Selective serotonin reuptake inhibitors (SSRIs) versus other antidepressants for depression (Review)

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ABSTRACT

Background
The relatively new class of antidepressant, the selective serotonin reputake inhibitors (SSRIs), may be better tolerated than the older tricyclic antidepressants. This review compares the efficacy of SSRIs with other antidepressants.

Objectives
To examine the relative efficacy of selective serotonin reuptake inhibitors (SSRIs) compared to other antidepressants.

Search strategy
The search strategy included a search of (a) Electronic bibliographic databases (MEDLINE, EMBASE); (b) reference lists of related reviews (c) reference lists of all located studies (d) contact with the manufacturer and (e) the Cochrane Group register of controlled trials

Selection criteria
Randomised controlled trials comparing selective serotonin reuptake inhibitors with other kinds of antidepressants in the treatment of patients with depressive disorders. The outcome measures assessed included measures of the severity of depression.

Data collection and analysis
Data were collected from each study the main outcome measurefrom each study. These included: mean Hamilton depression rating scale, mean Montgomery & Asberg depression rating scale, Clinical Global Impression rating scale. An analysis of standardised mean difference of these scales was performed using Review Manager 3.1 software. The presence of heterogeneity of treatment effect was assessed

Main results
Ninety-eight trials contributed data to the analysis of the relative efficacy of SSRIs and related drugs with comparator antidepressants (Figure 3 & Appendix 3). Analysis of efficacy was based upon 5044 patients treated with an SSRI or related drug, and 4510 treated with an alternative antidepressant. The standardised effect size for SSRIs and related drugs together versus alternative antidepressants using a fixed effects model was 0.035 (95% CI -0.006 to 0.076; Q = 149.25, df = 97, $p < 0.001$).

Authors' conclusions
There are no clinically significant differences in effectiveness between selective serotonin reuptake inhibitors and tricyclic antidepressants. Treatment decisions need to be based on considerations of relative patient acceptability, toxicity and cost.

PLAIN LANGUAGE SUMMARY

The efficacy of a new group of antidepressants (selective serotonin reuptake inhibitors-SSRIs), were compared to other tricyclic antidepressants (TCAs) for the treatment of depressive illness.

Ninety-eight randomised comparative trials were undertaken, where neither the patient nor the treating doctor knew which treatment was being given. This method provides the best estimates of treatment effect. Pooling the results from the trials, no clinically significant differences in efficacy were found between SSRIs and tricyclic antidepressants. Thus, the researchers suggest that treatment decisions between the two types of drug are to be based on considerations of drug toxicity, patient acceptability, and cost.

BACKGROUND

The development of a new and innovative group of antidepressants, the selective serotonin reuptake inhibitors, led to considerable interest in their relative effectiveness and efficiency in the treatment of depressive illness (EHC 1993; Song 1993 ; Freemantle 1994; Montgomery 1994; Montgomery 1994; Jonsson 1994; Owens 1994; Harrison 1994; Anon 1993; Anderson 1996; Hotopf 1996). Depressive disorders are common, affecting 5% of people seen in primary care settings in the UK (Blacker 1988). Depressive disorders are the fourth most important cause of disability world wide and are expected to become the second most important cause by 2020 (Murray 1997a; Murray 1997b). For the majority of people episodes of depression are short lived, but a minority experience a range of severe psychological and biological symptoms which may persist. Depression is one of the most common single reasons for attending a general practitioner and the majority of depressed people who receive treatment do so in the primary care setting (Goldberg 1992).

Although the relative tolerability of antidepressants has been examined by a number of investigators in meta analyses the issue of relative efficacy has received little attention (Song 1993). While it appears that SSRIs may be better tolerated than tricyclic antidepressants (Anderson 1996), it is not clear whether this may be at the cost of reduced efficacy (Song 1993).

OBJECTIVES

The objective of this review is to examine the relative efficacy of SSRIs compared to other antidepressant drugs. The main hypothesis to be tested is that SSRIs are more effective than alternative antidepressants.

CRITERIA FOR CONSIDERING STUDIES FOR THIS REVIEW

Types of studies

High quality randomised comparative trials that are conducted double blind (i.e. where neither the patient nor treating health professional knows which treatment is given) provide the best estimates of treatment effect of different pharmaceuticals as they enable comparisons to be made across groups that differ only in the exact compound ingested, and the play of chance. One investigation of the effects of blinding in systematic reviews found a 17% difference in the effect size between double blind and unblinded studies (Schulz 1995). The comparison of effects across trials (e.g. between two separate placebo controlled trials of different pharmaceuticals) is open to substantial bias, and unlikely to provide reliable estimates of treatment effect (Pocock 1983). Therefore, only double blind randomised controlled trials that compare directly an SSRI or related drug and a different antidepressant in the treatment of depression were included.

Types of participants

Patients suffering from major depressive illnesses diagnosed according to explicit criteria in a range of health care settings (primary/secondary/ inpatient/outpatient). This review focuses on the studies examining efficacy in uncomplicated major depressive disorder. In general studies in this area exclude patients with significant comorbidity. Although the reviewers did not plan a priori to exclude any age group, the majority of studies in this area focused on the 18-65 age group

Types of intervention

Trials were selected that directly compared a selective serotonin reuptake inhibitor (SSRI) or related drug and a different antidepressant.

Types of outcome measures

The main outcome measures used for the review were those used by the majority of studies as the primary endpoints. These included: mean Hamilton depression rating scale, mean Montgomery & Asberg depression rating scale, Clinical Global Impression rating scale.

SEARCH METHODS FOR IDENTIFICATION OF STUDIES

See: methods used in reviews.

a) Primary research
Electronic bibliographic databases was searched using optimally sensitive search terms:
1. text word '<SSRI drug name>' in title or abstracts without language restrictions in MEDLINE (from 1966-1998). Animal studies were excluded.
2. text word '<SSRI drug name>' across the basic index fields without language restrictions in EMBASE(from 1974-1998).

All studies that appeared to meet our entry criteria on the basis of the title and abstract were located and assessed. Where data necessary for the analyses or describing the context of a trial were not reported, the study authors were be written to, with reminders sent to non-responders after approximately one month.

(b) Secondary research

Reviews of related topics as a potential source of additional citations were identified.

(c) Citation lists

The reference lists of all located articles were checked for relevant references.

(d) Manufacturer

The manufacturers of all available SSRIs were contacted - data from any additional unpublished studies was requested.

(e) Cochrane Group Register of Trials

The Cochrane Group's register of trials was searched using the phrase '<SSRI drug name>'

METHODS OF THE REVIEW

DATA COLLECTION

In addition to including only randomised comparative double blind trials, the quality of included studies was assessed by NF primarily through the assessment of concealment of allocation during the randomisation process (Schulz 1995). Deviations from study protocols (such as inclusion of different patients from those stated in the protocol) is reported in the included trials table. Where studies are so compromised by faults in design or implementation (such as lack of randomisation) these were excluded from the analysis, and details reported in the excluded trials table.

Data were collected directly onto a computer database from each study using a checklist of items derived for this purpose. Questions include: mode of randomisation, comparison made, country, number randomised to each group, number discontinuing trial before end of treatment protocol, mean and standard deviation of main depression outcome scale for each patient group, setting of care (e.g. inpatient), planned age range.

STUDY QUALITY

The main quality criteria noted was reporting of the concealment of random allocation, which has been found to be related to study effect (Schulz 1995). Studies were given a quality rating ranging from C

(poorest quality) to A (best quality). C = inadequately concealed (e.g. via alternation or reference to an open random number table). B = no adequate details about how the randomisation procedure was carried out were given a rating of B. A = trials that were reported to have taken adequate measures to conceal allocation (e.g. serially numbered, opaque, sealed envelopes; numbered or coded bottles or containers).

DATA SYNTHESIS

An analysis of standardised mean difference of the primary study outcome measure (Cochrane Handbook 1996) was performed using Review Manager 3.1 software. The presence of heterogeneity of treatment effect was assessed using the Q statistic which approximates the chi square statistic with n - 1 degrees of freedom (DerSimonian 1986). A fixed effects model was used as the primary analysis, unless substantial heterogeneity was discovered in which case a random effects model was used as the primary analysis. The robustness of findings to the analysis used was assessed through sensitivity analyses.

Although the primary analyses examined comparisons between SSRIs and both tricyclic and other more recently developed drugs, we also undertook sensitivity analyses of this approach to determine the robustness of the analyses to the assumptions made, particularly limiting the comparison group to tricyclics.

DESCRIPTION OF STUDIES

We identified 126 studies, of which 98 contributed usable data for this review. The majority of the studies were small, phase three, double-blind randomised controlled trials. The duration was short - rarely longer than 6 weeks. There were 38 studies comparing fluoxetine to other antidepressants, 25 studies investigating the effectiveness of fluvoxamine, 8 studies on citalopram, 2 studies on nefazodone, 18 on paroxetine, 4 on venlafaxine and 4 on sertraline. Comparator antidepressants used in the trials included amineptine (1 study); amitriptyline (23 studies); clomipramine (12 studies); desipramine (2 studies); dothiepin (3 studies); imipramine (23 studies); lofepramine (1 study); maprotiline (6 studies); mianserin (8 studies); moclobemide (8 studies); trazodone (3 studies).

The majority of studies used on or other version of the Hamilton rating scale although the Mntgomery-Asberg and Clinical Global Impression scale were also used in a small minority of studies.

Out of a total of 7032 (27.7%) treated with an SSRI or related drug, 1948 patients dropped out of a trial prematurely, compared with 2072 treated with an alternative antidepressant out of a total treated of 6334 (32.7%); relative risk 0.87 (95% CI 0.80 to 0.95). That is a pooled risk difference using a random effects model of 4.1% (95% CI: 1.5% to 6.8%; Q = 376.95, df = 122, $p < 0.0001$) in absolute rate of drop-out (North of England Guidelines, in press).

METHODOLOGICAL QUALITY

Description of concealment of allocation was rated as B in all studies. We are currently obtaining the unpublished company reports for the trials - those we have obtained so far suggest that an adequate method of centrally concealed allocation was often used. Our findings will be reported in a future version of this review.

RESULTS

Comparative Efficacy

In the analyses, negative standardised mean differences (falling to the left of the midline) favour SSRIs. Positive standardised mean differences favour the alternative.

Ninety-nine trials contributed data to the analysis of the relative efficacy of SSRIs and related drugs with comparator antidepressants. Analysis of efficacy was based upon 5044 patients treated with an SSRI or related drug, and 4510 treated with an alternative antidepressant. The standardised effect size for SSRIs and related drugs together versus alternative antidepressants using a fixed effects model was 0.035 (95% CI -0.006 to 0.076; Q = 149.25, df = 97, p < 0.001).

This result was fairly robust to the assumptions on inclusion: the standardised effect size for SSRIs alone compared with tricyclics was 0.030 (95% CI -0.018 to 0.092; Q = 88.64, df = 66, p = 0.03). Results were also robust to the type of analysis used, with a standardised effect size for SSRIs and related antidepressants versus alternative antidepressants using a random effects model of 0.046 (95%CI -0.010 to 0.103), and the standardised effect size for SSRIs alone versus tricyclic antidepressants of 0.044 (95% CI -0.020 to 0.107). There was therefore no evidence of statistically or clinically significant differences between the drugs.

Analysis of the comparative efficacy of SSRIs and tricyclic antidepressants in inpatients (judged likely to be a more severely affected group) provided a slightly larger estimate of effect favouring tricyclic antidepressants, though this may be explained merely by chance. The overall estimate of effect in this grouping of studies (using a random effects model) was 0.10 (95% CI: -0.072 to 0.272; Q = 49.1, df = 22, p = 0.0008), equivalent to about one Hamilton Depression Rating Scale point.

We undertook further analyses comparing the 5 SSRIs currently licensed in the UK (citalopram, fluoxetine, fluvoxamine, paroxetine, sertraline) as a group, with individual alternative antidepressants. Twenty-three trials compared an SSRI with amitriptyline, and 23 with imipramine. The pooled standardised effect size for SSRIs versus amitriptyline was 0.057 (95% CI -0.027 to 0.140: Q = 21.03, df = 22, p = 0.49 - fixed effects), and for SSRIs versus imipramine was -0.040, (95% CI -0.126 to 0.046: Q = 25.47, df = 21, p = 0.227 - fixed effects).

Comparative efficacy data of last observation carried forward (closest to intention to treat, since the last available data from patients contributes to the final result, regardless of completion of the full trial period) were available only for 18 out of 64 trials of SSRIs versus tricyclics (these trials contributed nearly half of the statistical information in the meta analyses). Three studies had to be excluded from this analysis because it was not possible to detect if their analyses were last observation carried forward of endpoint. Although in some ways preferable to endpoint analysis, as all patients with some outcome data available contribute to the analysis, the results by last observation carried forward are confounded by the substantial improvement over time experienced by all patients regardless of treatment allocation, and the small systematic difference in treatment tolerability between SSRIs and related drugs and older antidepressants. These results are also further confounded when using a dimensionless outcome, as standardised effect sizes are based upon the trial variance which may be increased in those trials where a mixture of endpoints measured at different times in treatment are used. Consequently, we further analysed trials grouped by method of analysis (e.g. endpoint or last observation carried forward), and found a possible, but non-significant trend towards a greater effect in trials analysed by endpoint: standardised effect size 0.011 (95% CI -0.060 to 0.081: Q = 22.48, df = 17; p = 0.167) for last observation carried forward versus 0.045 (95% CI -0.023 to 0.113: Q = 55.74, df = 45, p = 0.13) for endpoint (see Figure 5). Thus, it is likely that high drop-out in the last observation carried forward trials (intention to treat) has lead to an underestimate of the true treatment effect at a common time period.

The sub-analysis comparing SSRIs with sedating (standardised mean difference 0.058; 95% CI -0.012 to 0.128) and non-sedating tricyclic drugs (standardised mean difference 0.005; 95% CI -0.080 to 0.090) revealed no clinically important effects.

In view of the substantial heterogeneity in the overall principal analysis of SSRIs v. alternative antidepressants, it is noteworthy that the sub-analyses of the individual SSRIs did not reveal any important differences between the drugs.

DISCUSSION

1. Methodological considerations

The majority of studies used continuous measure of depressive symptomatology as the primary outcome measure. It is uncertain how these translate into clinically meaningful measures. Some studies dichotomised the continuous measures into participants who experienced an arbitrary percentage reduction in symptoms. For example, a greater than 50% reduction in the total Hamilton score is often used. We have not used this approach in this review because, apart from being basically arbitrary and of uncertain clinical relevance, this approach sacrifices statistical power. In view of the relatively small differences that it would be realistic to expect between TCAs and SSRIs, we chose to use the most powerful method of analysis to give us a better chance of picking up any small, but clinically significant, differences.

However, there is a need for the use of more clinically meaningful, valid outcome measures in trials of antidepressants. “Hard” outcomes, such as suicide, are probably too rare to use. However deliberate self harm might be feasible to use in some studies, especially

in high risk samples. But other outcomes such as ability to work or admission to hospital are events which may be more clinically meaningful to patients and clinicians. Another approach which has sometimes been used is to count the number of participants who score below a prestated level on the continuous measure (for example <7 on the Hamilton) and to consider these as 'recovered'. The Macarthur Foundation Research Network have proposed an approach to defining remission, recovery, relapse and recurrence in depressive disorder and have also suggested cut points on commonly used scales such as the Hamilton and Beck for rating these events (Frank 1991). This approach may be fruitful because it avoids the arbitrary and relative nature of dichotomising around a percentage reduction.

Despite the large number of comparative trials, the total number of patients randomised is under 10,000. The mean size of each trial is therefore less than one hundred participants. Individually, each trial is underpowered for the purposes of demonstrating equivalence. Furthermore, most trials are very short - usually 6 weeks or less. This review highlights the need for better designed studies in this area. Other studies of the quality of this population of trials have been performed with similar findings (Hotopf 1996). It is possible that long-term differences would emerge in controlled trials of longer duration.

2. Quantitative findings

In the short-term, there does not appear to be a clinically significant difference in the effectiveness of selective serotonin reuptake inhibitors and any of the older antidepressants (including tricyclics such as clomipramine that are sometimes believed to be particularly effective). Treatment decisions therefore need to be based on the relative toxicity of the drugs, their tolerability and side effect profiles, and their costs.

In a separate review, we have used drop-out from trials as a proxy measure for patient acceptability, SSRIs appear to be slightly more acceptable (Eccles 1999). However, the difference is small: about 25 patients would need to be treated with an SSRI compared to an alternative drug to prevent one drop-out. A Cochrane systematic review of the relative drop-out from SSRI and alternative antidepressants is currently underway.

We have not assessed the relative costs of SSRIs and other antidepressants in this review. Previous economic studies (North of England Guidelines Group, in press; Trindade 1997) have concluded that the increased acquisition costs of SSRIs with limited benefit do not justify their routine first-line use. A more cost-effective strategy seems to be to use TCAs as a first-line treatment and to reserve SSRIs for patients in whom TCAs are medically contraindicated, who cannot tolerate them or, perhaps, those who have failed to respond to first-line SSRI treatment.

AUTHORS' CONCLUSIONS

Implications for practice

The main conclusion of this review is that there are no large differences between selective serotonin reuptake inhibitors and tricyclic antidepressants in terms of efficacy in the short-term treatment of depression. It is possible that differences may emerge in the longer term - we plan to investigate this issue in a future review of maintenance phase treatment of depression.

We have not investigated the comparative acceptability to patients and/or tolerability of these drugs in this review. These issues are the subjects of a complementary Cochrane review by Barbui et al (in preparation)

Implications for research

Trials comparing two or more active treatments need to be much larger than the studies that we identified for this review. Primary outcome measures in trials need to be clinically meaningful. In summary, there is a need for large, simple trials with meaningful outcome measures and heterogeneous subjects to ensure that the results are reliable and relevant to as many future patients as possible.

NOTES

This review is currently being updated, and is being split into a number of separate reviews of head to head drug comparisons.

POTENTIAL CONFLICT OF INTEREST

JG has received research funding and support from Sanofi-Aventis and GlaxoSmithKline and is currently in discussion with several other companies that manufacture SSRIs about collaboration on planned independent trials and systematic reviews.

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TABLES

Characteristics of included studies

Study	Ahlfors 1988
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Endpoint Active Treatment: 4 weeks
Participants	Inclusion Criteria: 'patients of either sex... referred to a psychiatric hosptial for a depression requiring treatment' Age: 18-70 Country: Finland Setting: Inpatients & outpatients
Interventions	Citalopram versus mianserin
Outcomes	MADRS* Drop Out*

Characteristics of included studies (*Continued*)

Notes	* includes unpublished data
Allocation concealment	B

Study	**Amin 1984**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Intention to treat Active Treatment: 6 weeks
Participants	Inclusion Criteria: DSM III R Depression (Major depression single or recurrent episodes, bipolar disorder with or without melancholia), 15+ HMD Age: 18+ Country: Canada, USA, UK, Netherlands Setting: Inpatients & outpatients
Interventions	Fluvoxamine versus imipramine
Outcomes	HMD Drop Out
Notes	
Allocation concealment	B

Study	**Amore 1989**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Not Applicable Active Treatment: 4 weeks
Participants	Inclusion Criteria: DSM III R Major Depression without psychotic features. 21+ on 21 item HMD Age: 20-70 Country: Italy Setting: Inpatients
Interventions	Fluvoxamine versus imipramine
Outcomes	Drop Out
Notes	
Allocation concealment	B

Study	**Anonymous 1986**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Not Applicable Active Treatment: 5 weeks
Participants	Inclusion Criteria: HMD 18+ Age: 19-65 Country: Denmark Setting: Inpatients (some with outpatient follow up)
Interventions	Citalopram versus clomipramine
Outcomes	Drop Out
Notes	
Allocation concealment	B

Characteristics of included studies (*Continued*)

Study	**Anonymous 1988**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Endpoint Active Treatment: 6 weeks
Participants	Inclusion Criteria: DSM III major depressive episode, 17+ HMD Age: 16-70 Country: Wales Setting: Inpatients & outpatients
Interventions	Fluoxetine versus dothiepin
Outcomes	HMD Drop Out
Notes	
Allocation concealment	B

Study	**Anonymous 1990**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Endpoint Active Treatment: 6 weeks
Participants	Inclusion Criteria: DSM III R major depressive disorder, 18+ HMD, 9+ Hamilton depression subscale Age: 19-68 Country: Denmark Setting: Inpatient
Interventions	Paroxetine versus clomipramine
Outcomes	HMD* Drop Out
Notes	*Includes unpublished data
Allocation concealment	B

Study	**Ansseau 1994**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Intention to treat Active Treatment: 6 weeks
Participants	Inclusion Criteria: DSM III R moderate or severe major depression or bipolar disorder depressed, and 27+ MADRS Age: 24-79 Country: Belgium Setting: Inpatients
Interventions	Nefazodone versus amitriptyline
Outcomes	HMD Drop Out
Notes	
Allocation concealment	B

Study	**Arminen 1992**
Methods	Double Blind RCT

Characteristics of included studies (*Continued*)

	Concealment of Allocation: Unclear Analysis: Endpoint Active Treatment: 12 weeks
Participants	Inclusion Criteria: DSM III R major depression, 18+ HMD Age: 18-70 Country: Finland Setting: Inpatients
Interventions	Paroxetine versus imipramine
Outcomes	*HMD *Drop Out
Notes	Includes unpublished data
Allocation concealment	B

Study	**Barrelet 1991**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Intention to treat Active Treatment: 4 weeks
Participants	Inclusion Criteria: DSM III Major Depression, 18+ points on HMD Age: mean 54 years Country: Switzerland Setting: Inpatients & outpatients
Interventions	Fluvoxamine versus moclobemide
Outcomes	HMD Drop Out
Notes	
Allocation concealment	B

Study	**Bascara 1989**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Not Applicable Active Treatment: 6 weeks
Participants	Inclusion Criteria: DSM III R major depressive episode, 18+ HMD (21 item) Age: mean age 33 Country: Phillipines Setting: Not Clear
Interventions	Paroxetine versus amitriptyline
Outcomes	Drop Out
Notes	
Allocation concealment	B

Study	**Battegay 1985**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Intention to treat Active Treatment: 6 weeks

Characteristics of included studies (*Continued*)

Participants	Inclusion Criteria: DSM III R major depressive episode, 20+ HMD Age: 18-60 Country: Switzerland Setting: Outpatients
Interventions	Paroxetine versus amitryptline
Outcomes	HMD* Drop Out
Notes	* includes unpublished data
Allocation concealment	B

Study	**Beasley 1991**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Intention to treat Active Treatment: 6 weeks
Participants	Inclusion Criteria: DSM III criteria for nonpsychotic major depressive episode for 4 weeks, 20 + HMD(21), >20 HMD 21 at end of wash out period, and less than 20% improvement. Age: 18+ Country: US Setting: Outpatients
Interventions	Fluoxetine versus trazodone
Outcomes	HMD (21 item) Drop Out
Notes	
Allocation concealment	B

Study	**Beasley 1993a**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Intention to treat Active Treatment: 6 weeks
Participants	Inclusion Criteria: DSM III major depressive disorder, 20+ HMD (21 item), no more than 20% decrease in HMD during placebo week, Raskin score of at least 8, and higher than covi score Age: 18-70 Country: US Setting: Inpatients for at least 3 days
Interventions	Fluoxetine versus imipramine
Outcomes	HMD (21 item) Drop Out
Notes	
Allocation concealment	B

Study	**Beasley 1993b**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Intention to treat Active Treatment: 5 weeks

Characteristics of included studies (*Continued*)

Participants	Inclusion Criteria: RDC Major depressive disorder, 20+ HMD (21 item), no more than 20% decrease in HMD during placebo week, Raskin score of at least 8, and higher than Covi score Age: 21-70 Country: US & Canada Setting: Outpatients
Interventions	Fluoxetine versus amitriptyline
Outcomes	HMD Drop Out
Notes	
Allocation concealment	B

Study	**Benkert 1996**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Not Applicable Active Treatment: 6 weeks
Participants	Inclusion Criteria: Major Depression DSM III R. 30+ MADRS at baseline & symptoms of depression for at least 1 month. Age: 18-70 Country: Germany Setting: Inpatients
Interventions	Venlafaxine versus imipramine
Outcomes	Drop Out*
Notes	* Unpublished data
Allocation concealment	B

Study	**Bersani 1994**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Endpoint Active Treatment: 8 weeks
Participants	Inclusion Criteria: DSM III R, major depression Age: 21-69 Country: Italy Setting: Outpatients
Interventions	Sertraline versus amitriptyline
Outcomes	HMD (21 item) Drop Out
Notes	
Allocation concealment	B

Study	**Besancon 1993**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Endpoint Active Treatment: 8 weeks
Participants	Inclusion Criteria: DSM III major depressive episode, 25+ MADRS

Characteristics of included studies (*Continued*)

	Age: 18-65 Country: France Setting: Outpatients
Interventions	Fluoxetine versus mianserin
Outcomes	MADRS Drop Out
Notes	
Allocation concealment	B

Study	**Bocksberger 1993**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Endpoint Active Treatment: 4 weeks
Participants	Inclusion Criteria: DSM III R, major Depression, and 20+ MADRS Age: over 65 Country: Switzerland Setting: inpatient
Interventions	Fluvoxamine versus moclobemide
Outcomes	MADRS Drop Out
Notes	
Allocation concealment	B

Study	**Bouchard 1987**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Endpoint Active Treatment: 6 weeks
Participants	Inclusion Criteria: 'patients ...who suffered from a depression which required drug treatment', 15+ on the MADRS post wash out Age: 18-75 Country: France Setting: Inpatients for at least the first 2 weeks.
Interventions	Citalopram versus maprotiline
Outcomes	MADRS Drop Out
Notes	
Allocation concealment	B

Study	**Bougerol 1992**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Intention to treat Active Treatment: 4 weeks
Participants	Inclusion Criteria: DSM III R, major depression, 17+ on HMD Age: 18+ Country: Switzerland & France

	Setting: Inpatients & outpatients
Interventions	Fluvoxamine versus moclobemide
Outcomes	HMD Drop Out
Notes	
Allocation concealment	B

Study	**Bowden 1993**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Not Applicable Active Treatment: 6 weeks
Participants	Inclusion Criteria: DSM III R major depressive disorder, 20+ HMD (21) at admission to study, 18+ HMD (21) at begining of active treatment phase, less than a 20% decrease in HMD (21) during washout phase. Age: 18-60 Country: US Setting: Inpatients & outpatients
Interventions	Fluoxetine versus desiparmine
Outcomes	Drop Out
Notes	
Allocation concealment	B

Study	**Bramanti 1988**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Intention to treat Active Treatment: 4 weeks
Participants	Inclusion Criteria: DSM III R major depression, 18+ 21 item HMD Age: 18+ Country: Italy Setting: Not Clear
Interventions	Fluvoxamine versus imipramine.
Outcomes	HMD 21 item Drop Out
Notes	
Allocation concealment	B

Study	**Bremner 1994**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Endpoint Active Treatment: 5 weeks
Participants	Inclusion Criteria: RDC major depressive disorder, at least 'moderately depressed', 20+ HMD (version unclear), 8+ Raskin and greater than Covi. Age: 23-69 Country: US Setting: Outpatients

Characteristics of included studies (*Continued*)

Interventions	Fluoxetine versus imipramine
Outcomes	CGI Drop Out
Notes	
Allocation concealment	B

Study	**Byerley 1988**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Endpoint Active Treatment: 6 weeks
Participants	Inclusion Criteria: DSM III R major depression of at least 1 month 20+ HMD (21) Age: mean age 39 Country: US Setting: Outpatients
Interventions	Fluoxetine versus imipramine
Outcomes	HMD (21 item) Drop Out
Notes	
Allocation concealment	B

Study	**Cohn 1984**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Endpoint Active Treatment: 6 weeks
Participants	Inclusion Criteria: DSM III major depression, 18+ HMD, less than 20% reduction in HMD during washout period. Age: Mean 42 Country: US Setting: Outpatients
Interventions	Fluoxetine versus imipramine
Outcomes	HMD Drop out
Notes	
Allocation concealment	B

Study	**Cohn 1985**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Not Applicable Active Treatment: 6 weeks
Participants	Inclusion Criteria: DSM III R major depression for 1 month, 20+ HMD (version unclear) Age: 20-64 Country: US Setting: Outpatients

Characteristics of included studies (*Continued*)

Interventions	Fluoxetine versus imipramine
Outcomes	Drop Out
Notes	
Allocation concealment	B

Study	**Cohn 1989**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Not Applicable Active Treatment: 6 weeks
Participants	Inclusion Criteria: DSM III bipolar disorder, 20+ HMD (21), 8+ Raskin score, At least 1 distinct manic episode in last 5 years. Age: 18-70 Country: US Setting: Outpatients
Interventions	Fluoxetine versus imipramine
Outcomes	Drop Out
Notes	
Allocation concealment	B

Study	**Cohn 1990**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Endpoint Active Treatment: 8 weeks
Participants	Inclusion Criteria: DSM III R major depressive episode, 18+ HMD (17) without 25% reduction during washout, higher score on Raskin than Covi. Age: 65+ Country: US Setting: Outpatients
Interventions	Sertraline versus amitriptyline
Outcomes	HMD Drop Out
Notes	
Allocation concealment	B

Study	**Cohn 1990a**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Endpoint Active Treatment: 6 weeks
Participants	Inclusion Criteria: DSM III r major depressive disorder, recurrent or single episode 18 + HMD (no more than 20% improvement during washout period) Age: 18+ Country: US Setting: outpatients
Interventions	Paroxetine versus imipramine

Characteristics of included studies (*Continued*)

Outcomes	HMD* Drop Out*
Notes	*Includes unpublished data
Allocation concealment	D

Study	**Corne 1989**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Endpoint Active Treatment: 6 weeks
Participants	Inclusion Criteria: RDC primary unipolar major depressive disorder, 17+ HMD Age: 18-70 Country: UK Setting: Family practice
Interventions	Fluoxetine versus dothiepin
Outcomes	HMD Drop Out
Notes	
Allocation concealment	B

Study	**Cunningham 1994**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Not Applicable Active Treatment: 6 weeks
Participants	Inclusion Criteria: DSM III R major Depression, HMD 21 item 20+ Age: 18+ Country: USA + Canada Setting: Not Clear
Interventions	Venlafaxine versus trazodone
Outcomes	HMD (21 item)* Drop Out
Notes	* includes unpublished data
Allocation concealment	B

Study	**Dalery 1992**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Endpoint Active Treatment: 90 days
Participants	Inclusion Criteria: DSM III R major depressive disorder, single or recurrent episode Age: 18-70 Country: France Setting: Outpatients
Interventions	Fluoxetine versus amineptine
Outcomes	MADRS Drop Out

Notes	
Allocation concealment	B

Study	**De Wilde 1983**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Endpoint Active Treatment: 4 weeks
Participants	Inclusion Criteria: 4+ Feighner Criteria, 16+ HMD, Endogenously depressed Age: 18-70 Country: Belgium Setting: Outpatients
Interventions	Fluvoxamine versus clomipramine
Outcomes	HMD* Drop Out*
Notes	* includes unpublished data
Allocation concealment	D

Study	**De Wilde 1985**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Intention to treat Active Treatment: 6 weeks
Participants	Inclusion Criteria: RDC Endogenous depression or chronic dystymic disorder. 25+ on 10 item CPRS. Age: 18-70 Country: Belgium Setting: Inpatients
Interventions	Citalopram versus mainserin
Outcomes	CGI Drop Out
Notes	
Allocation concealment	B

Study	**Dick 1983**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Endpoint Active Treatment: 4 weeks
Participants	Inclusion Criteria: 16+ HMD, Persistent depressed mood accompanied by at least 5 Feighner Criteria Age: mean 49 Country: Switzerland Setting: Inpatients
Interventions	Fluvoxamine versus clomipramine
Outcomes	HMD Drop Out
Notes	
Allocation concealment	B

Characteristics of included studies (*Continued*)

Study	**Dominguez 1985**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Endpoint Active Treatment: 4 weeks
Participants	Inclusion Criteria: DSM III R major depressive disorder (single or recurrent), 15+ HMD Age: 21-65 Country: US Setting: Outpatients
Interventions	Fluvoxamine versus imipramine
Outcomes	CGI Drop Out
Notes	
Allocation concealment	B

Study	**Dorman 1992**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Endpoint Active Treatment: 6 weeks
Participants	Inclusion Criteria: DSM III R unipolar depression, 17+ HMD Age: 65+ Country: UK Setting: Outpatients
Interventions	Paroxetine versus mainserin
Outcomes	HMD* Drop Out
Notes	*Includes unpublished data
Allocation concealment	B

Study	**Dowling 1990**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Not Applicable Active Treatment: 6 weeks
Participants	Inclusion Criteria:DSM III major depressive disorder, unipolar illness. 17+ HMD (version unclear) Age: mean 43 Country: Eire Setting: Not Clear
Interventions	Fluoxetine versus dothiepin
Outcomes	Drop Out
Notes	
Allocation concealment	B

Study	**Fabre 1991**
Methods	Double Blind RCT Concealment of Allocation: Unclear

	Analysis: Not Applicable Active Treatment: 5 weeks
Participants	Inclusion Criteria: DSM III R major depression (single episode or recurrent), 18-27 HMD (number of items unclear) Age: 18-65 Country: US Setting: Outpatients
Interventions	Fluoxetine versus nortriptyline
Outcomes	Drop Out
Notes	
Allocation concealment	B

Study	**Falk 1989**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Intention to treat Active Treatment: 6 weeks
Participants	Inclusion Criteria: DSM III major depressive episode, unipolar either single or recurrent, current episode at least 4 weeks, 20+ 21 item HMD Age: 62+ Country: US Setting: Outpatients
Interventions	Fluoxetine versus trazodone
Outcomes	HMD (21 item) Drop Out
Notes	
Allocation concealment	B

Study	**Feighner 1985a**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Not Applicable Active Treatment: 6 weeks
Participants	Inclusion Criteria: DSM III R major depression, at least 1 month, 20+ HMD (number of items unclear) Age: 61+ Country: US Setting: Outpatients
Interventions	Fluoxetine versus doxepin
Outcomes	Drop Out
Notes	
Allocation concealment	B

Study	**Feighner 1989a**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Endpoint Active Treatment: 6 weeks
Participants	Inclusion Criteria: DSM III major depression, 20+ HMD (21), 8+ Raskin scale, and greater than Covi

Characteristics of included studies (*Continued*)

	Age: 18-70 Country: US Setting: Outpatients
Interventions	Fluoxetine versus imipramine
Outcomes	HMD (21 item) Drop Out
Notes	
Allocation concealment	B

Study	**Feighner 1989d**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Not Applicable Active Treatment: 6 weeks
Participants	Inclusion Criteria: RDC Endogenous Major Depression, DSM III Major Depression with Melancholia. 18+ HMD Age: 27-64 Country: US Setting: Outpatients
Interventions	Nefazodone versus imipramine
Outcomes	Drop Out
Notes	
Allocation concealment	B

Study	**Feighner 1993**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Not Applicable Active Treatment: 6 weeks
Participants	Inclusion Criteria: DSM III R major depressive episode, 18+ HMD, Raskin score higher than Covi score. Age: 18-65 Country: US Setting: Outpatients
Interventions	Paroxetine versus imipramine
Outcomes	Drop Out
Notes	
Allocation concealment	B

Study	**Ferreri 1989**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Not Applicable Active Treatment: 6 weeks
Participants	Inclusion Criteria: DSM III major depressive disorder, 18-25 HMD (21) Age: 18-65 Country: France Setting: Outpatients

Characteristics of included studies (*Continued*)

Interventions	Fluoxetine versus amineptine
Outcomes	Drop Out
Notes	
Allocation concealment	B

Study	**Fontaine 1994**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Intention to treat Active Treatment: 6 weeks
Participants	Inclusion Criteria: RDC Major Depressive Disorder, 22+ HMD Age: 18-65 Country: Canada Setting: Outpatients
Interventions	Nefazodone versus imipramine
Outcomes	HMD* Drop Out
Notes	* unpublished data
Allocation concealment	B

Study	**Fudge 1990**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Endpoint Active Treatment: 6 weeks
Participants	Inclusion Criteria: DSM III Major depressive disorder unipolar affective illness, 20+ HMD (21) Age: 18+ Country: USA Setting: Outpatientsu
Interventions	Fluoxetine versus trazodone
Outcomes	HMD* Drop Out*
Notes	* Includes unpublished data
Allocation concealment	B

Study	**Gattaz 1995**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Intention to treat Active Treatment: 4 weeks
Participants	Inclusion Criteria: DSM III R Major Depression, and HMD 18 + Age: 18-65 Country: Germany Setting: Inpatients
Interventions	Fluoxetine versus moclobemide
Outcomes	HMD Drop Out

Notes	
Allocation concealment	B

Study	**Geerts 1994**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Endpoint Active Treatment: 6 weeks
Participants	Inclusion Criteria: DSM III R Major Depression without psychotic features. 17+ on 17 item HMD Age: 18 - 70 Country: Belgium Setting: inpatients & outpatients
Interventions	Fluoxetine versus moclobemide
Outcomes	HMD Drop Out
Notes	
Allocation concealment	B

Study	**Geretsegger 1995**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Endpoint Active Treatment: 6 weeks
Participants	Inclusion Criteria: DSM III R major depressive episode, 18+ HMD, Inpatient at least 3 weeks Age: 65+ Country: Germany & Austria Setting: Inpatient for at least 3 weeks
Interventions	Paroxetine versus amitriptyline
Outcomes	HMD* Drop Out
Notes	* Includes unpublished data
Allocation concealment	B

Study	**Ginestet 1989**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Not Clear Active Treatment: 8 weeks
Participants	Inclusion Criteria: DSM III major depressive disorder with melancholia, 20+ HMD 21 Age: 18-70 Country: France Setting: Inpatients
Interventions	Fluoxetine versus clomipramine.
Outcomes	HMD (21 item)
Notes	
Allocation concealment	B

Characteristics of included studies (*Continued*)

Study	**Gonella 1990**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Intention to treat Active Treatment: 4 weeks
Participants	Inclusion Criteria: DSM III R major depressive episode, 15+ HMD (21 item) Age: 20-70 Country: Italy Setting: Outpatients
Interventions	Fluvoxamine versus imipramine
Outcomes	HMD (21 item) Drop Out
Notes	
Allocation concealment	B

Study	**Gravem 1987**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Endpoint Active Treatment: 6 weeks
Participants	Inclusion Criteria: 'all patients .... can be regarded as severely depressed.' Age: 19-74 Country: Norway Setting: Inpatients & outpatients
Interventions	Citalopram versus amitriptyline
Outcomes	CGI Drop Out
Notes	
Allocation concealment	B

Study	**Guelfi 1983**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Endpoint Active Treatment: 4 weeks
Participants	Inclusion Criteria: Depressed patients 'with a clear and relatively persistent major depression', 25+ HMD (26 item) Age: Not Clear Country: France Setting: Inpatients
Interventions	Fluvoxamine versus imipramine
Outcomes	HMD (26 item) Drop Out
Notes	
Allocation concealment	B

Study	**Guillibert 1989**
Methods	Double Blind RCT

Characteristics of included studies (*Continued*)

	Concealment of Allocation: Unclear Analysis: Not Applicable Active Treatment: 6 weeks
Participants	Inclusion Criteria: DSM III R major depressive disorder, 20+ HMD (21 itemn) - declining less than 20% in washout period, Newcastle Scale score 6+ Age: 65+ Country: France Setting: Outpatients
Interventions	Paroxetine versus clomipramine
Outcomes	HMD* Drop Out
Notes	*Includes unpublished data
Allocation concealment	B

Study	**Harris 1991**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Endpoint Active Treatment: 6 weeks
Participants	Inclusion Criteria: DSM III R Major Depressive Episode, 17+ HMD Age: 18-65 Country: UK Setting: Outpatients
Interventions	Fluvoxamine versus amitriptyline
Outcomes	HMD Drop Out
Notes	
Allocation concealment	B

Study	**Hutchinson 1992**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Endpoint Active Treatment: 6 weeks
Participants	Inclusion Criteria: DSM III R major depressive episode, 18+ hmd (21 ITEM) Age: 65+ Country: UK Setting: Family practice
Interventions	Paroxetine versus amitriptyline.
Outcomes	HMD* Drop Out
Notes	*Includes unpublished data
Allocation concealment	B

Study	**Itil 1983**
Methods	Double Blind RCT Concealment of Allocation: Unclear

	Analysis: Endpoint Active Treatment: 4 weeks
Participants	Inclusion Criteria: RDC Major Affective Disorder Age: 21-68 Country: US Setting: Outpatients
Interventions	Fluvoxamine versus imipramine
Outcomes	HMD (16 item) Drop Out
Notes	
Allocation concealment	B

Study	**Judd 1993**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Endpoint Active Treatment: 6 weeks
Participants	Inclusion Criteria: DSM III R major depressive disorder, 1 month episode minimum, 17+ on HMD Age: 21-63 Country: Australia Setting: Inpatients and outpatients
Interventions	Fluoxetine versus amitriptyline
Outcomes	HMD Drop Out
Notes	
Allocation concealment	B

Study	**Kasper 1990**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Intention to treat Active Treatment: 4 weeks
Participants	Inclusion Criteria: Age: 28-71 Country: Germany Setting: Inpatients
Interventions	Fluvoxamine versus maprotiline
Outcomes	HMD (version unclear) Drop Out
Notes	Total sleep deprivation at day 1 and 8 for all patients (why?)
Allocation concealment	B

Study	**Keegan 1991**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Not Applicable Active Treatment: 6 weeks

Characteristics of included studies (*Continued*)

Participants	Inclusion Criteria: unipolar major depression on DSM III R or DIS, 20+ HMD (21) on entry to active treatment, and no more than 20% decrease during washout period, Raskin had to be higher than Covi Age: 18-70 Country: Canada Setting: Not Clear
Interventions	Fluoxetine versus amitriptyline
Outcomes	Drop Out
Notes	
Allocation concealment	B

Study	**Kerkhofs 1990**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Endpoint Active Treatment: 6 weeks
Participants	Inclusion Criteria: RDC, 17+ HMD (?) and less than 20% improvement during washout phase, Not receiving oxazepam within 5 days of sleep assessment. Age: 18-64 Country: Belgium Setting: Inpatient for at least part of time
Interventions	Fluoxetine versus amitriptyline
Outcomes	HMD (version unclear) Drop Out
Notes	
Allocation concealment	B

Study	**Klok 1981**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Endpoint Active Treatment: 4 weeks
Participants	Inclusion Criteria: 'vital depressive syndrom' comparable to endogenous depression, female Age: 23-66 Country: Netherlands Setting: Inpatients
Interventions	Fluvoxamine versus clomipramine
Outcomes	Drop Out HMD*
Notes	* Unpublished data
Allocation concealment	B

Study	**Kuha 1991**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Not Applicable Active Treatment: 5 weeks
Participants	Inclusion Criteria: RDC unipolar major depressive disorders, 17+ HMD, 8+ Raskin

	Age: 18-65 Country: Finland Setting: inpatients & outpatients
Interventions	Fluoxetine versus maprotiline
Outcomes	Drop Out
Notes	
Allocation concealment	B

Study	**Kuhs 1989**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Endpoint Active Treatment: 6 weeks
Participants	Inclusion Criteria: DSM III R major depressive illness, 18+ HMD (21 item) Age: 18-65 Country: Germany Setting: Inpatients
Interventions	Paroxetine versus amitriptyline.
Outcomes	HMD* Drop Out
Notes	* includes unpublished data
Allocation concealment	B

Study	**La Pia 1992**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Endpoint Active Treatment: 6 weeks
Participants	Inclusion Criteria: DSM III R major depressive disoders, 18+ HMD 21, 20+ Mini Mental State. Age: 60-80 Country: Italy Setting: Outpatients & inpatients
Interventions	Fluoxetine versus mianserin
Outcomes	HMD* Drop Out
Notes	* includes unpublished data
Allocation concealment	B

Study	**Laakmann 1988**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Endpoint Active Treatment: 5 weeks
Participants	Inclusion Criteria: depressive syndromes, 17+ HMD (17 item), 8+ raskin. Age: 19-74 Country: Germany Setting: Outpatients

Characteristics of included studies (*Continued*)

Interventions	Fluoxetine vs amitriptyline
Outcomes	HMD (21 item)* Drop Out*
Notes	* includes unpublished data
Allocation concealment	B

Study	**Laakmann 1991**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Endpoint Active Treatment: 6 weeks
Participants	Inclusion Criteria: ICD 9 Endogenous Depression, HMD 17+, Raskin 8+ Age: 18-70 Country: Germany Setting: Inpatients
Interventions	Fluoxetine versus amitriptyline
Outcomes	HMD* Drop Out*
Notes	Includes unpublished data
Allocation concealment	B

Study	**Lapierre 1987**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Endpoint Active Treatment: 6 weeks
Participants	Inclusion Criteria: DSM III R major depressive disorder, 15+ HMD Age: 20-69 Country: Canada Setting: Inpatients
Interventions	Fluvoxamine versus imipramine
Outcomes	HMD* Drop Out
Notes	* includes unpublished data
Allocation concealment	B

Study	**Laursen 1985**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Endpoint Active Treatment: 6 weeks
Participants	Inclusion Criteria: ICD 8 manic depressive psychoses, 15+ HMD Age: 18+ Country: Denmark Setting: Inpatients initially
Interventions	Paroxetine versus amitriptyline.

Outcomes	HMD Drop Out
Notes	
Allocation concealment	B

Study	**Levine 1989**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Not Applicable Active Treatment: 6 weeks
Participants	Inclusion Criteria: RDC major depressive illness, 17+ HMD (?) Age: Not Clear Country: UK Setting: Not Clear
Interventions	Fluoxetine versus imipramine
Outcomes	Drop Out
Notes	
Allocation concealment	B

Study	**Lonnqvist 1994**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Intention to treat Active Treatment: 6 weeks
Participants	Inclusion Criteria: DSM III R predominantly Major Depression, 16+ HMD Age: 18+ years Country: Finland Setting: Mostly outpatients
Interventions	Fluoxetine versus moclobemide
Outcomes	HMD Drop Out
Notes	
Allocation concealment	B

Study	**Lydiard 1989**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Endpoint Active Treatment: 6 weeks
Participants	Inclusion Criteria: DSM III R Major Depression, 22+ HMD Age: 18+ Country: US Setting: Outpatients
Interventions	Fluvoxamine versus imipramine
Outcomes	HMD* Drop Out*
Notes	* includes unpublished data

Allocation concealment	B

Study	**Mahapatra 1996**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Intention to treat Active Treatment: 6 weeks
Participants	Inclusion Criteria: DSM III R major depression with symptoms of depression for at least one month prior to study entry, at least 18 on HMD 21 item, minimum prestudy score of 23 on the Mini-Mental Status Examination Age: 64-87 Country: UK & Netherlands Setting: Inpatients, Outpatients, day treatment centre patients
Interventions	Venlafaxine versus dothiepin
Outcomes	HMD* Drop Out*
Notes	* includes unpublished data
Allocation concealment	D

Study	**Manna 1989**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Intention to treat Active Treatment: 6 weeks
Participants	Inclusion Criteria: DSM III major depressive disorder, 18+ HMD Age: mean 48 Country: Italy Setting: Inpatients
Interventions	Fluoxetine versus clomipramine
Outcomes	HMD
Notes	
Allocation concealment	B

Study	**March 1990**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Not Applicable Active Treatment: 6 weeks
Participants	Inclusion Criteria: DSM III R major affective disorder, illness duration 1-18 months, 22+ HMD Age: 18-67 Country: US Setting: Outpatients
Interventions	Fluvoxamine versus imipramine
Outcomes	Drop Out
Notes	
Allocation concealment	B

Characteristics of included studies (*Continued*)

Study	**Mertens 1988**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Intention to treat Active Treatment: 6 weeks
Participants	Inclusion Criteria: DSM III R major depressive episode - unipolar or bipolar, HMD (21 item) 18+ Age: 18-80 Country: Belgium Setting: Inpatient initially
Interventions	Paroxetine versus mianserin.
Outcomes	HMD (21 item) Drop Out
Notes	
Allocation concealment	B

Study	**Moller 1993**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Endpoint Active Treatment: 6 weeks
Participants	Inclusion Criteria: DSM III R major depression, 18+ HMD (21 item) Age: Not Clear Country: Germany + Hungary Setting: Inpatients
Interventions	Paroxetine versus amitriptyline
Outcomes	HMD Drop Out
Notes	
Allocation concealment	B

Study	**Moon 1994**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Not Applicable Active Treatment: 6 weeks
Participants	Inclusion Criteria: DSM IIIR Major Depressive Disorder, 18+ HMD, 16+ Hamilton Rating Scale for Anxiety, Age: 18-70 Country: England Setting: Family Practice
Interventions	Sertraline versus clomipramine
Outcomes	Drop Out
Notes	
Allocation concealment	B

Study	**Muijen 1988**
Methods	Double Blind RCT Concealment of Allocation: Unclear

Characteristics of included studies (*Continued*)

	Analysis: Endpoint Active Treatment: 6 weeks
Participants	Inclusion Criteria: RDC major depressive illness or bipolar illness depressive phase, 17+ HMD Age: 18-65 Country: UK Setting: Outpatients
Interventions	Fluoxetine versus mianserin
Outcomes	HMD Drop Out
Notes	
Allocation concealment	B

Study	**Mullin 1988**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Endpoint Active Treatment: 6 weeks
Participants	Inclusion Criteria: DSM III R major depressive episode, 17+ HMD Age: 18-70 Country: UK Setting: Outpatients
Interventions	Fluvoxamine versus dothiepin
Outcomes	HMD* Drop Out
Notes	* includes unpublished data
Allocation concealment	B

Study	**Nathan 1990**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Not Clear Active Treatment: 4 weeks
Participants	Inclusion Criteria: DSM III R major depressive episode, 15+ HMD, 7+ Rasking Severity of Depression Scale Age: mean 39.7 Country: US Setting: Inpatients
Interventions	Fluvoxamine versus desipramine
Outcomes	HMD
Notes	
Allocation concealment	B

Study	**Nielsen 1991**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Endpoint Active Treatment: 12 weeks*
Participants	Inclusion Criteria: DSM III Major depressive episode, 18+ HMD Age: 18-70

	Country: Denmark Setting: Inpatient & oupatients
Interventions	Paroxetine versus imipramine
Outcomes	HMD Drop Out
Notes	*Efficacy result at 4 weeks
Allocation concealment	B

Study	**Nielsen 1993**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Not Applicable Active Treatment: 8 weeks
Participants	Inclusion Criteria: DSM III major depressive disorder, Bech-Rafaelsen Melancholia Scale, 18+ HMD (21), remains 18+ after washout period, or less than 20% improvement. Age: 18-70 Country: Denmark Setting: Outpatients
Interventions	Fluoxetine versus imipramine
Outcomes	Drop Out
Notes	
Allocation concealment	B

Study	**Noguera 1991**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Intention to treat Active Treatment: 6 weeks
Participants	Inclusion Criteria: DSM III major unipolar depression, 17+ HMD, less than 20% reduction in hmd during washout period, 8+ Raskin, and > covi. Age: 18-65 Country: Spain Setting: Outpatients
Interventions	Fluoxetine versus clomipramine
Outcomes	HMD Drop Out
Notes	
Allocation concealment	B

Study	**Norton 1984**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Endpoint Active Treatment: 4 weeks
Participants	Inclusion Criteria: RDC for Major Depressive Disorder (probable or definite), 15+ HMD Age: 18-65 Country: UK

Characteristics of included studies (*Continued*)

	Setting: Outpatients
Interventions	Fluvoxamine versus imipramine
Outcomes	HMD* Drop Out
Notes	* includes unpublished data
Allocation concealment	B

Study	**Ohrberg 1992**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Endpoint Active Treatment: 6 weeks
Participants	Inclusion Criteria: Depressed patients of either sex requiring medical treatment Age: 18-70 Country: Denmark Setting: Outpatients
Interventions	Paroxetine versus imipramine
Outcomes	HMD* Drop Out
Notes	*Includes unpublished data
Allocation concealment	B

Study	**Ottevanger 1995**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Intention to treat Active Treatment: 4 weeks
Participants	Inclusion Criteria: Depression (Feighner Criteria), 17+ HMD, Age: mean 49 Country: Netherlands Setting: Inpatients
Interventions	Fluvoxamine versus clomipramine
Outcomes	HMD Drop Out
Notes	
Allocation concealment	B

Study	**Pakesch 1991**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Last observation carried forward Active Treatment: 4 weeks
Participants	Inclusion Criteria: Kielholz/Poeldinger scheme for depression, 11+ on 14 item HMD, 20% improvement in HMD during washout phase led to exclusion. Age: 19-79 Country: Germany Setting: Outpatients

Characteristics of included studies (*Continued*)

Interventions	Fluoxetine versus clomipramine
Outcomes	HMD* Drop Out*
Notes	* unpublished data
Allocation concealment	B

Study	**Pelicier 1993**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Not Applicable Active Treatment: 5 weeks
Participants	Inclusion Criteria: Reactive Depression according to Feighner criteria Age: 60+ Country: France Setting: Outpatients
Interventions	Paroxetine versus clomipramine
Outcomes	Drop Out
Notes	
Allocation concealment	B

Study	**Perez 1990**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Not Applicable Active Treatment: 6 weeks
Participants	Inclusion Criteria: DSM III R major depressive episode, 30+ MADRS Age: 18+ Country: UK Setting: Not Clear
Interventions	Fluvoxamine versus mianserin
Outcomes	Drop Out
Notes	
Allocation concealment	B

Study	**Peselow 1989**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Not Applicable Active Treatment: 6 weeks
Participants	Inclusion Criteria: DSM III R major depressive disorder, 18+ HMD, 9+ Raskin score, which is higher than covi score. Age: Not Clear Country: US Setting: Not Clear
Interventions	Paroxetine versus imipramine
Outcomes	Drop Out
Notes	

Allocation concealment	B

Study	**Peters 1990**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Endpoint Active Treatment: 5 weeks
Participants	Inclusion Criteria: 17+ HMD, 8+ Raskin, higher than Covi Age: 25-63 Country: Germany Setting: Outpatients
Interventions	Fluoxetine versus amitriptyline
Outcomes	HMD Drop Out
Notes	
Allocation concealment	B

Study	**Phanjoo 1991**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Endpoint Active Treatment: 6 weeks
Participants	Inclusion Criteria: DSM III R Major Depression, 30+ MADRS Age: 65+ Country: Scotland Setting: Inpatients & outpatients
Interventions	Fluvoxamine versus mianserin
Outcomes	MADRS* Drop Out
Notes	* includes unpublished data
Allocation concealment	B

Study	**Poelinger 1989**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Intention to treat Active Treatment: 4 weeks
Participants	Inclusion Criteria: Kielholz/Poeldinger scheme for depression, 14+ on 14 item HMD Age: 21-67 Country: Switzerland and Austria Setting: Outpatients & family practice
Interventions	Fluoxetine vs maprotiline
Outcomes	HMD (14 item) Drop Out
Notes	
Allocation concealment	B

Characteristics of included studies (*Continued*)

Study	**Rahman 1991**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Endpoint Active Treatment: 6 weeks
Participants	Inclusion Criteria: DSM III R Major Depression, 30+ MADRS Age: 65+ Country: UK Setting: Inpatients
Interventions	Fluvoxamine versus dothiepin
Outcomes	MADRS* Drop Out
Notes	* includes unpublished data
Allocation concealment	B

Study	**Ravindran 1995**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Endpoint Active Treatment: 8 weeks
Participants	Inclusion Criteria: DSM III R major depression (mild to moderate severity), 15+ on HMD Age: 18-65 Country: Canada Setting: Outpatients
Interventions	Sertraline versus desipramine
Outcomes	HMD* Drop Out
Notes	* includes unpublished data
Allocation concealment	B

Study	**Ravindran 1997**
Methods	Double-blind RCT
Participants	Patients with depression and associated anxiety MADRS score >20 and Clinical Anxiety score >11
Interventions	Paroxetine 20-40mg/day Clomipramine 75-150mg/day
Outcomes	MADRS CGI
Notes	
Allocation concealment	B

Study	**Reimherr 1990**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Intention to treat Active Treatment: 8 weeks

Characteristics of included studies (*Continued*)

Participants	Inclusion Criteria: DSM III R major depressive episode, 18+ HMD (18) without 25% reduction during washout, higher score on Raskin than Covi Age: 18-65 Country: US Setting: Outpatients
Interventions	Sertraline versus amitriptyline
Outcomes	HMD Drop Out
Notes	
Allocation concealment	B

Study	**Remick 1989**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Not Applicable Active Treatment: 6 weeks
Participants	Inclusion Criteria: DSM III major depressive disorder, 20+ HMD (21) (including after washout week) Age: mean 43 Country: Canada Setting: Outpatients & inpatients
Interventions	Fluoxetine versus doxepin
Outcomes	Drop Out
Notes	
Allocation concealment	B

Study	**Remick 1993**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Endpoint Active Treatment: 6 weeks
Participants	Inclusion Criteria: DSM III R major depressive disorder for 1 month minimum, 20+ HMD (21), 20% or below 20 on HMD after wash out led to exclusion. Age: 18-65 Country: Canada Setting: Outpatients & inpatients
Interventions	Fluoxetine versus desipramine
Outcomes	HMD (21 item)* Drop Out
Notes	* includes unpublished data
Allocation concealment	B

Study	**Remick 1994**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Intention to treat Active Treatment: 7 weeks
Participants	Inclusion Criteria: DSM III R major depressive episode, 20+ HMD

	Age: 18-65 Country: Canada Setting: Outpatients
Interventions	Fluvoxamine versus amitriptyline
Outcomes	HMD* Drop Out
Notes	* unpublished data
Allocation concealment	B

Study	**Reynaert 1995**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Endpoint Active Treatment: 6 weeks
Participants	Inclusion Criteria: DSM III R Major Depression, 16+ on 17 item HMD Age: mean 47 year Country: Belgium Setting: Inpatients & outpatientst
Interventions	Fluoxetine versus moclobemide
Outcomes	HMD Drop Out
Notes	
Allocation concealment	B

Study	**Rickels 1994**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Not Applicable Active Treatment: 8 weeks
Participants	Inclusion Criteria: 20+ HMD, DSM III R moderate to severe major depressive disorder or bipolar disorder depressed type but without rapid cycling. Age: 18+ Country: US Setting: Private psychiatric & family practice
Interventions	Nefazodone versus imipramine
Outcomes	Drop Out
Notes	
Allocation concealment	B

Study	**Robertson 1994**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Intention to treat Active Treatment: 6 weeks
Participants	Inclusion Criteria: DSM III R major depression, or bipolar disorder 18+ HMD Age: 18-70

	Country: UK Setting: Inpatients & outpatients
Interventions	Fluoxetine versus lofepramine
Outcomes	HMD Drop Out
Notes	
Allocation concealment	B

Study	**Ropert 1989**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Endpoint Active Treatment: 6 weeks
Participants	Inclusion Criteria: DSM III major depressive disorders, 18-25 HMD (21) Age: 18+ Country: France Setting: Outpatients
Interventions	Fluoxetine versus clomipramine
Outcomes	HMD (21 item) Drop Out
Notes	
Allocation concealment	B

Study	**Rosenberg 1994**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Intention to treat Active Treatment: 6 weeks
Participants	Inclusion Criteria: Assessed as being in need of antidepressant treatment, 14+ HMD Age: 18-65 Country: Denmark, Norway, Sweden, Finland. Setting: Family practice
Interventions	Citalopram 10 mg versus imipramine Citalopram 20 mg versus imipramine
Outcomes	HMD* Drop Out
Notes	* includes unpublished data Data combined across doses
Allocation concealment	B

Study	**Roth 1990**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Endpoint Active Treatment: 6 weeks
Participants	Inclusion Criteria: DSM III R major depressive epidosde, 22+ HMD Age: 18+

Characteristics of included studies (*Continued*)

	Country: USA Setting: Outpatients
Interventions	Fluvoxamine versus desipramine
Outcomes	HMD Drop Out
Notes	
Allocation concealment	B

Study	**Schweizer 1994**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Intention to treat Active Treatment: 6 weeks
Participants	Inclusion Criteria: DSM III R Major depression, 20+ 21 item HMD Age: 18+ Country: US Setting: Outpatients
Interventions	Venlafaxine versus imipramine
Outcomes	HMD (21 item) Drop Out
Notes	
Allocation concealment	B

Study	**Shaw 1986**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Intention to treat Active Treatment: 6 weeks
Participants	Inclusion Criteria: DSM III R major depressive illness. 18+ HMD Age: 18-70 Country: South Wales Setting: Inpatients & outpatients
Interventions	Citalopram versus amitriptyline.
Outcomes	HMD Drop Out
Notes	
Allocation concealment	B

Study	**Shillingford 1990**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Not Applicable Active Treatment: 6 weeks
Participants	Inclusion Criteria: DSM III R major depressive disorder, 18+ on HMD Age: Not Clear Country: UK Setting: Family practice

Characteristics of included studies (*Continued*)

Interventions	Paroxetine versus dothiepin
Outcomes	Drop Out
Notes	
Allocation concealment	B

Study	**Shrivastava 1994**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Intention to treat Active Treatment: 12 months
Participants	Inclusion Criteria: DSM III R Major depression Age: 18+ Country: US Setting: Outpatients
Interventions	Venlafaxine versus imipramine
Outcomes	CGI* Drop Out
Notes	*includes unpublished data
Allocation concealment	B

Study	**Staner 1995**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Intention to treat Active Treatment: 34 days
Participants	Inclusion Criteria: RDC major Depression, 18+ HMD Age: 18-65 Country: Belgium Setting: Inpatients
Interventions	Paroxetine versus amitriptyline
Outcomes	HMD Drop Out
Notes	
Allocation concealment	B

Study	**Stark 1985**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Intention to treat Active Treatment: 6 weeks
Participants	Inclusion Criteria: DSM III major depressive disorder for 4 weeks, 20+ HMD (21), less than 20% reduction in HMD during wash out period, 8+ on Raskin Scale, and greater than Covi scale. Age: 18-70 Country: US Setting: Outpatients
Interventions	Fluoxetine versus imipramine
Outcomes	HMD (21 item)

Characteristics of included studies (*Continued*)

	Drop Out
Notes	
Allocation concealment	B

Study	**Stott 1993**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Endpoint Active Treatment: 8 weeks
Participants	Inclusion Criteria: depression and associated anxiety, 16+ MADRS, 11+ Clinical Anxiety Scale Age: 18-65 Country: UK Setting: Family practice
Interventions	Paroxetine versus amitriptyline
Outcomes	MADRS* Drop Out
Notes	*Includes unpublished data
Allocation concealment	B

Study	**Stratta 1991**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Endpoint Active Treatment: 6 weeks
Participants	Inclusion Criteria: atypical depression Age: mean 35 Country: Italy Setting: Not Clear
Interventions	Fluoxetine versus imipramine
Outcomes	HMD (not clear which version) Drop Out
Notes	
Allocation concealment	B

Study	**Stuppaeck 1994**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Endpoint Active Treatment: 6 weeks
Participants	Inclusion Criteria: DSM III major depression, melancholic subtype, 18+ HMD (21item) Age: 18-65 Country: Austria & Germany Setting: Inpatients
Interventions	Paroxetine versus amitriptyline
Outcomes	HMD (21 item) Drop Out
Notes	

Allocation concealment	B

Study	**Tapani 1989**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Not Applicable Active Treatment: 5 weeks
Participants	Inclusion Criteria: RDC unipolar major depression, 17+ on HMD, Raskin at least 8, and equal or higher than Covi Age: 30-55 Country: Finland Setting: Inpatients & outpatients
Interventions	Fluoxetine versus doxepin
Outcomes	Drop Out
Notes	
Allocation concealment	B

Study	**Thompson 1991**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Not Applicable Active Treatment: 6 weeks
Participants	Inclusion Criteria: DSM III R major depressive disorder Age: Not clear Country: UK Setting: Not Clear
Interventions	Sertraline versus dothiepin
Outcomes	Drop Out
Notes	
Allocation concealment	B

Study	**Timmerman 1987**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Endpoint Active Treatment: 4 weeks
Participants	Inclusion Criteria: DSM III R major depressive disorder, 18+ HMD Age: 18-69 Country: Netherlands Setting: Inpatients (all women)
Interventions	Citalopram versus maprotiline
Outcomes	HMD Drop Out
Notes	
Allocation concealment	B

Characteristics of included studies (*Continued*)

Study	**Tollefson 1994**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Intention to treat Active Treatment: 8 weeks
Participants	Inclusion Criteria: DSM III R major depressive disorder (unipolar, non psychotic depressed) for 1 month + sub tag 'agitated' according to RDC, 14+ HMD at washout and for first 2 visits, 2+ score on at least 2 items on agitation rating scale. Age: 18-65 Country: US Setting: Outpatients
Interventions	Fluoxetine versus imipramine.
Outcomes	HMD Drop Out
Notes	
Allocation concealment	B

Study	**Upward 1988**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Not Applicable Active Treatment: 4 weeks
Participants	Inclusion Criteria: depressed patients Age: 24-63 Country: UK Setting: Outpatients
Interventions	Fluoxetine versus amitriptyline
Outcomes	Drop Out
Notes	
Allocation concealment	B

Study	**Williams 1993**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Endpoint Active Treatment: 6 weeks
Participants	Inclusion Criteria: DSM III R Major Depression, 17+ on 21 item HMD Age: 20-86 Country: New Zealand Setting: Not Clear
Interventions	Fluoxetine versus moclobemide
Outcomes	HMD* Drop Out
Notes	* unpublished data
Allocation concealment	B

Study	**Young 1987**
Methods	Double Blind RCT

	Concealment of Allocation: Unclear Analysis: Endpoint Active Treatment: 6 weeks
Participants	Inclusion Criteria: RDC moderately severe unipolar depression, 18+ HMD Age: 20-65 Country: UK Setting: Outpatients
Interventions	Fluoxetine versus amitriptyline
Outcomes	Drop Out HMD*
Notes	* unpublished data
Allocation concealment	B

Study	**de Jonghe 1991a**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Endpoint Active Treatment: 6 weeks
Participants	Inclusion Criteria: DSM III major depression without psychotic features, 18+ HMD (including after washout period), no more than 20% reductions in HMD during washout period Age: 18-70 Country: Netherlands Setting: Inpatients for first 3 weeks
Interventions	Fluoxetine versus maprotiline
Outcomes	HMD Drop Out
Notes	
Allocation concealment	B

Study	**de Jonghe 1991b**
Methods	Double Blind RCT Concealment of Allocation: Unclear Analysis: Endpoint Active Treatment: 6 weeks
Participants	Inclusion Criteria: DSM III R Major Depression or Dysthymic Disorder Age: 18-60 Country: Netherlands Setting: Outpatients
Interventions	Fluvoxamine versus maprotiline
Outcomes	HMD Drop Out
Notes	
Allocation concealment	B

HMD: Hamilton Depression Rating Scale- 17 item unless stated
MADRS: Montgomery & Asberg Depression Rating Scale
RDC: Research Diagnostic Criteria
CGI: Clinical Global Impression

Characteristics of excluded studies

Study	Reason for exclusion
Altamura 1989	No interpretable data available
Blanchard 1995	No interpretable data availalbe
Bressa 1989	No interpretable data available No address for correspondence
Chouinard 1985	Included in Beasley 1993b
De Wilde 1982	Repeated in De Wilde 1983
Debus 1988	Included in Beasley 1991
Doogan 1994	No interpretable data available
Dunbar 1991	Included in Feighner 1993
Entsuah 1994	Same study as Schwiezer 1994
Fairweather 1993	No interpretable data available
Feighner 1985b	Included in Beasley 1993b
Feighner 1989b	No interpretable data available
Feighner 1989c	Included in Feighner 1993
Fontaine 1991	No interpretable data available
Gagiano 1989	No interpretable data available
Guy 1984	No interpretable data available
Hewer 1994	No interpretable data available
Loeb 1989	No interpretable data available No address for correspondence
Masco 1985	Included in Beasley 1993b
Moon 1989	No interpretable data available
Perry 1989	Included in Beasley 1991
Taneri 1989	No interpretable data available No address for correspondence
Van Moffaert 1994	No interpretable data available

ANALYSES

Comparison 01. SSRIs versus alternative antidepressants

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Efficacy	98	9469	Weighted Mean Difference (Fixed) 95% CI	-0.06 [-0.28, 0.17]

Comparison 02. SSRIs versus tricyclic antidepressants

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Efficacy	66	6767	Weighted Mean Difference (Fixed) 95% CI	-0.09 [-0.37, 0.19]

Comparison 03. SSRI versus Tricyclics in Inpatients

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Efficacy	23	1347	Weighted Mean Difference (Fixed) 95% CI	0.13 [-0.36, 0.62]

Comparison 04. Tricyclics and related drugs versus SSRIs

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Efficacy	89	8478	Weighted Mean Difference (Fixed) 95% CI	-0.12 [-0.37, 0.13]

Comparison 05. SSRIs v. Tricyclics

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Drug efficacy by trial design	64	6674	Weighted Mean Difference (Fixed) 95% CI	-0.12 [-0.39, 0.16]

Comparison 06. SSRIs v. sedating/non-sedating tricyclic antidepressants

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 SSRIs v. TCAs group in sedating v. non-sedating categories	63	5571	Weighted Mean Difference (Fixed) 95% CI	-0.11 [-0.40, 0.18]

INDEX TERMS

Medical Subject Headings (MeSH)

Antidepressive Agents [*therapeutic use]; Depressive Disorder [*drug therapy]; Serotonin Uptake Inhibitors [*therapeutic use]

MeSH check words

Humans

COVER SHEET

Title	Selective serotonin reuptake inhibitors (SSRIs) versus other antidepressants for depression
Authors	Geddes JR, Freemantle N, Mason J, Eccles MP, Boynton J
Contribution of author(s)	Information not supplied by author
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Date new studies found but not yet included/excluded	Information not supplied by author
Date new studies found and included/excluded	Information not supplied by author
Date authors' conclusions section amended	Information not supplied by author
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GRAPHS AND OTHER TABLES

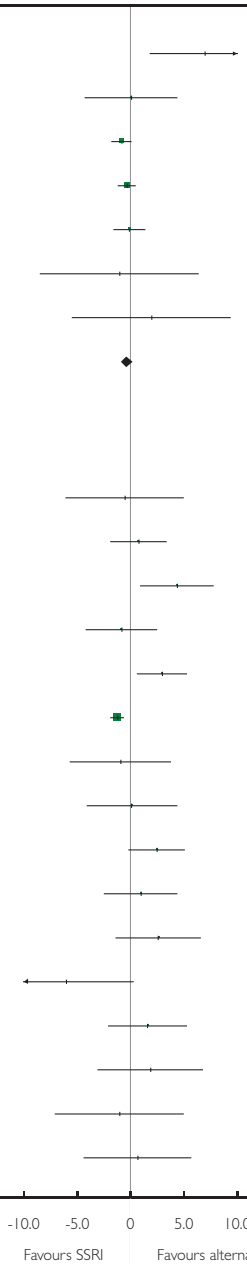
Analysis 01.01. Comparison 01 SSRIs versus alternative antidepressants, Outcome 01 Efficacy

Review: Selective serotonin reuptake inhibitors (SSRIs) versus other antidepressants for depression

Comparison: 01 SSRIs versus alternative antidepressants

Outcome: 01 Efficacy

Study	SSRI N	SSRI Mean(SD)	Alternative N	Alternative Mean(SD)	Weighted Mean Difference (Fixed) 95% CI	Weight (%)	Weighted Mean Difference (Fixed) 95% CI
01 Citalopram							
Ahlfors 1988	37	20.00 (12.00)	34	13.00 (10.00)		0.2	7.00 [1.88, 12.12]
Bouchard 1987	39	9.50 (10.30)	34	9.40 (8.50)		0.3	0.10 [-4.21, 4.41]
De Wilde 1985	29	1.20 (1.60)	29	2.00 (2.00)		5.9	-0.80 [-1.73, 0.13]
Gravem 1987	12	1.92 (1.08)	14	2.21 (1.05)		7.6	-0.29 [-1.11, 0.53]
Rosenberg 1994	380	10.65 (6.80)	85	10.70 (6.40)		2.2	-0.05 [-1.57, 1.47]
Shaw 1986	24	11.50 (14.00)	20	12.50 (11.20)		0.1	-1.00 [-8.45, 6.45]
Timmerman 1987	14	16.60 (9.70)	13	14.60 (10.10)		0.1	2.00 [-5.48, 9.48]
Subtotal (95% CI)	535		229			16.4	-0.34 [-0.90, 0.22]
Test for heterogeneity chi-square=9.42 df=6 p=0.15 I =36.3%							
Test for overall effect z=1.19 p=0.2							
02 Fluoxetine							
Anonymous 1988	16	9.50 (8.00)	21	10.00 (9.20)		0.2	-0.50 [-6.05, 5.05]
Beasley 1991	63	11.20 (7.20)	57	10.40 (7.70)		0.7	0.80 [-1.88, 3.48]
Beasley 1993a	54	19.50 (9.90)	60	15.10 (9.00)		0.4	4.40 [0.91, 7.89]
Beasley 1993b	65	15.60 (9.90)	71	16.40 (10.30)		0.4	-0.80 [-4.20, 2.60]
Besancon 1993	33	11.00 (4.50)	32	8.00 (5.00)		1.0	3.00 [0.69, 5.31]
Bremner 1994	16	1.69 (0.87)	19	2.89 (0.94)		14.2	-1.20 [-1.80, -0.60]
Byerley 1988	20	12.80 (7.70)	24	13.70 (8.50)		0.2	-0.90 [-5.69, 3.89]
Cohn 1984	35	14.72 (8.81)	31	14.54 (8.85)		0.3	0.18 [-4.09, 4.45]
Corne 1989	34	11.60 (6.20)	44	9.10 (5.80)		0.7	2.50 [-0.20, 5.20]
Dalery 1992	73	10.50 (12.40)	68	9.50 (8.50)		0.4	1.00 [-2.49, 4.49]
de Jonghe 1991a	28	19.00 (8.34)	34	16.38 (7.60)		0.3	2.62 [-1.39, 6.63]
Falk 1989	13	10.08 (7.57)	12	16.08 (8.53)		0.1	-6.00 [-12.34, 0.34]
Feighner 1989a	52	17.69 (9.20)	45	16.04 (9.20)		0.4	1.65 [-2.02, 5.32]
Fudge 1990	17	8.40 (9.00)	15	6.50 (5.10)		0.2	1.90 [-3.10, 6.90]
Gattaz 1995	34	12.00 (12.00)	36	13.00 (14.00)		0.1	-1.00 [-7.10, 5.10]
Geerts 1994	13	9.80 (6.20)	15	9.10 (7.30)		0.2	0.70 [-4.30, 5.70]



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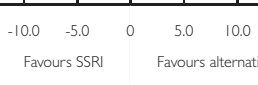
Study	SSRI N	SSRI Mean(SD)	Alternative N	Alternative Mean(SD)	Weighted Mean Difference (Fixed) 95% CI	Weight (%)	Weighted Mean Difference (Fixed) 95% CI
Ginestet 1989	28	10.40 (7.20)	26	5.30 (3.40)		0.6	5.10 [2.13, 8.07]
Judd 1993	23	9.60 (6.20)	23	11.60 (6.00)		0.4	-2.00 [-5.53, 1.53]
Kerkhofs 1990	9	8.44 (6.20)	10	9.80 (4.60)		0.2	-1.36 [-6.31, 3.59]
La Pia 1992	19	14.52 (6.65)	16	16.37 (4.92)		0.3	-1.85 [-5.69, 1.99]
Laakmann 1988	39	9.60 (6.30)	46	6.70 (4.70)		0.9	2.90 [0.50, 5.30]
Laakmann 1991	62	9.65 (7.86)	62	9.47 (7.56)		0.7	0.18 [-2.53, 2.89]
Lonnqvist 1994	107	10.60 (6.00)	102	9.60 (5.50)		2.1	1.00 [-0.56, 2.56]
Manna 1989	15	8.50 (5.00)	15	10.00 (5.00)		0.4	-1.50 [-5.08, 2.08]
Muijen 1988	14	10.50 (7.50)	14	14.50 (10.20)		0.1	-4.00 [-10.63, 2.63]
Noguera 1991	60	10.12 (8.66)	60	13.20 (9.09)		0.5	-3.08 [-6.26, 0.10]
Pakesch 1991	91	7.93 (6.19)	48	7.86 (7.52)		0.8	0.07 [-2.41, 2.55]
Peters 1990	40	11.00 (9.00)	41	10.00 (6.00)		0.5	1.00 [-2.34, 4.34]
Poelinger 1989	73	9.00 (8.00)	69	11.00 (8.00)		0.7	-2.00 [-4.63, 0.63]
Remick 1993	24	13.04 (8.20)	15	6.93 (5.92)		0.3	6.11 [1.67, 10.55]
Reynaert 1995	42	12.90 (9.00)	38	12.20 (7.60)		0.4	0.70 [-2.94, 4.34]
Robertson 1994	76	14.10 (7.20)	77	13.20 (6.80)		1.0	0.90 [-1.32, 3.12]
Ropert 1989	55	8.20 (4.50)	48	9.60 (5.30)		1.4	-1.40 [-3.31, 0.51]
Stark 1985	185	16.50 (10.10)	186	16.20 (10.10)		1.2	0.30 [-1.76, 2.36]
Stratta 1991	14	7.10 (4.80)	9	7.40 (11.70)		0.1	-0.30 [-8.35, 7.75]
Tollefson 1994	62	11.60 (7.60)	62	12.20 (7.90)		0.7	-0.60 [-3.33, 2.13]
Williams 1993	45	8.62 (7.27)	47	7.80 (6.67)		0.6	0.82 [-2.03, 3.67]
Young 1987	25	11.96 (5.24)	25	11.32 (6.76)		0.5	0.64 [-2.71, 3.99]
Subtotal (95% CI)	1674		1623			34.4	-0.15 [-0.53, 0.24]
Test for heterogeneity chi-square=78.32 df=37 p=<0.00011 =52.8%							
Test for overall effect z=0.75 p=0.5							
03 Fluvoxamine							
Amin 1984	105	13.90 (8.90)	106	14.90 (8.80)		0.9	-1.00 [-3.39, 1.39]
Barrelet 1991	30	11.00 (10.00)	31	9.40 (8.20)		0.2	1.60 [-3.00, 6.20]
Bocksberger 1993	18	23.50 (14.20)	18	11.90 (10.10)		0.1	11.60 [3.55, 19.65]
Bougerol 1992	63	13.02 (8.18)	67	12.71 (8.00)		0.7	0.31 [-2.47, 3.09]
Bramanti 1988	28	14.10 (4.83)	29	11.45 (4.28)		0.9	2.65 [0.28, 5.02]
de Jonghe 1991b	21	13.60 (6.10)	21	13.70 (7.80)		0.3	-0.10 [-4.34, 4.14]
De Wilde 1983	15	7.90 (6.70)	15	11.10 (8.50)		0.2	-3.20 [-8.68, 2.28]



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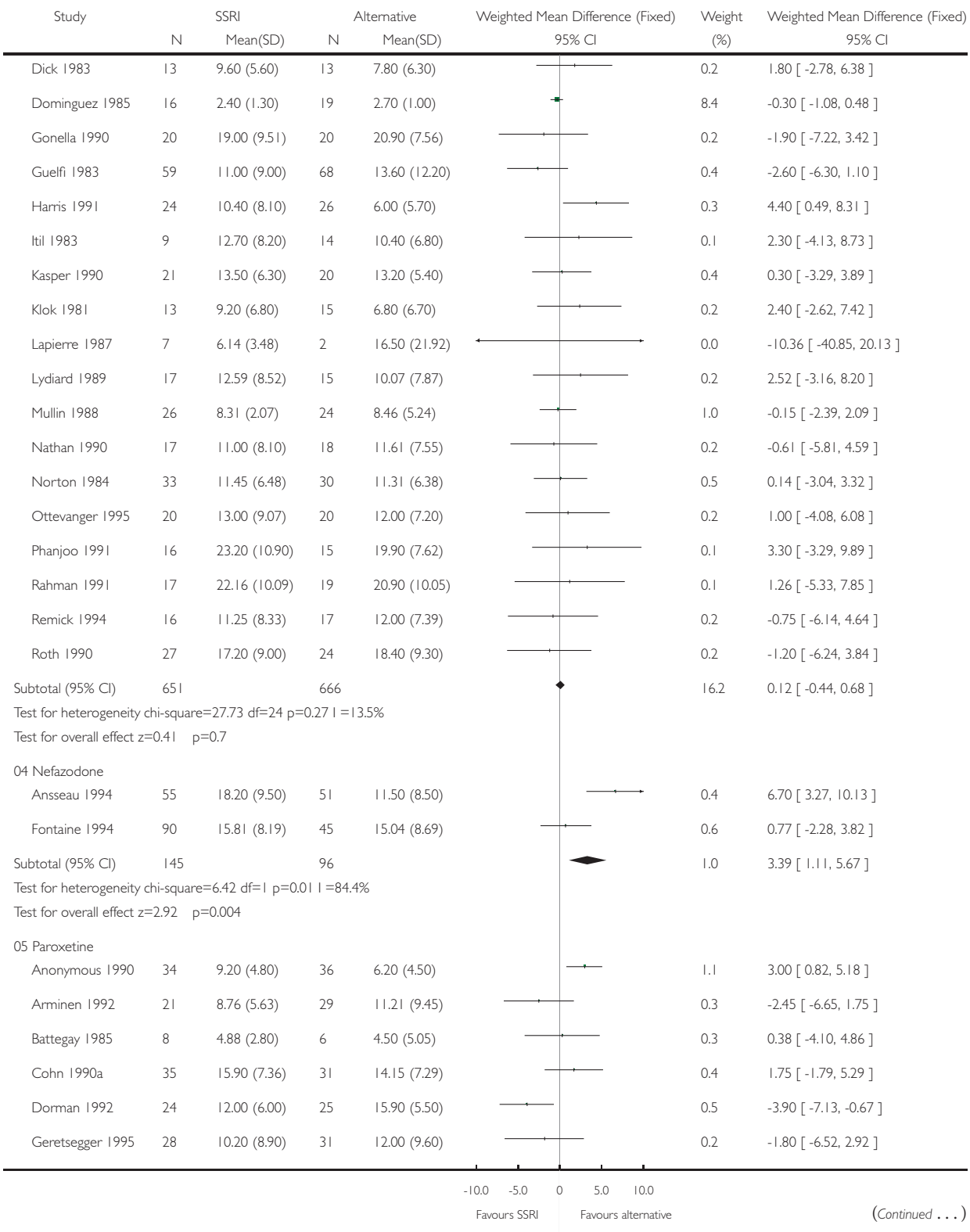

Study	SSRI N	SSRI Mean(SD)	Alternative N	Alternative Mean(SD)	Weighted Mean Difference (Fixed) 95% CI	Weight (%)	Weighted Mean Difference (Fixed) 95% CI
Dick 1983	13	9.60 (5.60)	13	7.80 (6.30)		0.2	1.80 [-2.78, 6.38]
Dominguez 1985	16	2.40 (1.30)	19	2.70 (1.00)		8.4	-0.30 [-1.08, 0.48]
Gonella 1990	20	19.00 (9.51)	20	20.90 (7.56)		0.2	-1.90 [-7.22, 3.42]
Guelfi 1983	59	11.00 (9.00)	68	13.60 (12.20)		0.4	-2.60 [-6.30, 1.10]
Harris 1991	24	10.40 (8.10)	26	6.00 (5.70)		0.3	4.40 [0.49, 8.31]
Itil 1983	9	12.70 (8.20)	14	10.40 (6.80)		0.1	2.30 [-4.13, 8.73]
Kasper 1990	21	13.50 (6.30)	20	13.20 (5.40)		0.4	0.30 [-3.29, 3.89]
Klok 1981	13	9.20 (6.80)	15	6.80 (6.70)		0.2	2.40 [-2.62, 7.42]
Lapierre 1987	7	6.14 (3.48)	2	16.50 (21.92)		0.0	-10.36 [-40.85, 20.13]
Lydiard 1989	17	12.59 (8.52)	15	10.07 (7.87)		0.2	2.52 [-3.16, 8.20]
Mullin 1988	26	8.31 (2.07)	24	8.46 (5.24)		1.0	-0.15 [-2.39, 2.09]
Nathan 1990	17	11.00 (8.10)	18	11.61 (7.55)		0.2	-0.61 [-5.81, 4.59]
Norton 1984	33	11.45 (6.48)	30	11.31 (6.38)		0.5	0.14 [-3.04, 3.32]
Ottevanger 1995	20	13.00 (9.07)	20	12.00 (7.20)		0.2	1.00 [-4.08, 6.08]
Phanjoo 1991	16	23.20 (10.90)	15	19.90 (7.62)		0.1	3.30 [-3.29, 9.89]
Rahman 1991	17	22.16 (10.09)	19	20.90 (10.05)		0.1	1.26 [-5.33, 7.85]
Remick 1994	16	11.25 (8.33)	17	12.00 (7.39)		0.2	-0.75 [-6.14, 4.64]
Roth 1990	27	17.20 (9.00)	24	18.40 (9.30)		0.2	-1.20 [-6.24, 3.84]
Subtotal (95% CI)	651		666			16.2	0.12 [-0.44, 0.68]
Test for heterogeneity chi-square=27.73 df=24 p=0.27 I =13.5%							
Test for overall effect z=0.41 p=0.7							
04 Nefazodone							
Ansseau 1994	55	18.20 (9.50)	51	11.50 (8.50)		0.4	6.70 [3.27, 10.13]
Fontaine 1994	90	15.81 (8.19)	45	15.04 (8.69)		0.6	0.77 [-2.28, 3.82]
Subtotal (95% CI)	145		96			1.0	3.39 [1.11, 5.67]
Test for heterogeneity chi-square=6.42 df=1 p=0.01 I =84.4%							
Test for overall effect z=2.92 p=0.004							
05 Paroxetine							
Anonymous 1990	34	9.20 (4.80)	36	6.20 (4.50)		1.1	3.00 [0.82, 5.18]
Arminen 1992	21	8.76 (5.63)	29	11.21 (9.45)		0.3	-2.45 [-6.65, 1.75]
Battegay 1985	8	4.88 (2.80)	6	4.50 (5.05)		0.3	0.38 [-4.10, 4.86]
Cohn 1990a	35	15.90 (7.36)	31	14.15 (7.29)		0.4	1.75 [-1.79, 5.29]
Dorman 1992	24	12.00 (6.00)	25	15.90 (5.50)		0.5	-3.90 [-7.13, -0.67]
Geretsegger 1995	28	10.20 (8.90)	31	12.00 (9.60)		0.2	-1.80 [-6.52, 2.92]

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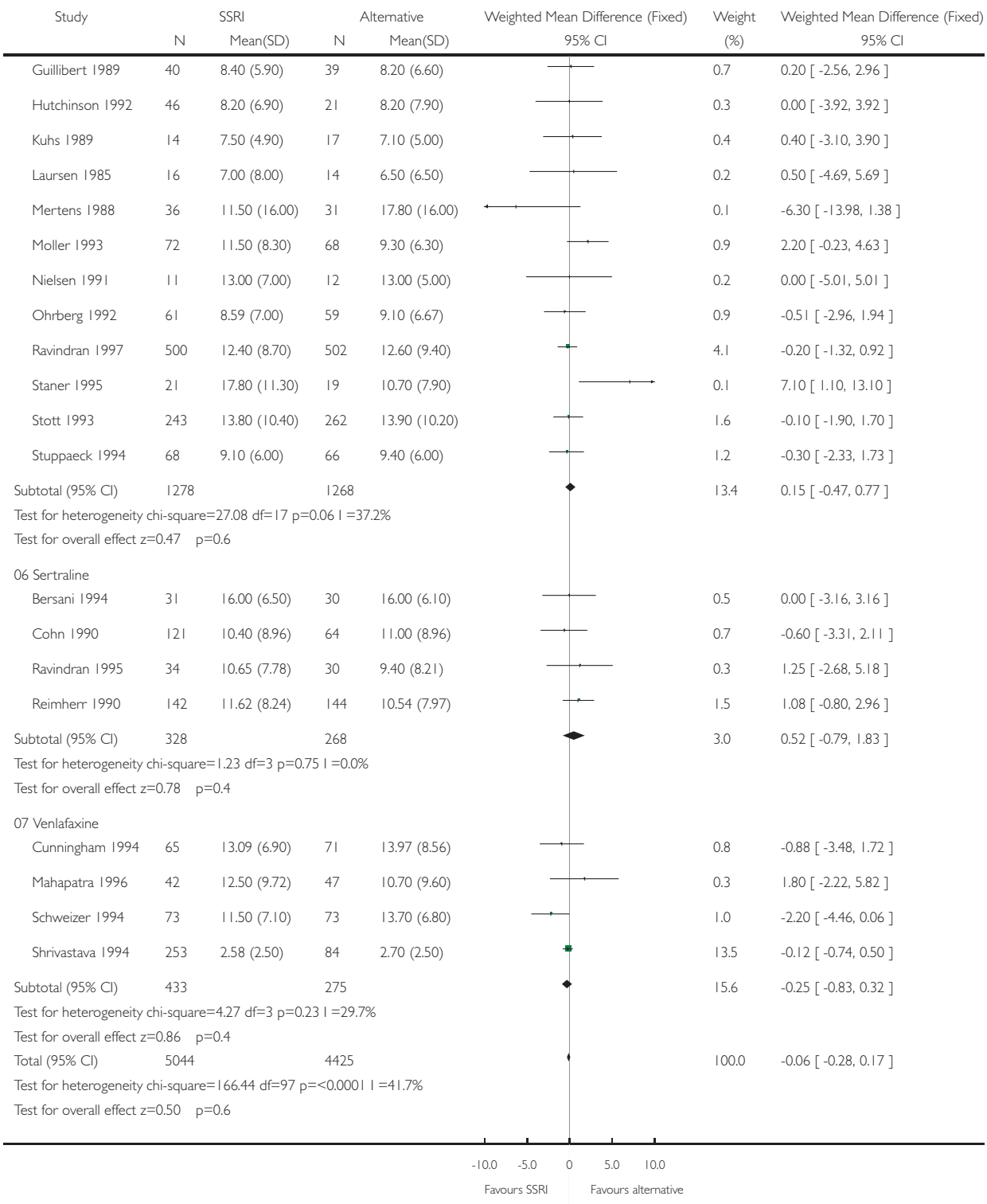


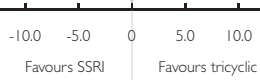
Analysis 02.01. Comparison 02 SSRIs versus tricyclic antidepressants, Outcome 01 Efficacy

Review: Selective serotonin reuptake inhibitors (SSRIs) versus other antidepressants for depression

Comparison: 02 SSRIs versus tricyclic antidepressants

Outcome: 01 Efficacy

Study	N	Mean(SD)	N	Mean(SD)	Weighted Mean Difference (Fixed) 95% CI	Weight (%)	Weighted Mean Difference (Fixed) 95% CI
01 Citalopram							
Gravem 1987	12	1.92 (1.08)	14	2.21 (1.05)		11.3	-0.29 [-1.11, 0.53]
Rosenberg 1994	380	10.65 (6.80)	85	10.70 (6.40)		3.3	-0.05 [-1.57, 1.47]
Shaw 1986	24	11.50 (14.00)	20	12.50 (11.20)		0.1	-1.00 [-8.45, 6.45]
Subtotal (95% CI)	416		119			14.8	-0.24 [-0.96, 0.48]
Test for heterogeneity chi-square=0.11 df=2 p=0.94 I =0.0%							
Test for overall effect z=0.66 p=0.5							
02 Fluoxetine							
Anonymous 1988	16	9.50 (8.00)	21	10.00 (9.20)		0.2	-0.50 [-6.05, 5.05]
Beasley 1993a	54	19.50 (9.90)	60	15.10 (9.00)		0.6	4.40 [0.91, 7.89]
Beasley 1993b	65	15.60 (9.90)	71	16.40 (10.30)		0.7	-0.80 [-4.20, 2.60]
Bremner 1994	16	1.69 (0.87)	19	2.89 (0.94)		21.3	-1.20 [-1.80, -0.60]
Byerley 1988	20	12.80 (7.70)	24	13.70 (8.50)		0.3	-0.90 [-5.69, 3.89]
Cohn 1984	35	14.72 (8.81)	31	14.54 (8.85)		0.4	0.18 [-4.09, 4.45]
Corne 1989	34	11.60 (6.20)	44	9.10 (5.80)		1.1	2.50 [-0.20, 5.20]
Dalery 1992	73	10.50 (12.40)	68	9.50 (8.50)		0.6	1.00 [-2.49, 4.49]
Feighner 1989a	52	17.69 (9.20)	45	16.04 (9.20)		0.6	1.65 [-2.02, 5.32]
Ginestet 1989	28	10.40 (7.20)	26	5.30 (3.40)		0.9	5.10 [2.13, 8.07]
Judd 1993	23	9.60 (6.20)	23	11.60 (6.00)		0.6	-2.00 [-5.53, 1.53]
Kerkhofs 1990	9	8.44 (6.20)	10	9.80 (4.60)		0.3	-1.36 [-6.31, 3.59]
Laakmann 1988	39	9.60 (6.30)	46	6.70 (4.70)		1.3	2.90 [0.50, 5.30]
Laakmann 1991	62	9.65 (7.86)	62	9.47 (7.56)		1.0	0.18 [-2.53, 2.89]
Manna 1989	15	8.50 (5.00)	15	10.00 (5.00)		0.6	-1.50 [-5.08, 2.08]
Noguera 1991	60	10.12 (8.66)	60	13.20 (9.09)		0.8	-3.08 [-6.26, 0.10]
Pakesch 1991	91	7.93 (6.19)	48	7.86 (7.52)		1.2	0.07 [-2.41, 2.55]
Peters 1990	40	11.00 (9.00)	41	10.00 (6.00)		0.7	1.00 [-2.34, 4.34]
Remick 1993	24	13.04 (8.20)	15	6.93 (5.92)		0.4	6.11 [1.67, 10.55]
Robertson 1994	76	14.10 (7.20)	77	13.20 (6.80)		1.6	0.90 [-1.32, 3.12]



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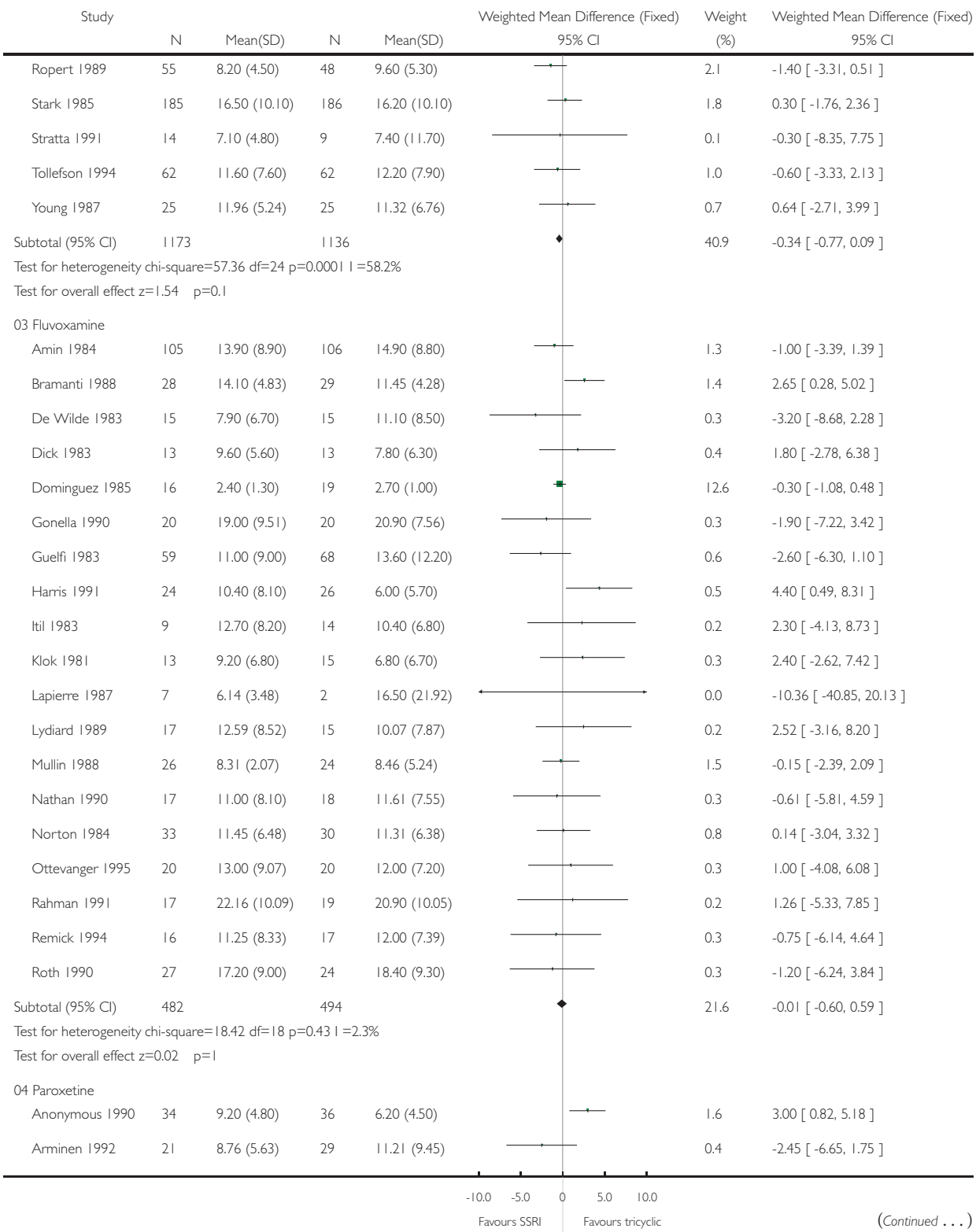

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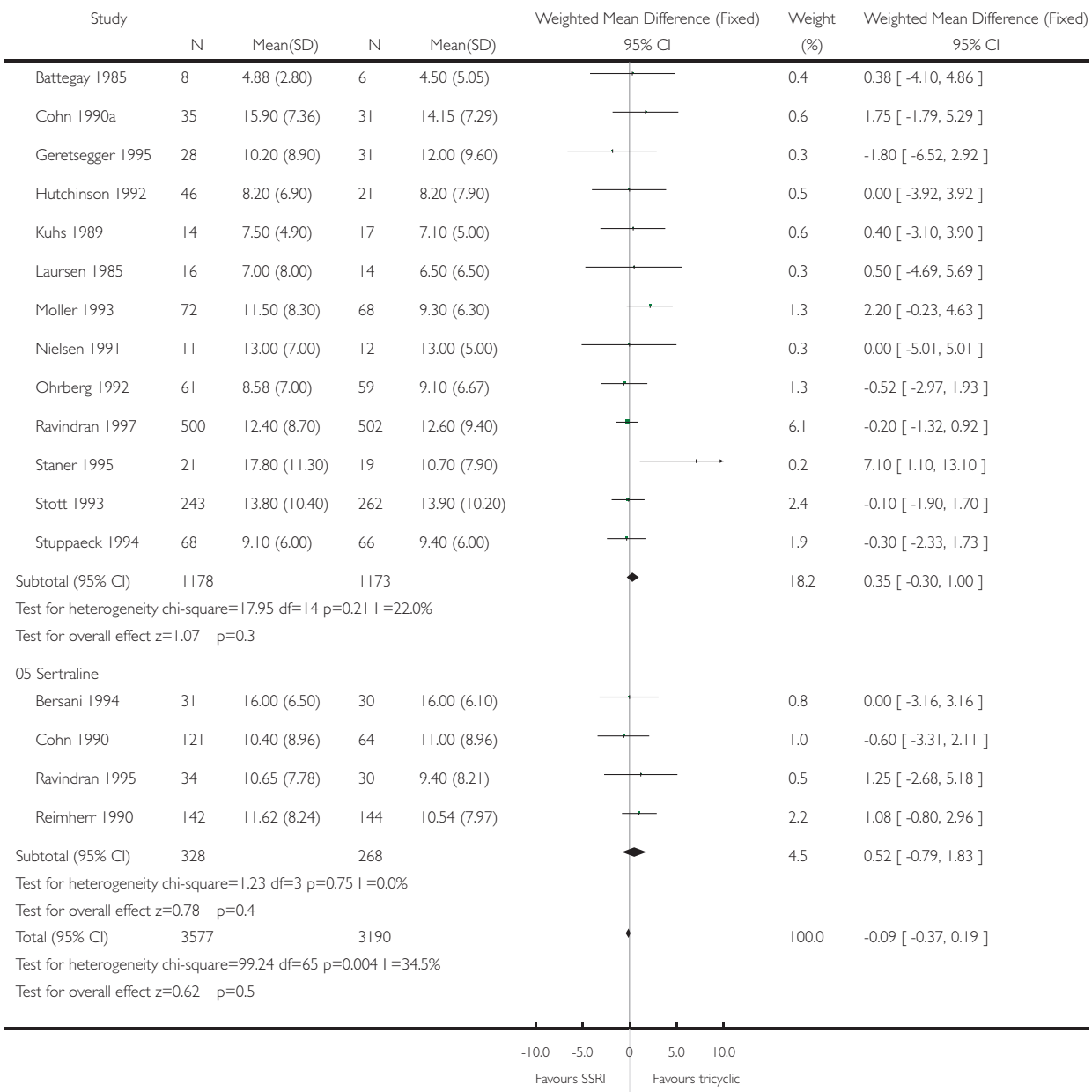

Analysis 03.01. Comparison 03 SSRI versus Tricyclics in Inpatients, Outcome 01 Efficacy

Review: Selective serotonin reuptake inhibitors (SSRIs) versus other antidepressants for depression

Comparison: 03 SSRI versus Tricyclics in Inpatients

Outcome: 01 Efficacy

Study	N	Mean(SD)	N	Mean(SD)	Weighted Mean Difference (Fixed) 95% CI	Weight (%)	Weighted Mean Difference (Fixed) 95% CI
01 Citalopram							
De Wilde 1985	29	1.20 (1.60)	29	2.00 (2.00)		27.2	-0.80 [-1.73, 0.13]
Gravem 1987	12	1.92 (1.08)	14	2.21 (1.05)		35.0	-0.29 [-1.11, 0.53]
Subtotal (95% CI)	41		43			62.2	-0.51 [-1.13, 0.10]
Test for heterogeneity chi-square=0.65 df=1 p=0.42 I =0.0%							
Test for overall effect z=1.63 p=0.1							
02 Fluoxetine							
Beasley 1993a	54	19.50 (9.90)	60	15.10 (9.00)		1.9	4.40 [0.91, 7.89]
Ginestet 1989	28	10.40 (7.20)	26	5.30 (3.40)		2.7	5.10 [2.13, 8.07]
Kerkhofs 1990	9	8.44 (6.20)	10	9.80 (4.60)		1.0	-1.36 [-6.31, 3.59]
Laakmann 1991	62	9.65 (7.86)	62	9.47 (7.56)		3.2	0.18 [-2.53, 2.89]
Manna 1989	15	8.50 (5.00)	15	10.00 (5.00)		1.8	-1.50 [-5.08, 2.08]
Subtotal (95% CI)	168		173			10.6	1.76 [0.27, 3.25]
Test for heterogeneity chi-square=13.07 df=4 p=0.011 =69.4%							
Test for overall effect z=2.31 p=0.02							
03 Fluvoxamine							
Dick 1983	13	9.60 (5.60)	13	7.80 (6.30)		1.1	1.80 [-2.78, 6.38]
Guelfi 1983	59	11.00 (9.00)	68	13.60 (12.20)		1.7	-2.60 [-6.30, 1.10]
Klok 1981	13	9.20 (6.80)	15	6.80 (6.70)		0.9	2.40 [-2.62, 7.42]
Lapierre 1987	7	6.14 (3.48)	2	16.50 (21.92)		0.0	-10.36 [-40.85, 20.13]
Nathan 1990	17	11.00 (8.10)	18	11.61 (7.55)		0.9	-0.61 [-5.81, 4.59]
Ottevanger 1995	20	13.00 (9.07)	20	12.00 (7.20)		0.9	1.00 [-4.08, 6.08]
Rahman 1991	17	22.16 (10.09)	19	10.90 (10.05)		0.5	11.26 [4.67, 17.85]
Subtotal (95% CI)	146		155			6.2	0.98 [-0.98, 2.94]
Test for heterogeneity chi-square=14.27 df=6 p=0.031 =58.0%							
Test for overall effect z=0.98 p=0.3							
04 Paroxetine							
Anonymous 1990	34	9.20 (4.80)	36	6.20 (4.50)		5.0	3.00 [0.82, 5.18]
Arminen 1992	21	8.76 (5.63)	29	11.21 (9.45)		1.3	-2.45 [-6.65, 1.75]
Geretsegger 1995	28	10.20 (8.90)	31	12.00 (9.60)		1.1	-1.80 [-6.52, 2.92]

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Study	SSRI N	SSRI Mean(SD)	tricyclic N	tricyclic Mean(SD)	Weighted Mean Difference (Fixed) 95% CI	Weight (%)	Weighted Mean Difference (Fixed) 95% CI
Kuhs 1989	14	7.50 (4.90)	17	7.10 (5.00)		1.9	0.40 [-3.10, 3.90]
Laursen 1985	16	7.00 (8.00)	14	6.50 (6.50)		0.9	0.50 [-4.69, 5.69]
Mertens 1988	36	11.50 (16.00)	31	17.80 (16.00)		0.4	-6.30 [-13.98, 1.38]
Moller 1993	72	11.50 (8.30)	68	9.30 (6.30)		4.0	2.20 [-0.23, 4.63]
Staner 1995	21	17.80 (11.30)	19	10.70 (7.90)		0.7	7.10 [1.10, 13.10]
Stuppaeck 1994	68	9.10 (6.00)	66	9.40 (6.00)		5.7	-0.30 [-2.33, 1.73]
Subtotal (95% CI)	310		311			21.0	0.96 [-0.10, 2.02]
Test for heterogeneity chi-square=17.26 df=8 p=0.03 I =53.7%							
Test for overall effect z=1.77 p=0.08							
05 Sertraline							
Subtotal (95% CI)	0		0			0.0	Not estimable
Test for heterogeneity: not applicable							
Test for overall effect: not applicable							
Total (95% CI)	665		682			100.0	0.13 [-0.36, 0.62]
Test for heterogeneity chi-square=57.09 df=22 p=<0.00011 =61.5%							
Test for overall effect z=0.52 p=0.6							

Analysis 04.01. Comparison 04 Tricyclics and related drugs versus SSRIs, Outcome 01 Efficacy

Review: Selective serotonin reuptake inhibitors (SSRIs) versus other antidepressants for depression

Comparison: 04 Tricyclics and related drugs versus SSRIs

Outcome: 01 Efficacy

Study	SSRI N	SSRI Mean(SD)	tricyclic N	tricyclic Mean(SD)	Weighted Mean Difference (Fixed) 95% CI	Weight (%)	Weighted Mean Difference (Fixed) 95% CI
01 Amineptine							
Dalery 1992	73	10.50 (12.40)	68	9.50 (8.50)		0.5	1.00 [-2.49, 4.49]
Subtotal (95% CI)	73		68			0.5	1.00 [-2.49, 4.49]
Test for heterogeneity: not applicable							
Test for overall effect z=0.56 p=0.6							
02 Amitriptyline							
Battegay 1985	8	4.88 (2.80)	6	4.50 (5.05)		0.3	0.38 [-4.10, 4.86]
Beasley 1993b	65	15.60 (9.90)	71	16.40 (10.30)		0.5	-0.80 [-4.20, 2.60]
Bersani 1994	31	16.00 (6.50)	30	16.00 (6.10)		0.6	0.00 [-3.16, 3.16]

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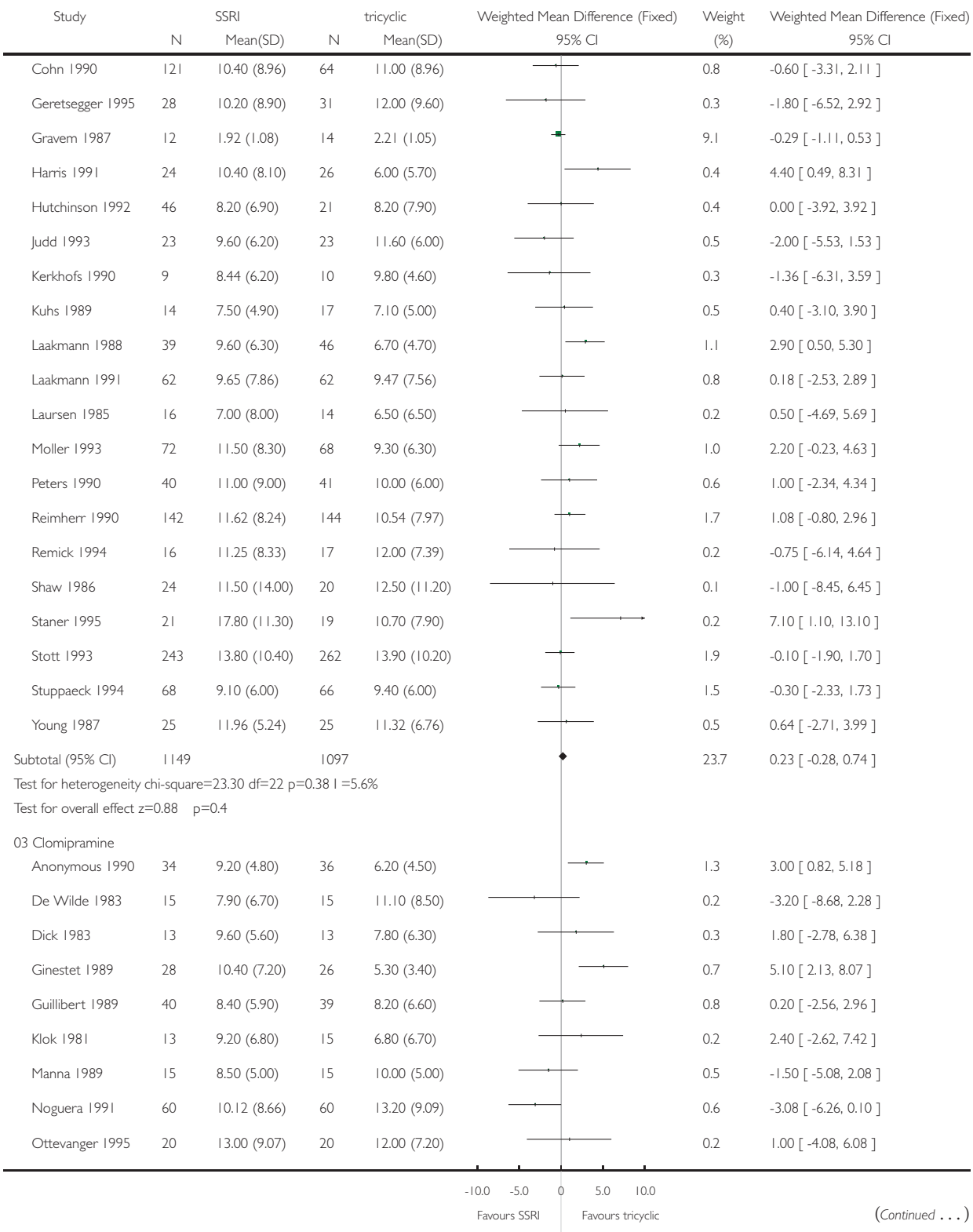

Study	SSRI N	SSRI Mean(SD)	tricyclic N	tricyclic Mean(SD)	Weighted Mean Difference (Fixed) 95% CI	Weight (%)	Weighted Mean Difference (Fixed) 95% CI
Cohn 1990	121	10.40 (8.96)	64	11.00 (8.96)		0.8	-0.60 [-3.31, 2.11]
Geretsegger 1995	28	10.20 (8.90)	31	12.00 (9.60)		0.3	-1.80 [-6.52, 2.92]
Gravem 1987	12	1.92 (1.08)	14	2.21 (1.05)		9.1	-0.29 [-1.11, 0.53]
Harris 1991	24	10.40 (8.10)	26	6.00 (5.70)		0.4	4.40 [0.49, 8.31]
Hutchinson 1992	46	8.20 (6.90)	21	8.20 (7.90)		0.4	0.00 [-3.92, 3.92]
Judd 1993	23	9.60 (6.20)	23	11.60 (6.00)		0.5	-2.00 [-5.53, 1.53]
Kerkhofs 1990	9	8.44 (6.20)	10	9.80 (4.60)		0.3	-1.36 [-6.31, 3.59]
Kuhs 1989	14	7.50 (4.90)	17	7.10 (5.00)		0.5	0.40 [-3.10, 3.90]
Laakmann 1988	39	9.60 (6.30)	46	6.70 (4.70)		1.1	2.90 [0.50, 5.30]
Laakmann 1991	62	9.65 (7.86)	62	9.47 (7.56)		0.8	0.18 [-2.53, 2.89]
Laursen 1985	16	7.00 (8.00)	14	6.50 (6.50)		0.2	0.50 [-4.69, 5.69]
Moller 1993	72	11.50 (8.30)	68	9.30 (6.30)		1.0	2.20 [-0.23, 4.63]
Peters 1990	40	11.00 (9.00)	41	10.00 (6.00)		0.6	1.00 [-2.34, 4.34]
Reimherr 1990	142	11.62 (8.24)	144	10.54 (7.97)		1.7	1.08 [-0.80, 2.96]
Remick 1994	16	11.25 (8.33)	17	12.00 (7.39)		0.2	-0.75 [-6.14, 4.64]
Shaw 1986	24	11.50 (14.00)	20	12.50 (11.20)		0.1	-1.00 [-8.45, 6.45]
Staner 1995	21	17.80 (11.30)	19	10.70 (7.90)		0.2	7.10 [1.10, 13.10]
Stott 1993	243	13.80 (10.40)	262	13.90 (10.20)		1.9	-0.10 [-1.90, 1.70]
Stuppaeck 1994	68	9.10 (6.00)	66	9.40 (6.00)		1.5	-0.30 [-2.33, 1.73]
Young 1987	25	11.96 (5.24)	25	11.32 (6.76)		0.5	0.64 [-2.71, 3.99]
Subtotal (95% CI)	1149		1097			23.7	0.23 [-0.28, 0.74]
Test for heterogeneity chi-square=23.30 df=22 p=0.38 I =5.6%							
Test for overall effect z=0.88 p=0.4							
03 Clomipramine							
Anonymous 1990	34	9.20 (4.80)	36	6.20 (4.50)		1.3	3.00 [0.82, 5.18]
De Wilde 1983	15	7.90 (6.70)	15	11.10 (8.50)		0.2	-3.20 [-8.68, 2.28]
Dick 1983	13	9.60 (5.60)	13	7.80 (6.30)		0.3	1.80 [-2.78, 6.38]
Ginestet 1989	28	10.40 (7.20)	26	5.30 (3.40)		0.7	5.10 [2.13, 8.07]
Guillibert 1989	40	8.40 (5.90)	39	8.20 (6.60)		0.8	0.20 [-2.56, 2.96]
Klok 1981	13	9.20 (6.80)	15	6.80 (6.70)		0.2	2.40 [-2.62, 7.42]
Manna 1989	15	8.50 (5.00)	15	10.00 (5.00)		0.5	-1.50 [-5.08, 2.08]
Noguera 1991	60	10.12 (8.66)	60	13.20 (9.09)		0.6	-3.08 [-6.26, 0.10]
Ottevanger 1995	20	13.00 (9.07)	20	12.00 (7.20)		0.2	1.00 [-4.08, 6.08]

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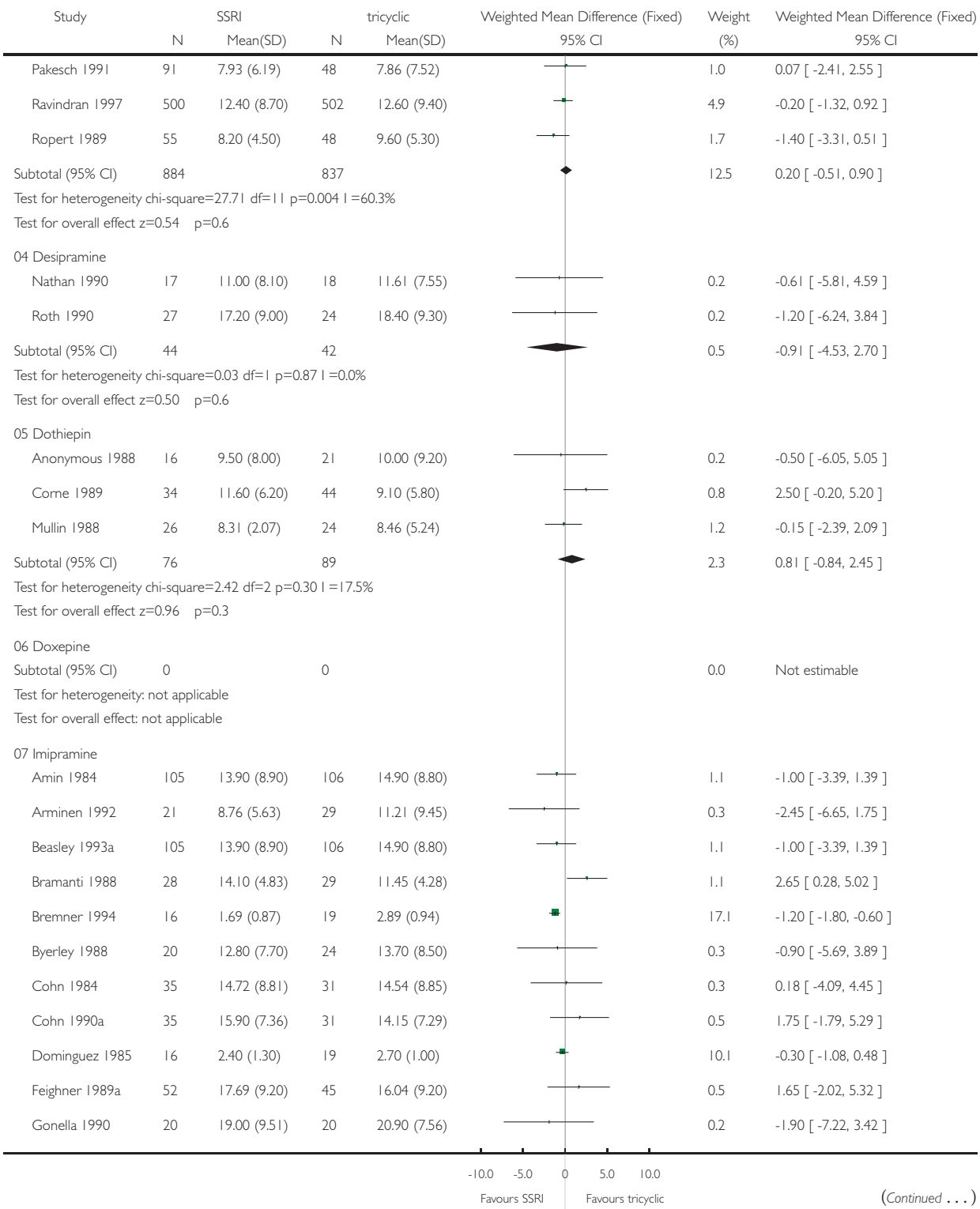

Study	SSRI N	SSRI Mean(SD)	tricyclic N	tricyclic Mean(SD)	Weighted Mean Difference (Fixed) 95% CI	Weight (%)	Weighted Mean Difference (Fixed) 95% CI
Pakesch 1991	91	7.93 (6.19)	48	7.86 (7.52)		1.0	0.07 [-2.41, 2.55]
Ravindran 1997	500	12.40 (8.70)	502	12.60 (9.40)		4.9	-0.20 [-1.32, 0.92]
Ropert 1989	55	8.20 (4.50)	48	9.60 (5.30)		1.7	-1.40 [-3.31, 0.51]
Subtotal (95% CI)	884		837			12.5	0.20 [-0.51, 0.90]
Test for heterogeneity chi-square=27.71 df=11 p=0.004 I =60.3%							
Test for overall effect z=0.54 p=0.6							
04 Desipramine							
Nathan 1990	17	11.00 (8.10)	18	11.61 (7.55)		0.2	-0.61 [-5.81, 4.59]
Roth 1990	27	17.20 (9.00)	24	18.40 (9.30)		0.2	-1.20 [-6.24, 3.84]
Subtotal (95% CI)	44		42			0.5	-0.91 [-4.53, 2.70]
Test for heterogeneity chi-square=0.03 df=1 p=0.87 I =0.0%							
Test for overall effect z=0.50 p=0.6							
05 Dothiepin							
Anonymous 1988	16	9.50 (8.00)	21	10.00 (9.20)		0.2	-0.50 [-6.05, 5.05]
Corne 1989	34	11.60 (6.20)	44	9.10 (5.80)		0.8	2.50 [-0.20, 5.20]
Mullin 1988	26	8.31 (2.07)	24	8.46 (5.24)		1.2	-0.15 [-2.39, 2.09]
Subtotal (95% CI)	76		89			2.3	0.81 [-0.84, 2.45]
Test for heterogeneity chi-square=2.42 df=2 p=0.30 I =17.5%							
Test for overall effect z=0.96 p=0.3							
06 Doxepine							
Subtotal (95% CI)	0		0			0.0	Not estimable
Test for heterogeneity: not applicable							
Test for overall effect: not applicable							
07 Imipramine							
Amin 1984	105	13.90 (8.90)	106	14.90 (8.80)		1.1	-1.00 [-3.39, 1.39]
Arminen 1992	21	8.76 (5.63)	29	11.21 (9.45)		0.3	-2.45 [-6.65, 1.75]
Beasley 1993a	105	13.90 (8.90)	106	14.90 (8.80)		1.1	-1.00 [-3.39, 1.39]
Bramanti 1988	28	14.10 (4.83)	29	11.45 (4.28)		1.1	2.65 [0.28, 5.02]
Bremner 1994	16	1.69 (0.87)	19	2.89 (0.94)		17.1	-1.20 [-1.80, -0.60]
Byerley 1988	20	12.80 (7.70)	24	13.70 (8.50)		0.3	-0.90 [-5.69, 3.89]
Cohn 1984	35	14.72 (8.81)	31	14.54 (8.85)		0.3	0.18 [-4.09, 4.45]
Cohn 1990a	35	15.90 (7.36)	31	14.15 (7.29)		0.5	1.75 [-1.79, 5.29]
Dominguez 1985	16	2.40 (1.30)	19	2.70 (1.00)		10.1	-0.30 [-1.08, 0.48]
Feighner 1989a	52	17.69 (9.20)	45	16.04 (9.20)		0.5	1.65 [-2.02, 5.32]
Gonella 1990	20	19.00 (9.51)	20	20.90 (7.56)		0.2	-1.90 [-7.22, 3.42]

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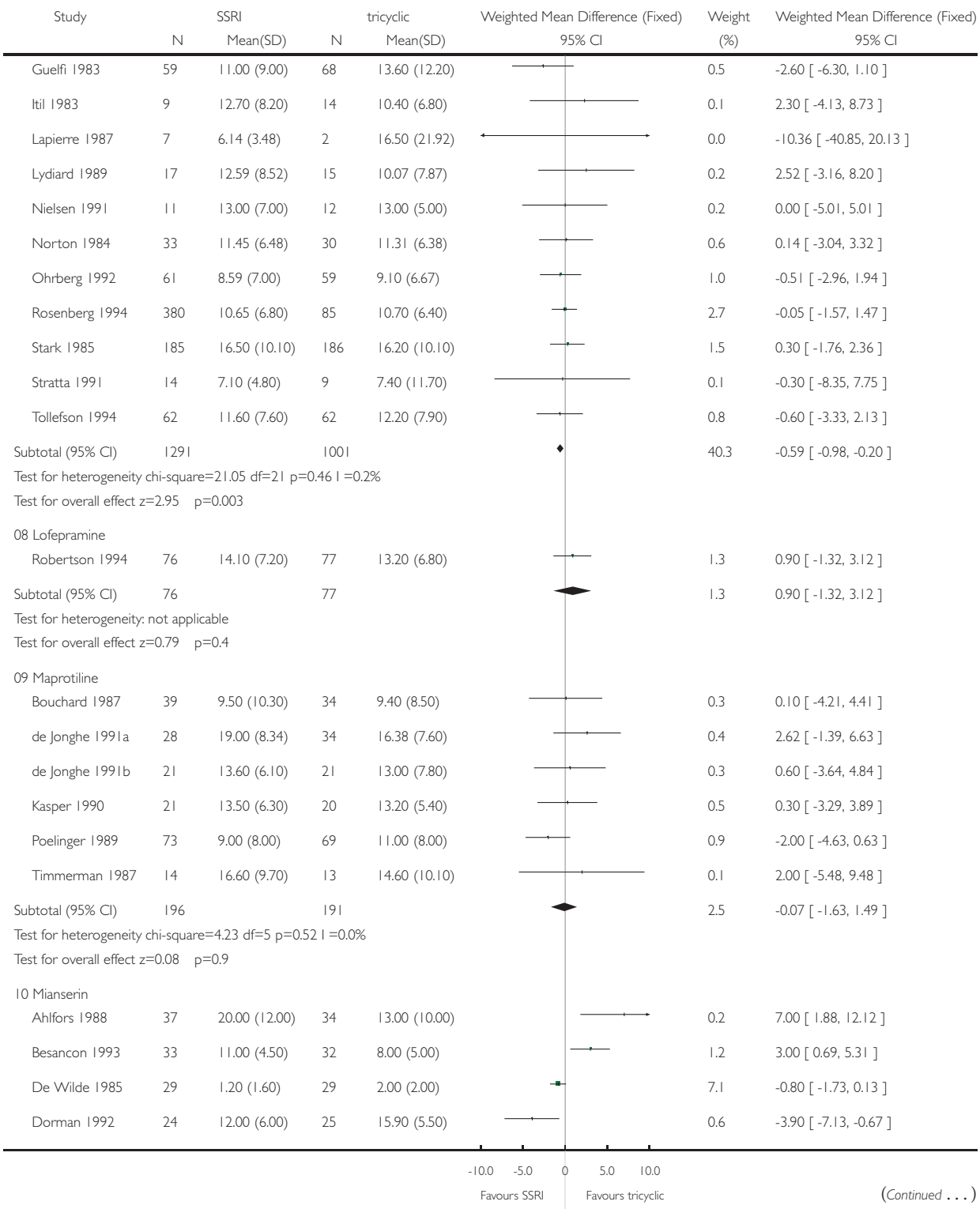

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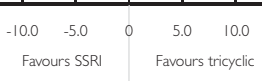
Study	SSRI N	SSRI Mean(SD)	tricyclic N	tricyclic Mean(SD)	Weighted Mean Difference (Fixed) 95% CI	Weight (%)	Weighted Mean Difference (Fixed) 95% CI
La Pia 1992	19	14.52 (6.65)	16	16.37 (4.92)		0.4	-1.85 [-5.69, 1.99]
Mertens 1988	36	11.50 (16.00)	31	17.80 (16.00)		0.1	-6.30 [-13.98, 1.38]
Muijen 1988	14	10.50 (7.50)	14	14.50 (10.20)		0.1	-4.00 [-10.63, 2.63]
Phanjoo 1991	16	23.20 (10.90)	15	19.90 (7.62)		0.1	3.30 [-3.29, 9.89]
Subtotal (95% CI)	208		196			9.9	-0.45 [-1.24, 0.34]
Test for heterogeneity chi-square=26.67 df=7 p=0.0004 I =73.8%							
Test for overall effect z=1.11 p=0.3							
11 Moclobemide							
Barrelet 1991	30	11.00 (10.00)	31	9.40 (8.20)		0.3	1.60 [-3.00, 6.20]
Bocksberger 1993	18	23.50 (14.20)	18	11.90 (10.10)		0.1	11.60 [3.55, 19.65]
Bougerol 1992	63	13.02 (8.18)	67	12.71 (8.00)		0.8	0.31 [-2.47, 3.09]
Gattaz 1995	34	12.00 (12.00)	36	13.00 (14.00)		0.2	-1.00 [-7.10, 5.10]
Geerts 1994	13	9.80 (6.20)	15	9.10 (7.30)		0.2	0.70 [-4.30, 5.70]
Lonnqvist 1994	107	10.60 (6.00)	102	9.60 (5.50)		2.5	1.00 [-0.56, 2.56]
Reynaert 1995	42	12.90 (9.00)	38	12.20 (7.60)		0.5	0.70 [-2.94, 4.34]
Williams 1993	45	8.62 (7.27)	47	7.80 (6.67)		0.8	0.82 [-2.03, 3.67]
Subtotal (95% CI)	352		354			5.4	0.99 [-0.08, 2.06]
Test for heterogeneity chi-square=7.43 df=7 p=0.39 I =5.8%							
Test for overall effect z=1.81 p=0.07							
12 Nortriptyline							
Subtotal (95% CI)	0		0			0.0	Not estimable
Test for heterogeneity: not applicable							
Test for overall effect: not applicable							
13 Trazodone							
Beasley 1991	63	11.20 (7.20)	57	10.40 (7.70)		0.9	0.80 [-1.88, 3.48]
Falk 1989	13	10.08 (7.57)	12	16.08 (8.53)		0.2	-6.00 [-12.34, 0.34]
Fudge 1990	17	8.40 (9.00)	15	6.50 (5.10)		0.2	1.90 [-3.10, 6.90]
Subtotal (95% CI)	93		84			1.3	0.19 [-2.02, 2.40]
Test for heterogeneity chi-square=4.31 df=2 p=0.12 I =53.6%							
Test for overall effect z=0.17 p=0.9							
Total (95% CI)	4442		4036			100.0	-0.12 [-0.37, 0.13]
Test for heterogeneity chi-square=132.71 df=88 p=0.001 I =33.7%							
Test for overall effect z=0.94 p=0.3							



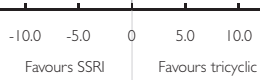
Analysis 05.01. Comparison 05 SSRIs v. Tricyclics, Outcome 01 Drug efficacy by trial design

Review: Selective serotonin reuptake inhibitors (SSRIs) versus other antidepressants for depression

Comparison: 05 SSRIs v. Tricyclics

Outcome: 01 Drug efficacy by trial design

Study	Treatment N	Treatment Mean(SD)	Control N	Control Mean(SD)	Weighted Mean Difference (Fixed) 95% CI	Weight (%)	Weighted Mean Difference (Fixed) 95% CI
01 Intention to treat analysis							
Amin 1984	105	13.90 (8.90)	106	14.90 (8.30)		1.4	-1.00 [-3.32, 1.32]
Battegay 1985	8	4.88 (2.80)	6	4.50 (5.05)		0.4	0.38 [-4.10, 4.86]
Beasley 1993a	54	19.50 (9.90)	60	15.10 (9.00)		0.6	4.40 [0.91, 7.89]
Beasley 1993b	65	15.60 (9.90)	71	16.40 (10.30)		0.7	-0.80 [-4.20, 2.60]
Bramanti 1988	28	14.10 (4.83)	29	11.45 (4.28)		1.4	2.65 [0.28, 5.02]
Gonella 1990	20	19.00 (9.51)	20	20.90 (7.56)		0.3	-1.90 [-7.22, 3.42]
Manna 1989	15	8.50 (5.00)	15	10.00 (5.00)		0.6	-1.50 [-5.08, 2.08]
Noguera 1991	60	10.12 (8.66)	60	13.20 (9.09)		0.8	-3.08 [-6.26, 0.10]
Ottevanger 1995	20	13.00 (9.07)	20	12.00 (7.20)		0.3	1.00 [-4.08, 6.08]
Pakesch 1991	91	7.93 (6.19)	48	7.86 (7.52)		1.2	0.07 [-2.41, 2.55]
Ravindran 1995	500	12.40 (8.70)	502	12.60 (9.40)		6.1	-0.20 [-1.32, 0.92]
Reimherr 1990	142	11.62 (8.24)	144	10.54 (7.97)		2.2	1.08 [-0.80, 2.96]
Remick 1994	16	11.25 (8.33)	17	12.00 (7.93)		0.2	-0.75 [-6.31, 4.81]
Rosenberg 1994	380	10.65 (6.80)	85	10.70 (6.40)		3.3	-0.05 [-1.57, 1.47]
Shaw 1986	24	11.50 (14.00)	20	12.50 (11.20)		0.1	-1.00 [-8.45, 6.45]
Staner 1995	21	17.80 (11.30)	19	10.70 (7.90)		0.2	7.10 [1.10, 13.10]
Stark 1985	185	16.50 (10.10)	186	16.20 (10.10)		1.8	0.30 [-1.76, 2.36]
Tollefson 1994	62	11.60 (7.60)	62	12.20 (7.90)		1.0	-0.60 [-3.33, 2.13]
Subtotal (95% CI)	1796		1470			22.6	0.15 [-0.44, 0.73]
Test for heterogeneity chi-square=23.74 df=17 p=0.131 =28.4%							
Test for overall effect z=0.49 p=0.6							
02 Endpoint analysis							
Anonymous 1988	16	9.50 (8.00)	21	10.00 (9.20)		0.2	-0.50 [-6.05, 5.05]
Anonymous 1990	34	9.20 (4.80)	36	6.20 (4.50)		1.6	3.00 [0.82, 5.18]
Arminen 1992	21	8.76 (5.63)	29	11.21 (9.45)		0.4	-2.45 [-6.65, 1.75]
Bersani 1994	31	16.00 (6.50)	30	16.00 (6.10)		0.8	0.00 [-3.16, 3.16]
Bremner 1994	16	1.69 (0.87)	19	2.89 (0.94)		21.2	-1.20 [-1.80, -0.60]



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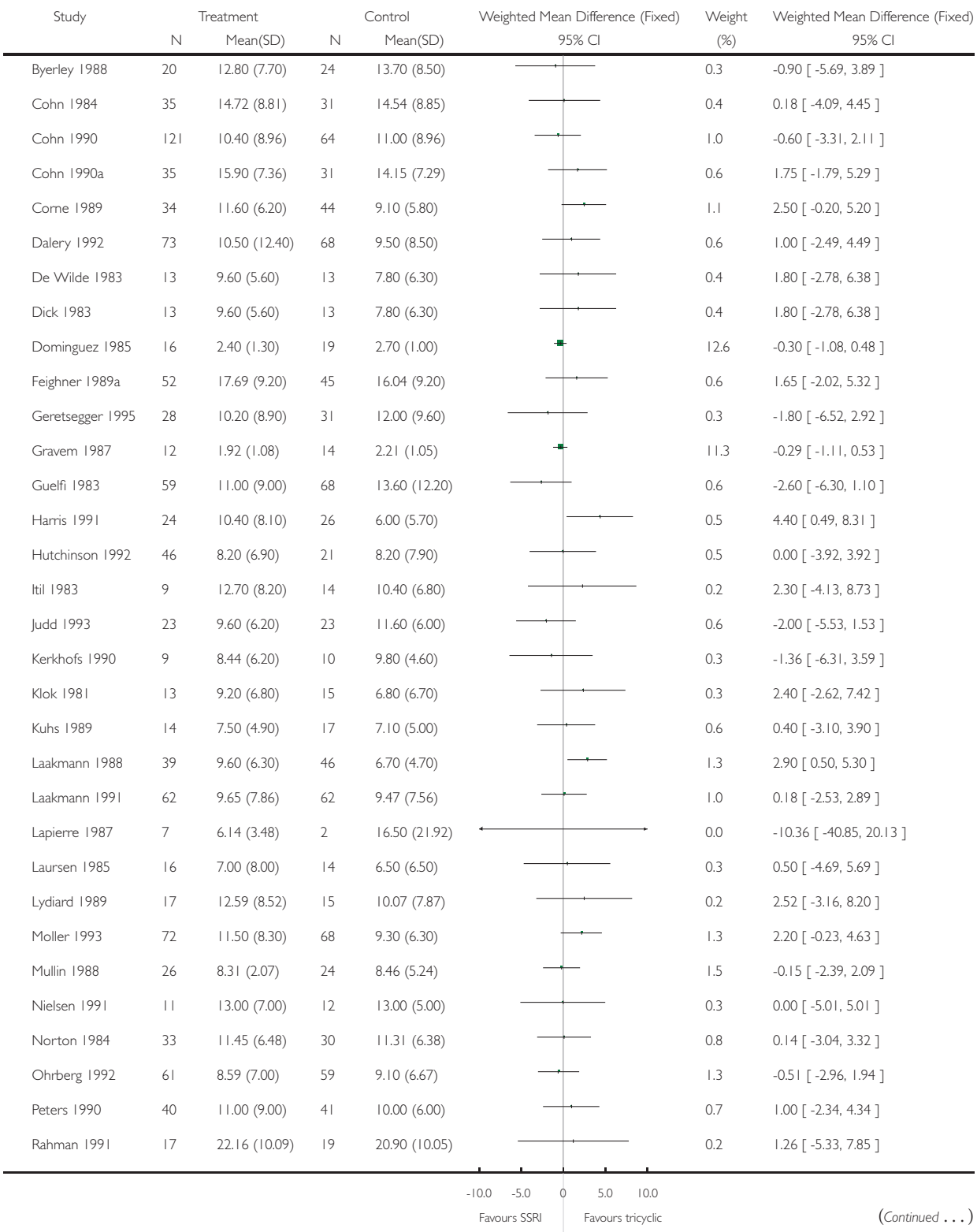

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Study	Treatment N	Treatment Mean(SD)	Control N	Control Mean(SD)	Weighted Mean Difference (Fixed) 95% CI	Weight (%)	Weighted Mean Difference (Fixed) 95% CI
Ravindran 1995	34	10.65 (7.78)	30	9.40 (8.21)		0.5	1.25 [-2.68, 5.18]
Remick 1993	24	13.04 (8.20)	15	6.93 (5.92)		0.4	6.11 [1.67, 10.55]
Robertson 1994	76	14.10 (7.20)	77	13.20 (6.80)		1.6	0.90 [-1.32, 3.12]
Ropert 1989	55	8.20 (4.50)	48	9.60 (5.30)		2.1	-1.40 [-3.31, 0.51]
Roth 1990	27	17.20 (9.00)	24	18.40 (9.30)		0.3	-1.20 [-6.24, 3.84]
Stott 1993	243	13.80 (10.40)	262	13.90 (6.00)		3.4	-0.10 [-1.60, 1.40]
Stratta 1991	14	7.10 (4.80)	9	7.40 (11.70)		0.1	-0.30 [-8.35, 7.75]
Stuppaeck 1994	68	9.10 (6.00)	66	9.40 (6.00)		1.9	-0.30 [-2.33, 1.73]
Young 1987	25	11.96 (5.24)	25	11.32 (6.76)		0.7	0.64 [-2.71, 3.99]
Subtotal (95% CI)	1734		1674			77.4	-0.19 [-0.51, 0.12]
Test for heterogeneity chi-square=62.12 df=45 p=0.05 I =27.6%							
Test for overall effect z=1.21 p=0.2							
Total (95% CI)	3530		3144			100.0	-0.12 [-0.39, 0.16]
Test for heterogeneity chi-square=86.87 df=63 p=0.02 I =27.5%							
Test for overall effect z=0.83 p=0.4							

Analysis 06.01. Comparison 06 SSRIs v. sedating/non-sedating tricyclic antidepressants, Outcome 01 SSRIs v. TCAs group in sedating v. non-sedating categories

Review: Selective serotonin reuptake inhibitors (SSRIs) versus other antidepressants for depression

Comparison: 06 SSRIs v. sedating/non-sedating tricyclic antidepressants

Outcome: 01 SSRIs v. TCAs group in sedating v. non-sedating categories

Study	Treatment N	Treatment Mean(SD)	Control N	Control Mean(SD)	Weighted Mean Difference (Fixed) 95% CI	Weight (%)	Weighted Mean Difference (Fixed) 95% CI
01 Sedating tricyclics							
Anonymous 1988	16	9.50 (8.00)	21	10.00 (9.20)		0.3	-0.50 [-6.05, 5.05]
Anonymous 1990	34	9.20 (4.80)	36	6.20 (4.50)		1.7	3.00 [0.82, 5.18]
Battegay 1985	8	4.88 (2.80)	6	4.50 (5.05)		0.4	0.38 [-4.10, 4.86]
Beasley 1993b	65	15.60 (9.90)	71	16.40 (10.30)		0.7	-0.80 [-4.20, 2.60]
Bersani 1994	31	16.00 (6.50)	30	16.00 (6.10)		0.8	0.00 [-3.16, 3.16]
Cohn 1990	121	10.40 (8.96)	31	12.00 (9.60)		0.6	-1.60 [-5.34, 2.14]
Corne 1989	34	11.60 (6.20)	44	9.10 (5.80)		1.1	2.50 [-0.20, 5.20]
Dalery 1992	73	10.50 (12.40)	68	9.50 (8.50)		0.7	1.00 [-2.49, 4.49]
De Wilde 1983	15	7.90 (6.70)	15	11.10 (8.50)		0.3	-3.20 [-8.68, 2.28]
Dick 1983	13	9.60 (5.60)	13	7.80 (6.30)		0.4	1.80 [-2.78, 6.38]
Geretsegger 1995	28	10.20 (8.90)	31	12.00 (9.60)		0.4	-1.80 [-6.52, 2.92]
Ginestet 1989	28	10.40 (7.20)	26	5.30 (3.40)		0.9	5.10 [2.13, 8.07]
Gravem 1987	12	1.92 (1.08)	14	2.21 (1.05)		12.3	-0.29 [-1.11, 0.53]
Guillibert 1989	40	8.40 (5.90)	39	8.20 (6.60)		1.1	0.20 [-2.56, 2.96]
Harris 1991	24	10.40 (8.10)	26	6.00 (5.70)		0.5	4.40 [0.49, 8.31]
Hutchinson 1992	46	8.20 (6.90)	21	8.20 (7.90)		0.5	0.00 [-3.92, 3.92]
Judd 1993	23	9.60 (6.20)	23	11.60 (6.00)		0.7	-2.00 [-5.53, 1.53]
Kerkhofs 1990	9	8.44 (6.20)	10	9.80 (4.60)		0.3	-1.36 [-6.31, 3.59]
Klok 1981	13	9.20 (6.80)	15	6.80 (6.70)		0.3	2.40 [-2.62, 7.42]
Kuhs 1989	14	7.50 (4.90)	17	7.10 (5.00)		0.7	0.40 [-3.10, 3.90]
Laakmann 1988	39	9.60 (6.30)	46	6.70 (4.70)		1.4	2.90 [0.50, 5.30]
Laakmann 1991	62	9.65 (7.86)	62	9.47 (7.56)		1.1	0.18 [-2.53, 2.89]
Laursen 1985	16	7.00 (8.00)	14	6.50 (6.50)		0.3	0.50 [-4.69, 5.69]
Manna 1989	15	8.50 (5.00)	15	10.00 (5.00)		0.6	-1.50 [-5.08, 2.08]
Moller 1993	72	11.50 (8.30)	68	9.30 (6.30)		1.4	2.20 [-0.23, 4.63]

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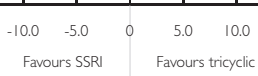
Study	Treatment N	Treatment Mean(SD)	Control N	Control Mean(SD)	Weighted Mean Difference (Fixed) 95% CI	Weight (%)	Weighted Mean Difference (Fixed) 95% CI
Mullin 1988	26	8.31 (2.07)	24	8.46 (5.24)		1.6	-0.15 [-2.39, 2.09]
Noguera 1991	60	10.20 (8.66)	60	13.20 (9.09)		0.8	-3.00 [-6.18, 0.18]
Ottevanger 1995	20	13.00 (9.07)	20	12.00 (7.20)		0.3	1.00 [-4.08, 6.08]
Pakesch 1991	91	7.93 (6.19)	48	7.86 (7.52)		1.3	0.07 [-2.41, 2.55]
Peters 1990	40	11.00 (9.00)	41	10.00 (6.00)		0.7	1.00 [-2.34, 4.34]
Reimherr 1990	142	11.62 (8.24)	144	10.54 (7.97)		2.3	1.08 [-0.80, 2.96]
Remick 1994	16	11.25 (8.33)	17	12.00 (7.39)		0.3	-0.75 [-6.14, 4.64]
Ropert 1989	55	8.20 (4.50)	48	9.60 (5.30)		2.3	-1.40 [-3.31, 0.51]
Shaw 1986	24	11.50 (14.00)	20	12.50 (11.20)		0.1	-1.00 [-8.45, 6.45]
Staner 1995	21	17.80 (11.30)	19	10.70 (7.90)		0.2	7.10 [1.10, 13.10]
Stott 1993	243	13.80 (10.40)	262	13.90 (10.20)		2.6	-0.10 [-1.90, 1.70]
Stuppaeck 1994	68	9.10 (6.00)	66	9.40 (6.00)		2.0	-0.30 [-2.33, 1.73]
Young 1987	25	11.96 (5.24)	25	11.32 (6.76)		0.7	0.64 [-2.71, 3.99]
Subtotal (95% CI)	1682		1556			45.2	0.33 [-0.10, 0.76]
Test for heterogeneity chi-square=53.70 df=37 p=0.041 =31.1%							
Test for overall effect z=1.50 p=0.1							
02 Non-sedating tricyclics							
Amin 1984	105	13.90 (8.90)	106	14.90 (8.80)		1.5	-1.00 [-3.39, 1.39]
Arminen 1992	21	8.76 (5.63)	29	11.21 (9.45)		0.5	-2.45 [-6.65, 1.75]
Beasley 1993a	54	19.50 (9.90)	60	15.10 (9.00)		0.7	4.40 [0.91, 7.89]
Bramanti 1988	28	14.10 (4.83)	29	11.45 (4.28)		1.5	2.65 [0.28, 5.02]
Bremner 1994	16	1.69 (0.87)	19	2.89 (0.94)		23.0	-1.20 [-1.80, -0.60]
Byerley 1988	20	12.80 (7.70)	24	13.70 (8.50)		0.4	-0.90 [-5.69, 3.89]
Cohn 1984	35	14.72 (8.81)	31	14.54 (8.85)		0.5	0.18 [-4.09, 4.45]
Cohn 1990a	35	15.90 (7.36)	31	14.15 (7.29)		0.7	1.75 [-1.79, 5.29]
Dominguez 1985	16	2.40 (1.30)	19	2.70 (1.00)		13.6	-0.30 [-1.08, 0.48]
Feighner 1989a	52	17.69 (9.20)	45	16.04 (9.20)		0.6	1.65 [-2.02, 5.32]
Gonella 1990	20	19.00 (9.51)	20	20.90 (7.56)		0.3	-1.90 [-7.22, 3.42]
Guelfi 1983	59	11.00 (9.00)	68	13.60 (12.20)		0.6	-2.60 [-6.30, 1.10]
Itil 1983	9	12.70 (8.20)	14	10.40 (6.80)		0.2	2.30 [-4.13, 8.73]
Lapierre 1987	7	6.14 (3.48)	2	16.50 (21.92)		0.0	-10.36 [-40.85, 20.13]
Lydiard 1989	17	12.59 (8.52)	15	10.07 (7.87)		0.3	2.52 [-3.16, 8.20]
Nathan 1990	17	11.00 (8.10)	18	11.61 (7.55)		0.3	-0.61 [-5.81, 4.59]



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Study	Treatment N	Treatment Mean(SD)	Control N	Control Mean(SD)	Weighted Mean Difference (Fixed) 95% CI	Weight (%)	Weighted Mean Difference (Fixed) 95% CI
Nielsen 1991	11	13.00 (7.00)	12	13.00 (5.00)		0.3	0.00 [-5.01, 5.01]
Norton 1984	33	11.45 (6.48)	30	11.31 (6.38)		0.8	0.14 [-3.04, 3.32]
Ohrberg 1992	61	8.59 (7.00)	59	9.10 (6.67)		1.4	-0.51 [-2.96, 1.94]
Robertson 1994	76	14.10 (7.20)	77	13.20 (6.80)		1.7	0.90 [-1.32, 3.12]
Rosenberg 1994	380	10.65 (6.80)	85	10.70 (6.40)		3.6	-0.05 [-1.57, 1.47]
Roth 1990	27	17.20 (9.00)	24	18.40 (9.30)		0.3	-1.20 [-6.24, 3.84]
Stark 1985	185	16.50 (10.10)	186	16.20 (10.10)		2.0	0.30 [-1.76, 2.36]
Stratta 1991	14	7.10 (4.80)	9	7.40 (11.70)		0.1	-0.30 [-8.35, 7.75]
Tollefson 1994	14	7.10 (4.80)	9	7.40 (11.70)		0.1	-0.30 [-8.35, 7.75]
Subtotal (95% CI)	1312		1021			54.8	-0.47 [-0.86, -0.08]
Test for heterogeneity chi-square=30.25 df=24 p=0.181 =20.7%							
Test for overall effect z=2.38 p=0.02							
Total (95% CI)	2994		2577			100.0	-0.11 [-0.40, 0.18]
Test for heterogeneity chi-square=91.31 df=62 p=0.009 1 =32.1%							
Test for overall effect z=0.75 p=0.5