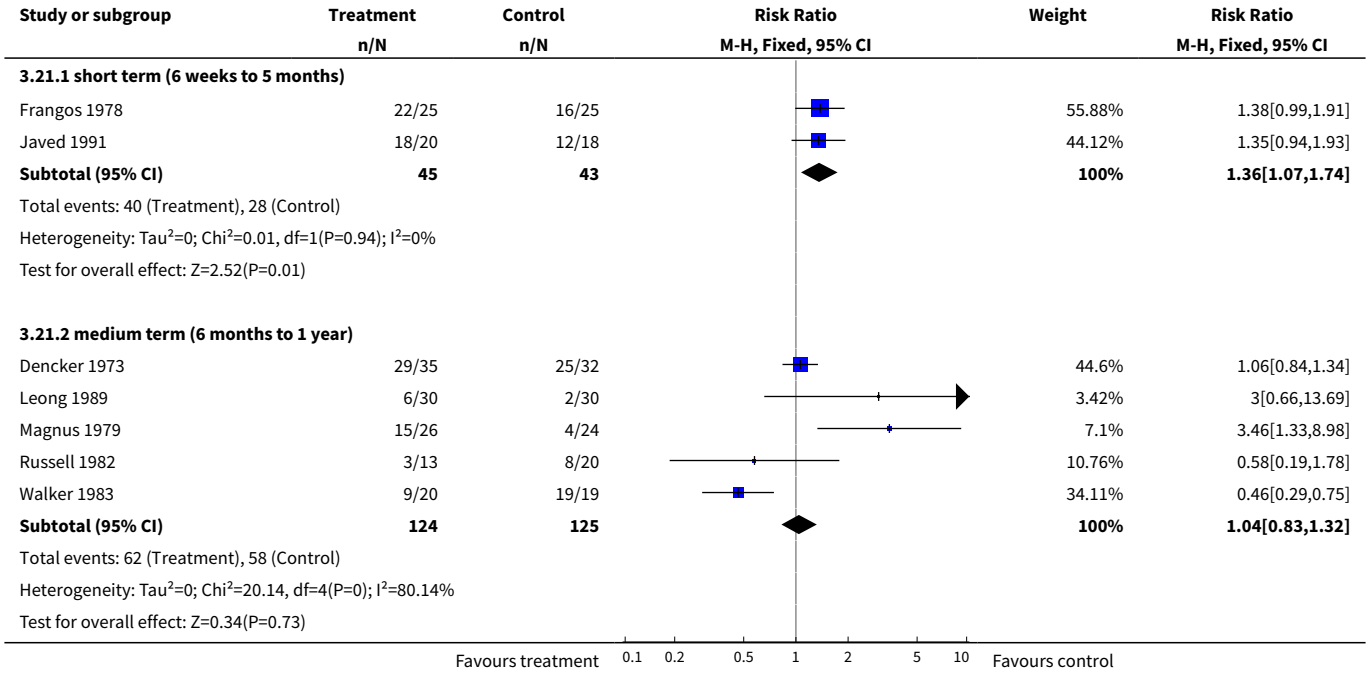
Analysis 3.20. Comparison 3 FLUPHENAZINE DECANOATE vs OTHER DEPOT NEUROLEPTICS, Outcome 20 Adverse effects: 3. Dry mouth: longer term (more than 1 year).

Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Wistedt 1983	7/15	11/17		100%	0.72[0.38,1.37]





Analysis 3.21. Comparison 3 FLUPHENAZINE DECANOATE vs OTHER DEPOT NEUROLEPTICS, Outcome 21 Adverse effects: 4. General adverse effects.



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]

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
3.2 psychiatrist rated	1	40	Risk Ratio (M-H, Fixed, 95% CI)	1.15 [0.77, 1.74]
4 Behaviour: 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]

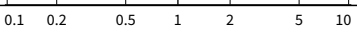
Analysis 4.1. Comparison 4 FLUPHENAZINE DECANOATE - DOSAGE STUDIES - HIGH DOSE vs STANDARD, Outcome 1 Global state: 1. Relapse (medium term - 6 months to 1 year).

Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Kreisman 1988	30/66	6/66		57.18%	5[2.23,11.21]
McClelland 1976	2/25	3/25		42.82%	0.67[0.12,3.65]
Total (95% CI)	**91**	**91**		**100%**	**2.11[0.3,14.91]**
Total events: 32 (Treatment), 9 (Control)					
Heterogeneity: Tau^2=1.57; Chi^2=4.4, df=1(P=0.04); I^2=77.3%					
Test for overall effect: Z=0.75(P=0.45)					

Favours Treatment — Favours Control

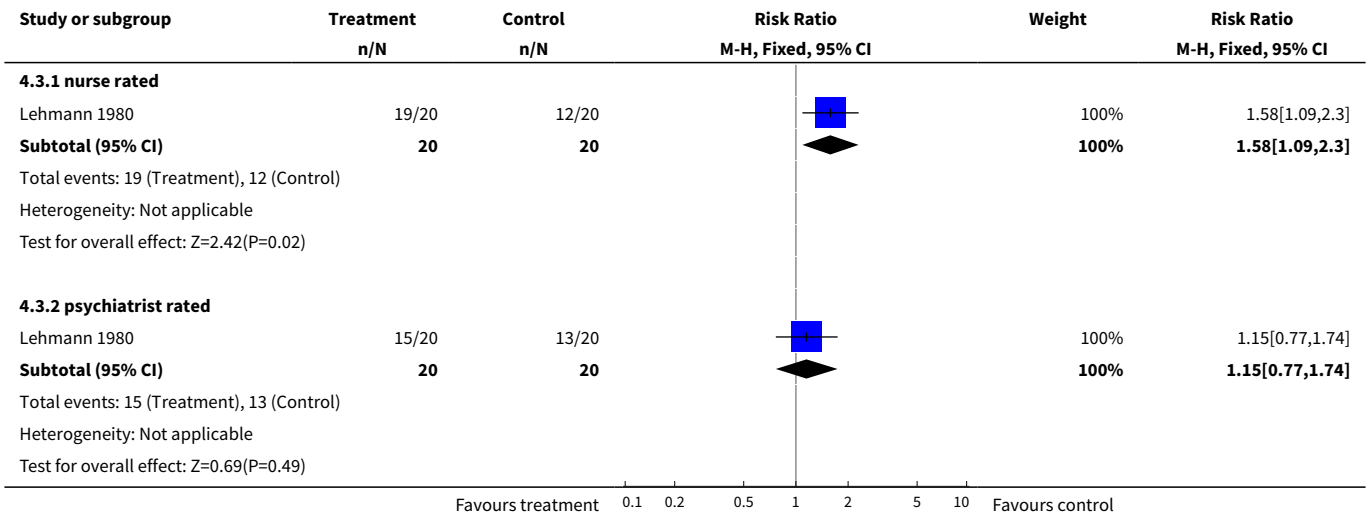
Analysis 4.2. Comparison 4 FLUPHENAZINE DECANOATE - DOSAGE STUDIES - HIGH DOSE vs STANDARD, Outcome 2 Global state: 2. Needing additional antispsychotic treatment (medium term - 6 months to 1 year).

Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
McClelland 1976	5/25	3/25		100%	1.67[0.45,6.24]
Total (95% CI)	**25**	**25**		**100%**	**1.67[0.45,6.24]**
Total events: 5 (Treatment), 3 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.76(P=0.45)					

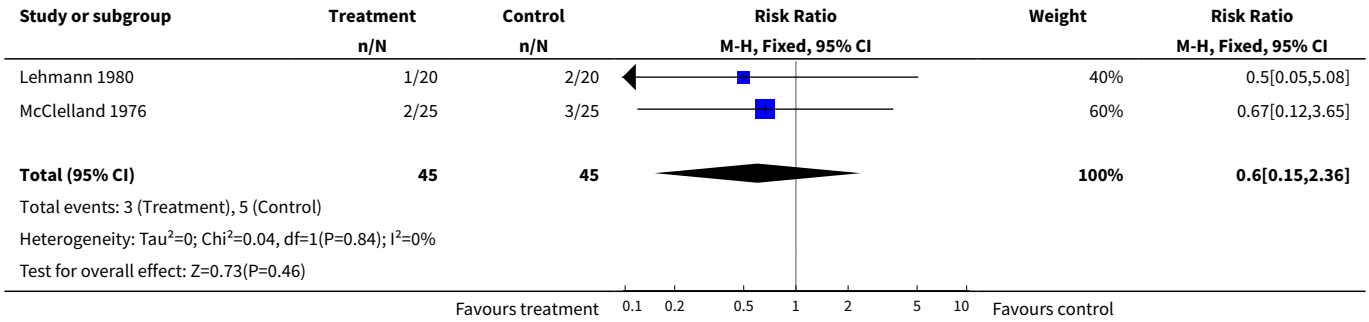


Favours Treatment — Favours Control

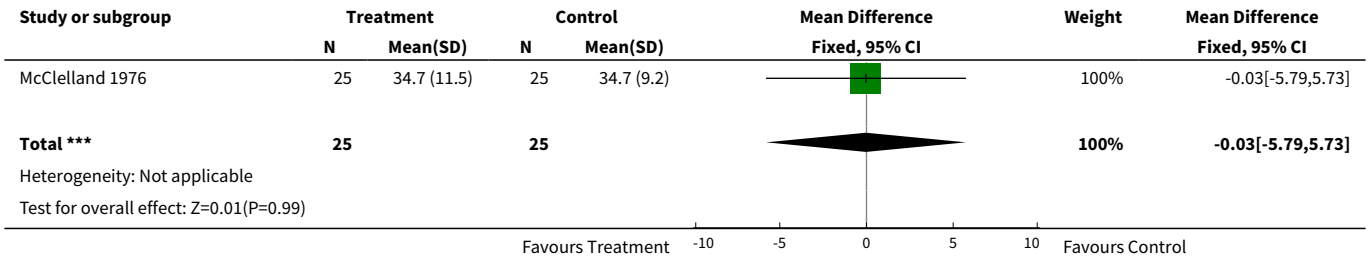
Analysis 4.3. Comparison 4 FLUPHENAZINE DECANOATE - DOSAGE STUDIES - HIGH DOSE vs STANDARD, Outcome 3 Global state: 3. Not improved (medium term - 6 months to 1 year).



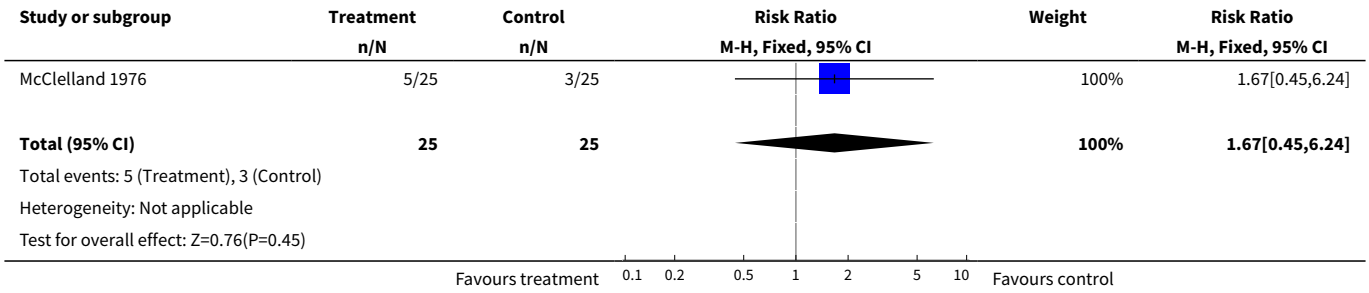
Analysis 4.4. Comparison 4 FLUPHENAZINE DECANOATE - DOSAGE STUDIES - HIGH DOSE vs STANDARD, Outcome 4 Behaviour: Leaving the study early (medium term - 6 months to 1 year).



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).



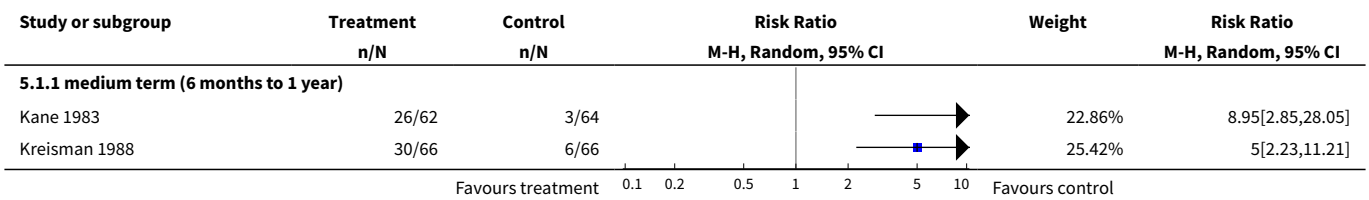
Analysis 4.6. Comparison 4 FLUPHENAZINE DECANOATE - DOSAGE STUDIES - HIGH DOSE vs STANDARD, Outcome 6 Adverse effects: Movement disorders - needing anticholinergic drugs (medium term - 6 months to 1 year).

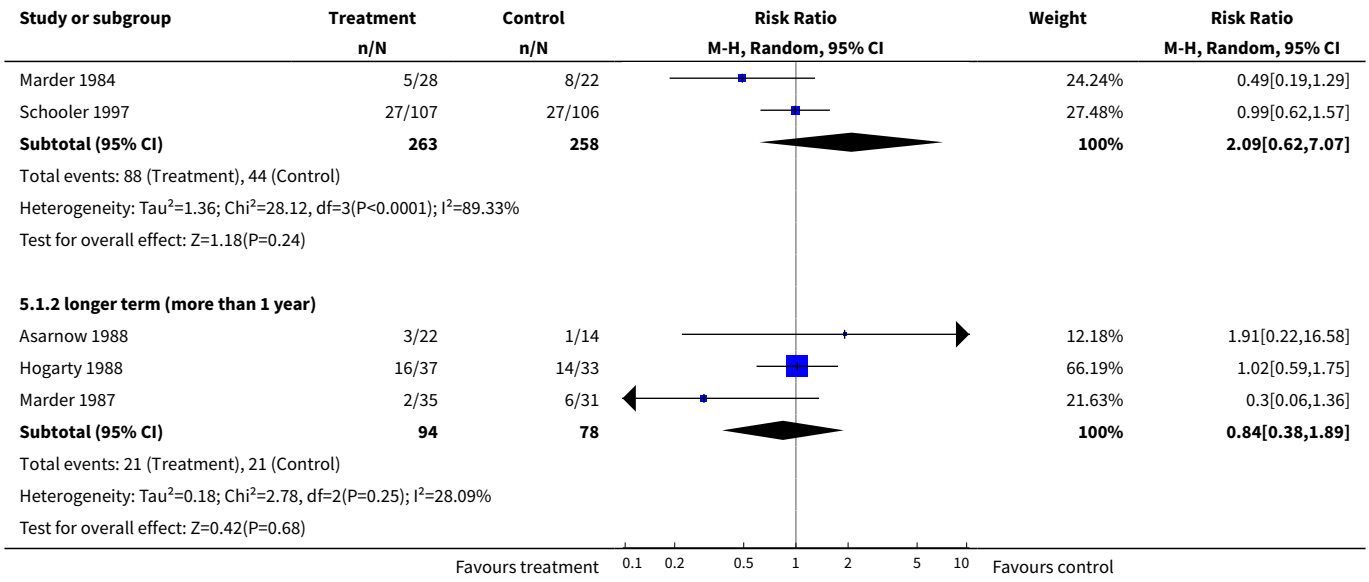


Comparison 5. FLUPHENAZINE DECANOATE - DOSAGE STUDIES - LOW DOSE vs STANDARD

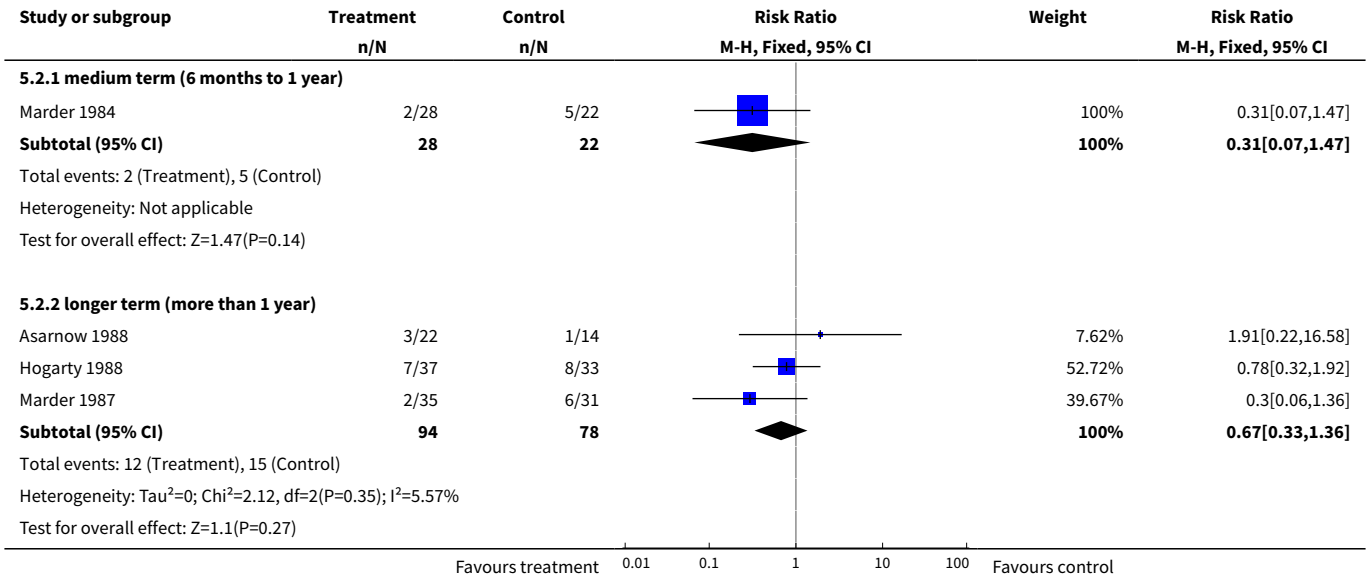
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Global state: Relapse	7		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
1.1 medium term (6 months to 1 year)	4	521	Risk Ratio (M-H, Random, 95% CI)	2.09 [0.62, 7.07]
1.2 longer term (more than 1 year)	3	172	Risk Ratio (M-H, Random, 95% CI)	0.84 [0.38, 1.89]
2 Behaviour: Leaving the study early	4		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
2.1 medium term (6 months to 1 year)	1	50	Risk Ratio (M-H, Fixed, 95% CI)	0.31 [0.07, 1.47]
2.2 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]
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

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

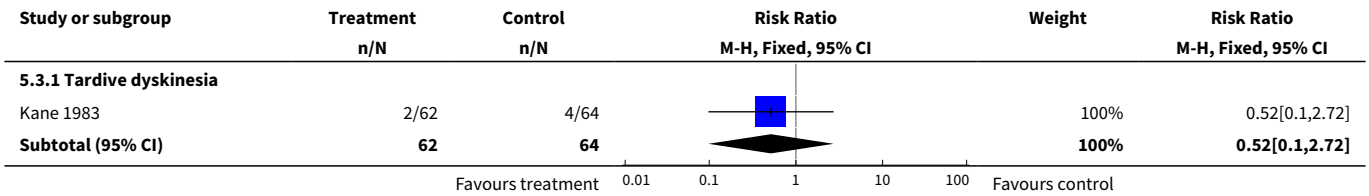


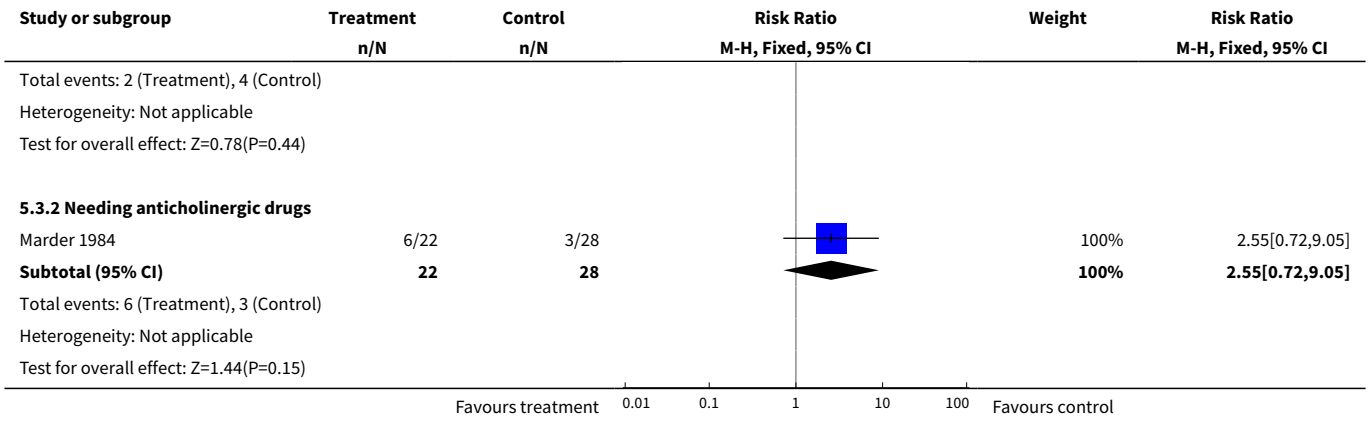


Analysis 5.2. Comparison 5 FLUPHENAZINE DECANOATE - DOSAGE STUDIES - LOW DOSE vs STANDARD, Outcome 2 Behaviour: Leaving the study early.



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).





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).

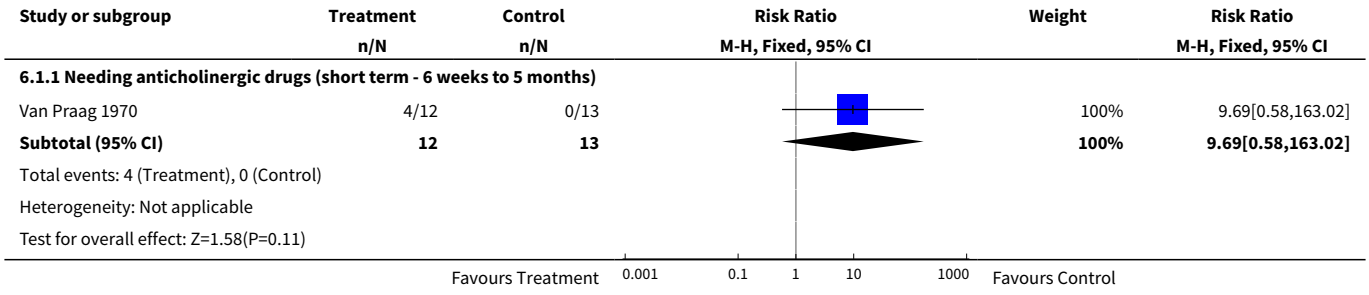
Adverse effects: 2. Continuous data - skewed data (endpoint scores, high = poor)

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

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]

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



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]

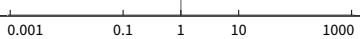
Analysis 7.1. Comparison 7 FLUPHENAZINE ENANTHATE vs ORAL NEUROLEPTICS, Outcome 1 Global state: No clinically important global change (immediate - 0 to 5 weeks).

Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Chien 1973	5/16	7/15		100%	0.67[0.27,1.66]
Total (95% CI)	**16**	**15**		**100%**	**0.67[0.27,1.66]**
Total events: 5 (Treatment), 7 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.87(P=0.39)					

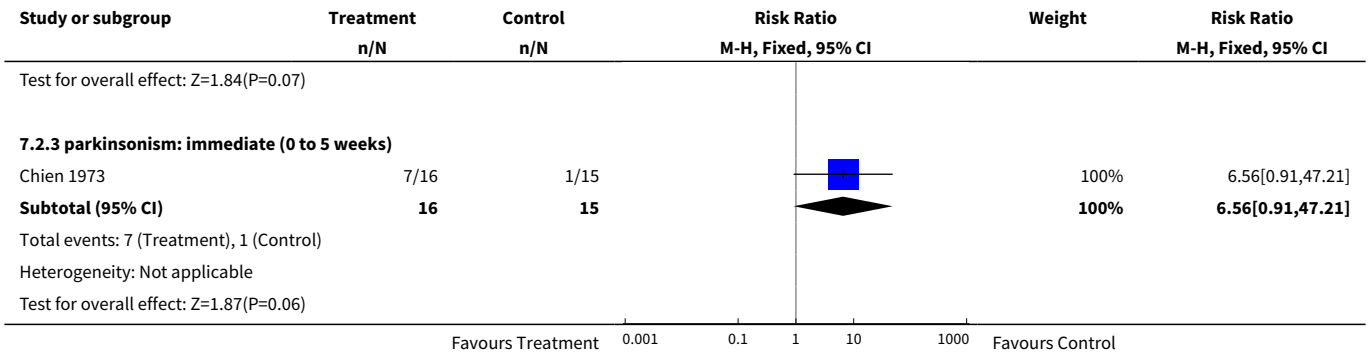
Favours Treatment — Favours Control

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

Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
7.2.1 movement disorders: immediate (0 to 5 weeks)					
Chien 1973	5/16	2/15		100%	2.34[0.53,10.3]
Subtotal (95% CI)	**16**	**15**		**100%**	**2.34[0.53,10.3]**
Total events: 5 (Treatment), 2 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=1.13(P=0.26)					
7.2.2 side effects: immediate (0 to 5 weeks)					
Chien 1973	9/16	3/15		100%	2.81[0.94,8.45]
Subtotal (95% CI)	**16**	**15**		**100%**	**2.81[0.94,8.45]**
Total events: 9 (Treatment), 3 (Control)					
Heterogeneity: Not applicable					



Favours Treatment — Favours Control



Comparison 8. FLUPHENAZINE ENANTHATE vs OTHER DEPOT NEUROLEPTICS

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
1 Global state: 1. Needing additional antipsy-chotic 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
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 Behaviour: 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]

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
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]

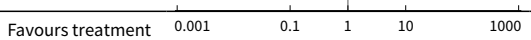
Analysis 8.1. Comparison 8 FLUPHENAZINE ENANTHATE vs OTHER DEPOT NEUROLEPTICS, Outcome 1 Global state: 1. Needing additional antipsychotic treatment (6 months to 1 year).

Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Albert 1980	4/11	13/22		59.09%	0.62[0.26,1.45]
Chouinard 1978	2/16	6/16		40.91%	0.33[0.08,1.41]
Total (95% CI)	**27**	**38**		**100%**	**0.5[0.24,1.05]**
Total events: 6 (Treatment), 19 (Control)					
Heterogeneity: Tau^2=0; Chi^2=0.53, df=1(P=0.47); I^2=0%					
Test for overall effect: Z=1.84(P=0.07)					

Favours Treatment — Favours Control

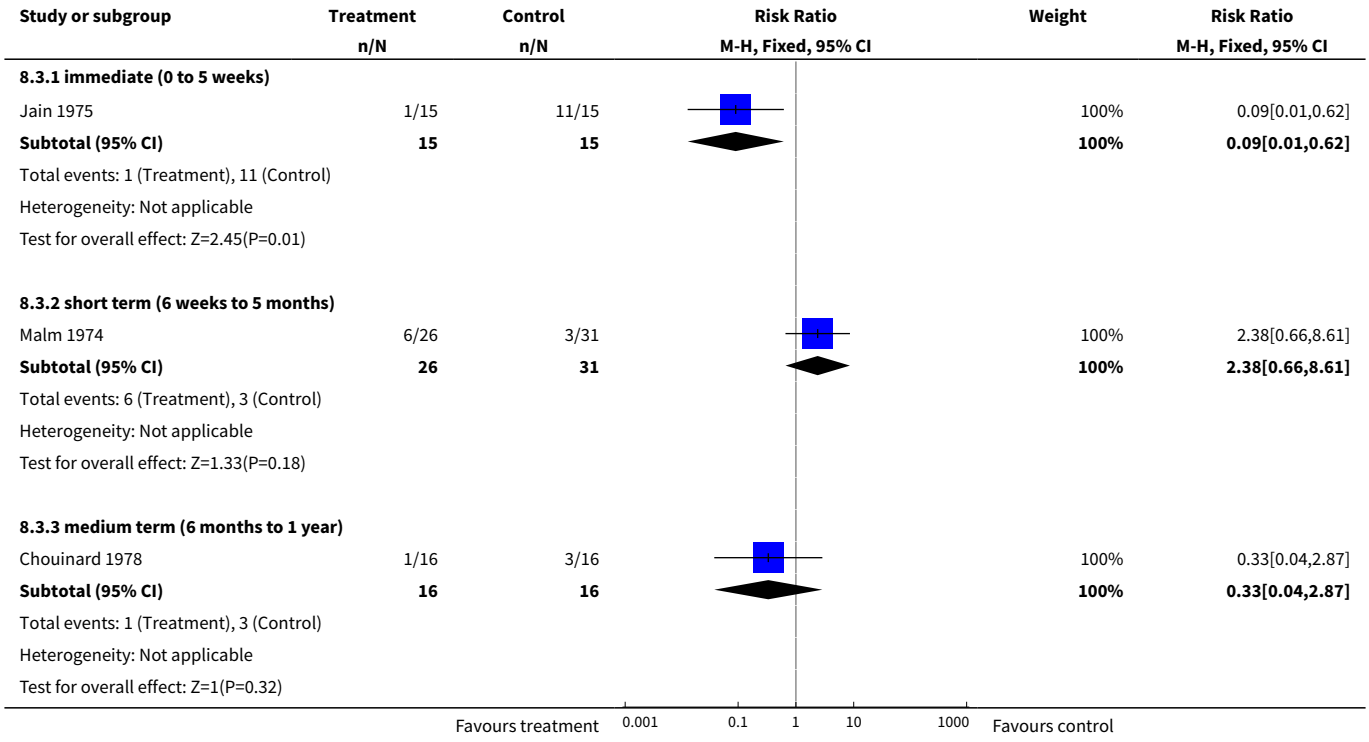
Analysis 8.2. Comparison 8 FLUPHENAZINE ENANTHATE vs OTHER DEPOT NEUROLEPTICS, Outcome 2 Global state: 2. Relapse.

Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
8.2.1 short term (6 weeks to 5 months)					
Malm 1974	6/26	3/31		100%	2.38[0.66,8.61]
Subtotal (95% CI)	**26**	**31**		**100%**	**2.38[0.66,8.61]**
Total events: 6 (Treatment), 3 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=1.33(P=0.18)					
8.2.2 medium term (6 months to 1 year)					
Chouinard 1978	1/16	3/16		100%	0.33[0.04,2.87]
Subtotal (95% CI)	**16**	**16**		**100%**	**0.33[0.04,2.87]**
Total events: 1 (Treatment), 3 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=1(P=0.32)					

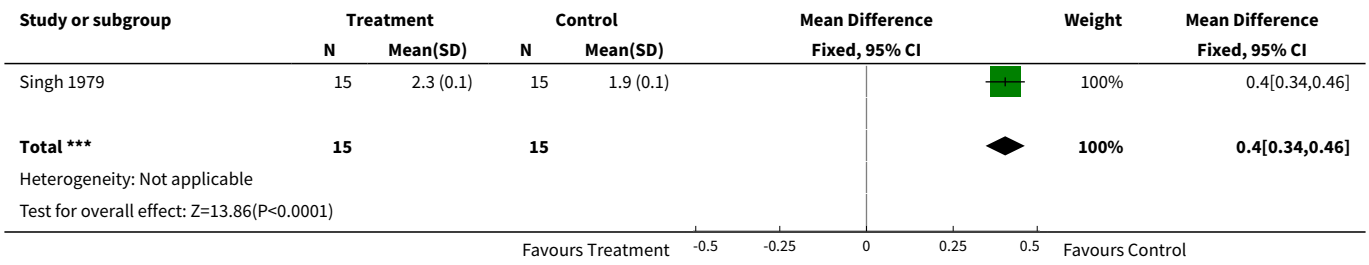


Favours treatment — Favours control

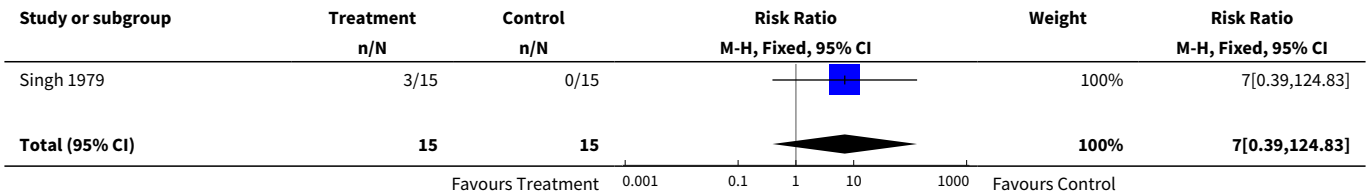
Analysis 8.3. Comparison 8 FLUPHENAZINE ENANTHATE vs OTHER DEPOT NEUROLEPTICS, Outcome 3 Behaviour: Leaving the study early.

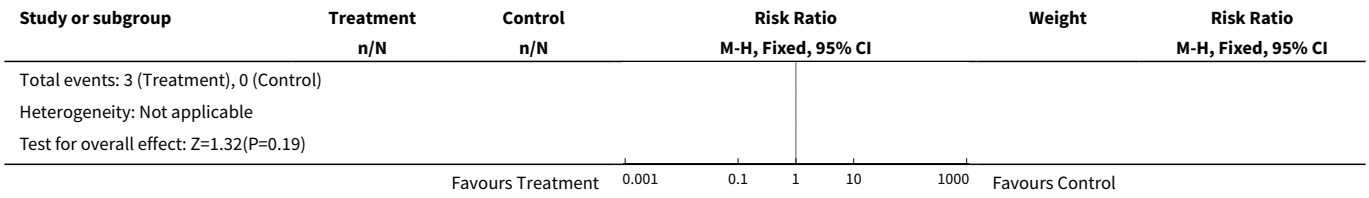


Analysis 8.4. Comparison 8 FLUPHENAZINE ENANTHATE vs OTHER DEPOT NEUROLEPTICS, Outcome 4 Mental state: 1. BPRS - endpoint scores (medium term - 6 months to 1 year) (high score =poor).

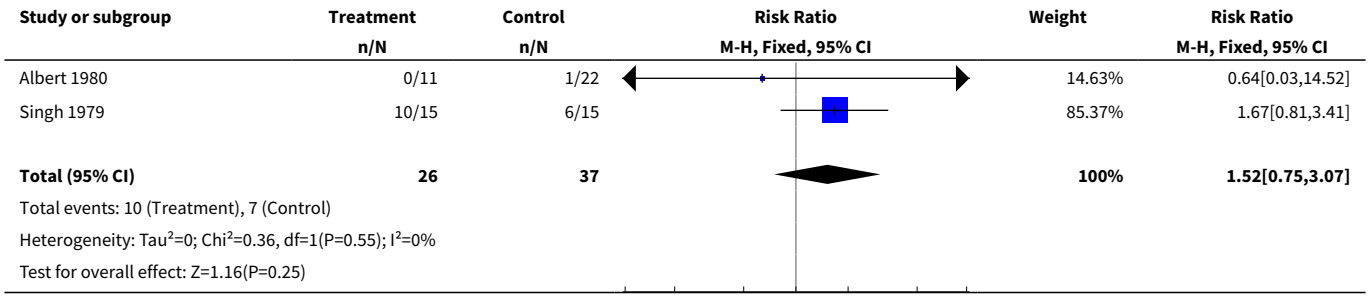


Analysis 8.5. Comparison 8 FLUPHENAZINE ENANTHATE vs OTHER DEPOT NEUROLEPTICS, Outcome 5 Mental state: 2. Depression (medium term - 6 months to 1 year).

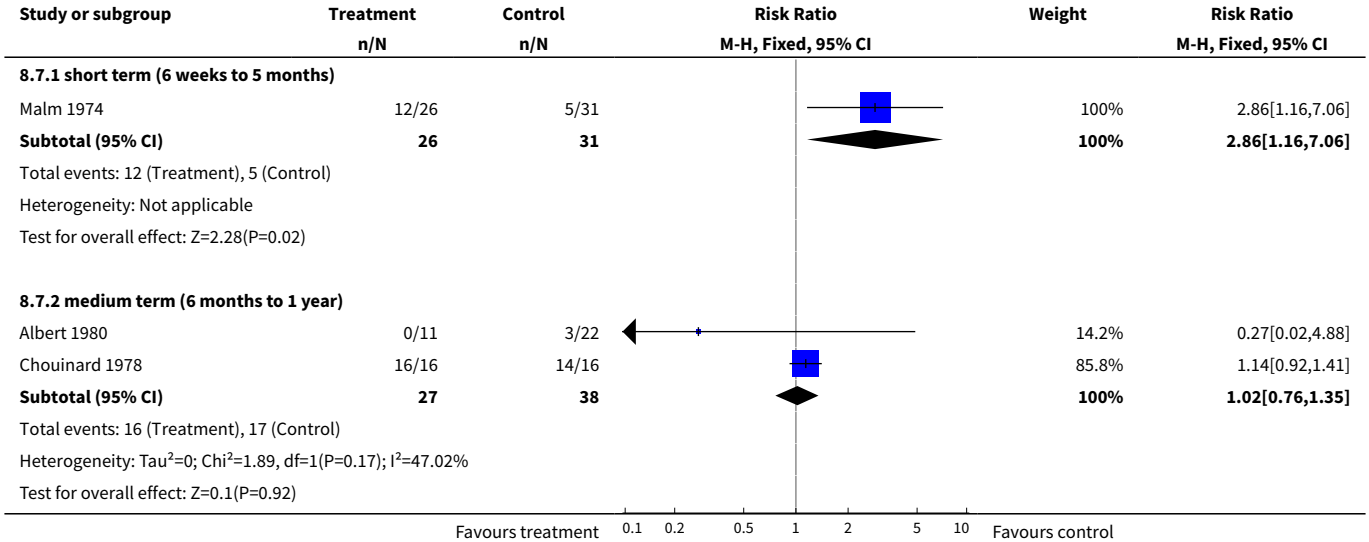




Analysis 8.6. Comparison 8 FLUPHENAZINE ENANTHATE vs OTHER DEPOT NEUROLEPTICS, Outcome 6 Adverse effects: 1a. Movement disorders - general (medium term - 6 months to 1 year).



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



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).

Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Chouinard 1978	8/16	9/16		100%	0.89[0.46,1.71]
Total (95% CI)	**16**	**16**		**100%**	**0.89[0.46,1.71]**
Total events: 8 (Treatment), 9 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.35(P=0.72)					

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).

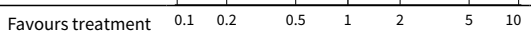
Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Albert 1980	5/11	10/22		32.26%	1[0.45,2.21]
Chouinard 1978	9/16	8/16		38.71%	1.13[0.59,2.16]
Singh 1979	10/15	6/15		29.03%	1.67[0.81,3.41]
Total (95% CI)	**42**	**53**		**100%**	**1.24[0.82,1.87]**
Total events: 24 (Treatment), 24 (Control)					
Heterogeneity: $Tau^2=0$; $Chi^2=1.02$, df=2(P=0.6); $I^2=0\%$					
Test for overall effect: Z=1.03(P=0.3)					

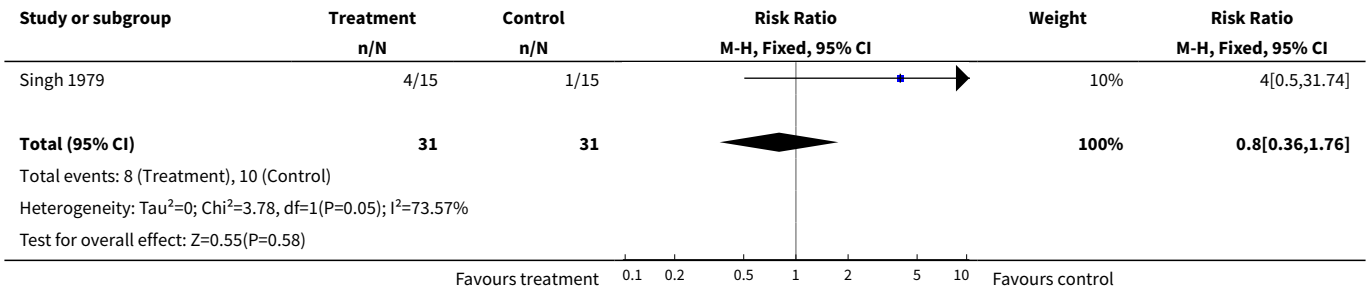
Analysis 8.10. Comparison 8 FLUPHENAZINE ENANTHATE vs OTHER DEPOT NEUROLEPTICS, Outcome 10 Adverse effects: 2. Blurred vision (medium term - 6 months to 1 year).

Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Singh 1979	1/15	0/15		100%	3[0.13,68.26]
Total (95% CI)	**15**	**15**		**100%**	**3[0.13,68.26]**
Total events: 1 (Treatment), 0 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.69(P=0.49)					

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).

Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Chouinard 1978	4/16	9/16		90%	0.44[0.17,1.15]

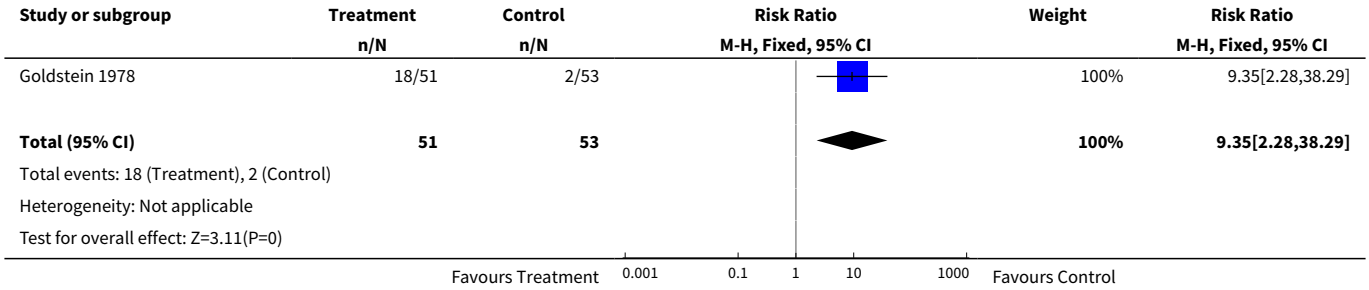




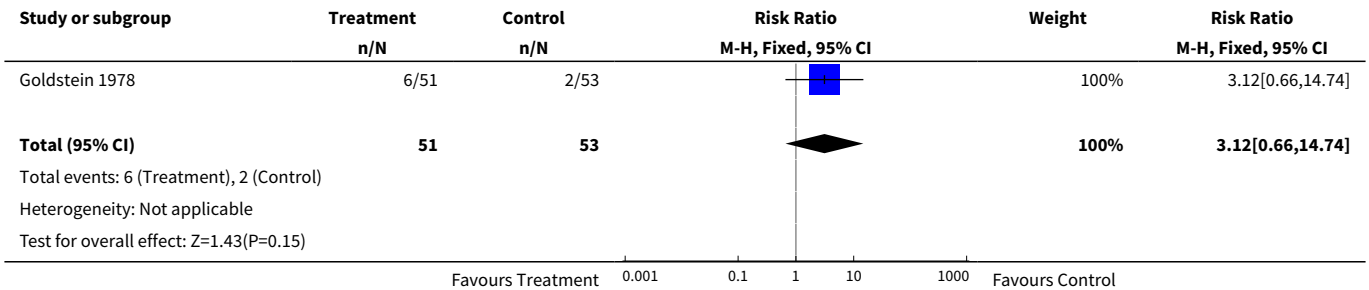
Comparison 9. FLUPHENAZINE ENANTHATE - DOSAGE STUDIES - LOW DOSE vs INTERMEDIATE/HIGH DOSE

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 Behavior: 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]

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).



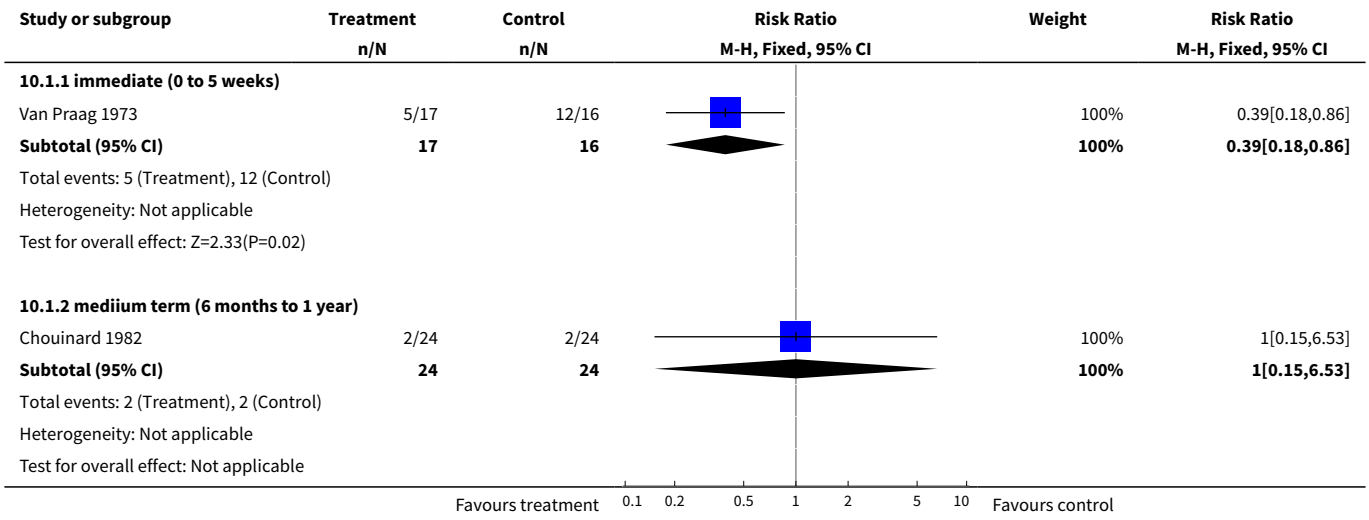
Analysis 9.2. Comparison 9 FLUPHENAZINE ENANTHATE - DOSAGE STUDIES - LOW DOSE vs INTERMEDIATE/HIGH DOSE, Outcome 2 Behavior: Leaving the study early (short term - 6 weeks to 5 months).



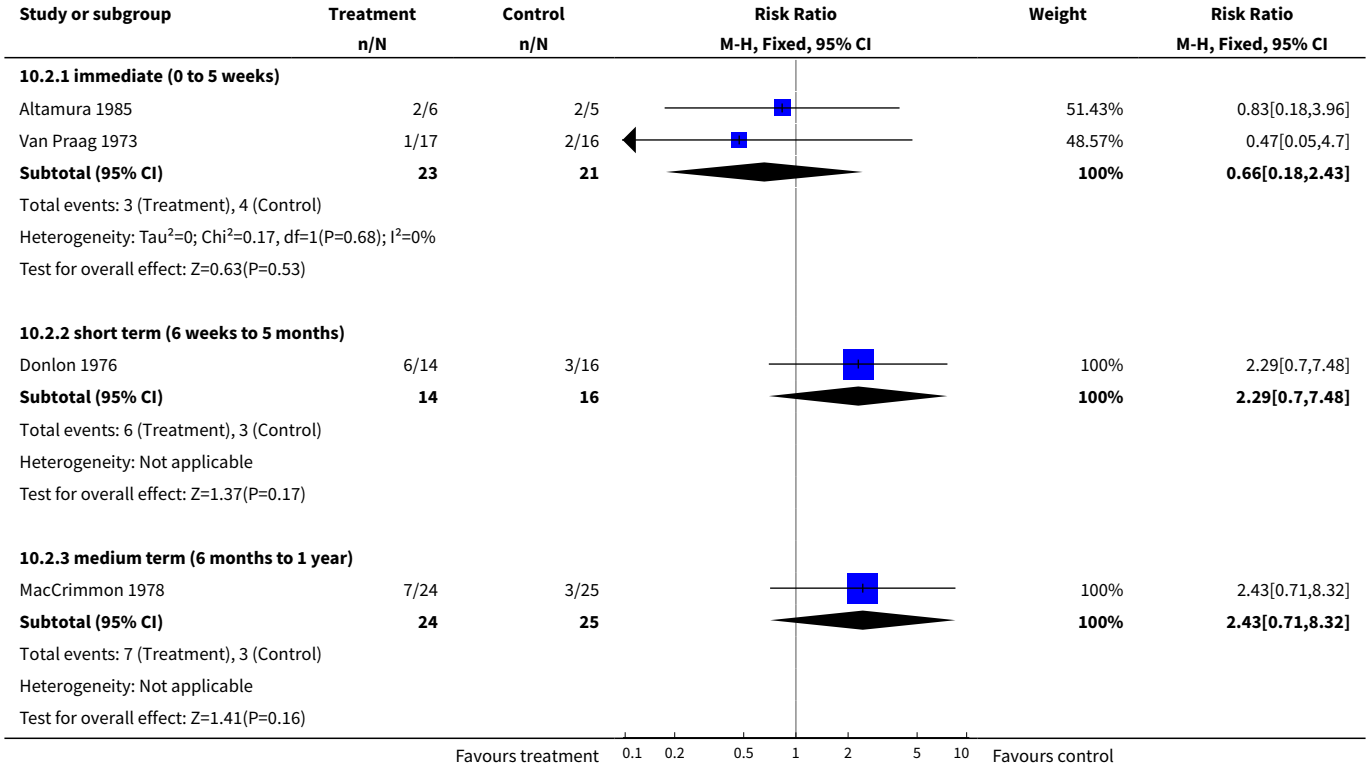
Comparison 10. FLUPHENAZINE DECANAOTE vs FLUPHENAZINE ENANTHATE

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	2		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
5.1 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]
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: 2. General adverse effects (immediate - 0 to 5 weeks)	1	11	Risk Ratio (M-H, Fixed, 95% CI)	0.08 [0.01, 1.14]

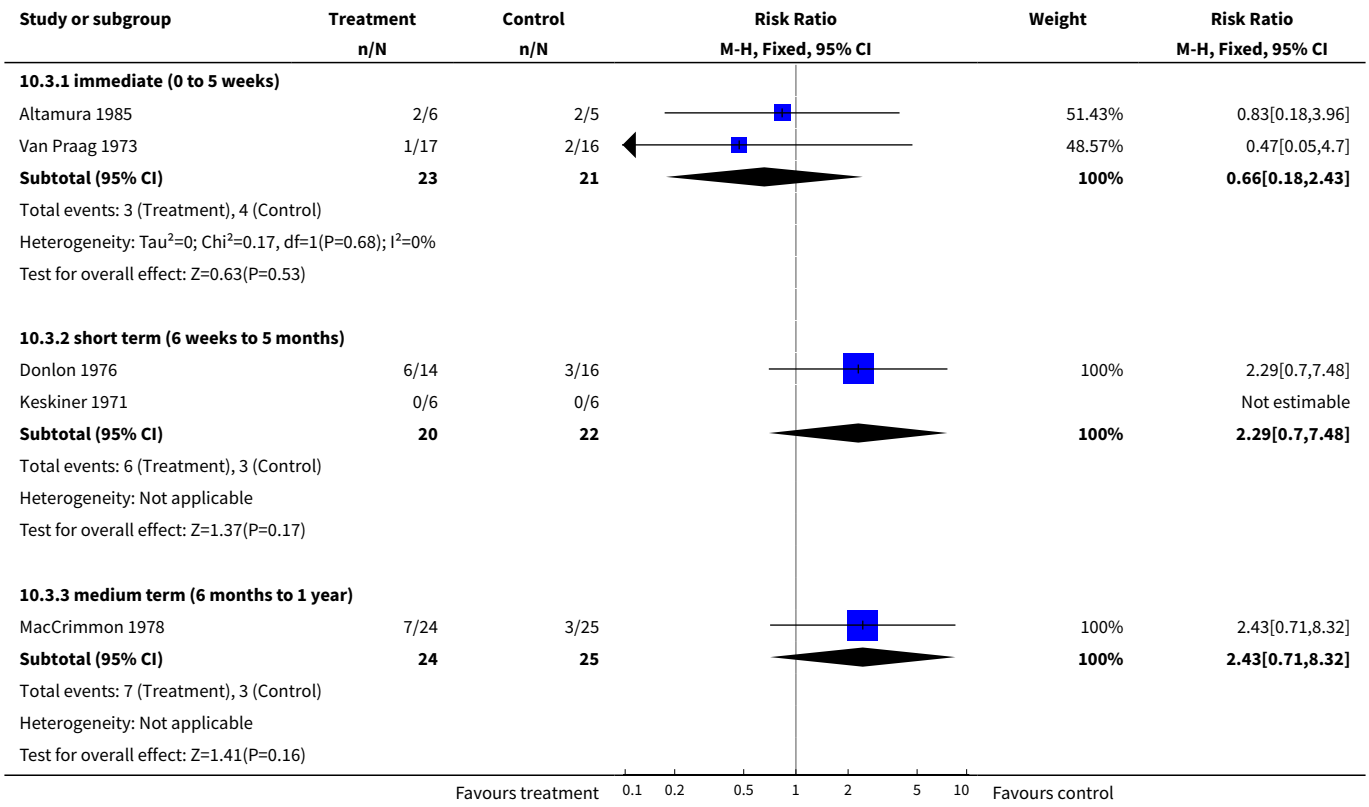
Analysis 10.1. Comparison 10 FLUPHENAZINE DECANAOTE vs FLUPHENAZINE ENANTHATE, Outcome 1 Global state: 1. Needing additional antipsychotic treatment.



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

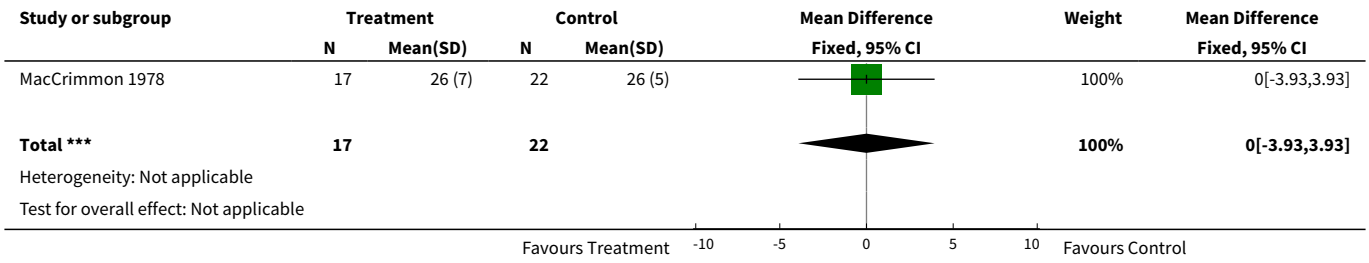


Analysis 10.3. Comparison 10 FLUPHENAZINE DECANAOTE vs FLUPHENAZINE ENANTHATE, Outcome 3 Behavioiur: Leaving the study early.



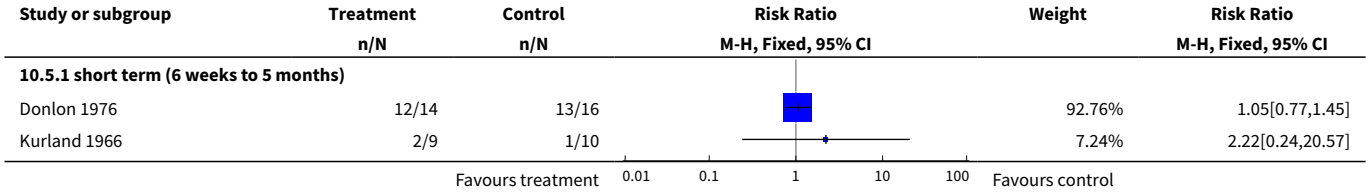
Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
10.3.1 immediate (0 to 5 weeks)					
Altamura 1985	2/6	2/5		51.43%	0.83[0.18,3.96]
Van Praag 1973	1/17	2/16		48.57%	0.47[0.05,4.7]
Subtotal (95% CI)	**23**	**21**		**100%**	**0.66[0.18,2.43]**
Total events: 3 (Treatment), 4 (Control)					
Heterogeneity: Tau²=0; Chi²=0.17, df=1(P=0.68); I²=0%					
Test for overall effect: Z=0.63(P=0.53)					
10.3.2 short term (6 weeks to 5 months)					
Donlon 1976	6/14	3/16		100%	2.29[0.7,7.48]
Keskiner 1971	0/6	0/6			Not estimable
Subtotal (95% CI)	**20**	**22**		**100%**	**2.29[0.7,7.48]**
Total events: 6 (Treatment), 3 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=1.37(P=0.17)					
10.3.3 medium term (6 months to 1 year)					
MacCrimmon 1978	7/24	3/25		100%	2.43[0.71,8.32]
Subtotal (95% CI)	**24**	**25**		**100%**	**2.43[0.71,8.32]**
Total events: 7 (Treatment), 3 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=1.41(P=0.16)					

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).

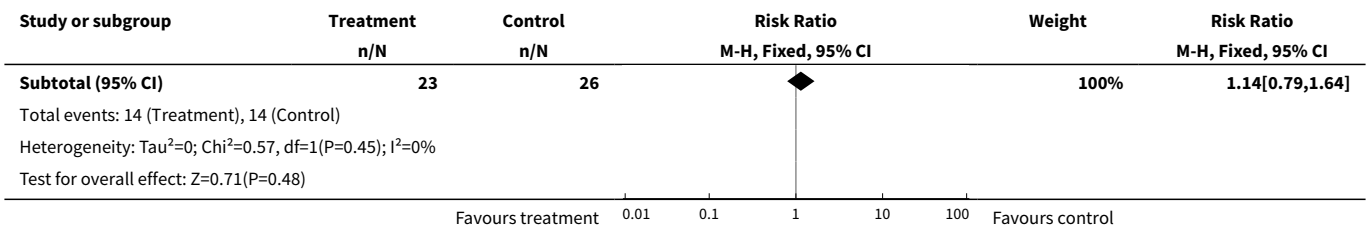


Study or subgroup	Treatment N	Treatment Mean(SD)	Control N	Control Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
MacCrimmon 1978	17	26 (7)	22	26 (5)		100%	0[-3.93,3.93]
Total ***	**17**		**22**			**100%**	**0[-3.93,3.93]**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							

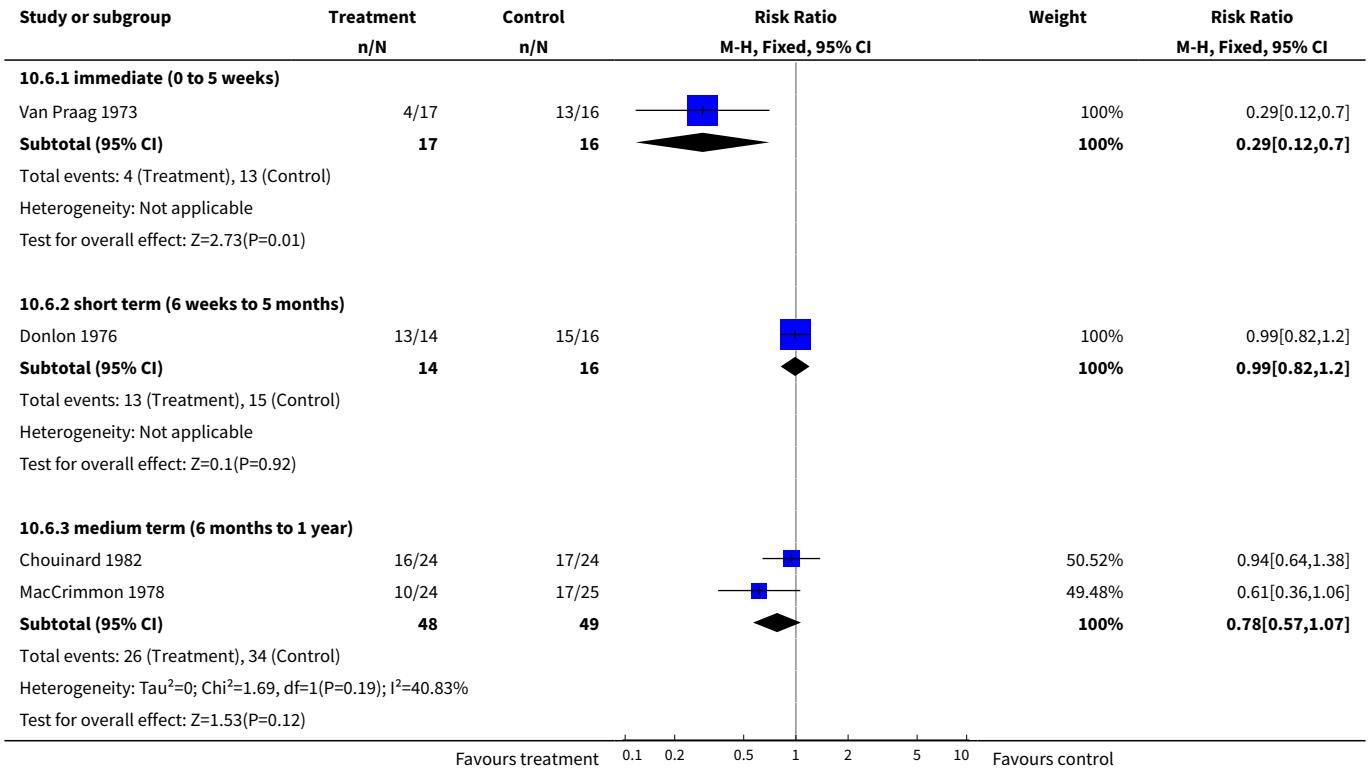
Analysis 10.5. Comparison 10 FLUPHENAZINE DECANAOTE vs FLUPHENAZINE ENANTHATE, Outcome 5 Adverse effects: 1a. Movement disorders - general.



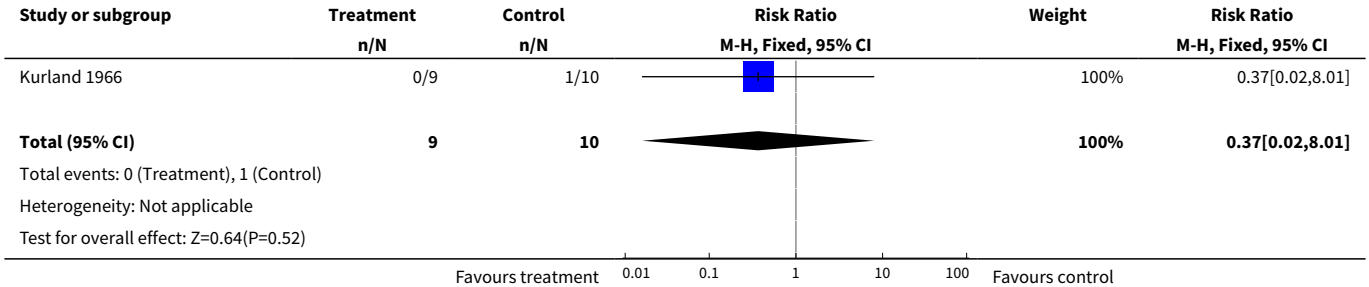
Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
10.5.1 short term (6 weeks to 5 months)					
Donlon 1976	12/14	13/16		92.76%	1.05[0.77,1.45]
Kurland 1966	2/9	1/10		7.24%	2.22[0.24,20.57]



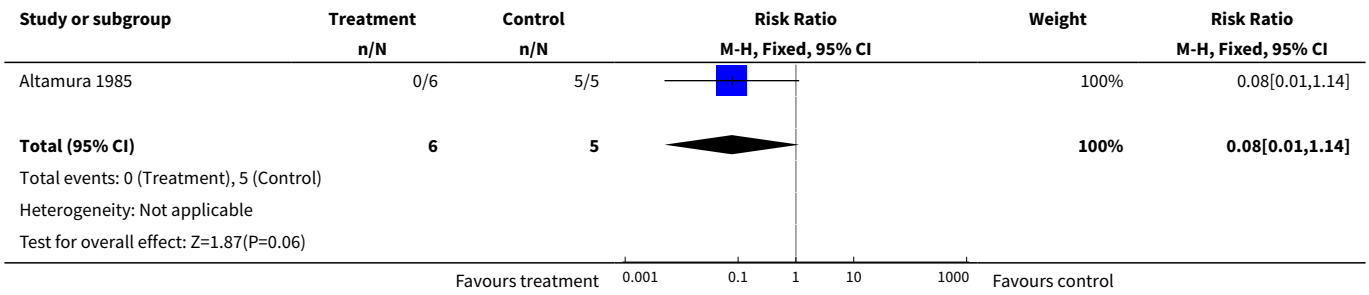
Analysis 10.6. Comparison 10 FLUPHENAZINE DECANAOTE vs FLUPHENAZINE ENANTHATE, Outcome 6 Adverse effects: 1b. Movement disorders - needing anticholinergic drugs.



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).



Analysis 10.8. Comparison 10 FLUPHENAZINE DECANAOTE vs FLUPHENAZINE ENANTHATE, Outcome 8 Adverse effects: 2. General adverse effects (immediate - 0 to 5 weeks).



WHAT'S NEW

Date	Event	Description
25 January 2011	Amended	byline corrected

HISTORY

Protocol first published: Issue 2, 1996
Review first published: Issue 4, 1997

Date	Event	Description
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.

Maurice Eisenbruch - prepared protocol, undertook searches, selected and acquired studies, extracted data, summated data, produced report.

Anthony David - acquired funding, helped prepare protocol, select studies, extract data, and produce the report.

Clive Adams - acquired funding, helped prepare protocol, undertook searches, selected and acquired studies, extracted and summated data, produce the report and prepared the updated review.

John Rathbone - selected and acquired studies, extracted and summated data and prepared the updated review (2004).

DECLARATIONS OF INTEREST

None known.

SOURCES OF SUPPORT

Internal sources

- No sources of support supplied

External sources

- NHS-ROCD Health Technology Assessment Programme., UK.

INDEX TERMS

Medical Subject Headings (MeSH)

Administration, Oral; Antipsychotic Agents [administration & dosage] [*therapeutic use]; Delayed-Action Preparations [administration & dosage] [therapeutic use]; Fluphenazine [administration & dosage] [*analogs & derivatives] [therapeutic use]; Injections, Intramuscular; Randomized Controlled Trials as Topic; Schizophrenia [drug therapy]

MeSH check words

Humans