Paroxetine versus other anti-depressive agents for depression (Review)

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This is a reprint of a Cochrane review, prepared and maintained by The Cochrane Collaboration and published in *The Cochrane Library* 2014, Issue 4

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[Intervention Review]

Paroxetine versus other anti-depressive agents for depression

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Editorial group: Cochrane Depression, Anxiety and Neurosis Group.
Publication status and date: New, published in Issue 4, 2014.
Review content assessed as up-to-date: 30 September 2012.

Citation: Purgato M, Papola D, Gastaldon C, Trespidi C, Magni LR, Rizzo C, Furukawa TA, Watanabe N, Cipriani A, Barbui C. Paroxetine versus other anti-depressive agents for depression. *Cochrane Database of Systematic Reviews* 2014, Issue 4. Art. No.: CD006531. DOI: 10.1002/14651858.CD006531.pub2.

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ABSTRACT

Background

Paroxetine is the most potent inhibitor of the reuptake of serotonin of all selective serotonin reuptake inhibitors (SSRIs) and has been studied in many randomised controlled trials (RCTs). However, these comparative studies provided contrasting findings and systematic reviews of RCTs have always considered the SSRIs as a group, and evidence applicable to this group of drugs might not be applicable to paroxetine alone. The present systematic review assessed the efficacy and tolerability profile of paroxetine in comparison with tricyclics (TCAs), SSRIs and newer or non-conventional agents.

Objectives

1. To determine the efficacy of paroxetine in comparison with other anti-depressive agents in alleviating the acute symptoms of Major Depressive Disorder.

2. To review acceptability of treatment with paroxetine in comparison with other anti-depressive agents.

3. To investigate the adverse effects of paroxetine in comparison with other anti-depressive agents.

Search methods

We searched the Cochrane Depression, Anxiety and Neurosis Review Group's Specialized Register (CCDANCTR, to 30 September 2012), which includes relevant randomised controlled trials from the following bibliographic databases: *The Cochrane Library* (all years), EMBASE (1974 to date), MEDLINE (1950 to date) and PsycINFO (1967 to date). Reference lists of relevant papers and previous systematic reviews were handsearched. Pharmaceutical companies marketing paroxetine and experts in this field were contacted for supplemental data.

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Selection criteria

All randomised controlled trials allocating participants with major depression to paroxetine versus any other antidepressants (ADs), both conventional (such as TCAs, SSRIs) and newer or non-conventional (such as hypericum). For trials which had a cross-over design, only results from the first randomisation period were considered.

Data collection and analysis

Two review authors independently checked eligibility and extracted data using a standard form. Data were then entered in RevMan 5.2 with a double-entry procedure. Information extracted included study and participant characteristics, intervention details, settings and efficacy, acceptability and tolerability measures.

Main results

A total of 115 randomised controlled trials (26,134 participants) were included. In 54 studies paroxetine was compared with older ADs, in 21 studies with another SSRI, and in 40 studies with a newer or non-conventional antidepressant other than SSRIs. For the primary outcome (patients who responded to treatment), paroxetine was more effective than reboxetine at increasing patients who responded early to treatment (Odds Ratio (OR): 0.66, 95% Confidence Interval (CI) 0.50 to 0.87, number needed to treat to provide benefit (NNTb) = 16, 95% CI 10 to 50, at one to four weeks, 3 RCTs, 1375 participants, moderate quality of evidence), and less effective than mirtazapine (OR: 2.39, 95% CI 1.42 to 4.02, NNTb = 8, 95% CI 5 to 14, at one to four weeks, 3 RCTs, 726 participants, moderate quality of evidence). Paroxetine was less effective than citalopram in improving response to treatment (OR: 1.54, 95% CI 1.04 to 2.28, NNTb = 9, 95% CI 5 to 102, at six to 12 weeks, 1 RCT, 406 participants, moderate quality of evidence). We found no clear evidence that paroxetine was more or less effective compared with other antidepressants at increasing response to treatment at acute (six to 12 weeks), early (one to four weeks), or longer term follow-up (four to six months). Paroxetine was associated with a lower rate of adverse events than amitriptyline, imipramine and older ADs as a class, but was less well tolerated than agomelatine and hypericum. Included studies were generally at unclear or high risk of bias due to poor reporting of allocation concealment and blinding of outcome assessment, and incomplete reporting of outcomes.

Authors' conclusions

Some possibly clinically meaningful differences between paroxetine and other ADs exist, but no definitive conclusions can be drawn from these findings. In terms of response, there was a moderate quality of evidence that citalopram was better than paroxetine in the acute phase (six to 12 weeks), although only one study contributed data. In terms of early response to treatment (one to four weeks) there was moderate quality of evidence that mirtazapine was better than paroxetine and that paroxetine was better than reboxetine. However there was no clear evidence that paroxetine was better or worse compared with other antidepressants at increasing response to treatment at any time point. Even if some differences were identified, the findings from this review are better thought as hypothesis forming rather than hypothesis testing and it would be reassuring to see the conclusions replicated in future trials. Finally, most of included studies were at unclear or high risk of bias, and were sponsored by the drug industry. The potential for overestimation of treatment effect due to sponsorship bias should be borne in mind.

PLAIN LANGUAGE SUMMARY

Paroxetine versus other anti-depressive agents for depression

Major depression is a severe mental illness characterised by a persistent and unreactive low mood and loss of all interest and pleasure, usually accompanied by a range of symptoms such as appetite change, sleep disturbance, fatigue, loss of energy, poor concentration, inappropriate guilt and morbid thoughts of death. Although medication and psychological treatments are both effective for major depression, antidepressant drugs remain the mainstay of treatment in moderate to severe major depression. However, head-to-head comparisons of such drugs provide contrasting findings as to whether they are effective.

This review of the research on the effect of an antidepressant drug called paroxetine was conducted to shed light on the field of drug treatment for depression. In September 2012 we searched, in a wide ranging way, for all the useful studies (randomised controlled trials) which had been completed which compared paroxetine with any other antidepressant in treating people with depression. One hundred and fifteen studies were included in this review, with a total of 26,134 people. We grouped the studies according to the types of drug they compared paroxetine against; we then analysed the combined findings of these groups of studies.

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For the primary outcome (number of people who responded to treatment) paroxetine was more effective than reboxetine, but less effective than mirtazapine (in the early phase: one to four weeks follow-up) and probably citalopram (at endpoint: six weeks follow-up). There was some evidence that paroxetine is less well tolerated than agomelatine and St John's Wort, as more patients allocated to paroxetine experienced at least some side effects (though this finding for St John's Wort was only based on one study).

In conclusion, some possibly meaningful differences between paroxetine and other antidepressants exist, but no definitive concluions can be drawn due to the limited number of studies per comparison. In addition, most of included studies were sponsored by the drug industry, which means they might potentially have overestimated the effect of paroxetine. Therefore, the results of this review should be interpreted with caution.

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SUMMARY OF FINDINGS FOR THE MAIN COMPARISON [Explanation]

Paroxetine compared with older ADs for depression

Patient or population: patients with depression
Settings: in- and out-patients
Intervention: paroxetine
Comparison: older ADs

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Older ADs	Paroxetine				
Failure to respond at endpoint (6-12 weeks)	**416 per 1000**	**426 per 1000** (396 to 455)	**OR 1.04** (0.92 to 1.17)	4647 (34 studies)	⊕⊕⊕◯ **moderate**[1]	
Failure to respond at 1-4 weeks	**670 per 1000**	**416 per 1000** (328 to 509)	**OR 0.90** (0.61 to 1.33)	526 (4 studies)	⊕⊕◯◯ **low**[1]	
Failure to respond at 16-24 weeks	See comment	See comment	Not estimable	0 (0)	See comment	No trial reported this outcome.
Failure to remit at endpoint	**550 per 1000**	**365 per 1000** (180 to 601)	**OR 1.23** (0.49 to 3.07)	401 (3 studies)	⊕⊕◯◯ **low**[1,2]	
SMD at endpoint		The mean SMD at endpoint in the intervention groups was **0.01 standard deviations higher** (0.08 lower to 0.09 higher)		4745 (35 studies)	⊕⊕⊕◯ **moderate**[1]	This effect approaches zero.

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Failure to complete - any cause -	**312 per 1000**	**276 per 1000** (249 to 303)	**OR 0.84** (0.73 to 0.96)	6810 (44 studies)	⊕⊕⊕○ **moderate**[1]
Participants with at least some Side Effects	**707 per 1000**	**606 per 1000** (565 to 650)	**OR 0.64** (0.54 to 0.77)	6132 (42 studies)	⊕⊕⊕○ **moderate**[1]

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

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

[1] Blinding stated but not tested. No information on randomisation procedures and allocation concealment.
[2] I squared 79%.

BACKGROUND

Description of the condition

Major depression is a severe mental illness characterised by a persistent low mood and/or loss of interest and pleasure accompanied by a range of symptoms including appetite loss, insomnia, fatigue, loss of energy, poor concentration, psychomotor symptoms, inappropriate guilt and morbid thoughts of death (APA 1994). This condition is associated with marked personal, social and economic morbidity, loss of functioning and productivity, and creates significant demands on service providers in terms of workload (NICE 2010). It was the third leading cause of burden among all diseases in the year 2002, and it is expected to show a rising trend during the coming 20 years (WHO 2006).

Description of the intervention

Although pharmacological and psychological interventions are both effective for major depression, in primary and secondary care settings antidepressant (AD) drugs remain the mainstay of treatment (APA 2000; Ellis 2004; NICE 2010). Paroxetine hydrochloride is a component of the class of AD known as selective serotonin reuptake inhibitors (SSRIs). In vitro studies suggest that paroxetine is a potent and highly selective inhibitor of neuronal serotonin reuptake and has only very weak effects on norepinephrine and dopamine neuronal reuptake. (Germann 2013).

How the intervention might work

Paroxetine is the most potent inhibitor of the reuptake of serotonin (Ki = 65 pmol/L) of all SSRIs and shows an intermediate affinity profile between the other SSRIs and tricyclic antidepressants (TCAs) with regards to the norepinephrine transporter (Ki = 45 nmol/L). At higher concentrations paroxetine loses its serotonin transporter (SERT) selectivity and may therefore act as a dual serotonin/norepinephrine uptake inhibitor (SNRI), nevertheless it is necessary to administer high doses of paroxetine (40 mg/day and higher) to determine a sufficient plasma level (higher than 100 ng/mL). (Gibiino 2012; Germann 2013).

Why it is important to do this review

Amongst ADs many different agents are available for the treatment of depression, including TCAs, monoamine oxidase inhibitors (MAOIs), SSRIs, SNRIs, and other newer agents (such as agomelatine, mirtazapine, reboxetine, bupropion). During the last 20 years, AD consumption has risen dramatically worldwide, mainly because of the increasing consumption of SSRIs and newer ADs, which have progressively become the most commonly prescribed ADs (Ciuna 2004). SSRIs are generally better tolerated than TCAs and there is evidence of similar efficacy (Anderson 2000). However, head-to-head comparison has provided contrasting findings. Amitriptyline, for example, may have the edge over SSRIs in terms of efficacy, and individual SSRIs and SNRIs may differ in terms of efficacy and tolerability (Hansen 2005; Cipriani 2009). Starting from this consideration, and with the aim to shed light on the field of AD trials and treatment of major depression, a group of researchers agreed to join forces under the rubric of the Meta-Analyses of New Generation Antidepressants Study Group (MANGA Study Group) to systematically review all available evidence for each specific newer AD to inform clinical practice and mental health policies. We have up to now completed some individual reviews (about fluoxetine (Magni 2013), duloxetine (Cipriani 2012a), citalopram (Cipriani 2012b), sertraline (Cipriani 2009a), escitalopram (Cipriani 2009b), mirtazapine (Watanabe 2011), fluvoxamine (Omori 2010), milnacipran (Nakagawa 2009), and a number of other reviews are now underway.

OBJECTIVES

1. To determine the efficacy of paroxetine in comparison with other anti-depressive agents in alleviating the acute symptoms of Major Depressive Disorder.

2. To review acceptability of treatment with paroxetine in comparison with other anti-depressive agents.

3. To investigate the adverse effects of paroxetine in comparison with other anti-depressive agents.

METHODS

Criteria for considering studies for this review

Types of studies

Randomised controlled trials (RCTs) comparing paroxetine with all other active anti-depressive agents as monotherapy in the acute-phase treatment of major depression were included. Quasi-randomised trials, such as those allocating by using alternate days of the week, were excluded. Cluster-randomised trials were eligible for inclusion. For trials which have a cross-over design only results from the first randomisation phase were considered.

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Types of participants

The review included participants 18 years or older, of both sexes, with a primary diagnosis of unipolar major depression according to standardised criteria, DSM-III, DSM-III-R, DSM-IV (APA 2000), ICD-10 (WHO 1992), Feighner criteria (Feighner 1972) or Research Diagnostic Criteria (Spitzer 1972). Studies using ICD-9 were excluded, as it only lists disease names and does not have diagnostic criteria.

We included participants with the following subtypes of depression: chronic, with catatonic features, with melancholic features, with atypical features, with postpartum onset, and with seasonal pattern. We included studies in which up to 20% of participants presented depressive episodes in bipolar affective disorder. We also included participants with a concurrent secondary diagnosis of another psychiatric disorder.

We excluded participants with a concurrent primary diagnosis of Axis I or II disorders and participants with a serious concomitant medical illness.

Types of interventions

We examined paroxetine in comparison with conventional treatments for acute depression. We also examined paroxetine in comparison with the non-conventional antidepressant hypericum.

We excluded trials in which paroxetine was compared with another type of psychopharmacological agent (i.e., anxiolytics, anticonvulsants, antipsychotics or mood-stabilisers), and trials in which paroxetine was used as an augmentation strategy.

Eligible intervention

1. Paroxetine: any dose and pattern of administration

Eligible comparators

Conventional anti-depressive agents: any dose and mode or pattern of administration:

1. Older ADs:
   - Tricyclics;
   - Heterocyclics;
   - MAOIs.
2. SSRIs
3. Newer or non-conventional anti-depressive agents, for example:
   - SNRIs;
   - Hypericum.

Types of outcome measures

Primary outcomes

1. Efficacy: response rate

(1) Number of patients who responded to treatment, showing a reduction of at least 50% on the Hamilton rating scale for depression (HDRS) (Hamilton 1960) or Montgomery and Asberg Depression Rating Scale (MADRS) (Montgomery 1979), or any other depression scale, or "much or very much improved" (score one or two) on Clinical Global Impression (CGI) - Improvement. All response rates were calculated out of the total number of randomised patients. Where more than one criterion was provided, we preferred the former criterion for judging response. We used the first criterion whenever possible, even when we needed to impute standard deviations (SDs) or response rates according to the procedures described below. We applied intention-to-treat (ITT) analyses, whereby all the dropouts not included in the analyses were considered non-responders.

When studies reported response rates at various time points of the trial, we decided a priori to subdivide the treatment indices as follows.

(a) Early response: between one and four weeks; the time point closest to two weeks was given preference.

(b) Acute phase treatment response: between six and 12 weeks; the time point given in the original study as the study endpoint was given preference.

(c) Follow-up response: between four and six months; the time point closest to 24 weeks was given preference.

The acute phase treatment response (between six and 12 weeks) was our primary outcome of interest.

Secondary outcomes

2. Efficacy: remission rate and continuous outcomes

(1) Number of patients who achieved remission. The cut-off point for remission was set a priori:

(a) at seven or less on the 17-item HDRS and at eight or less for all the other longer versions of HDRS, or

(b) at 10 or less on the MADRS (Zimmerman 2004), or

(c) "not ill or borderline mentally ill" (score one or two) on CGI-Severity (Guy 1970).

All remission rates were calculated out of the total number of randomised patients. Where two or more were provided, we preferred the first criteria for judging remission. We applied the ITT analyses, whereby all the dropouts not included in the analyses were considered non-remitters.

(2) Change scores from baseline to the time point in question (early response, acute phase response, or follow-up response as defined above) on HDRS or MADRS, or any other depression scale. We applied a looser form of ITT analyses, whereby all the patients with at least one post-baseline measurement were represented by their Last Observations Carried Forward (LOCF).

(3) Social adjustment, social functioning including the Global Assessment of Function (GAF) (Luborsky 1962) scores.

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(4) Health-related quality of life: we limited ourselves to SF-12/SF-36 (Ware 1993), HoNOS (Wing 1994) and WHO-QOL (WHOQOL Group 1998).
(5) Costs to healthcare services.

3. Acceptability

(1) Number of patients who dropped out during the trial as a proportion of the total number of randomised patients - Total dropout rate.
(2) Number of patients who dropped out due to inefficacy during the trial as a proportion of the total number of randomised patients - Dropout rates due to inefficacy.
(3) Number of patients who dropped out due to side effects during the trial as a proportion of the total number of randomised patients - Dropout rates due to side effects.

4. Tolerability

(1) Total number of patients experiencing at least some side effects.
(2) Total number of patients experiencing the following specific side effects.
(a) Sleepiness/drowsiness.
(b) Insomnia.
(c) Dry mouth.
(d) Constipation.
(e) Urination problem.
(f) Hypotension.
(g) Agitation/anxiety.
(h) Suicide wishes/gestures/attempts.
(i) Completed suicide.
(j) Vomiting/nausea.
(k) Diarrhoea.
In order not to miss any relatively rare or unexpected yet important side effects, in the data extraction phase, we collected all side effects data reported in the literature and discussed ways to summarise them post hoc.

Search methods for identification of studies

The Cochrane, Depression, Anxiety and Neurosis Review Group's Specialised Register (CCDANCTR)

The Cochrane Depression, Anxiety and Neurosis Group (CCDAN) registers were searched up to September, 2012. The CCDAN maintain two clinical trials registers at their editorial base in Bristol, UK, a references register and a studies based register. The CCDANCTR-References Register contains over 31,500 reports of randomised controlled trials in depression, anxiety and neurosis. Approximately 65% of these references have been tagged to individual, coded trials. The coded trials are held in the CCDANCTR-Studies Register and records are linked between the two registers through the use of unique Study ID tags. Coding of trials is based on the EU-Psi coding manual, please contact the CCDAN Trials Search Coordinator for further details. Reports of trials for inclusion in the Group's registers are collated from routine (weekly), generic searches of MEDLINE (1950-), EMBASE (1974-) and PsycINFO (1967-); quarterly searches of the Cochrane Central Register of Controlled Trials (CENTRAL) and review specific searches of additional databases. Reports of trials are also sourced from international trials registers c/o the World Health Organization's trials portal (ICTRP), ClinicalTrials.gov, drug companies, the handsearching of key journals, conference proceedings and other (non-Cochrane) systematic reviews and meta-analyses.
Details of CCDAN's generic search strategies can be found on the Group's website.

Electronic searches

1. CCDANCTR

CDANCTR-Studies was searched using the following search strategy:
Diagnosis = Depress* or Dysthymi* or "Adjustment Disorder*" or "Mood Disorder*" or "Affective Disorder" or "Affective Symptoms"
and
Intervention = Paroxetine
CCDANCTR-References was searched using a similar set of terms to find additional untagged/uncoded references:
Keyword = Depress* or Dysthymi* or "Adjustment Disorder*" or "Mood Disorder*" or "Affective Disorder" or "Affective Symptoms"
and
Free-Text = Paroxetine
There was no restriction on date, language or publication status applied to the search.

2. International Regulatory Authorities and Trial Registries

Websites of the following drug regulatory authorities were searched for additional unpublished data: The Food and Drug Administration (FDA) in the USA, the Medicines and Healthcare products Regulatory Agency (MHRA) in the UK, the European Medicines Agency (EMEA) in the EU, the Pharmaceuticals and Medical Devices Agency (PMDA) in Japan, the Therapeutic Goods Administration (TGA) in Australia). International trial registries were also searched for unpublished or ongoing research: Clinicaltrials.gov, ISRCTN, Nederlands Trial Register, EUDRACT, UMIN-CTR and the Australian New Zealand Clinical Trials Registry.

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Searching other resources

Personal communication

Pharmaceutical companies and experts in this field were contacted for additional information on studies meeting the inclusion criteria for this review.

Handsearching

Appropriate journals and conference proceedings relating to the treatment of depression with paroxetine have already been handsearched and incorporated into the CCDANCTR.
Reference lists of all included studies, previous systematic reviews and major textbooks of affective disorder written in English were checked for published reports and citations of unpublished research. A cited reference search was conducted (on the Web of Science) to identify new reports citing any of the included studies.

Data collection and analysis

Data were entered into RevMan 5.2 (RevMan 2012) software by two review authors (DP and CT) (double data entry).

Selection of studies

Studies which met the following rough inclusion criteria constituted the preliminary list and their full texts were retrieved. The rough inclusion criteria were:
(a) randomised trial;
(b) comparing paroxetine against any other antidepressant;
(c) patients with major depression, regardless of the diagnostic criteria used.
Studies relating to paroxetine generated by the search strategies of the CCDANCTR-References and the other complementary searches were checked by review authors CR and CT to see if they meet the rough inclusion criteria, firstly based on the title and abstracts. All the studies rated as possible candidates by either of the two review authors were added to the preliminary list and their full texts retrieved. All the full text articles in this preliminary list were then assessed by MP and DP to see if they met the strict inclusion criteria. If the raters disagreed the final rating was made by consensus with the involvement (if necessary) of CB. Considerable care was taken to exclude duplicate publications.

Data extraction and management

Two review authors, working independently and in duplicate (CR and CT) extracted data from the included studies. Data were extracted on: participant characteristics (age, sex, depression diagnosis, comorbidity, depression severity, antidepressant treatment history for the index episode, study setting); intervention details (dosage range, mean daily dosage actually prescribed, co-intervention if any, paroxetine as investigational drug or as comparator drug, sponsorship); and outcome measures of interest from the included studies. The results were compared with those in the completed reviews of individual antidepressants in *The Cochrane Library*. If there were any discrepancies, a third review author (AC) intervened and the agreed-upon results were used in the review as well as fed back to the authors of the completed reviews. If the trial was a three (or more) -armed trial involving a placebo arm, the data were extracted from the placebo arm as well.

Assessment of risk of bias in included studies

Two review authors (MP and CR) independently assessed trial risk of bias in accordance with the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). The Cochrane Collaboration's tool for assessing risk of bias covers six domains of bias: selection bias (random sequence generation, allocation concealment), performance bias (blinding of participants and personnel), detection bias (blinding of outcome assessment), attrition bias (incomplete outcome data), reporting bias (selective reporting), and other bias not covered elsewhere. Particular attention was given to the adequacy of the random allocation concealment and double blinding. Where inadequate details of methodological characteristics of trials were provided, the authors were contacted in order to obtain further information. If the raters disagreed the final rating was made by consensus with the involvement (if necessary) of another member of the review group (CB). The ratings were also compared with those in the completed reviews of individual antidepressants in *The Cochrane Library*. If there were any discrepancies, they were fed back to the authors of the completed reviews.

Measures of treatment effect

All comparisons were performed between paroxetine and comparator ADs considered as individual ADs and as a class.

Dichotomous data

For dichotomous data, odds ratios (ORs) were calculated with a 95% confidence interval (CI). For statistically significant results, we calculated the number needed to treat to provide benefit (NNTb) and the number needed to treat to induce harm (NNTh).

Continuous data

For continuous data we calculated the standardized mean differences (SMDs) with a 95% CI.

Unit of analysis issues

Cross-over trials

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A major concern of cross-over trials is the carry-over effect. It occurs if an effect (e.g. pharmacological, physiological or psychological) of the treatment in the first phase is carried over to the second phase. As a consequence, on entry to the second phase, the participants can differ systematically from their initial state, despite a wash-out phase. For the same reason, cross-over trials are not appropriate if the condition of interest is unstable (Elbourne 2002). As both effects are very likely in major depression, we only used data from the first phase of the cross-over studies.

Cluster-randomised trials

No cluster-randomised trials were identified for this version of the review. Should they be identified in a future update, we plan to use the generic inverse variance technique, if such trials have been appropriately analysed taking into account intra-class correlation coefficients to adjust for cluster effects.

Multiple intervention groups

Studies that compared more than two intervention groups of the same drug (i.e. different dosages) were included in meta-analysis by combining group arms of the study into a single group, for the intervention and for the control group respectively, as recommended in section 16.5 of the *Cochrane Handbook* (Higgins 2011).

Dealing with missing data

When dichotomous or continuous outcomes were not reported, we asked the trial authors to supply the data.

For dichotomous data, we applied intention-to-treat (ITT) analyses, whereby all the dropouts not included in the analyses were considered as non-responders or non-remitters (i.e. it was assumed they would have experienced the negative outcome by the end of the trial, e.g. failure to respond to treatment).

For continuous data, we applied a looser form of ITT analyses, whereby all patients with at least one post-baseline measurement were represented by their Last Observations Carried Forward (LOCF). When only the standard error (SE) or t-statistics or P values were reported, standard deviations (SDs) were calculated according to Altman (Altman 1996).

In the absence of supplemental data from the authors, the SDs of the HDRS (or any other depression scale) and response/remission rates were calculated according to the validated imputation methods (Furukawa 2005; Furukawa 2006). We examined the validity of these imputations in the sensitivity analyses.

Assessment of heterogeneity

Skewed data and non-quantitative data were presented descriptively. An outcome whose minimum score is zero could be considered skewed when the mean was smaller than twice the SD. Heterogeneity between studies was investigated using the I^2 statistic (Higgins 2003; Ioannidis 2008) and by visual inspection of the forest plots.

According to the *Cochrane Handbook* (Higgins 2011), the following thresholds for the interpretation of I^2 were used: 0% to 40%: might not be important; 30% to 60%: may represent moderate heterogeneity; 50% to 90%: may represent substantial heterogeneity; 75% to 100%: considerable heterogeneity. Moreover, we considered the sample size, the magnitude and the direction of the treatment effects.

Assessment of reporting biases

Data from included studies were entered into a funnel plot (trial effect against trial variance) to investigate small-study effects (Sterne 2000). We used the tests for funnel plot asymmetry only when there were at least 10 studies included in the meta-analysis, and results were interpreted cautiously, with visual inspection of the funnel plots (Higgins 2011). When evidence of small-study effects was identified, possible reasons for funnel plot asymmetry, including publication bias, were investigated.

Data synthesis

For dichotomous data, odds ratios (OR) were calculated with 95% confidence intervals. The primary analysis used a random-effects model, which had the highest generalisability in our empirical examination of summary effect measures for meta-analyses (Furukawa 2002a). The robustness of this summary measure was routinely examined by checking the results under a fixed-effect model. Material differences between the models were reported.

Continuous data were analysed using standardized mean differences (SMD) (with 95% CIs) as different measurement scales were used. A random-effects model was employed. Fixed-effect analyses were used routinely for continuous outcomes to investigate the effect of the choice of method on the estimates. Material differences between the models were reported.

Subgroup analysis and investigation of heterogeneity

Subgroup analyses should be performed and interpreted with caution because multiple analyses will lead to false positive conclusions (Oxman 1992). However, we performed the following subgroup analyses for the following a priori reasons.

1. Paroxetine dosing (fixed low dosage, fixed standard dosage, fixed high dosage; flexible low dosage, flexible standard dosage, flexible high dosage), because there is evidence to suspect that low dosage antidepressant may be associated with better outcomes both in terms of effectiveness and side effects than standard or high dosage antidepressants (Bollini 1999; Furukawa 2002b) and also because fixed versus flexible dosing schedule may affect estimates of treatment effectiveness (Khan 2003).
2. Comparator dosing (low effective range, medium to high effective range), as it is easy to imagine that there are greater

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chances of completing the study on the experimental drug than on the comparator drug that is increased to the maximum dosage.

3. Depression severity (severe major depression, moderate/mild major depression).

4. Treatment settings (psychiatric inpatients, psychiatric outpatients, primary care).

5. Elderly patients (≥ 65 years of age), separately from other adult patients.

Sensitivity analysis

Funnel plot analysis was performed to check for existence of small-study effects including publication bias. We performed the following sensitivity analyses. By limiting the studies to be included to those with higher quality, we examined if the results changed, and checked for the robustness of the observed findings.

1. Excluding trials with unclear concealment of random allocation and/or unclear double blinding.

2. Excluding trials whose dropout rate was greater than 20%.

3. Performing the worst-case scenario ITT (all the patients in the experimental group experienced the negative outcome and all those allocated to the comparison group experienced the positive outcome) and the best-case scenario ITT (all the patients in the experimental group experienced the positive outcome and all those allocated to the comparison group experienced the negative outcome).

4. Excluding trials for which the response rates had to be calculated based on the imputation method (Furukawa 2005) and those for which the SD had to be borrowed from other trials (Furukawa 2006).

5. Examination of "wish bias" by comparing paroxetine as investigational drug versus paroxetine as comparator, as there is evidence to suspect that a new antidepressant might perform worse when used as a comparator than when used as an experimental agent (Barbui 2004; Lundh 2012).

6. Excluding studies funded by the pharmaceutical company marketing paroxetine. This sensitivity analysis is particularly important in view of the recent repeated findings that funding strongly affects outcomes of research studies (Als-Nielsen 2003; Bhandari 2004; Lexchin 2003; Montgomery 2004b; Perlis 2005; Procyshyn 2004) and because industry sponsorship and authorship of clinical trials are increasing over 20 years (Buchkowsky 2004).

We planned that if subgroups within any of the subgroup or sensitivity analyses turned out to be significantly different from one another, we would run meta-regression for exploratory analyses of additive or multiplicative influences of the variables in question. Our routine application of random-effects and fixed-effect models as well as our secondary outcomes of remission rates and continuous severity measures may be considered additional forms of sensitivity analyses.

Summary of findings

The GRADE approach was employed to interpret findings (Langendam 2013) and the GRADE profiler (GRADEPRO) allowed us to import data from Review Manager 5.2 (Review Manager) to create 'Summary of findings' tables. These tables provide outcome-specific information concerning the overall quality of evidence from studies included in the comparison, the magnitude of effect of the interventions examined, and the sum of available data on the outcomes we considered.

The following outcomes were included in the 'Summary of findings' tables.

1. Failure to respond at endpoint (six to 12 weeks).
2. Failure to respond at one to four weeks.
3. Failure to respond at 16 to 24 weeks.
4. Failure to remit at endpoint.
5. SMD at endpoint.
6. Failure to complete - any cause.
7. Participants with at least some SE.

RESULTS

Description of studies

See Characteristics of included studies; Characteristics of excluded studies; Characteristics of studies awaiting classification

Results of the search

The original searches yielded 691 records: after reading abstracts, 187 papers were considered potentially relevant for this review. Of these, 13 were excluded because of the not relevant diagnostic status or other reasons, 58 studies were defined as awaiting assessment and one study was ongoing. The remaining 115 studies, retrieved for more detailed evaluation, met the inclusion criteria and were included in the review. A total of 94 studies contributed to the quantitative synthesis (meta-analysis) (see Figure 1).

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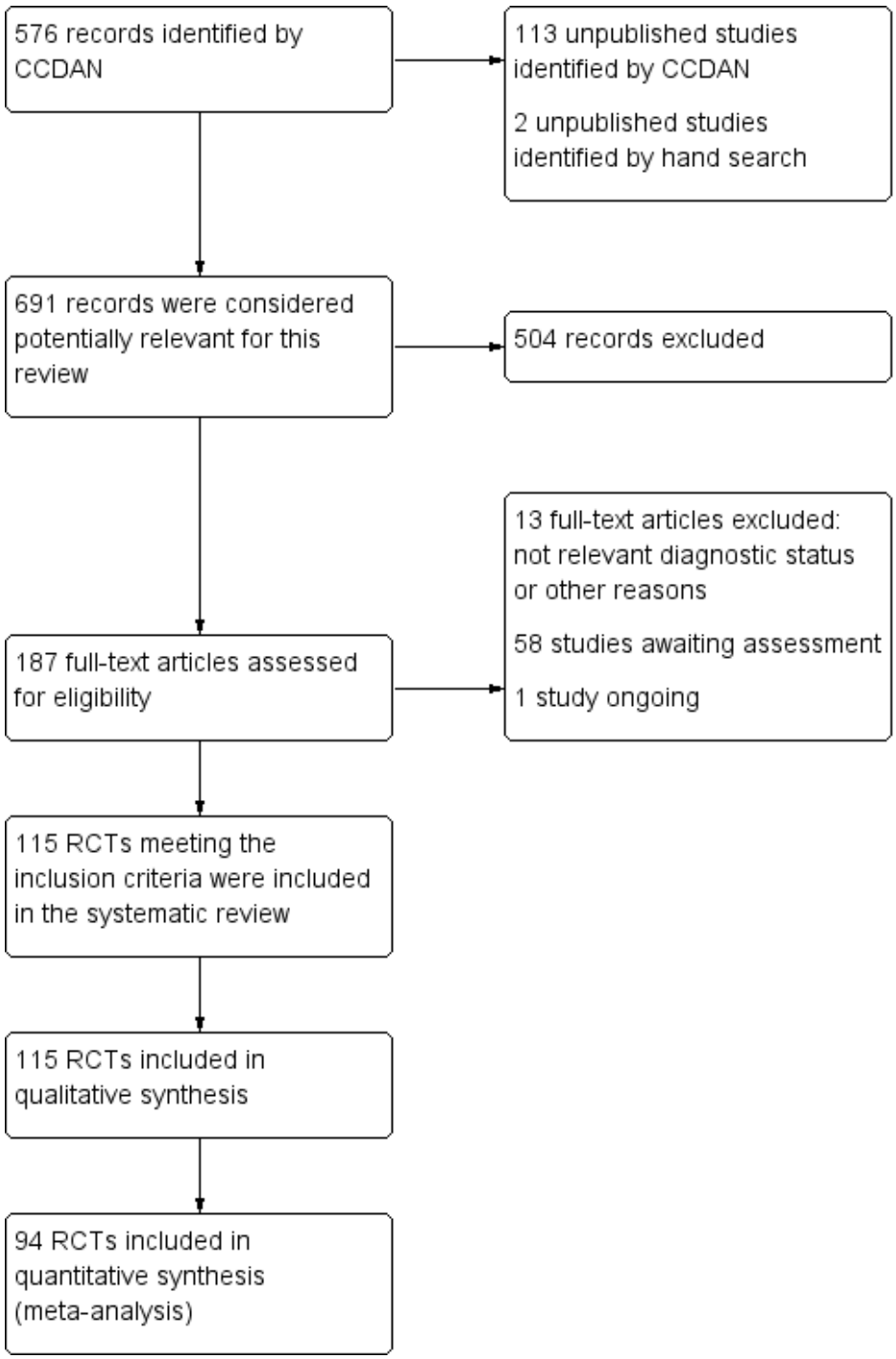
Figure 1. Flow diagram.



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Included studies

See: Characteristics of included studies

Overall, a total of 115 studies (of which 25 were unpublished) were included in the present systematic review (26,134 participants). Unpublished data were obtained from the websites of pharmaceutical industries sponsoring the drugs under evaluation (23 trials), from the European Medicine Agency (one trial) and from conference proceedings (one trial).

Design

The great majority of included studies were reported to be double-blind (99 out of 115 RCTs, that is 86%). The participants were followed up for six weeks (range: three to 52 weeks) in 57 trials.

Sample sizes

The mean number of participants per study was 226, with a minimum sample size of 10 (Javors 2000) and a maximum of 1057 (NCT00463242).

Setting

A total of 54 trials enrolled only outpatients, 14 trials enrolled only inpatients, and both inpatients and outpatients were enrolled in 18 trials. Twelve trials were conducted in general practice setting and for the remaining 17 trials the setting was unclear. Fifty-two out of 115 trials took place in Europe; 34 trials took place in America (United States, Central America) and Canada; nine trials took place in Asia and two in Australia, For the remaining trials the country was unclear.

Participants

The majority of included trials (100 RCTs) enrolled patients with a diagnosis of major depression based on DSM-III (30 studies), DSM-III-R (26 studies), DSM-IV or ICD 10 criteria (44 studies). The remaining studies used other diagnostic criteria (15 studies). Forty-one trials excluded patients over 65 years, while 15 trials included only elderly patients. We also included a minority of studies in which up to 20% of patients presented depressive episodes in bipolar disorder (six studies).

Intervention and Comparators

In 54 studies paroxetine was compared with older ADs (two RCTs versus dothiepin, two RCTs versus nortriptyline, 19 RCTs versus amitriptyline, 12 RCTs versus imipramine, three RCTs versus desipramine, three RCTs versus maprotiline, five RCTs versus mianserin, five RCTs versus clomipramine, two RCTs versus lofepramine, and one RCT versus doxepine). Twenty-one RCTs compared paroxetine with other SSRIs (one RCT versus sertraline, two RCTs versus escitalopram, 14 RCTs versus fluoxetine and two RCTs versus fluvoxamine. There was one three-armed study comparing paroxetine with fluoxetine and sertraline (Fava 2002), and one three-armed study comparing paroxetine with citalopram and sertraline (Jefferson 2001 29060/785)). Forty studies compared paroxetine with newer or non-conventional ADs (one RCT versus trazodone, three RCTs versus milnacipran, eight RCTs versus venlafaxine, two RCTs versus nefazodone, three RCTs versus reboxetine, two RCTs versus bupropion, one RCT versus hypericum, three RCTs versus tianeptine, four RCTs versus mirtazapine, six RCTs versus duloxetine, one RCT versus amisulpride, four RCTs versus agomelatine,one RCT versus aprepitant (MK-869), and one RCT versus substance P).

Outcomes

At the end of the reviewing process, 94 RCTs were included in the meta-analysis. For efficacy outcomes, 76 RCTs provided continuous data, and 81 dichotomous data. For acceptability outcomes, 94 RCTs provided data on total dropouts, 61 on dropouts due to inefficacy and 78 on dropouts due to side effects. In the majority of trials (93 out of 115, 81%) the HDRS scale was used for reporting outcomes.

Overall, 15,863 patients were included in the efficacy analysis, dichotomous outcome (7776 participants randomised to paroxetine and 8087 randomised to another antidepressant) and 14,637 were included in the efficacy analysis, continuous outcome (7326 participants randomised to paroxetine and 7311 randomised to another antidepressant). A total of 18,658 patients were included in the acceptability analysis (9037 partIcipants randomised to paroxetine and 9621 randomised to another antidepressant).

Excluded studies

See: Characteristics of excluded studies; Characteristics of studies awaiting classification

Thirteen articles initially selected did not meet our inclusion criteria and were excluded because of the wrong diagnosis or other reasons A total of 58 records were classified as “awaiting classification”.

Ongoing studies

There is one ongoing study (Thomas 2008), This is a large multicentre trial including more than 500 participants with a primary diagnosis of major depression.

See Characteristics of ongoing studies

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Studies awaiting classification

There were 58 studies for which sufficient information was not currently available to make a decision about inclusion or exclusion. The majority of studies in this section were written in Chinese (39 out of 58 studies). For the remaining studies, the number of participants or the outcomes were unclear.
See Characteristics of studies awaiting classification

Risk of bias in included studies

See:Characteristics of included studies.

Our judgment about the overall risk of bias in the individual studies is illustrated in Figure 2 and Figure 3. The Cochrane 'Risk of bias' tool highlighted poor reporting for a number of items in many of the included studies, although judging articles from some time ago by today's standards can be problematic (Begg 1996; Turner 2012). Moreover, many articles failed to report methodologically relevant information on study procedure (in these cases the judgement was defined as "unclear"). In general, the reporting of studies was not good. This type of reporting has been associated with an overestimate of the estimate of effect (Schulz 1995) and this should be considered when interpreting the results.

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

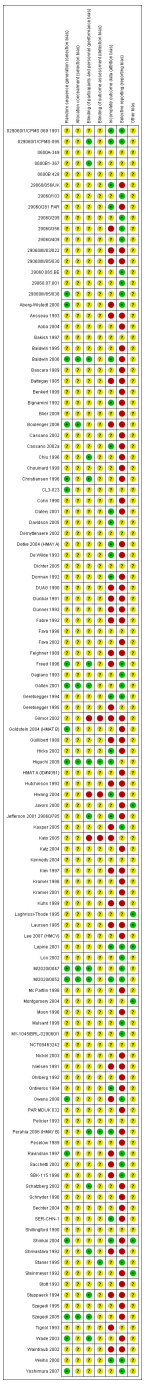

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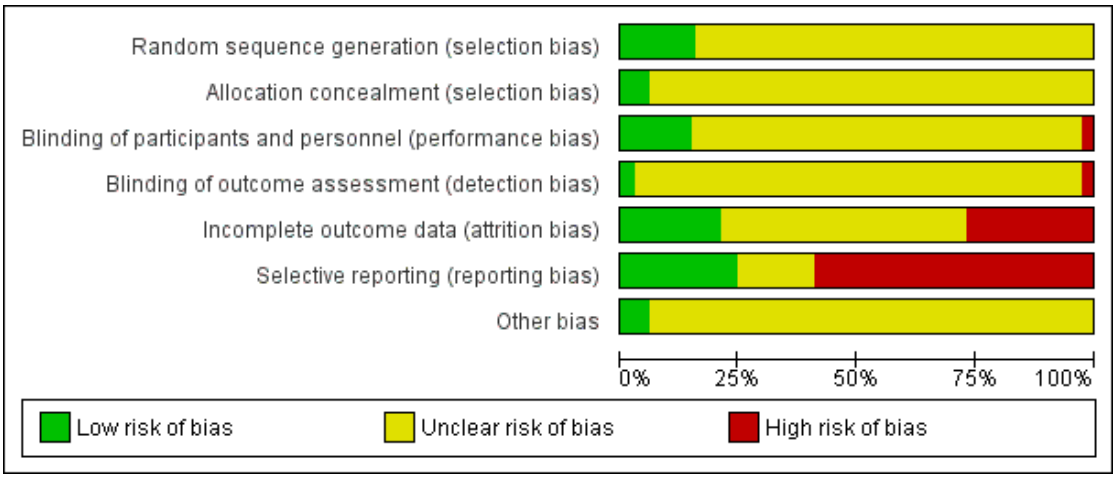
Figure 3. 'Risk of bias' graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.



Allocation

Random sequence generation

The majority of studies (96 RCTs) did not report the methods of random sequence generation, while 18 studies (CL3-023; 29060III/85/038; Aberg-Wistedt 2000; Baldwin 2006; Boulenger 2006; Christiansen 1996; Freed 1996; Gallen 2001; Goldstein 2004 (HMAT B); Higuchi 2009; M/2020/0047; M/2020/0052; Owens 2008; Ravindran 1997; Shinkai 2004; Szegedi 2005; Wade 2003; Yoshimura 2007) specified this information, and they were classified as "low risk of bias".

Allocation concealment

Only a few trials (seven out of 115) (Baldwin 2006; Boulenger 2006; Gallen 2001; Higuchi 2009; M/2020/0047; M/2020/0052; Szegedi 2005) reported details on allocation concealment and were classified as "low risk".

Blinding

The great majority of included trials were undertaken under double-blind conditions (99 out of 115 RCTs), however in many cases blinding was stated but not tested; two trials employed an open-label design and for the remaining studies the design was unclear.

Incomplete outcome data

Twenty-four trials were rated as "low" in terms of addressing incomplete outcome data, while 60 studies were classified as "unclear risk" and 31 as "high risk".

Selective reporting

The study protocol was not available for almost all studies so it is difficult to make a judgment on the possibility of outcome reporting bias. However, in 28 studies results were consistent with what was stated in the study protocols.

Other potential sources of bias

Most of the included studies were funded by the pharmaceutical industry or do not specify the source of funding. Seven studies were independent from commercial sponsorship (Javors 2000; Laghrissi-Thode 1995; Laursen 1985; Montgomery 2004; Shinkai 2004; Steinmeyer 1992; Lepine 2001).

Effects of interventions

See: **Summary of findings for the main comparison** Paroxetine compared with older ADs for depression; **Summary of findings 2** Paroxetine compared with agomelatine for depression; **Summary of findings 3** Paroxetine compared with amisulpride for

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depression; **Summary of findings 4** Paroxetine compared with aprepitant for depression; **Summary of findings 5** Paroxetine compared with bupropion for depression; **Summary of findings 6** Paroxetine compared with citalopram for depression; **Summary of findings 7** Paroxetine compared with duloxetine for depression; **Summary of findings 8** Paroxetine compared with escitalopram for depression; **Summary of findings 9** Paroxetine compared with fluoxetine for depression; **Summary of findings 10** Paroxetine compared with fluvoxamine for depression; **Summary of findings 11** Paroxetine compared with hypericum for depression; **Summary of findings 12** Paroxetine compared with milnacipran for depression; **Summary of findings 13** Paroxetine compared with mirtazapine for depression; **Summary of findings 14** Paroxetine compared with nefazodone for depression; **Summary of findings 15** Paroxetine compared with reboxetine for depression; **Summary of findings 16** Paroxetine compared with sertraline for depression; **Summary of findings 17** Paroxetine compared with tianeptine for depression; **Summary of findings 18** Paroxetine compared with trazodone for depression; **Summary of findings 19** Paroxetine compared with venlafaxine for depression

All the results of this systematic review need to be interpreted considering the characteristics and the risk of bias profile of each included study (Characteristics of included studies).

Comparison 1: Paroxetine versus older ADs

Pirmary outcome: Efficacy. Number of patients who responded to treatment

1.1 Responders at endpoint (six to 12 weeks)

We found no statistically significant difference in terms of response rate between paroxetine and older ADs as a class (odds ratio (OR): 1.04, 95% confidence interval (CI) 0.92 to 1.17, 34 RCTs, 4647 participants), and in head-to-head comparisons (see Analysis 1.1).

1.2 Early response rate (one to four weeks)

We found no difference between paroxetine and older ADs for this outcome (see Analysis 2.1).

1.3 Follow-up response rate (16 to 24 weeks)

No studies provided data for this outcome.

Secondary outcome: Efficacy. Number of patients who remitted

1.4 Remission at endpoint (six to 12 weeks)

There was no evidence that paroxetine was more effective than older ADs as a class in terms of remission rates at endpoint (see Analysis 4.1). In head-to-head comparisons we found a difference in favour of clomipramine over paroxetine (OR: 3.39, 95% CI 1.50 to 7.65, number needed to treat to provide benefit (NNTb) = 4, 95% CI 2 to 11, 1 RCT, 120 participants).

1.5. Early remission rate (one to four weeks)

There was no evidence that paroxetine was more effective than older ADs in terms of early remissions (see Analysis 5.1).

1.6. Follow-up remission rate (16 to 24 weeks)

No studies provided data for this outcome.

Secondary outcome: Efficacy. Standardized mean difference (SMD)

1.7 Standardized mean difference at endpoint (six to 12 weeks)

On this outcome, we found no statistically significant differences between paroxetine and older ADs (SMD: 0.01, 95% CI -0.08 to 0.10, 34 RCTs, 4712 participants), nor between paroxetine and individual ADs (see Analysis 7.1).

1.8 Standardized mean difference at one to four weeks

We found a difference in favour of desipramine over paroxetine (SMD: 0.86, 95% CI 0.28 to 1.44, 1 RCT, 50 participants) (see Analysis 8.1).

1.9 Standardized mean difference at 16 to 24 weeks

No studies provided data for this outcome.

Secondary outcome: Acceptability

1.10 Failure to complete due to any cause

In terms of participants who dropped out due to any cause, we found a difference between paroxetine and older ADs as a class (OR: 0.84, 95% CI 0.73 to 0.96, number needed to treat to induce harm (NNTh) = 23, 95% CI 15 to 44, 43 RCTs, 6777 participants). In head-to-head comparisons paroxetine was better

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tolerated than clomipramine (OR: 0.67, 95% CI 0.52 to 0.87, NNTh = 14, 95% CI 8 to 39, 4 RCTs, 1273 participants), and than imipramine (OR: 0.65, 95% CI 0.50 to 0.85, NNTh= 8, 95% CI 6 to 14, 9 RCTs, 1268 participants) (see.Analysis 10.1)

1.11 Failure to complete due to inefficacy

We found no differences in terms of dropouts due to inefficacy between paroxetine and older ADs (OR: 1.22, 95% CI 0.93 to 1.61, 27 RCTs, 4436 participants) (see Analysis 11.1).

1.12 Failure to complete due to side effects

The analysis of dropouts due to side effects revealed that amitriptyline (OR: 0.74, 95% CI 0.56 to 0.98, NNTh = 29, 95% CI 15 to 1318, 12 RCTs, 1698 participants), clomipramine (OR: 0.59, 95% CI 0.41 to 0.84, NNTh = 19, 95% CI 11 to 61, 4 RCTs, 1273 participants), imipramine (OR: 0.58, 95% CI 0.43 to 0.77, NNTh = 10, 95% CI 7 to 17, 9 RCTs, 1268 participants) and overall older ADs (OR: 0.76, 95% CI 0.63 to 0.92, NNTh = 25, 95% CI 17 to 49, 34 RCTs, 5175 participants) were significantly less well tolerated than paroxetine (see Analysis 12.1).

Secondary outcome: Tolerability

1.13 Total number of patients experiencing at least some side effects

There was evidence that paroxetine was associated with a lower rate of adverse events than amitriptyline (OR: 0.53, 95% CI 0.39 to 0.72, NNTh = 7, 95% CI 6 to 10, 16 RCTs, 2492 participants), imipramine (OR: 0.62, 95% CI 0.42 to 0.94, NNTh = 10, 95% CI 7 to 19, 9 RCTs, 1189 participants) and than older ADs as a class (OR: 0.64, 95% CI 0.53 to 0.77, NNTh = 11, 95% CI 9 to 14, 41 RCTs, 6099 participants) (see Analysis 13.1).

1.14 Number of patients experiencing specific side effects

(a) Sleepiness/drowsiness. We found a difference in favour of paroxetine over maprotiline (OR: 0.37, 95% CI 0.17 to 0.82, NNTh = 13, 95% CI 7 to 52, 2 RCTs, 358 participants) (see Analysis 79.1).

(b) Insomnia. There was evidence that paroxetine was associated with a higher rate of insomnia than older ADs (OR: 2.17, 95% CI 1.51 to 3.12, NNTh = 17, 95% CI 12 to 29, 15 RCTs, 1986 participants). In head-to-head comparisons, paroxetine was associated with a higher rate of insomnia than amitriptyline (OR: 3.66, 95% CI 1.36 to 9.85, NNTh = 13, 95% CI 8 to 36, 4 RCTs, 352 participants), dothiepin (OR: 2.34, 95% CI 1.03 to 5.31, NNTh = 19, 95% CI 10 to 246, 2 RCTs, 405 participants) and than maprotiline (OR: 4.38, 95% CI 1.72 to 11.15, NNTh = 9, 95% CI 6 to 22, 1 RCTs, 298 participants) (see Analysis 54.1).

(c) Dry mouth. Paroxetine was associated with a lower rate of dry mouth than amitriptyline (OR: 0.27, 95% CI 0.17 to 0.43, NNTh = 4, 95% CI 4 to 5, 12 RCTs, 1576 participants), clomipramine (OR: 0.35, 95% CI 0.26 to 0.48, NNTh = 6, 95% CI 5 to 8, 2 RCTs, 1111 participants), dothiepin (OR: 0.22, 95% CI 0.10 to 0.50, NNTh = 3, 95% CI 3 to 5, 2 RCTs, 405 participants), imipramine (OR: 0.16, 95% CI 0.10 to 0.26, NNTh = 3, 95% CI 2 to 3, 8 RCTs, 835 participants), maprotiline (OR: 0.13, 95% CI 0.08 to 0.23, NNTh = 3, 95% CI 2 to 4, 3 RCTs, 429 participants), and older ADs as a class (OR: 0.23, 95% CI 0.18 to 0.30, NNTh = 4, 95% CI 3 to 5, 29 RCTs, 4578 participants) (see Analysis 38.1).

(d) Constipation. Paroxetine was associated with a lower rate of constipation than older ADs as a class (OR: 0.49, 95% CI 0.40 to 0.60, NNTh = 12, 95% CI 9 to 16, 26 RCTs, 3934 participants). In head-to-head comparisons, paroxetine was associated with a lower rate of constipation than amitriptyline (OR: 0.61, 95% CI 0.37 to 0.99, NNTh = 18, 95% CI 11 to 65, 10 RCTs, 1146 participants), clomipramine (OR: 0.57, 95% CI 0.38 to 0.85, NNTh = 19, 95% CI 12 to 64, 2 RCTs, 1111 participants), dothiepin (OR: 0.57, 95% CI 0.32 to 0.99, NNTh = 10, 95% CI 5 to 378, 1 RCT, 271 participants), imipramine (OR: 0.40, 95% CI 0.25 to 0.63, NNTh = 6, 95% CI 5 to 11, 7 RCTs, 633 participants), and maprotiline (OR: 0.31, 95% CI 0.17 to 0.55, NNTh = 7, 95% CI 5 to 12, 3 RCTs, 429 participants) (see Analysis 31.1).

(e) Urination/Urogenital problems. There was evidence in favour of paroxetine over imipramine for urinary retention (OR: 0.04, 95% CI 0.00 to 0.73, NNTh = 4, 95% CI 3 to 10, 1 RCT, 80 participants) (see Analysis 90.4) and for urogenital problems (Not Otherwise Specified) (OR: 0.10, 95% CI 0.01 to 0.82, NNTh = 10, 95% CI 6 to 38, 1 RCT, 159 participants) (see Analysis 90.5).

(f) Hypotension. We found no difference between paroxetine and older ADs (see Analysis 50.1).

(g) Agitation/anxiety. We found no difference between paroxetine and older ADs (see Analysis 18.1).

(h) Suicide wishes/gestures/attempts. We found no difference between paroxetine and older ADs (see Analysis 96.1; Analysis 96.3).

(i) Completed suicide. We found no difference between paroxetine and older ADs (see Analysis 96.2).

(j) Vomiting/nausea. Paroxetine was associated with a higher rate of vomiting/nausea than older ADs as a class (OR: 2.10, 95% CI 1.59 to 2.77, NNTh = 12, 95% CI 10 to 17, 30 RCTs, 4545 participants). In head-to-head comparisons we found evidence in favour of amitriptyline (OR: 2.17, 95% CI 1.43 to 3.29, NNTh = 15, 95% CI 10 to 29, 10 RCTs, 1282 participants), dothiepin (OR: 3.12, 95% CI 1.1 to 8.78, NNTh = 8, 95% CI 5 to 15, 2 RCTs, 405 participants), imipramine (OR: 2.05, 95% CI 1.23 to 3.42, NNTh = 11, 95% CI 7 to 26, 8 RCTs, 835 participants), and lofepramine (OR: 2.97, 95% CI 1.12 to 7.92, NNTh = 9, 95% CI 5 to 34, 2 RCTs, 228 participants) over paroxetine (see Analysis 59.1).

(k) Diarrhoea. We found that paroxetine was associated with a

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higher rate of diarrhoea than older ADs as a class (OR: 2.41, 95% CI 1.56 to 3.73, NNTh = 20, 95% CI 14 to 36, 13 RCTs, 1743 participants) and than dothiepin (OR: 3.47, 95% CI 1.23 to 9.75, NNTh = 12, 95% CI 7 to 56, 1 RCTs, 271 participants) and maprotiline (OR: 2.94, 95% CI 1.34 to 6.47, NNTh = 11, 95% CI 7 to 33, 2 RCTs, 358 participants) (see Analysis 36.1).
(l) Other side effects. Other statistically significant side effects are reported in Table 1.

Comparison 2: Paroxetine versus SSRIs

Primary outcome: Efficacy. Number of patients who responded to treatment

2.1 Responders at endpoint (six to 12 weeks)

We found a difference in favour of citalopram over paroxetine (OR: 1.54, 95% CI 1.04 to 2.28, NNTb = 9, 95% CI 5 to 102, 1 RCT, 406 participants).

2.2 Early response rate (one to four weeks) and follow-up response rate (16 to 24 weeks)

We found no differences between paroxetine and individual SSRIs (see Analysis 2.2; Analysis 3.1).

Secondary outcome: Efficacy. Number of patients who remitted

2.3 Remission rate at endpoint (six to 12 weeks)

We found no differences between paroxetine and individual SSRIs (see Analysis 4.2).

2.4 Early remission rate (one to four weeks)

We found no difference between paroxetine and other SSRIs in terms of early remission rates (see Analysis 5.2).

2.5. Follow-up remission rate (16 to 24 weeks)

No studies provided data for this outcome.

Secondary outcome: Efficacy. Standardized mean difference

2.6 Standardized mean difference at endpoint (six to 12 weeks)

For this continuous outcome at endpoint, we found no difference between paroxetine and other SSRIs (see Analysis 7.2).

2.7 Standardized mean difference at one to four weeks

For this outcome we found no difference between paroxetine and other SSRIs (see Analysis 8.2).

2.8 Standardized mean difference at 16 to 24 weeks

No difference was found for this outcome.

Secondary outcome: Acceptability

2.9 Failure to complete due to any cause

In terms of patients who dropped out during the trial for any reason, we found no difference between paroxetine and individual SSRIs (see Analysis 10.2).

2.10 Failure to complete due to inefficacy

We found no difference in terms of dropouts due to inefficacy (see Analysis 11.2).

2.11 Failure to complete due to side effects

In terms of dropouts due to side effects, we found that paroxetine was less well tolerated than fluoxetine (OR: 1.34, 95% CI 1.06 to 1.70, NNTh = 29, 95% CI 16 to 137, 11 RCTs, 2491 participants) (see Analysis 12.2).

Secondary outcome: Tolerability

2.13 Total number of patients experiencing at least some side effects

We found no difference between paroxetine and other SSRIs in terms of number of patients experiencing side effects (see Analysis 13.2).

2.14 Number of patients experiencing specific side effects

(a) Sleepiness/drowsiness. We found a difference in favour of fluoxetine over paroxetine (OR: 1.48, 95% CI 1.16 to 1.88, NNTh = 20, 95% CI 12 to 53, 8 RCTs, 2116 participants) (see Analysis 79.2).
(b) Insomnia. We found no difference between paroxetine and SSRIs (see Analysis 54.2).
(c) Dry mouth. Paroxetine was associated with a higher rate of dry mouth than fluoxetine (OR: 1.67, 95% CI 1.17 to 2.38, NNTh = 18, 95% CI 12 to 38, 6 RCTs, 1920 participants) (see Analysis 38.2).
(d) Constipation. Paroxetine was associated with a higher rate of constipation than fluoxetine (OR: 2.71, 95% CI 1.47 to 5.01,

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NNTh = 14, 95% CI 9 to 26, 3 RCTs, 1001 participants) and sertraline (OR: 3.26, 95% CI 1.73 to 6.14, NNTh = 10, 95% CI 7 to 20, 2 RCTs, 545 participants) (see Analysis 31.2).
(e) Urination/Urogenital problems. There was difference in favour of sertraline over paroxetine for this outcome (OR: 11.60, 95% CI 1.48 to 90.81, NNTh = 18, 95% CI 11 to 52, 1 RCT, 353 participants) (see Analysis 90.5).
(f) Hypotension. We found no difference between paroxetine and other SSRIs (see Analysis 50.2).
(g) Agitation/anxiety. We found no difference between paroxetine and other SSRIs (see Analysis 18.2).
(h) Suicide wishes/gestures/attempts. We found no difference between paroxetine and other SSRIs (see Analysis 96.1; Analysis 96.3)..
(i) Completed suicide. We found no difference between paroxetine and other SSRIs (see Analysis 96.2).
(j) Vomiting/nausea. We found a difference in favour of fluoxetine over paroxetine (OR: 1.24, 95% CI 1.02 to 1.51, NNTh = 26, 95% CI 14 to 298, 10 RCTs, 2336 participants) (see Analysis 59.2).
(k) Diarrhoea. We found a difference in favour of paroxetine over sertraline (OR: 0.40, 95% CI 0.26 to 0.60, NNTh = 6, 95% CI 4 to 11, 2 RCTs, 545 participants) (see Analysis 36.2).
(l) Other side effects. Other statistically significant side effects are reported in Table 1.

Comparison 3: Paroxetine versus newer or non-conventional ADs

Primary outcome: Efficacy. Number of patients who responded to treatment

3.1 Responders at endpoint (six to 12 weeks)

In terms of efficacy as number of patients who responded to treatment, there was a trend in favour of paroxetine over reboxetine (OR: 0.82, 95% CI 0.66 to 1.02, 3 RCTs, 1369 participants) (see Analysis 1.3).

3.2 Early response rate (one to four weeks)

In terms of efficacy as number of patients who responded to treatment at one to four weeks, we found a difference in favour of paroxetine over reboxetine (OR: 0.66, 95% CI 0.50 to 0.87, NNTb = 16, 95% CI 10 to 50, 3 RCTs, 1375 participants). By contrast, we found a difference in favour of mirtazapine over paroxetine for this outcome (OR: 2.39, 95% CI 1.42 to 4.02, NNTb = 8, 95% CI 5 to 14, 3 RCTs, 726 participants) (see Analysis 2.3).

3.3 Follow-up response rate (16 to 24 weeks)

In terms of efficacy as number of patients who responded to treatment at 16-24 weeks, we found no difference between paroxetine and newer or non-conventional ADs (see Analysis 3.2).

Secondary outcome: Efficacy. Number of patients who remitted

3.4 Remission rate at endpoint (six to 12 weeks)

In terms of efficacy as number of patients who remitted, we found a difference in favour of hypericum (OR: 1.84, 95% CI 1.11 to 3.06, NNTb = 7, 95% CI 4 to 38, 1 RCT, 251 participants), mirtazapine (OR: 1.52, 95% CI 1.13 to 2.06, NNTb = 11, 95% CI 6 to 37, 4 RCTs, 766 participants) and venlafaxine (OR: 1.57, 95% CI 1.08 to 2.29, NNTb = 11, 95% CI 6 to 54, 4 RCTs, 807 participants) over paroxetine (see Analysis 4.3).

3.5 Early remission rate (one to four weeks)

In terms of efficacy as number of patients who remitted at one to four weeks, we found a difference between paroxetine and mirtazapine, in favour of mirtazapine (OR: 2.31, 95% CI 1.04 to 5.11, NNTb = 18, 95% CI 11 to 54, 3 RCTs, 726 participants) (see Analysis 5.3).

3.6. Follow-up remission rate (16 to 24 weeks)

We found a difference in favour of mirtazapine over paroxetine for this outcome (OR: 1.89, 95% CI 1.01 to 3.54, NNTb = 8, 95% CI 4 to 265, 1 RCT, 197 participants) (see Analysis 6.1).

Secondary outcome: Efficacy. Standardized mean difference

3.7 Standardized mean difference at endpoint (six to 12 weeks)

In terms of continuous outcomes at 6-12 weeks, we found a difference in favour of mirtazapine over paroxetine (SMD: 0.33, 95% CI 0.08 to 0.58, 1 RCTs, 246 participants). Moreover, there was a trend in favour of paroxetine over reboxetine (SMD: -0.10, 95% CI -0.21 to 0.00, 3 RCTs, 1291 participants). There was no evidence that paroxetine was different from other newer or non-conventional ADs (see Analysis 7.3).

3.8 Standardized mean difference at one to four weeks

For this outcome we found a difference in favour of paroxetine over reboxetine (SMD: -0.17, 95% CI -0.31 to -0.03, 2 RCTs, 805 participants) (see Analysis 8.3).

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3.9 Standardized mean difference at 16 to 24 weeks

For this outcome, we found no difference between paroxetine and newer or non-conventional ADs (see Analysis 9.2).

Secondary outcome: Acceptability

3.10 Failure to complete due to any cause

In terms of patients who dropped out for any reason, we found no difference between paroxetine and newer or non-conventional ADs (see Analysis 10.3).

3.11 Failure to complete due to inefficacy

No difference was found between paroxetine and newer or non-conventional ADs in terms of discontinuation due to inefficacy (see Analysis 11.3).

3.12 Failure to complete due to side effects

In terms of patients who dropped out due to side effects, we found a difference between paroxetine and reboxetine (OR: 0.38, 95% CI 0.17 to 0.86, NNTh = 16, 95% CI 10 to 30, 3 RCTs, 1375 participants) in favour of paroxetine; and a difference between paroxetine and tianeptine (OR: 3.38, 95% CI 1.31 to 8.71, NNTh = 13, 95% CI 7 to 47, 1 RCT, 327 participants) in favour of tianeptine (see Analysis 12.3).

Secondary outcome: Tolerability

3.13 Total number of patients experiencing at least some side effects

There was evidence that paroxetine was less well tolerated than hypericum (OR: 2.60, 95% CI 1.51 to 4.46, NNTh = 5, 95% CI 3 to 10, 1 RCT, 251 participants) (see Analysis 13.3).

3.14 Number of patients experiencing specific side effects

(a) Sleepiness/drowsiness. We found a difference in favour of bupropion (OR: 7.63, 95% CI 2.51 to 23.16, NNTh = 5, 95% CI 4 to 9, 2 RCTs, 240 participants) and in favour of reboxetine (OR: 2.66, 95% CI 1.45 to 4.89, NNTh = 13, 95% CI 9 to 22, 3 RCTs, 1375 participants) over paroxetine (see Analysis 79.3).
(b) Insomnia. There was evidence that paroxetine was associated with a lower rate of insomnia than reboxetine (OR: 0.48, 95% CI 0.31 to 0.74, NNTh = 8, 95% CI 6 to 11, 3 RCTs, 1375 participants) (see Analysis 54.3).
(c) Dry mouth. Paroxetine was associated with a lower rate of dry mouth than reboxetine (OR: 0.35, 95% CI 0.27 to 0.45, NNTh = 5, 95% CI 4 to 6, 3 RCTs, 1375 participants). By contrast, we found a difference in favour of hypericum (OR: 2.62, 95% CI 1.36 to 5.04, NNTh = 7, 95% CI 4 to 19, 1 RCT, 251 participants) over paroxetine (see Analysis 38.3).
(d) Constipation. Paroxetine was associated with a lower rate of constipation than reboxetine (OR: 0.48, 95% CI 0.36 to 0.63, NNTh = 9, 95% CI 7 to 15, 3 RCTs, 1375 participants) (see Analysis 31.3).
(e) Urination/Urogenital problems. There was evidence in favour of paroxetine over reboxetine, in particular for dysuria (OR: 0.16, 95% CI 0.04 to 0.75, NNTh = 42, 95% CI 25 to 151, 2 RCTs, 855 participants) (see Analysis 90.2) and urinary retention (OR: 0.28, 95% CI 0.14 to 0.54, NNTh = 22, 95% CI 15 to 40, 3 RCTs, 1375 participants) (see Analysis 90.4).
(f) Hypotension. We found a difference in favour of paroxetine over reboxetine (OR: 0.37, 95% CI 0.19 to 0.75, NNTh = 19, 95% CI 13 to 36, 3 RCTs, 1375 participants) (see Analysis 50.3).
(g) Agitation/anxiety. We found no difference between paroxetine and newer or non-conventional ADs (see Analysis 18.3).
(h) Suicide wishes/gestures/attempts. We found no difference between paroxetine and newer or non-conventional ADs (see Analysis 96.1; Analysis 96.3).
(i) Completed suicide. We found no difference between paroxetine and newer or non-conventional ADs (see Analysis 96.2) .
(j) Vomiting/nausea. Paroxetine was associated with a higher rate of vomiting/nausea than agomelatine (OR: 6.81, 95% CI 2.31 to 20.14, NNTh = 7, 95% CI 5 to 14, 1 RCT, 284 participants), amisulpride (OR: 7.13, 95% CI 2.06 to 24.68, NNTh = 9, 95% CI 6 to 19, 1 RCT, 277 participants), hypericum (OR: 2.58, 95% CI 1.13 to 5.88, NNTh = 11, 95% CI 6 to 65, 1 RCT, 251 participants), mirtazapine (OR: 3.03, 95% CI 1.91 to 4.82, NNTh = 8, 95% CI 6 to 14, 3 RCTs, 726 participants), reboxetine (OR: 2.07, 95% CI 1.60 to 2.69, NNTh = 8, 95% CI 6 to 12, 3 RCTs, 1375 participants) and tianeptine (OR: 2.54, 95% CI 1.38 to 4.67, NNTh = 14, 95% CI 9 to 38, 2 RCTs, 604 participants). By contrast, paroxetine was better than duloxetine (OR: 0.68, 95% CI 0.52 to 0.88, NNTh = 34, 95% CI 14 to 78, 5 RCTs, 1573 participants) (see Analysis 59.3).
(k) Diarrhoea. We found that paroxetine was associated with a higher rate of diarrhoea than bupropion (OR: 3.03, 95% CI 1.35 to 6.84, NNTh = 8, 95% CI 5 to 25, 2 RCTs, 240 participants) and reboxetine (OR: 3.45, 95% CI 2.31 to 5.15, NNTh = 9, 95% CI 7 to 13, 3 RCTs, 1375 participants). Moreover, a trend in favour of hypericum over paroxetine (OR: 2.10, 95% CI 1.00 to 4.44, 1 RCT, 251 participants) was found (see Analysis 36.3).
(l) Other side effects. Other statistically significant side effects are reported in Table 1.

Subgroup analyses

1. Paroxetine dosing

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The great majority of studies used paroxetine within the standard dose range of 20-40 mg/day. Therefore, it was not meaningful to carry out this pre-planned subgroup analysis.

2. Comparator dosing

All comparator doses were within the therapeutic range. Due to the small number of trials outside the therapeutic range, it was not considered meaningful to carry out this pre-planned subgroup analysis.

3. Depression severity

The great majority of studies reported a mean baseline score corresponding to moderate to severe major depression. Therefore, it was not meaningful to carry out this pre-planned subgroup analysis.

4. Treatment settings

Results from this subgroup analysis did not materially change the main findings (full details available on request from authors).

5. Elderly patients

Results from this subgroup analysis did not materially change the main findings (full details available on request from authors).

Sensitivity analysis

1. Excluding trials with unclear concealment of random allocation and/or unclear double blinding

Although technically possible to carry out these sensitivity analyses, they were not performed, because they would not have contributed useful information due to the small number of studies (only seven out of 115 trials) reporting clear details on concealment of random allocation (Baldwin 2006; Boulenger 2006; Gallen 2001; Higuchi 2009; M/2020/0047; M/2020/0052; Szegedi 2005).

2. Excluding trials whose dropout rate was greater than 20%

It was not meaningful to carry out this pre-planned sensitivity analysis.

3. Performing the worst- and best-case scenario analyses

Results from these sensitivity analyses did not materially change the main findings (full details available on request from authors).

4. Excluding trials for which the imputation methods were used

Excluding trials for which the SDs had to be borrowed from other trials, results for all comparisons did not materially change.

5. Examination of "wish bias" and exclusion of studies funded by the pharmaceutical company marketing paroxetine

These pre-planned sensitivity analyses were not carried out because we found only a few studies per comparison.

6. Excluding studies funded by the pharmaceutical company marketing paroxetine

These pre-planned sensitivity analyses were not carried out because we found only a few studies per comparison.

Assessment of heterogeneity

For primary outcomes (response rate at endpoint), we found I^2 indicative of substantial heterogeneity level (I^2 between 50 and 90%) in the comparison between paroxetine and mianserin (I^2 = 61%), and between paroxetine and venlafaxine (I^2 = 76%) . For the secondary outcome failure to remit at endpoint, substantial heterogeneity was found in the comparison between paroxetine and older ADs as a class (I^2 = 79%) and between paroxetine and escitalopram (I^2 = 81%). Moreover, for the secondary outcome standardized mean difference at endpoint, substantial heterogeneity was found in the comparison between paroxetine and clomipramine (I^2 = 78%) and between paroxetine and escitalopram (I^2 = 78%). For the outcome failure to complete (any cause), substantial heterogeneity was found in the comparisons between paroxetine and lofepramine (I^2 = 68%), sertraline (I^2 = 69%) and reboxetine (I^2 = 65%). For the outcome failure to complete (due to side effects) heterogeneity was found in the comparison between paroxetine and maprotiline (I^2 = 84%), fluvoxamine (I^2 = 75%) and reboxetine (I^2 = 71%) . For the secondary outcome failure to complete (due to inefficacy), substantial heterogeneity was found in the comparison between paroxetine and tianeptine (I^2 = 74%).

Assessment of publication bias

Visual inspection of funnel plots did not reveal substantial asymmetry in any of the comparisons between paroxetine and other conventional and unconventional ADs.

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ADDITIONAL SUMMARY OF FINDINGS *[Explanation]*

Paroxetine compared with agomelatine for depression

Patient or population: patients with depression
Settings: in- and out-patients
Intervention: paroxetine
Comparison: agomelatine

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Agomelatine	Paroxetine				
Failure to respond at endpoint (6-12 weeks) Follow-up: 6-12 weeks	**394 per 1000**	**449 per 1000** (337 to 567)	**OR 1.25** (0.78 to 2.01)	284 (1 study)	⊕⊕⊕◯ **moderate**[1]	
Failure to respond at 1-4 weeks	See comment	See comment	Not estimable	0 (0)	See comment	No trial reported this outcome.
Failure to respond at 16-24 weeks	See comment	See comment	Not estimable	0 (0)	See comment	No trial reported this outcome.
Failure to remit at endpoint HDRS Follow-up: 6-12 weeks	**701 per 1000**	**748 per 1000** (637 to 834)	**OR 1.27** (0.75 to 2.14)	284 (1 study)	⊕⊕⊕◯ **moderate**[1]	
SMD at endpoint HDRS Follow-up: 6-12 weeks		The mean SMD at endpoint in the intervention groups was **0.18 standard deviations lower** (0.38 lower to 0.02 higher)		1074 (4 studies)	⊕⊕⊕◯ **moderate**[1]	The point estimate of the effect size corresponds to a small effect according to Cohen 1992.

Failure to complete - any cause -	**234 per 1000**	**232 per 1000** (148 to 343)	**OR 0.99** (0.57 to 1.71)	284 (1 study)	⊕⊕⊕○ **moderate**[1]
Participants with at least some Side Effects	**547 per 1000**	**659 per 1000** (545 to 758)	**OR 1.60** (0.99 to 2.59)	284 (1 study)	⊕⊕⊕○ **moderate**[1]

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

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

[1] Blinding stated but not tested. No information on randomisation procedures and allocation concealment.

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Paroxetine compared with amisulpride for depression

Patient or population: patients with depression
Settings: in- and out-patients
Intervention: paroxetine
Comparison: amisulpride

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Amisulpride	Paroxetine				
Failure to respond at endpoint (6-12 weeks)	**254 per 1000**	**181 per 1000** (109 to 281)	**OR 0.65** (0.36 to 1.15)	277 (1 study)	⊕⊕⊕◯ **moderate**[1]	
Failure to respond at 1-4 weeks	See comment	See comment	Not estimable	0 (0)	See comment	No trial reported this outcome.
Failure to respond at 16-24 weeks	See comment	See comment	Not estimable	0 (0)	See comment	No trial reported this outcome.
Failure to remit at endpoint	**268 per 1000**	**237 per 1000** (152 to 348)	**OR 0.85** (0.49 to 1.46)	277 (1 study)	⊕⊕⊕◯ **moderate**[1]	
SMD at endpoint		The mean SMD at endpoint in the intervention groups was **0.13 standard deviations lower** (0.37 lower to 0.10 higher)		272 (1 study)	⊕⊕⊕◯ **moderate**[1]	The point estimate of the effect size corresponds to a small effect according to Cohen 1992.
Failure to complete - any cause -	See comment	See comment	Not estimable	0 (0)	See comment	No trial reported this outcome.

Participants with at least some Side Effects	**Study population**		**OR 1.49** (0.89 to 2.50)	277 (1 study)	⊕⊕⊕◯ **moderate**[1]
	261 per 1000	**345 per 1000** (239 to 469)			
	Moderate				

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

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

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paroxetine compared with aprepitant for depression

Patient or population: patients with depression
Settings: in- and out-patients
Intervention: paroxetine
Comparison: aprepitant

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Aprepitant	Paroxetine				
Failure to respond at endpoint (6-12 weeks)	See comment	See comment	See comment	0 (0)	See comment	No trial reported this outcome.
Failure to respond at 1-4 weeks	See comment	See comment	Not estimable	0 (0)	See comment	No trial reported this outcome.
Failure to respond at 16-24 weeks	See comment	See comment	Not estimable	0 (0)	See comment	No trial reported this outcome.
Failure to remit at endpoint	**444 per 1000**	**557 per 1000** (464 to 647)	**OR 1.57** (1.08 to 2.29)	807 (4 studies)	⊕⊕⊕⊕ **high**	
SMD at endpoint		The mean SMD at endpoint in the intervention groups was **0.00 standard deviations higher** (0.39 lower to 0.39 higher)		102 (1 study)	⊕⊕⊕⊕ **high**	This correspond to no treatment effect.
Failure to complete - any cause -	**282 per 1000**	**375 per 1000** (230 to 548)	**OR 1.53** (0.76 to 3.09)	143 (1 study)	⊕⊕⊕◯ **moderate**[1]	

Participants with at least some Side Effects	See comment	See comment	Not estimable	0 (0)	See comment	No trial reported this outcome.

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

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

[1] Blinding stated but not tested. No information on randomisation procedures and allocation concealment.

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Paroxetine compared with bupropion for depression

Patient or population: patients with depression
Settings: in- and out-patients
Intervention: paroxetine
Comparison: bupropion

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Bupropion	Paroxetine				
Failure to respond at endpoint (6-12 weeks)	**292 per 1000**	**231 per 1000** (110 to 424)	**OR 0.73** (0.3 to 1.79)	100 (1 study)	⊕⊕⊕◯ **moderate**[1]	
Failure to respond at 1-4 weeks	See comment	See comment	Not estimable	0 (0)	See comment	No trial reported this outcome.
Failure to respond at 16-24 weeks	See comment	See comment	Not estimable	0 (0)	See comment	No trial reported this outcome.
Failure to remit at endpoint	See comment	See comment	Not estimable	0 (0)	See comment	No trial reported this outcome.
SMD at endpoint		The mean SMD at endpoint in the intervention groups was **0.04 standard deviations lower** (0.38 lower to 0.3 higher)		132 (1 study)	⊕⊕⊕◯ **moderate**[1]	This effect approaches zero.
Failure to complete - any cause -	**188 per 1000**	**212 per 1000** (126 to 338)	**OR 1.16** (0.62 to 2.2)	240 (2 studies)	⊕⊕⊕◯ **moderate**[1]	

Participants with at least some Side Effects	**913 per 1000**	**944 per 1000** (819 to 984)	**OR 1.60** (0.43 to 5.92)	140 (1 study)	⊕⊕⊕○ **moderate**[1]

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

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

[1] Blinding stated but not tested. No information on randomisation procedures and allocation concealment.

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Paroxetine compared with citalopram for depression

Patient or population: patients with depression
Settings: in- and out-patients
Intervention: paroxetine
Comparison: citalopram

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Citalopram	Paroxetine				
Failure to respond at endpoint (6-12 weeks)	**507 per 1000**	**613 per 1000** (517 to 701)	**OR 1.54** (1.04 to 2.28)	406 (1 study)	⊕⊕⊕◯ **moderate**	
Failure to respond at 1-4 weeks	See comment	See comment	Not estimable	0 (0)	See comment	No trial reported this outcome.
Failure to respond at 16-24 weeks	See comment	See comment	Not estimable	0 (0)	See comment	No trial reported this outcome.
Failure to remit at endpoint	See comment	See comment	Not estimable		See comment	No trial reported this outcome.
SMD at endpoint		The mean SMD at endpoint in the intervention groups was **0.16 standard deviations lower** (0.44 lower to 0.11 higher)		201 (1 study)	⊕⊕⊕◯ **moderate**[1]	The point estimate of the effect size corresponds to a small effect according to Cohen 1992.
Failure to complete - any cause -	**208 per 1000**	**206 per 1000** (138 to 296)	**OR 0.99** (0.61 to 1.6)	406 (1 study)	⊕⊕⊕◯ **moderate**[1]	

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Participants with at least some Side Effects	**Study population**		**OR 0.74** (0.46 to 1.21)	406 (1 study)	⊕⊕⊕○ **moderate**[1]
	821 per 1000	**773 per 1000** (679 to 848)			
	Moderate				

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

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

[1] Blinding stated but not tested. No information on randomisation procedures and allocation concealment.

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Paroxetine compared with duloxetine for depression

Patient or population: patients with depression
Settings: in- and out-patients
Intervention: paroxetine
Comparison: duloxetine

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Duloxetine	Paroxetine				
Failure to respond at endpoint (6-12 weeks)	**459 per 1000**	**431 per 1000** (373 to 492)	**OR 0.89** (0.70 to 1.14)	1821 (6 studies)	⊕⊕⊕○ **moderate**[1]	
Failure to respond at 1-4 weeks	See comment	See comment	Not estimable	0 (0)	See comment	No trial reported this outcome.
Failure to respond at 16-24 weeks	See comment	See comment	Not estimable	0 (0)	See comment	No trial reported this outcome.
Failure to remit at endpoint	**592 per 1000**	**587 per 1000** (537 to 633)	**OR 0.98** (0.80 to 1.19)	1821 (6 studies)	⊕⊕⊕○ **moderate**[1]	
SMD at endpoint		The mean SMD at endpoint in the intervention groups was **0.04 standard deviations higher** (0.06 lower to 0.15 higher)		1481 (6 studies)	⊕⊕⊕○ **moderate**[1]	This effect approaches zero.
Failure to complete - any cause -	**237 per 1000**	**232 per 1000** (193 to 277)	**OR 0.97** (0.77 to 1.23)	1821 (6 studies)	⊕⊕⊕○ **moderate**[1]	

Participants with at least some Side Effects	**700 per 1000**	**654 per 1000** (599 to 702)	**OR 0.81** (0.64 to 1.01)	1870 (6 studies)	⊕⊕⊕○ **moderate**[1]

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

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

[1] Blinding stated but not tested. No information on randomisation procedures and allocation concealment.

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Paroxetine compared with escitalopram for depression

Patient or population: depression
Settings: in- and out-patients
Intervention: paroxetine
Comparison: escitalopram

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Escitalopram	Paroxetine				
Failure to respond at endpoint (6-12 weeks)	**312 per 1000**	**336 per 1000** (256 to 427)	**OR 1.12** (0.76 to 1.65)	784 (2 studies)	⊕⊕⊕◯ **moderate**[1]	
Failure to respond at 1-4 weeks	See comment	See comment	Not estimable	0 (0)		No trial reported this outcome.
Failure to respond at 16-24 weeks	**Study population**		**OR 1.36** (0.87 to 2.12)	459 (1 study)	⊕⊕⊕◯ **moderate**[1]	
	194 per 1000	**247 per 1000** (173 to 338)				
	Moderate					
Failure to remit at endpoint	**407 per 1000**	**441 per 1000** (292 to 604)	**OR 1.15** (0.6 to 2.22)	784 (2 studies)	⊕⊕◯◯ **low**[1,2]	
SMD at endpoint		The mean SMD at endpoint in the intervention groups was **0.05 standard deviations higher**		772 (2 studies)	⊕⊕◯◯ **low**[1,3]	This effect approaches zero.

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		(0.26 lower to 0.36 higher)			
Failure to complete - any cause -	**156 per 1000**	**213 per 1000** (124 to 340)	**OR 1.47** (0.77 to 2.79)	784 (2 studies)	⊕⊕⊕◯ **moderate**[1]
Participants with at least some Side Effects	**Study population**		**OR 1.28** (0.86 to 1.91)	454 (1 study)	⊕⊕⊕◯ **moderate**[1]
	668 per 1000	**720 per 1000** (634 to 794)			
	Moderate				

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

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

[1] Blinding stated but not tested. No information on randomisation procedures and allocation concealment.
[2] I squared 81%
[3] I squared 78%

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Paroxetine compared with fluoxetine for depression

Patient or population: patients with depression
Settings: in- and out-patients
Intervention: paroxetine
Comparison: fluoxetine

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Fluoxetine	Paroxetine				
Failure to respond at endpoint (6-12 weeks)	**386 per 1000**	**555 per 1000** (332 to 436)	**OR 1.98** (0.79 to 1.23)	2418 (11 studies)	⊕⊕⊕○ **moderate**[1]	
Failure to respond at 1-4 weeks	See comment	See comment	Not estimable	0 (0)	See comment	No trial reported this outcome.
Failure to respond at 16-24 weeks	See comment	See comment	Not estimable	0 (0)	See comment	No trial reported this outcome.
Failure to remit at endpoint	See comment	See comment	Not estimable	0 (0)	See comment	No trial reported this outcome.
SMD at endpoint		The mean SMD at endpoint in the intervention groups was **0.04 standard deviations higher** (0.05 lower to 0.12 higher)		2109 (9 studies)	⊕⊕⊕○ **moderate**[1]	This effect approaches zero.
Failure to complete - any cause - total drop out rate	**325 per 1000**	**336 per 1000** (300 to 372)	**OR 1.05** (0.89 to 1.23)	2798 (13 studies)	⊕⊕⊕○ **moderate**[1]	

Participants with at least some Side Effects	**774 per 1000**	**763 per 1000** (703 to 814)	**OR 0.94** (0.69 to 1.28)	2255 (9 studies)	⊕⊕⊕○ **moderate**[1]

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

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

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Paroxetine compared with fluvoxamine for depression

Patient or population: patients with depression
Settings: in- and out-patients
Intervention: paroxetine
Comparison: fluvoxamine

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Fluvoxamine	Paroxetine				
Failure to respond at endpoint (6-12 weeks)	**466 per 1000**	**510 per 1000** (386 to 629)	**OR 1.19** (0.72 to 1.94)	261 (3 studies)	⊕⊕⊕○ **moderate**[1]	
Failure to respond at 1-4 weeks	**Study population**		**OR 0.71** (0.41 to 1.24)	281 (3 studies)	⊕⊕⊕○ **moderate**[1]	
	769 per 1000	**703 per 1000** (577 to 805)				
	Moderate					
Failure to respond at 16-24 weeks	See comment	See comment	Not estimable	0 (0)		No trial reported this outcome.
Failure to remit at endpoint	**752 per 1000**	**703 per 1000** (571 to 807)	**OR 0.78** (0.44 to 1.38)	261 (3 studies)	⊕⊕⊕○ **moderate**[1]	
SMD at endpoint		The mean SMD at endpoint in the intervention groups was **0.09 standard deviations higher**		58 (1 study)	⊕⊕⊕○ **moderate**[1]	This effect approaches zero.

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		(0.43 lower to 0.6 higher)			
Failure to complete - any cause -	**293 per 1000**	**285 per 1000** (183 to 416)	**OR 0.96** (0.54 to 1.72)	261 (3 studies)	⊕⊕⊕◯ **moderate**[1]
Participants with at least some Side Effects	**609 per 1000**	**636 per 1000** (395 to 822)	**OR 1.12** (0.42 to 2.97)	261 (3 studies)	⊕⊕⊕◯ **moderate**[1]

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

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

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Paroxetine compared with hypericum for depression

Patient or population: patients with depression
Settings: in- and out-patients
Intervention: paroxetine
Comparison: hypericum

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Hypericum	Paroxetine				
Failure to respond at endpoint (6-12 weeks)	**312 per 1000**	**420 per 1000** (301 to 550)	**OR 1.60** (0.95 to 2.69)	251 (1 study)	⊕⊕⊕◯ **moderate**[1]	
Failure to respond at 1-4 weeks	See comment	See comment	Not estimable	0 (0)	See comment	No trial reported this outcome.
Failure to respond at 16-24 weeks	See comment	See comment	Not estimable	0 (0)	See comment	No trial reported this outcome.
Failure to remit at endpoint	**512 per 1000**	**659 per 1000** (538 to 762)	**OR 1.84** (1.11 to 3.06)	251 (1 study)	⊕⊕⊕◯ **moderate**[1]	
SMD at endpoint		The mean SMD at endpoint in the intervention groups was **0.35 standard deviations higher** (0.09 to 0.6 higher)		244 (1 study)	⊕⊕⊕◯ **moderate**[1]	The point estimate of the effect size corresponds to a small effect according to Cohen 1992.
Failure to complete - any cause -	**136 per 1000**	**230 per 1000** (134 to 366)	**OR 1.90** (0.98 to 3.67)	251 (1 study)	⊕⊕⊕◯ **moderate**[1]	

Participants with at least some Side Effects	**552 per 1000**	**762 per 1000** (650 to 846)	**OR 2.60** (1.51 to 4.46)	251 (1 study)	⊕⊕⊕○ **moderate**[1]

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

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

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Paroxetine compared with milnacipran for depression

Patient or population: patients with depression
Settings: in- and out-patients
Intervention: paroxetine
Comparison: milnacipran

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Milnacipran	Paroxetine				
Failure to respond at endpoint (6-12 weeks)	**423 per 1000**	**405 per 1000** (302 to 519)	**OR 0.93** (0.59 to 1.47)	302 (1 study)	⊕⊕⊕◯ **moderate**[1]	
Failure to respond at 1-4 weeks	See comment	See comment	Not estimable	0 (0)	See comment	No trial reported this outcome.
Failure to respond at 16-24 weeks	See comment	See comment	Not estimable	0 (0)	See comment	No trial reported this outcome.
Failure to remit at endpoint	**Study population**		**OR 0.92** (0.57 to 1.49)	302 (1 study)	⊕⊕⊕◯ **moderate**[1]	
	671 per 1000	**652 per 1000** (538 to 753)				
	Moderate					
SMD at endpoint		The mean SMD at endpoint in the intervention groups was **0.05 standard deviations lower**		299 (1 study)	⊕⊕⊕◯ **moderate**[1]	This effect approaches zero.

		(0.28 lower to 0.18 higher)			
Failure to complete - any cause -	**172 per 1000**	**195 per 1000** (122 to 323)	**OR 1.17** (0.67 to 2.3)	343 (2 studies)	⊕⊕⊕◯ **moderate**[1]
Participants with at least some Side Effects	**772 per 1000**	**700 per 1000** (581 to 795)	**OR 0.69** (0.41 to 1.15)	302 (1 study)	⊕⊕⊕◯ **moderate**[1]

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

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

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Paroxetine compared with mirtazapine for depression

Patient or population: patients with depression
Settings: in- and out-patients
Intervention: paroxetine
Comparison: mirtazapine

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Mirtazapine	Paroxetine				
Failure to respond at endpoint (6-12 weeks)	**509 per 1000**	**554 per 1000** (483 to 625)	**OR 1.20** (0.90 to 1.61)	766 (4 studies)	⊕⊕⊕○ **moderate**[1]	
Failure to respond at 1-4 weeks	**735 per 1000**	**869 per 1000** (797 to 918)	**OR 2.39** (1.42 to 4.02)	726 (3 studies)	⊕⊕⊕○ **moderate**[1]	
Failure to respond at 16-24 weeks	**Study population**		**OR 1.41** (0.81 to 2.48)	726 (3 studies)	⊕⊕⊕○ **moderate**[1]	
	735 per 1000	**869 per 1000** (797 to 918)				
	Moderate					
Failure to remit at endpoint	**597 per 1000**	**692 per 1000** (626 to 753)	**OR 1.52** (1.13 to 2.06)	766 (4 studies)	⊕⊕⊕○ **moderate**[1]	
SMD at endpoint		The mean SMD at endpoint in the intervention groups was **0.33 standard deviations higher**		246 (1 study)	⊕⊕⊕○ **moderate**[1]	The point estimate of the effect size corresponds to a small effect according to Cohen 1992.

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		(0.08 to 0.58 higher)			
Failure to complete - any cause -	**306 per 1000**	**357 per 1000** (286 to 434)	**OR 1.26** (0.91 to 1.74)	726 (3 studies)	⊕⊕⊕◯ **moderate**[1]
Participants with at least some Side Effects	**743 per 1000**	**756 per 1000** (687 to 813)	**OR 1.07** (0.76 to 1.50)	726 (3 studies)	⊕⊕⊕◯ **moderate**[1]

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

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

[1] Blinding stated but not tested. No information on randomisation procedures and allocation concealment.

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Paroxetine compared with nefazodone for depression

Patient or population: patients with depression
Settings: in- and out-patients
Intervention: paroxetine
Comparison: nefazodone

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Nefazodone	Paroxetine				
Failure to respond at endpoint (6-12 weeks)	**450 per 1000**	**202 per 1000** (54 to 506)	**OR 0.31** (0.07 to 1.25)	40 (1 study)	⊕⊕⊕◯ **moderate**[1]	
Failure to respond at 1-4 weeks	See comment	See comment	Not estimable	0 (0)	See comment	No trial reported this outcome.
Failure to respond at 16-24 weeks	**Study population**		**OR 0.64** (0.17 to 2.38)	40 (1 study)	⊕⊕⊕◯ **moderate**[1]	
	400 per 1000	**299 per 1000** (102 to 613)				
	Moderate					
Failure to remit at endpoint			Not estimable	0 (0)		
SMD at endpoint		The mean SMD at endpoint in the intervention groups was **0.12 standard deviations lower**		235 (2 studies)	⊕⊕⊕◯ **moderate**[1]	The point estimate of the effect size corresponds to a small effect according to Cohen 1992.

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		(0.37 lower to 0.14 higher)			
Failure to complete - any cause -	**250 per 1000**	**150 per 1000** (35 to 464)	**OR 0.53** (0.11 to 2.60)	40 (1 study)	⊕⊕⊕◯ **moderate**[1]
Participants with at least some Side Effects	**838 per 1000**	**781 per 1000** (638 to 879)	**OR 0.69** (0.34 to 1.40)	206 (1 study)	⊕⊕⊕◯ **moderate**[1]

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

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

[1] Blinding stated but not tested. No information on randomisation procedures and allocation concealment.

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Paroxetine compared with reboxetine for depression

Patient or population: patients with depression
Settings: in- and out-patients
Intervention: paroxetine
Comparison: reboxetine

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Reboxetine	Paroxetine				
Failure to respond at endpoint (6-12 weeks)	**500 per 1000**	**451 per 1000** (398 to 505)	**OR 0.82** (0.66 to 1.02)	1369 (3 studies)	⊕⊕⊕○ **moderate**[1]	
Failure to respond at 1-4 weeks	**846 per 1000**	**784 per 1000** (733 to 827)	**OR 0.66** (0.5 to 0.87)	1375 (3 studies)	⊕⊕⊕○ **moderate**[1]	
Failure to respond at 16-24 weeks	See comment	See comment	Not estimable	0 (0)	See comment	No trial reported this outcome.
Failure to remit at endpoint	See comment	See comment	Not estimable	0 (0)	See comment	No trial reported this outcome.
SMD at endpoint		The mean SMD at endpoint in the intervention groups was **0.10 standard deviations lower** (0.21 lower to 0 higher)		1291 (3 studies)	⊕⊕⊕○ **moderate**[1]	The point estimate of the effect size corresponds to a small effect according to Cohen 1992.
Failure to complete - any cause -	**277 per 1000**	**230 per 1000** (164 to 313)	**OR 0.78** (0.51 to 1.19)	1375 (3 studies)	⊕⊕⊕○ **moderate**[1]	

Participants with at least some Side Effects	**849 per 1000**	**859 per 1000** (806 to 899)	**OR 1.08** (0.74 to 1.58)	1375 (3 studies)	⊕⊕⊕○ **moderate**[1]

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

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

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Paroxetine compared with sertraline for depression

Patient or population: patients with depression
Settings: in- and out-patients
Intervention: paroxetine
Comparison: sertraline

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Sertraline	Paroxetine				
Failure to respond at endpoint (6-12 weeks)	**292 per 1000**	**340 per 1000** (269 to 422)	**OR 1.25** (0.89 to 1.77)	618 (3 studies)	⊕⊕⊕◯ **moderate**[1]	
Failure to respond at 1-4 weeks	See comment	See comment	Not estimable	0 (0)	See comment	No trial reported this outcome.
Failure to respond at 16-24 weeks	See comment	See comment	Not estimable	0 (0)	See comment	No trial reported this outcome.
Failure to remit at endpoint	**577 per 1000**	**562 per 1000** (478 to 647)	**OR 0.94** (0.67 to 1.34)	545 (2 studies)	⊕⊕⊕◯ **moderate**[1]	
SMD at endpoint		The mean SMD at endpoint in the intervention groups was **0.13 standard deviations lower** (0.34 lower to 0.07 higher)		353 (1 study)	⊕⊕⊕◯ **moderate**[1]	The point estimate of the effect size corresponds to a small effect according to Cohen 1992.
Failure to complete - any cause -	**338 per 1000**	**411 per 1000** (210 to 648)	**OR 1.37** (0.52 to 3.6)	426 (2 studies)	⊕⊕⊕◯ **moderate**[1]	

Participants with at least some Side Effects	See comment	See comment	Not estimable	0 (0)	See comment	No trial reported this outcome.

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

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

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Paroxetine compared with tianeptine for depression

Patient or population: patients with depression
Settings: in- and out-patients
Intervention: paroxetine
Comparison: tianeptine

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Tianeptine	Paroxetine				
Failure to respond at endpoint (6-12 weeks)	**370 per 1000**	**379 per 1000** (294 to 473)	**OR 1.04** (0.71 to 1.53)	648 (3 studies)	⊕⊕⊕◯ **moderate**[1]	
Failure to respond at 1-4 weeks	See comment	See comment	Not estimable	0 (0)	See comment	No trial reported this outcome.
Failure to respond at 16-24 weeks	See comment	See comment	Not estimable	0 (0)	See comment	No trial reported this outcome.
Failure to remit at endpoint	**727 per 1000**	**638 per 1000** (324 to 863)	**OR 0.66** (0.18 to 2.36)	44 (1 study)	⊕⊕⊕◯ **moderate**[1]	
SMD at endpoint		The mean SMD at endpoint in the intervention groups was **0.04 standard deviations higher** (0.12 lower to 0.2 higher)		586 (3 studies)	⊕⊕⊕◯ **moderate**[1]	This effect approaches zero.
Failure to complete - any cause -	**174 per 1000**	**235 per 1000** (136 to 375)	**OR 1.46** (0.75 to 2.85)	648 (3 studies)	⊕⊕⊕◯ **moderate**[1]	

Participants with at least some Side Effects	**427 per 1000**	**484 per 1000** (398 to 570)	**OR 1.26** (0.89 to 1.78)	604 (2 studies)	⊕⊕⊕○ **moderate**[1]

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

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

[1] Blinding stated but not tested. No information on randomisation procedures and allocation concealment.

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Paroxetine compared with trazodone for depression

Patient or population: patients with depression
Settings: in- and out-patients
Intervention: paroxetine
Comparison: trazodone

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Trazodone	Paroxetine				
Failure to respond at endpoint (6-12 weeks)	**127 per 1000**	**94 per 1000** (30 to 260)	**OR 0.71** (0.21 to 2.41)	108 (1 study)	⊕⊕⊕○ **moderate**[1]	
Failure to respond at 1-4 weeks	**Study population**		**OR 0.54** (0.25 to 1.19)	108 (1 study)	⊕⊕⊕○ **moderate**[1]	
	691 per 1000	**547 per 1000** (358 to 727)				
	Moderate					
Failure to respond at 16-24 weeks	See comment	See comment	Not estimable	0 (0)	See comment	No trial reported this outcome.
Failure to remit at endpoint	**309 per 1000**	**322 per 1000** (174 to 516)	**OR 1.06** (0.47 to 2.38)	108 (1 study)	⊕⊕⊕○ **moderate**[1]	
SMD at endpoint		The mean SMD at endpoint in the intervention groups was **0.08 standard deviations lower**		108 (1 study)	⊕⊕⊕○ **moderate**[1]	This effect approaches zero.

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		(0.46 to 0.30 lower)				
Failure to complete - any cause -	See comment	See comment	Not estimable	0 (0)	See comment	No trial reported this outcome.
Participants with at least some Side Effects	**345 per 1000**	**264 per 1000** (137 to 450)	**OR 0.68** (0.30 to 1.55)	108 (1 study)	⊕⊕⊕○ **moderate**[1]	

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

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

[1] Blinding stated but not tested. No information on randomisation procedures and allocation concealment.

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Paroxetine compared with venlafaxine for depression

Patient or population: patients with depression
Settings: in- and out-patients
Intervention: paroxetine
Comparison: venlafaxine

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Venlafaxine	Paroxetine				
Failure to respond at endpoint (6-12 weeks)	**433 per 1000**	**457 per 1000** (307 to 617)	**OR 1.10** (0.58 to 2.11)	747 (4 studies)	⊕⊕◯◯ **low**[1,2]	
Failure to respond at 1-4 weeks	See comment	See comment	Not estimable	0 (0)	See comment	No trial reported this outcome.
Failure to respond at 16-24 weeks	See comment	See comment	Not estimable	0 (0)	See comment	No trial reported this outcome.
Failure to remit at endpoint	**444 per 1000**	**557 per 1000** (464 to 647)	**OR 1.57** (1.08 to 2.29)	807 (4 studies)	⊕⊕⊕◯ **moderate**[1]	
SMD at endpoint		The mean SMD at endpoint in the intervention groups was **0.07 standard deviations higher** (0.13 lower to 0.26 higher)		411 (2 studies)	⊕⊕⊕◯ **moderate**[1]	This effect approaches zero.
Failure to complete - any cause -	**250 per 1000**	**265 per 1000** (215 to 324)	**OR 1.08** (0.82 to 1.44)	1079 (6 studies)	⊕⊕⊕◯ **moderate**[1]	

Participants with at least some Side Effects	**500 per 1000**	**502 per 1000** (342 to 661)	**OR 1.01** (0.52 to 1.95)	200 (2 studies)	⊕⊕⊕○ **moderate**[1]

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

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

[1] Blinding stated but not tested. No information on randomisation procedures and allocation concealment.
[2] I squared 76%

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DISCUSSION

Summary of main results

The present systematic review included a total of 115 randomised controlled trials (RCTs), involving 26,134 participants. The included studies did not report all the outcomes that were pre-specified in the protocol and for some comparisons only a small number of trials provided data. Overall, we detected differences between paroxetine and some comparator ADs in terms of efficacy, acceptability and tolerability. For the primary outcome, response rate, paroxetine was less effective than citalopram at endpoint. In head-to-head comparisons with newer or non-conventional ADs, we found a difference in favour of paroxetine over reboxetine and in favour of mirtazapine over paroxetine in the early phase. For the secondary outcome remission rate, we found a difference in favour of clomipramine, hypericum, mirtazapine and venlafaxine over paroxetine. For the secondary outcome acceptability, paroxetine was better than reboxetine and amitriptyline (dropouts due to side effects) and better than clomipramine, imipramine and than older ADs as a class (dropouts due to side effects and dropouts due to any cause). By contrast, paroxetine was associated with a higher rate of dropouts due to side effects than fluoxetine and tianeptine. For the secondary outcome tolerability - number of patients experiencing at least some side effects - paroxetine was better than amitriptyline, imipramine and older ADs as a class, and worse than hypericum.

Overall completeness and applicability of evidence

All studies included in the present review recruited participants with a formal diagnosis of depression according to operationalised diagnostic criteria such as DSM-III or DSM-IV criteria, and therefore there was considerable homogeneity in the study populations. However, we have to consider that the majority of included studies were short in duration and some analyses were underpowered to demonstrate clinically meaningful differences between treatments. There was also considerable variation in the type of control medication used in the trials, and in some cases trials did not provide data for all the outcomes specified in the protocol, thus limiting the overall completeness of evidence. Another weakness of this analysis is that different subgroups of studies provided data for each efficacy and acceptability analyses, therefore raising the possibility of outcome reporting bias (Furukawa 2007).

The great majority of included trials were conducted in developed countries (Europe, United States, Canada) and this issue may be of limit in the application of these results in other countries of the world. Moreover, even though we collected a considerable amount of data on efficacy and acceptability, for some comparisons only a few trials were identified. In consequence, the reader is left with the decision of whether the findings from trials carried out in developed countries with standardized methods can be translated to routine clinical practice.

It has long been argued that placebo-controlled trials are required to adequately demonstrate the efficacy of novel antidepressant drugs (Cipriani 2009), however, in the present review we focused only on the comparison between paroxetine and other active treatments. The background logic that guided the development of the present review was based on two considerations. First, the efficacy of paroxetine versus placebo has already been quantified in a systematic review of published and unpublished studies (Barbui 2008); second, the need to provide real-world evidence for patients in need of pharmacological treatment. We therefore made the choice of including only studies that compared paroxetine with another active treatment, as we reasoned that clinicians need to know how paroxetine, a reference AD agent, compares with a selection of possible comparator ADs. Although the search was thorough, and we did our very best to retrieve as much data as possible (through asking pharmaceutical companies and study authors to supply all available information and searching the GSK website to retrieve unpublished data), it is still possible that there are unpublished studies that have not been identified. Of consequence, we can assume that data from some trials are still lacking, most of which are likely to be studies with negative findings. We are also aware of the possibility that a number of further RCTs comparing paroxetine with other antidepressant drugs are currently being conducted and will be included in future updates of this review.

Quality of the evidence

The 'Risk of bias' assessment is crucial in influencing the results' interpretation and deserves therefore due attention. All included studies were RCTs and were very similar in design and conduct. Using high-quality research evidence is relevant to review results and to speed up the translation of research in a way that really responds to clinically relevant questions. However, the quality of RCTs is not easy to assess. Even though RCTs are the design of choice for evaluating the efficacy and acceptability of healthcare interventions (Jüni 2001; Purgato 2010), the evidence upon which the findings of this review are based is relatively poor as evaluated with the Cochrane 'Risk of bias' tool, and this is also reflected in our grading within the 'Summary of findings' tables. For example, allocation concealment and blinding of outcome assessment were "unclear" in the great majority of included studies and there is evidence that non-blinded assessors in RCTs might generate biased results (Hróbjartsson 2013). The great majority of studies included in our review were described as "double-blind", but information on the procedure followed to guarantee the blindness, and if blindness was successful was not reported in many cases. The investigators' and participants' belief about what treatment the participant is taking is a crucial issue that could influence the trIal's results. Also, the reporting of outcomes was often unclear

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or incomplete (for example, many RCTs did not report SDs) and the figures used to report or summarise the analyses were not immediately understandable. However, we have to consider that the scant information about allocation concealment may be a matter of reporting in the text than a real defect in the study design. The quality of evidence evaluated with the GRADE methodology (within-study risk of bias, directness of evidence, heterogeneity, precision of effect estimates and risk of publication bias) was in general, from moderate to low.

Potential biases in the review process

Some possible limitations of this review should be noted and this means that the interpretation of results should remain tentative.
Although the search was thorough, it is possible that there are still unpublished studies which have not been identified. Moreover, the search date is September 2012 and there are a number of studies classified as "awaiting assessment", the eligibility of which has yet to be determined and the impact of which on the results of the review is uncertain.
It is important to bear in mind that the majority of the included studies were funded by the pharmaceutical industry;Hamilton 1960.
To assess efficacy, we used rating scales administered by clinicians or expert assessors. Even though both the Hamilton rating scale for depression (HDRS) and Montgomery and Asberg Depression Rating Scale (MADRS) are standardized tools commonly used in antidepressant trials, they are all potentially prone to observer bias. Self-administered questionnaires were not used in the included studies, so this might represent a limitation of the methods used in the primary studies of the present review.
In this review we decided to consider the response rate as the primary outcome because it is one of the main goals for the treatment of major depressive disorder. The term "treatment response" describes a state of improvement in the patient's condition of sufficient quality to result in the treating physician's impression of at least a moderate degree of global improvement, conventionally defined as a reduction of at least 50% in depressive symptomatology. However, from a clinical point of view, the ultimate goal of the acute treatment phase of major depressive disorder may well be to achieve remission. Full remission from depression correlates with better longer-term functional recovery, lower risk of relapse and higher level of patients satisfaction than partial response (without remission). Thus, one important limitation of the included trials (and consequently of the present review) is that only a few studies reported remission rates, underpowering the analysis and undermining the possibility to find significant differences between comparisons. Moreover, outcomes of clear relevance to patients and clinicians, in particular, patients' and their carers' attitudes to treatment, and the patient's ability to return to work and resume normal social functioning, were not reported in the included studies.

Agreements and disagreements with other studies or reviews

Even though it is a matter of ongoing discussion in the scientific literature (Gartlehner 2011), there is now robust evidence that there are statistically and clinically significant differences among antidepressants (Cipriani 2009). Results from this review suggest some differences in terms of efficacy, acceptability and tolerability between paroxetine and certain ADs, and might contribute to developing and keeping up to date an evidence-based hierarchy of antidepressants to be used by clinicians (both specialists and general practitioners) when prescribing an antidepressant drug for moderate to severe acute major depression.

AUTHORS' CONCLUSIONS

Implications for practice

The effects we have found in terms of efficacy, acceptability and tolerability of paroxetine compared with certain antidepressants (ADs), are of generally moderate quality. Data from the present review suggest some possible differences between paroxetine and other ADs, but the clinical meaning of these differences is uncertain, and no definitive implications for clinical practice can be drawn. Considering the methodological limitation of standard systematic reviews that rely only on evidence from direct comparisons and given the wide spectrum of available comparisons for the treatment of major depression, the use of the methodology of multiple treatments meta-analysis (MTM) may provide a more informative and clinically useful summary of the results that can be used to guide treatment decisions.

Implications for research

Results described in this systematic review come from evidence assessed as of *low or moderate quality* according to the GRADE methodology, a tool providing outcome-specific information concerning the overall quality of evidence from each included study in the comparison and the magnitude of effect of the interventions examined. Moreover, in many cases studies were financially supported by pharmaceutical industries. Industry-sponsored trials tend to follow a standard design which involves short-term, double-blind, parallel-group studies of patients with acute episodes or exacerbations of chronic illness. Often, patients with medical and psychiatric comorbidity or taking concomitant medication are excluded. Moreover, it is known that economic support by drug manufacturers can strongly influence progress of research and its results. Consequently, there is a risk that these studies do not provide sufficient and adequate information to clinicians in real-world settings. Studies should be conducted following high methodological standards and with the primary intent of providing clinicians with useful practical data regarding the comparative

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effectiveness of marketed medications, and consider rating scales but also pragmatic outcome measures (for example hospitalisations, return to work, social functioning and so on). If not, there is a risk that research will be guided only by economic interests instead of being based on clinical grounds.

Moreover, when dealing with summary statistics, the quality and the completeness of information is important. Meta-analyses of poor quality studies may be seriously misleading (Savović 2012), because the bias associated with defects in the conduct of primary studies (randomised trials) can seriously affect the overall estimate of intervention. Systematic review authors (not only within The Cochrane Collaboration) should routinely assess the risk of bias in the results of trials, and should report meta-analyses restricted to trials at low risk of bias (Wood 2008).

ACKNOWLEDGEMENTS

We would like to thank the CCDAN Editorial Team for their support, information and advice.

We also would like to thank all authors that provided additional data to be used in the present report and especially Drs. Jonathan Davidson, Stuart Montgomery and David Baldwin.

CRG Funding Acknowledgement

The National Institute for Health Research (NIHR) is the largest single funder of the Cochrane Depression, Anxiety and Neurosis Group.

Disclaimer

The views and opinions expressed therein are those of the review authors and do not necessarily reflect those of the NIHR, NHS or the Department of Health.

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* *Indicates the major publication for the study*

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CHARACTERISTICS OF STUDIES

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

029060/1/CPMS 069 1991

Methods	Nine-week, randomised, double-blind, double-dummy, parallel group, multicentre study
Participants	Participants of either sex, over the age of 60 years, with a diagnosis of a major episode of depression according to the DSM III, scoring 18 or more on the Hamilton rating scale for depression (HDRS-21), and being a hospital inpatient who gave written informed consent
Interventions	Paroxetine: 45 participants. Clomipramine: 47 participants. Paroxetine dose range: 20-50 mg/day. Clomipramine dose range: 150-150 mg/day.
Outcomes	HDRS-21, Montgomery and Asberg Depression Rating Scale (MADRS), Clinical Global Impression (CGI), the Widlocher rating scale, the Wang anxiety rating scale. Total dropout, dropout due to side effects, dropout due to inefficacy. Number of patients experiencing at least one side effect, side-effect profile
Notes	None.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "randomly assigned", no further details.
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double blind, double dummy".
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No information provided.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "the analyses were based on the Intention-to-treat (ITT). This consisted of the all subjects who had received at least one dose of study medication and for whom any data were available after the start of treatment (...) the safety analysis was based on the ITT population"

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029060/1/CPMS 069 1991 (*Continued*)

Selective reporting (reporting bias)	Low risk	Outcomes data were reported.
Other bias	Unclear risk	Sponsorship bias cannot be ruled out.

029060/1/CPMS-095

Methods	Randomised, double-blind, double-dummy, parallel group, multicentre study
Participants	In- or out-patients of either sex in the age range of 18-65 with a major depressive episode (DSM III-R) and who had a score of at least 18 in the Hamilton rating scale for depression (HDRS-17) total were included in the trial. A total of 210 participants were enrolled in the study and 202 participants proceeded to the active treatment phase; 68 were randomised to low-dose paroxetine, 66 to high-dose paroxetine and 68 to imipramine. All these participants were included in the intent-to-treat analysis
Interventions	Paroxetine: 134 participants. Imipramine: 68 participants. Paroxetine dose range: 20-40 mg/day. Imipramine dose: 150 mg/day.
Outcomes	HDRS-17, HDRS factor sub-scales (anxiety, melancholia, retardation and sleep disturbance), Clinical Global Impression (CGI), Hamilton rating scale for anxiety (HAM-A). Total dropout, dropout due to side effects, dropout due to inefficacy. Number of patients experiencing at least one side effect, side-effect profile
Notes	Funding: paroxetine manufacturer.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: "randomized". No further details.
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "double blind (...) a double dummy technique was used. Paroxetine was given as white, oval, film-coated tablets containing 20 mg paroxetine. Placebo tablets of identical appearance were supplied. Subjects took two tablets in the morning. (...) Imipramine was given as brown capsules containing 50 mg imipramine. Placebo capsules of identical appearance were supplied"

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029060/1/CPMS-095 (*Continued*)

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double blind".
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "the Intention-to-treat (ITT) population for efficacy was defined as subjects who were randomized and received treatment and if at least one efficacy assessment was made. The ITT population for safety and tolerability was defined as those subjects who were randomized and received treatment. The withdrawal effects population was defined as those included in the last 10 days of the run-out period" Withdrawn: paroxetine 7/134 participants; imipramine 6/68 participants
Selective reporting (reporting bias)	Low risk	Outcome data were reported.
Other bias	Unclear risk	Sponsorship bias cannot be ruled out.

0600A-349

Methods	Data from eight randomised, double-blind, controlled studies were pooled to compare efficacy in depressed patients receiving venlafaxine/venlafaxine extended release (XR), SSRIs or placebo for < 8 weeks
Participants	Patients could be enrolled in the studies if they were at least 18 and met the criteria of the DSM-III-R or DSM-IV for major depression or major depressive disorder, respectively, for at least 1 month before enrolment
Interventions	Paroxetine: 85 participants. Venlafaxine XR: 82 participants. Paroxetine dose range: 20-40 mg/day. Venlafaxine dose range: 75-150 mg/day.
Outcomes	Hamilton rating scale for depression (HDRS-21), Montgomery and Asberg Depression Rating Scale (MADRS), Clinical Global Impression (CGI) Improvement, Severity. Total dropout, dropout due to side effects, dropout due to inefficacy
Notes	Funding: venlafaxine manufacturer.

Risk of bias

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

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0600A-349 (*Continued*)

Random sequence generation (selection bias)	Unclear risk	Quote: "randomized". No further details.
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double blind".
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double blind".
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Quote: "analyses were performed on data from Intention-to-treat (ITT) patients; this ITT population included all patients who began the double blind treatment phase, received at least one dose of study medication, and had at least one HDRS evaluation during therapy or within 3 days of the last treatment day. The Last Observation Carried Forward (LOCF) approach was used for missing observations and to include results from the 6-week studies in the week 8 efficacy assessment"
Selective reporting (reporting bias)	Unclear risk	Outcomes data not clearly reported.
Other bias	Unclear risk	Sponsorship bias cannot be ruled out.

0600B 428

Methods	A multicentre, double-blind, randomised study.
Participants	Patients who had symptoms of major depression meeting DSM-IV criteria for at least 2 weeks
Interventions	Paroxetine: 56 participants. Venlafaxine XR: 58 participants. Paroxetine dose: 20 mg/day. Venlafaxine dose: 75 mg/day.
Outcomes	Montgomery and Asberg Depression Rating Scale (MADRS), Hamilton rating scale for depression (HDRS), Clinical Global Impression (CGI). Total dropout, dropout due to side effects
Notes	Funding: venlafaxine manufacturer.

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0600B 428 (*Continued*)

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: "randomized". No further details.
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double blind". No further details.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double blind". No further details.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	No information on data analysis and patients missed during the follow-up
Selective reporting (reporting bias)	Unclear risk	Baseline characteristics and outcomes data not clearly reported
Other bias	Unclear risk	Sponsorship bias cannot be ruled out.

0600B1-367

Methods	Pooled analysis of data from 5 double-blind, parallel group trials conducted in depressed patients in the USA, Canada and Europe
Participants	Participants were 18 years of age who met the criteria for moderate to severe depression. Patients were eligible if they reported symptoms of depression for at least 1 month before the beginning of the study and scored a minimum of 20 on the Hamilton rating scale for depression (HDRS-21 or 26 items) on the Montgomery and Asberg Depression Rating Scale (MADRS)
Interventions	Paroxetine: 81 participants. Venlafaxine XR: 165 participants. Paroxetine dose: 20 mg/day. Venlafaxine dose range: 75-150 mg/day.
Outcomes	HDRS-21, MADRS, Clinical Global Impression (CGI) Severity. Total dropout, dropout due to side effects, dropout due to inefficacy
Notes	Exclusion criteria included significant cardiovascular, renal, hepatic or seizure disorders. In addition, patients were excluded if they had significant abnormalities on baseline physical examination, laboratory tests, ECG or a history of alcohol or drug abuse. Funding: venlafaxine manufacturer

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0600B1-367 (*Continued*)

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: "randomized (...) patients were randomly assigned". No further details
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "all study medications, including placebo, were given with food in the morning and were provided in identical capsules"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No information provided.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Quote: "scores based on the HDRS-17 were generated for all Intention-to-treat (ITT) patients and were calculated on a Last Observation Carried Forward (LOCF) basis, such that the last observation for a patient who withdrew prematurely from the study was carried forward into all subsequent periods, up to 8 weeks"
Selective reporting (reporting bias)	Unclear risk	Outcomes data not clearly reported.
Other bias	Unclear risk	Sponsorship bias cannot be ruled out.

29060.065.BE

Methods	Six-week, randomised, double-blind, double-dummy, active-controlled, parallel group study
Participants	Hospital in-patients of either sex in the age range 18-65 years with a major depressive episode according to the DSM-III and a Hamilton rating scale for depression (HDRS-21) score of 18 or more in the 21-item total after a 1-week placebo wash-out
Interventions	Paroxetine: 28 participants. Maprolitine: 32 participants. Paroxetine dose range: 30-40 mg/day. Maprolitine dose range: 100-150 mg/day.
Outcomes	HDRS-21, Clinical Global Impression (CGI) Severity, Montgomery and Asberg Depression Rating Scale (MADRS), the Hopkins' Symtom Checklist (HSCL-58). Total

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29060.065.BE (*Continued*)

	dropout, dropout due to side effects. Number of patients experiencing at least one side effect, side-effect profile
Notes	Funding: paroxetine manufacturer.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: "randomized". No further details.
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double blind, double dummy".
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double blind, double dummy".
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Quote: "analyses were based on the Intention-to-treat (ITT) population. The ITT population consists of subjects who received at least one dose of active trial medication and a subsequent assessment. primary efficacy results were presented for the ITT population using the visit-wise data set which consists of each person assessment at each visit" More than 20% of participants in the paroxetine group abandoned the study prematurely
Selective reporting (reporting bias)	Low risk	Outcomes data were reported.
Other bias	Unclear risk	Sponsorship bias cannot be ruled out.

29060.07.001

Methods	Six-week, multicentre, double-blind, randomised, parallel group controlled trial
Participants	Inpatients, aged 18 or older, diagnosed with moderately severe to severe major depressive disorder with melancholia (DSM-III), characterized by disorder of mood with symptoms such as depressed mood, sadness, hopelessness and worthlessness were eligible for the study

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29060.07.001 (*Continued*)

Interventions	Paroxetine: 13 participants. Amitriptyline: 13 participants. Paroxetine dose range: 10-60 mg/day. Amitriptyline dose: 100 mg/day.
Outcomes	Hamilton rating scale for depression (HDRS), Symptom checklist (SCL), Clinical Global Impression (CGI), Montgomery and Asberg Depression Rating Scale (MADRS). Endpoint was identified at week 6. Total dropout, dropout due to side effects, dropout due to inefficacy. Number of patients experiencing at least one side effect, side-effect profile
Notes	Funding: paroxetine manufacturer.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: "randomized". No further details.
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double blind (...) subjects received two bottles of screen medication (a morning and evening bottle) and were instructed to take two capsules from each bottle morning and evening"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No information provided.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Quote: "the primary analysis of the study is based on the all efficacy subject population using the extender data set and analysis of variance (...) The Intention to treat (ITT) population consisted of subjects who were evaluable for safety analysis. These subjects must have entered the active treatment phase of the study, taken double blind medication, and at least had an opportunity to report the presence or absence of an adverse event"
Selective reporting (reporting bias)	Low risk	Outcomes data were reported.
Other bias	Unclear risk	Sponsorship bias cannot be ruled out.

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29060/056/UK

Methods	A double-blind, multicentre, parallel group study.
Participants	Inclusion criteria: male and female participants, aged > 65 years; major depressive illness according to the DSM-III-R; total score >18 on the Montgomery and Asberg Depression Rating Scale (MADRS) Exclusion criteria: participants with other psychiatric disorders; participants with suicidal tendencies
Interventions	Paroxetine: 67 participants. Dotiepine: 67 participants. Paroxetine dose: 20 mg/day. Dotiepine dose: 75 mg/day.
Outcomes	MADRS, Clinical Global Impression (CGI), Leeds Sleep Evaluation Questionnaire (LSEQ). Total dropout, dropout due to side effects, dropout due to inefficacy. Number of patients experiencing at least one side effect, side-effect profile
Notes	Funding: paroxetine manufacturer.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: "randomized". No further details.
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double blind". No further details.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double blind". No further details.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "the Intention-to-treat (ITT) population included all subjects who received at least one dose of study medication and had at least one assessment. All subjects who took active medication were analyzed for safety. MADRS, CGI and LSEQ data were subject to a Last Observation Carried Forward (LOCF) procedure before analysis" Withdrawn: paroxetine 12/67 participants; dothiepin 8/67 participants

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29060/056/UK (*Continued*)

Selective reporting (reporting bias)	High risk	Standard deviations for rating scales scores not reported.
Other bias	Unclear risk	Sponsorship bias cannot be ruled out.

29060/103

Methods	A double-blind, multicentre, randomised, comparative study.
Participants	Male or female hospital inpatients or outpatients aged 65 to 85 years suffering a major depressive episode defined according to DSM-III-R were eligible for inclusion. Participants scored > 20 on the Montgomery and Asberg Depression Rating Scale (MADRS) and 23 on the Folstein Mini Mental State Examination (FMMSE) at day -7 were included as well
Interventions	Paroxetine: 57 participants. Lofepramine: 49 participants. Paroxetine dose range: 20-30 mg/day. Lofepramine dose range: 70-210 mg/day.
Outcomes	MADRS, Global Deterioration Scale (GDS), Clinical Global Impression (CGI). Total dropout, dropout due to side effects, dropout due to inefficacy. Number of patients experiencing at least one side effect, side-effect profile
Notes	Participants with severe disease, dementia, mania, bipolar affective disorder and schizophrenia were excluded from the study Funding: paroxetine manufacturer.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: "randomized". No further details.
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double blind". No further details.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double blind". No further details.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Quote: "all subjects randomized to active treatment and not excluded by failure to take > or = 1 dose of study medication and

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		who had data captured were included in the Intention-to-treat (ITT), clinical, safety, and tolerability analyses. Subjects who also had > or = 1 valid efficacy evaluation after the start of treatment were eligible for the ITT efficacy analysis. Subjects included in the ITT analysis were also included in the Per Protocol (PP) analysis" More than 20% of participants in the lofepramine group abandoned the study prematurely
Selective reporting (reporting bias)	Low risk	Outcome data were reported.
Other bias	Unclear risk	Sponsorship bias cannot be ruled out.

29060/281 PAR

Methods	Seven-week, double-blind, double-dummy, parallel group study
Participants	Participants aged 18 to 70 years; suffering from unipolar (endogenous or reactive) depression; fulfilling Feighner's criteria for depression; had a minimum Hamilton rating scale for depression (HDRS-21) score of 18
Interventions	Paroxetine: 82 participants. Amitriptyline: 80 participants. Paroxetine dose: 30 mg/day. Amitriptyline dose range: 75-150 mg/day.
Outcomes	HDRS-21, Clinical Global Impression (CGI), Self-Rating Scale. Total dropout, dropout due to side effects, dropout due to inefficacy. Number of patients experiencing at least one side effect, side-effect profile
Notes	Funding: paroxetine manufacturer.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: "subjects were randomly allocated". No further details
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double blind, double dummy (. ..) all medication was administered orally once daily in the evening with matching placebo tablets or capsules according to a

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29060/281 PAR (*Continued*)

		double dummy design"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double blind". No further details.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "the main analyses were carried out on the Intention-to-treat (ITT) population - patients who were randomized and had on-treatment data available. An "extender" dataset was created using a Last Observation Carried Forward (LOCF) technique to impute missing values using the previous on-treatment data for that subject"
Selective reporting (reporting bias)	High risk	Outcomes data reported without standard deviations.
Other bias	Unclear risk	Sponsorship bias cannot be ruled out.

29060/299

Methods	A double-blind, multicentre, randomised, flexible dose, parallel group study
Participants	Male or non-pregnant, non-lactating female patients using adequate contraception were eligible if they were aged 18 to 65 years; were hospitalised; had a diagnosis of severe, unipolar depression (without psychotic symptoms), defined according to ICD-10 criteria; and had a score of at least 24 points on the Hamilton rating scale for depression (HDRS-17) at screening and at the baseline assessment
Interventions	Paroxetine: 109 participants. Amitriptyline: 108 participants. Paroxetine dose range: 20-50 mg/day. Amitriptyline dose range: 100-250 mg/day.
Outcomes	Clinical Global Impression (CGI), Hospital Anxiety and Depression scale (HAD). Total dropout, dropout due to side effects. Number of patients experiencing at least one side effect, side-effect profile
Notes	Funding: paroxetine manufacturer.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: "patients were randomized (1:1) to either paroxetine or amitriptyline"

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Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double blind". No further details.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double blind". No further details.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Quote: "the primary analysis was on the Intention-to-treat (ITT) data set at endpoint. No efficacy data was available for 15 of the randomized patients. The ITT analysis was therefore performed on 202 subjects of whom 102 were randomized to paroxetine and 100 to amitriptyline. The safety population included all randomized subjects"
Selective reporting (reporting bias)	Low risk	Outcomes data were reported.
Other bias	Unclear risk	Sponsorship bias cannot be ruled out.

29060/356

Methods	Eight-week, double-blind, multicentre, randomised, comparative study	
Participants	Moderate to moderately severe depression with a diagnosis of Major Depressive Disorder (MDD) (DSM-III-R), male or female at least 18 years old, inpatients or outpatients with a Hamilton rating scale for depression (HDRS-17) total score 18 or more, HAMD-10 of 1 or more	
Interventions	Fluoxetine: 68 participants. Paroxetine: 70 participants. Fluoxetine dose: 20 mg/day. Paroxetine dose: 20 mg/day.	
Outcomes	HDRS, Hamilton rating scale for anxiety (HAM-A), Clinical Global Impression (CGI). Total dropout, dropout due to side effects, dropout due to inefficacy. Number of patients experiencing at least one side effect, side-effect profile	
Notes	Funding: paroxetine manufacturer.	
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**

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Random sequence generation (selection bias)	Unclear risk	Quote: "randomized". No further details.
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double blind". No further details.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double blind". No further details.
Incomplete outcome data (attrition bias) All outcomes	High risk	Quote: "Intention-to-treat (ITT) population consisted of all subjects randomized to active treatment and for whom one valid post-randomization evaluation was available. Per Protocol (PP) population consisted of all subjects who had no major protocol violation with regard to inclusion/exclusion criteria, duration of treatment was at least 42 days, and no major protocol violation occurred during the first 2 weeks of active treatment. Safety population consisted of all subjects who were randomized to treatment. Primary efficacy analysis was based on both ITT and PP population" More than 20% of participants abandoned the study prematurely
Selective reporting (reporting bias)	Low risk	Outcomes data were reported.
Other bias	Unclear risk	Sponsorship bias cannot be ruled out.

29060/409

Methods	Controlled,double-blind, double-dummy study.
Participants	Male and female participants with a diagnosis of MDD (DSM-III), Hamilton rating scale for depression (HDRS-17) total score >/= 22 Age range: 18-65 years old.
Interventions	Paroxetine: 38 participants. Imipramine: 37 participants. Paroxetine dose: 20 mg/day. Imipramine dose range: 150-300 mg/day.

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Outcomes	HDRS-25, HDRS-17, Hamilton rating scale for anxiety (HAM-A), Clinical Global Impression (CGI).Total dropout, dropout due to side effects, dropout due to inefficacy. Number of patients experiencing at least one side effect, side-effect profile
Notes	Funding: paroxetine manufacturer.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: "randomized". No further details.
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double blind, double dummy".
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double blind, double dummy".
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Quote: "the subject population used for the efficacy analysis was the Intent-to-treat (ITT) Last Observation Carried Forward (LOCF)." More than 20% of participants abandoned the study prematurely
Selective reporting (reporting bias)	Low risk	Outcome data were reported.
Other bias	Unclear risk	Sponsorship bias cannot be ruled out.

29060/III/83/022

Methods	Double-blind, randomised, double-dummy, parallel group study
Participants	Male or female participants with reactive or endogenous unipolar depression, and who were considered suitable for treatment with tricyclic-like anti-depressant, could be eligible for inclusion in the study. Participants also had to meet Spizer's criteria for depression and score a minimum of 15 on the Hamilton rating scale for depression (HDRS-17) at baseline Age range: 18-70 years.
Interventions	Paroxetine: 18 participants. Mianserin: 18 participants.

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	Paroxetine dose range: 15-45 mg/day. Mianserine dose range: 30-90 mg/day.
Outcomes	HDRS-17, Clinical Global Impression (CGI). Total dropout, dropout due to side effects, dropout due to inefficacy. Number of patients experiencing at least one side effect, side-effect profile
Notes	None.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: "subject were randomized". No further details.
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double blind, double dummy".
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double blind, double dummy".
Incomplete outcome data (attrition bias) All outcomes	High risk	No details on the Intention-to-treat (ITT) population. Number of randomized, and number of subjects withdrawn not reported for the paroxetine arm
Selective reporting (reporting bias)	High risk	Outcomes data not clearly reported. Standard deviations on rating scales scores not reported
Other bias	Unclear risk	Sponsorship bias cannot be ruled out.

29060/III/85/030

Methods	Randomised, double-blind, double-dummy parallel group study.
Participants	Participants suffering from reactive or endogenous depression (fulfilling the DSM criteria for major depressive illness) and having a minimum score of 17 on the Hamilton rating scale for depression (HDRS-17) at baseline were eligible for inclusion in the study Age range: 18-65 years.

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29060/III/85/030 (*Continued*)

Interventions	Paroxetine: 18 participants. Mianserin: 15 participants. Paroxetine dose range: 15-30 mg/day. Mianserine dose range: 30-90 mg/day.
Outcomes	HDRS-17. Total dropout, dropout due to side effects. Number of patients experiencing at least one side effect
Notes	No specific exclusion criteria were defined. Funding: paroxetine manufacturer

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: "subject were randomized". No further details.
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double blind". No further details.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double blind". No further details.
Incomplete outcome data (attrition bias) All outcomes	High risk	Quote: "the population of interest was the Intent-to-treat (ITT) population and the timepoint of interest was the 6 week extender endpoint" More than 20% of participants in both groups abandoned the study prematurely
Selective reporting (reporting bias)	High risk	Outcomes data not clearly reported. Standard deviations for rating scales scores not reported
Other bias	Unclear risk	Sponsorship bias cannot be ruled out.

29060III/85/038

Methods	A double-bind, parallel group, active controlled, double-dummy, randomised study
Participants	Participants suffering from either reactive or endogenous unipolar depression considered suitable for treatment with "tricyclic-like" antidepressants were eligible for the study. Participants had to score al least 17 on the first 17-itemof the Hamilton rating scale for depression (HDRS-21) and fulfil the DSM-III criteria for the diagnosis of depression.

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29060III/85/038 (*Continued*)

	Subjects were excluded in they were suffering from severe co-existing diseases, intolerant to "tricyclic-like" drugs, scored 4 on the suicide item of the HDRS-21, had received ECT in the previous 3 months required hospitalisation for ECT treatment, had taken IMAO with 2 weeks of the active phase of the study and female participants who were pregnant or lactating Age range: 18-70 years old.
Interventions	Paroxetine: 30 participants. Mianserin: 29 participants. Paroxetine dose range: 15-30 mg/day Mianserine dose range: 30-90 mg/day.
Outcomes	HDRS-21, Clinical Global Impression (CGI). Total dropout, dropout due to side effects, dropout due to inefficacy. Number of patients experiencing at least one side effect, side-effect profile
Notes	None.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Quote: "subjects were randomized (...) allocation of treatment by random code"
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double blind, using a double dummy technique". No further details
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double blind, using a double dummy technique". No further details
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Quote: "results are presented for the Intention-to-treat (ITT) population, extender data set" Less than 20% of participants in each study arm abandoned the study prematurely
Selective reporting (reporting bias)	Low risk	Outcomes data were reported.
Other bias	Unclear risk	Sponsorship bias cannot be ruled out.

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Aberg-Wistedt 2000

Methods	Twenty-four week, double-blind, randomised study.
Participants	Outpatients meeting DSM-III-R criteria for major depression (no patients with bipolar disorder). Age range: over 18 years.
Interventions	Paroxetine: 177 participants Sertraline: 176 participants. Paroxetine dose: 20-40 mg/day. Sertraline dose: 50-150 mg/day. The association of short half-time benzodiazepines was allowed for insomnia in those patients who already been receiving concomitant treatment before the study began
Outcomes	Montgomery-Asberg Depression Rating Scale (MADRS), Clinical Global Impression (CGI) Total dropout, side-effect profile.
Notes	Funding: sertraline manufacturer.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Quote: "randomly assigned". Probably done, as a similar trial by these investigators included the same phrase and used a proper method of allocation
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double-blind"; no further information.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double-blind"; no further information.
Incomplete outcome data (attrition bias) All outcomes	High risk	Three efficacy analyses were performed: an ITT analysis performed on all randomly assigned patients who were available at each study visit; an Intention-to-treat-Last Observation Carried Forward (ITT-LOCF) analysis and an analysis performed on all patients who completed study treatment with no major protocol deviation Study endpoint: 61/177 missing from paroxetine group; 64/176 missing from control group

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Aberg-Wistedt 2000 (*Continued*)

Selective reporting (reporting bias)	Low risk	The study protocol is not available but it is clear that the published reports include all expected outcomes, including those that were pre-specified
Other bias	Unclear risk	Sponsorship bias cannot be ruled out.

Ansseau 1993

Methods	Six-week, randomised, double-blind, multicentre study.
Participants	Psychiatric in- and outpatients meeting DSM-III-R for major depressive episode, with a minimum baseline score of 18 on the Hamilton rating scale for depression (HRSD-21). Age range: 18-65 years.
Interventions	Fluvoxamine: 64 participants. Paroxetine: 56 participants. Fluvoxamine dose range: 50-200 mg/day. Paroxetine dose range: 20-30 mg/day. For patients who had received benzodiazepines for at least two weeks prior to continue these agents, providing the dose remained unchanged throughout the study period. In addition, low dose lormethazepam or chloral hydrate were permitted in case of severe insomnia
Outcomes	HRSD-21, Clinical Global Impression- Severity (CGI-S), Hamilton rating scale for anxiety (HAM-A) Total dropout, dropout due to inefficacy, dropout due to side effects, number of patients experiencing at least one side effect, side-effect profile
Notes	Funding: paroxetine manufacturer. Patients with major depressive episode (DSM-III-R) were included, so there might be some bipolar depression, but correct number was not reported

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: "randomly assigned", no further details.
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "the trial used a double-blind design", no further details

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Ansseau 1993 (*Continued*)

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "the trial used a double-blind design", no further details
Incomplete outcome data (attrition bias) All outcomes	High risk	The Intention-to-treat (ITT) population was analysed using an endpoint dataset as well as a visit-wise dataset Study endpoint: 16/56 missing from paroxetine group; 23/64 missing from control group
Selective reporting (reporting bias)	High risk	Standard deviations of change score for depression were not reported
Other bias	Unclear risk	Sponsorship bias cannot be ruled out.

Aoba 2004

Methods	Six-week, double-blind, randomised study.
Participants	Inpatients and outpatients meeting DSM-IV criteria for major depression (no patients with bipolar disorder). Age range: 18-65 years.
Interventions	Paroxetine: 106 participants. Imipramine: 104 participants. Paroxetine dose: 20-40 mg/day. Imipramine dose: 50-150 mg/day.
Outcomes	Hamilton rating scale for depression (HDRS-17), Clinical Global Impression (CGI) Total dropout, dropout due to inefficacy, dropout due to side effects, number of patients experiencing at least one side effect, side-effect profile
Notes	Funding: paroxetine manufacturer.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: "randomized". No further details.
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double blind". No further details.

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Aoba 2004 (*Continued*)

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double blind". No further details.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Study endpoint: 22/106 missing from paroxetine group; 31/104 missing from control group All safety analyses were performed on safety population. Efficacy analyses were performed on FAS population and the Last Observation Carried Forward (LOCF) dataset was used. The FAS population consisted in all subjects who have entered the treatment phase with the exception of those who did not meet the major eligibility criteria, those who did not take any study medication during the treatment phase and those with no valid post baseline assessment
Selective reporting (reporting bias)	High risk	Mean change from baseline only reported as "rate of decrease from baseline at endpoint"
Other bias	Unclear risk	Sponsorship bias cannot be ruled out.

Bakish 1997

Methods	Double-blind, active-controlled study comparing the efficacy of paroxetine and fluoxetine
Participants	All patients fulfilled the DSM III-R criteria for Major Affective Disorder, unipolar (either first episode or recurrent) and had met the diagnostic criteria for major depressive episode for at least one month prior to entering the study. To be included in the study, patients had to score 18 or more on the Hamilton rating scale for depression (HDRS-17), with a score of two or more on item one Patients with a concurrent DSM III-R Axis I diagnosis or an unstable medical condition were excluded from the study
Interventions	Paroxetine: 12 participants. Fluoxetine: 9 participants. Paroxetine dose: 20-50 mg/day. Fluoxetine dose: 20-80 mg/day. No concomitant psychotropic medications were allowed with the exception of chloral hydrate at bedtime on an "as needed" basis to a maximum dose of 1000 mg/day
Outcomes	HDRS-17, Clinical Global Impression (CGI).

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Bakish 1997 (*Continued*)

Notes	This study was partly supported by SmithKline Beecham. Outcomes data were not available. The study was primarily designed to investigate the effect of antidepressants on platelet serotonin parameters

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "randomly assigned". No further details.
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double blind". No further details.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double blind". No further details.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	No clear information on incomplete outcome data management.
Selective reporting (reporting bias)	Unclear risk	Outcomes data not available.
Other bias	Unclear risk	Sponsorship bias cannot be ruled out.

Baldwin 1995

Methods	Eight-week, double-blind, randomised study.
Participants	Outpatients meeting DSM-III-R criteria for major depression (there are some bipolars but less than 20% of the total randomised sample). Age range: over 18 years.
Interventions	Paroxetine: 101 participants. Nefazodone: 105 participants. Paroxetine dose: 20-40 mg/day. Nefazodone dose: 200-600 mg/day. The association of short half-time benzodiazepines was allowed for insomnia in those patients who already been receiving concomitant treatment before the study began
Outcomes	Montgomery and Asberg Depression Rating Scale (MADRS), Hamilton rating scale for depression (HDRS-17), Clinical Global Impression (CGI) Total dropout, dropout due to inefficacy, dropout due to side effects, number of patients experiencing at least one side effect, side-effect profile

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Baldwin 1995 (*Continued*)

Notes	Funding: nefazodone manufacturer. Adverse events reported only if occurring in >= 10% of any treatment group

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "randomly assigned", no further details.
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "a double dummy technique was used to maintain the blind"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "a double dummy technique was used to maintain the blind"
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Safety analyses comprised the data from all patients who were randomly assigned to treatment and received the study medication. Efficacy analyses were performed on all patients who had received study medication and who had undergone at least one efficacy evaluation during treatment Study endpoint: 28/101 missing from paroxetine group; 28/105 missing from control group
Selective reporting (reporting bias)	High risk	Standard deviations of change score for depression were not reported Adverse events were reported only if occurring in >= 10% of any treatment group
Other bias	Unclear risk	Sponsorship bias cannot be ruled out.

Baldwin 2006

Methods	Twenty-seven-week double-blind, randomised, multicentre study. For efficacy data we consider only the first eight weeks
Participants	Setting unclear, patients meeting DSM-IV for major depressive episode, with a minimum baseline score of 22 on the Montgomery and Asberg Depression Rating Scale (MADRS) . Age: older than 18 years.

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Baldwin 2006 (*Continued*)

Interventions	Paroxetine: 101 participants. Escitalopram: 105 participants. Paroxetine dose range: 20-40 mg/day. Escitalopram dose range: 10-20 mg/day. For patients who had received benzodiazepines for at least 6 months prior to continue these agents, providing the dose remained unchanged throughout the study period
Outcomes	MADRS, Arizona sexual experience scale (ASEX). Total dropout, dropout due to inefficacy, dropout due to side effects, number of patients experiencing at least one side effect, side-effect profile
Notes	Funding: escitalopram manufacturer. Adverse events reported only if occurring in >= 5% of any treatment group

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Quote: "patients were assigned to escitalopram or paroxetine treatment according to a computer-generated randomization list"
Allocation concealment (selection bias)	Low risk	Quote: "the details of the randomization series were unknown to any of the investigators and were unknown to any of the investigators and were contained in a set of opaque envelops"
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "all study personnel and participants were blinded to treatment assignment for the duration of the study" "Treatment was in the form of tablets of identical appearance, taste and smell"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "all study personnel and participants were blinded to treatment assignment for the duration of the study"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Efficacy analyses were conducted for the modified Intention-to-treat (ITT) population which included all randomized patients who took at least one dose of double blind study medication and who had least one valid post baseline MADRS assessment
Selective reporting (reporting bias)	High risk	Standard deviations of change score for depression were not reported Adverse events were reported only if occur-

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Baldwin 2006 (*Continued*)

		ring in >= 5% of any treatment group
Other bias	Unclear risk	Sponsorship bias cannot be ruled out

Bascara 1989

Methods	Six-week, double-blind, randomised study.
Participants	Setting unclear, patients meeting DSM-III criteria for major depression with a minimum score of 18 on the Hamilton rating scale for depression (HDRS-21). Age: over 18 years.
Interventions	Paroxetine: 27 participants. Amitriptyline: 23 participants. Paroxetine dose: 30 mg/day. Amitriptyline dose: 75 mg/day.
Outcomes	HDRS-21. Dropout due to side effects.
Notes	None.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: "patients were randomly allocated". No further details
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: " in a double blind fashion (...) material was prepared using a double dummy technique. all study medication was given in the morning"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double blind".
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	No information on incomplete outcome data management.
Selective reporting (reporting bias)	High risk	Standard deviations of change scores for depression were not reported Efficay and safety analyses reported only as rate of patients who "improved" and for whom treatment was "well tolerated"

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Bascara 1989 (*Continued*)

Other bias	Unclear risk	Sponsorship bias cannot be ruled out.

Battegay 1985

Methods	Seven-week, double-blind, randomised study.
Participants	Outpatients meeting DSM III endogenous and reactive depression, with a minimum score of 20 on the Hamilton rating scale for depression (HDRS-17). Age range: 18-60 years.
Interventions	Paroxetine: 11 participants. Amitriptyline: 10 participants. Paroxetine dose range: 10-30 mg/day. Amitriptyline dose range: 50-100 mg/day. In case of severe insomnia tranquillisers with a short half life were permitted
Outcomes	HDRS-17, Montgomery and Asberg Depression Rating Scale (MADRS), Clinical Global Impression (CGI) Dropout, number of patients experiencing at least one side effect, side-effect profile
Notes	Small sample; more than 50% of patients did not complete the trial

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: "the patients received (...) in a randomized procedure (...)". No further details
Allocation concealment (selection bias)	Unclear risk	No informations provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "the patients received in a double blind procedure identically looking white tablets containing either 10 mg paroxetine ore 50 mg amitriptyline"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double blind".
Incomplete outcome data (attrition bias) All outcomes	High risk	Study endpoint: 3/11 missing from paroxetine group; 8/10 missing from control group
Selective reporting (reporting bias)	High risk	Standard deviations of change scores for depression were not reported

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Battegay 1985 (*Continued*)

Other bias	Unclear risk	Sponsorship bias cannot be ruled out.

Benkert 1999

Methods	Six-week, randomised, double-blind, multicentre study.
Participants	Outpatients meeting DSM-IV criteria for major depression (no patients with bipolar disorder). Age range: 18-70 years.
Interventions	Paroxetine: 136 participants. Mirtazapine: 139 participants. Paroxetine dose range: 20-40 mg/day. Mirtazapine dose range:15-45 mg/day. In case of severe insomnia chloral hydrate was permitted.
Outcomes	The measure used for response and remission in the review: Hamilton rating scale for depression (HDRS-17) Other measures: Hamilton rating scale for anxiety (HAM-A), Beck Depression Inventory (BDI), Welzil-Kohnen Color Scales (WKFS), Short Form-36, Clinical Global Impression (CGI) improvement, CGI-severity
Notes	Funding: mirtazapine manufacturer. Adverse events reported only if occurring in >= 5% of any treatment group

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: "randomized". No further details.
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double-blind", "both drugs were given once daily, mirtazapine in the evening and paroxetine in the morning using a double dummy technique
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double-blind".
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	More than 20% of the allocated patients to both of the intervention arms dropped out during the study Efficacy analyses were based on the In-

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Benkert 1999 (*Continued*)

		tention-to-treat (ITT) patients sample, including all randomly assigned patients who received at least one dose of study medication and had at least one post-baseline efficacy assessment. A Last Observation Carried Forward (LOCF) analysis was performed for the endpoint assessment
Selective reporting (reporting bias)	High risk	Both the response and the remission outcomes at end of the acute-phase treatment are reported with the proportion of the patients who achieved these Standard deviations of change scores were not reported. Adverse events were reported only if occurring in >= 5% of any treatment group
Other bias	Unclear risk	Sponsorship bias cannot be ruled out.

Bignamini 1992

Methods	Six-week, randomised, double-blind, multicentre study.
Participants	Outpatients meeting DSM-III diagnostic criteria for depression Age range: 18-70 years.
Interventions	Paroxetine: 156 participants. Amitriptyline: 153 participants. Paroxetine dose range: 20-30 mg/day. Amitriptyline dose range: 75-150 mg/day.
Outcomes	Hamilton rating scale for depression (HDRS-21). Total dropout, dropout due to inefficacy, dropout due to side effects, number of patients experiencing at least one side effect, side-effect profile
Notes	Funding: paroxetine manufacturer. Adverse events reported only if occurring in >=5% and only on graphs

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: "randomized". No further details.
Allocation concealment (selection bias)	Unclear risk	No information provided.

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Bignamini 1992 (*Continued*)

Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double blind"; "double dummy".
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double blind"; "double dummy".
Incomplete outcome data (attrition bias) All outcomes	Low risk	Study endpoint: 31/156 missing from Paroxetine group; 20/153 missing from control group. The population on which efficacy and safety analyses have been conducted was not well specified
Selective reporting (reporting bias)	High risk	Two rating scales for depression Clinical Global Impression (CGI) and HDRS listed in methods but only one is reported (HDRS) Adverse events were reported only if occurring in >=5% and only on graphs
Other bias	Unclear risk	Sponsorship bias cannot be ruled out.

Blier 2009

Methods	Eight-week, randomised, double-blind study. We consider only the first six weeks of treatment because in the subsequent two weeks the possibility of combining the two treatment is introduced and randomisation is lost
Participants	In and outpatients meeting DSM IV diagnostic criteria for major depression (no bipolar patients included in the study) Age range:18-65 years.
Interventions	Paroxetine: 19 participants. Mirtazapine: 21 participants. Paroxetine dose range: 20-30 mg/day. Mirtazapine dose range: 30-45 mg/day.
Outcomes	Montgomery and Asberg Depression Rating Scale (MADRS), Hamilton rating scale for depression (HDRS-17), Clinical Global Impression (CGI)
Notes	Funding: mirtazapine manufacturer.

Risk of bias

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

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Blier 2009 (*Continued*)

Random sequence generation (selection bias)	Unclear risk	Quote: "randomized". No further details.
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "patients received either two mirtazapine tablets at bedtime with two placebo in the morning or two paroxetine tablets in the morning with placebo in the evening"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double blind".
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Number of total dropout not specified.
Selective reporting (reporting bias)	High risk	Three rating scales in method, but only one reported in results (MADRS)
Other bias	Unclear risk	Quote: "this investigator-initiated study was fully funded by Organon Pharmaceuticals. The sponsor had no role in the study design, in the collection and interpretation of the data, in the preparation of this report and in the decision to publish this manuscript

Boulenger 2006

Methods	Twenty-four-week, randomised, double-blind, multicentre study
Participants	Outpatients meeting DSM-IV criteria for major depression (no patients with bipolar disorder) with a minimum score of 30 on the Montgomery and Asberg Depression Rating Scale (MADRS) rating scale (severe depression). Age range: 18-75 years.
Interventions	Paroxetine: 227 participants. Escitalopram: 232 participants. Paroxetine dose: 40 mg/day. Escitalopram dose: 20 mg/day.
Outcomes	MADRS (primary outcome), Hamilton rating scale for depression (HDRS-24, HDRS-17), Clinical Global Impression (CGI) Total dropout, dropout due to inefficacy, dropout due to side effects, number of patients experiencing at least one side effect, side-effect profile

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Notes	Funding: escitalopram manufacturer. Adverse events reported only if occurring in >=5%.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "patients (...) were assigned in a 1:1 ratio of escitalopram or paroxetine according to a computer generated randomization list. (...) At each study centre, sequentially enrolled patients were assigned to the lowest randomization number in blocks of four"
Allocation concealment (selection bias)	Low risk	Quote: "the details of the randomization series were unknown to any of the investigators and were contained in a set of sealed opaque envelopes"
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "all study personnel and participants were blinded to treatment assignment for the duration of the entire study"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "all study personnel and participants were blinded to treatment assignment for the duration of the entire study"
Incomplete outcome data (attrition bias) All outcomes	High risk	Study endpoint (24 week) : 72/227 missing from paroxetine group; 44/232 missing from control group Efficacy analyses were based on the Intention-to-treat (ITT) set and using Last Observation Carried Forward (LOCF). The ITT population comprised 451 patients (paroxetine: 223, escitalopram: 228)
Selective reporting (reporting bias)	High risk	Proportion of remitters and responders reported only for endpoint, data for other weeks reported only as a proportion on graphs Standard deviations of change scores for depression were not reported Adverse events were reported only if occurring in >=5%.
Other bias	Unclear risk	Sponsorship bias cannot be ruled out.

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Cassano 2002

Methods	Fifty-two-week double-blind, randomised, multicentre study.
Participants	Outpatients fulfilling ICD-10 criteria for major depression, with a Mini Mental State Examination (MMSE) score of at least 22, Hamilton rating scale for depression (HDRS) score of at least 18. Age range: over 65 years.
Interventions	Paroxetine: 123 participants. Fluoxetine: 119 participants. Paroxetine dose range: 20-40 mg/day. Fluoxetine dose range: 20-60 mg/day. Stabilised treatment for concomitant systemic disease, temazepam for occasional treatment of insomnia and short or intermediate half-life benzodiazepine for anxiety were permitted
Outcomes	HDRS-21, Clinical Anxiety Scale (CAS), Buschke Selective Reminding Test (BSRT), Blessed Information and Memory Test (BIMT), Clifton Assessment Schedule (CLAS) , Cancellation Task Test (CTT), Wechsler Paired Word Test (WPW), MMSE, Clinical Global Impression (CGI) Total dropout, number of patients experiencing at least one side effect, side-effect profile
Notes	Funding: paroxetine manufacturer.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "randomized". No further details.
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double blind". No further details.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double blind". No further details.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Study endpoint: 50/123 missing from paroxetine group; 45/119 missing from control group. Statistical evaluation was performed on the basis of an endpoint analysis and all the data were analysed on an observed-case basis
Selective reporting (reporting bias)	High risk	Standard deviations of change scores for depression were not reported

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Cassano 2002 (*Continued*)

Other bias	Unclear risk	Sponsorship bias cannot be ruled out.

Cassano 2002a

Methods	Eight-week, double-blind, randomised, multicentre study.
Participants	Outpatients meeting DSM-IV criteria for major depression (no patients with bipolar disorder) with a minimum score of 18 on the Hamilton rating scale for depression (HDRS) Age range: 18-75 years.
Interventions	Paroxetine: 139 participants. Amisulpride: 138 participants. Paroxetine dose range: 20 mg/day. Amisulpride dose range: 50 mg/day. Benzodiazepine or hypnotic given at a stable dose were permitted
Outcomes	HDRS, Montgomery and Asberg Depression Rating Scale (MADRS), Clinical Global Impression (CGI) Total dropout, dropout due to inefficacy, dropout due to side effects, number of patients experiencing at least one side effect, side-effect profile
Notes	Funding: amisulpride manufacturer.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: "randomized". No further details.
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double blind". No further details.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double blind". No further details.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Less than 20% of the allocated patients to both of the intervention arms dropped out during the study The primary efficacy analysis was performed on the Per Protocol (PP) population that included all randomized patients

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		fully compliant with the protocol during the active treatment period and having at least one evaluation of the primary end-point after baseline. Consistency of results was assessed in the Intention-to-treat (ITT) population. For patients not completing the trial the Last Observation Carried Forward (LOCF) was analysed
Selective reporting (reporting bias)	High risk	Side effects reported only if statistically significant.
Other bias	Unclear risk	Sponsorship bias cannot be ruled out.

Chiu 1996

Methods	Six-week, double-blind, randomised study.
Participants	Inpatients and Outpatients meeting DSM-III-R criteria for major depression with a minimum score of 18 at the Hamilton rating scale for depression (HDRS) rating scale. Age range: 18-70 years.
Interventions	Paroxetine: 20 participants. Imipramine: 20 participants. Paroxetine dose: 20-30 mg/day. Imipramine dose: 75-150 mg/day. No other psychoactive drugs were used except for patients who had initiated benzodiazepines within 14 days before the screening visit. Patients requiring hypnotics were allowed only one benzodiazepine on a p.n.r basis at night
Outcomes	HDRS, Clinical Global Impression (CGI), Treatment Emergent Symptom Scale (TESS) . Total dropout. Dropout due inefficacy. Side-effect profile
Notes	Funding: paroxetine manufacturer.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: "randomized". No further details.
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "the blindness of the study was maintained by using a double dummy technique. Paroxetine Imipramine and placebo were all prepared in physically identical

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Chiu 1996 (*Continued*)

		capsules. To maintain a double blind condition blister packs containing either active drugs or placebo capsules and the blisters used daily were the same in each group"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double blind".
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Study endpoint: 5/20 missing from paroxetine group; 5/20 missing from control group. 35 patients who did not violate the trial protocol were included in the analysis of adverse effects. 30 patients who had completed six weeks of active treatment according to the trail protocol were included for calculation of mean reduction of HDRS score
Selective reporting (reporting bias)	High risk	HDRS scores for each week of treatment reported only on graphs. Side effects reported only on graphs
Other bias	Unclear risk	Sponsorship bias cannot be ruled out.

Chouinard 1999

Methods	Twelve-week, double-blind, randomised, multicentre study.
Participants	Patients fulfilling DSM-III criteria for major depressive disorder, with a score of at least 20 on Hamilton rating scale for depression (HDRS-21) Age range: not stated.
Interventions	Paroxetine: 102 participants. Fluoxetine: 101 participants. Paroxetine dose range: 20-50 mg/day. Fluoxetine dose range: 20-80 mg/day. Chloral hydrate was allowed just during the first two weeks of the study
Outcomes	HDRS-21, Clinical Global Impression(CGI), Hamilton rating scale for anxiety (HAM-A) Total dropout, dropout due to inefficiency, dropout due to side effects, side-effect profile
Notes	Two participants abandoned prematurely the trial (1 in the fluoxetine and 1 in the paroxetine group) due to attempted suicide. Funding: paroxetine manufacturer. Adverse events reported only if occurring in >= 5% of any treatment group

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Chouinard 1999 (*Continued*)

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: "randomized". No further details.
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double blind".
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double blind".
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	A total of 203 patients were randomized and 130 (64.04%) completed the study. A total of 100 patients in the paroxetine group and 98 in the fluoxetine one were evaluable for the Last Observation Carried Forward (LOCF) endpoint analysis
Selective reporting (reporting bias)	High risk	Adverse events were reported only if occurring in >= 5% of any treatment group
Other bias	Unclear risk	Sponsorship bias cannot be ruled out.

Christiansen 1996

Methods	Eight-week, double-blind, randomised, multicentre study.
Participants	General practise patients with depression (unclear diagnostic criteria used) with a minimum score of 15 on the Hamilton rating scale for depression (HDRS) Age range: 18-65 years.
Interventions	Paroxetine: 71 participants. Amitriptyline: 73 participants. Paroxetine dose range: 20-40 mg/day. Amitriptyline dose range: 100-150 mg/day. In case of severe insomnia tranquillisers with a short half life were permitted
Outcomes	HDRS, Clinical Global Impression (CGI), Visual Analogue Scale (VAS). Total dropout, dropout due to side effect, dropout due to lack of efficacy. Tolerability profile
Notes	Funding: paroxetine manufacturer.

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Christiansen 1996 (*Continued*)

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Quote:"patient identification numbers were randomly generated to indicate treatment options. These numbers were randomized and packed in blocks of four"
Allocation concealment (selection bias)	Unclear risk	Patients who fulfilled the entrance criteria were allocated.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "a double dummy technique was employed using placebo tablets identical in appearance to the active drugs. The number of tablets taken daily was four at low dose and eight at high dose"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double blind".
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Study endpoint: 15/71 missing from paroxetine group, 16/73 from control group Two different set of data were analysed for efficacy: the actual data produced at each visit from day 7 to day 55 and a Intention-to-treat (ITT) analysis of every randomised patient participating in the study and including for withdrawals last values carried forward
Selective reporting (reporting bias)	High risk	Side effects reported only if statistically significant and only as a percentage
Other bias	Unclear risk	Sponsorship bias cannot be ruled out.

CL3-023

Methods	Double-blind, randomised study.
Participants	Male and female adults, 18-70 years of age, with a diagnosis of Major Depressive Disorder according to DSM-IV criteria. Hamilton Depression Rating Scale (HDRS) total score > or = 22 at screening and baseline
Interventions	Paroxetine: 20 mg/day. Agomelatine: 25 mg/day.

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CL3-023 (*Continued*)

Outcomes	Change from baseline to endpoint at HDRS, remission, sexual functions	
Notes	Funding: by industry.	
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Quote: "The randomisation of treatments (agomelatine, placebo, fluoxetine or paroxetine) was non-adaptive, non-centralised, and balanced with a 1:1:1 ratio. There was no stratification and permutation blocks were of fixed size = 6"
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Double blind. Quote: "Agomelatine, placebo and fluoxetine (or paroxetine) were disguised in tablets or capsules (or tablets) of identical appearance and taste"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Double blind. Quote: "Agomelatine, placebo and fluoxetine (or paroxetine) were disguised in tablets or capsules (or tablets) of identical appearance and taste"
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Insufficient information.
Selective reporting (reporting bias)	Unclear risk	Insufficient information.
Other bias	Unclear risk	Sponsorship bias cannot be ruled out.

Cohn 1990

Methods	Six-week, double-blind, randomised, single-centre, placebo-controlled
Participants	Outpatients meeting DSM-III criteria for major depression with a minimum score of 18 on Hamilton rating scale for depression (HDRS-17). Age: older than 18 years.
Interventions	Paroxetine: 40 participants Imipramine: 40 participants Placebo:40 participants. Paroxetine dose range: 10-50 mg/day (mean dose: 30.9 mg/day) Imipramine dose range: 65-275 mg/day (mean dose: 144.9 mg/day) Chloral hydrate (500 mg) was allowed for a maximum of 4 consecutive nights during the first two weeks of the study

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Cohn 1990 (*Continued*)

Outcomes	HDRS-21, Clinical Global Impression (CGI) Improvement, Severity, Patient Global Experience (PGE). Total dropout, dropout due to side effect, dropout due to lack of efficacy. Number of patients experiencing at least one side effect, side-effect profile
Notes	Funding: unclear.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Randomized". No further details.
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double blind". No further details.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double blind". No further details.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Study endpoint: 21/40 missing from paroxetine group, 22/40 missing from control group
Selective reporting (reporting bias)	High risk	Dichotomous outcome not reported.
Other bias	Unclear risk	Sponsorship bias cannot be ruled out.

Dalery 2001

Methods	Six-week, double-blind, randomised, multicentre study.
Participants	Inpatients and outpatients meeting DSM-III-R criteria for major depression with a minimum score of 25 on the Montgomery and Asberg Depression Rating Scale (MADRS) rating scale. Age: older than 60 years.
Interventions	Paroxetine: 54 participants. Mianserin: 62 participants. Paroxetine dose range: 20 mg/day. Mianserin dose range: 30 mg/day. No other psychoactive drugs were used except for patients who had initiated benzodiazepines within 14 days before the screening visit

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Dalery 2001 (*Continued*)

Outcomes	MADRS, Mini Mental State Examination (MMSE), Aubin Jouvent Rating Scale (AJRS). Total dropout, dropout due to side effect, dropout due to lack of efficacy. Tolerability profile
Notes	None.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: "Randomized". No further details.
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double blind". No further details.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double blind". No further details.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Study endpoint: 11/54 missing from Paroxetine group; 9/62 missing from control group. Efficacy analyses were based on the Intention-to-treat (ITT) patients sample, including all randomly assigned patients who received at least one dose of study medication and had at least one post-baseline efficacy assessment
Selective reporting (reporting bias)	High risk	Side-effect profile incomplete.
Other bias	Unclear risk	Sponsorship bias cannot be ruled out.

Davidson 2005

Methods	Three-week, double-blind, randomised, study.
Participants	Outpatients fulfilling DSM-IV criteria for major depressive disorder. (No patients with bipolar disorder) Age range: 20-60 years.
Interventions	Paroxetine: 25 participants. Venlafaxine XR: 24 participants. Paroxetine dose range: 20-40 mg/day.

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Davidson 2005 (*Continued*)

	Venlafaxine dose range: 150-225 mg/day.
Outcomes	Heart rate variability. Total dropout. Responders at endpoint (3 weeks)
Notes	This study has been conducted in order to evaluate cardiological effects of both paroxetine and venlafaxine in the treatment of depression. For this reason most efficacy and safety data are not available

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: "medication assignment was based on a predetermined randomized allocation to treatment"
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double blind". No further details.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double blind". No further details.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Efficacy analyses were based on the Intention-to-treat (ITT) patients sample, including all randomly assigned patients who received at least one dose of study medication and had at least one post-baseline efficacy assessment Study endpoint: 11/54 missing from Paroxetine group; 9/62 missing from control group
Selective reporting (reporting bias)	Unclear risk	Protocol not available. Reported cardiological parameters only
Other bias	Unclear risk	Sponsorship bias cannot ruled out.

De Wilde 1993

Methods	Six-week, double-blind, randomised, study.
Participants	Patients fulfilling DSM-III criteria for major depression, with a score of at least 18 on the Hamilton rating scale for depression (HDRS-21). Age range: 18-65 years.

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De Wilde 1993 (*Continued*)

Interventions	Paroxetine: 50 participants. Fluoxetine: 50 participants. Paroxetine dose range: 20-40 mg/day. Fluoxetine dose range: 20-60 mg/day. Temazepam or other short-acting benzodiazepines were permitted as hypnotic
Outcomes	HDRS-21, Montgomery and Asberg Depression Rating Scale (MADRS), Hopkins Symptoms Check List (HSCL), Clinical Global Impression (CGI) Total dropout, dropout due to side effects, number of patients experiencing at least one side effect, side-effect profile
Notes	Funding: paroxetine manufacturer.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: "randomized". No further details.
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double blind". No further details.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double blind". No further details.
Incomplete outcome data (attrition bias) All outcomes	Low risk	For the evaluation of efficacy data, the extender Last Observation Carried Forward (LOCF) dataset was used Study endpoint: 6/37 missing from paroxetine group; 9/41 missing from control group
Selective reporting (reporting bias)	High risk	Total number of randomised patients not reported. Only reported Intention-to-treat (ITT) population. Data per week reported only when statistically significant. Side effects were reported only by body
Other bias	Unclear risk	Sponsorhip bias cannot be ruled out.

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Demyttenaere 2002

Methods	Double-blind, randomised, multicentre study.
Participants	Patients with DSM-IV diagnosis of major depressive disorder.
Interventions	Paroxetine: 43 participants. Fluoxetine: 42 participants. Paroxetine dose: 20 mg/day. Fluoxetine dose: 20 mg/day.
Outcomes	Hamilton rating scale for depression (HDRS-17).
Notes	None.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "randomized". No further details.
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double blind". No further details.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double blind". No further details.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	No clear information on incomplete data management. Number and reasons for dropouts not clear
Selective reporting (reporting bias)	Unclear risk	The type of adverse events was not reported.
Other bias	Unclear risk	Sponsorhip bias cannot be ruled out.

Detke 2004 (HMAY A)

Methods	Eight-week, double-blind, randomised, multicentre, placebo- and active comparator-controlled study comparing paroxetine with placebo and duloxetine. The protocol consisted of two identical studies conducted in parallel. Investigators were divided into the two separate study groups prior to beginning the studies

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Detke 2004 (HMAY A) (*Continued*)

Participants	Outpatients of at least 18 years of age with a primary diagnosis of major depression as defined by the DSM-IV. Patients were required to have a Hamilton rating scale for depression (HDRS-17) total score ≥15 and a CGI-Severity total score ≥4 at both Visits 1 and 2
Interventions	Paroxetine: 86 participants. Duloxetine 80 mg: 95 participants. Duloxetine 120 mg: 93 participants. Placebo: 93 participants. Paroxetine dose range: 20 mg once daily. Duloxetine 80 mg dose range: 40 mg twice daily. Duloxetine 120 mg dose range: 60 mg twice daily.
Outcomes	HDRS-17, Montgomery and Asberg Depression Rating Scale (MADRS), Clinical Global Impression (CGI), Visual Analogue Scale (VAS), Patient Global Impression (PGI) , Self-rating depression scale (SDS), Scale for Suicidal Ideation (SSI). Total dropout, dropout due to side effects, side-effect profile
Notes	Funding: duloxetine manufacturer.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: "patients were randomly assigned in a 1:1:1:1 ratio to placebo, duloxetine 80 mg/day, duloxetine 120 mg/day or paroxetine 20 mg/day"
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Treatments were administered in a double-blind fashion via the use of a double-dummy study drug design
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double blind".
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "All analyses were conducted on an Intention-to-treat (ITT) basis. (...) The change from baseline to endpoint in the HDRS- 17 item total score and other continuous efficacy variables were also calculated using the Last Observation Carried Forward (LOCF) Study endpoint: 10/86 missing from Paroxetine group, 12/95 from Duloxetine 80 mg,

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Detke 2004 (HMAY A) (*Continued*)

		9/93 missing from Duloxetine 120 mg, 18/93 missing from placebo group
Selective reporting (reporting bias)	High risk	In the duloxetine 120 mg/day arm only treatment emergent side effects experienced by > or = 5% of patients are reported
Other bias	Unclear risk	Sponsorship bias cannot be ruled out.

Dichter 2005

Methods	Twelve-week, randomised trial.
Participants	Participants were adult outpatients who met DSM-IV criteria for major depression as determined by the Structured Clinical Interview for DSM-IV patient version Participants: (1) had scores on the Hamilton rating scale for depression (HDRS-17) that were greater than 17; (2) were free of benzodiazepines for at least 2 weeks prior to their baseline assessment, antidepressant medication for at least 3 weeks prior to their baseline assessment, and fluoxetine, antipsychotics, lithium, carbamazepine, or valproate for at least 5 weeks prior to their baseline assessment; and (3) did not have: (a) any clinically significant physical illness that would limit treatment with either study drug; (b) a history of bipolar affective disorder; (c) any history of a psychotic Axis I disorder, including major depression with psychotic features; (d) current predominant nonpsychotic Axis I disorder, antisocial, borderline, or schizotypal Axis II personality disorders; (e) subnormal intellectual potential; (f) a history of substance abuse in the past 6 months or substance dependence in the past 12 months; (g) a known hypersensitivity to either study drug; or (h) any history of a seizure disorder
Interventions	20 participants were randomly assigned to receive either venlafaxine XR (n = 10; age range: 27.3-54.5 years, mean (S.D.)=42.6 (9.2), 6 women) or paroxetine (n = 10; age range: 22.2-50.2 years, mean (S.D.) = 37.6 (9.0), 7 women) Paroxetine dose range:10-30 mg/day. Venlafaxine dose range: 75-225 mg/day.
Outcomes	HDRS-17, Clinical Global Impression (CGI), Hamilton rating scale for anxiety (HAM-A), Beck Depression Inventory (BDI), Beck Anxiety Scale (BAI)
Notes	None.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: "participants were randomly assigned". No further details
Allocation concealment (selection bias)	Unclear risk	No information provided.

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Dichter 2005 (*Continued*)

Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No information provided.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No information provided.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	No information on incomplete outcome data management.
Selective reporting (reporting bias)	Unclear risk	Outcomes data not clearly reported.
Other bias	Unclear risk	Sponsorship bias cannot be ruled out.

Dorman 1992

Methods	Six-week double-blind, randomised, study.
Participants	Outpatients fulfilling DSM-III criteria for major depression, with a score of at least 17 on the Hamilton rating scale for depression (HDRS-17). Age: older than 65 years.
Interventions	Paroxetine: 29 participants. Mianserin: 28 participants. Paroxetine dose range: 15-30 mg/day. Mianserin dose range: 30-60 mg/day. With the exception of short- acting benzodiazepines for hypnotic purposes, no other concomitant psychotropic medication was permitted during the study
Outcomes	HDRS-17 Total dropout, dropout due to side effects, number of patients experience at least once side effect, side-effect profile
Notes	This study has been conducted in order to evaluate the effects on sleeping of both paroxetine and mianserin in the treatment of depression. For this reason most efficacy and safety data were not available

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: "randomized". No further details.
Allocation concealment (selection bias)	Unclear risk	No information provided.

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Dorman 1992 (*Continued*)

Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "Double-blind, double-dummy".
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "Double-blind, double-dummy".
Incomplete outcome data (attrition bias) All outcomes	Low risk	Study endpoint: 5/29 missing from paroxetine group, 3/28 missing from control group
Selective reporting (reporting bias)	High risk	Side effects reported only per body system. Mean difference reported on graphs only.
Other bias	Unclear risk	Sponsorship bias cannot be ruled out.

DUAG 1990

Methods	Six-week double-blind, randomised, multicentre study.
Participants	Inpatients fulfilling DSM III criteria for major depressive disorder with a minimum score of 18 on the Hamilton rating scale for depression (HDRS-17) rating scale. Patients remained hospitalised throughout the trial period, except that patients who responded were permitted to be discharged after two weeks of active treatment but only if the trial program could be followed strictly Age range: 19-67 years.
Interventions	Paroxetine: 62 participants. Clomipramine: 58 participants. Paroxetine dose range: 30 mg/day. Clomipramine dose range: 150 mg/day. No other psychotropic medication was allowed except occasional use of oxazepam as a sedative/hypnotic
Outcomes	HDRS, HDRS subscales, Bech-Rafaelsen Melancholia Scale (BRMS), UKU side effect scale. Total dropout. Reasons for dropout
Notes	We considered dropout at 4 weeks instead of 6 because patients who were rated non-responders after 4 weeks of active treatment "were terminated" in the study

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: "randomly assigned". No further details.

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DUAG 1990 (*Continued*)

Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double blind". No further details.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double blind". No further details.
Incomplete outcome data (attrition bias) All outcomes	High risk	Patients who were rated non-responders after 4 weeks of active treatment "were terminated" in the study 27/62 completed 6 weeks of treatment in the paroxetine group (23 were considered non-responders, 12 were dropout); 33/58 completed 6 weeks treatment in the clomipramine group (4 were considered non-responders, 19 were dropout)
Selective reporting (reporting bias)	High risk	Number of patients experiencing each side effect not reported. Mean change on HAMD reported only on graph
Other bias	Unclear risk	Sponsorship bias cannot be ruled out.

Dunbar 1991

Methods	Six-week double-blind, randomised, parallel group, single-centre, placebo-controlled
Participants	Outpatients meeting DSM-III criteria for major depression with a minimum score of 18 on Hamilton rating scale for depression (HDRS-17). Age range:18-65 years.
Interventions	Paroxetine: 41 participants. Imipramine: 42 participants. Placebo: 42 participants. Paroxetine dose range: 10-50 mg/day. Imipramine dose range: 65-275 mg/day.
Outcomes	HDRS-21, Clinical Global Impression (CGI) Improvement, Severity, Montgomery and Asberg Depression Rating Scale (MADRS), Patient Global Experience (PGE). Total dropout, dropout due to side effect, dropout due to lack of efficacy. Number of patients experiencing at least one side effect, side-effect profile
Notes	Funding: paroxetine manufacturer.

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Dunbar 1991 (*Continued*)

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: "randomized". No further details.
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double blind". No further details.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double blind". No further details.
Incomplete outcome data (attrition bias) All outcomes	High risk	Study endpoint: 21/41 missing from paroxetine group, 25/42 missing from control group
Selective reporting (reporting bias)	High risk	Dichotomous outcome not reported.
Other bias	Unclear risk	Sponsorship bias cannot be ruled out.

Dunner 1992

Methods	Six-week, double-blind, randomised, multicentre study.
Participants	Outpatients fulfilling DSM-III diagnostic criteria for major depression (moderate to severe) Age: older than 60 years.
Interventions	Paroxetine: 136 participants. Doxepin: 135 participants. Paroxetine dose-range: 10-40 mg/day (mean dose: 23.4 mg/day) Doxepin dose-range: max 200 mg/day (mean dose: 105.2 mg/day) Occasional use of chloral hydrate 500 mg as a hypnotic, for a maximum of 4 consecutive nights during the first 2 weeks of the study
Outcomes	Hamilton rating scale for depression (HDRS), Clinical Global Impression (CGI), Montgomery and Asberg Depression Rating Scale (MADRS), Hopkins Symptom Checklist (SCL) Total dropout, dropout due to inefficiency, dropout due to side effects
Notes	Adverse events reported only on graphs.

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Dunner 1992 (*Continued*)

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: "randomized". No further details.
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double blind". No further details.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double blind". No further details.
Incomplete outcome data (attrition bias) All outcomes	High risk	Standard deviations for mean change not reported (borrowed from *The Cochrane Library*); side effects reported incompletely. Number of patients experiencing each side effect not reported
Selective reporting (reporting bias)	High risk	Standard deviation for mean change not reported (borrowed from *The Cochrane Library*); side effects reported incompletely. Number of patients experiencing each side effect not reported
Other bias	Unclear risk	Sponsorship bias cannot be ruled out.

Fabre 1992

Methods	Six-week double-blind, randomised, parallel group, single-centre, placebo-controlled study
Participants	Outpatients meeting DSM-III criteria for major depression with a minimum score of 18 on Hamilton rating scale for depression (HDRS-17). Age: older than 18 years.
Interventions	Paroxetine: 40 participants. Imipramine: 40 participants. Placebo: 40 participants. Paroxetine dose range: 10-50 mg/day. Imipramine dose range: 65-275 mg/day. Chloral hydrate (500 mg) was allowed for a maximum of 4 consecutive nights during the first two weeks of the study

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Fabre 1992 (*Continued*)

Outcomes	HDRS-21, Clinical Global Impression (CGI) Improvement, Severity, Montgomery and Asberg Depression Rating Scale (MADRS), Patient Global Experience (PGE). Total dropout, dropout due to side effect, dropout due to lack of efficacy. Number of patients experiencing at least one side effect, side-effect profile
Notes	Funding: paroxetine manufacturer.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: "randomized". No further details.
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double blind". No further details.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double blind". No further details.
Incomplete outcome data (attrition bias) All outcomes	High risk	Study endpoint: 24/40 missing from paroxetine group, 24/40 missing from control group
Selective reporting (reporting bias)	High risk	Dichotomous outcome not reported.
Other bias	Unclear risk	Sponsorship bias cannot be ruled out.

Fava 1998

Methods	Twelve-week randomised, double-blind, multicentre study.
Participants	Outpatients fulfilling DSM-III-R criteria for moderate to moderately severe major depression without a history of mania or hypomania, with a score of at least 18 on the Hamilton Rating Scale for Depression-21 item (HDRS-21), of at least 8 on the Raskin Depression Scale (and grater than Covi Anxiety Scale [CAS] score).Mean age: 41.3 years. Exclusion criteria: schizophrenia, adjustment disorder, bipolar disorder, panic disorder, social phobia, obsessive compulsive disorder, psychotic depression, atypical depression, serious concomitant medical illness, significant abnormal laboratory values, history of seizure disorder, high suicidal risk, recent history of alcohol or drug abuse, use other psychotropic drug within 14 days of baseline, ECT within 3 months of baseline, any investigational drug within 30 days of baseline, previous treatment with paroxetine, pregnancy, childbearing potential without contraceptive

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Fava 1998 (*Continued*)

Interventions	Paroxetine: 55 participants. Fluoxetine: 54 participants. Placebo: 19 participants. Paroxetine dose range: 20-50 mg/day. Fluoxetine dose range: 20-80 mg/day.
Outcomes	HDRS-21, Covy Anxiety Scale (CAS), Raskin Depression Scale.
Notes	Response: decrease of at least 50% in the HDRS-21 total. score Funding: by industry.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Randomised, no further information.
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Double-blind, no further information.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Double-blind, no further information.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Quote: "we chose to conduct all analyses with an ITT approach". Number and reasons of dropout reported
Selective reporting (reporting bias)	Unclear risk	Adverse events reported. Primary and secondary endpoint reported with standard deviations
Other bias	Unclear risk	Sponsorship bias can not be ruled out.

Fava 2002

Methods	Ten-week randomised, double-blind, multicentre study.
Participants	Outpatients fulfilling DSM-IV criteria for major depression or atypical major depression, with a baseline score of at least 16 on the first 17 items of the Hamilton rating scale for depression (HDRS-28). No patients with bipolar disorder

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Interventions	Paroxetine: 96 participants. Fluoxetine: 92 participants. Sertraline: 96 participants. Paroxetine dose range: 20-60 mg/day. Fluoxetine dose range: 20-60 mg/day. Sertraline dose range: 50-200 mg/day.
Outcomes	HDRS-17 , Clinical Global Impression (CGI) Severity and HDRSsleep disturbance, A/S, R, Cognitive Disturbance (COG) factors Total dropout, dropout due to side effects, side-effect profile
Notes	Funding: fluoxetine manufacturer. Adverse events reported only if occurring in >=10%.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: "randomized". No further details.
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double blind". No further details.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double blind". No further details.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Study endpoint: 27/96 missing from paroxetine group; 24/92 missing from fluoxetine one, 26/96 from sertraline one. All enrolled patients who had at least one post-baseline visit at which appropriate assessment was taken were included in the analyses of efficacy. All randomly assigned patients were included in the analyses of safety
Selective reporting (reporting bias)	High risk	Adverse events reported only if occurring in >=10%.
Other bias	Unclear risk	Sponsorship bias cannot be ruled out.

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Feighner 1989

Methods	Six-week double-blind, randomised, parallel group, single-centre, placebo-controlled study
Participants	Outpatients meeting DSM-III criteria for major depression with a minimum score of 18 on Hamilton rating scale for depression (HDRS-17). Age: older than 18 years.
Interventions	Paroxetine: 40 participants. Imipramine: 40 participants. Placebo: 40 participants. Paroxetine dose range: 10-50 mg/day. Imipramine dose range: 65-275 mg/day.
Outcomes	HDRS-21, Clinical Global Impression (CGI) Improvement, Severity, Montgomery and Asberg Depression Rating Scale (MADRS), Patient Global Experience (PGE). Total dropout, dropout due to side effect, dropout due to lack of efficacy. Number of patients experiencing at least one side effect, side-effect profile
Notes	Funding: paroxetine manufacturer.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "randomized". No further details.
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double blind". No further details.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double blind". No further details.
Incomplete outcome data (attrition bias) All outcomes	High risk	Study endpoint: 19/40 missing from paroxetine group, 26/40 missing from control group
Selective reporting (reporting bias)	High risk	Dichotomous outcome not reported.
Other bias	Unclear risk	Sponsorship bias cannot be ruled out.

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Freed 1996

Methods	Nine-week, randomised, double-blind study.
Participants	Inclusion criteria: patients with Montgomery and Asberg Depression Rating Scale (MADRS) 20+. Age range: 19-85 years. Country: Australia. Setting: family practice.
Interventions	Paroxetine versus amitriptyline
Outcomes	Montgomery and Asberg Depression Rating Scale (MADRS), Clinical Global Impression (CGI), dropouts
Notes	None.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "patients were randomly assigned (...) using a computer generated randomization list"
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "double blind (...) medication was blinded by over-encapsulation of marketed forms of paroxetine and amitriptyline in identical capsules. To maintain the blinding, placebo was given at night to patients receiving paroxetine and in the morning to patients receiving amitriptyline"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double blind". No further details.
Incomplete outcome data (attrition bias) All outcomes	High risk	Quote: "all patients randomized to active treatment and fro whom one valid post-randomization evaluation was available within 4 days of intake of medication, were included in the Intention-to-treat (ITT) analysis. Three hundred and six patients were eligible for the ITT analysis and all efficacy variables were analysed using this population. All patients (381) were included in the safety analysis; however, six patients were not evaluable by treatment due to inconsistent treatment allocation"

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Freed 1996 (*Continued*)

Selective reporting (reporting bias)	Low risk	Outcomes data were reported.
Other bias	Unclear risk	Sponsorship bias cannot be ruled out.

Gagiano 1993

Methods	Six-week randomised, double-blind study.
Participants	Outpatients fulfilling DSM-III-R criteria for major depressive episode, with a score of at least 18 on the Hamilton rating scale for depression (HDRS-21). Age range: 18-65 years.
Interventions	Paroxetine: 45 participants. Fluoxetine: 45 participants. Paroxetine dose range: 20-40 mg/day. Fluoxetine dose range: 20-60 mg/day. Short acting benzodiazepines were permitted for use as hypnotics during the study period
Outcomes	HDRS, Montgomery and Asberg Depression Rating Scale (MADRS), Hamilton rating scale for anxiety (HAM-A), Clinical Global Impression (CGI) Total dropout, dropout due to inefficiency, dropout due to side effects, side-effect profile
Notes	Funding: paroxetine manufacturer. Adverse events reported only if occurring in >=10%. Unpublished data were retrieved.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: "randomized". No further details.
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "The double dummy technique using matching placebos was employed to maintain the double blind"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double blind".
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Study endpoint: 8/45 missing from paroxetine group; 10/45 missing from control group All data from the Intention-to-treat (ITT)

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Gagiano 1993 (*Continued*)

		population were included in the analyses up to the time of withdrawal; thereafter the last observed value of a variable was carried forward for all subsequent missing data points
Selective reporting (reporting bias)	Low risk	The study protocol was not available but the unpublished reports retrieved include all expected outcomes
Other bias	Unclear risk	Sponsorship bias cannot be ruled out.

Gallen 2001

Methods	Multicentre, randomised, double-blind, placebo- and active-controlled, parallel-group study
Participants	Inclusion Criteria: To be included in the study, patients must have met all of the following criteria: diagnosis of Major Depressive Disorder (MDD) without psychotic features, as defined by DSM-IV; male or female, of any race, between the ages of 18 and 65 years. If female, must have been postmenopausal or must have met all of the following criteria: agreed to avoid pregnancy during the study; had a negative serum pregnancy test at screen; used an accepted means of birth control (as determined by the investigator), such as abstinence, oral contraceptive, implantable or injectable contraceptive, intrauterine device, or barrier method, or have been surgically sterilized; total score of $\geq$20 on the Hamilton rating scale for depression (HDRS-17), which was administered via the IVRS prior to the screening visit; general good health, as confirmed by routine clinical laboratory safety findings. Voluntary consent to participate in the study, documented in a written Patient Informed Consent Form that was signed prior to the start of any study procedures at the screening visit Exclusion Criteria: Patients were excluded from the study for any of the following reasons: DSM-IV diagnosis of the following concomitant psychiatric disorders: MDD with psychotic features, cyclothymic disorder, bipolar I or bipolar II disorders, substance-related disorders (within the preceding 12 months), schizophrenia, or other psychotic disorders; resistance to antidepressive treatment, defined as a lack of response to at least 2 previous courses of antidepressant medications administered at full doses for more than 1 month; participation in a previous clinical trial of reboxetine or lack of response to previous treatment with paroxetine, administered at a dose of $\geq$20 mg/day for more than 1 month; use of antidepressant medication for the treatment of depression in the 2 months preceding the start of the study; history of MDD associated with endocrine disorders: hypo- or hyper-thyroidism tested by thyroid-stimulating hormone and thyroxine, adrenal insufficiency, or Cushing's syndrome; positive pregnancy test for females of childbearing potential; breast-feeding by female patients; refusal by female patients of childbearing age to use an effective contraceptive method during the study; participation in any clinical study with an investigational compound in the 4 weeks preceding the study; history or presence of gastrointestinal, liver, or kidney disease or other conditions known to interfere with the absorption, distribution, metabolism, and excretion of drugs; history of seizures or brain injury; current evidence of clinically important

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	hematopoietic, respiratory, or cardiovascular diseases; current evidence of urinary retention or glaucoma. Clinically significant illness in the 4 weeks preceding the study that might have interfered with the conduct of the trial. Clinically relevant abnormal findings in the physical examination, laboratory tests, or ECG at admission. Positive urine drug screen for amphetamines, barbiturates, marijuana metabolites, cocaine metabolites, methadone, methaqualone, opiates, phencyclidine, or propoxyphene. A positive urine drug screen for benzodiazepines did not exclude the patient. Treatment with electroconvulsive therapy in the 6 months preceding the study. Major risk of suicide as assessed by the investigator, a score of $\geq$3 on Item 3 of the HDRS at screen or baseline, or a history of suicide attempt during the current depressive episode. History of hypersensitivity to reboxetine or paroxetine. Use of the following medications, which are potent inhibitors of the drug-metabolizing enzyme cytochrome p450-3A4: azole antifungals, macrolide antibiotics, or fluvoxamine. Use of the following medications, which are known to be substrates or inhibitors of the drug-metabolizing enzyme cytochrome p450-2D6: Type 1C antiarrhythmics, quinidine, or cimetidine. Use of oral anticoagulants that are known to inhibit vitamin K-dependent coagulation factors. Use of concomitant psychotropic medications other than the protocol-specified sedatives/hypnotics, which could be taken on an as-needed basis for sleep. Inability of the patient to comply with the conditions of the study, based on the investigator's assessment
Interventions	Paroxetine: 265 participants. Reboxetine: 265 participants. Placebo: 257 participants.
Outcomes	Montgomery Asberg Depression Rating Scale (MADRS) total score at day 56 in the intent-to-treat (ITT) patient population.Total dropout, dropout due to side effects, dropout due to inefficacy. Number of patients experiencing at least one side effect, side-effect profile
Notes	Funding: reboxetine manufacturer.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Quote: "Pharmacia & Upjohn (P&U) prepared a randomization list for assignment of the patients to 1 of the 3 treatment groups. Study medication for each treatment group was prepared on this basis by P&U and was labeled with the corresponding patient number"
Allocation concealment (selection bias)	Low risk	Quote: "at the baseline visit, the investigator assigned each patient to a treatment group based on the patient's temporal entry into the study (i.e. by assigning the lowest patient number available). A list of patient numbers and medication assignments was

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Gallen 2001 (*Continued*)

		provided only after the data for the study had been analyzed"
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "double blind (...) study medications were provided as identically appearing capsules (...) Study medications for the randomized treatments consisted of identically appearing capsules that contained , paroxetine or placebo. The capsules were provided in clinical supply packages that were labeled with the protocol number, patient number, treatment period, dosing, directions and storage conditions. Investigators were given sealed drug-disclosure sheets that contained information about each patient's treatment"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double blind".
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Quote: "the Intention-to-treat (ITT) population includes all patients who were randomized into the trial and who received at least one dose of study medication. All analyses were based on the ITT population. Efficacy analyses were based on the population of ITT patients who had at least one post-baseline evaluation for the specified efficacy measure"
Selective reporting (reporting bias)	Low risk	Outcomes data were reported.
Other bias	Unclear risk	Sponsorship bias cannot be ruled out.

Geretsegger 1994

Methods	Six-week, double-blind, randomised, multicentre study.
Participants	Patients fulfilling DSM-III criteria for major depression, with a score of at least 18 on the Hamilton rating scale for depression (HDRS-21). Age range: 61-85 years.
Interventions	Paroxetine: 54 participants. Fluoxetine: 52 participants. Paroxetine dose range: 20-40 mg/day. Fluoxetine dose range: 20-60 mg/day.

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Geretsegger 1994 (*Continued*)

Outcomes	HDRS-21 item, Clinical Global Impression (CGI), Montgomery and Asberg Depression Rating Scale (MADRS) Total dropout, dropout due to side effects, number of patients experiencing at least one side effect, side-effect profile
Notes	Funding: paroxetine manufacturer.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: "randomized". No further details.
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double blind". No further details.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double blind". No further details.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Less than 20% of patients abandoned the study prematurely. Patients with at least one valid evaluation during treatment were included in the Intention-to-treat (ITT) analysis of efficacy (visit-wise data) All randomised patients who received active treatment were included in ITT analysis of clinical tolerability and safety
Selective reporting (reporting bias)	Low risk	The study protocol was not available but the unpublished reports we retrieved include all expected outcomes
Other bias	Unclear risk	Sponsorship bias cannot be ruled out.

Geretsegger 1995

Methods	Six-week, double-blind, randomised, multicentre study.
Participants	Inpatients for the first 3 weeks fulfilling DSM-III criteria for major depression, with a score of at least 18 on the Hamilton rating scale for depression (HDRS-17). Age: older than 65 years.

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Geretsegger 1995 (*Continued*)

Interventions	Paroxetine: 78 participants. Amitriptyline: 75 participants. Paroxetine dose range: 20-30 mg/day. Amitriptyline dose range: 100-150 mg/day. No other psychotropic medication was allowed except temazepam or oxazepam or chloral hydrate as hypnotics
Outcomes	HDRS, Clinical Global Impression (CGI), Montgomery and Asberg Depression Rating Scale (MADRS) Total dropout, dropout due to side effects, number of patients experiencing at least one side effect, side-effect profile
Notes	Funding: paroxetine manufacturer.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: "randomly allocated", no further details.
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double-blind, double dummy technique".
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double-blind, double dummy technique".
Incomplete outcome data (attrition bias) All outcomes	High risk	More than 20% of patients abandoned the study prematurely. Study endpoint: 32/78 missing from paroxetine group; 30/75 missing from control group
Selective reporting (reporting bias)	Unclear risk	Mean change on HDRS and MADRS reported only on graph.
Other bias	Unclear risk	Sponsorship bias cannot be ruled out.

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Gilmor 2002

Methods	Seven-week randomised, open-label, parallel-group, forced-titration multicentre study
Participants	Outpatients fulfilling DSM-IV criteria for major depressive disorder, with a score of at least > or = 20 on the Montgomery and Asberg Depression Rating Scale (MADRS). Age range: 18-57 years.
Interventions	Paroxetine: 38 participants. Desipramine: 14 participants. Paroxetine dose range: 10-60 mg/day. Desipramine dose range: 50-300 mg/day.
Outcomes	MADRS, Clinical Global Impression (CGI). Total dropout.
Notes	Funding: paroxetine manufacturer. This study was conducted in order to evaluate inhibition of norepinephrine uptake in patient with major depression, so it is not a study of efficacy or tolerability

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: "randomly assigned to paroxetine or desipramine in a 3-to-1 ratio respectively"
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "open-label". No further details.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote: "open-label". No further details.
Incomplete outcome data (attrition bias) All outcomes	High risk	Dichotomous outcome not reported. Adverse events were not reported. Incomplete reporting of dropout due to side effects, dropout due to inefficacy
Selective reporting (reporting bias)	High risk	Dichotomous outcome not reported. Adverse events were not reported. Incomplete reporting of dropout due to side effects, dropout due to inefficacy
Other bias	Unclear risk	Sponsorship bias cannot be ruled out.

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Goldstein 2004 (HMAT B)

Methods	Multicentre, parallel, double-blind, randomised, placebo- and active comparator-controlled study with blinded placebo lead-in and placebo lead-out. The protocol consisted of two identical studies conducted in parallel and reported separately (Study Group A and Study Group B). The study consisted of two study periods. Study Period I was the 1-week screening phase of the study, and Study Period II was an 11-week acute therapy phase in which patients were assessed weekly from Visit 2 (Week 0) to Visit 5 (Week 3) and every other week from Visit 5 (Week 3) to Visit 9 (Week 11). This study design employed double-blind, variable-duration placebo lead-in and lead-out periods to blind patients and investigators at the start and end of active therapy
Participants	Planned: 356 patients (89 per treatment group) Randomized: 87 Paroxetine 20 mg once daily; 86 Duloxetine 20 mg BID (twice daily); 91 Duloxetine 40 mg BID ; 89 Placebo Completed:49 Paroxetine 20 mg once daily; 55 Duloxetine 20 mg BID; 53 Duloxetine 40 mg BID; 52 Placebo Criteria for Inclusion: Male and female outpatients of at least 18 years of age with a primary diagnosis of MDD as defined by the DSM-IV, and confirmed by use of the Mini International Neuropsychiatric Interview. Patients were required to have a HAMD17 total score $\geq$15 and a CGI-Severity total score $\geq$4 at both Visit 1 and Visit 2
Interventions	Paroxetine 20 mg once daily (20 mg/day) Duloxetine 20 mg twice daily (40 mg/day) Duloxetine 40 mg twice daily (80 mg/day) Placebo
Outcomes	Efficacy: the primary efficacy measure was the Hamilton rating scale for depression (HDRS-17) total score. Secondary efficacy measures included HDRS-17 response rates (50% reduction from baseline to endpoint), HDRS-17 remission rates (endpoint score $\leq$7), time to sustained response, and time to sustained remission. Other secondary measures included the HDRS-17 subfactors and individual items, Montgomery and Asberg Depression Rating Scale (MADRS), Clinical Global Impression (CGI) Severity, Patient Global Impression (PGI) Improvement, Hamilton rating scale for anxiety (HAM-A), Somatic Symptom Inventory 26- and 28-item scale (SSI), and Visual Analog Scales for pain (VAS) Safety: safety was evaluated through the collection and reporting of discontinuation rates, treatment-emergent adverse events, discontinuation-emergent adverse events, laboratory analyses, vital signs, ECGs, and the Arizona Sexual Experiences (ASEX) Health Outcomes: Health outcomes were evaluated using the Quality of Life in Depression (QLDS) scale and Health Resource Utilization scales (HRUS)
Notes	Funding: duloxetine manufacturer.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "patients were allocated within each study site by a computer-generated random table and had an equal probability of re-

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Goldstein 2004 (HMAT B) (*Continued*)

		ceiving placebo, duloxetine 40 mg/day, administered as 20 mg twice daily, duloxetine 80 mg/day, administered as 40 mg twice daily, or paroxetine 20 mg/day administered once daily during the 8 week acute therapy phase. No stratification was employed"
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double blind". No further details.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double blind". No further details.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Number of patients experiencing each side effect not reported Study endpoint: 38/87 missing from paroxetine group; 69/177 missing from control group
Selective reporting (reporting bias)	High risk	Quote: "Treatment emergent adverse events experience by at least 5% of patients treated with duloxetine 80 mg/day and statistically significantly different from placebo are reported"
Other bias	Unclear risk	Sponsorship bias cannot be ruled out.

Guillibert 1989

Methods	Six-week double-blind, randomised, multicentre study.
Participants	Outpatients fulfilling DSM-III diagnostic criteria for major depressive disorder with a minimum score at baseline of 20 on the Hamilton rating scale for depression (HDRS-21) rating scale Age: over 60 years.
Interventions	Paroxetine: 40 randomised. Clomipramine: 39 randomised. Paroxetine dose range: 20-30 mg/day. Clomipramine dose range: 25-75 mg/day. No other psychotropic medication was permitted except short half-life benzodiazepine of the oxazepam type for the control of agitation, anxiety or insomnia

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Guillibert 1989 (*Continued*)

Outcomes	HDRS, Wang Anxiety and Widlocher scales (WAW), Clinical global Impression (CGI) Total dropout, dropout due to inefficiency, dropout due to side effects, side-effect profile
Notes	None.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "randomized". No further details.
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double blind". No further details.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double blind". No further details.
Incomplete outcome data (attrition bias) All outcomes	High risk	Study endpoint: 9/40 missing from Paroxetine group, 12/39 missing from Clomipramine one. All 79 patients were evaluable for tolerability and for an ITT evaluation with the respect of the HAMD scale
Selective reporting (reporting bias)	High risk	SD for mean change not reported (borrowed from *The Cochrane Library*); side effects reported incompletely.
Other bias	Unclear risk	Sponsorship bias cannot be ruled out.

Hicks 2002

Methods	Eight-week, double-blind, randomised study.
Participants	Outpatients fulfilling DSM-IV diagnostic criteria for major depression with a minimum score of 18 on the Hamilton rating scale for depression (HDRS) Age range: 18-65 years.
Interventions	Paroxetine: 20 randomised. Nefazodone: 20 randomised. Paroxetine dose range: 20-40 mg/day (mean daily dose: 29.5 [SD 8.9]) Nefazodone dose range: 400-600 mg/day (mean daily dose: 495 [SD 82.6]) No addition psychoactive medication was allowed during the study period

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Hicks 2002 (*Continued*)

Outcomes	HDRS, Clinical Global Impression (CGI), Montgomery and Asberg Depression Rating Scale (MADRS), sleeping analysis, dropout, side-effect profile
Notes	Funding: nefazodone manufacturer.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "randomized". No further details.
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double blind". No further details.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double blind". No further details.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Study endpoint: 3/20 missing from paroxetine group, 5/20 missing from nefazodone group
Selective reporting (reporting bias)	High risk	Three rating scales reported in the methods but just one reported in the results; side effect reported only if occurring in more than 5% of participants
Other bias	Unclear risk	Sponsorship bias cannot be ruled out.

Higuchi 2009

Methods	Multicentre, parallel, double-blind, randomised, placebo- and active comparator-controlled study comparing duloxetine with placebo and paroxetine in the acute treatment of patients with DSM-IV MDD
Participants	Male and female patients with a primary diagnosis of MDD as defined by the DSM-IV, and confirmed by use of the MINI. Patients were required to have a HAM-D17 total score $\geq$ 15 and a CGI-S total score $\geq$ 4 at both Visit 1 and Visit 2 Country: Japan Setting: inpatients and outpatients Age: 18 to 65 years inclusive

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Interventions	Paroxetine 20-40 mg/day, once in the evening. Duloxetine 40 mg/day, once in the morning. Duloxetine 60 mg/day, once in the morning. Placebo. Duration: 6 weeks active treatment with 1-week placebo lead-in and 2-week lead-out periods Cointervention: No psychotropic drug except for one short or ultra-short acting benzodiazepine sleeping pill
Outcomes	Efficacy: Primary efficacy measure was the HAM-D17 total score. Secondary efficacy measures included HAM-D17 response rates (a 50% reduction from baseline to endpoint) and HDRS 17 remission rates (endpoint score <7), VAS for pain, CGI-I
Notes	Randomised: 495 patients, however the first 50 patients were randomised according to a wrong randomisation scheme and were therefore omitted from the main analyses. The correct ITT sample would then be: 75 for duloxetine 40 mg, 76 for duloxetine 60 mg, 148 for paroxetine and 146 for placebo

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Probably done. Quote: "The sequence was generated by an independent investigator."
Allocation concealment (selection bias)	Low risk	Probably done. Quote: "The allocation was handled by an independent investigator."
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Both the clinician and the patient were blinded. The capsules have been tested to be indistinguishable. The clinician was the assessor
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Both the clinician and the patient were blinded. The capsules have been tested to be indistinguishable. The clinician was the assessor
Incomplete outcome data (attrition bias) All outcomes	Low risk	Of the 445 patients appropriately randomised, 5 patients did not contribute at all to the analysis and about 10% of the patients had to have their outcomes LOCFed (the exact numbers cannot be known due to the way the authors summarised the data.)
Selective reporting (reporting bias)	Unclear risk	The protocol has not been published and we do not know if all the intended outcomes are reported

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Other bias	Unclear risk	Five-armed placebo- and active drug-controlled trial appears more trustworthy than straightforward 2-arm trial

HMAT A (ID#4091)

Methods	Multicentre, parallel, double-blind, randomised, placebo- and active comparator-controlled study
Participants	Planned: 356 patients (89 per treatment arm). Randomized: Duloxetine 20 mg BID 91; Duloxetine 40 mg BID 84; Placebo 90; Paroxetine 89 Completed: Duloxetine 20 mg BID 61; Duloxetine 40 mg BID 56; Placebo 61; Paroxetine 58 Criteria for Inclusion: Male and female outpatients of at least 18 years of age with a primary diagnosis of MDD as defined by the DSM-IV, and confirmed by use of the Mini International Neuropsychiatric Interview. Patients were required to have a HAMD17 total score of $\geq$15 and a CGI-Severity total score of $\geq$4 at both Visit 1 and Visit 2
Interventions	Duloxetine 20 mg BID (40 mg/day). Duloxetine 40 mg BID (80 mg/day). Paroxetine 20 mg once daily (20 mg/day). Placebo.
Outcomes	Efficacy: the primary efficacy measure was the Hamilton rating scale for depression (HDRS-17) total score. Secondary efficacy measures included HAMD17 response rates (a 50% reduction from baseline to endpoint), HDRS-17 remission rates (endpoint score of $\leq$7), time to sustained response, and time to sustained remission. Other secondary measures included the HDRS-17 subfactors and individual items, Montgomery and Asberg Depression Rating Scale (MADRS), Clinical Global Impression (CGI) Severity, Patient Global Impression (PGI) Improvement, Hamilton rating scale for anxiety (HAM-A), Somatic Symptom Inventory (SSI), and Visual Analog Scales for pain (VAS). Safety: safety was evaluated through the collection and reporting of discontinuation rates, Treatment Emergent Adverse Effects, discontinuation-emergent adverse events, laboratory analyses, vital signs, ECGs, and the Arizona Sexual Experiences (ASEX). Health Outcomes: Health outcomes were evaluated using the Quality of Life in Depression scale and Health Resource Utilization scales
Notes	Date first patient enrolled: 10 March 2000. Date last patient completed: 10 April 2001. For all total scores calculated from individual items, if any of the individual items was missing, the corresponding total score was considered missing. Sites with fewer than 8 randomly assigned patients with baseline and at least one post baseline (Visit 4 to Visit 8) HAMD17 total score were pooled. If this resulted in a pooled site with fewer than 8 patients, these patients were pooled with the next smallest site

Risk of bias

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HMAT A (ID#4091) (*Continued*)

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "randomized". No further details.
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double blind". No further details.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double blind". No further details.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Quote: "an Intention-to-treat (ITT) principle was applied in all efficacy and safety analyses"
Selective reporting (reporting bias)	High risk	Only adverse effects with total incidence > or = 2% were reported
Other bias	Unclear risk	Sponsorship bias cannot be ruled out.

Hutchinson 1992

Methods	Six-week, double-blind, randomised study.
Participants	General practice patients fulfilling DSM-III diagnostic criteria for major depression with a minimum score of 18 on the Hamilton rating scale for depression (HDRS) Age:older than 65 years.
Interventions	Paroxetine: 58 randomised. Amitriptyline: 32 randomised. Paroxetine dose range: 20-30 mg/day. Amitriptyline dose range: 50-100 mg/day. No other psychotropic medication was allowed during the study period except temazepam as hypnotic
Outcomes	HDRS, Clinical Global Impression (CGI), Leeds Sleep Evaluation Questionnaire (LSEQ) Total dropout, dropout due to inefficiency, dropout due to side effects, number of patients experiencing at least one side effect, side-effect profile
Notes	Funding: paroxetine manufacturer.
Risk of bias	

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Hutchinson 1992 (*Continued*)

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "a biased randomization of treatment was adopted to ensure that two-thirds of the patients received paroxetine and one-third amitriptyline"
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double blind, double dummy".
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double blind, double dummy".
Incomplete outcome data (attrition bias) All outcomes	High risk	Study endpoint: 12/58 missing from paroxetine group, 11/32 missing from Amitriptyline one
Selective reporting (reporting bias)	High risk	Only "the most commonly" adverse events were reported. Mean change on HDRS reported only on graph.
Other bias	Unclear risk	Sponsorship bias cannot be ruled out.

Hwang 2004

Methods	Four-week, open-label, randomised study.
Participants	Inpatients fulfilling DSM-IV diagnostic criteria for major depression Age:older than 65 years.
Interventions	Paroxetine: 53 randomised. Venlafaxine: 52 randomised. Paroxetine dose range: 20-40 mg/day (mean daily dose: 37.4 mg/day [SD 20.9]) Venlfaxine dose range: 75-150 mg/day (mean daily dose: 131.6 mg/day [SD 24.4]) Benzodiazepines were given to patients with anxiety or insomnia
Outcomes	Hamilton rating scale for depression (HDRS), Clinical Global Impression (CGI). Total dropouts
Notes	None.
Risk of bias	

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Hwang 2004 (*Continued*)

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "randomized". No further details.
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "open label trial". No further details.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote: "open label trial". No further details.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Study endpoint: 3/53 missing from paroxetine group; 3/52 missing from venlafaxine one
Selective reporting (reporting bias)	High risk	Incomplete reporting of dropout due to side effects, dropout due to inefficiency. Incomplete reporting of number of patients experiencing at least one side effect
Other bias	Unclear risk	No sufficient information in order to establish if other bias are present

Javors 2000

Methods	Six-week, randomised study.
Participants	Inpatients fulfilling DSM-IV diagnostic criteria for major depression Age range: unclear.
Interventions	Paroxetine: 3 participants. Desipramine: 5 participants.. Paroxetine dose range: 30-60 mg/day. Desipramine dose range: 50-250 mg/day.
Outcomes	Hamilton rating scale for depression (HDRS); platelet serotonin content
Notes	The study was primarily designed to assess the reduction of platelet serotonin content in depressed patients treated with paroxetine or desipramine

Risk of bias

Bias	Authors' judgement	Support for judgement

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Javors 2000 (*Continued*)

Random sequence generation (selection bias)	Unclear risk	Quote: "randomly assigned".
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No information provided.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No information provided.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	No clear information on incomplete outcome data management.
Selective reporting (reporting bias)	High risk	Adverse events, dropouts and side effects were not reported. As dichotomous outcome, only endpoint response rate are reported. (The study was primarily designed to assess the reduction of platelet serotonin content in depressed patients treated with paroxetine or desipramine)
Other bias	Low risk	This study was independent from pharmaceutical industry.

Jefferson 2001 29060/785

Methods	Six-week, double-blind, placebo-controlled, multicentre, parallel-group, randomised study
Participants	Patients with major depressive disorder (DSM-IV criteria), with a Montgomery and Asberg Depression Rating Scale (MADRS) score of at least 17 (both at the screening and baseline visits) Exclusion criteria: patient who have taken other psychotropic drugs, had a history of schizophrenia or schizoaffective disorder, had current (or within 6 months prior to screening) Axis I anxiety disorder or Axis I affective disorder other than major depressive disorder. Patient who, in the investigator's judgement, posed a current homicidal or suicidal risk. Woman who had a positive pregnancy test or who were lactating, women of childbearing potential who were not practicing a clinically accepted method of contraception. Subject with a serious medical disorder or condition that, in the investigator's opinion, precluded the administration of paroxetine controlled release (CR) or citalopram. Patient undergoing any form of psychotherapy Age range: 18-65 years.
Interventions	Citalopram 20 mg/day: 107 participants. Citalopram 40 mg/day: 100 participants. Paroxetine CR 12.5 mg/day: 96 participants.

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Jefferson 2001 29060/785 (*Continued*)

	Paroxetine CR 25 mg/day: 103 participants. Placebo: 105 participants.
Outcomes	MADRS, Clinical Global Impression (CGI), Hamilton rating scale for anxiety (HAM-A), Hospital Anxiety and Depression (HAD), Self-rating depression scale (SDS) Total dropout, dropout due to inefficacy, dropout due to side effects, number of patients experiencing at least one side effect, side-effect profile
Notes	Funding: paroxetine manufacturer. One suicide in placebo group.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: "subject were randomized (1:1:1:1: 1) to either paroxetine CR 12.5 mg, paroxetine CR 25 mg, citalopram 20 mg, citalopram 40 mg, or placebo"
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "paroxetine CR and citalopram were provided as over-encapsulated tablets (...) placebo capsules were identical in appearance to the active study medication capsules"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double blind".
Incomplete outcome data (attrition bias) All outcomes	Low risk	Study endpoint: "23/103 missing from paroxetine 25 mg group, 18/96 from paroxetine 12.5 one, 17/107 from citalopram 20 mg one, 26/100 from citalopram 40 mg one Quote: "all subjects who were randomized to double-blind medication and had at least one valid post baseline efficacy assessment comprised the Intention-to-treat (ITT) efficacy population. The Last Observation Carried Forward (LOCF) data at week 6 were the primary dataset of interest"
Selective reporting (reporting bias)	High risk	Only most frequent adverse events reported.

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Other bias	Unclear risk	Sponsorship bias cannot be ruled out.

Kasper 2005

Methods	Six-week, double-blind,multicentre, parallel-group, randomised study
Participants	Outpatients fulfilling DSM-IV diagnostic criteria for major depression with a minimum score of 18 on the Hamilton rating scale for depression (HDRS-17) Age range: 18-65 years.
Interventions	Paroxetine: 53 randomised Trazodone: 55 randomised Paroxetine dose range: 20-40 mg/day. Trazodone dose range: 300-450 mg/day. No other psychotropic medication was allowed during the study period, with the exception of patients stabilised on BDZ
Outcomes	HDRS, Clinical Global Impression (CGI), Montgomery and Asberg Depression Rating Scale (MADRS). Total dropout, dropout due to inefficiency, dropout due to side effects, number of patients experiencing at least one side effect and side-effect profile
Notes	Funding: paroxetine and trazodone manufacturer.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: "randomly assigned". No further details.
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "Double-blind, double-dummy".
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "Double-blind, double-dummy".
Incomplete outcome data (attrition bias) All outcomes	High risk	More than 20% of patients abandoned the study prematurely. Study endpoint: 14/53 missing from paroxetine group; 19/55 missing from trazodone one

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Kasper 2005 (*Continued*)

Selective reporting (reporting bias)	Low risk	CGI-Improvement and CGI-Severity reported only on graphs.
Other bias	Unclear risk	Sponsorship bias cannot be ruled out.

Kato 2005

Methods	Open-label study with two parallel groups of patients randomly assigned to either paroxetine or fluvoxamine
Participants	Eighty-one patients meeting DSM-IV diagnosis of major depressive disorder (excluding bipolar disorder) were included in the study Exclusion criteria were additional diagnoses on Axis 1 and Axis 2, pregnancy and major medical and neurological disorders
Interventions	Fluvoxamine: 39 participants. Paroxetine: 42 participants. Fluvoxamine dose range: 50-150 mg/day. Paroxetine dose range: 20-40 mg/day. Patients who had been receiving benzodiazepines for at least 10 days before entering the study were permitted to continue these agents, providing that the dose remained unchanged throughout the study period. A low-dose sleep-inducing hypnotic agent, either brotizolam or triazolam, was permitted for severe insomnia as an additional medication
Outcomes	Hamilton rating scale for depression (HDRS). Total dropout, dropout due to side effects. Number of patients experiencing at least one side effect, side-effect profile
Notes	In this study "lack of response" was defined as a 40% of less reduction of the HDRS This study was partly sponsored by Glaxo Smith Kline and Meiji Seika Kaisha Ltd

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: "patients randomly assigned".
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "open label". No further details.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote: "open label". No further details.

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Incomplete outcome data (attrition bias) All outcomes	High risk	No information regarding incomplete outcome data management. This study was primarily designed to assess the influence of the serotonin type 2A, 3A and 3B receptor genes in addition to a polymorphism in the promoter region of the serotonin transporter
Selective reporting (reporting bias)	Unclear risk	Outcomes data not clearly reported.
Other bias	Unclear risk	Sponsorship bias cannot be ruled out.

Katz 2004

Methods	Six-week double-blind, parallel-group, randomised study.
Participants	Inpatients fulfilling DSM-III-R diagnostic criteria for major depression with a minimum score of 18 on the Hamilton rating scale for depression (HDRS) Age range: 20-69 years.
Interventions	Paroxetine: 28 participants. Desipramine: 29 participants. Placebo: 25 participants. Paroxetine dose range: 20-60 mg/day. Desipramine dose range: 50-350 mg/day.
Outcomes	HDRS, Clinical Global Impression (CGI), Global Assessment Scale (GAS), Schedule for Affective Disorders and Schizophrenia (SADS), VIBES, Symptom checklist (SCL-90), National Institute of Mental Health Mood Scale (NIMH)
Notes	None.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: "randomly assigned", no further details.
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double blind". No further details.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double blind". No further details.

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Katz 2004 (*Continued*)

Incomplete outcome data (attrition bias) All outcomes	Unclear risk	No information provided about number of patients missing from paroxetine group and desipramine group at study endpoint
Selective reporting (reporting bias)	High risk	Adverse events, dropouts and side effects were not reported. As dichotomous outcome, only endpoint response rate were reported
Other bias	Unclear risk	No sufficient information in order to establish if other biases are present

Kennedy 2004

Methods	Eight-week, double-blind, double-dummy, parallel-group, randomised study
Participants	Males and non-pregnant females using adequate contraception were eligible if they were between 18 and 65. Participants had to have a diagnosis of moderate to severe major depressive disorder without psychotic features Participants were excluded if they had a predisposition to seizures, serious suicidal risk, poor previous therapeutic response to antidepressant medication, significant DSM-IV Axis II diagnosis, history of or current diagnosis of anorexia nervosa or bulimia, recent history of drug dependence or abuse, including alcohol Age range: 18-65 years.
Interventions	Paroxetine: 71 randomised. Bupropion: 69 randomised. Paroxetine dose: 20-40 mg/day. Bupropion dose: 150-300 mg/day.
Outcomes	Hamilton rating scale for depression (HDRS-17), Clinical Global Impression (CGI), Hamilton rating scale for anxiety (HAM-A), Quality of Life in Depression (QLDS). Total dropout, dropout due to side effects. Number of patients experiencing at least one side effect, side - profile
Notes	Poor therapeutic response is defined as at least two failed responses to antidepressant medications to from two different antidepressant classes, at adequate dose and duration Funding: bupropion manufacturer.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: "patients were randomly assigned". No further details
Allocation concealment (selection bias)	Unclear risk	No information provided.

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Kennedy 2004 (*Continued*)

Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double blind, double dummy". No further details.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double blind, double dummy". No further details.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Quote: "we performed statistical analysis using the Last Observation Carried Forward (LOCF) method on all subjects who took at least one dose of medication and completed at least a second visit"
Selective reporting (reporting bias)	Unclear risk	Outcomes data not clearly reported (the study was primarily designed to evaluate sexual functioning during paroxetine or bupropion treatment)
Other bias	Unclear risk	Sponsorship bias cannot be ruled out.

Kiev 1997

Methods	Seven-week, double-blind, multicentre, randomised study.
Participants	Psychiatric outpatients meeting DSM-III-R for recurrent major depressive disorder, with a minimum baseline score of 20 on the Hamilton rating scale for depression (HDRS-21). Age range: 18-65 years.
Interventions	Paroxetine: 30 participants. Fluvoxamine: 30 participants. Paroxetine dose range: 20-50 mg/day. Fluvoxamine dose range: 50-150 mg/day. Concomitant use of any psychotropic medication was prohibited. While medications to treat gastrointestinal disturbances (antacids, laxatives), and headache (acetaminophen, aspirin, ibuprofen) and to provide nighttime sedation (chloral hydrate only) were permitted, all other medication use was prohibited unless approved by the study physician
Outcomes	HRSD-21, Clinical Global Impression (CGI), Hamilton rating scale for anxiety (HAM-A), Symptom checklist (SCL-56) Total dropout, dropout due to inefficiency, dropout due to side effects, number of patients experiencing at least one side effect, side-effect profile
Notes	Funding: fluvoxamine manufacturer.
Risk of bias	

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Kiev 1997 (*Continued*)

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "randomly assigned", no further details.
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double blind". No further details.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double blind". No further details.
Incomplete outcome data (attrition bias) All outcomes	High risk	Study endpoint: 11/30 missing from paroxetine group (1 due to lack of efficacy, 2 due to adverse effects); 9/30 missing from control group (3 due to lack of efficacy, 5 due to adverse effects)
Selective reporting (reporting bias)	High risk	Standard deviations of endpoint score for depression were not reported
Other bias	Unclear risk	Sponsorship bias cannot be ruled out.

Kramer 1998

Methods	Six-week, randomised, double-blind, placebo-controlled study
Participants	Out-patients with a DSM-IV diagnosis of major depression disorder (single or recurrent) , a current episode of depression lasting at least 4 weeks (but less than 2 years) a score ≥22 (moderately depressed) on the Hamilton rating scale for depression (HDRS-17), a score ≥15 (moderately high anxiety) on the Hamilton rating scale for anxiety (HAM-A) and a score ≥4 (moderately ill) on the Clinical Global Impression (CGI) Severity. Patients considered at risk for suicide or violence were excluded
Interventions	Paroxetine:72 participants. Aprepitant (MK-869): 71 participants. Paroxetine dose: 20 mg/day. Aprepitant (MK-869): 300 mg/day.
Outcomes	HDRS-21, HAM-A, CGI-S.
Notes	Funding: aprepitant manufacturer.
Risk of bias	

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Kramer 1998 (*Continued*)

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "randomized". No further details.
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double blind". No further details.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double blind". No further details.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	More than 20% of participants in each arm abandoned the study prematurely
Selective reporting (reporting bias)	High risk	Outcomes data not clearly reported. Only side effects with an incidence of > or = 5% were reported
Other bias	Unclear risk	Sponsorship bias cannot be ruled out.

Kramer 2001

Methods	Eight-week, randomised, multicentre study.
Participants	Outpatients with Major Depressive Disorder (MDD).
Interventions	Paroxetine: 20 mg/day. Compound A: low dose (not specified). Compound A: high dose (not specified). Placebo.
Outcomes	Hamilton rating scale for depression (HDRS), Hamilton rating scale for anxiety (HAM-A), adverse effects
Notes	None.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "randomized". No further details.
Allocation concealment (selection bias)	Unclear risk	No information provided.

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Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No information provided.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No information provided.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	No information on incomplete outcome data management.
Selective reporting (reporting bias)	High risk	Efficacy and tolerability data not clearly reported.
Other bias	Unclear risk	Insufficient information to establish the presence of other biases

Kuhs 1989

Methods	Six-week, double-blind, randomised, double-dummy, parallel-group, comparative study
Participants	Inclusion criteria: DSM III major depression, Hamilton rating scale for depression (HDRS-21) 18+. Age: 18-65 years. Country: Germany. Setting: inpatients.
Interventions	Paroxetine: 20 participants. Amitriptyline: 20 participants. Paroxetine dose: 30 mg/day. Amitriptyline dose: 150 mg/day. During the study 13 patients were treated with oxazepam (<20mg/d) as a co-medication in cases of psychomotor agitation (paroxetine n = 5; amitriptyline n = 8) Short-acting benzodiazepines (triazolam, lorazepam) were given in case of persistent insomnia (paroxetine n = 3; amitriptyline n = 1) Because of postural hypotension, 3 patients in the paroxetine group and 7 in the amitriptyline group were treated with dihydroergotamine (<5 mg/d)
Outcomes	HDRS-21. Total dropout, dropout due to side effects, dropout due to inefficacy. Number of patients experiencing at least one side effect, side-effect profile
Notes	None.

Risk of bias

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

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Kuhs 1989 (*Continued*)

Random sequence generation (selection bias)	Unclear risk	Quote: "randomized". No further details.
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double blind". No further details.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double blind". No further details.
Incomplete outcome data (attrition bias) All outcomes	High risk	Quote: "all subjects entered were eligible for the Intention-to-treat (ITT) population. Safety assessment were performed on the ITT population". No further details More than 20% of participants in both arms abandoned the study prematurely
Selective reporting (reporting bias)	High risk	Outcomes data not clearly reported. Continuous data not reported
Other bias	Unclear risk	Sponsorship bias cannot be ruled out.

Laghrissi-Thode 1995

Methods	Six-week, randomised, double-blind study.
Participants	Patients suffering from a major depressive episode according to DSM III criteria using the Structured Clinical Interview for DSM III R. The current episode must have lasted at least 1 month and the Hamilton rating scale for depression (HDRS) score must have been 15 or higher for patient inclusion. Patients were excluded from the study if they suffered from an instable medical illness, had taken psychotropic medications within 2 weeks (or within 6 weeks for fluoxetine) or had contraindications to nortriptyline treatment
Interventions	Paroxetine: 20 mg/day. Nortriptyline: 50/120 ng/mL.
Outcomes	Postural stability in older depressed patients.
Notes	This study was independent from pharmaceutical industry.

Risk of bias

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

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Laghrissi-Thode 1995 (*Continued*)

Random sequence generation (selection bias)	Unclear risk	Quote: "patients were randomized". No further details.
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double blind". No further details.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double blind". No further details.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	No clear information on incomplete outcome data management.
Selective reporting (reporting bias)	Unclear risk	No efficacy and tolerability data. This study was primarily designed to investigate the effect of antidepressants on postural stability in older depressed patients
Other bias	Low risk	This study was independent from pharmaceutical industry.

Laursen 1985

Methods	Six-week, randomised, double-blind,parallel-group.
Participants	Inclusion criteria: ICD 8 Manic-depressive psychosis, Hamilton rating scale for depression (HDRS-17) 15+; three of the four following criteria had to be present: phasic course of illness, changes in psychomotor activity, diurnal variation in symptom and unfounded lost of self-esteem. Age: 35-81 years. Country: Denmark. Setting: inpatients with outpatient follow-up.
Interventions	Paroxetine: 21 participants. Amitriptyline: 23 participants. Paroxetine dose range: 30-60 mg/day. Amitriptyline dose range: 150-200 mg/day. In the event of need for an anxiolytic or hypnotic drug, benzodiazepines and chlorhydrate could be used
Outcomes	HDRS-17 and 6-item subscale ratings.Total dropout, dropout due to side effects, dropout due to inefficacy. Number of patients experiencing at least one side effect, side-effect profile
Notes	Funding: independent from industry.

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Laursen 1985 (*Continued*)

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: "random allocation to treatment (. ..) randomized".
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double blind". No further details.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double blind". No further details.
Incomplete outcome data (attrition bias) All outcomes	High risk	The statistical analyses were based on results from completers. No further details
Selective reporting (reporting bias)	High risk	Outcomes data not clearly reported. Rating scales scores reported only in figures
Other bias	Low risk	This study was independent from pharmaceutical industry.

Lee 2007 (HMCV)

Methods	Randomised, double-blind, double-dummy, parallel-group study
Participants	Planned: Total 480, duloxetine 240, paroxetine 240. Randomised: Total 478, duloxetine 238, paroxetine 240. Completed: Total 349, duloxetine 166, paroxetine 183. Criteria for Inclusion: Patients of either sex and at least 18 years of age who met the DSM-IV criteria for nonpsychotic Major Depressive Disorder (MDD), and had a Hamilton rating scale for depression (HDRS-17) total score $\geq$15 and Clinical Global Impression (CGI) Severity score $\geq$4 were included
Interventions	Duloxetine: 60 mg/day (given orally once a day as two 30 mg capsules). Paroxetine: 20 mg/day, given orally once a day as two 10 mg capsules
Outcomes	Efficacy: The primary measure of efficacy was to assess the severity of depression and its improvement during the course of therapy, using the HDRS-17. Secondary measures of efficacy included: presence and severity of anxiety (HAM-A), severity of illness (CGI-Severity), degree of improvement (PGI-Improvement), degree to which physical complaints were bothersome to patient (SSI), and experience of overall pain (VAS). Safety: Assessment of adverse events, including serious adverse events, routine laboratory

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	tests, vital signs, and ECGs
Notes	For the primary efficacy analysis, a one-sided 97.5% confidence interval of the adjusted mean HDRS-17 total score was used to determine whether duloxetine was noninferior to paroxetine. Non-inferiority was declared if the upper bound of the one-sided 97.5% confidence interval was less than 2.2 Date of first patient enrolled: 17 February 2004. Date of last patient completed: 12 June 2005.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: "Patients meeting the entry criteria were randomized in a ratio of 1:1 to either duloxetine 60 mg/day or paroxetine 20 mg/day"
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double blind, double dummy".
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double blind, double dummy".
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Quote: "the primary analysis was based on the Per Protocol (PP) population. The analysis of treatment emergent adverse effects was based on all randomized patients with at least one post-baseline observation and taking at least one dose of their randomzed medication (safety set). All other results are based on all randomized patients with at least one post-baseline observation (Intention-to-treat population)"
Selective reporting (reporting bias)	High risk	Only adverse events occurring with frequency > or = 5% were reported
Other bias	Unclear risk	Sponsorship bias cannot be ruled out.

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Lepine 2001

Methods	Multicentre, randomised, double-blind study.
Participants	Male of female, in- or outpatients fulfilling DSM-IV criteria for Major Depressive Disorder (MDD) single episode or recurrent, severity moderate to severe, without psychotic features, with or without melancholic features and, for recurrent disorders, with or without seasonal pattern and inter-episode recovery), were eligible for the study To be selected, patients had to present at D7 a minimum severity score of 25 on the Montgomery and Asberg Depression Rating Scale (MADRS) and of 9 on the Hamilton rating scale for depression (HDRS) (items 1,2,7,8,10 and 13). These severity criteria also had to be present at inclusion, and those patients with a decrease of 30% or more on MADRS or HDRS global scores were excluded Patients fulfilling DSM-IV criteria for other Major Depressive Disorders: Bipilar I or II Disorders, dysthymic disorder, cyclothymic disorder, mixed anxio-depressive disorder, recurrent brief depressive disorder, schizophrenia or any other acute or chronic psychosis and patients whose present disorder was due to a general medical condition or to a substance were not eligible for the study
Interventions	Paroxetine: 165 participants. Tianeptine: 162 participants. Paroxetine dose: 20 mg/day. Tianeptine dose: 37,5 mg/day. Treatment with a benzodiazepine during the last 2 weeks, or for more then 1 month during the last 6 months, or at daily dose equal to or greater the an equivalent of 15mg of diazepam on a lifetime period, were also non-inclusion criteria
Outcomes	MADRS, CPRS, HDRS, Hamilton rating scale for anxiety (HAM-A), Clinical Global Impression (CGI), Severity of Depression Questionnaire (QSD), Hospital Anxiety and Depression (HAD), Mood and Anxiety Symptom Questionnaire (MASQ), Visual Analogue Scale (VAS). Total dropout, dropout due to side effects, dropout due to inefficacy. Number of patients experiencing at least one side effect, side-effect profile
Notes	This study was independent from pharmaceutical industry.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: "randomized". No further details.
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double blind". No further details.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double blind". No further details.

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Lepine 2001 (*Continued*)

Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "analysis of the efficacy data was performed both on the Intention-to-treat (ITT) population (ITT: all patients with at least one evaluation under treatment) and on the Per Protocol (PP) population (PP: all completed patients without major deviation, according to the study protocol). The analysis was done at the endpoint for the ITT population and visit by visit for the PP population. The analysis of safety used all patients who had taken at least one dose of randomized treatment" Less than 20% of participants in both arms withdrew from the study prematurely
Selective reporting (reporting bias)	Low risk	Outcomes data were reported.
Other bias	Low risk	This study was independent from pharmaceutical industry.

Loo 2002

Methods	Eight-week, double-blind, randomised multicentre study.
Participants	Seven hundred and eleven patients (238 males, 33.5%; 473 females, 66.5%; mean age 42.3 years) in 102 centres located in Belgium, France and the UK were included in this study. There was no significant difference between groups at inclusion for demo-graphic characteristics or disease factors: 67.1% of patients met DSM-IV criteria for a recurrent major depressive disorder, 33.5% of patients had an episode of severe intensity
Interventions	Patients were to take orally one capsule twice daily: one in the morning, one in the evening. Following a placebo run-in period of 1 week, patients were randomised in double-blind conditions to receive fixed doses of agomelatine (1mg, 5mg or 25mg in the evening capsule), paroxetine 20 mg (in the morning capsule) or placebo Concomitant treatment with psychotropic drugs was not allowed with the exception of benzodiazepines at restricted doses. High potency benzodiazepines, such as alprazolam and triazolam, were not permitted Drugs which were thought to be able to influence study evaluations by acting on patient's mood or circadian rhythms, such as b-blockers, central a-blockers,non-steroidal anti-inflammatory drugs and exogenous melatonin,were not allowed
Outcomes	The Hamilton rating scale for depression (HDRS) and the Clinical Global Impression (CGI) were assessed at baseline, and at weeks 1, 2, 4, 6and 8.The Montgomery and Asberg Depression Rating Scale (MADRS) and the Hamilton rating scale for anxiety (HAM-A) were assessed at baseline, and at weeks 4 and 8. Total dropout, dropout due to side effects, dropout due to inefficacy. Number of patients experiencing at least one side effect, side-effect profile

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Notes	In this Cochrane Review data referring to dichotomic outcomes were add up together, data referring to continuous outcomes were matched together as suggested by the Cochrane Handbook (Table 7.7.a: Formulae for combining groups)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "patients were randomized". No further details.
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double blind conditions". No further details.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double blind conditions". No further details.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Primary measure of efficacy was based on the Intention-to-treat (ITT) population, defined as "patients who has received at least one post-randomization capsule and had a baseline measurement and at least one post-baseline measurement"
Selective reporting (reporting bias)	Low risk	Outcomes data were reported.
Other bias	Unclear risk	Sponsorship bias cannot be ruled out.

M/2020/0047

Methods	Multicentre, randomised, double-blind, placebo- and active-controlled, parallel-group study
Participants	Inclusion Criteria. To be included in the study, patients must have met all of the following criteria: diagnosis of Major Depressive Disorder (MDD) without psychotic features, as defined by DSM-IV. Male or female, of any race, between the ages of 18 and 65 years. If female, must have been postmenopausal or must have met all of the following criteria: agreed to avoid pregnancy during the study; had a negative serum pregnancy test at screen; used an accepted means of birth control (as determined by the investigator), such as abstinence, oral contraceptive, implantable or injectable contraceptive, intrauterine device, or barrier method, or have been surgically sterilized. Total score of $\geq$20 on the Hamilton rating scale for depression (HDRS-17), which was administered via the IVRS prior to the screening visit. General good health, as confirmed by routine clinical laboratory safety findings. Voluntary consent to participate in the study, documented in

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	a written Patient Informed Consent Form that was signed prior to the start of any study procedures at the screening visit Exclusion Criteria. Patients were excluded from the study for any of the following reasons: DSM-IV diagnosis of the following concomitant psychiatric disorders: MDD with psychotic features, cyclothymic disorder, bipolar I or bipolar II disorders, substance-related disorders (within the preceding 12 months), schizophrenia, or other psychotic disorders. Resistance to antidepressive treatment, defined as a lack of response to at least 2 previous courses of antidepressant medications administered at full doses for more than 1 month. Participation in a previous clinical trial of reboxetine or lack of response to previous treatment with paroxetine, administered at a dose of ≥20 mg/day for more than 1 month. Use of antidepressant medication for the treatment of depression in the 2 months preceding the start of the study. History of MDD associated with endocrine disorders: hypo- or hyper-thyroidism tested by thyroid-stimulating hormone and thyroxine, adrenal insufficiency, or Cushing's syndrome. Positive pregnancy test for females of childbearing potential. Breast-feeding by female patients. Refusal by female patients of childbearing age to use an effective contraceptive method during the study. Participation in any clinical study with an investigational compound in the 4 weeks preceding the study. History or presence of gastrointestinal, liver, or kidney disease or other conditions known to interfere with the absorption, distribution, metabolism, and excretion of drugs. History of seizures or brain injury; current evidence of clinically important hematopoietic, respiratory, or cardiovascular diseases; current evidence of urinary retention or glaucoma. Clinically significant illness in the 4 weeks preceding the study that might have interfered with the conduct of the trial. Clinically relevant abnormal findings in the physical examination, laboratory tests, or ECG at admission. Positive urine drug screen for amphetamines, barbiturates, marijuana metabolites, cocaine metabolites, methadone, methaqualone, opiates, phencyclidine, or propoxyphene. A positive urine drug screen for benzodiazepines did not exclude the patient. Treatment with electroconvulsive therapy in the 6 months preceding the study. Major risk of suicide as assessed by the investigator, a score of ≥3 on Item 3 of the HDRS at screen or baseline, or a history of suicide attempt during the current depressive episode. History of hypersensitivity to reboxetine or paroxetine. Use of the following medications, which are potent inhibitors of the drug-metabolizing enzyme cytochrome p450-3A4: azole antifungals, macrolide antibiotics , or fluvoxamine. Use of the following medications, which are known to be substrates or inhibitors of the drug-metabolizing enzyme cytochrome p450-2D6: Type 1C antiarrhythmics, quinidine, or cimetidine. Use of oral anticoagulants that are known to inhibit vitamin K-dependent coagulation factors. Use of concomitant psychotropic medications other than the protocol-specified sedatives/hypnotics, which could be taken on an as-needed basis for sleep. Inability of the patient to comply with the conditions of the study, based on the investigator's assessment
Interventions	Paroxetine: 262 participants. Reboxetine: 258 participants. Placebo: 254 participants.
Outcomes	Montgomery Asberg Depression Rating Scale (MADRS) total score at day 56 in the Intent-to-treat (ITT) patient population.Total dropout, dropout due to side effects, dropout due to inefficacy. Number of patients experiencing at least one side effect, side-effect profile

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Notes	Funding: reboxetine manufacturer.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Pharmacia & Upjohn (P&U) prepared a randomization list for assignment of the patients to 1 of the 3 treatment groups. Study medication for each treatment group was prepared on this basis by P&U and was labeled with the corresponding patient number"
Allocation concealment (selection bias)	Low risk	Quote: "at the baseline visit, the investigator assigned each patient to a treatment group based on the patient's temporal entry into the study (i.e. by assigning the lowest patient number available). A list of patient numbers and medication assignments was provided only after the data for the study had been analyzed"
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "double blind (...) study medications were provided as identically appearing capsules (...) The randomized medications consisted of identically appearing capsules containing reboxetine, paroxetine or placebo. The capsules were provided in clinical supply packages that were labeled with the protocol number, patient number, treatment period, dosing, directions and storage conditions. Investigators were given sealed drug-disclosure sheets that contained information about each patient's treatment"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double blind".
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Quote: "the Intention-to-treat (ITT) dataset, which includes all patients who were randomized into the trial and who received at least one dose of study medication, was used for all the analyses. Two types of analyses were performed for all efficacy variables: Last Observation Carried For-

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M/2020/0047 (*Continued*)

		ward (LOCF) and Observed Cases (OC). The LOCF analyses used the last valid assessment as an estimate for all subsequent missing values. The OC analysis did not replace missing data. The LOCF analyses were the primary analyses and the OC analyses were the secondary analyses"
Selective reporting (reporting bias)	Low risk	Outcomes data were reported.
Other bias	Unclear risk	Sponsorship bias cannot be ruled out.

M/2020/0052

Methods	Eight-week, multicentre, randomised, double-blind, parallel-group study
Participants	Inclusion Criteria. To be included in the study, patients must have met all of the following criteria: diagnosis of Major depressive Disorder (MDD) without psychotic features, as defined by DSM-IV. Male or female, of any race, between the ages of 18 and 65 years. If female, must have been postmenopausal or must have met all of the following criteria: agreed to avoid pregnancy during the study; had a negative serum pregnancy test at screen; used an accepted means of birth control (as determined by the investigator), such as oral contraceptive, implantable or injectable contraceptive, intrauterine device, or barrier method, or have been surgically sterilized. Total score of $\geq$22 and $\leq$35 on the 21-Item Hamilton rating scale for depression (HDRS) at screen and confirmed at baseline. Voluntary consent to participate in the study documented in a written Patient Informed Consent Form that was signed prior to the start of any study procedures at the screening visit Exclusion Criteria. Patients were excluded from the study for any of the following reasons: DSM-IV diagnosis of the following concomitant psychiatric disorders: MDD with psychotic features, dysthymic or cyclothymic disorder, bipolar I or bipolar II disorders, substance-related disorders, schizophrenia, or other psychotic disorders; a lack of response to a previous course of either reboxetine or paroxetine; history of MDD associated with endocrine disorders: hypo- or hyper-thyroidism tested by thyroid-stimulating hormone and thyroxine, adrenal insufficiency, or Cushing's syndrome, etc.; positive serum pregnancy test for females of childbearing potential. Breast-feeding female patients. Participation in a clinical study with an investigational compound in the 4 weeks preceding the study. Presence of gastrointestinal, liver, or kidney disease or other conditions known to interfere with the absorption, distribution, metabolism, and excretion of drugs. History of seizures or brain injury; current evidence of clinically important hematopoietic, respiratory, or cardiovascular diseases; current evidence of urinary retention or glaucoma. Clinically significant illness in the 4 weeks preceding the study that might have interfered with the conduct of the trial. Clinically relevant abnormal findings in the physical examination, laboratory tests, or ECG at admission. Treatment with electroconvulsive therapy in the 6 months preceding the study. Major risk of suicide as assessed by the investigator, a score of $\geq$3 on Item 3 of the HDRS at screen or baseline, or a history of suicide attempt during the current depressive episode. History of hypersensitivity to reboxetine or paroxetine. Use of the following medications, which are known to inhibit major drug-

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	metabolizing enzymes other than cytochrome p450-2D6: azole antifungals, macrolide antibiotics, or fluvoxamine. Use of oral anticoagulants that are known to inhibit vitamin K-dependent coagulation factors. Use of concomitant psychotropic medications other than the protocol-specified sedatives/hypnotics, which could be taken on an as-needed basis for sleep. Inability of the patient to comply with the conditions of the study based on the investigator's assessment
Interventions	Paroxetine: 166 participants. Reboxetine: 159 participants.
Outcomes	To assess efficacy and tolerability of reboxetine in comparison with paroxetine in patients suffering from MDD as determined by the HDRS scale. Total dropout, dropout due to side effects, dropout due to inefficacy. Number of patients experiencing at least one side effect, side-effect profile
Notes	Funding: reboxetine manufacturer.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Quote: "Pharmacia & Upjohn (P&U) prepared a randomization list for assignment of the patients to 1 of the 2 treatment groups. Study medication for each treatment group was prepared on this basis by P&U and was labled with the corresponding patient number"
Allocation concealment (selection bias)	Low risk	Quote: "at the baseline visit, the investigator assigned each patient to a treatment group based on the patient's temporal entry into the study (i.e. by assigning the lowest patient number available). A list of patient numbers and medication assignments was provided only after the data for the study had been analyzed"
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "double blind (...) study medications were provided in product packages that were labeled with the protocol number, the patient number, the study week, and the dose level. The randomized medications consisted of identically appearing capsules containing reboxetine, paroxetine with placebo. The capsules were provided in clinical supply packages that were labeled with the protocol number, patient

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		number, treatment period, dosing, directions and storage conditions. Investigators were given sealed drug-disclosure sheets that contained information about each patient's treatment assignment"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "the Intention-to-treat (ITT) dataset, which includes all patients randomized into the trial and who received at least one treatment dose with at least one post-baseline efficacy follow up evaluation, was to be used for the analysis. Two types of analyses were performed for all efficacy variables: Last Observation Carried Forward (LOCF) and Observed Cases (OC). The LOCF analyses used the last valid assessment as an estimate for all subsequent missing values. The OC analysis did not replace missing data. The ITT dataset using the LOCF technique was to be the primary analysis and the OC analysis was to be included as a secondary analysis"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Outcomes data were reported.
Selective reporting (reporting bias)	Low risk	Outcomes data were reported.
Other bias	Unclear risk	Sponsorship bias cannot be ruled out.

Mc Partlin 1998

Methods	Twelve-week, parallel-group, randomised, double-blind trial.
Participants	Outpatients at least 18 years of age were eligible if they satisfied DSM-IV criteria for major depression, had symptoms of depression for at least 14 days, and had a minimum baseline score of 19 on the Montgomery and Asberg Depression Rating Scale (MADRS)
Interventions	Paroxetine: 178 participants. Venlafaxine XR: 183 participants. Paroxetine dose: 20 mg/day. Venlafaxine dose: 75 mg/day.
Outcomes	MADRS, Hamilton rating scale for depression (HDRS), Clinical Global Impression (CGI). Total dropout, dropout due to side effects, dropout due to inefficacy. Side-effect profile
Notes	Funding: venlafaxine manufacturer.

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Mc Partlin 1998 (*Continued*)

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: "randomized". No further details.
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double blind". No further details.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double blind". No further details.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Quote: "data from patients who took at least one dose of study medication and who had at least one efficacy evaluation during the treatment period comprised the Intention-to-treat (ITT) population"
Selective reporting (reporting bias)	High risk	Only most common adverse effects were reported.
Other bias	Unclear risk	Sponsorship bias cannot be ruled out.

Montgomery 2004

Methods	Twelve-week, randomised, double-blind study.
Participants	Depressed outpatients, aged 18 years or above, who fulfilled the diagnostic criteria for Major Depressive Disorder (MDD) of DSM IV, single or recurrent episode. The diagnosis of MDD and any comorbid psychiatric disorders was documented using the Mini International Neuropsychiatric Interview (MINI). No other Axis I or II disorders could be included. Patients having any concomitant severe and/or unstable medical illnesses likely to interfere with the conduct of the study were also excluded
Interventions	Paroxetine:168 participants. Agomelatine: 167 participants. Paroxetine dose: 20 mg/day. Agomelatine dose: 25 mg/day.
Outcomes	Montgomery and Asberg Depression Rating Scale (MADRS), Hamilton rating scale for anxiety (HAM-A), side effects

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Montgomery 2004 (*Continued*)

Notes	This study was independent from pharmaceutical industry.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "randomized". No further details.
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double blind conditions". No further details.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double blind conditions". No further details.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	No information on incomplete outcome data management.
Selective reporting (reporting bias)	Unclear risk	Some data were not reported.
Other bias	Low risk	This study was independent from pharmaceutical industry.

Moon 1996

Methods	Six-week, multicentre, randomised, double-blind, comparative study
Participants	Inclusion criteria: male and female patients; aged 18-65 years; patients who met DSM-III criteria for a major depressive episode; subjects with Montgomery and Asberg Depression Rating Scale (MADRS) score of 18+ Exclusion criteria: patients with significant suicidal tendencies; psychosis or rapid cyclic manic-depressive disorder; patients who had received other psychotropic agents, such as IMAO within 2 weeks of entering the study, or concurrent treatment with clonidine or anticoagulants
Interventions	Paroxetine: 60 participants. Lofepramine: 62 participants. Paroxetine dose range: 20-30 mg/day. Lofepramine dose range: 140-210 mg/day.
Outcomes	MADRS, Clinical Global Impression (CGI). Total dropout, dropout due to side effects, dropout due to inefficacy. Number of patients experiencing at least one side effect, side-effect profile

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Moon 1996 (*Continued*)

Notes	Only side effects occurring in >5% of patients.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "patients were randomly allocated". No further details
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double blind". No further details.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double blind". No further details.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Quote: "the intent-to-treat (ITT) population comprised all subjects who received at least 1 dose of trial medication and were assessed at least once during the active phase of the study" Less than 20% of participants in both arms withdrew from the study prematurely
Selective reporting (reporting bias)	High risk	Only side effects occurring in >5% of patients were reported
Other bias	Unclear risk	Sponsorship bias cannot be ruled out.

Mulsant 1999

Methods	Six-week, randomised, double-blind study.
Participants	For inclusion in the analyses, patients had to meet the following criteria: age of 60 years or older, DSM-IV major depressive episode without psychotic features or history of bipolar or schizoaffective disorder, baseline Hamilton rating scale for depression (HDRS) score of 15 or above, Mini Mental State Examination (MMSE) score of 18 or above, no history of alcohol or other substance abuse or dependency during at least the past year, and no specific medical condition contraindicating treatment with either nortriptyline or paroxetine (e.g., QRS longer than 120 ms or bradycardia with heart rate below 50 beats per minute)
Interventions	Paroxetine: 43 participants. Nortriptyilne: 37 participants. Paroxetine dose range: 20-30 mg/day.

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Mulsant 1999 (*Continued*)

	Nortriptyline dose range: 50 mg/day. Patients complaining of severe anxiety and/or insomnia were prescribed lorazepam on a regular basis (e.g., twice a day or at bedtime); the lowest possible doses were used and, as much as clinically possible, doses were kept constant
Outcomes	Study participants were also evaluated with the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-IV) and several rating scales, including a semi-structured version of the HDRS-17, the Cumulative Illness Rating Scale adapted for Geriatrics (CIRS-G), the UKU side effect rating scale (UKU), and a standardised version of MMSE
Notes	Sponsor unclear.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: "Subjects were randomly assigned". No further details
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double blind conditions". No further details.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double blind conditions". No further details.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	An Intention-to-treat (ITT) Last Observation Carried Forward (LOCF) analysis was performed
Selective reporting (reporting bias)	Low risk	Outcomes data were reported.
Other bias	Unclear risk	Sponsorship bias cannot be ruled out.

MY-1045/BRL-029060/1

Methods	Multicentre, randomised, double-blind, placebo-controlled study
Participants	Outpatients >18 years old with a primary diagnosis meeting DSM-III-R criteria for Major depressive Disorder (MDD) (single or recurrent episode) with a total score of >18 on the first 17 items of the Hamilton rating scale for depression (HDRS-21). Total score could not have decreased by 25% between the screen and baseline visits Exclusion criteria: other diagnosis than MDD, serious suicidal or homicidal risk, substance abuse/dependence, prior ECT (within 3 months of the study), serious concomi-

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	tant medical conditions and patients with a history of hypersensitivity to fluoxetine or who had previously taken paroxetine
Interventions	Paroxetine:357 participants. Fluoxetine: 251 participants. Paroxetine dose range: 20-50 mg/day. Fluoxetine dose range: 20-80 mg/day.
Outcomes	HDRS, Clinical Global Impression (CGI), Raskin Depression Score (RDS), Global Assessment of Functioning (GAF), Symptoms Checklist (SCL-90). Total dropout, dropout due to side effects, dropout due to inefficacy. Number of patients experiencing at least one side effect, side-effect profile
Notes	Funding: paroxetine manufacturer.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: "randomized". No further details.
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double blind". No further details.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double blind". No further details.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Quote: "the Intention-to-treat (ITT) analysis included all randomized subjects. All randomized subjects who had an on-therapy efficacy evaluation were included in the efficacy analysis; all randomized subjects were included in the safety analysis. The main analysis was based on the extender dataset which modified the observed data so that missing data for a given week were estimated by bringing forward (extending) the data from the previous week. If week 1 data were missing, no estimate was made"
Selective reporting (reporting bias)	Low risk	Outcomes data were reported.
Other bias	Unclear risk	Sponsorship bias cannot be ruled out.

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NCT00463242

Methods	Double-blind, randomised study.
Participants	Male and female adults, 18-70 years of age, with a diagnosis of Major Depressive Disorder according to DSM-IV criteria. Hamilton Depression Rating Scale (HDRS) total score > or = 22 at screening and baseline
Interventions	Paroxetine: 20-40 mg/day. Agomelatine: 25-50 mg/day.
Outcomes	Change from baseline to endpoint at HDRS, remission, sexual functions
Notes	Funding: by industry.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Randomised, no further information.
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Double-blind. No further information.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Double-blind. No further information.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Insufficient information.
Selective reporting (reporting bias)	Unclear risk	Insufficient information.
Other bias	Unclear risk	Sponsorship bias cannot be ruled out.

Nickel 2003

Methods	Double-blind, randomised, controlled study of depressed inpatients
Participants	Hospitalised patients of either sex (25-65 years of age) fulfi lling the DSM-IV criteria for a major depressive episode or bipolar I or II disorder (single-episode or recurrent depression, without psychotic features) and having a total score of 18 on the Hamilton rating scale for depression (HDRS-21) were eligible for enrolment in the study. The difference in the total HDRS score between selection and inclusion on day 1 had to be 6 points in order to minimise confounding by spontaneous remission. Patients with other affective disorders, i.e., dysthymia, double depression, recurrent brief

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	depressed disorder, anxiety disorder, or acute or chronic psychotic disorder, were not enrolled. Other exclusion criteria were pregnancy and absences of effective contraception in women of childbearing potential; suicidality; history of drug or alcohol abuse or dependence; other severe diseases such as uncontrolled cardiovascular, neurological, or metabolic disorders
Interventions	Paroxetine: 22 participants. Tianeptine: 22 participants. Paroxetine dose range: 20-40 mg/day. Tianeptine dose range: 37,5- 75 mg/day. During the study, no other psychotropic drugs was allowed except chloralhydrate in a dosage of up to 2 g/d on an as-required basis. The prescription of medications that would not interfere with the antidepressant treatment was acceptable
Outcomes	HDRS, Montgomery and Asberg Depression Rating Scale (MADRS), Clinical Global Impression (CGI), Beck Depression Inventory (BDI). Total dropout, dropout due to inefficacy
Notes	Funding: tianeptine manufacturer.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: "patients were enrolled and randomly assigned". No further details"
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double blind". No further details.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double blind". No further details.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Quote: "the analysis of changes in the efficacy measures was performed on the Intention-to-treat (ITT) population with use of the Last Observation Carried Forward (LOCF) method"
Selective reporting (reporting bias)	High risk	Side effects not reported.
Other bias	Unclear risk	Sponsorship bias cannot be ruled out.

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Nielsen 1991

Methods	Double-blind, randomised, multicentre study.
Participants	Inclusion criteria were depression (unipolar or bipolar) calling for pharmacotherapeutic treatment, Hamilton rating scale for depression (HDRS) 18+, age 18-70 years and all patients met the DSM-III criteria for major depressive episode Exclusion criteria were concurrent somatic conditions contraindicating treatment with antidepressants, i.e. cardiovascular conditions, severe liver or renal disease, severe hypertension and unstable endocrinological disease
Interventions	Paroxetine: 16 participants. Imipramine: 15 participants. Paroxetine dose: 30 mg/day. Imipramine dose: 150 mg/day. Concomitant medications was restricted to occasional doses of oxazepam (or similar benzodiazepines) as sedative and paracetamol as analgesic, when necessary. Other psychotropic medication, including lithium, was not allowed
Outcomes	HDRS-17, Melancholia Scale (MES), UKU scale. Total dropout, dropout due to side effects, dropout due to inefficacy. Number of patients experiencing at least one side effect
Notes	Funding unclear.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: "the patients were randomly allocated". No further details
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double blind". No further details.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double blind". No further details.
Incomplete outcome data (attrition bias) All outcomes	High risk	Quote: "to reduce bias caused by patient withdrawals, the last value was carried forward in the analyses" More than 20% of participants in both arms withdrew from the study prematurely
Selective reporting (reporting bias)	High risk	Side effects were not reported. Continuous outcomes only in graph

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Nielsen 1991 (*Continued*)

Other bias	Unclear risk	Sponsorship bias cannot be ruled out.

Ohrberg 1992

Methods	Multicentre, randomised, double-blind, parallel-group, active-controlled study
Participants	Male and female participants, aged 18 to 70 years inclusive, with depression requiring drug treatment, with a diagnosis confirmed by observation of signs and symptoms, and a score >15 on the Hamilton rating scale for depression (HDRS) scale. Key exclusion criteria: other mental disorder, serious suicidal risk (score of >3 on HDRS item 3), treatment with a IMAO within the 14 days preceding entry to the study
Interventions	Paroxetine: 79 participants. Imipramine:80 participants. Paroxetine dose range: 10-50 mg/day. Imipramine dose range: 50-250 mg/day. With the exception of oxazepam or lorazepam as sedative/hypnotics, no other psychopharmacological drugs were allowed
Outcomes	HDRS, Bech-Rafaelsen Melancholia Scale (BRMS). Total dropout, dropout due to side effects, dropout due to inefficacy. Side-effect profile
Notes	Only side effects occurring in >5% of patients. Funding unclear.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: "subjects were randomized". No further details.
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double blind". No further details.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double blind". No further details.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Quote: "the Intention-to-treat (ITT) dataset included all participants who were randomised and received study medication. The efficacy dataset was the subset of the ITT population who completed at least

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Ohrberg 1992 (*Continued*)

		two weeks of treatment. To reduce bias due to subjects who withdrew prematurely, the last value recorded was carried forward" More than 20% of participants in the imipramine arm withdrew from the study prematurely
Selective reporting (reporting bias)	High risk	Only side effects occurring in >5% of patients were reported
Other bias	Unclear risk	Insufficient information to establish the presence of other biases

Ontiveros 1994

Methods	Randomised, double-blind, parallel-group study.
Participants	Male and female participants, aged 18 to 75 years inclusive, who were suffering from a major depressive episode according to the DSM-III criteria, with a diagnosis confirmed by observation of signs and symptoms, and a score >18 on the Hamilton rating scale for depression (HDRS) scale at the pretreatment and baseline assessment. Participants with severe co-existing disease, who had received ECT therapy in the previous 3 months, IMAO in the previous 2 weeks, lithium in the previous 3 months, oral neuroleptics in the previous 2 weeks, depot neuroleptics in the previous 4 weeks, benzodiazepines in the previous 3 days or coadministration of any drug with know psychotropic effects, participants at severe risk of suicide were excluded from the study
Interventions	Paroxetine: 60 participants. Fluoxetine: 62 participants. Paroxetine dose: 20 mg/day. Fluoxetine dose: 20 mg/day.
Outcomes	HDRS, Clinical Global Impression (CGI). Total dropout, dropout due to side effects, dropout due to inefficacy. Number of patients experiencing at least one side effect, side-effect profile
Notes	Funding: paroxetine manufacturer.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: "randomized". No further details.
Allocation concealment (selection bias)	Unclear risk	No information provided.

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Ontiveros 1994 (*Continued*)

Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double blind (...) in order to maintain the blind, all medication was concealed in coloured capsules"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double blind".
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "the primary analyses were performed on the Intention-to-treat (ITT) population, which included all subjects who were randomized to active treatment and had at least one valid efficacy evaluation after the start of treatment". The primary dataset was the ITT endpoint assessment (defined as the patient's last available assessment between weeks 4 and 6) Less than 20% of participants withdrew from the study prematurely
Selective reporting (reporting bias)	High risk	Only adverse events by more than 5% of participants were reported
Other bias	Unclear risk	Sponsorship bias cannot be ruled out.

Owens 2008

Methods	Eight-week, prospective, multicentre, randomised, double-blind, parallel-group study
Participants	Male and female patients (18-65 years) meeting diagnostic criteria for Major Depressive Disorder (MDD) were eligible (American Psychiatric Association, 1994). The diagnosis of MDD was made by the principal investigator using the Mini International Neuropsychiatric Interview (MINI) - a structured diagnostic interview for DSM-IV. A total score of >20 on the Montgomery and Asberg Depression Rating Scale (MADRS) was required at screening and baseline. Patients were excluded if they had a clinically predominant axis I disorder other than MDD. Other key exclusion criteria were: history of unresponsiveness to either paroxetine or venlafaxine or exhibited prior hypersensitivity/intolerance to either paroxetine CR or venlafaxine XR, substance abuse/dependence, prior non-response to SSRIs, suicidal/homicidal risk, concurrent psychotherapy or psychotropic pharmacotherapy, or any serious medical condition or clinically significant finding in the screening or baseline evaluation that would preclude the administration of paroxetine CR or venlafaxine XR. Patients were excluded if they required concomitant therapy with psychoactive medication or patients who have taken other psychoactive medication within the time frames specified below prior to the screening visit: antidepressants other than MAOIs or fluoxetine (e.g., tricyclic antidepressants, SSRIs, and NSRIs), lithium and oral antipsychotics-14 days; hypnotics, benzodiazepines, and all other sedatives (including chlorpheniramine and other sedating antihistamines)-14 days; fluoxetine, MAOIs-4 weeks; depot neuroleptics-12 weeks; any CNS-active herbal preparations/supplement

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	(e.g., St John's wort, kava kava, etc.)F-14 days
Interventions	Paroxetine: 42 participants. Venlafaxine XR: 44 participants. Paroxetine dose range: 12.5-75 mg/day. Venlafaxine dose range: 75-375 mg/day.
Outcomes	MADRS, Clinical Global Impression (CGI). Total dropout, dropout due to side-effects. Number of patients experiencing at least one side effect
Notes	Funding: paroxetine manufacturer.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Quote: "randomized (...) patients meeting eligibility criteria at baseline were randomized (1:1) to receive over-encapsulated paroxetine or venlafaxine tables using a computer-generated randomization list"
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double blind (...) over-encapsulated paroxetine or venlafaxine tables"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double blind".
Incomplete outcome data (attrition bias) All outcomes	High risk	Quote: "all patients who were randomized, received at least one dose of study medication and had at least one post-baseline efficacy assessment, were included in the modified intent-to-treat (ITT) efficacy analyses (...) Patients withdrawing before week 2 without MADRS assessments are not included in the analyses of the MADRS. The analyses on observed data were repeated using the Last Observation Carried Forward (LOCF) approach to impute missing values (...). Because five of the randomized patients did not have a post-baseline efficacy assessment, the evaluable population (modified ITT) consisted of 81 patients" More than 20% of participants withdrew from the study prematurely

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Selective reporting (reporting bias)	Low risk	Outcomes data were reported.
Other bias	Unclear risk	Sponsorship bias cannot be ruled out.

PAR MDUK 032

Methods	Six-week, randomised, double-blind, double-dummy, parallel-group comparative study
Participants	Male and female patients, aged 18 to 75 years, suffering from reactive or endogenous unipolar depression according to the DSM-III criteria, considered suitable for treatment with anti-depressant drugs, and also having a minimum score of 17 on the first 17 items of the Hamilton rating scale for depression (HDRS-21), were eligible for the inclusion in the study
Interventions	Paroxetine: 29 participants. Amitriptyline: 30 participants. Paroxetine dose range: 20-30 mg/day. Amitriptyline dose range: 100-150 mg/day.
Outcomes	HDRS-21, Physician's Global Assessment of Severity of Illness (PGAS). Total dropout, dropout due to side-effects, dropout due to inefficacy. Number of patients experiencing at least one side effect, side-effect profile
Notes	Funding: paroxetine manufacturer.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: "randomized". No further details.
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double blind". No further details.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double blind". No further details.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Quote: "the main analyses were carried out on the Inten-to-treat (ITT) population using the extender dataset - a dataset that has missing values imputed by Last Observation Carried Forward (LOCF)"

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Selective reporting (reporting bias)	High risk	Continuous outcomes data reported without Standard deviations
Other bias	Unclear risk	Sponsorship bias cannot be ruled out.

Pelicier 1993

Methods	Five-week, multicentre, randomised, double-blind, double-dummy, parallel group, comparative study
Participants	Male and female patients, aged 60 or more, with moderate reactive depression who could be treated as out-patients were eligible for the study. Participants also had to have moderate reactive depression by Feighner's Criteria and the Zung self-rating depressions scale
Interventions	Paroxetine: 51 participants. Clomipramine: 42 participants. Paroxetine dose: 20 mg/day. Clomipramine dose: 60 mg/day.
Outcomes	Montgomery and Asberg Depression Rating Scale (MADRS), Zung Self-rating Depressions Scale (SDS), the Visual Analogue Scale (VAS), Global Assessment Scale (GAS). Total dropout, dropout due to side effects, dropout due to inefficacy. Number of patients experiencing at least one side effect, side-effect profile
Notes	Funding: unclear.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: "subjects were randomized". No further details.
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double blind, double dummy (. ..) placebo tablets were used to maintain blinding"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double blind".
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	No clear information regarding the management of incomplete outcomes data

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Pelicier 1993 (*Continued*)

Selective reporting (reporting bias)	Unclear risk	Outcomes data not clearly reported. Only most frequent adverse effects were reported
Other bias	Unclear risk	Insufficient information to establish the presence of other biases

Perahia 2006 (HMAY B)

Methods	Eight-week, double-blind, randomised multicentre study, followed by a 26-week continuation phase for responders
Participants	Outpatients of at least 18 years of age with a primary diagnosis of major depression as defined by the DSM-IV. Patients were required to have a Hamilton rating scale for depression (HDRS) total score $\geq$15 and a Clinical Global Impression (CGI) Severity total score $\geq$4 at both Visits 1 and 2 No patients with bipolar disorder were included.
Interventions	Duloxetine 40 mg twice daily (80 mg/day): 93 participants. Duloxetine 60 mg twice daily (120 mg/day): 103 participants. Paroxetine 20 mg once daily (20 mg/day): 97 participants. Placebo: 99 participants.
Outcomes	Efficacy: HDRS-17 total score; HDRS-17 response rates (a 50% reduction from baseline to endpoint), and HAMD17 remission rates (endpoint score $\leq$7); Montgomery and Asberg Depression Rating Scale (MADRS), CGI-Severity, Patient Global Impression (PGI) Improvement, Hamilton rating scale for anxiety (HAM-A), Scale for Suicidal Ideation (SSI), and Visual Analogue Scale (VAS) for pain Total dropout, dropout due to inefficiency, dropout due to side effects, number of patients experiencing at least one side effect, side-effect profile
Notes	Funding: duloxetine manufacturer.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: Patients were randomly assigned in a 1:1:1:1 ratio to placebo, duloxetine 80 mg/day, duloxetine 120 mg/day or paroxetine 20 mg/day"
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "The study utilized a double blind, variable duration placebo lead-in at the beginning of the acute phase and a placebo lead out at the end of the continuation

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Perahia 2006 (HMAY B) (*Continued*)

		phase to minimize possible bias in the ratings of efficacy and tolerability associated with patients and investigators knowledge of the onset and conclusion of active drug therapy"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "The study utilized a double blind, variable duration placebo lead-in at the beginning of the acute phase and a placebo lead out at the end of the continuation phase to minimize possible bias in the ratings of efficacy and tolerability associated with patients and investigators knowledge of the onset and conclusion of active drug therapy"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Study endpoint: 11/97 missing from paroxetine group; 23/196 missing from control group
Selective reporting (reporting bias)	High risk	In duloxetine 120 mg/day group only adverse events with an incidence > or = 2.5% were reported
Other bias	Unclear risk	Sponsorship bias cannot be ruled out.

Peselow 1989

Methods	Six-week, single-centre, double-blind, randomised, parallel-group study
Participants	Only moderate to moderately severe depressed patients with a DSM-III diagnosis of major depressive disorder without mania, characterised by disorder of mood with symptoms such as depressed mood, sadness, hopelessness, and worthlessness-were to be admitted to the study. In addition to the DSM-III diagnostic criteria, the participant had to: (1) be al least 18 years old and (2) have Hamilton rating scale for depression (HDRS-21) score at the screen and baseline visits of at least 18 on the first 17 items of the 21-item scale, and the HDRS-21 total could not decrease by 20% or more between the screen and baseline visits, and (3) have a Raskin Depression Scale (RDS) score at baseline of at least 8, and the RDS score had to be higher than the Covi Anxiety Scale score (CAS)
Interventions	Paroxetine: 40 participants. Imipramine: 39 participants. Paroxetine dose: 20-50 mg/day. Imipramine dose: 65-275 mg/day.
Outcomes	HDRS-21, RDS, Clinical Global Impression (CGI) Severity, Improvement, Patients Global Evaluation (PGE). Total dropout, dropout due to side-effects, dropout due to inefficacy. Number of patients experiencing at least one side effect, side-effect profile

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Peselow 1989 (*Continued*)

Notes	Funding: unclear.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "patients were randomized". No further details.
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double blind (...) the subject received two medication bottles and was instructed to take two capsules from the bottle labeled "morning" and one capsule from the bottle labeled "evening"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double blind".
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Quote: "the primary analysis of the study is based on the wee 6 evaluation from the All Efficacy Population using a Last Observation Carried Forward (LOCF) approach" More than 20% of participants in the paroxetine arm withdrew from the study prematurely
Selective reporting (reporting bias)	High risk	Only most frequent adverse effects were reported.
Other bias	Unclear risk	Insufficient information to establish the presence of other biases

Ravindran 1997

Methods	Twelve-week, randomised, double-blind, multicentre, parallel-group study
Participants	Patients with a diagnosis of depression with associated anxiety, suitable for treatment with antidepressant, a Montgomery and Asberg Depression Rating Scale (MADRS) score of at least 20 and a Covi Anxiety Score (CAS) score of at least 11 could qualify for study entry
Interventions	Paroxetine: 513 participants. Clomipramine: 503 participants. Paroxetine dose range: 20-40 mg/day.

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	Clomipramine dose range: 75-150 mg/day. The only concurrent psychotropic medication permitted during active treatment was temazepam, up to 20 mg at night as a hypnotic, on an as-needed basis
Outcomes	MADRS, CAS, Clinical Global Impression (CGI). Total dropout, dropout due to side effects, dropout due to inefficacy. Number of patients experiencing at least one side effect, side-effect profile
Notes	Only side effects occurring in >10% of patients. Funding: paroxetine manufacturer.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Quote: "patients were randomly assigned on the basis of a computer-generated schedule in which treatments were balanced within blocks of consecutive patients to receive double blind treatment with either paroxetine or clomipramine for 12 weeks"
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double blind". No further details.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double blind". No further details.
Incomplete outcome data (attrition bias) All outcomes	High risk	Quote: "endpoint data were generated from the last available on-treatment assessment for each patient. The endpoint for each analysis was taken as the visit at which at least 70% of the Intent-to-treat (ITT) population (randomized patient with at least one valid on-treatment efficacy assessment) remained" More than 20% of participants in both arms withdrew from the study prematurely
Selective reporting (reporting bias)	Low risk	Outcomes data were reported.
Other bias	Unclear risk	Sponsorship bias cannot be ruled out.

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Sacchetti 2002

Methods	Twelve-week, randomised double-blind, double-dummy, parallel-group study
Participants	Adult male and female patients aged between 18 and 70 years were eligible for inclusion if they met DSM-III-R criteria for recurrent major depression, had a total score of 518 on the Hamilton Rating Scale for Depression (HDRS-21) 16 and had scores of one or more for each of the HDRS core symptoms of depressed mood, suicide, insomnia, and retardation. In addition, patients had to have experienced at least one of the following: one or more episodes of affective illness per year for the previous 3 years; three or more episodes of affective illness in the previous 2 years; two or more episodes of affective illness in the previous year Patients were excluded if they had a schizoaffective disorder; had a high risk of suicide, serious concurrent physical disease or abnormal laboratory findings; were pregnant or lactating or likely to become pregnant; were taking certain prescribed medications including oral anticoagulants, non-steroidal anti-inflammatory drugs, diuretics, Type 1C anti-arrhythmics or any investigational drugs; were known to be abusing drugs or alcohol; or had a history of allergic drug reactions. Patients were excluded who had recently received other psychoactive therapy including: electroconvulsive therapy (ECT) in the previous 3 months; depot neuroleptics in the past 4 weeks; oral neuroleptics in the past 2 weeks; monoamine oxidase inhibitors in the past 2 weeks; other prophylactic antidepressant or antiepileptic drugs in the previous 2 weeks. In addition, patients stabilised on lithium therapy in the previous 3 months were excluded
Interventions	Paroxetine: 64 participants. Amitriptyline: 65 participants. Paroxetine dose range: 20-50 mg/day. Amitriptyline dose range: 100-250 mg/day. The only psychotropic medication permitted was temazepam, which could be used as a hypnotic if required
Outcomes	HDRS, Clinical Global Impression (CGI). Total dropout, dropout due to side effects, dropout due to inefficacy. Number of patients experiencing at least one side effect, side-effect profile
Notes	Patients taking essential non-psychotropic medication (unless specifically excluded) which had been started at least one month before study entry were permitted to continue with it throughout,preferably at unchanged dosage

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: "randomized". No further details.
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double blind, double dummy".

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Sacchetti 2002 (*Continued*)

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double blind, double dummy".
Incomplete outcome data (attrition bias) All outcomes	High risk	Quote: the Intention-to-treat (ITT) study endpoint assessment was assessed at the 70% Last Observation Carried Forward (LOCF) endpoint, the latest visit during the acute phase at which at least 70% of patients provided data. For the remaining patients, data were carried forward from the last visit where the relevant measure was recorded. All patients who were randomly allocated to treatment, received their treatment, and for whom at least one assessment was available after taking active treatment, were eligible for inclusion in the ITT population (...) week 5 was the last visit in the acute phase where at least 70% of subjects had efficacy data" More than 20% of participants in both arms withdrew from the study prematurely
Selective reporting (reporting bias)	Low risk	Outcomes data were reported.
Other bias	Unclear risk	Sponsorship bias cannot be ruled out.

SBK-115 1998

Methods	Twelve-week, randomised, double-blind, comparative, placebo-controlled study
Participants	Outpatients >18 years old with moderate to moderately severe depression (DSM: single episode or recurrent). At both the screen visit and baseline the Hamilton rating scale for depression (HDRS-21) had to be at least 18 for the HDRS-21 first 17 items; the could not decrease by more than 25% between screen and baseline visit. The Raskin depression score had to be at least 8 at baseline and must have exceeded the Covi Anxiety Score (CAS) Key exclusion criteria were patients with a primary psychiatric diagnosis other than depression, or those with serious concomitant diseases. Patients were excluded who had a serious suicidal threat, recent ECT or with substance abuse
Interventions	Paroxetine:287 participants. Fluoxetine: 289 participants. Paroxetine dose range: 20-50 mg/day. Fluoxetine dose range: 20-80 mg/day.

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SBK-115 1998 (*Continued*)

Outcomes	HDRS, Clinical Global Impression (CGI), the Raskin Depression score (RDS), CAS. Total dropout, dropout due to side effects, dropout due to inefficacy. Number of patients experiencing at least one side effect, side-effect profile
Notes	Funding: paroxetine manufacturer.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "subjects were randomized". No further details.
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double blind". No further details.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double blind". No further details.
Incomplete outcome data (attrition bias) All outcomes	High risk	Quote: "analyses were performed on the Intention-to-treat (ITT) population, which included all subjects who were randomized to study medication. For the safety analysis, this included the total patient population. The efficacy ITT population (depression, anxiety) only included all randomized patients with at least one on-therapy efficacy evaluation" More than 20% of participants in both arms abandoned the study prematurely
Selective reporting (reporting bias)	Low risk	Outcomes data were reported.
Other bias	Unclear risk	Sponsorship bias cannot be ruled out.

Schatzberg 2002

Methods	Eight-week, double-blind, randomised, comparative trial.
Participants	Patients at least 65 years of age were eligible. Participant in the study were outpatients recruited through advertising, private practices, and routine intake at clinics and other healthcare facilities. At the screening visit, patients were required to satisfy DSM-IV criteria for a single or recurrent major depressive episode, have a Mini-Mental State Exam

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	(MMSE) score above the 25th percentile for age and educational level, and score at least 18 on the Hamilton rating scale for depression (HDRS-17). Patients were excluded if their HDRS score decreased by 20% or more between the screening and baseline visits. Patients with concomitant medical illnesses were eligible for the study if their condition was stable for at least 3 months and they had been receiving standard therapy for the condition for at least 1 month
Interventions	Paroxetine: 126 participants. Mirtazapine: 128 participants. Paroxetine dose range: 10-40 mg/day (mean daily dose: 26.5 [SD 5.5]). Mirtazapine dose range: 15-45 mg/day (mean daily dose: 25.7 [SD 6.7]) Patients were allowed to take chloral hydrate (500mg-1000mg) or zolpidem (5mg-10mg) as needed for sleep induction
Outcomes	HDRS, Clinical Global Impression (CGI). Total dropout, dropout due to side effects, dropout due to inefficacy. Number of patients experiencing at least one side effect, side-effect profile
Notes	Only side effects occurring in >10% of patients. Funding: paroxetine manufacturer.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: "randomized". No further details.
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "study drugs were supplied as identical-appearing capsules of mirtazapine 15 mg and paroxetine 10 mg. Because active treatment would involve fewer capsules of mirtazapine than paroxetine, matching placebo capsules were supplied for use with mirtazapine, to maintain the blind"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double blind".
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Quote: the primary analysis was conducted on the Intent-to-treat (ITT) population, which included all randomized patients who received at least one dose of study medication and at least one post treatment assessment of efficacy. we used a Last Observation Carried Forward (LOCF) analysis (i.

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Schatzberg 2002 (*Continued*)

		e., missing data were replaced by the last recorded value)"
Selective reporting (reporting bias)	High risk	Outcomes data not clearly reported (continuous data not reported, only side effects occurring in at least 10% of participants reported)
Other bias	Unclear risk	Sponsorship bias cannot be ruled out.

Schnyder 1996

Methods	Phase III multicentre, double-blind, randomised, parallel-group study
Participants	Patients were in- or out-patients of either sex, aged 18 to 65 years, had been diagnosed with major depression according to the DSM-III-R criteria, and had a score of at least 18 on the Hamilton rating scale for depression (HDRS-21) on the day before the start of treatment Exclusion criteria were pregnancy or lactation period, severe co-existing physical diseases, MAOI or neuroleptics shortly prior to the study, chronic lithium therapy, intolerance to tricyclic antidepressants, schizophrenia, dementia, or a history of ECT treatment, manic episodes or bipolar disorder. Before entering the study, all patients had to undergo a general medical examination
Interventions	Paroxetine: 37 participants. Maprolitine: 34 participants. Paroxetine dose range: 20-40 mg/day. Maprolitine dose range: 50-150 mg/day. In case of sleep disturbances, the following concurrent medications were permitted: lormetazepam, dipotassium chloracepate, chloral hydrate, diazepam, flurazepam, oxazepam, bromazepam, flunitrazepam and zolpidem
Outcomes	HDRS, Montgomery and Asberg Depression Rating Scale (MADRS), Clinical Global Impression (CGI). Total dropout, dropout due to side effects, dropout due to inefficacy. Number of patients experiencing at least one side effect, side-effect profile
Notes	Reasons for withdrawal were reported. Funding: paroxetine manufacturer.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: "patients were randomly assigned to treatment".
Allocation concealment (selection bias)	Unclear risk	No information provided.

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Schnyder 1996 (*Continued*)

Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double-blind study". No further details.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double-blind study". No further details.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	No clear information about data analysis.
Selective reporting (reporting bias)	High risk	Rating scales scores at follow-up assessments were not clearly reported. The denominators (for continuous outcomes) were unclear
Other bias	Unclear risk	Sponsorship bias cannot be ruled out.

Sechter 2004

Methods	Double-blind, randomised controlled study conducted in 42 European centres
Participants	Outpatients meeting DSM-IV criteria for unipolar major depression, without psychotic features, with Montgomery and Asberg Depression Rating Scale (MADRS) total score >20, aged 18-70 years, were included in the study. Patients with a significant suicide risk, a lack of response to two adequate antidepressant treatments, a history of psychotic disorder, a major personality disorder, a current primary diagnosis of panic disorder, agoraphobia, social phobia, or obsessive compulsive disorder, current alcohol or drug abuse or dependence, were excluded
Interventions	Paroxetine: 153 participants. Milnacipran: 149 participants. Patients were randomized to receive milnacipran 100 mg/day (50 mg bid) or paroxetine 20 mg/day (20 mg od) for 6 weeks
Outcomes	Patients were evaluated at inclusion and on Day 7; 14; 28; 42; with a post-treatment assessment 7 days after treatment discontinuation. The Hamilton rating scale for depression (HDRS-17) total score, the MADRS total score, the Clinical Global Impression (CGI) for severity of illness and global improvement from Day 0 were determined at each visit Total dropout, dropout due to side effects, dropout due to inefficacy. Number of patients experiencing at least one side effect, side-effect profile
Notes	Only events reported more than once were included. Funding: milnacipran manufacturer.

Risk of bias

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Sechter 2004 (*Continued*)

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "randomized (...) patients were randomized".
Allocation concealment (selection bias)	Unclear risk	no information provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double blind". No further details.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double blind". No further details.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Quote: "data were analyzed on an Intention-to-treat (ITT) basis with Last Observation Carried Forward (LOCF)"
Selective reporting (reporting bias)	High risk	Continuous outcomes data were reported without Standard deviations
Other bias	Unclear risk	Sponsorship bias cannot be ruled out.

SER-CHN-1

Methods	Double-blind randomised comparative control study.
Participants	Inclusion criteria: after 1 week placebo single blind wash out, only patients with Hamilton rating scale for depression (HDRS) score of 18 or more, or total score decreased less than 20% at baseline were enrolled. Male and female patients aged 18-65 years who met the diagnostic criteria for depression on DSM-III-R and Chinese Classification of Mental Disease Exlusion criteria: Patients with severe renal disease, severe cardiac disease, active thyroid disease, severe gastrointestinal or hepatic disease, unstable diabetes, Addison's disease, severe neurological diseases including Parkinsonism and organic brain pathology, rapid and cycling type of depression, epilepsy, schizophrenia or psychosis. Patients who have received ECT in the previous 12 weeks, lithium in the previous 4 weeks, oral neuroleptics in the previous 2 weeks or depot neuroleptics in the previous 4 weeks, MAOIs in the previous 2 weeks, investigational drugs in the previous 12 weeks, SSRIs in the previous 4-5 weeks
Interventions	Paroxetine: 113 participants. Amitriptyline: 118 participants. Paroxetine dose range: 20-30 mg/day. Amitriptyline dose: 150 mg/day.

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SER-CHN-1 (*Continued*)

Outcomes	HDRS, Hamilton rating scale for anxiety (HAM-A), Clinical Global Impression (CGI). Total dropout, dropout due to side effects, dropout due to inefficacy. Number of patients experiencing at least one side effect, side-effect profile
Notes	Funding: paroxetine manufacturer.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "randomized study". No further details.
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double blind". No further details.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double blind". No further details.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "Intention-to-treat (ITT) population consisted of all subjects who received treatment and had one post treatment evaluation" Less than 20% of participants in both arms withdrew from the study prematurely
Selective reporting (reporting bias)	High risk	Outcomes data not clearly reported.
Other bias	Unclear risk	Sponsorship bias cannot be ruled out.

Shillingford 1990

Methods	Six-week, randomised, double-blind study.
Participants	Patients with major depressive episode according to DSM III criteria, in general practice setting
Interventions	Paroxetine versus dothiepin.
Outcomes	Efficacy and tolerability.
Notes	None.

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Shillingford 1990 (*Continued*)

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: "randomized". No further details.
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double blind". No further details.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double blind". No further details.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	No information on incomplete outcome data management.
Selective reporting (reporting bias)	Unclear risk	No information provided.
Other bias	Unclear risk	Insufficient information to establish the presence of other biases

Shinkai 2004

Methods	Four-week, randomised, double-blind study.
Participants	Inpatients with DSM-IV major depressive disorder without psychotic features with a minimum score of 15 on the Hamilton rating scale for depression (HDRS). Age range: 20-78 years.
Interventions	Paroxetine: 21 participants. Milnacipram: 20 participants. Paroxetine mean dose: 34.28 mg. Milnacipran mean dose: 80.25 mg. No other drugs were administered throughout the study with the exception of a few patients who received benzodiazepines for insomnia
Outcomes	HDRS-17.
Notes	Funding: independent from industry.

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

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Shinkai 2004 (*Continued*)

Random sequence generation (selection bias)	Low risk	Quote: "randomly divided into either milnacipran or the paroxetine group using StatView, a computerized statistical package"
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double blind". No further details.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double blind". No further details.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Study endpoint: 1/21 missing from paroxetine group, 0/20 missing from control group
Selective reporting (reporting bias)	High risk	Adverse events were not reported so that could not be entered in to the meta-analysis
Other bias	Low risk	This study was independent from pharmaceutical industry.

Shrivastava 1992

Methods	Six-week, randomised, double-blind study.
Participants	Outpatients of at least 18 years of age with a primary diagnosis of major depression as defined by the DSM-III. Patients were required to have a Hamilton rating scale for depression (HDRS-17) total score $\geq$18
Interventions	Paroxetine: 40 participants. Imipramine: 40 participants. Placebo: 40 participants. Paroxetine dose range: 10-50 mg/day. Imipramine dose range: 65-275 mg/day. 500-mg dose of chloral hydrate was permitted for treatment of insomnia
Outcomes	HDRS-21. Total dropout, dropout due to inefficiency, dropout due to side effects, number of patients experiencing at least one side effect, side-effect profile
Notes	Funding: paroxetine manufacturer.
Risk of bias	

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Shrivastava 1992 (*Continued*)

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "randomized". No further details.
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "After randomization to double blind treatment at a baseline visit, the subject received two medication bottles and was instructed to take two capsules from the bottle labeled "morning" (each capsule 10 mg paroxetine, 15 mg imipramine or placebo) and one from the bottle labeled "evening" (each capsule 50 mg imipramine or placebo)"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double blind".
Incomplete outcome data (attrition bias) All outcomes	High risk	Study endpoint: "16/40 missing from Paroxetine group, 30/40 missing from Imipramine group"
Selective reporting (reporting bias)	High risk	Response and remission rates not reported. On the published paper adverse events reported only if occurring with frequency > or = 20%
Other bias	Unclear risk	Sponsorship bias cannot be ruled out.

Staner 1995

Methods	Four-week, double-blind, parallel-group trial.
Participants	Inclusion criteria: RDC major depression, Hamilton rating scale for depression (HDRS-21) of 18+. Exclusion criteria: pregnant or lactating women; patients with severe concomitant disease; schizophrenics, known abusers of alcohol or illicit drugs; those who had received ECT in the previous 3 months, MAOIs or oral neuroleptics in the previous 14 days and/or depot neuroleptics in the previous 4 weeks Age: 18-65 years. Country: Belgium. Setting: inpatients.

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Staner 1995 (*Continued*)

Interventions	Paroxetine: 21 participants. Amitriptyline: 19 participants. Paroxetine dose range: 20-30 mg/day. Amitriptyline dose range: 100-150 mg/day.
Outcomes	HDRS. Total dropout, dropout due to side effects, dropout due to inefficacy. Number of patients experiencing at least one side effect, side-effect profile
Notes	Only the most common side effects were reported. Funding: paroxetine manufacturer.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: "patients were randomized". No further details.
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: double blind". No further details.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "double blind". The evaluation of sleep (sleep EEG changes during antidepressant treatment was the primary outcome) consisted in sleep recording. Records were scored blind to group membership (paroxetine and amitriptyline)
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Quote: "for the evaluation of the antidepressant effect, the Intention-to-treat (ITT) population extended or Last Observation Carried Forward (LOCF) dataset was used"
Selective reporting (reporting bias)	Low risk	Outcomes data were reported.
Other bias	Unclear risk	Sponsorship bias cannot be ruled out.

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Steinmeyer 1992

Methods	Six-week, double-blind, randomised study.
Participants	The inclusion criteria were: a diagnosis of a major depressive disorder according to DSM-III, a score of 18 or more on the Hamilton rating scale for depression (HDRS-21) and the status of inpatients All patients with an organic illness, a psychosis, psychosomatic disorder, addiction, or severe suicidal tendencies had to be excluded
Interventions	Paroxetine: 112 participants Amitriptyline: 110 participants Paroxetine dose: 30 mg/day Amitriptyline dose: 150 mg/day Additional psychopharmacological treatment was not allowed, apart from temazepam in case of sleep disturbance
Outcomes	The main efficacy measures were: HDRS, Clinical Global Impression (CGI). In addition, the subfactors of the HDRS were taken into consideration. Safety and tolerance were assessed from spontaneous adverse-event reports, a standardised symptom checklist, laboratory data, physical examination, and vital signs". Total dropout, dropout due to side effects, dropout due to inefficacy
Notes	Funding: independent from industry.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: "patients were randomly allocated". No further details
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double blind". No further details.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double blind". No further details.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	No clear information on incomplete outcome data management.
Selective reporting (reporting bias)	High risk	Only side effects experienced by more than 10% of participants reported (only in figure)

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Steinmeyer 1992 (*Continued*)

Other bias	Low risk	This study was independent from pharmaceutical industry.

Stott 1993

Methods	Eight-week, double-blind study.
Participants	Inclusion criteria: patients with depression and anxiety, Montgomery and Asberg Depression Rating Scale (MADRS) 16+, Covi Anxiety Score (CAS) 11+. Age range: 18-65 years. Country: UK. Setting: family practice.
Interventions	Paroxetine: 243 participants. Amitriptyline: 262 participants. Paroxetine: 20 mg/day. Amitriptyline: 25-75 mg/day.
Outcomes	MADRS, CAS, adverse events.
Notes	Outcomes data not available.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Randomised.
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double blind". No further details.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double blind". No further details.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Quote "patients (...) were evaluated on an Intention-to-treat basis"
Selective reporting (reporting bias)	High risk	Outcomes data not available.
Other bias	Unclear risk	Sponsorship bias cannot be ruled out.

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Stuppaeck 1994

Methods	Six-week, randomised, double-blind study.
Participants	Inclusion criteria: DSM III major depression, melancholic subtype, Hamilton rating scale for depression (HDRS) 18+ Exclusion criteria: senile dementia (DSM-III) alcohol or drug addiction, patients with a high risk for suicide, or ECT during the last 3 months, as well as relevant somatic diseases. Patients were also excluded if they received long-term treatment with lithium. Age: 18-65 years. Country: Austria, Germany. Setting: inpatients.
Interventions	Paroxetine: 78 participants. Amitriptyline: 75 participants. Paroxetine dose range: 20-50 mg/day (mean daily dose: 33.3). Amitriptyline dose range: 50-250 mg/day (mean daily dose: 166)
Outcomes	Montgomery and Asberg Depression Rating Scale (MADRS), Clinical Global Impression (CGI). Total dropout. Number of patients experiencing at least one side effect, side-effect profile
Notes	Funding: paroxetine manufacturer. quality rating: 21

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: patients were randomly allocated". No further details
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "double blind (...) paroxetine was administered as a single daily dose in the morning, whereas amitriptyline was given each morning, noon, and evening. Patients in the paroxetine group received matching placebo tablets at noon and in the evening"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double blind".
Incomplete outcome data (attrition bias) All outcomes	High risk	Quote: "analyses were performed on the Intention-to-treat (ITT) population with the Last Observation Carried Forward (LOCF) and visit wise datasets" More than 20% of participants in both arms abandoned the study prematurely

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Stuppaeck 1994 (*Continued*)

Selective reporting (reporting bias)	High risk	Only most frequent adverse effects reported.
Other bias	Unclear risk	Sponsorship bias cannot be ruled out.

Szegedi 1995

Methods	Randomised, multicentre, parallel-group, double- blind clinical trial in depressed outpatients
Participants	Age range: 18-71 years. Exclusion criteria were requirement of hospitalisation, presence of psychotic symptoms, acute risk of suicidality or severe existing physical disease, pregnancy or lactation, or the need of additional benzodiazepine treatment
Interventions	Paroxetine: 145 participants. Maprolitine: 153 participants. Paroxetine dose range: 20-40 mg/day. Maprolitine dose range: 100-150 mg/day.
Outcomes	Hamilton rating scale for depression (HDRS), Clinical Global Impression (CGI), Montgomery and Asberg Depression Rating Scale (MADRS), Hamilton rating scale for anxiety (HAM-A), Bech-Rafaelsen Mania Scale (BRMS), Raskin Depression score (RDS), Covi Anxiety Score (CAS)
Notes	Funding: unclear. The study population includes subjects with diagnoses of major and minor depression. According to the protocol of this review, only data referring to patients with major depression were considered

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: "randomized". No further details.
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double blind (...) a double dummy design was used". No further details
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double blind (...) a double dummy design was used". No further details

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Szegedi 1995 (*Continued*)

Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Quote: "for all patients receiving active medication an Intention-to-treat (ITT) analysis was performed using the Last Observation Carried Forward (LOCF) method"
Selective reporting (reporting bias)	High risk	Only most often experienced adverse effects reported.
Other bias	Unclear risk	Sponsorship bias cannot be ruled out.

Szegedi 2005

Methods	Double-blind, double-dummy, randomised, phase III trial.
Participants	All participants were 18-70 years old and had single or recurrent moderate or severe episodes of unipolar major depression without psychotic features (DSM-IV) persisting for two weeks to a year. At screening and baseline all participants had to have a total score $\geq$ 22 points on the Hamilton rating scale for depression (HDRS-17) and $\geq$ 2 points for the item "depressive mood." The diagnosis of depression was based on the mini-international neuropsychiatric interview. There were no restrictions regarding ethnic group. We excluded anyone with a decrease in total depression score of $\geq$ 25% during the run-in, or with a diagnosis of schizophrenia, acute anxiety disorder, adjustment disorder, depressive disorder of any type not stated above, bipolar disorder, organic mental disorder, acute post-traumatic stress disorder, or substance abuse disorder. We also excluded patients with increased risk of suicide (defined by a score $\geq$ 4 for item 10 of the Montgomery and Asberg Depression Rating Scale (MADRS), who had previously attempted suicide, or who had not responded to more than one adequate treatment (equivalent to 150 mg/day amitriptyline for $\geq$ 6 weeks) in the present episode
Interventions	Paroxetine: 126 participants. Hypericum: 125 participants. Paroxetine dose range: 20-40 mg/day. Hypericum dose range: 15-45 mg/day.
Outcomes	HDRS, MADRS, Clinical Global Impression (CGI). Total dropout, dropout due to side-effects, dropout due to inefficacy. Number of patients experiencing at least one side effect, side-effect profile
Notes	Funding: hypericum manufacturer.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Quote: "randomized (...) randomization was performed in blocks stratified by trial

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		centre. A biometrician otherwise not involved in the trial generated the code using a validated computer program. The study drugs were dispensed to the centres in numbered containers"
Allocation concealment (selection bias)	Low risk	Quote: "On inclusion of a patient into randomized treatment the local investigator allocated each participants the lowest available number. The block size was withheld from the investigators"
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "double blind, double dummy (...) coated tables; high and low dose tablets were indistinguishable in all aspects of their outward appearance. For each drug an identically matched placebo was available (the success of blinding was evaluated by examining the drugs before distribution). During the six weeks randomized treatment patients allocated to hypericum always took three coated tablets of hypericum/day plus one paroxetine placebo capsule in the morning whereas those in the paroxetine group took one capsule of paroxetine in the morning and three coated tables of hypericum placebo/day"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double blind, double dummy".
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Quote: "the primary analysis was based on the Intention-to-treat (ITT) analysis to mirror clinical practice. we also performed as per protocol (PP) analysis to demonstrate robustness of the trial result to the choice of the analysis set" More than 20% of participants in the paroxetine arm abandoned the study prematurely
Selective reporting (reporting bias)	High risk	Only adverse effects that occurred in at least 10 patients in one group reported
Other bias	Unclear risk	Sponsorship bias cannot be ruled out.

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Tignol 1993

Methods	Multicentre, randomised, double-blind, double-dummy, parallel group, comparative study
Participants	Inclusion criteria: patients meeting criteria for Major depression (DSM-III); patients with Montgomery and Asberg Depression Rating Scale (MADRS) score of >24 Age range 18-65 years. Exclusion criteria: subjects with severe risk of suicide; patients who were schizophrenic or psychotic; patients who had received 1 or more specified psychiatric drugs prior to the study
Interventions	Paroxetine: 89 participants. Fluoxetine: 87 participants. Paroxetine dose: 20 mg/day. Fluoxetine dose: 20 mg/day.
Outcomes	MADRS, Clinical Global Impression (CGI), Hamilton rating scale for anxiety (HAM-A), Hospital Anxiety and Depression (HAD).Total dropout, dropout due to side effects, dropout due to inefficacy. Number of patients experiencing at least one side effect, side-effect profile
Notes	Funding: paroxetine manufacturer.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: "eligible patients were randomized".
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double blind". No further details.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double blind". No further details.
Incomplete outcome data (attrition bias) All outcomes	High risk	Quote: "the Intent-to-treat (ITT) population comprised all subjects who received at least one dose of randomized active treatment and who had at least one post-treatment assessment" More than 20% of participants in both arms abandoned the study prematurely
Selective reporting (reporting bias)	Unclear risk	Only endpoint outcomes data were reported.

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Tignol 1993 (*Continued*)

Other bias	Unclear risk	Sponsorship bias cannot be ruled out.

Wade 2003

Methods	Twenty-four-week, prospective, multicentre, randomised, double-blind study
Participants	Male and female patients who were at least 18 years old, fulfilling DSM-IV criteria for a single or recurrent depressive episode according to the DSM-IV checklist, with a total baseline score > 18 on the Hamilton rating scale for depression (HDRS-17) and who provided their written informed consent were eligible for participation in the study. Patients were excluded if they were suffering from schizophrenia or bipolar affective disorder, were suicidal, or were diagnosed with current illicit drugs abuse or alcohol dependence. Treatment with any other psychotropic drug, including any anxiolytic or hypnotic within 1 week before entry to the study, with mirtazapine or paroxetine during the present episode or hypersensitivity to either compound, with fluoxetine within 5 weeks, or with any other antidepressant within 2 weeks of entry, prohibited inclusion. In addition, patients of both sexes were not eligible if they had any clinically meaningful renal, hepatic, respiratory, cardiovascular or cerebrovascular disease. Pregnant or lactating women and those of childbearing age not employing any adequate contraception were also excluded
Interventions	Paroxetine: 98 participants. Mirtazapine: 99 participants. Paroxetine dose range: 20-30 mg/day (mean daily dose: 23.9 [SD 3.96]). Mirtazapine dose range: 30-45 mg/day (mean daily dose: 34.6 [SD 5.7]) Use of any psychotropic concomitant drug, including anxiolytics (benzodiazepines) and hypnotics was prohibited during the study
Outcomes	HDRS-17, Clinical Global Impression (CGI). Total dropout, dropout due to side effects, dropout due to inefficacy. Number of patients experiencing at least one side effect, side-effect profile
Notes	Only side effects occurring in >5% of patients in either groups Funding: mirtazapine manufacturer.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Quote: "randomization was performed according to centrally prepared randomization lists"
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "double blind oral treatment with either drug, prepared as indistinguishable-looking capsules containing 15 mg mir-

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Wade 2003 (*Continued*)

		tazapine or 10 mg paroxetine"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double blind".
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Quote: "efficacy analyses were based on the Intention-to-treat (ITT) sample, thus including all randomly assigned subjects who received at least one dose of blinded study medication, and who had at least one post-dose efficacy assessment. The primary inferences concerning efficacy were made using the Last Observation Carried Forward (LOCF) method at endpoint. Additional Observed Case (OC) analysis was used at the week 24 assessment to ensure robustness of the LOCF results and at other visits (for the primary efficacy variable only) to determine effect of treatment. Tolerability assessments were performed on All Subjects Treated (AST) group, consisting of all randomized patients who took at least one dose of blinded medication" More than 20% of participants in both arms abandoned the study prematurely
Selective reporting (reporting bias)	High risk	Outcomes data not clearly reported. Only side effects experienced by > or = 5% of participants were reported
Other bias	Unclear risk	Sponsorship bias cannot be ruled out.

Waintraub 2002

Methods	Three-month controlled, randomised, double-blind, clinical trial
Participants	Male and female patients aged 18 to 60 years who met, according to the investigator, the DSM-IV criteria for a major depressive episode of moderate or severe intensity were included. Patients had to have a total Montgomery and Asberg Depression Rating Scale (MADRS) score $\geq$20, a total Hamilton rating scale for depression (HDRS) score $\geq$18, a MADRS item 10 score (suicidal thoughts) $\leq$2, and a HDRS item 3 score (suicide) $\leq$1. Patients with significant physical illness or epilepsy, or who were pregnant or drug abusers were excluded, as were patients who were currently being treated with barbiturates, thymoregulators, antipsychotics, electroconvulsive therapy, or other antidepressant treatments during 7 days prior to the start of the trial. Other exclusion criteria were anxiety disorders, acute or chronic psychoses, or neurodegenerative diseases

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Interventions	Paroxetine: 139 participants. Tianeptine: 138 participants. Paroxetine dose range: 20-40 mg/day. Tianeptine dose range: 37,5-75 mg/day. If clinically required, bromazepam (maximal dosage 9 mg/day) and zopiclone (maximal dosage 7.5 mg/day) could be prescribed
Outcomes	MADRS, HDRS, Clinical Global Impression (CGI). Total dropout. Number of patients experiencing at least one side effect, side-effect profile
Notes	Funding: tianeptine manufacturer.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: "patients were randomly allocated".
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double blind conditions". No further details.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double blind conditions". No further details.
Incomplete outcome data (attrition bias) All outcomes	High risk	Quote: "the efficacy analysis was performed both on the full analysis set (FAS), which is a 'complete as possible' and a 'close as possible' to the Intention-to-treat (ITT) ideal of including all randomized subjects, and on the per protocol (PP) populations. The safety analysis was performed on all patients who received at least one dose of the study drug (...) Seven patients with no data inclusion visit were excluded from the randomized population" Dropout not clearly reported.
Selective reporting (reporting bias)	High risk	Dropout not clearly reported.
Other bias	Unclear risk	Sponsorship bias cannot be ruled out.

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Weihs 2000

Methods	Six-week randomised, double-blind, double-dummy, parallel-group, active-treatment phase
Participants	Men and women 60 years of age and older with a minimum baseline score of 18 on theHamilton rating scale for depression (HDRS-21) who presented with a recurrent episode of nonpsychotic major depressive disorder (DSM-IV) with a duration of at least 8 weeks, but not more than 24 months, and who were considered clinically appropriate for treatment with either bupropion SR or paroxetine were eligible for the study. Patients who had a known predisposition to seizures were excluded from the study. Patients taking medications or treatments that lower the seizure threshold were also excluded. Patients were excluded if they were actively suicidal, had a history or current diagnosis of anorexia nervosa or bulimia nervosa, had an unstable medical disorder, or had a history of non-responsiveness to pharmacotherapy for depression. Patients were also excluded if they had a history of alcohol or substance abuse within 1 year prior to the study or myocardial infarction, uncontrolled hypertension, or unstable heart disease within 6 months prior to the study
Interventions	Paroxetine: 52 participants. Bupropion: 48 participants. Paroxetine dose range: 10-40 mg/day (mean daily dose: 22 [SD 7]). Bupropion: dose range: 100-300 mg/day.(mean daily dose: 197 [SD 53])
Outcomes	HDRS, Clinical Global Impression (CGI), Hamilton rating scale for anxiety (HAM-A) . Total dropout, dropout due to side effects. Side-effect profile
Notes	Funding: paroxetine manufacturer.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: "Of the 100 patients enrolled in the study, 48 were randomly assigned to treatment with bupropion SR and 52 were randomly assigned to treatment with paroxetine."
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double blind, double dummy".
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double blind, double dummy".
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "all patients who received at least one dose of study medication and com-

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Weihs 2000 (*Continued*)

		pleted one or more treatment-phase efficacy assessments beyond baseline were included in the efficacy analyses (Intent-to-treat ITT population). Both Observed and Last Observation Carried Forward (LOCF) scores were analyzed" Less than 20% of participants in both arms abandoned the study prematurely
Selective reporting (reporting bias)	Low risk	Outcomes data were reported.
Other bias	Unclear risk	Sponsorship bias cannot be ruled out.

Yoshimura 2007

Methods	Eight-week, randomised study.
Participants	In- or out-patients who met the DSM-IV-TR criteria for major depressive disorder (MDD) without psychotic features and who scored at least 16 on the Hamilton Rating Scale for Depression (HDRS). Fifteen patients were male and 27 were female. The age of the participants ranged from 28 to 74 years old
Interventions	Paroxetine: 21 participants. Milnacipran: 21 participants. Paroxetine dose range: 10-40 mg/day (mean: 31; SD: 13). Milnacipran dose range: 25-150 mg/day (mean 83; SD: 31).
Outcomes	Serum brain-derived neurotrophic factor (BDNF); HDRS.
Notes	Sponsorship bias cannot be ruled out.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Quote: "the patients were randomly divided into either a paroxetine group or a milnacipran group using StatView, a computerized statistical package"
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No information provided.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No information provided.

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Yoshimura 2007 (*Continued*)

Incomplete outcome data (attrition bias) All outcomes	Unclear risk	No information on incomplete outcome data management.
Selective reporting (reporting bias)	Low risk	Outcomes data were reported.
Other bias	Unclear risk	Sponsorship bias cannot be ruled out.

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

Study	Reason for exclusion
Arminen 1992	More than 20% of bipolars included in this study.
Benkert 1997	Not a relevant diagnostic status and study design.
Bird 2000	Not a relevant diagnostic status (comorbidity with other disorders)
Cocchi 1997	Not a relevant diagnostic status (comorbidity with alcohol dependence)
Ferrando 1997	Not a relevant diagnostic status (comorbidity with other disorders)
Gulseren 2005	Not a relevant diagnostic status (comorbidity with other disorders)
Hazleman 1997	Not a relevant diagnostic status (comorbidity with other disorders)
Katona 1998	Not a relevant diagnostic status (comorbidity with dementia)
Poirier 1997	Patients with treatment resistant depression.
Rapaport 2003	Wrong design (no active comparator).
Sacchetti 1997	Patients with treatment resistant depression.
SAD-PD 2004	Not a relevant diagnostic status (comorbidity with other disorders)
Zanardi 1996	More than 20% of people with bipolar included in this study.

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

29060/III/83/12

Methods	Six-week double-blind, double-dummy, randomised study.
Participants	Paroxetine: 19 participants. Mianserin: 16 participants. Placebo: 10 participants.
Interventions	Paroxetine: 30 mg/day. Mianserin: 30-90 mg/day. Placebo.
Outcomes	Hamilton rating scale for depression (HDRS), Global Assessment and Final Assessment of efficacy and tolerance
Notes	Funding: probably by industry.

Ballus 1997

Methods	Twenty-four-week double-blind, randomised study.
Participants	Paroxetine: 43 participants. Venlafaxine: 41 participants.
Interventions	Paroxetine: 20-40 mg/day. Venlafaxine: 75-150 mg/day.
Outcomes	Hamilton rating scale for depression (HDRS), Clinical Global Impression (CGI), Montgomery and Asberg Depression Rating Scale (MADRS)
Notes	Unclear diagnosis.

Benattia 2004

Methods	Randomised, double-blind, multicentre study.
Participants	Paroxetine: 39 participants. Mianserin: 34 participants.
Interventions	Paroxetine: 30 mg/day. Mianserin: 60 mg/day.
Outcomes	Hamilton rating scale for depression (HDRS), dropout.
Notes	The number of bipolar participants was unclear.

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Blackwell 1967

Methods	Unclear.
Participants	Unclear.
Interventions	Psychotropic drugs.
Outcomes	Unclear.
Notes	No abstract available.

Chen 2001

Methods	Controlled study. Unclear design.
Participants	Patients with depression.
Interventions	Venlafaxine and paroxetine.
Outcomes	Unclear.
Notes	Unclear study design; waiting for translation from Chinese to English

Deuschle 2003

Methods	Double-blind study.
Participants	A total of 126 adult inpatients were included in this study.
Interventions	Paroxetine: 40 mg/day. Amitriptyline: 150 mg/day.
Outcomes	Saliva cortisol concentrations, Hamilton rating scale for depression (HDRS)
Notes	Unclear study design.

Feng 2005

Methods	Comparative study. Unclear design.
Participants	Patients with depression.
Interventions	Paroxetine and clomipramine.
Outcomes	Unclear outcomes.
Notes	Waiting for translation from Chinese to English.

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Geiger 1998

Methods	Randomised, open-label, multicentre trial.
Participants	Paroxetine: 176 participants. Fluoxetine: 322 participants. Nortriptyline: 79 participants.
Interventions	Paroxetine: 20-30 mg/day. Fluoxetine: unclear. Nortriptyline: unclear.
Outcomes	Hamilton rating scale for depression (HDRS), Clinical Global Impression (CGI)
Notes	Funding: unclear. Waiting for data from study authors.

Gonul 1999

Methods	Randomised, single blind study.
Participants	Fluoxetine: number of randomised unclear. Paroxetine: number of randomised unclear. Setraline: number of randomised unclear. Flovoxamine: number of randomised unclear.
Interventions	Fluoxetine: 20 mg/day. Paroxetine: 20 mg/day. Setraline: 50 mg/day. Flovoxamine: 150 mg/day.
Outcomes	Hamilton rating scale for depression (HDRS), dropout.
Notes	Funding: unclear.

Gou 2002

Methods	A clinical control study. Unclear design.
Participants	Patients with depression.
Interventions	Paroxetine and venlafaxine.
Outcomes	Unclear.
Notes	Waiting for translation from Chinese to English.

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Guan 2001

Methods	Unclear study design.
Participants	Patients with depression.
Interventions	Sertraline, fluoxetine and paroxetine.
Outcomes	Quality of life and cost of treatment.
Notes	Waiting for translation from Chinese to English.

Gurovich 1997

Methods	Six-week, parallel group study.
Participants	Toatal number of participants: 150 outpatients.
Interventions	Amitriptyline; Fluoxetine; Paroxetine; Sertraline; Tianeptine
Outcomes	Hamilton rating scale for depression (HDRS).
Notes	Unclear study design.

Han 2004

Methods	A controlled study. Unclear design.
Participants	Patients with depression.
Interventions	Trazodone and paroxetine.
Outcomes	Unclear.
Notes	Waiting for translation from Chinese to English.

Hang 2005

Methods	A comparative study.
Participants	Patients with depression.
Interventions	Mirtazapine and paroxetine.
Outcomes	Unclear.
Notes	Waiting for translation from Chinese to English.

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Henning 2002

Methods	Parallel group study.
Participants	Paroxetine: 23 participants. Amitriptyline: 17 participants.
Interventions	Paroxetine: 40 mg/day. Amitriptyline: 150 mg/day.
Outcomes	Peripheral Nervous System functions.
Notes	Unclear study design.

Huang 2006

Methods	Control study. Unclear design.
Participants	Patients with depression.
Interventions	Paroxetine and imipramine.
Outcomes	Unclear.
Notes	Waiting for translation from Chinese to English.

Jakitowicz 2000

Methods	Parallel group study.
Participants	Paroxetine: 14 participants. Tianeptine: 16 participants.
Interventions	Paroxetine: 20-50 mg/day. Tianeptine: 37.5 mg/day.
Outcomes	EEG profile, Clinical Global Impression (CGI).
Notes	Funding: unclear.

Lemoine 1998

Methods	Eight-week, randomised, double-blind study.
Participants	Toatal number of participants: 173 outpatients.
Interventions	Nefazodone, paroxetine.

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Lemoine 1998 (*Continued*)

Outcomes	Hamilton rating scale for depression (HDRS), Clinical Global Impression (CGI) - Improvement
Notes	Funding: unclear. Waiting for data from study authors.

Li 2001

Methods	A contrast study. Unclear design.
Participants	Patients with depression.
Interventions	Paroxetine and amitriptyline.
Outcomes	Unclear.
Notes	Waiting for translation from Chinese to English.

Li 2003

Methods	A comparative study. Unclear design.
Participants	Patients with depression.
Interventions	Paroxetine and amitriptyline.
Outcomes	Unclear.
Notes	Waiting for translation from Chinese to English.

Li 2004

Methods	Eight-weeks, randomised study.
Participants	Patients with depression.
Interventions	Paroxetine and venlafaxine.
Outcomes	Efficacy (HDRS) and side effects.
Notes	Waiting for translation from Chinese to English.

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Li 2006

Methods	A comparative study. Unclear design.
Participants	Patients with depression.
Interventions	Citalopram and paroxetine.
Outcomes	Unclear.
Notes	Waiting for translation from Chinese to English.

Liao 2002

Methods	Unclear design.
Participants	Patients with depression.
Interventions	Fluoxetine, paroxetine, and venlafaxine.
Outcomes	Pharmcy-economic evaluation.
Notes	Waiting for translation from Chinese to English.

Liu 2002

Methods	A comparative study. Unclear design.
Participants	Patients with senile melancholia.
Interventions	Paroxetine and amitriptyline.
Outcomes	Unclear.
Notes	Waiting for translation from Chinese to English.

Liu 2005

Methods	A comparative study. Unclear design.
Participants	Patients with depression.
Interventions	Venlafaxine and paroxetine.
Outcomes	Unclear.
Notes	Waiting for translation from Chinese to English.

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Ma 2000

Methods	Clinical comparative study. Unclear design.
Participants	Patients with depression.
Interventions	Study on paroxetine (8 comparators unclear).
Outcomes	Unclear.
Notes	Waiting for translation from Chinese to English.

Mertens 1988

Methods	Randomised, open-label study.
Participants	Outpatients with major depression.
Interventions	Paroxetine, fluoxetine, venlafaxine, citalopram, sertraline.
Outcomes	Hamilton rating scale for depression (HDRS).
Notes	Pooled data.

Montoya 1998

Methods	Six-week, randomised, double-blind study.
Participants	Toatal number of participants: 38 outpatients.
Interventions	Imipramine, paroxetine.
Outcomes	Sexual functioning, dropout.
Notes	Funding: unclear. Waiting for data from study authors.

Peng 2004a

Methods	A comparative study. Unclear design.
Participants	Depressed patients.
Interventions	Mirtazapine and paroxetine.
Outcomes	Unclear.
Notes	Waiting for translation from Chinese to English.

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Peng 2004b

Methods	A comparative study. Unclear design.
Participants	Depressed patients.
Interventions	Tianeptine and paroxetine.
Outcomes	Unclear.
Notes	Waiting for translation from Chinese to English.

Qiao 2005

Methods	A comparative study. Unclear design.
Participants	Depressed patients.
Interventions	Citalopram and paroxetine.
Outcomes	Unclear.
Notes	Waiting for translation from Chinese to English.

R228060 2004

Methods	Six-week, randomised, double-blind study.
Participants	Toatal number of participants: 688 outpatients.
Interventions	R228060, paroxetine, placebo.
Outcomes	Unclear.
Notes	Funding: by industry.

Ren 2004

Methods	A comparative study. Unclear design.
Participants	Depressed patients.
Interventions	Mirtazapine and paroxetine.
Outcomes	Unclear.
Notes	Waiting for translation from Chinese to English.

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Salzman 1993

Methods	Thirteen-week, parallel group study.
Participants	Outpatients with major depression.
Interventions	Fluoxetine, paroxetine, placebo.
Outcomes	Prolactin levels, tryptophan levels, neutral amino acids levels
Notes	Unclear study design.

Serretti 2001

Methods	Six-week, double-blind study.
Participants	Patients with major and bipolar depression.
Interventions	Paroxetine, fluvoxamine and either placebo or pindolol.
Outcomes	Hamilton rating scale for depression (HDRS).
Notes	The number of bipolar patients included in this study was unclear

Shu 2004

Methods	Control study. Unclear design.
Participants	Elderly patients with depression.
Interventions	Paroxetine and mianserin.
Outcomes	Unclear.
Notes	Waiting for translation from Chinese to English.

Song 2004

Methods	A comparative study. Unclear design.
Participants	Elderly patients with depression.
Interventions	Paroxetine and amitriptyline.
Outcomes	Unclear.
Notes	Waiting for translation from Chinese to English.

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Starmer 1996

Methods	Four-week, randomised, double-blind study.
Participants	Patients with depression in general practice.
Interventions	Paroxetine, amitriptyline.
Outcomes	To assess the effect of paroxetine and amitriptyline on driving and psychomotor performance
Notes	Funding: unclear.

Su 2005

Methods	Comparative study. Unclear design.
Participants	Patients with depression.
Interventions	Mirtazapine and paroxetine.
Outcomes	Unclear.
Notes	Waiting for translation from Chinese to English.

Sun 2001

Methods	Comparative study. Unclear design.
Participants	Patients with depression.
Interventions	Paroxetine and amitriptyline.
Outcomes	Unclear.
Notes	Waiting for translation from Chinese to English.

Tao 2005

Methods	Comparative study. Unclear design.
Participants	Patients with depression.
Interventions	Citalopram and paroxetine.
Outcomes	Unclear.
Notes	Waiting for translation from Chinese to English.

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Tao 2006

Methods	Comparative study. Unclear design.
Participants	Patients with depression.
Interventions	Tianeptine and paroxetine.
Outcomes	Unclear.
Notes	Waiting for translation from Chinese to English.

Wang 2003

Methods	Unclear.
Participants	Patients with depressive disorder.
Interventions	Fluoxetine, paroxetine and venlafaxine.
Outcomes	Unclear.
Notes	Waiting for translation from Chinese to English.

Wang 2004

Methods	Unclear.
Participants	Patients with depressive disorder.
Interventions	Paroxetine and tricyclic antidepressants.
Outcomes	Unclear.
Notes	Waiting for translation from Chinese to English.

Wang 2005

Methods	Unclear.
Participants	Patients with depressive disorder.
Interventions	Paroxetine (unclear comparators).
Outcomes	Unclear.
Notes	Waiting for translation from Chinese to English.

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Wang 2007

Methods	Unclear.
Participants	Patients with depressive disorder.
Interventions	Participants assigned to fluoxetine or paroxetine.
Outcomes	Quality of life.
Notes	Waiting for translation from Chinese to English.

Wieck 2001

Methods	Randomised, double-blind study.
Participants	Patients with major depression.
Interventions	Paroxetine, reboxetine.
Outcomes	Hamilton rating scale for depression (HDRS).
Notes	Funding: unclear.

Wu 2000

Methods	Double-blind, randomised study.
Participants	Patients with major depressive disorder.
Interventions	Paroxetine and doxepine.
Outcomes	Unclear.
Notes	Waiting for translation from Chinese to English.

Wu 2007

Methods	Twenty-four-week, open-label study.
Participants	Patients with major depressive disorder.
Interventions	Venlafaxine and paroxetine.
Outcomes	HDRS scores, remission rate at endpoint.
Notes	Waiting for translation from Chinese to English.

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Xie 1999

Methods	A randomised double-blind -controlled study.
Participants	Patients with major depressive disorder.
Interventions	Paroxetine and amitriptyline.
Outcomes	Unclear.
Notes	Waiting for translation from Chinese to English.

Yang 1998

Methods	Double-blind, randomised study.
Participants	Toatal number of participants: 30 outpatients.
Interventions	Paroxetine, amitriptyline, fluoxetine.
Outcomes	Hamilton rating scale for depression (HDRS).
Notes	Funding: unclear.

Yang 2004

Methods	Unclear design.
Participants	Patients with depression.
Interventions	Paroxetine and amitriptyline.
Outcomes	Adverse reactions, Hamilton rating scale for depression (HDRS)
Notes	Waiting for translation from Chinese to English.

Yang 2006

Methods	Comparative study. Unclear design.
Participants	Patients with depression.
Interventions	Reboxetine and paroxetine.
Outcomes	Unclear.
Notes	Waiting for translation from Chinese to English.

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Ye 2002

Methods	A clinical control study. Unclear design.
Participants	Outpatients with depression.
Interventions	Paroxetine and venlafaxine.
Outcomes	Unclear.
Notes	Waiting for translation from Chinese to English.

Zhang 2003

Methods	Comparative study. Unclear design.
Participants	Patients with depression.
Interventions	Venlafaxine extended release versus paroxetine.
Outcomes	Unclear.
Notes	Waiting for translation from Chinese to English.

Zhou 2005

Methods	Comparative study. Unclear design.
Participants	Patients with depression.
Interventions	Paroxetine and imipramine.
Outcomes	Unclear.
Notes	Waiting for translation from Chinese to English.

Zimbroff 2004

Methods	Two-week, open-label, randomised study.
Participants	Non responders outpatients.
Interventions	Paroxetine, citalopram, fluoxetine, sertraline.
Outcomes	Montgomery-Asberg Depression Rating Scale (MADRS).
Notes	Funding: pharmaceutical industry.

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Zou 2006

Methods	Comparative study. Unclear design.
Participants	Patients with depression.
Interventions	Mirtazapine and paroxetine.
Outcomes	Unclear.
Notes	Waiting for translation from Chinese to English.

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

Thomas 2008

Trial name or title	Thomas 2008 (GENPOD study).
Methods	Multicentre randomised controlled trial.
Participants	Patients with a primary diagnosis of depression according to ICD10 criteria and a Beck Depression Inventory (BDI) score > 14
Interventions	Antidepressant treatments.
Outcomes	BDI score at 6 weeks.
Starting date	2008
Contact information	Thomas L.
Notes	

ICD: International Classification of Disease

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DATA AND ANALYSES

Comparison 1. Failure to respond at endpoint (6 - 12 weeks)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Paroxetine versus older ADs	34	4647	Odds Ratio (M-H, Random, 95% CI)	1.04 [0.92, 1.17]
1.1 versus amitriptyline	13	1671	Odds Ratio (M-H, Random, 95% CI)	1.12 [0.92, 1.37]
1.2 versus clomipramine	4	1273	Odds Ratio (M-H, Random, 95% CI)	0.92 [0.73, 1.15]
1.3 versus desipramine	1	57	Odds Ratio (M-H, Random, 95% CI)	1.90 [0.66, 5.46]
1.4 versus dothiepin	1	134	Odds Ratio (M-H, Random, 95% CI)	1.43 [0.73, 2.83]
1.5 versus imipramine	6	587	Odds Ratio (M-H, Random, 95% CI)	0.84 [0.57, 1.24]
1.6 versus lofepramine	2	228	Odds Ratio (M-H, Random, 95% CI)	0.79 [0.47, 1.34]
1.7 versus maprolitine	3	429	Odds Ratio (M-H, Random, 95% CI)	1.24 [0.84, 1.82]
1.8 versus mianserin	4	268	Odds Ratio (M-H, Random, 95% CI)	1.30 [0.56, 3.05]
2 Paroxetine versus other SSRIs	17		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 versus citalopram	1	406	Odds Ratio (M-H, Random, 95% CI)	1.54 [1.04, 2.28]
2.2 versus escitalopram	2	784	Odds Ratio (M-H, Random, 95% CI)	1.12 [0.76, 1.65]
2.3 versus fluoxetine	10	2353	Odds Ratio (M-H, Random, 95% CI)	0.98 [0.77, 1.24]
2.4 versus fluvoxamine	3	261	Odds Ratio (M-H, Random, 95% CI)	1.19 [0.72, 1.94]
2.5 versus sertraline	2	545	Odds Ratio (M-H, Random, 95% CI)	1.21 [0.85, 1.73]
3 Paroxetine versus newer or non-conventional ADs	27		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
3.1 versus agomelatine	1	284	Odds Ratio (M-H, Random, 95% CI)	1.25 [0.78, 2.01]
3.2 versus amisulpride	1	277	Odds Ratio (M-H, Random, 95% CI)	0.65 [0.36, 1.15]
3.3 versus bupropion	1	100	Odds Ratio (M-H, Random, 95% CI)	0.73 [0.30, 1.79]
3.4 versus duloxetine	6	1821	Odds Ratio (M-H, Random, 95% CI)	0.89 [0.70, 1.14]
3.5 versus hypericum	1	251	Odds Ratio (M-H, Random, 95% CI)	1.60 [0.95, 2.69]
3.6 versus milnacipran	1	302	Odds Ratio (M-H, Random, 95% CI)	0.93 [0.59, 1.47]
3.7 versus mirtazapine	4	766	Odds Ratio (M-H, Random, 95% CI)	1.20 [0.90, 1.61]
3.8 versus nefazodone	1	40	Odds Ratio (M-H, Random, 95% CI)	0.31 [0.07, 1.25]
3.9 versus reboxetine	3	1369	Odds Ratio (M-H, Random, 95% CI)	0.82 [0.66, 1.02]
3.10 versus tianeptine	3	648	Odds Ratio (M-H, Random, 95% CI)	1.04 [0.71, 1.53]
3.11 versus trazodone	1	108	Odds Ratio (M-H, Random, 95% CI)	0.71 [0.21, 2.41]
3.12 versus venlafaxine	4	747	Odds Ratio (M-H, Random, 95% CI)	1.10 [0.58, 2.11]

Comparison 2. Failure to respond (at 1 - 4 weeks)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Paroxetine versus older ADs	4	526	Odds Ratio (M-H, Fixed, 95% CI)	0.90 [0.61, 1.33]
1.1 versus amitriptyline	1	153	Odds Ratio (M-H, Fixed, 95% CI)	1.06 [0.52, 2.15]
1.2 versus clomipramine	1	92	Odds Ratio (M-H, Fixed, 95% CI)	0.58 [0.25, 1.37]
1.3 versus imipramine	1	159	Odds Ratio (M-H, Fixed, 95% CI)	1.43 [0.61, 3.33]
1.4 versus lofepramine	1	122	Odds Ratio (M-H, Fixed, 95% CI)	0.74 [0.35, 1.55]
2 Paroxetine versus SSRIs	3		Odds Ratio (M-H, Fixed, 95% CI)	Subtotals only

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2.1 versus fluvoxamine	3	281	Odds Ratio (M-H, Fixed, 95% CI)	0.71 [0.41, 1.24]
3 Paroxetine versus newer or non-conventional ADs	7		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
3.1 versus mirtazapine	3	726	Odds Ratio (M-H, Random, 95% CI)	2.39 [1.42, 4.02]
3.2 versus reboxetine	3	1375	Odds Ratio (M-H, Random, 95% CI)	0.66 [0.50, 0.87]
3.3 versus trazodone	1	108	Odds Ratio (M-H, Random, 95% CI)	0.54 [0.25, 1.19]

Comparison 3. Failure to respond (at 16 - 24 weeks)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Paroxetine versus SSRIs	1		Odds Ratio (M-H, Fixed, 95% CI)	Subtotals only
1.1 versus escitalopram	1	459	Odds Ratio (M-H, Fixed, 95% CI)	1.36 [0.87, 2.12]
2 Paroxetine versus newer or non-conventional ADs	2		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 versus mirtazapine	1	197	Odds Ratio (M-H, Random, 95% CI)	1.41 [0.81, 2.48]
2.2 versus nefazodone	1	40	Odds Ratio (M-H, Random, 95% CI)	0.64 [0.17, 2.38]

Comparison 4. Failure to remit at endpoint (6 - 12 weeks)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Paroxetine versus older ADs	3	401	Odds Ratio (M-H, Random, 95% CI)	1.23 [0.49, 3.07]
1.1 versus clomipramine	1	120	Odds Ratio (M-H, Random, 95% CI)	3.39 [1.50, 7.65]
1.2 versus imipramine	1	159	Odds Ratio (M-H, Random, 95% CI)	0.75 [0.39, 1.43]
1.3 versus lofepramine	1	122	Odds Ratio (M-H, Random, 95% CI)	0.80 [0.38, 1.66]
2 Paroxetine versus other SSRIs	7		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 versus escitalopram	2	784	Odds Ratio (M-H, Random, 95% CI)	1.15 [0.60, 2.22]
2.2 versus fluvoxamine	3	261	Odds Ratio (M-H, Random, 95% CI)	0.78 [0.44, 1.38]
2.3 versus sertraline	2	545	Odds Ratio (M-H, Random, 95% CI)	0.94 [0.67, 1.34]
3 Paroxetine versus newer or non-conventional ADs	20		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
3.1 versus agomelatine	1	284	Odds Ratio (M-H, Random, 95% CI)	1.27 [0.75, 2.14]
3.2 versus amisulpride	1	277	Odds Ratio (M-H, Random, 95% CI)	0.85 [0.49, 1.46]
3.3 versus duloxetine	6	1821	Odds Ratio (M-H, Random, 95% CI)	0.98 [0.80, 1.19]
3.4 versus hypericum	1	251	Odds Ratio (M-H, Random, 95% CI)	1.84 [1.11, 3.06]
3.5 versus milnacipran	1	302	Odds Ratio (M-H, Random, 95% CI)	0.92 [0.57, 1.49]
3.6 versus mirtazapine	4	766	Odds Ratio (M-H, Random, 95% CI)	1.52 [1.13, 2.06]
3.7 versus tianeptine	1	44	Odds Ratio (M-H, Random, 95% CI)	0.66 [0.18, 2.36]
3.8 versus trazodone	1	108	Odds Ratio (M-H, Random, 95% CI)	1.06 [0.47, 2.38]
3.9 versus venlafaxine	4	807	Odds Ratio (M-H, Random, 95% CI)	1.57 [1.08, 2.29]

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Comparison 5. Failure to remit (at 1 - 4 weeks)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Paroxetine versus older ADs	2	279	Odds Ratio (M-H, Random, 95% CI)	2.38 [0.38, 14.85]
1.1 versus clomipramine	1	120	Odds Ratio (M-H, Random, 95% CI)	10.32 [0.54, 196.06]
1.2 versus imipramine	1	159	Odds Ratio (M-H, Random, 95% CI)	1.35 [0.45, 4.09]
2 Paroxetine versus other SSRIs	3		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 versus fluvoxamine	3	268	Odds Ratio (M-H, Random, 95% CI)	1.17 [0.41, 3.35]
3 Paroxetine versus newer or non-conventional ADs	5		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
3.1 versus milnacipran	1	41	Odds Ratio (M-H, Random, 95% CI)	0.62 [0.18, 2.13]
3.2 versus mirtazapine	3	726	Odds Ratio (M-H, Random, 95% CI)	2.31 [1.04, 5.11]
3.3 versus trazodone	1	108	Odds Ratio (M-H, Random, 95% CI)	0.68 [0.27, 1.73]

Comparison 6. Failure to remit (at 16 - 24 weeks)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Paroxetine versus newer or non-conventional ADs	2		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
1.1 versus mirtazapine	1	197	Odds Ratio (M-H, Random, 95% CI)	1.89 [1.01, 3.54]
1.2 versus trazodone	1	108	Odds Ratio (M-H, Random, 95% CI)	1.06 [0.47, 2.38]

Comparison 7. Standardized mean difference at endpoint (6 - 12 weeks)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Paroxetine versus older ADs	34	4712	Std. Mean Difference (IV, Random, 95% CI)	0.01 [-0.08, 0.10]
1.1 versus amitriptyline	13	1919	Std. Mean Difference (IV, Random, 95% CI)	0.07 [-0.06, 0.20]
1.2 versus clomipramine	5	1242	Std. Mean Difference (IV, Random, 95% CI)	0.14 [-0.21, 0.49]
1.3 versus doxepin	2	306	Std. Mean Difference (IV, Random, 95% CI)	-0.12 [-0.35, 0.10]
1.4 versus imipramine	7	572	Std. Mean Difference (IV, Random, 95% CI)	-0.10 [-0.37, 0.17]
1.5 versus lofepramine	1	92	Std. Mean Difference (IV, Random, 95% CI)	-0.06 [-0.47, 0.35]
1.6 versus maprolitine	2	336	Std. Mean Difference (IV, Random, 95% CI)	-0.01 [-0.23, 0.20]
1.7 versus nortriptyline	1	56	Std. Mean Difference (IV, Random, 95% CI)	0.20 [-0.32, 0.73]
1.8 versus mianserin	3	189	Std. Mean Difference (IV, Random, 95% CI)	-0.21 [-0.50, 0.07]
2 Paroxetine versus other SSRIs	13		Std. Mean Difference (IV, Random, 95% CI)	Subtotals only
2.1 versus citalopram	1	201	Std. Mean Difference (IV, Random, 95% CI)	-0.16 [-0.44, 0.11]
2.2 versus escitalopram	2	772	Std. Mean Difference (IV, Random, 95% CI)	0.05 [-0.26, 0.36]
2.3 versus fluoxetine	8	2044	Std. Mean Difference (IV, Random, 95% CI)	0.04 [-0.05, 0.12]
2.4 versus fluvoxamine	1	58	Std. Mean Difference (IV, Random, 95% CI)	0.09 [-0.43, 0.60]
2.5 versus sertraline	1	353	Std. Mean Difference (IV, Random, 95% CI)	-0.13 [-0.34, 0.07]

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3 Paroxetine versus newer or non-conventional ADs	27		Std. Mean Difference (IV, Random, 95% CI)	Subtotals only
3.1 versus agomelatine	4	1074	Std. Mean Difference (IV, Random, 95% CI)	-0.18 [-0.38, 0.02]
3.2 versus amisulpride	1	272	Std. Mean Difference (IV, Random, 95% CI)	-0.13 [-0.37, 0.10]
3.3 versus aprepitant (MK-869)	1	102	Std. Mean Difference (IV, Random, 95% CI)	-0.00 [-0.39, 0.39]
3.4 versus bupropion	1	132	Std. Mean Difference (IV, Random, 95% CI)	-0.04 [-0.38, 0.30]
3.5 versus duloxetine	6	1481	Std. Mean Difference (IV, Random, 95% CI)	0.04 [-0.06, 0.15]
3.6 versus hypericum	1	244	Std. Mean Difference (IV, Random, 95% CI)	0.35 [0.09, 0.60]
3.7 versus milnacipran	1	299	Std. Mean Difference (IV, Random, 95% CI)	-0.05 [-0.28, 0.18]
3.8 versus mirtazapine	1	246	Std. Mean Difference (IV, Random, 95% CI)	0.33 [0.08, 0.58]
3.9 versus nefazodone	2	235	Std. Mean Difference (IV, Random, 95% CI)	-0.12 [-0.37, 0.14]
3.10 versus reboxetine	3	1291	Std. Mean Difference (IV, Random, 95% CI)	-0.10 [-0.21, 0.00]
3.11 versus tianeptine	3	586	Std. Mean Difference (IV, Random, 95% CI)	0.04 [-0.12, 0.20]
3.12 versus trazodone	1	108	Std. Mean Difference (IV, Random, 95% CI)	-0.08 [-0.46, 0.30]
3.13 versus venlafaxine	2	411	Std. Mean Difference (IV, Random, 95% CI)	0.07 [-0.13, 0.26]

Comparison 8. Standardized mean difference (at 1 - 4 weeks)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Paroxetine versus older ADs	7	723	Std. Mean Difference (IV, Random, 95% CI)	0.19 [-0.02, 0.39]
1.1 versus amitriptyline	4	566	Std. Mean Difference (IV, Random, 95% CI)	0.14 [-0.02, 0.31]
1.2 versus clomipramine	1	84	Std. Mean Difference (IV, Random, 95% CI)	-0.15 [-0.58, 0.28]
1.3 versus desipramine	1	50	Std. Mean Difference (IV, Random, 95% CI)	0.86 [0.28, 1.44]
1.4 versus imipramine	1	23	Std. Mean Difference (IV, Random, 95% CI)	0.21 [-0.61, 1.03]
2 Paroxetine versus other SSRIs	1		Std. Mean Difference (IV, Random, 95% CI)	Subtotals only
2.1 versus fluoxetine	1	132	Std. Mean Difference (IV, Random, 95% CI)	-0.03 [-0.37, 0.32]
3 Paroxetine versus newer or non-conventional ADs	6		Std. Mean Difference (IV, Random, 95% CI)	Subtotals only
3.1 versus aprepitant (MK-869)	1	121	Std. Mean Difference (IV, Random, 95% CI)	-0.15 [-0.50, 0.21]
3.2 versus duloxetine	2	353	Std. Mean Difference (IV, Random, 95% CI)	0.12 [-0.09, 0.33]
3.3 versus reboxetine	2	805	Std. Mean Difference (IV, Random, 95% CI)	-0.17 [-0.31, -0.03]
3.4 versus tianeptine	1	246	Std. Mean Difference (IV, Random, 95% CI)	0.13 [-0.12, 0.38]

Comparison 9. Standardized mean difference (at 16 - 24 weeks)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Paroxetine versus SSRIs	1		Std. Mean Difference (IV, Random, 95% CI)	Subtotals only
1.1 versus sertraline	1	353	Std. Mean Difference (IV, Random, 95% CI)	0.01 [-0.20, 0.22]
2 Paroxetine versus newer or non-conventional ADs	1		Std. Mean Difference (IV, Random, 95% CI)	Subtotals only
2.1 versus mirtazapine	1	177	Std. Mean Difference (IV, Random, 95% CI)	0.21 [-0.09, 0.51]

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Comparison 10. Failure to complete (any cause)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Paroxetine versus older ADs	43	6777	Odds Ratio (M-H, Random, 95% CI)	0.84 [0.73, 0.96]
1.1 versus amitriptyline	19	2908	Odds Ratio (M-H, Random, 95% CI)	0.86 [0.70, 1.06]
1.2 versus clomipramine	4	1273	Odds Ratio (M-H, Random, 95% CI)	0.67 [0.52, 0.87]
1.3 versus dothiepin	3	499	Odds Ratio (M-H, Random, 95% CI)	1.25 [0.84, 1.87]
1.4 versus imipramine	9	1268	Odds Ratio (M-H, Random, 95% CI)	0.65 [0.50, 0.85]
1.5 versus lofepramine	2	228	Odds Ratio (M-H, Random, 95% CI)	0.94 [0.31, 2.80]
1.6 versus maprolitine	3	429	Odds Ratio (M-H, Random, 95% CI)	1.05 [0.49, 2.25]
1.7 versus mianserin	2	92	Odds Ratio (M-H, Random, 95% CI)	0.84 [0.21, 3.41]
1.8 versus nortriptyline	1	80	Odds Ratio (M-H, Random, 95% CI)	1.30 [0.50, 3.42]
2 Paroxetine versus other SSRIs	19		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 versus citalopram	1	406	Odds Ratio (M-H, Random, 95% CI)	0.99 [0.61, 1.60]
2.2 versus escitalopram	2	784	Odds Ratio (M-H, Random, 95% CI)	1.47 [0.77, 2.79]
2.3 versus fluoxetine	12	2733	Odds Ratio (M-H, Random, 95% CI)	1.05 [0.89, 1.24]
2.4 versus fluvoxamine	3	261	Odds Ratio (M-H, Random, 95% CI)	0.96 [0.54, 1.72]
2.5 versus sertraline	2	426	Odds Ratio (M-H, Random, 95% CI)	1.37 [0.52, 3.60]
3 Paroxetine versus newer or non-conventional ADs	29		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
3.1 versus agomelatine	1	284	Odds Ratio (M-H, Random, 95% CI)	0.99 [0.57, 1.71]
3.2 versus aprepitant (MK-869)	1	143	Odds Ratio (M-H, Random, 95% CI)	1.53 [0.76, 3.09]
3.3 versus bupropion	2	240	Odds Ratio (M-H, Random, 95% CI)	1.16 [0.62, 2.20]
3.4 versus duloxetine	6	1821	Odds Ratio (M-H, Random, 95% CI)	0.97 [0.77, 1.23]
3.5 versus hypericum	1	251	Odds Ratio (M-H, Random, 95% CI)	1.90 [0.98, 3.67]
3.6 versus mirtazapine	3	726	Odds Ratio (M-H, Random, 95% CI)	1.26 [0.91, 1.74]
3.7 versus milnacipram	2	343	Odds Ratio (M-H, Random, 95% CI)	1.17 [0.67, 2.03]
3.8 versus nefazodone	1	40	Odds Ratio (M-H, Random, 95% CI)	0.53 [0.11, 2.60]
3.9 versus reboxetine	3	1375	Odds Ratio (M-H, Random, 95% CI)	0.78 [0.51, 1.19]
3.10 versus tianeptine	3	648	Odds Ratio (M-H, Random, 95% CI)	1.46 [0.75, 2.85]
3.11 versus venlafaxine	6	1079	Odds Ratio (M-H, Random, 95% CI)	1.08 [0.82, 1.44]

Comparison 11. Failure to complete (due to inefficacy)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Paroxetine versus older ADs	27	4436	Odds Ratio (M-H, Random, 95% CI)	1.22 [0.93, 1.61]
1.1 versus amitriptyline	9	1191	Odds Ratio (M-H, Random, 95% CI)	1.20 [0.77, 1.86]
1.2 versus clomipramine	4	1273	Odds Ratio (M-H, Random, 95% CI)	1.50 [0.76, 2.97]
1.3 versus dothiepin	2	405	Odds Ratio (M-H, Random, 95% CI)	0.59 [0.18, 1.96]
1.4 versus imipramine	9	1268	Odds Ratio (M-H, Random, 95% CI)	1.27 [0.80, 2.02]
1.5 versus lofepramine	2	228	Odds Ratio (M-H, Random, 95% CI)	0.87 [0.13, 6.08]
1.6 versus maprolitine	1	71	Odds Ratio (M-H, Random, 95% CI)	2.84 [0.11, 71.99]
2 Paroxetine versus other SSRIs	13		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 versus citalopram	1	406	Odds Ratio (M-H, Random, 95% CI)	1.75 [0.41, 7.43]

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2.2 versus escitalopram	2	784	Odds Ratio (M-H, Random, 95% CI)	0.72 [0.09, 5.96]
2.3 versus fluoxetine	8	2214	Odds Ratio (M-H, Random, 95% CI)	0.91 [0.60, 1.39]
2.4 versus fluvoxamine	2	180	Odds Ratio (M-H, Random, 95% CI)	1.00 [0.15, 6.93]
2.5 versus sertraline	1	192	Odds Ratio (M-H, Random, 95% CI)	0.53 [0.17, 1.65]
3 Paroxetine versus newer or non-conventional ADs	19		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
3.1 versus agomelatine	1	284	Odds Ratio (M-H, Random, 95% CI)	1.15 [0.46, 2.87]
3.2 versus aprepitant (MK-869)	1	143	Odds Ratio (M-H, Random, 95% CI)	0.32 [0.01, 8.09]
3.3 versus duloxetine	5	1557	Odds Ratio (M-H, Random, 95% CI)	1.05 [0.55, 2.00]
3.4 versus hypericum	1	251	Odds Ratio (M-H, Random, 95% CI)	0.48 [0.12, 1.98]
3.5 versus milnacipran	1	302	Odds Ratio (M-H, Random, 95% CI)	0.63 [0.22, 1.83]
3.6 versus mirtazapine	2	451	Odds Ratio (M-H, Random, 95% CI)	0.41 [0.04, 4.58]
3.7 versus reboxetine	3	1375	Odds Ratio (M-H, Random, 95% CI)	0.66 [0.20, 2.16]
3.8 versus tianeptine	2	371	Odds Ratio (M-H, Random, 95% CI)	1.22 [0.05, 27.06]
3.9 versus venlafaxine	3	774	Odds Ratio (M-H, Random, 95% CI)	0.75 [0.33, 1.66]

Comparison 12. Failure to complete (due to side effects)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Paroxetine versus older ADs	34	5175	Odds Ratio (M-H, Random, 95% CI)	0.76 [0.63, 0.92]
1.1 versus amitriptyline	12	1698	Odds Ratio (M-H, Random, 95% CI)	0.74 [0.56, 0.98]
1.2 versus clomipramine	4	1273	Odds Ratio (M-H, Random, 95% CI)	0.59 [0.41, 0.84]
1.3 versus dothiepin	2	405	Odds Ratio (M-H, Random, 95% CI)	1.70 [0.78, 3.70]
1.4 versus imipramine	9	1268	Odds Ratio (M-H, Random, 95% CI)	0.58 [0.43, 0.77]
1.5 versus lofepramine	2	228	Odds Ratio (M-H, Random, 95% CI)	1.19 [0.45, 3.15]
1.6 versus maprolitine	2	131	Odds Ratio (M-H, Random, 95% CI)	0.77 [0.01, 70.98]
1.7 versus mianserin	2	92	Odds Ratio (M-H, Random, 95% CI)	2.26 [0.38, 13.50]
1.8 versus nortriptyline	1	80	Odds Ratio (M-H, Random, 95% CI)	1.46 [0.43, 4.93]
2 Paroxetine versus other SSRIs	17		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 versus citalopram	1	406	Odds Ratio (M-H, Random, 95% CI)	1.15 [0.48, 2.78]
2.2 versus escitalopram	2	784	Odds Ratio (M-H, Random, 95% CI)	1.43 [0.51, 4.00]
2.3 versus fluoxetine	11	2491	Odds Ratio (M-H, Random, 95% CI)	1.34 [1.06, 1.70]
2.4 versus fluvoxamine	3	261	Odds Ratio (M-H, Random, 95% CI)	1.16 [0.19, 7.16]
2.5 versus sertraline	1	192	Odds Ratio (M-H, Random, 95% CI)	1.94 [0.69, 5.48]
3 Paroxetine versus newer or non-conventional ADs	24		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
3.1 versus agomelatine	1	284	Odds Ratio (M-H, Random, 95% CI)	0.84 [0.34, 2.04]
3.2 versus aprepitant (MK-869)	1	143	Odds Ratio (M-H, Random, 95% CI)	1.66 [0.67, 4.13]
3.3 versus bupropion	2	240	Odds Ratio (M-H, Random, 95% CI)	0.61 [0.24, 1.55]
3.4 versus duloxetine	6	1821	Odds Ratio (M-H, Random, 95% CI)	0.84 [0.57, 1.25]
3.5 versus hypericum	1	251	Odds Ratio (M-H, Random, 95% CI)	2.05 [0.60, 6.99]
3.6 versus milnacipran	1	302	Odds Ratio (M-H, Random, 95% CI)	1.17 [0.59, 2.33]
3.7 versus mirtazapine	3	726	Odds Ratio (M-H, Random, 95% CI)	1.35 [0.83, 2.21]
3.8 versus reboxetine	3	1375	Odds Ratio (M-H, Random, 95% CI)	0.38 [0.17, 0.86]
3.9 versus tianeptine	1	327	Odds Ratio (M-H, Random, 95% CI)	3.38 [1.31, 8.71]

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3.10 versus venlafaxine	5	974	Odds Ratio (M-H, Random, 95% CI)	0.88 [0.50, 1.56]

Comparison 13. SE - Participants with at least one TEAE

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Paroxetine versus older ADs	41	6099	Odds Ratio (M-H, Random, 95% CI)	0.64 [0.53, 0.77]
1.1 versus amitriptyline	16	2492	Odds Ratio (M-H, Random, 95% CI)	0.53 [0.39, 0.72]
1.2 versus clomipramine	4	1273	Odds Ratio (M-H, Random, 95% CI)	0.56 [0.28, 1.10]
1.3 versus dothiepin	2	405	Odds Ratio (M-H, Random, 95% CI)	1.04 [0.61, 1.76]
1.4 versus imipramine	9	1189	Odds Ratio (M-H, Random, 95% CI)	0.62 [0.42, 0.94]
1.5 versus lofepramine	2	228	Odds Ratio (M-H, Random, 95% CI)	1.25 [0.74, 2.12]
1.6 versus maprolitine	2	131	Odds Ratio (M-H, Random, 95% CI)	0.66 [0.28, 1.55]
1.7 versus mianserin	5	301	Odds Ratio (M-H, Random, 95% CI)	0.71 [0.41, 1.22]
1.8 versus nortriptyline	1	80	Odds Ratio (M-H, Random, 95% CI)	1.46 [0.43, 4.93]
2 Paroxetine versus other SSRIs	14		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 versus citalopram	1	406	Odds Ratio (M-H, Random, 95% CI)	0.74 [0.46, 1.21]
2.2 versus escitalopram	1	454	Odds Ratio (M-H, Random, 95% CI)	1.28 [0.86, 1.91]
2.3 versus fluoxetine	9	2255	Odds Ratio (M-H, Random, 95% CI)	0.94 [0.69, 1.28]
2.4 versus fluvoxamine	3	261	Odds Ratio (M-H, Random, 95% CI)	1.12 [0.42, 2.97]
3 Paroxetine versus newer or non-conventional ADs	23		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
3.1 versus agomelatine	1	284	Odds Ratio (M-H, Random, 95% CI)	1.60 [0.99, 2.59]
3.2 versus amisulpride	1	277	Odds Ratio (M-H, Random, 95% CI)	1.49 [0.89, 2.50]
3.3 versus bupropion	1	140	Odds Ratio (M-H, Random, 95% CI)	1.60 [0.43, 5.92]
3.4 versus duloxetine	6	1870	Odds Ratio (M-H, Random, 95% CI)	0.81 [0.64, 1.01]
3.5 versus hypericum	1	251	Odds Ratio (M-H, Random, 95% CI)	2.60 [1.51, 4.46]
3.6 versus milnacipran	1	302	Odds Ratio (M-H, Random, 95% CI)	0.69 [0.41, 1.15]
3.7 versus mirtazapine	3	726	Odds Ratio (M-H, Random, 95% CI)	1.07 [0.76, 1.50]
3.8 versus nefazodone	1	206	Odds Ratio (M-H, Random, 95% CI)	0.69 [0.34, 1.40]
3.9 versus reboxetine	3	1375	Odds Ratio (M-H, Random, 95% CI)	1.08 [0.74, 1.58]
3.10 versus tianeptine	2	604	Odds Ratio (M-H, Random, 95% CI)	1.26 [0.89, 1.78]
3.11 versus trazodone	1	108	Odds Ratio (M-H, Random, 95% CI)	0.68 [0.30, 1.55]
3.12 versus venlafaxine	2	200	Odds Ratio (M-H, Random, 95% CI)	1.01 [0.52, 1.95]

Comparison 14. SE - Abnormal dreams

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Paroxetine versus older ADs	1		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
1.1 versus maprolitine	1	71	Odds Ratio (M-H, Random, 95% CI)	2.84 [0.11, 71.99]
2 Paroxetine versus other SSRIs	1		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 versus fluvoxamine	1	60	Odds Ratio (M-H, Random, 95% CI)	13.16 [0.69, 249.48]
3 Paroxetine versus newer or non-conventional ADs	3		Odds Ratio (M-H, Random, 95% CI)	Subtotals only

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3.1 versus milnacipran	1	302	Odds Ratio (M-H, Random, 95% CI)	4.93 [0.23, 103.64]
3.2 versus reboxetine	2	1050	Odds Ratio (M-H, Random, 95% CI)	0.99 [0.33, 2.99]

Comparison 15. SE - Abnormal laboratory values

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Abnormal white blood cells	1		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
1.1 versus fluoxetine	1	138	Odds Ratio (M-H, Random, 95% CI)	0.34 [0.01, 8.45]
2 Leucocytosis	1		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 versus amitriptyline	1	40	Odds Ratio (M-H, Random, 95% CI)	1.0 [0.06, 17.18]
3 ALT/AST increase	2		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
3.1 versus amitriptyline	2	262	Odds Ratio (M-H, Random, 95% CI)	2.13 [0.27, 16.88]
4 NOS	1		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
4.1 versus clomipramine	1	83	Odds Ratio (M-H, Random, 95% CI)	0.33 [0.01, 8.42]

Comparison 16. SE - Abnormal thinking

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Paroxetine versus newer or non-conventional ADs	4		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
1.1 versus duloxetine	2	528	Odds Ratio (M-H, Random, 95% CI)	0.93 [0.16, 5.46]
1.2 versus reboxetine	2	1050	Odds Ratio (M-H, Random, 95% CI)	1.18 [0.06, 24.15]

Comparison 17. SE - Accidental injury

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Paroxetine versus other SSRIs	1		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
1.1 versus fluoxetine	1	573	Odds Ratio (M-H, Random, 95% CI)	1.02 [0.49, 2.12]
2 Paroxetine versus newer or non-conventional ADs	5		Odds Ratio (M-H, Fixed, 95% CI)	Subtotals only
2.1 versus duloxetine	2	528	Odds Ratio (M-H, Fixed, 95% CI)	1.00 [0.37, 2.72]
2.2 versus reboxetine	3	1375	Odds Ratio (M-H, Fixed, 95% CI)	1.74 [0.88, 3.43]

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Comparison 18. SE - Agitation/anxiety

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Paroxetine versus older ADs	15	2240	Odds Ratio (M-H, Random, 95% CI)	1.12 [0.67, 1.86]
1.1 versus amitriptyline	6	1001	Odds Ratio (M-H, Random, 95% CI)	1.21 [0.36, 4.03]
1.2 versus clomipramine	1	92	Odds Ratio (M-H, Random, 95% CI)	0.2 [0.01, 4.28]
1.3 versus dothiepin	1	271	Odds Ratio (M-H, Random, 95% CI)	2.52 [0.86, 7.35]
1.4 versus imipramine	2	282	Odds Ratio (M-H, Random, 95% CI)	0.63 [0.18, 2.16]
1.5 versus lofepramine	1	106	Odds Ratio (M-H, Random, 95% CI)	0.28 [0.01, 7.06]
1.6 versus maprolitine	3	429	Odds Ratio (M-H, Random, 95% CI)	0.95 [0.38, 2.39]
1.7 versus mianserin	1	59	Odds Ratio (M-H, Random, 95% CI)	2.0 [0.17, 23.34]
2 Paroxetine versus other SSRIs	8		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 versus fluoxetine	5	713	Odds Ratio (M-H, Random, 95% CI)	1.15 [0.75, 1.77]
2.2 versus fluvoxamine	1	60	Odds Ratio (M-H, Random, 95% CI)	2.15 [0.36, 12.76]
2.3 versus sertraline	2	545	Odds Ratio (M-H, Random, 95% CI)	1.19 [0.66, 2.13]
3 Paroxetine versus newer or non-conventional ADs	14		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
3.1 versus agomelatine	1	284	Odds Ratio (M-H, Random, 95% CI)	0.74 [0.19, 2.81]
3.2 versus bupropion	2	240	Odds Ratio (M-H, Random, 95% CI)	0.45 [0.19, 1.08]
3.3 versus duloxetine	4	1095	Odds Ratio (M-H, Random, 95% CI)	0.82 [0.35, 1.91]
3.4 versus milnacipran	1	302	Odds Ratio (M-H, Random, 95% CI)	0.73 [0.16, 3.30]
3.5 versus mirtazapine	2	472	Odds Ratio (M-H, Random, 95% CI)	1.40 [0.63, 3.15]
3.6 versus reboxetine	3	1375	Odds Ratio (M-H, Random, 95% CI)	0.74 [0.47, 1.17]
3.7 versus tianeptine	1	277	Odds Ratio (M-H, Random, 95% CI)	0.33 [0.01, 8.14]

Comparison 19. SE - Akathisia

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Paroxetine versus older ADs	1		Odds Ratio (M-H, Fixed, 95% CI)	Subtotals only
1.1 versus amitriptyline	1	21	Odds Ratio (M-H, Fixed, 95% CI)	0.28 [0.01, 7.57]
2 Paroxetine versus newer or non-conventional ADs	2		Odds Ratio (M-H, Fixed, 95% CI)	Subtotals only
2.1 versus reboxetine	2	1050	Odds Ratio (M-H, Fixed, 95% CI)	1.37 [0.55, 3.44]

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Comparison 20. SE - Anorexia

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Paroxetine versus other SSRIs	1		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
1.1 versus fluoxetine	1	138	Odds Ratio (M-H, Random, 95% CI)	3.90 [0.78, 19.50]
2 Paroxetine versus newer or non-conventional ADs	10		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 versus aprepitant (MK-869)	1	143	Odds Ratio (M-H, Random, 95% CI)	2.83 [0.72, 11.15]
2.2 versus bupropion	1	100	Odds Ratio (M-H, Random, 95% CI)	6.13 [0.71, 52.93]
2.3 versus duloxetine	4	1299	Odds Ratio (M-H, Random, 95% CI)	0.64 [0.39, 1.05]
2.4 versus reboxetine	3	1375	Odds Ratio (M-H, Random, 95% CI)	0.71 [0.47, 1.08]
2.5 versus tianeptine	1	277	Odds Ratio (M-H, Random, 95% CI)	0.33 [0.01, 8.14]

Comparison 21. SE - Anticholinergic

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 paroxetine versus older ADs	3		Odds Ratio (M-H, Fixed, 95% CI)	Subtotals only
1.1 versus amitriptyline	2	130	Odds Ratio (M-H, Fixed, 95% CI)	0.22 [0.07, 0.76]
1.2 versus clomipramine	1	79	Odds Ratio (M-H, Fixed, 95% CI)	0.30 [0.11, 0.86]
2 paroxerine versus other SSRIs	2		Odds Ratio (M-H, Fixed, 95% CI)	Subtotals only
2.1 versus fluoxetine	2	296	Odds Ratio (M-H, Fixed, 95% CI)	0.79 [0.31, 2.05]

Comparison 22. SE - Appetite decreased

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Paroxetine versus older ADs	4	685	Odds Ratio (M-H, Random, 95% CI)	4.00 [1.65, 9.71]
1.1 versus amitriptyline	1	26	Odds Ratio (M-H, Random, 95% CI)	12.79 [0.61, 266.66]
1.2 versus imipramine	2	361	Odds Ratio (M-H, Random, 95% CI)	2.45 [0.76, 7.90]
1.3 versus maprotiline	1	298	Odds Ratio (M-H, Random, 95% CI)	6.81 [1.50, 30.99]
2 Paroxetine versus other SSRIs	1		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 versus fluoxetine	1	122	Odds Ratio (M-H, Random, 95% CI)	0.58 [0.20, 1.70]
3 Paroxetine versus newer or non-conventional ADs	3		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
3.1 versus duloxetine	2	752	Odds Ratio (M-H, Random, 95% CI)	1.09 [0.59, 2.01]
3.2 versus reboxetine	1	325	Odds Ratio (M-H, Random, 95% CI)	0.76 [0.20, 2.88]

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Comparison 23. SE - Appetite increased

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Paroxetine versus newer or non-conventional ADs	4		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
1.1 versus bupropion	1	100	Odds Ratio (M-H, Random, 95% CI)	0.29 [0.03, 2.93]
1.2 versus reboxetine	3	1375	Odds Ratio (M-H, Random, 95% CI)	1.43 [0.22, 9.41]

Comparison 24. SE - Asthenia

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Paroxetine versus older ADs	17		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
1.1 versus amitriptyline	5	779	Odds Ratio (M-H, Random, 95% CI)	0.44 [0.12, 1.55]
1.2 versus dothiepin	2	405	Odds Ratio (M-H, Random, 95% CI)	1.58 [0.30, 8.47]
1.3 versus imipramine	6	680	Odds Ratio (M-H, Random, 95% CI)	1.29 [0.73, 2.28]
1.4 versus lofepramine	1	122	Odds Ratio (M-H, Random, 95% CI)	4.36 [0.47, 40.16]
1.5 versus maprolitine	3	429	Odds Ratio (M-H, Random, 95% CI)	0.76 [0.49, 1.16]
2 Paroxetine versus other SSRIs	7		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 versus citalopram	1	406	Odds Ratio (M-H, Random, 95% CI)	0.59 [0.33, 1.04]
2.2 versus fluoxetine	5	1680	Odds Ratio (M-H, Random, 95% CI)	1.27 [0.91, 1.77]
2.3 versus fluvoxamine	1	60	Odds Ratio (M-H, Random, 95% CI)	0.51 [0.13, 1.95]
3 Paroxetine versus newer ADs	13		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
3.1 versus aprepitant (MK-869)	1	143	Odds Ratio (M-H, Random, 95% CI)	1.47 [0.61, 3.58]
3.2 versus bupropion	1	140	Odds Ratio (M-H, Random, 95% CI)	4.25 [0.87, 20.80]
3.3 versus duloxetine	3	1006	Odds Ratio (M-H, Random, 95% CI)	0.79 [0.45, 1.38]
3.4 versus nefazodone	2	246	Odds Ratio (M-H, Random, 95% CI)	1.15 [0.36, 3.62]
3.5 versus reboxetine	3	1375	Odds Ratio (M-H, Random, 95% CI)	2.07 [1.19, 3.60]
3.6 versus tianeptine	1	277	Odds Ratio (M-H, Random, 95% CI)	0.99 [0.06, 16.03]
3.7 versus venlafaxine	1	361	Odds Ratio (M-H, Random, 95% CI)	0.46 [0.17, 1.23]
3.8 versus trazodone	1	108	Odds Ratio (M-H, Random, 95% CI)	3.17 [0.13, 79.60]

Comparison 25. SE - Behaviour

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Euphoria	1		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
1.1 versus reboxetine	1	520	Odds Ratio (M-H, Random, 95% CI)	0.14 [0.01, 2.71]
2 Hostility	1		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 versus reboxetine	1	325	Odds Ratio (M-H, Random, 95% CI)	0.48 [0.04, 5.30]
3 Impulsive	1		Odds Ratio (M-H, Random, 95% CI)	Subtotals only

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3.1 versus tianeptine	1	277	Odds Ratio (M-H, Random, 95% CI)	0.33 [0.01, 8.14]
4 Irritability	4	557	Odds Ratio (M-H, Random, 95% CI)	1.34 [0.15, 12.23]
4.1 versus amitriptyline	1	21	Odds Ratio (M-H, Random, 95% CI)	15.75 [1.42, 174.25]
4.2 versus aprepitant (MK-869)	1	143	Odds Ratio (M-H, Random, 95% CI)	0.19 [0.02, 1.63]
4.3 versus mianserin	1	116	Odds Ratio (M-H, Random, 95% CI)	0.38 [0.02, 9.43]
4.4 versus tianeptine	1	277	Odds Ratio (M-H, Random, 95% CI)	3.0 [0.12, 74.28]
5 Paranoid reaction	1		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
5.1 versus maprolitine	1	71	Odds Ratio (M-H, Random, 95% CI)	4.86 [0.23, 104.92]
6 Psychotic symptoms	1		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
6.1 versus fluvoxamine	1	81	Odds Ratio (M-H, Random, 95% CI)	9.23 [0.48, 177.35]

Comparison 26. SE - Body as a whole

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Paroxetine versus older ADs	6	463	Odds Ratio (M-H, Random, 95% CI)	1.40 [0.83, 2.36]
1.1 versus amitriptyline	2	221	Odds Ratio (M-H, Random, 95% CI)	1.87 [1.08, 3.23]
1.2 versus clomipramine	1	83	Odds Ratio (M-H, Random, 95% CI)	0.40 [0.11, 1.41]
1.3 versus mianserin	1	33	Odds Ratio (M-H, Random, 95% CI)	2.5 [0.41, 15.29]
1.4 versus mianserin	3	126	Odds Ratio (M-H, Random, 95% CI)	1.29 [0.48, 3.52]
2 Paroxetine versus other SSRIs	1		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 versus fluoxetine	1	242	Odds Ratio (M-H, Random, 95% CI)	1.57 [0.65, 3.78]

Comparison 27. SE - Bronchitis

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Paroxetine versus other SSRIs	1		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
1.1 versus fluoxetine	1	138	Odds Ratio (M-H, Random, 95% CI)	0.19 [0.02, 1.71]
2 Paroxetine versus newer or non-conventional ADs	2		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 versus reboxetine	2	845	Odds Ratio (M-H, Random, 95% CI)	0.42 [0.06, 2.85]

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Comparison 28. SE - Cardiovascular system

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Syncope	1		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
1.1 versus maprolitine	1	60	Odds Ratio (M-H, Random, 95% CI)	1.16 [0.21, 6.27]
2 NOS	8	693	Odds Ratio (M-H, Random, 95% CI)	0.73 [0.41, 1.31]
2.1 versus amitriptyline	3	242	Odds Ratio (M-H, Random, 95% CI)	1.01 [0.24, 4.31]
2.2 versus clomipramine	1	83	Odds Ratio (M-H, Random, 95% CI)	0.69 [0.20, 2.40]
2.3 versus fluoxetine	1	242	Odds Ratio (M-H, Random, 95% CI)	0.85 [0.32, 2.28]
2.4 versus mianserin	3	126	Odds Ratio (M-H, Random, 95% CI)	0.24 [0.05, 1.06]

Comparison 29. SE - Chills

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Paroxetine versus newer or non-conventional ADs	3		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
1.1 versus reboxetine	3	1375	Odds Ratio (M-H, Random, 95% CI)	0.37 [0.18, 0.74]

Comparison 30. SE - Confusion

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Paroxetine versus older ADs	5	738	Odds Ratio (M-H, Random, 95% CI)	0.48 [0.18, 1.30]
1.1 versus amitriptyline	1	153	Odds Ratio (M-H, Random, 95% CI)	0.96 [0.13, 7.00]
1.2 versus clomipramine	1	92	Odds Ratio (M-H, Random, 95% CI)	1.05 [0.14, 7.76]
1.3 versus dothiepin	1	271	Odds Ratio (M-H, Random, 95% CI)	0.14 [0.02, 1.12]
1.4 versus lofepramine	1	106	Odds Ratio (M-H, Random, 95% CI)	0.17 [0.01, 3.53]
1.5 versus mianserin	1	116	Odds Ratio (M-H, Random, 95% CI)	0.57 [0.05, 6.42]
2 Paroxetine versus newer or non-conventional ADs	3		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 versus nefazodone	1	40	Odds Ratio (M-H, Random, 95% CI)	4.75 [0.48, 46.91]
2.2 versus reboxetine	2	1050	Odds Ratio (M-H, Random, 95% CI)	1.58 [0.20, 12.39]

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Comparison 31. SE - Constipation

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Paroxetine versus older ADs	26	3934	Odds Ratio (M-H, Random, 95% CI)	0.49 [0.40, 0.60]
1.1 versus amitriptyline	10	1146	Odds Ratio (M-H, Random, 95% CI)	0.61 [0.37, 0.99]
1.2 versus clomipramine	2	1111	Odds Ratio (M-H, Random, 95% CI)	0.57 [0.38, 0.85]
1.3 versus dothiepin	1	271	Odds Ratio (M-H, Random, 95% CI)	0.57 [0.32, 0.99]
1.4 versus imipramine	7	633	Odds Ratio (M-H, Random, 95% CI)	0.40 [0.25, 0.63]
1.5 versus lofepramine	2	228	Odds Ratio (M-H, Random, 95% CI)	0.49 [0.20, 1.23]
1.6 versus maprolitine	3	429	Odds Ratio (M-H, Random, 95% CI)	0.31 [0.17, 0.55]
1.7 versus mianserin	1	116	Odds Ratio (M-H, Random, 95% CI)	0.22 [0.01, 4.73]
2 Paroxetine versus other SSRIs	7		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 versus escitalopram	1	454	Odds Ratio (M-H, Random, 95% CI)	2.52 [0.87, 7.29]
2.2 versus fluoxetine	3	1001	Odds Ratio (M-H, Random, 95% CI)	2.71 [1.47, 5.01]
2.3 versus fluvoxamine	1	60	Odds Ratio (M-H, Random, 95% CI)	2.15 [0.36, 12.76]
2.4 versus sertraline	2	545	Odds Ratio (M-H, Random, 95% CI)	3.26 [1.73, 6.14]
3 Paroxetine versus newer or non-conventional ADs	16		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
3.1 versus bupropion	2	240	Odds Ratio (M-H, Random, 95% CI)	2.00 [0.59, 6.81]
3.2 versus duloxetine	5	1573	Odds Ratio (M-H, Random, 95% CI)	0.74 [0.46, 1.18]
3.3 versus mirtazapine	2	529	Odds Ratio (M-H, Random, 95% CI)	0.93 [0.51, 1.69]
3.4 versus nefazodone	1	40	Odds Ratio (M-H, Random, 95% CI)	3.35 [0.32, 35.36]
3.5 versus reboxetine	3	1375	Odds Ratio (M-H, Random, 95% CI)	0.48 [0.36, 0.63]
3.6 versus tianeptine	1	277	Odds Ratio (M-H, Random, 95% CI)	7.10 [0.36, 138.80]
3.7 versus venlafaxine	2	466	Odds Ratio (M-H, Random, 95% CI)	1.16 [0.33, 4.12]

Comparison 32. SE - Cough

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Paroxetine versus older ADs	1		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
1.1 versus lofepramine	1	106	Odds Ratio (M-H, Random, 95% CI)	0.12 [0.01, 2.29]
2 Paroxetine versus newer or non-conventional ADs	5		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 versus duloxetine	2	528	Odds Ratio (M-H, Random, 95% CI)	1.22 [0.43, 3.42]
2.2 versus reboxetine	3	1375	Odds Ratio (M-H, Random, 95% CI)	1.32 [0.50, 3.48]

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Comparison 33. SE - Delirium

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Paroxetine versus other SSRIs	1		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
1.1 versus fluoxetine	1	90	Odds Ratio (M-H, Random, 95% CI)	3.07 [0.12, 77.32]
2 Paroxetine versus older ADs	1		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 versus clomipramine	1	92	Odds Ratio (M-H, Random, 95% CI)	0.2 [0.01, 4.28]

Comparison 34. SE - Depersonalization

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Paroxetine versus older ADs	2		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
1.1 versus amitriptyline	1	21	Odds Ratio (M-H, Random, 95% CI)	5.53 [0.23, 130.34]
1.2 versus lofepramine	1	106	Odds Ratio (M-H, Random, 95% CI)	2.63 [0.10, 66.00]
2 Paroxetine versus other SSRIs	2		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 versus fluoxetine	1	176	Odds Ratio (M-H, Random, 95% CI)	2.97 [0.12, 73.81]
2.2 versus fluvoxamine	1	60	Odds Ratio (M-H, Random, 95% CI)	0.46 [0.08, 2.75]
3 Paroxetine versus newer or non-conventional ADs	1		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
3.1 versus tianeptine	1	277	Odds Ratio (M-H, Random, 95% CI)	3.0 [0.12, 74.28]

Comparison 35. SE - Depression

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Paroxetine versus older ADs	2	323	Odds Ratio (M-H, Random, 95% CI)	0.92 [0.09, 9.38]
1.1 versus amitriptyline	1	217	Odds Ratio (M-H, Random, 95% CI)	3.0 [0.12, 74.46]
1.2 versus lofepramine	1	106	Odds Ratio (M-H, Random, 95% CI)	0.28 [0.01, 7.06]
2 Paroxetine versus other SSRIs	4		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 versus fluoxetine	4	1128	Odds Ratio (M-H, Random, 95% CI)	0.97 [0.45, 2.09]
3 Paroxetine versus newer or non-conventional ADs	3		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
3.1 versus agomelatine	1	284	Odds Ratio (M-H, Random, 95% CI)	1.41 [0.39, 5.13]
3.2 versus reboxetine	2	1050	Odds Ratio (M-H, Random, 95% CI)	0.76 [0.23, 2.46]

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Comparison 36. SE - Diarrhoea

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Paroxetine versus older ADs	13	1743	Odds Ratio (M-H, Random, 95% CI)	2.41 [1.56, 3.73]
1.1 versus amitriptyline	5	653	Odds Ratio (M-H, Random, 95% CI)	1.91 [0.88, 4.14]
1.2 versus dothiepin	1	271	Odds Ratio (M-H, Random, 95% CI)	3.47 [1.23, 9.75]
1.3 versus imipramine	2	159	Odds Ratio (M-H, Random, 95% CI)	1.88 [0.58, 6.02]
1.4 versus lofepramine	1	106	Odds Ratio (M-H, Random, 95% CI)	6.36 [0.32, 126.19]
1.5 versus maprolitine	2	358	Odds Ratio (M-H, Random, 95% CI)	2.94 [1.34, 6.47]
1.6 versus nortriptyline	1	80	Odds Ratio (M-H, Random, 95% CI)	4.52 [0.21, 97.16]
1.7 versus mianserin	1	116	Odds Ratio (M-H, Random, 95% CI)	0.22 [0.01, 4.73]
2 Paroxetine versus other SSRIs	12		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 versus citalopram	1	406	Odds Ratio (M-H, Random, 95% CI)	1.36 [0.76, 2.45]
2.2 versus escitalopram	1	454	Odds Ratio (M-H, Random, 95% CI)	1.62 [0.82, 3.20]
2.3 versus fluoxetine	7	1940	Odds Ratio (M-H, Random, 95% CI)	0.85 [0.63, 1.15]
2.4 versus fluvoxamine	1	60	Odds Ratio (M-H, Random, 95% CI)	2.79 [0.75, 10.33]
2.5 versus sertraline	2	545	Odds Ratio (M-H, Random, 95% CI)	0.40 [0.26, 0.60]
3 Paroxetine versus newer or non-conventional ADs	19		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
3.1 versus agomelatine	1	284	Odds Ratio (M-H, Random, 95% CI)	1.12 [0.33, 3.77]
3.2 versus aprepitant (MK-869)	1	143	Odds Ratio (M-H, Random, 95% CI)	1.27 [0.47, 3.43]
3.3 versus bupropion	2	240	Odds Ratio (M-H, Random, 95% CI)	3.03 [1.35, 6.84]
3.4 versus duloxetine	5	1573	Odds Ratio (M-H, Random, 95% CI)	1.38 [0.68, 2.77]
3.5 versus hypericum	1	251	Odds Ratio (M-H, Random, 95% CI)	2.10 [1.00, 4.44]
3.6 versus mirtazapine	3	726	Odds Ratio (M-H, Random, 95% CI)	1.12 [0.69, 1.83]
3.7 versus reboxetine	3	1375	Odds Ratio (M-H, Random, 95% CI)	3.45 [2.31, 5.15]
3.8 versus tianeptine	1	277	Odds Ratio (M-H, Random, 95% CI)	7.10 [0.36, 138.80]
3.9 versus venlafaxine	1	361	Odds Ratio (M-H, Random, 95% CI)	1.16 [0.44, 3.09]
3.10 versus trazodone	1	108	Odds Ratio (M-H, Random, 95% CI)	3.17 [0.13, 79.60]

Comparison 37. SE - Dizziness

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Paroxetine versus older ADs	21	2554	Odds Ratio (M-H, Random, 95% CI)	0.80 [0.62, 1.03]
1.1 versus amitriptyline	7	777	Odds Ratio (M-H, Random, 95% CI)	0.42 [0.25, 0.72]
1.2 versus clomipramine	1	92	Odds Ratio (M-H, Random, 95% CI)	0.19 [0.02, 1.70]
1.3 versus dothiepin	2	405	Odds Ratio (M-H, Random, 95% CI)	1.73 [0.94, 3.18]
1.4 versus imipramine	6	558	Odds Ratio (M-H, Random, 95% CI)	0.80 [0.53, 1.22]
1.5 versus lofepramine	2	228	Odds Ratio (M-H, Random, 95% CI)	0.76 [0.32, 1.81]
1.6 versus maprotiline	1	298	Odds Ratio (M-H, Random, 95% CI)	1.08 [0.66, 1.78]
1.7 versus mianserin	1	116	Odds Ratio (M-H, Random, 95% CI)	0.57 [0.05, 6.42]
1.8 versus nortriptyline	1	80	Odds Ratio (M-H, Random, 95% CI)	0.28 [0.01, 7.08]
2 Paroxetine versus other SSRIs	10		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 versus escitalopram	1	454	Odds Ratio (M-H, Random, 95% CI)	0.97 [0.51, 1.84]

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2.2 versus fluoxetine	6	1737	Odds Ratio (M-H, Random, 95% CI)	1.50 [1.11, 2.04]
2.3 versus fluvoxamine	1	60	Odds Ratio (M-H, Random, 95% CI)	1.45 [0.44, 4.86]
2.4 versus sertraline	2	545	Odds Ratio (M-H, Random, 95% CI)	1.40 [0.61, 3.22]
3 Paroxetine versus newer or non-conventional ADs	23		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
3.1 versus aprepitant (MK-869)	1	143	Odds Ratio (M-H, Random, 95% CI)	1.2 [0.35, 4.13]
3.2 versus bupropion	2	240	Odds Ratio (M-H, Random, 95% CI)	0.81 [0.37, 1.76]
3.3 versus duloxetine	5	1573	Odds Ratio (M-H, Random, 95% CI)	0.83 [0.58, 1.18]
3.4 versus hypericum	1	251	Odds Ratio (M-H, Random, 95% CI)	3.03 [1.35, 6.82]
3.5 versus milnacipran	1	302	Odds Ratio (M-H, Random, 95% CI)	9.00 [0.48, 168.64]
3.6 versus mirtazapine	3	726	Odds Ratio (M-H, Random, 95% CI)	1.19 [0.66, 2.11]
3.7 versus nefazodone	2	246	Odds Ratio (M-H, Random, 95% CI)	0.48 [0.23, 1.03]
3.8 versus reboxetine	3	1375	Odds Ratio (M-H, Random, 95% CI)	0.84 [0.59, 1.21]
3.9 versus tianeptine	2	604	Odds Ratio (M-H, Random, 95% CI)	7.02 [1.25, 39.32]
3.10 versus trazodone	1	108	Odds Ratio (M-H, Random, 95% CI)	0.51 [0.04, 5.79]
3.11 versus venlafaxine	2	466	Odds Ratio (M-H, Random, 95% CI)	1.39 [0.18, 10.62]

Comparison 38. SE - Dry mouth

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Paroxetine versus older ADs	29	4578	Odds Ratio (M-H, Random, 95% CI)	0.23 [0.18, 0.30]
1.1 versus amitriptyline	12	1576	Odds Ratio (M-H, Random, 95% CI)	0.27 [0.17, 0.43]
1.2 versus clomipramine	2	1111	Odds Ratio (M-H, Random, 95% CI)	0.35 [0.26, 0.48]
1.3 versus dothiepin	2	405	Odds Ratio (M-H, Random, 95% CI)	0.22 [0.10, 0.50]
1.4 versus imipramine	8	835	Odds Ratio (M-H, Random, 95% CI)	0.16 [0.10, 0.26]
1.5 versus lofepramine	1	106	Odds Ratio (M-H, Random, 95% CI)	1.16 [0.25, 5.44]
1.6 versus maprolitine	3	429	Odds Ratio (M-H, Random, 95% CI)	0.13 [0.08, 0.23]
1.7 versus mianserin	1	116	Odds Ratio (M-H, Random, 95% CI)	0.76 [0.12, 4.70]
2 Paroxetine versus other SSRIs	11		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 versus citalopram	1	406	Odds Ratio (M-H, Random, 95% CI)	0.97 [0.56, 1.68]
2.2 versus escitalopram	1	454	Odds Ratio (M-H, Random, 95% CI)	1.44 [0.74, 2.83]
2.3 versus fluoxetine	6	1920	Odds Ratio (M-H, Random, 95% CI)	1.67 [1.17, 2.38]
2.4 versus fluvoxamine	1	60	Odds Ratio (M-H, Random, 95% CI)	0.63 [0.21, 1.88]
2.5 versus sertraline	2	545	Odds Ratio (M-H, Random, 95% CI)	1.01 [0.52, 1.99]
3 Paroxetine versus newer or non-conventional ADs	22		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
3.1 versus agomelatine	1	284	Odds Ratio (M-H, Random, 95% CI)	4.79 [0.55, 41.52]
3.2 versus aprepitant (MK-869)	1	143	Odds Ratio (M-H, Random, 95% CI)	0.98 [0.30, 3.21]
3.3 versus bupropion	2	240	Odds Ratio (M-H, Random, 95% CI)	0.71 [0.27, 1.87]
3.4 versus duloxetine	5	1571	Odds Ratio (M-H, Random, 95% CI)	0.78 [0.55, 1.10]
3.5 versus hypericum	1	251	Odds Ratio (M-H, Random, 95% CI)	2.62 [1.36, 5.04]
3.6 versus mirtazapine	3	726	Odds Ratio (M-H, Random, 95% CI)	0.58 [0.27, 1.24]
3.7 versus nefazodone	2	246	Odds Ratio (M-H, Random, 95% CI)	0.80 [0.35, 1.82]
3.8 versus reboxetine	3	1375	Odds Ratio (M-H, Random, 95% CI)	0.35 [0.27, 0.45]
3.9 versus tianeptine	1	277	Odds Ratio (M-H, Random, 95% CI)	0.70 [0.22, 2.26]
3.10 versus trazodone	1	108	Odds Ratio (M-H, Random, 95% CI)	10.09 [0.53, 192.17]

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3.11 versus venlafaxine	2	466	Odds Ratio (M-H, Random, 95% CI)	1.16 [0.44, 3.06]

Comparison 39. SE - Dyspepsia

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Paroxetine versus older ADs	5		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
1.1 versus amitriptyline	3	552	Odds Ratio (M-H, Random, 95% CI)	0.44 [0.05, 3.72]
1.2 versus dothiepin	1	271	Odds Ratio (M-H, Random, 95% CI)	0.68 [0.25, 1.84]
1.3 versus maprotiline	1	298	Odds Ratio (M-H, Random, 95% CI)	0.47 [0.20, 1.12]
2 Paroxetine versus other SSRIs	4		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 versus fluoxetine	3	1371	Odds Ratio (M-H, Random, 95% CI)	0.77 [0.54, 1.09]
2.2 versus fluvoxamine	1	60	Odds Ratio (M-H, Random, 95% CI)	0.51 [0.13, 1.95]
3 Paroxetine versus newer or non-conventional ADs	6		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
3.1 versus duloxetine	3	802	Odds Ratio (M-H, Random, 95% CI)	0.67 [0.28, 1.61]
3.2 versus mirtazapine	1	197	Odds Ratio (M-H, Random, 95% CI)	1.33 [0.47, 3.72]
3.3 versus reboxetine	2	1050	Odds Ratio (M-H, Random, 95% CI)	1.12 [0.64, 1.96]

Comparison 40. SE - Dyspnea

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Paroxetine versus older ADs	1		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
1.1 versus imipramine	1	75	Odds Ratio (M-H, Random, 95% CI)	0.25 [0.07, 0.85]
2 Paroxetine versus other SSRIs	1		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 versus fluoxetine	1	203	Odds Ratio (M-H, Random, 95% CI)	2.31 [0.84, 6.35]
3 Paroxetine versus newer or non-conventional ADs	3		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
3.1 versus duloxetine	1	274	Odds Ratio (M-H, Random, 95% CI)	0.43 [0.02, 9.08]
3.2 versus reboxetine	2	845	Odds Ratio (M-H, Random, 95% CI)	4.30 [1.21, 15.26]

Comparison 41. SE - ECG abnormailities

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Paroxetine versus older ADs	3	382	Odds Ratio (M-H, Random, 95% CI)	0.33 [0.08, 1.40]
1.1 versus amitriptyline	1	231	Odds Ratio (M-H, Random, 95% CI)	0.25 [0.05, 1.19]
1.2 versus maprolitine	1	71	Odds Ratio (M-H, Random, 95% CI)	2.84 [0.11, 71.99]
1.3 versus nortriptyline	1	80	Odds Ratio (M-H, Random, 95% CI)	0.11 [0.01, 2.27]

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Comparison 42. SE - Emotional lability

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Paroxetine versus older ADs	7	953	Odds Ratio (M-H, Random, 95% CI)	1.18 [0.54, 2.57]
1.1 versus amitriptyline	4	503	Odds Ratio (M-H, Random, 95% CI)	1.66 [0.65, 4.20]
1.2 versus clomipramine	1	92	Odds Ratio (M-H, Random, 95% CI)	0.34 [0.01, 8.58]
1.3 versus maprolitine	2	358	Odds Ratio (M-H, Random, 95% CI)	0.60 [0.12, 2.91]
2 Paroxetine versus other SSRIs	4		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 versus fluoxetine	4	1139	Odds Ratio (M-H, Random, 95% CI)	0.83 [0.31, 2.22]
3 Paroxetine versus newer or non-conventional ADs	2		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
3.1 versus reboxetine	2	1050	Odds Ratio (M-H, Random, 95% CI)	0.62 [0.08, 5.05]

Comparison 43. SE - Fatigue

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Paroxetine versus older ADs	2		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
1.1 versus lofepramine	1	106	Odds Ratio (M-H, Random, 95% CI)	0.17 [0.01, 3.53]
1.2 versus mianserin	1	116	Odds Ratio (M-H, Random, 95% CI)	3.50 [0.14, 87.83]
2 Paroxetine versus other SSRIs	3		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 versus fluoxetine	1	138	Odds Ratio (M-H, Random, 95% CI)	0.21 [0.04, 0.99]
2.2 versus sertraline	2	545	Odds Ratio (M-H, Random, 95% CI)	2.41 [1.21, 4.77]
3 Paroxetine versus newer or non-conventional ADs	8		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
3.1 versus duloxetine	3	1045	Odds Ratio (M-H, Random, 95% CI)	1.19 [0.60, 2.39]
3.2 versus hypericum	1	251	Odds Ratio (M-H, Random, 95% CI)	1.15 [0.54, 2.48]
3.3 versus mirtazapine	3	726	Odds Ratio (M-H, Random, 95% CI)	0.58 [0.32, 1.06]
3.4 versus reboxetine	1	325	Odds Ratio (M-H, Random, 95% CI)	4.91 [0.57, 42.47]

Comparison 44. SE - Fever

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Paroxetine versus older ADs	2		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
1.1 versus imipramine	1	80	Odds Ratio (M-H, Random, 95% CI)	0.33 [0.01, 8.22]
1.2 versus mianserin	1	116	Odds Ratio (M-H, Random, 95% CI)	3.50 [0.14, 87.83]
2 Paroxetine versus newer or non-conventional ADs	2		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 versus reboxetine	2	1050	Odds Ratio (M-H, Random, 95% CI)	0.99 [0.28, 3.54]

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Comparison 45. SE - Flatulence

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Paroxetine versus older ADs	1		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
1.1 versus amitriptyline	1	21	Odds Ratio (M-H, Random, 95% CI)	3.0 [0.11, 82.40]
2 Paroxetine versus other SSRIs	2		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 versus fluoxetine	1	573	Odds Ratio (M-H, Random, 95% CI)	1.69 [0.87, 3.29]
2.2 versus fluvoxamine	1	60	Odds Ratio (M-H, Random, 95% CI)	0.22 [0.02, 2.14]
3 Paroxetine versus newer or non-conventional ADs	6		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
3.1 versus aprepitant (MK-869)	1	143	Odds Ratio (M-H, Random, 95% CI)	0.38 [0.07, 2.01]
3.2 versus mirtazapine	1	254	Odds Ratio (M-H, Random, 95% CI)	4.19 [1.35, 13.00]
3.3 versus reboxetine	2	1050	Odds Ratio (M-H, Random, 95% CI)	1.84 [0.87, 3.87]
3.4 versus duloxetine	2	528	Odds Ratio (M-H, Random, 95% CI)	2.34 [0.83, 6.59]

Comparison 46. SE - Gastrointestinal disorder

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Appendicitis	1		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
1.1 versus fluoxetine	1	138	Odds Ratio (M-H, Random, 95% CI)	3.13 [0.13, 78.26]
2 Cholelithiasis	1		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 versus imipramine	1	202	Odds Ratio (M-H, Random, 95% CI)	0.17 [0.01, 4.16]
3 Colitis	1		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
3.1 versus fluoxetine	1	122	Odds Ratio (M-H, Random, 95% CI)	7.61 [0.38, 150.51]
4 Eructation	1		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
4.1 versus reboxetine	1	520	Odds Ratio (M-H, Random, 95% CI)	0.14 [0.01, 2.71]
5 Melena	1		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
5.1 versus maprolitine	1	60	Odds Ratio (M-H, Random, 95% CI)	3.55 [0.14, 90.59]
6 Gastritis	1		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
6.1 versus imipramine	1	202	Odds Ratio (M-H, Random, 95% CI)	1.53 [0.16, 15.03]
7 Gastroenteritis	2		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
7.1 versus reboxetine	2	1050	Odds Ratio (M-H, Random, 95% CI)	1.13 [0.42, 2.98]
8 Intestinal obstruction	1		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
8.1 versus fluoxetine	1	138	Odds Ratio (M-H, Random, 95% CI)	3.13 [0.13, 78.26]
9 Intestinal perforation	1		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
9.1 versus lofepramine	1	106	Odds Ratio (M-H, Random, 95% CI)	0.28 [0.01, 7.06]
10 Peptic ulcer hemorrhage	1		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
10.1 versus fluoxetine	1	573	Odds Ratio (M-H, Random, 95% CI)	3.06 [0.12, 75.52]
11 NOS	18		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
11.1 versus amisulpride	2	298	Odds Ratio (M-H, Random, 95% CI)	1.77 [0.14, 21.98]
11.2 versus amitriptyline	4	478	Odds Ratio (M-H, Random, 95% CI)	0.68 [0.35, 1.33]
11.3 versus clomipramine	1	83	Odds Ratio (M-H, Random, 95% CI)	0.56 [0.23, 1.38]
11.4 versus imipramine	1	159	Odds Ratio (M-H, Random, 95% CI)	1.69 [0.53, 5.41]
11.5 versus fluoxetine	2	950	Odds Ratio (M-H, Random, 95% CI)	0.75 [0.37, 1.49]

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11.6 versus fluvoxamine	1	81	Odds Ratio (M-H, Random, 95% CI)	0.92 [0.27, 3.12]
11.7 versus maprolitine	1	71	Odds Ratio (M-H, Random, 95% CI)	0.54 [0.17, 1.71]
11.8 versus mianserin	3	126	Odds Ratio (M-H, Random, 95% CI)	3.56 [1.62, 7.79]
11.9 versus reboxetine	2	855	Odds Ratio (M-H, Random, 95% CI)	1.04 [0.08, 14.21]
11.10 versus sertraline	1	192	Odds Ratio (M-H, Random, 95% CI)	1.28 [0.48, 3.39]

Comparison 47. SE - Gynecological

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Dysmenorrhea	3		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
1.1 versus fluvoxamine	1	60	Odds Ratio (M-H, Random, 95% CI)	0.13 [0.01, 2.61]
1.2 versus reboxetine	2	1050	Odds Ratio (M-H, Random, 95% CI)	0.42 [0.07, 2.57]
2 Mestrual disorder	1		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 versus reboxetine	1	325	Odds Ratio (M-H, Random, 95% CI)	4.85 [0.23, 101.77]
3 Vaginal moniliasis	2		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
3.1 versus reboxetine	2	1050	Odds Ratio (M-H, Random, 95% CI)	0.80 [0.19, 3.36]
4 Ectopic pregnancy	1		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
4.1 versus fluoxetine	1	573	Odds Ratio (M-H, Random, 95% CI)	0.20 [0.01, 4.23]
5 Polycystic granuloma	1		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
5.1 versus fluoxetine	1	573	Odds Ratio (M-H, Random, 95% CI)	0.34 [0.01, 8.33]

Comparison 48. SE - Headache

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Paroxetine versus older ADs	29	4496	Odds Ratio (M-H, Random, 95% CI)	1.38 [1.13, 1.68]
1.1 versus amitriptyline	10	1323	Odds Ratio (M-H, Random, 95% CI)	0.93 [0.59, 1.48]
1.2 versus clomipramine	2	1111	Odds Ratio (M-H, Random, 95% CI)	1.23 [0.85, 1.78]
1.3 versus dothiepin	2	405	Odds Ratio (M-H, Random, 95% CI)	2.46 [1.35, 4.48]
1.4 versus imipramine	8	835	Odds Ratio (M-H, Random, 95% CI)	1.29 [0.87, 1.93]
1.5 versus lofepramine	2	228	Odds Ratio (M-H, Random, 95% CI)	1.58 [0.55, 4.54]
1.6 versus maprolitine	3	419	Odds Ratio (M-H, Random, 95% CI)	1.96 [1.13, 3.39]
1.7 versus mianserin	2	175	Odds Ratio (M-H, Random, 95% CI)	1.14 [0.16, 7.93]
2 Paroxetine versus other SSRIs	14		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 versus citalopram	1	406	Odds Ratio (M-H, Random, 95% CI)	0.80 [0.51, 1.27]
2.2 versus escitalopram	1	454	Odds Ratio (M-H, Random, 95% CI)	0.79 [0.51, 1.24]
2.3 versus fluoxetine	8	2116	Odds Ratio (M-H, Random, 95% CI)	1.02 [0.84, 1.23]
2.4 versus fluvoxamine	2	141	Odds Ratio (M-H, Random, 95% CI)	0.91 [0.10, 8.45]
2.5 versus sertraline	2	545	Odds Ratio (M-H, Random, 95% CI)	0.80 [0.55, 1.14]
3 Paroxetine versus newer or non-conventional ADs	23		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
3.1 versus agomelatine	1	284	Odds Ratio (M-H, Random, 95% CI)	1.43 [0.57, 3.62]
3.2 versus aprepitant (MK-869)	1	143	Odds Ratio (M-H, Random, 95% CI)	0.80 [0.39, 1.64]

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3.3 versus bupropion	2	240	Odds Ratio (M-H, Random, 95% CI)	0.92 [0.23, 3.75]
3.4 versus duloxetine	5	1573	Odds Ratio (M-H, Random, 95% CI)	1.01 [0.73, 1.40]
3.5 versus hypericum	1	251	Odds Ratio (M-H, Random, 95% CI)	1.08 [0.48, 2.39]
3.6 versus mirtazapine	3	726	Odds Ratio (M-H, Random, 95% CI)	1.77 [1.12, 2.79]
3.7 versus nefazodone	2	246	Odds Ratio (M-H, Random, 95% CI)	1.14 [0.65, 1.99]
3.8 versus tianeptine	2	604	Odds Ratio (M-H, Random, 95% CI)	1.34 [0.67, 2.67]
3.9 versus reboxetine	3	1375	Odds Ratio (M-H, Random, 95% CI)	1.13 [0.84, 1.53]
3.10 versus trazodone	1	108	Odds Ratio (M-H, Random, 95% CI)	0.11 [0.01, 2.04]
3.11 versus venlafaxine	2	466	Odds Ratio (M-H, Random, 95% CI)	1.37 [0.70, 2.66]

Comparison 49. SE - Hypertension

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Paroxetine versus older ADs	3	202	Odds Ratio (M-H, Random, 95% CI)	0.82 [0.22, 3.14]
1.1 versus amitriptyline	1	26	Odds Ratio (M-H, Random, 95% CI)	0.17 [0.01, 3.92]
1.2 versus maprolitine	1	60	Odds Ratio (M-H, Random, 95% CI)	1.8 [0.28, 11.64]
1.3 versus mianserin	1	116	Odds Ratio (M-H, Random, 95% CI)	0.57 [0.05, 6.42]
2 Paroxetine versus other SSRIs	1		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 versus fluoxetine	1	573	Odds Ratio (M-H, Random, 95% CI)	3.06 [0.12, 75.52]
3 Paroxetine versus newer or non-conventional ADs	4		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
3.1 versus duloxetine	1	274	Odds Ratio (M-H, Random, 95% CI)	2.21 [0.31, 15.99]
3.2 versus reboxetine	2	855	Odds Ratio (M-H, Random, 95% CI)	0.65 [0.15, 2.77]
3.3 versus venlafaxine	1	361	Odds Ratio (M-H, Random, 95% CI)	3.12 [0.32, 30.28]

Comparison 50. SE - Hypotension

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Paroxetine versus older ADs	6	670	Odds Ratio (M-H, Random, 95% CI)	1.07 [0.30, 3.84]
1.1 versus amitriptyline	1	153	Odds Ratio (M-H, Random, 95% CI)	0.31 [0.03, 3.07]
1.2 versus clomipramine	2	175	Odds Ratio (M-H, Random, 95% CI)	2.46 [0.35, 17.21]
1.3 versus imipramine	2	282	Odds Ratio (M-H, Random, 95% CI)	0.40 [0.02, 7.79]
1.4 versus maprolitine	1	60	Odds Ratio (M-H, Random, 95% CI)	8.92 [0.44, 180.67]
2 Paroxetine versus other SSRIs	2		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 versus fluoxetine	2	276	Odds Ratio (M-H, Random, 95% CI)	0.65 [0.18, 2.41]
3 Paroxetine versus newer or non-conventional ADs	4		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
3.1 versus reboxetine	3	1375	Odds Ratio (M-H, Random, 95% CI)	0.37 [0.19, 0.75]
3.2 versus trazodone	1	108	Odds Ratio (M-H, Random, 95% CI)	3.17 [0.13, 79.60]
4 Postural hypotension	4		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
4.1 versus clomipramine	1	92	Odds Ratio (M-H, Random, 95% CI)	1.05 [0.14, 7.76]
4.2 versus dothiepin	1	134	Odds Ratio (M-H, Random, 95% CI)	3.05 [0.12, 76.10]
4.3 versus nortriptyline	1	80	Odds Ratio (M-H, Random, 95% CI)	2.65 [0.10, 66.96]

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4.4 versus reboxetine	1	530	Odds Ratio (M-H, Random, 95% CI)	0.25 [0.03, 2.23]

Comparison 51. SE - Hypertonia

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Paroxetine versus newer or non-conventional ADs	3		Odds Ratio (M-H, Fixed, 95% CI)	Subtotals only
1.1 versus reboxetine	3	1375	Odds Ratio (M-H, Fixed, 95% CI)	0.84 [0.39, 1.84]

Comparison 52. SE - Infection

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Meningitis	1		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
1.1 versus amitriptyline	1	162	Odds Ratio (M-H, Random, 95% CI)	2.96 [0.12, 73.82]
2 Otitis media	1		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 versus reboxetine	1	530	Odds Ratio (M-H, Random, 95% CI)	0.33 [0.03, 3.20]
3 Respiratory upper	4		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
3.1 versus agomelatine	1	572	Odds Ratio (M-H, Random, 95% CI)	0.36 [0.04, 2.88]
3.2 versus aprepitant (MK-869)	1	143	Odds Ratio (M-H, Random, 95% CI)	1.52 [0.41, 5.64]
3.3 versus lofepramine	1	122	Odds Ratio (M-H, Random, 95% CI)	3.21 [0.32, 31.76]
3.4 versus tianeptine	1	277	Odds Ratio (M-H, Random, 95% CI)	0.33 [0.01, 8.14]
4 Urinary	9		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
4.1 versus amitriptyline	1	153	Odds Ratio (M-H, Random, 95% CI)	0.08 [0.00, 1.50]
4.2 versus clomipramine	1	92	Odds Ratio (M-H, Random, 95% CI)	0.33 [0.03, 3.33]
4.3 versus fluoxetine	2	212	Odds Ratio (M-H, Random, 95% CI)	4.39 [0.71, 27.09]
4.4 versus lofepramine	1	106	Odds Ratio (M-H, Random, 95% CI)	6.36 [0.32, 126.19]
4.5 versus mianserin	1	116	Odds Ratio (M-H, Random, 95% CI)	1.15 [0.07, 18.85]
4.6 versus reboxetine	3	1375	Odds Ratio (M-H, Random, 95% CI)	0.54 [0.19, 1.55]
5 NOS	6		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
5.1 versus amitriptyline	1	217	Odds Ratio (M-H, Random, 95% CI)	11.42 [0.62, 209.13]
5.2 versus bupropion	1	100	Odds Ratio (M-H, Random, 95% CI)	0.29 [0.03, 2.93]
5.3 versus mirtazapine	1	197	Odds Ratio (M-H, Random, 95% CI)	0.65 [0.22, 1.91]
5.4 versus reboxetine	3	1375	Odds Ratio (M-H, Random, 95% CI)	0.64 [0.38, 1.07]

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Comparison 53. SE - Influenza-like symptoms

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Paroxetine versus newer or non-conventional ADs	4		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
1.1 versus nefazodone	1	40	Odds Ratio (M-H, Random, 95% CI)	2.25 [0.36, 13.97]
1.2 versus reboxetine	3	1375	Odds Ratio (M-H, Random, 95% CI)	2.01 [0.84, 4.80]

Comparison 54. SE - Insomnia

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Paroxetine versus older ADs	15	1986	Odds Ratio (M-H, Random, 95% CI)	2.17 [1.51, 3.12]
1.1 versus amitriptyline	4	352	Odds Ratio (M-H, Random, 95% CI)	3.66 [1.36, 9.85]
1.2 versus clomipramine	1	92	Odds Ratio (M-H, Random, 95% CI)	4.49 [0.48, 41.79]
1.3 versus dothiepin	2	405	Odds Ratio (M-H, Random, 95% CI)	2.34 [1.03, 5.31]
1.4 versus imipramine	5	601	Odds Ratio (M-H, Random, 95% CI)	1.54 [0.89, 2.66]
1.5 versus lofepramine	1	122	Odds Ratio (M-H, Random, 95% CI)	0.5 [0.09, 2.84]
1.6 versus maprotiline	1	298	Odds Ratio (M-H, Random, 95% CI)	4.38 [1.72, 11.15]
1.7 versus mianserin	1	116	Odds Ratio (M-H, Random, 95% CI)	3.50 [0.14, 87.83]
2 Paroxetine versus other SSRIs	11		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 versus citalopram	1	406	Odds Ratio (M-H, Random, 95% CI)	1.09 [0.63, 1.89]
2.2 versus fluoxetine	7	1994	Odds Ratio (M-H, Random, 95% CI)	0.93 [0.74, 1.16]
2.3 versus fluvoxamine	1	60	Odds Ratio (M-H, Random, 95% CI)	0.58 [0.18, 1.91]
2.4 versus sertraline	2	545	Odds Ratio (M-H, Random, 95% CI)	0.95 [0.61, 1.48]
3 Paroxetine versus newer or non-conventional ADs	18		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
3.1 versus agomelatine	1	284	Odds Ratio (M-H, Random, 95% CI)	1.66 [0.48, 5.81]
3.2 versus aprepitant (MK-869)	1	143	Odds Ratio (M-H, Random, 95% CI)	0.76 [0.28, 2.06]
3.3 versus bupropion	2	240	Odds Ratio (M-H, Random, 95% CI)	1.19 [0.61, 2.33]
3.4 versus duloxetine	4	1095	Odds Ratio (M-H, Random, 95% CI)	0.62 [0.37, 1.04]
3.5 versus milnacipran	1	302	Odds Ratio (M-H, Random, 95% CI)	1.96 [0.18, 21.85]
3.6 versus mirtazapine	2	451	Odds Ratio (M-H, Random, 95% CI)	1.46 [0.54, 3.95]
3.7 versus reboxetine	3	1375	Odds Ratio (M-H, Random, 95% CI)	0.48 [0.31, 0.74]
3.8 versus tianeptine	2	604	Odds Ratio (M-H, Random, 95% CI)	1.32 [0.06, 31.66]
3.9 versus trazodone	1	108	Odds Ratio (M-H, Random, 95% CI)	1.04 [0.20, 5.40]
3.10 versus venlafaxine	1	361	Odds Ratio (M-H, Random, 95% CI)	0.81 [0.31, 2.11]

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Comparison 55. SE - Metabolic and nutritional system

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Paroxetine versus older ADs	5	441	Odds Ratio (M-H, Random, 95% CI)	1.34 [0.50, 3.55]
1.1 versus amitriptyline	2	221	Odds Ratio (M-H, Random, 95% CI)	0.98 [0.30, 3.19]
1.2 versus clomipramine	1	83	Odds Ratio (M-H, Random, 95% CI)	1.03 [0.06, 16.95]
1.3 versus nortriptyline	1	80	Odds Ratio (M-H, Random, 95% CI)	2.65 [0.10, 66.96]
1.4 versus mianserin	1	57	Odds Ratio (M-H, Random, 95% CI)	7.53 [0.37, 152.73]
2 Paroxetine versus other SSRIs	2		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 versus fluoxetine	2	1281	Odds Ratio (M-H, Random, 95% CI)	1.00 [0.10, 9.64]
3 Paroxetine versus newer or non-conventional ADs	1		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
3.1 versus amisulpride	1	277	Odds Ratio (M-H, Random, 95% CI)	1.62 [0.52, 5.09]

Comparison 56. SE - Musculoskeletal and connective tissue disorders

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Paroxetine versus older ADs	3	566	Odds Ratio (M-H, Random, 95% CI)	1.34 [0.26, 7.03]
1.1 versus amitriptyline	1	162	Odds Ratio (M-H, Random, 95% CI)	1.98 [0.18, 22.22]
1.2 versus lofepramine	1	106	Odds Ratio (M-H, Random, 95% CI)	0.28 [0.01, 7.06]
1.3 versus maprotiline	1	298	Odds Ratio (M-H, Random, 95% CI)	3.19 [0.13, 78.86]
2 Paroxetine versus newer or non-conventional ADs	5		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 versus duloxetine	3	802	Odds Ratio (M-H, Random, 95% CI)	0.89 [0.36, 2.20]
2.2 versus mirtazapine	1	197	Odds Ratio (M-H, Random, 95% CI)	1.83 [0.52, 6.45]
2.3 versus reboxetine	1	530	Odds Ratio (M-H, Random, 95% CI)	3.01 [0.12, 74.26]

Comparison 57. SE - Myalgia

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Paroxetine versus other SSRIs	1		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
1.1 versus fluoxetine	1	90	Odds Ratio (M-H, Random, 95% CI)	0.13 [0.01, 2.66]
2 Paroxetine versus newer or non-conventional ADs	2		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 versus reboxetine	2	1050	Odds Ratio (M-H, Random, 95% CI)	0.65 [0.16, 2.56]

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Comparison 58. SE - Nervousness

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Paroxetine versus older ADs	1		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
1.1 versus imipramine	1	80	Odds Ratio (M-H, Random, 95% CI)	1.37 [0.29, 6.56]
2 Paroxetine versus other SSRIs	6		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 versus fluoxetine	4	1660	Odds Ratio (M-H, Random, 95% CI)	1.07 [0.75, 1.52]
2.2 versus fluvoxamine	1	60	Odds Ratio (M-H, Random, 95% CI)	1.3 [0.31, 5.40]
2.3 versus sertraline	1	192	Odds Ratio (M-H, Random, 95% CI)	0.93 [0.43, 2.00]
3 Paroxetine versus newer or non-conventional ADs	7		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
3.1 versus aprepitant (MK-869)	1	143	Odds Ratio (M-H, Random, 95% CI)	4.12 [0.45, 37.78]
3.2 versus milnacipran	1	302	Odds Ratio (M-H, Random, 95% CI)	2.96 [0.30, 28.78]
3.3 versus reboxetine	3	1375	Odds Ratio (M-H, Random, 95% CI)	0.80 [0.48, 1.35]
3.4 versus duloxetine	2	528	Odds Ratio (M-H, Random, 95% CI)	0.56 [0.22, 1.47]

Comparison 59. SE - Nausea/vomiting

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Paroxetine versus older ADs	30	4545	Odds Ratio (M-H, Random, 95% CI)	2.10 [1.59, 2.77]
1.1 versus amitriptyline	10	1282	Odds Ratio (M-H, Random, 95% CI)	2.17 [1.43, 3.29]
1.2 versus clomipramine	2	1111	Odds Ratio (M-H, Random, 95% CI)	1.29 [0.94, 1.78]
1.3 versus dothiepin	2	405	Odds Ratio (M-H, Random, 95% CI)	3.12 [1.11, 8.78]
1.4 versus imipramine	8	835	Odds Ratio (M-H, Random, 95% CI)	2.05 [1.23, 3.42]
1.5 versus lofepramine	2	228	Odds Ratio (M-H, Random, 95% CI)	2.97 [1.12, 7.92]
1.6 versus maprolitine	3	429	Odds Ratio (M-H, Random, 95% CI)	2.56 [0.86, 7.60]
1.7 versus mianserin	2	175	Odds Ratio (M-H, Random, 95% CI)	0.55 [0.04, 8.50]
1.8 versus nortriptyline	1	80	Odds Ratio (M-H, Random, 95% CI)	4.52 [0.21, 97.16]
2 Paroxetine versus other SSRIs	15		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 versus citalopram	1	406	Odds Ratio (M-H, Random, 95% CI)	0.87 [0.51, 1.48]
2.2 versus escitalopram	1	454	Odds Ratio (M-H, Random, 95% CI)	1.05 [0.69, 1.60]
2.3 versus fluoxetine	10	2336	Odds Ratio (M-H, Random, 95% CI)	1.24 [1.02, 1.51]
2.4 versus fluvoxamine	1	60	Odds Ratio (M-H, Random, 95% CI)	1.51 [0.54, 4.24]
2.5 versus sertraline	2	545	Odds Ratio (M-H, Random, 95% CI)	0.89 [0.52, 1.54]
3 Paroxetine versus newer or non-conventional ADs	23		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
3.1 versus agomelatine	1	284	Odds Ratio (M-H, Random, 95% CI)	6.81 [2.31, 20.14]
3.2 versus amisulpride	1	277	Odds Ratio (M-H, Random, 95% CI)	7.13 [2.06, 24.68]
3.3 versus aprepitant (MK-869)	1	143	Odds Ratio (M-H, Random, 95% CI)	1.72 [0.78, 3.79]
3.4 versus bupropion	2	240	Odds Ratio (M-H, Random, 95% CI)	1.22 [0.65, 2.27]
3.5 versus duloxetine	5	1573	Odds Ratio (M-H, Random, 95% CI)	0.68 [0.52, 0.88]
3.6 versus hypericum	1	251	Odds Ratio (M-H, Random, 95% CI)	2.58 [1.13, 5.88]
3.7 versus milnacipran	1	302	Odds Ratio (M-H, Random, 95% CI)	0.97 [0.06, 15.71]

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3.8 versus mirtazapine	3	726	Odds Ratio (M-H, Random, 95% CI)	3.03 [1.91, 4.82]
3.9 versus nefazodone	1	206	Odds Ratio (M-H, Random, 95% CI)	0.71 [0.30, 1.69]
3.10 versus reboxetine	3	1375	Odds Ratio (M-H, Random, 95% CI)	2.07 [1.60, 2.69]
3.11 versus tianeptine	2	604	Odds Ratio (M-H, Random, 95% CI)	2.54 [1.38, 4.67]
3.12 versus trazodone	1	108	Odds Ratio (M-H, Random, 95% CI)	6.89 [0.80, 59.35]
3.13 versus venlafaxine	1	361	Odds Ratio (M-H, Random, 95% CI)	1.04 [0.67, 1.63]

Comparison 60. SE - Neoplasm

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Basal cell carcinoma	1		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
1.1 versus fluoxetine	1	573	Odds Ratio (M-H, Random, 95% CI)	0.20 [0.01, 4.23]
2 Bone	1		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 versus amitriptyline	1	217	Odds Ratio (M-H, Random, 95% CI)	0.33 [0.01, 8.12]
3 Meningioma	1		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
3.1 versus fluoxetine	1	176	Odds Ratio (M-H, Random, 95% CI)	0.32 [0.01, 8.02]
4 Pulmonary	1		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
4.1 versus lofepramine	1	106	Odds Ratio (M-H, Random, 95% CI)	0.28 [0.01, 7.06]
5 NOS	3		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
5.1 versus clomipramine	1	92	Odds Ratio (M-H, Random, 95% CI)	3.20 [0.13, 80.68]
5.2 versus fluoxetine	2	1281	Odds Ratio (M-H, Random, 95% CI)	1.49 [0.24, 9.15]

Comparison 61. SE - Nervous system

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Amnesia	3		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
1.1 versus fluoxetine	1	122	Odds Ratio (M-H, Random, 95% CI)	1.58 [0.25, 9.80]
1.2 versus reboxetine	2	855	Odds Ratio (M-H, Random, 95% CI)	4.87 [0.83, 28.50]
2 Concentration impaired	1		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 versus reboxetine	1	325	Odds Ratio (M-H, Random, 95% CI)	4.85 [0.23, 101.77]
3 Hyperesthesia	2		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
3.1 versus reboxetine	2	1050	Odds Ratio (M-H, Random, 95% CI)	0.75 [0.05, 10.74]
4 Parkinsonism	1		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
4.1 versus nortriptyline	1	80	Odds Ratio (M-H, Random, 95% CI)	0.28 [0.01, 7.08]
5 Seizure	1		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
5.1 versus nortriptyline	1	80	Odds Ratio (M-H, Random, 95% CI)	0.28 [0.01, 7.08]
6 Stroke	1		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
6.1 versus lofepramine	1	106	Odds Ratio (M-H, Random, 95% CI)	0.28 [0.01, 7.06]
7 NOS	11		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
7.1 versus amitriptyline	3	261	Odds Ratio (M-H, Random, 95% CI)	0.76 [0.46, 1.26]
7.2 versus clomipramine	1	83	Odds Ratio (M-H, Random, 95% CI)	0.49 [0.19, 1.23]
7.3 versus fluoxetine	2	342	Odds Ratio (M-H, Random, 95% CI)	0.38 [0.14, 1.04]
7.4 versus imipramine	1	202	Odds Ratio (M-H, Random, 95% CI)	0.24 [0.04, 1.36]

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7.5 versus maprolitine	1	71	Odds Ratio (M-H, Random, 95% CI)	1.5 [0.47, 4.78]
7.6 versus mianserin	2	90	Odds Ratio (M-H, Random, 95% CI)	0.25 [0.09, 0.68]
7.7 versus sertraline	1	353	Odds Ratio (M-H, Random, 95% CI)	0.62 [0.23, 1.63]

Comparison 62. SE - Pain (back)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Paroxetine versus older ADs	2		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
1.1 versus maprotiline	1	298	Odds Ratio (M-H, Random, 95% CI)	3.19 [0.13, 78.86]
1.2 versus mianserin	1	116	Odds Ratio (M-H, Random, 95% CI)	3.50 [0.14, 87.83]
2 Paroxetine versus other SSRIs	2		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 versus fluoxetine	2	663	Odds Ratio (M-H, Random, 95% CI)	0.63 [0.30, 1.31]
3 Paroxetine versus newer or non-conventional ADs	8		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
3.1 versus duloxetine	1	293	Odds Ratio (M-H, Random, 95% CI)	1.35 [0.22, 8.24]
3.2 versus duloxetine	4	1095	Odds Ratio (M-H, Random, 95% CI)	0.85 [0.37, 1.97]
3.3 versus mirtazapine	1	197	Odds Ratio (M-H, Random, 95% CI)	1.24 [0.51, 3.02]
3.4 versus reboxetine	3	1375	Odds Ratio (M-H, Random, 95% CI)	1.36 [0.71, 2.62]

Comparison 63. SE - Pain (chest)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Paroxetine versus older ADs	3	235	Odds Ratio (M-H, Random, 95% CI)	1.11 [0.17, 7.08]
1.1 versus amitriptyline	1	21	Odds Ratio (M-H, Random, 95% CI)	3.0 [0.11, 82.40]
1.2 versus dothiepin	1	134	Odds Ratio (M-H, Random, 95% CI)	3.05 [0.12, 76.10]
1.3 versus imipramine	1	80	Odds Ratio (M-H, Random, 95% CI)	0.19 [0.01, 4.09]
2 Paroxetine versus other SSRIs	1		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 versus fluoxetine	1	90	Odds Ratio (M-H, Random, 95% CI)	7.49 [0.38, 149.40]
3 Paroxetine versus newer or non-conventional ADs	3		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
3.1 versus duloxetine	1	264	Odds Ratio (M-H, Random, 95% CI)	1.49 [0.33, 6.81]
3.2 versus reboxetine	2	1050	Odds Ratio (M-H, Random, 95% CI)	0.86 [0.31, 2.40]

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Comparison 64. SE - Pain (abdominal)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Paroxetine versus older ADs	5		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
1.1 versus amitriptyline	2	330	Odds Ratio (M-H, Random, 95% CI)	0.61 [0.18, 2.07]
1.2 versus imipramine	1	80	Odds Ratio (M-H, Random, 95% CI)	0.19 [0.01, 4.09]
1.3 versus maprolitine	2	369	Odds Ratio (M-H, Random, 95% CI)	1.58 [0.76, 3.28]
2 Paroxetine versus other SSRIs	3		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 versus fluoxetine	3	1022	Odds Ratio (M-H, Random, 95% CI)	0.55 [0.20, 1.53]
3 Paroxetine versus newer or non-conventional ADs	13		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
3.1 versus agomelatine	1	284	Odds Ratio (M-H, Random, 95% CI)	0.93 [0.26, 3.28]
3.2 versus aprepitant (MK-869)	1	143	Odds Ratio (M-H, Random, 95% CI)	0.64 [0.17, 2.36]
3.3 versus bupropion	1	100	Odds Ratio (M-H, Random, 95% CI)	0.92 [0.22, 3.89]
3.4 versus duloxetine	4	1095	Odds Ratio (M-H, Random, 95% CI)	0.75 [0.33, 1.69]
3.5 versus hypericum	1	251	Odds Ratio (M-H, Random, 95% CI)	0.72 [0.29, 1.79]
3.6 versus mirtazapine	1	197	Odds Ratio (M-H, Random, 95% CI)	1.01 [0.34, 3.00]
3.7 versus reboxetine	3	1375	Odds Ratio (M-H, Random, 95% CI)	1.04 [0.59, 1.83]
3.8 versus tianeptine	1	277	Odds Ratio (M-H, Random, 95% CI)	0.39 [0.07, 2.04]

Comparison 65. SE - Pain (general)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Paroxetine versus older ADs	2		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
1.1 versus dothiepin	1	134	Odds Ratio (M-H, Random, 95% CI)	9.57 [0.50, 181.29]
1.2 versus mianserin	1	116	Odds Ratio (M-H, Random, 95% CI)	3.50 [0.14, 87.83]
2 Paroxetine versus SSRIs	3		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 versus fluoxetine	1	90	Odds Ratio (M-H, Random, 95% CI)	7.49 [0.38, 149.40]
2.2 versus sertraline	2	545	Odds Ratio (M-H, Random, 95% CI)	1.54 [0.26, 9.00]
3 Paroxetine versus newer or non-conventional ADs	7		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
3.1 versus duloxetine	2	530	Odds Ratio (M-H, Random, 95% CI)	1.48 [0.74, 2.94]
3.2 versus mirtazapine	1	197	Odds Ratio (M-H, Random, 95% CI)	0.56 [0.16, 1.97]
3.3 versus reboxetine	3	1375	Odds Ratio (M-H, Random, 95% CI)	0.93 [0.27, 3.25]
3.4 versus tianeptine	1	277	Odds Ratio (M-H, Random, 95% CI)	0.33 [0.01, 8.14]

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Comparison 66. SE - Pain (neck)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Paroxetine versus newer or non-conventional ADs	2		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
1.1 versus duloxetine	1	264	Odds Ratio (M-H, Random, 95% CI)	0.13 [0.01, 2.30]
1.2 versus reboxetine	1	325	Odds Ratio (M-H, Random, 95% CI)	1.93 [0.17, 21.46]

Comparison 67. SE - Palpitations

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Paroxetine versus older ADs	9	1171	Odds Ratio (M-H, Random, 95% CI)	0.63 [0.27, 1.51]
1.1 versus amitriptyline	3	374	Odds Ratio (M-H, Random, 95% CI)	0.42 [0.06, 2.74]
1.2 versus dothiepin	1	134	Odds Ratio (M-H, Random, 95% CI)	7.33 [0.37, 144.63]
1.3 versus imipramine	3	441	Odds Ratio (M-H, Random, 95% CI)	0.54 [0.18, 1.61]
1.4 versus lofepramine	1	106	Odds Ratio (M-H, Random, 95% CI)	0.17 [0.01, 3.53]
1.5 versus mianserin	1	116	Odds Ratio (M-H, Random, 95% CI)	3.50 [0.14, 87.83]
2 Paroxetine versus other SSRIs	2		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 versus fluoxetine	1	100	Odds Ratio (M-H, Random, 95% CI)	0.33 [0.01, 8.21]
2.2 versus fluvoxamine	1	60	Odds Ratio (M-H, Random, 95% CI)	0.22 [0.02, 2.14]
3 Paroxetine versus newer or non-conventional ADs	7		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
3.1 versus duloxetine	4	1280	Odds Ratio (M-H, Random, 95% CI)	0.86 [0.34, 2.18]
3.2 versus reboxetine	3	1375	Odds Ratio (M-H, Random, 95% CI)	0.69 [0.36, 1.35]

Comparison 68. SE - Paraesthesia

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Paroxetine versus older ADs	4		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
1.1 versus amitriptyline	1	21	Odds Ratio (M-H, Random, 95% CI)	0.9 [0.05, 16.59]
1.2 versus imipramine	2	282	Odds Ratio (M-H, Random, 95% CI)	0.77 [0.17, 3.43]
1.3 versus maprotiline	1	298	Odds Ratio (M-H, Random, 95% CI)	3.19 [0.13, 78.86]
2 Paroxetine versus SSRIs	2	528	Odds Ratio (M-H, Random, 95% CI)	1.21 [0.17, 8.41]
2.1 versus duloxetine	2	528	Odds Ratio (M-H, Random, 95% CI)	1.21 [0.17, 8.41]
3 Paroxetine versus newer or non-conventional ADs	3		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
3.1 versus reboxetine	3	1375	Odds Ratio (M-H, Random, 95% CI)	0.44 [0.20, 0.96]

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Comparison 69. SE - Pharyngitis

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Paroxetine versus older ADs	2		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
1.1 versus amitriptyline	1	217	Odds Ratio (M-H, Random, 95% CI)	3.09 [0.61, 15.65]
1.2 versus imipramine	1	80	Odds Ratio (M-H, Random, 95% CI)	3.16 [0.31, 31.78]
2 Paroxetine versus SSRIs	1		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 versus fluoxetine	1	203	Odds Ratio (M-H, Random, 95% CI)	3.0 [0.12, 74.52]
3 Paroxetine versus newer or non-conventional ADs	3		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
3.1 versus duloxetine	1	264	Odds Ratio (M-H, Random, 95% CI)	2.06 [0.29, 14.87]
3.2 versus reboxetine	2	1050	Odds Ratio (M-H, Random, 95% CI)	0.74 [0.37, 1.48]

Comparison 70. SE - Pruritus

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Paroxetine versus other SSRIs	1		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
1.1 versus fluoxetine	1	176	Odds Ratio (M-H, Random, 95% CI)	0.32 [0.03, 3.12]
2 Paroxetine versus newer or non-conventional ADs	4		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 versus reboxetine	3	1375	Odds Ratio (M-H, Random, 95% CI)	0.81 [0.19, 3.43]
2.2 versus duloxetine	1	264	Odds Ratio (M-H, Random, 95% CI)	1.36 [0.22, 8.32]

Comparison 71. SE - RARE

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Abdomen enlarged	1		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
1.1 versus reboxetine	1	520	Odds Ratio (M-H, Random, 95% CI)	0.98 [0.24, 3.98]
2 Acute pyelonephritis	1		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 versus fluoxetine	1	573	Odds Ratio (M-H, Random, 95% CI)	0.20 [0.01, 4.23]
3 Alcohol abuse	3		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
3.1 versus fluoxetine	1	573	Odds Ratio (M-H, Random, 95% CI)	3.06 [0.12, 75.52]
3.2 versus maprotiline	1	298	Odds Ratio (M-H, Random, 95% CI)	0.35 [0.01, 8.65]
3.3 versus tianeptine	1	278	Odds Ratio (M-H, Random, 95% CI)	0.33 [0.01, 8.19]
4 Angina attack	1		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
4.1 versus dothiepin	1	134	Odds Ratio (M-H, Random, 95% CI)	0.33 [0.01, 8.21]
5 Coronary artery disorder	1		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
5.1 versus fluoxetine	1	708	Odds Ratio (M-H, Random, 95% CI)	0.33 [0.01, 8.05]
6 Deep thrombophlebitis	3		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
6.1 versus fluoxetine	3	1419	Odds Ratio (M-H, Random, 95% CI)	0.33 [0.05, 2.13]

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7 Edema generalized	2		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
7.1 versus reboxetine	2	1050	Odds Ratio (M-H, Random, 95% CI)	0.99 [0.10, 9.57]
8 Balance difficulty	1		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
8.1 versus dothiepin	1	134	Odds Ratio (M-H, Random, 95% CI)	0.33 [0.01, 8.21]
9 Enucleation of eyeball	1		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
9.1 versus dothiepin	1	134	Odds Ratio (M-H, Random, 95% CI)	0.33 [0.01, 8.21]
10 Epistaxis	2		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
10.1 versus fluoxetine	2	911	Odds Ratio (M-H, Random, 95% CI)	0.99 [0.10, 9.53]
11 Falls	2		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
11.1 versus dothiepin	1	134	Odds Ratio (M-H, Random, 95% CI)	3.05 [0.12, 76.10]
11.2 versus mianserin	1	116	Odds Ratio (M-H, Random, 95% CI)	3.50 [0.14, 87.83]
12 Hiccup	1		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
12.1 versus tianeptine	1	277	Odds Ratio (M-H, Random, 95% CI)	3.0 [0.12, 74.28]
13 Hot flushes	1		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
13.1 versus tianeptine	1	277	Odds Ratio (M-H, Random, 95% CI)	0.99 [0.06, 16.03]
14 Hyperkinesia	2		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
14.1 versus reboxetine	2	1050	Odds Ratio (M-H, Random, 95% CI)	1.49 [0.42, 5.33]
15 Incoordination	1		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
15.1 versus reboxetine	1	530	Odds Ratio (M-H, Random, 95% CI)	3.02 [0.31, 29.25]
16 Irregular pulse	1		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
16.1 versus dothiepin	1	134	Odds Ratio (M-H, Random, 95% CI)	5.15 [0.24, 109.38]
17 Light headedness	2		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
17.1 versus dothiepin	1	134	Odds Ratio (M-H, Random, 95% CI)	3.05 [0.12, 76.10]
17.2 versus tianeptine	1	277	Odds Ratio (M-H, Random, 95% CI)	0.33 [0.01, 8.14]
18 Malaise	1		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
18.1 versus tianeptine	1	277	Odds Ratio (M-H, Random, 95% CI)	3.0 [0.12, 74.28]
19 Overdose	2		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
19.1 versus mianserin	1	36	Odds Ratio (M-H, Random, 95% CI)	0.32 [0.01, 8.27]
19.2 versus fluoxetine	1	138	Odds Ratio (M-H, Random, 95% CI)	0.68 [0.11, 4.18]
20 Peripheal vascular disorder	1		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
20.1 versus reboxetine	1	530	Odds Ratio (M-H, Random, 95% CI)	0.33 [0.03, 3.20]
21 Pregnancy	1		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
21.1 versus amitriptyline	1	217	Odds Ratio (M-H, Random, 95% CI)	0.33 [0.01, 8.12]
22 Psychosomatic disorders	1		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
22.1 versus fluoxetine	1	176	Odds Ratio (M-H, Random, 95% CI)	0.32 [0.01, 8.02]
23 Renal failure	1		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
23.1 versus fluoxetine	1	138	Odds Ratio (M-H, Random, 95% CI)	3.13 [0.13, 78.26]
24 Stage 1 coma	1		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
24.1 versus fluoxetine	1	176	Odds Ratio (M-H, Random, 95% CI)	2.97 [0.12, 73.81]
25 Tooth disorder	3		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
25.1 versus reboxetine	3	1375	Odds Ratio (M-H, Random, 95% CI)	0.90 [0.12, 6.97]
26 Voice alteration	1		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
26.1 versus reboxetine	1	325	Odds Ratio (M-H, Random, 95% CI)	4.85 [0.23, 101.77]

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Comparison 72. SE - Rash, itching, allergic reactions

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Paroxetine verus older ADs	3	444	Odds Ratio (M-H, Random, 95% CI)	0.47 [0.08, 2.87]
1.1 versus imipramine	1	75	Odds Ratio (M-H, Random, 95% CI)	0.13 [0.01, 2.57]
1.2 versus maprolitine	2	369	Odds Ratio (M-H, Random, 95% CI)	0.99 [0.10, 9.63]
2 Paroxetine versus other SSRIs	2		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 versus duloxetine	1	264	Odds Ratio (M-H, Random, 95% CI)	0.18 [0.01, 3.28]
2.2 versus fluoxetine	1	138	Odds Ratio (M-H, Random, 95% CI)	0.34 [0.01, 8.45]
3 Paroxetine versus newer or non-conventional ADs	4		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
3.1 versus reboxetine	3	1375	Odds Ratio (M-H, Random, 95% CI)	0.62 [0.36, 1.05]
3.2 versus tianeptine	1	277	Odds Ratio (M-H, Random, 95% CI)	3.0 [0.12, 74.28]

Comparison 73. SE - Respiratory disorder

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Paroxetine versus older ADs	11	1102	Odds Ratio (M-H, Random, 95% CI)	1.08 [0.54, 2.18]
1.1 versus amitriptyline	2	221	Odds Ratio (M-H, Random, 95% CI)	0.47 [0.15, 1.42]
1.2 versus dothiepin	1	271	Odds Ratio (M-H, Random, 95% CI)	1.35 [0.55, 3.33]
1.3 vesus imipramine	4	319	Odds Ratio (M-H, Random, 95% CI)	2.62 [0.90, 7.64]
1.4 versus lofepramine	1	106	Odds Ratio (M-H, Random, 95% CI)	6.36 [0.32, 126.19]
1.5 versus mianserin	3	185	Odds Ratio (M-H, Random, 95% CI)	0.17 [0.03, 1.02]
2 Paroxetine versus other SSRIs	5		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 versus fluoxetine	5	1674	Odds Ratio (M-H, Random, 95% CI)	0.95 [0.66, 1.35]

Comparison 74. SE - Restlessness

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Paroxetine versus SSRIs	1	274	Odds Ratio (M-H, Random, 95% CI)	6.61 [0.27, 164.02]
1.1 versus duloxetine	1	274	Odds Ratio (M-H, Random, 95% CI)	6.61 [0.27, 164.02]
2 Paroxetine versus newer or non-conventional ADs	1		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 versus reboxetine	1	325	Odds Ratio (M-H, Random, 95% CI)	4.85 [0.23, 101.77]

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Comparison 75. SE - Rhinitis

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Paroxetine versus older ADs	1		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
1.1 versus mianserin	1	116	Odds Ratio (M-H, Random, 95% CI)	0.38 [0.02, 9.43]
2 Paroxetine versus SSRIs	1		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 versus sertraline	1	192	Odds Ratio (M-H, Random, 95% CI)	0.94 [0.46, 1.92]
3 Paroxetine versus newer or non-conventional ADs	7		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
3.1 versus agomelatine	1	284	Odds Ratio (M-H, Random, 95% CI)	0.31 [0.03, 2.98]
3.2 versus mirtazapine	1	197	Odds Ratio (M-H, Random, 95% CI)	1.38 [0.46, 4.13]
3.3 versus reboxetine	3	1375	Odds Ratio (M-H, Random, 95% CI)	1.39 [0.32, 6.05]
3.4 versus duloxetine	2	528	Odds Ratio (M-H, Random, 95% CI)	1.10 [0.59, 2.06]

Comparison 76. SE - Sexual problems

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Anorgasmia	7		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
1.1 versus duloxetine	2	538	Odds Ratio (M-H, Random, 95% CI)	0.69 [0.22, 2.18]
1.2 versus reboxetine	3	1375	Odds Ratio (M-H, Random, 95% CI)	9.84 [2.23, 43.46]
1.3 versus sertraline	2	545	Odds Ratio (M-H, Random, 95% CI)	2.22 [0.43, 11.36]
2 Ejaculation disorder	11		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 versus aprepitant (MK-869)	1	143	Odds Ratio (M-H, Random, 95% CI)	8.33 [1.82, 38.16]
2.2 versus fluoxetine	1	708	Odds Ratio (M-H, Random, 95% CI)	3.17 [1.62, 6.20]
2.3 versus fluvoxamine	1	60	Odds Ratio (M-H, Random, 95% CI)	3.22 [0.32, 32.89]
2.4 versus imipramine	1	79	Odds Ratio (M-H, Random, 95% CI)	12.24 [0.65, 229.29]
2.5 versus maprolitine	1	71	Odds Ratio (M-H, Random, 95% CI)	2.84 [0.11, 71.99]
2.6 versus reboxetine	3	1375	Odds Ratio (M-H, Random, 95% CI)	0.73 [0.37, 1.46]
2.7 versus sertraline	2	545	Odds Ratio (M-H, Random, 95% CI)	3.49 [1.67, 7.26]
2.8 versus tianeptine	1	277	Odds Ratio (M-H, Random, 95% CI)	3.0 [0.12, 74.28]
3 Impotence	6		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
3.1 versus aprepitant (MK-869)	1	143	Odds Ratio (M-H, Random, 95% CI)	3.72 [0.74, 18.54]
3.2 versus duloxetine	1	264	Odds Ratio (M-H, Random, 95% CI)	1.02 [0.25, 4.17]
3.3 versus fluvoxamine	1	60	Odds Ratio (M-H, Random, 95% CI)	1.56 [0.24, 10.05]
3.4 versus reboxetine	3	1375	Odds Ratio (M-H, Random, 95% CI)	0.60 [0.30, 1.17]
4 Libido decreased	11		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
4.1 versus aprepitant (MK-869)	1	143	Odds Ratio (M-H, Random, 95% CI)	9.39 [0.50, 177.78]
4.2 versus bupropion	1	140	Odds Ratio (M-H, Random, 95% CI)	1.93 [0.67, 5.53]
4.3 versus duloxetine	3	802	Odds Ratio (M-H, Random, 95% CI)	1.36 [0.36, 5.14]
4.4 versus fluvoxamine	1	60	Odds Ratio (M-H, Random, 95% CI)	1.3 [0.31, 5.40]
4.5 versus maprotiline	1	298	Odds Ratio (M-H, Random, 95% CI)	5.35 [0.25, 112.36]
4.6 versus reboxetine	3	1375	Odds Ratio (M-H, Random, 95% CI)	2.34 [1.14, 4.82]

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4.7 versus tianeptine	1	277	Odds Ratio (M-H, Random, 95% CI)	0.99 [0.06, 16.03]
5 Penis disorder	1		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
5.1 versus reboxetine	1	530	Odds Ratio (M-H, Random, 95% CI)	0.14 [0.01, 2.75]
6 NOS	14		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
6.1 versus amitriptyline	1	21	Odds Ratio (M-H, Random, 95% CI)	2.0 [0.15, 26.19]
6.2 versus aprepitant (MK-869)	1	143	Odds Ratio (M-H, Random, 95% CI)	11.65 [0.63, 214.77]
6.3 versus bupropion	1	140	Odds Ratio (M-H, Random, 95% CI)	2.35 [0.77, 7.15]
6.4 versus citalopram	1	406	Odds Ratio (M-H, Random, 95% CI)	0.87 [0.38, 2.00]
6.5 versus clomipramine	1	1019	Odds Ratio (M-H, Random, 95% CI)	1.60 [0.72, 3.55]
6.6 versus duloxetine	2	528	Odds Ratio (M-H, Random, 95% CI)	1.25 [0.40, 3.90]
6.7 versus fluvoxamine	1	81	Odds Ratio (M-H, Random, 95% CI)	1.36 [0.39, 4.70]
6.8 versus mirtazapine	1	275	Odds Ratio (M-H, Random, 95% CI)	5.15 [1.69, 15.64]
6.9 versus nefazodone	1	40	Odds Ratio (M-H, Random, 95% CI)	14.55 [0.75, 283.37]
6.10 versus nortriptyline	1	80	Odds Ratio (M-H, Random, 95% CI)	2.65 [0.10, 66.96]
6.11 versus reboxetine	2	1050	Odds Ratio (M-H, Random, 95% CI)	1.95 [0.48, 7.98]
6.12 versus venlafaxine	1	361	Odds Ratio (M-H, Random, 95% CI)	1.29 [0.34, 4.90]

Comparison 77. SE - Skin and appendages

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Paroxetine versus older ADs	5	659	Odds Ratio (M-H, Random, 95% CI)	1.26 [0.63, 2.52]
1.1 versus amitriptyline	2	221	Odds Ratio (M-H, Random, 95% CI)	1.36 [0.61, 3.05]
1.2 versus clomipramine	1	83	Odds Ratio (M-H, Random, 95% CI)	1.03 [0.19, 5.41]
1.3 versus maprotiline	1	298	Odds Ratio (M-H, Random, 95% CI)	3.19 [0.13, 78.86]
1.4 versus mianserin	1	57	Odds Ratio (M-H, Random, 95% CI)	0.31 [0.01, 7.95]
2 Paroxetine versus other SSRIs	1		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 versus fluoxetine	1	100	Odds Ratio (M-H, Random, 95% CI)	0.13 [0.01, 1.06]
3 Paroxetine versus newer or non-conventional ADs	2		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
3.1 versus reboxetine	2	1050	Odds Ratio (M-H, Random, 95% CI)	0.35 [0.10, 1.20]

Comparison 78. SE - Sleep disorders

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Paroxetine versus older ADs	2		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
1.1 versus imipramine	1	159	Odds Ratio (M-H, Random, 95% CI)	0.49 [0.12, 2.02]
1.2 versus mianserin	1	116	Odds Ratio (M-H, Random, 95% CI)	0.38 [0.02, 9.43]
2 Paroxetine versus newer or non-conventional ADs	9		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 versus duloxetine	2	538	Odds Ratio (M-H, Random, 95% CI)	2.92 [0.70, 12.22]
2.2 versus hypericum	1	251	Odds Ratio (M-H, Random, 95% CI)	2.07 [0.69, 6.24]
2.3 versus mirtazapine	2	451	Odds Ratio (M-H, Random, 95% CI)	1.46 [0.54, 3.95]

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2.4 versus reboxetine	3	1375	Odds Ratio (M-H, Random, 95% CI)	3.13 [1.04, 9.43]
2.5 versus trazodone	1	108	Odds Ratio (M-H, Random, 95% CI)	0.11 [0.01, 2.04]

Comparison 79. SE - Sleepiness/drowsiness

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Paroxetine versus older ADs	22	2711	Odds Ratio (M-H, Random, 95% CI)	0.72 [0.50, 1.02]
1.1 versus amitriptyline	8	985	Odds Ratio (M-H, Random, 95% CI)	0.72 [0.36, 1.43]
1.2 versus clomipramine	1	92	Odds Ratio (M-H, Random, 95% CI)	0.51 [0.04, 5.84]
1.3 versus dothiepin	2	405	Odds Ratio (M-H, Random, 95% CI)	0.45 [0.14, 1.41]
1.4 versus imipramine	7	633	Odds Ratio (M-H, Random, 95% CI)	0.95 [0.58, 1.55]
1.5 versus lofepramine	1	122	Odds Ratio (M-H, Random, 95% CI)	2.14 [0.38, 12.16]
1.6 versus maprolitine	2	358	Odds Ratio (M-H, Random, 95% CI)	0.37 [0.17, 0.82]
1.7 versus mianserin	1	116	Odds Ratio (M-H, Random, 95% CI)	0.37 [0.04, 3.68]
2 Paroxetine versus other SSRIs	12		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 versus citalopram	1	406	Odds Ratio (M-H, Random, 95% CI)	0.61 [0.34, 1.08]
2.2 versus fluoxetine	8	2116	Odds Ratio (M-H, Random, 95% CI)	1.48 [1.16, 1.88]
2.3 versus fluvoxamine	1	60	Odds Ratio (M-H, Random, 95% CI)	0.64 [0.22, 1.87]
2.4 versus sertraline	2	426	Odds Ratio (M-H, Random, 95% CI)	1.29 [0.30, 5.60]
3 Paroxetine versus newer or non-conventional ADs	19		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
3.1 versus agomelatine	1	284	Odds Ratio (M-H, Random, 95% CI)	2.69 [0.84, 8.66]
3.2 versus aprepitant (MK-869)	1	143	Odds Ratio (M-H, Random, 95% CI)	0.98 [0.43, 2.24]
3.3 versus bupropion	2	240	Odds Ratio (M-H, Random, 95% CI)	7.63 [2.51, 23.16]
3.4 versus duloxetine	5	1571	Odds Ratio (M-H, Random, 95% CI)	1.03 [0.70, 1.51]
3.5 versus mirtazapine	3	726	Odds Ratio (M-H, Random, 95% CI)	0.81 [0.55, 1.19]
3.6 versus nefazodone	2	246	Odds Ratio (M-H, Random, 95% CI)	0.73 [0.13, 4.13]
3.7 versus reboxetine	3	1375	Odds Ratio (M-H, Random, 95% CI)	2.66 [1.45, 4.89]
3.8 versus trazodone	1	108	Odds Ratio (M-H, Random, 95% CI)	0.33 [0.03, 3.31]
3.9 versus venlafaxine	1	361	Odds Ratio (M-H, Random, 95% CI)	1.03 [0.42, 2.54]

Comparison 80. SE - Sinusitis

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Paroxetine versus newer or non-conventional ADs	3		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
1.1 versus reboxetine	3	1375	Odds Ratio (M-H, Random, 95% CI)	1.31 [0.60, 2.86]

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Comparison 81. SE - Special senses

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 NOS	6		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
1.1 versus amitriptyline	2	221	Odds Ratio (M-H, Random, 95% CI)	1.22 [0.59, 2.53]
1.2 versus clomipramine	1	83	Odds Ratio (M-H, Random, 95% CI)	0.75 [0.16, 3.58]
1.3 versus mianserin	3	126	Odds Ratio (M-H, Random, 95% CI)	1.23 [0.32, 4.73]
2 Taste perversion	3		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 versus amitriptyline	2	150	Odds Ratio (M-H, Random, 95% CI)	0.71 [0.05, 10.26]
2.2 versus reboxetine	1	530	Odds Ratio (M-H, Random, 95% CI)	1.25 [0.33, 4.73]
3 Auditory disorders	1		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
3.1 versus reboxetine	1	325	Odds Ratio (M-H, Random, 95% CI)	0.19 [0.01, 3.97]

Comparison 82. SE - Surgical procedure

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Paroxetine versus older ADs	1		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
1.1 versus dothiepin	1	134	Odds Ratio (M-H, Random, 95% CI)	3.05 [0.12, 76.10]
2 Paroxetine versus other SSRIs	2		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 versus fluoxetine	2	663	Odds Ratio (M-H, Random, 95% CI)	4.87 [0.55, 43.27]

Comparison 83. SE - Sweating

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Paroxetine versus older ADs	15	2970	Odds Ratio (M-H, Random, 95% CI)	0.75 [0.50, 1.12]
1.1 versus amitriptyline	5	774	Odds Ratio (M-H, Random, 95% CI)	1.72 [0.60, 4.90]
1.2 versus clomipramine	2	1111	Odds Ratio (M-H, Random, 95% CI)	0.73 [0.48, 1.10]
1.3 versus imipramine	6	681	Odds Ratio (M-H, Random, 95% CI)	0.43 [0.29, 0.65]
1.4 versus lofepramine	1	106	Odds Ratio (M-H, Random, 95% CI)	0.13 [0.01, 1.10]
1.5 versus maprotiline	1	298	Odds Ratio (M-H, Random, 95% CI)	1.51 [0.77, 2.96]
2 Paroxetine versus other SSRIs	8		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 versus escitalopram	1	454	Odds Ratio (M-H, Random, 95% CI)	1.49 [0.81, 2.72]
2.2 versus fluoxetine	6	1431	Odds Ratio (M-H, Random, 95% CI)	0.95 [0.43, 2.12]
2.3 versus fluvoxamine	1	60	Odds Ratio (M-H, Random, 95% CI)	4.5 [1.09, 18.50]
3 Paroxetine versus newer or non-conventional ADs	18		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
3.1 versus aprepitant (MK-869)	1	143	Odds Ratio (M-H, Random, 95% CI)	4.31 [0.88, 21.07]
3.2 versus bupropion	1	140	Odds Ratio (M-H, Random, 95% CI)	1.36 [0.53, 3.46]
3.3 versus duloxetine	5	1573	Odds Ratio (M-H, Random, 95% CI)	0.80 [0.50, 1.28]

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3.4 versus hypericum	1	251	Odds Ratio (M-H, Random, 95% CI)	1.48 [0.61, 3.61]
3.5 versus mirtazapine	3	726	Odds Ratio (M-H, Random, 95% CI)	3.12 [1.61, 6.03]
3.6 versus nefazodone	1	40	Odds Ratio (M-H, Random, 95% CI)	22.78 [1.20, 432.58]
3.7 versus reboxetine	3	1375	Odds Ratio (M-H, Random, 95% CI)	0.48 [0.34, 0.68]
3.8 versus tianeptine	1	277	Odds Ratio (M-H, Random, 95% CI)	13.49 [0.75, 241.76]
3.9 versus trazodone	1	108	Odds Ratio (M-H, Random, 95% CI)	3.17 [0.13, 79.60]
3.10 versus venlafaxine	1	361	Odds Ratio (M-H, Random, 95% CI)	2.95 [0.92, 9.44]

Comparison 84. SE - Tachycardia

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Paroxetine versus older ADs	5	717	Odds Ratio (M-H, Random, 95% CI)	0.37 [0.12, 1.13]
1.1 versus amitriptyline	2	360	Odds Ratio (M-H, Random, 95% CI)	0.43 [0.04, 4.44]
1.2 versus imipramine	3	357	Odds Ratio (M-H, Random, 95% CI)	0.36 [0.09, 1.47]
2 Paroxetine versus SSRIs	1		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 versus sertraline	1	353	Odds Ratio (M-H, Random, 95% CI)	1.29 [0.47, 3.55]
3 Paroxetine versus newer or non-conventional ADs	4		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
3.1 versus duloxetine	1	293	Odds Ratio (M-H, Random, 95% CI)	0.67 [0.07, 6.53]
3.2 versus reboxetine	3	1375	Odds Ratio (M-H, Random, 95% CI)	0.39 [0.15, 1.01]

Comparison 85. SE - Tension

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Paroxetine versus newer or non-conventional ADs	1		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
1.1 versus duloxetine	1	293	Odds Ratio (M-H, Random, 95% CI)	0.50 [0.06, 4.53]

Comparison 86. SE - Thirst

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Paroxetine versus newer or non-conventional ADs	2		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
1.1 versus reboxetine	2	1050	Odds Ratio (M-H, Random, 95% CI)	1.74 [0.51, 6.01]

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Comparison 87. SE - Tinnitus

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Paroxetine versus older ADs	1		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
1.1 versus mianserin	1	116	Odds Ratio (M-H, Random, 95% CI)	0.38 [0.02, 9.43]
2 Paroxetine versus newer or non-conventional ADs	3		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 versus duloxetine	2	538	Odds Ratio (M-H, Random, 95% CI)	0.56 [0.11, 2.77]
2.2 versus tianeptine	1	277	Odds Ratio (M-H, Random, 95% CI)	3.0 [0.12, 74.28]

Comparison 88. SE - Tremor

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Paroxetine versus older ADs	23	3313	Odds Ratio (M-H, Random, 95% CI)	0.69 [0.50, 0.94]
1.1 versus amitriptyline	9	1014	Odds Ratio (M-H, Random, 95% CI)	0.44 [0.22, 0.90]
1.2 versus clomipramine	2	1111	Odds Ratio (M-H, Random, 95% CI)	0.76 [0.52, 1.12]
1.3 versus imipramine	8	835	Odds Ratio (M-H, Random, 95% CI)	0.85 [0.51, 1.42]
1.4 versus lofepramine	1	106	Odds Ratio (M-H, Random, 95% CI)	0.85 [0.12, 6.30]
1.5 versus maprolitine	2	131	Odds Ratio (M-H, Random, 95% CI)	0.84 [0.03, 25.65]
1.6 versus mianserin	1	116	Odds Ratio (M-H, Random, 95% CI)	3.50 [0.14, 87.83]
2 Paroxetine versus other SSRIs	10		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 versus fluoxetine	7	1994	Odds Ratio (M-H, Random, 95% CI)	0.98 [0.67, 1.44]
2.2 versus fluvoxamine	1	60	Odds Ratio (M-H, Random, 95% CI)	1.38 [0.28, 6.80]
2.3 versus sertraline	2	545	Odds Ratio (M-H, Random, 95% CI)	1.82 [1.07, 3.09]
3 Paroxetine versus newer or non-conventional ADs	13		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
3.1 versus bupropion	1	100	Odds Ratio (M-H, Random, 95% CI)	0.91 [0.25, 3.38]
3.2 versus duloxetine	4	1095	Odds Ratio (M-H, Random, 95% CI)	1.45 [0.64, 3.29]
3.3 versus mirtazapine	2	529	Odds Ratio (M-H, Random, 95% CI)	3.67 [1.43, 9.42]
3.4 versus nefazodone	1	40	Odds Ratio (M-H, Random, 95% CI)	11.18 [0.56, 222.98]
3.5 versus reboxetine	3	1375	Odds Ratio (M-H, Random, 95% CI)	2.75 [1.35, 5.57]
3.6 versus tianeptine	1	277	Odds Ratio (M-H, Random, 95% CI)	2.0 [0.18, 22.31]
3.7 versus trazodone	1	108	Odds Ratio (M-H, Random, 95% CI)	1.04 [0.14, 7.66]

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Comparison 89. SE - Upper respiratory tract infection

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Paroxetine versus newer or non-conventional ADs	1		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
1.1 versus reboxetine	1	325	Odds Ratio (M-H, Random, 95% CI)	2.63 [0.69, 10.11]

Comparison 90. SE - Urination/Urogenital problems

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Difficulty micturating	2		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
1.1 versus amitriptyline	2	65	Odds Ratio (M-H, Random, 95% CI)	0.85 [0.23, 3.19]
2 Dysuria	2		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 versus reboxetine	2	855	Odds Ratio (M-H, Random, 95% CI)	0.16 [0.04, 0.75]
3 Urination frequency	5		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
3.1 versus bupropion	1	100	Odds Ratio (M-H, Random, 95% CI)	0.12 [0.01, 2.46]
3.2 versus duloxetine	1	293	Odds Ratio (M-H, Random, 95% CI)	1.01 [0.09, 11.28]
3.3 versus imipramine	1	79	Odds Ratio (M-H, Random, 95% CI)	0.08 [0.00, 1.45]
3.4 versus reboxetine	2	1050	Odds Ratio (M-H, Random, 95% CI)	1.30 [0.56, 2.99]
4 Urinary retention	6		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
4.1 versus amitriptyline	1	129	Odds Ratio (M-H, Random, 95% CI)	1.02 [0.14, 7.44]
4.2 versus imipramine	1	80	Odds Ratio (M-H, Random, 95% CI)	0.04 [0.00, 0.73]
4.3 versus nortriptyline	1	80	Odds Ratio (M-H, Random, 95% CI)	4.52 [0.21, 97.16]
4.4 versus reboxetine	3	1375	Odds Ratio (M-H, Random, 95% CI)	0.28 [0.14, 0.54]
5 Not Otherwise Specified	9		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
5.1 versus amitriptyline	2	221	Odds Ratio (M-H, Random, 95% CI)	1.83 [0.51, 6.52]
5.2 versus clomipramine	1	83	Odds Ratio (M-H, Random, 95% CI)	0.20 [0.01, 4.19]
5.3 versus duloxetine	2	557	Odds Ratio (M-H, Random, 95% CI)	0.87 [0.22, 3.41]
5.4 versus imipramine	1	159	Odds Ratio (M-H, Random, 95% CI)	0.10 [0.01, 0.82]
5.5 versus mianserin	2	394	Odds Ratio (M-H, Random, 95% CI)	1.38 [0.21, 8.87]
5.6 versus sertraline	1	353	Odds Ratio (M-H, Random, 95% CI)	11.60 [1.48, 90.81]

Comparison 91. SE - Visual problems (accommodation disorders, amblyopia, blepharoptosis, blurred vision, detached retina, dry eye, eye strain, mydriasis)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Paroxetine versus older ADs	8	830	Odds Ratio (M-H, Random, 95% CI)	1.21 [0.74, 1.98]
1.1 versus amitriptyline	3	278	Odds Ratio (M-H, Random, 95% CI)	0.76 [0.37, 1.58]
1.2 versus clomipramine	1	92	Odds Ratio (M-H, Random, 95% CI)	2.20 [0.38, 12.62]
1.3 versus imipramine	2	238	Odds Ratio (M-H, Random, 95% CI)	1.60 [0.65, 3.92]

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1.4 versus lofepramine	1	106	Odds Ratio (M-H, Random, 95% CI)	6.36 [0.32, 126.19]
1.5 versus mianserin	1	116	Odds Ratio (M-H, Random, 95% CI)	1.15 [0.07, 18.85]
2 Paroxetine versus SSRIs	1		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 versus sertraline	1	353	Odds Ratio (M-H, Random, 95% CI)	1.21 [0.51, 2.87]
3 Paroxetine versus newer or non-conventional ADs	10		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
3.1 versus duloxetine	4	1299	Odds Ratio (M-H, Random, 95% CI)	1.06 [0.61, 1.82]
3.2 versus nefazodone	1	206	Odds Ratio (M-H, Random, 95% CI)	0.6 [0.21, 1.72]
3.3 versus reboxetine	3	1375	Odds Ratio (M-H, Random, 95% CI)	0.72 [0.30, 1.71]
3.4 versus tianeptine	1	277	Odds Ratio (M-H, Random, 95% CI)	3.0 [0.12, 74.28]
3.5 versus venlafaxine	1	105	Odds Ratio (M-H, Random, 95% CI)	2.0 [0.18, 22.75]

Comparison 92. SE - Vertigo

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Paroxetine versus older ADs	6	767	Odds Ratio (M-H, Random, 95% CI)	0.70 [0.32, 1.50]
1.1 versus amitriptyline	4	636	Odds Ratio (M-H, Random, 95% CI)	0.57 [0.17, 1.91]
1.2 versus maprolitine	2	131	Odds Ratio (M-H, Random, 95% CI)	0.91 [0.27, 3.03]
2 Paroxetine versus other SSRIs	2		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 versus fluoxetine	1	106	Odds Ratio (M-H, Random, 95% CI)	0.96 [0.23, 4.06]
2.2 versus fluvoxamine	1	81	Odds Ratio (M-H, Random, 95% CI)	1.9 [0.17, 21.82]
3 Paroxetine versus newer or non-conventional ADs	3		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
3.1 versus duloxetine	1	293	Odds Ratio (M-H, Random, 95% CI)	1.01 [0.09, 11.28]
3.2 versus reboxetine	1	325	Odds Ratio (M-H, Random, 95% CI)	0.48 [0.04, 5.30]
3.3 versus trazodone	1	108	Odds Ratio (M-H, Random, 95% CI)	0.34 [0.01, 8.52]

Comparison 93. SE - Weight gain

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Paroxetine versus older ADs	6	729	Odds Ratio (M-H, Random, 95% CI)	0.52 [0.14, 1.98]
1.1 versus amitryptline	1	231	Odds Ratio (M-H, Random, 95% CI)	1.05 [0.36, 3.09]
1.2 versus clomipramine	1	92	Odds Ratio (M-H, Random, 95% CI)	5.46 [0.25, 116.92]
1.3 versus imipramine	1	159	Odds Ratio (M-H, Random, 95% CI)	0.12 [0.01, 0.95]
1.4 versus maprolitine	2	131	Odds Ratio (M-H, Random, 95% CI)	0.10 [0.01, 0.81]
1.5 versus mianserin	1	116	Odds Ratio (M-H, Random, 95% CI)	3.50 [0.14, 87.83]
2 Paroxetine versus other SSRIs	2		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 versus fluoxetine	2	276	Odds Ratio (M-H, Random, 95% CI)	0.99 [0.27, 3.59]
3 Paroxetine versus newer or non-conventional ADs	9		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
3.1 versus duloxetine	2	567	Odds Ratio (M-H, Random, 95% CI)	0.59 [0.09, 3.63]
3.2 versus mirtazapine	3	726	Odds Ratio (M-H, Random, 95% CI)	0.26 [0.08, 0.84]
3.3 versus reboxetine	2	855	Odds Ratio (M-H, Random, 95% CI)	4.12 [1.02, 16.62]

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3.4 versus tianeptine	1	277	Odds Ratio (M-H, Random, 95% CI)	3.0 [0.12, 74.28]
3.5 versus venlafaxine	1	105	Odds Ratio (M-H, Random, 95% CI)	2.09 [0.49, 8.82]

Comparison 94. SE - Weight loss

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Paroxetine versus older ADs	1		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
1.1 versus maprolitine	1	71	Odds Ratio (M-H, Random, 95% CI)	2.84 [0.11, 71.99]
2 Paroxetine versus other SSRIs	3		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 versus fluoxetine	3	398	Odds Ratio (M-H, Random, 95% CI)	0.42 [0.11, 1.55]
3 Paroxetine versus newer or non-conventional ADs	6		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
3.1 versus duloxetine	2	567	Odds Ratio (M-H, Random, 95% CI)	0.37 [0.06, 2.18]
3.2 versus mirtazapine	1	275	Odds Ratio (M-H, Random, 95% CI)	7.31 [0.37, 142.96]
3.3 versus reboxetine	3	1375	Odds Ratio (M-H, Random, 95% CI)	0.88 [0.37, 2.07]

Comparison 95. SE - Yawning

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Paroxetine versus older ADs	1		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
1.1 versus imipramine	1	80	Odds Ratio (M-H, Random, 95% CI)	5.57 [0.62, 50.03]
2 Paroxetine versus newer or non-conventional ADs	3		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 versus reboxetine	2	1050	Odds Ratio (M-H, Random, 95% CI)	12.13 [1.57, 93.64]
2.2 versus tianeptine	1	277	Odds Ratio (M-H, Random, 95% CI)	3.0 [0.12, 74.28]

Comparison 96. Deaths, suicide and suicidality

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Suicide - attempted	8		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
1.1 versus agomelatine	1	572	Odds Ratio (M-H, Random, 95% CI)	1.16 [0.22, 6.04]
1.2 versus amitriptyline	2	351	Odds Ratio (M-H, Random, 95% CI)	0.33 [0.03, 3.19]
1.3 versus clomipramine	1	1019	Odds Ratio (M-H, Random, 95% CI)	0.49 [0.15, 1.63]
1.4 versus fluoxetine	2	314	Odds Ratio (M-H, Random, 95% CI)	0.25 [0.03, 2.30]
1.5 versus reboxetine	1	325	Odds Ratio (M-H, Random, 95% CI)	2.89 [0.12, 71.50]
1.6 versus tianeptine	1	277	Odds Ratio (M-H, Random, 95% CI)	7.10 [0.36, 138.80]
2 Suicide - completed	4		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 versus agomelatine	1	572	Odds Ratio (M-H, Random, 95% CI)	2.90 [0.18, 46.73]
2.2 versus amitriptyline	1	217	Odds Ratio (M-H, Random, 95% CI)	0.33 [0.01, 8.12]

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2.3 versus clomipramine	1	1019	Odds Ratio (M-H, Random, 95% CI)	0.99 [0.06, 15.81]
2.4 versus fluoxetine	1	138	Odds Ratio (M-H, Random, 95% CI)	1.03 [0.06, 16.80]
3 Suicide - tendency/ideation	6		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
3.1 versus amitriptyline	1	26	Odds Ratio (M-H, Random, 95% CI)	5.87 [0.25, 135.15]
3.2 versus fluoxetine	3	952	Odds Ratio (M-H, Random, 95% CI)	1.54 [0.35, 6.71]
3.3 versus lofepramine	1	106	Odds Ratio (M-H, Random, 95% CI)	2.63 [0.10, 66.00]
3.4 versus tianeptine	1	277	Odds Ratio (M-H, Random, 95% CI)	3.0 [0.12, 74.28]
4 Deaths (any cause)	3		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
4.1 versus fluoxetine	2	711	Odds Ratio (M-H, Random, 95% CI)	0.64 [0.08, 5.23]
4.2 versus lofepramine	1	106	Odds Ratio (M-H, Random, 95% CI)	0.86 [0.05, 14.07]

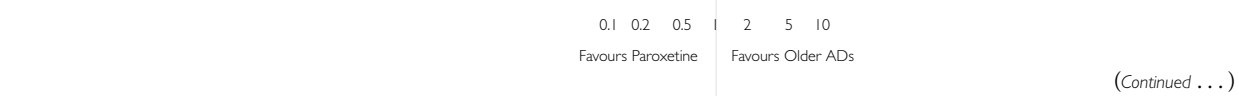
Analysis 1.1. Comparison 1 Failure to respond at endpoint (6 - 12 weeks), Outcome 1 Paroxetine versus older ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 1 Failure to respond at endpoint (6 - 12 weeks)

Outcome: 1 Paroxetine versus older ADs

Study or subgroup	Paroxetine n/N	Older ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
1 versus amitriptyline					
29060/281 PAR	44/82	34/80		3.7 %	1.57 [0.84, 2.91]
29060/299	43/109	51/108		5.0 %	0.73 [0.42, 1.25]
Bascara 1989	0/27	1/23		0.1 %	0.27 [0.01, 7.02]
Battegay 1985	4/11	4/10		0.5 %	0.86 [0.15, 5.00]
Bignamini 1992	81/156	66/153		7.2 %	1.42 [0.91, 2.23]
Christiansen 1996	25/71	25/73		3.1 %	1.04 [0.53, 2.07]
Geretsegger 1995	26/44	29/46		2.0 %	0.85 [0.36, 1.98]
Hutchinson 1992	26/58	13/32		1.9 %	1.19 [0.50, 2.85]
Laursen 1985	10/21	10/23		1.0 %	1.18 [0.36, 3.88]
Sacchetti 2002	42/64	47/65		2.6 %	0.73 [0.35, 1.55]
Staner 1995	14/21	10/19		0.9 %	1.80 [0.50, 6.46]
Steinmeyer 1992	50/112	44/110		5.1 %	1.21 [0.71, 2.06]
Stuppaeck 1994	35/78	29/75		3.5 %	1.29 [0.68, 2.46]
Subtotal (95% CI)	**854**	**817**		**36.5 %**	**1.12 [0.92, 1.37]**
Total events: 400 (Paroxetine), 363 (Older ADs)					
Heterogeneity: Tau^2 = 0.0; Chi^2 = 8.02, df = 12 (P = 0.78); I^2 =0.0%					



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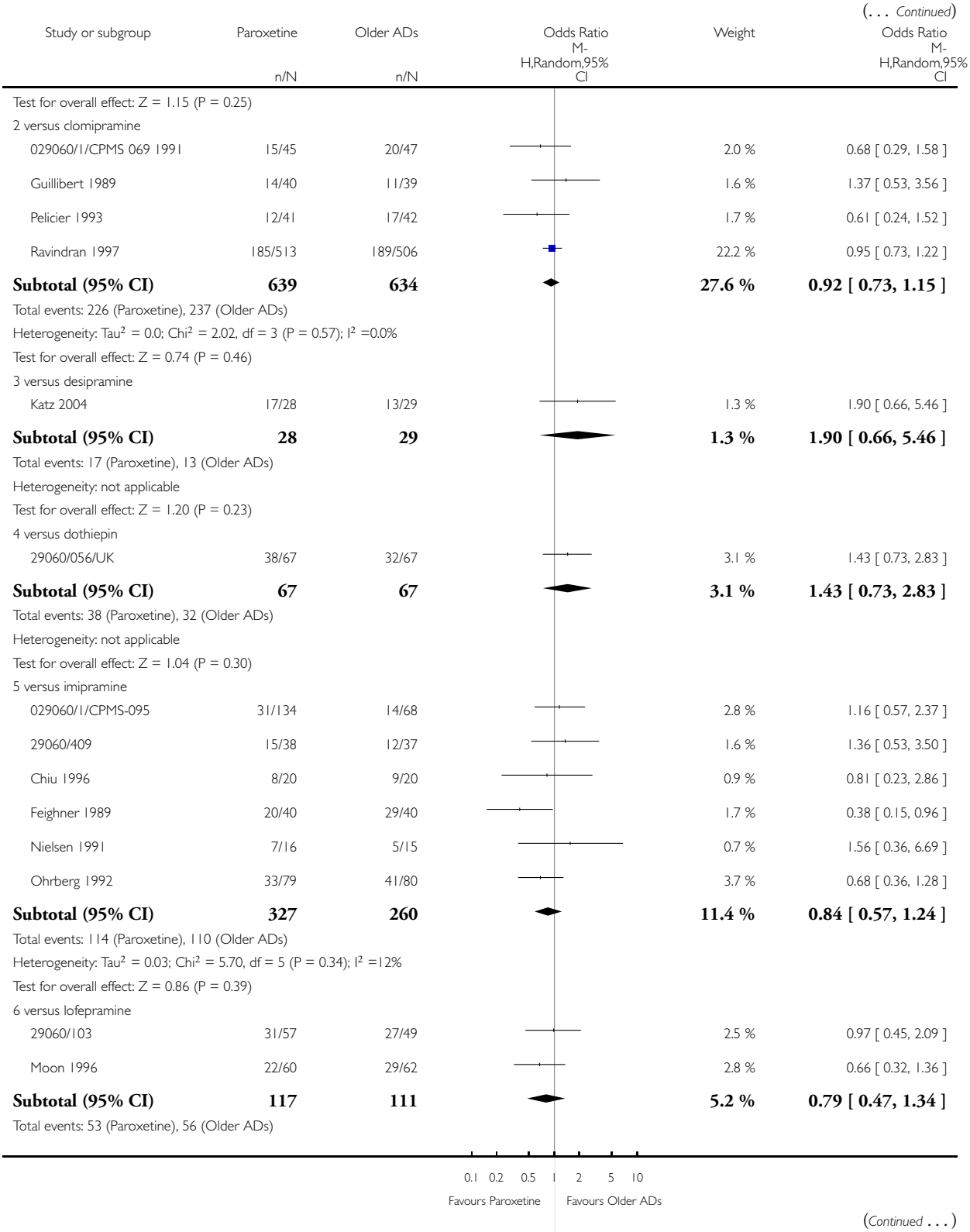

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Study or subgroup	Paroxetine n/N	Older ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.52$, df = 1 (P = 0.47); $I^2 = 0.0\%$					
Test for overall effect: Z = 0.87 (P = 0.38)					
7 versus maprolitine					
29060.065.BE	18/28	17/32		1.3 %	1.59 [0.56, 4.49]
Schnyder 1996	18/37	18/34		1.7 %	0.84 [0.33, 2.14]
Szegedi 1995	59/145	53/153		6.5 %	1.29 [0.81, 2.07]
Subtotal (95% CI)	**210**	**219**		**9.5 %**	**1.24 [0.84, 1.82]**
Total events: 95 (Paroxetine), 88 (Older ADs)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.91$, df = 2 (P = 0.63); $I^2 = 0.0\%$					
Test for overall effect: Z = 1.07 (P = 0.29)					
8 versus mianserin					
29060/III/83/022	9/18	7/18		0.8 %	1.57 [0.42, 5.90]
29060III/85/038	13/30	18/29		1.3 %	0.47 [0.16, 1.32]
Dalery 2001	17/54	18/62		2.3 %	1.12 [0.51, 2.48]
Dorman 1992	14/29	5/28		1.0 %	4.29 [1.28, 14.41]
Subtotal (95% CI)	**131**	**137**		**5.4 %**	**1.30 [0.56, 3.05]**
Total events: 53 (Paroxetine), 48 (Older ADs)					
Heterogeneity: $Tau^2 = 0.45$; $Chi^2 = 7.60$, df = 3 (P = 0.06); $I^2 = 61\%$					
Test for overall effect: Z = 0.61 (P = 0.54)					
Total (95% CI)	**2373**	**2274**		**100.0 %**	**1.04 [0.92, 1.17]**
Total events: 996 (Paroxetine), 947 (Older ADs)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 32.15$, df = 33 (P = 0.51); $I^2 = 0.0\%$					
Test for overall effect: Z = 0.60 (P = 0.55)					
Test for subgroup differences: $Chi^2 = 7.03$, df = 7 (P = 0.43), $I^2 = 0\%$					

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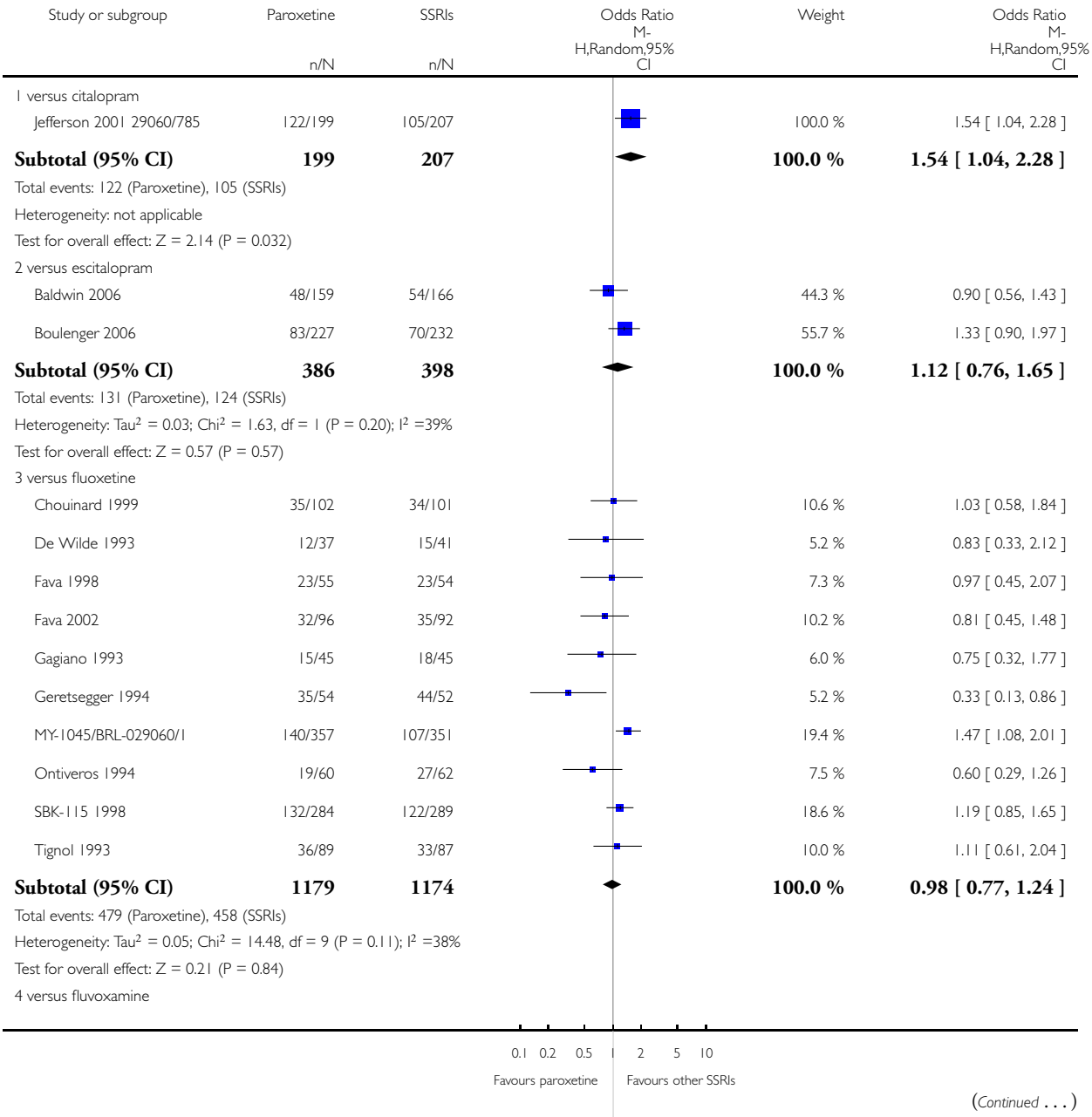
Analysis 1.2. Comparison 1 Failure to respond at endpoint (6 - 12 weeks), Outcome 2 Paroxetine versus other SSRIs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 1 Failure to respond at endpoint (6 - 12 weeks)

Outcome: 2 Paroxetine versus other SSRIs



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Study or subgroup	Paroxetine n/N	SSRIs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Ansseau 1993	34/56	34/64		46.1 %	1.36 [0.66, 2.82]
Kato 2005	16/42	15/39		30.3 %	0.98 [0.40, 2.41]
Kiev 1997	14/30	13/30		23.5 %	1.14 [0.41, 3.17]
Subtotal (95% CI)	**128**	**133**		**100.0 %**	**1.19 [0.72, 1.94]**
Total events: 64 (Paroxetine), 62 (SSRIs)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.31$, df = 2 (P = 0.86); $I^2 = 0.0\%$					
Test for overall effect: Z = 0.68 (P = 0.50)					
5 versus sertraline					
Aberg-Wistedt 2000	66/177	60/176		66.8 %	1.15 [0.74, 1.78]
Fava 2002	32/96	26/96		33.2 %	1.35 [0.73, 2.50]
Subtotal (95% CI)	**273**	**272**		**100.0 %**	**1.21 [0.85, 1.73]**
Total events: 98 (Paroxetine), 86 (SSRIs)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.17$, df = 1 (P = 0.68); $I^2 = 0.0\%$					
Test for overall effect: Z = 1.05 (P = 0.29)					

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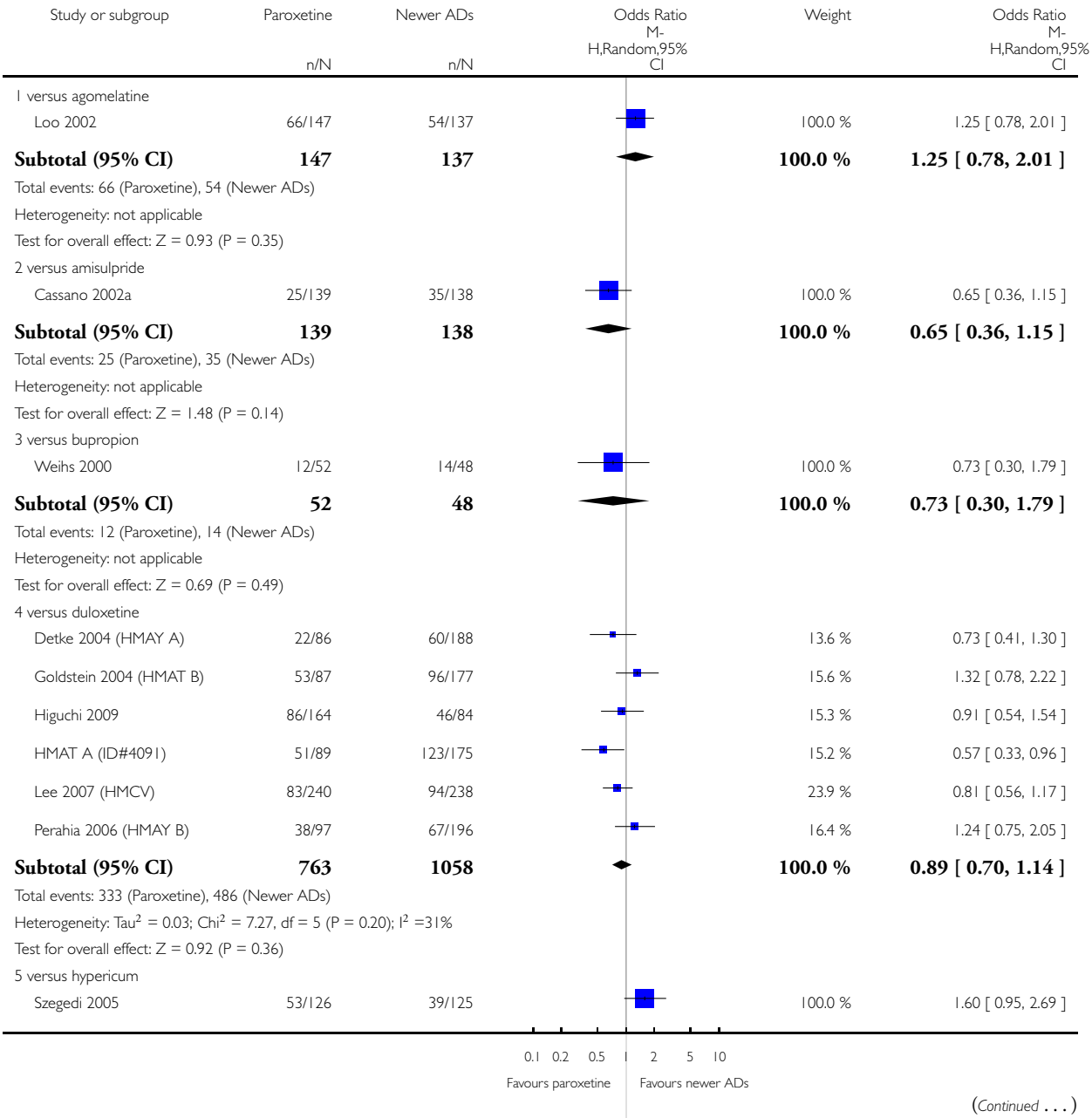
Analysis 1.3. Comparison 1 Failure to respond at endpoint (6 - 12 weeks), Outcome 3 Paroxetine versus newer or non-conventional ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 1 Failure to respond at endpoint (6 - 12 weeks)

Outcome: 3 Paroxetine versus newer or non-conventional ADs



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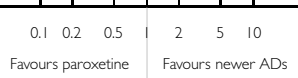
Study or subgroup	Paroxetine n/N	Newer ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Subtotal (95% CI)	**126**	**125**		**100.0 %**	**1.60 [0.95, 2.69]**
Total events: 53 (Paroxetine), 39 (Newer ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.78 (P = 0.075)					
6 versus milnacipran					
Sechter 2004	62/153	63/149		100.0 %	0.93 [0.59, 1.47]
Subtotal (95% CI)	**153**	**149**		**100.0 %**	**0.93 [0.59, 1.47]**
Total events: 62 (Paroxetine), 63 (Newer ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.31 (P = 0.76)					
7 versus mirtazapine					
Benkert 1999	70/136	65/139		36.8 %	1.21 [0.75, 1.94]
Blier 2009	10/19	15/21		4.8 %	0.44 [0.12, 1.64]
Schatzberg 2002	66/126	56/128		33.8 %	1.41 [0.86, 2.32]
Wade 2003	64/98	61/99		24.5 %	1.17 [0.66, 2.10]
Subtotal (95% CI)	**379**	**387**		**100.0 %**	**1.20 [0.90, 1.61]**
Total events: 210 (Paroxetine), 197 (Newer ADs)					
Heterogeneity: Tau^2 = 0.0; Chi^2 = 2.65, df = 3 (P = 0.45); I^2 =0.0%					
Test for overall effect: Z = 1.27 (P = 0.20)					
8 versus nefazodone					
Hicks 2002	4/20	9/20		100.0 %	0.31 [0.07, 1.25]
Subtotal (95% CI)	**20**	**20**		**100.0 %**	**0.31 [0.07, 1.25]**
Total events: 4 (Paroxetine), 9 (Newer ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.65 (P = 0.098)					
9 versus reboxetine					
Gallen 2001	109/265	121/265		38.5 %	0.83 [0.59, 1.17]
M/2020/0047	138/262	138/252		37.9 %	0.92 [0.65, 1.30]
M/2020/0052	66/166	79/159		23.6 %	0.67 [0.43, 1.04]
Subtotal (95% CI)	**693**	**676**		**100.0 %**	**0.82 [0.66, 1.02]**
Total events: 313 (Paroxetine), 338 (Newer ADs)					
Heterogeneity: Tau^2 = 0.0; Chi^2 = 1.25, df = 2 (P = 0.53); I^2 =0.0%					
Test for overall effect: Z = 1.82 (P = 0.069)					
10 versus tianeptine					
Lepine 2001	60/165	66/162		48.9 %	0.83 [0.53, 1.30]
Nickel 2003	12/22	13/22		9.7 %	0.83 [0.25, 2.74]
Waintraub 2002	51/139	40/138		41.4 %	1.42 [0.86, 2.35]
Subtotal (95% CI)	**326**	**322**		**100.0 %**	**1.04 [0.71, 1.53]**



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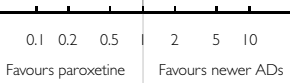
Study or subgroup	Paroxetine n/N	Newer ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Total events: 123 (Paroxetine), 119 (Newer ADs)					
Heterogeneity: Tau^2 = 0.03; Chi^2 = 2.57, df = 2 (P = 0.28); I^2 =22%					
Test for overall effect: Z = 0.19 (P = 0.85)					
11 versus trazodone					
Kasper 2005	5/53	7/55		100.0 %	0.71 [0.21, 2.41]
Subtotal (95% CI)	**53**	**55**		**100.0 %**	**0.71 [0.21, 2.41]**
Total events: 5 (Paroxetine), 7 (Newer ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.54 (P = 0.59)					
12 versus venlafaxine					
0600B 428	27/56	15/58		22.6 %	2.67 [1.21, 5.87]
0600B1-367	37/81	67/105		26.5 %	0.48 [0.26, 0.86]
Mc Partlin 1998	73/178	70/183		29.7 %	1.12 [0.74, 1.71]
Owens 2008	18/42	17/44		21.2 %	1.19 [0.50, 2.82]
Subtotal (95% CI)	**357**	**390**		**100.0 %**	**1.10 [0.58, 2.11]**
Total events: 155 (Paroxetine), 169 (Newer ADs)					
Heterogeneity: Tau^2 = 0.32; Chi^2 = 12.40, df = 3 (P = 0.01); I^2 =76%					
Test for overall effect: Z = 0.29 (P = 0.77)					



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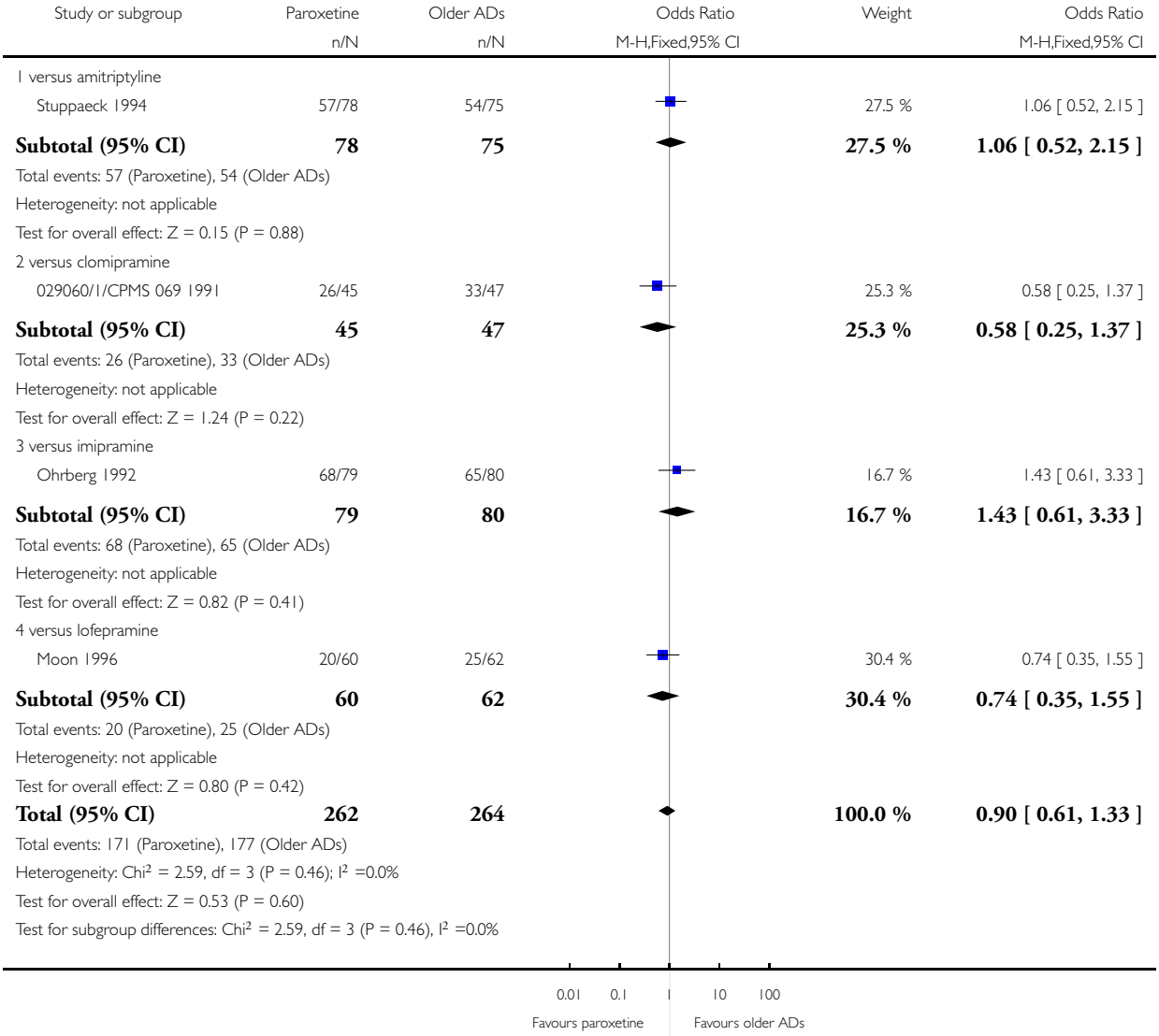
Analysis 2.1. Comparison 2 Failure to respond (at 1 - 4 weeks), Outcome 1 Paroxetine versus older ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 2 Failure to respond (at 1 - 4 weeks)

Outcome: 1 Paroxetine versus older ADs



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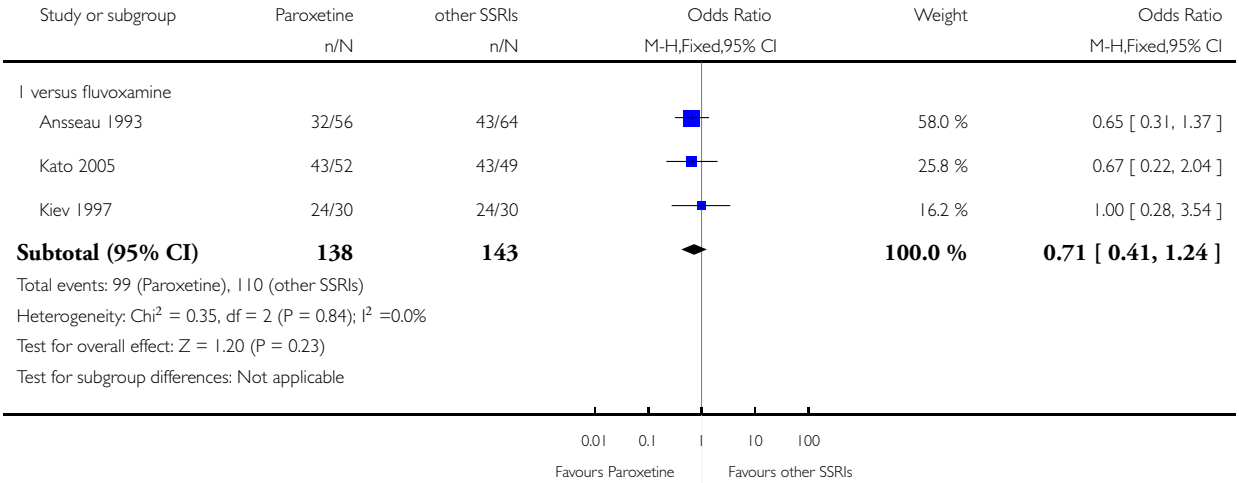
Analysis 2.2. Comparison 2 Failure to respond (at 1 - 4 weeks), Outcome 2 Paroxetine versus SSRIs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 2 Failure to respond (at 1 - 4 weeks)

Outcome: 2 Paroxetine versus SSRIs



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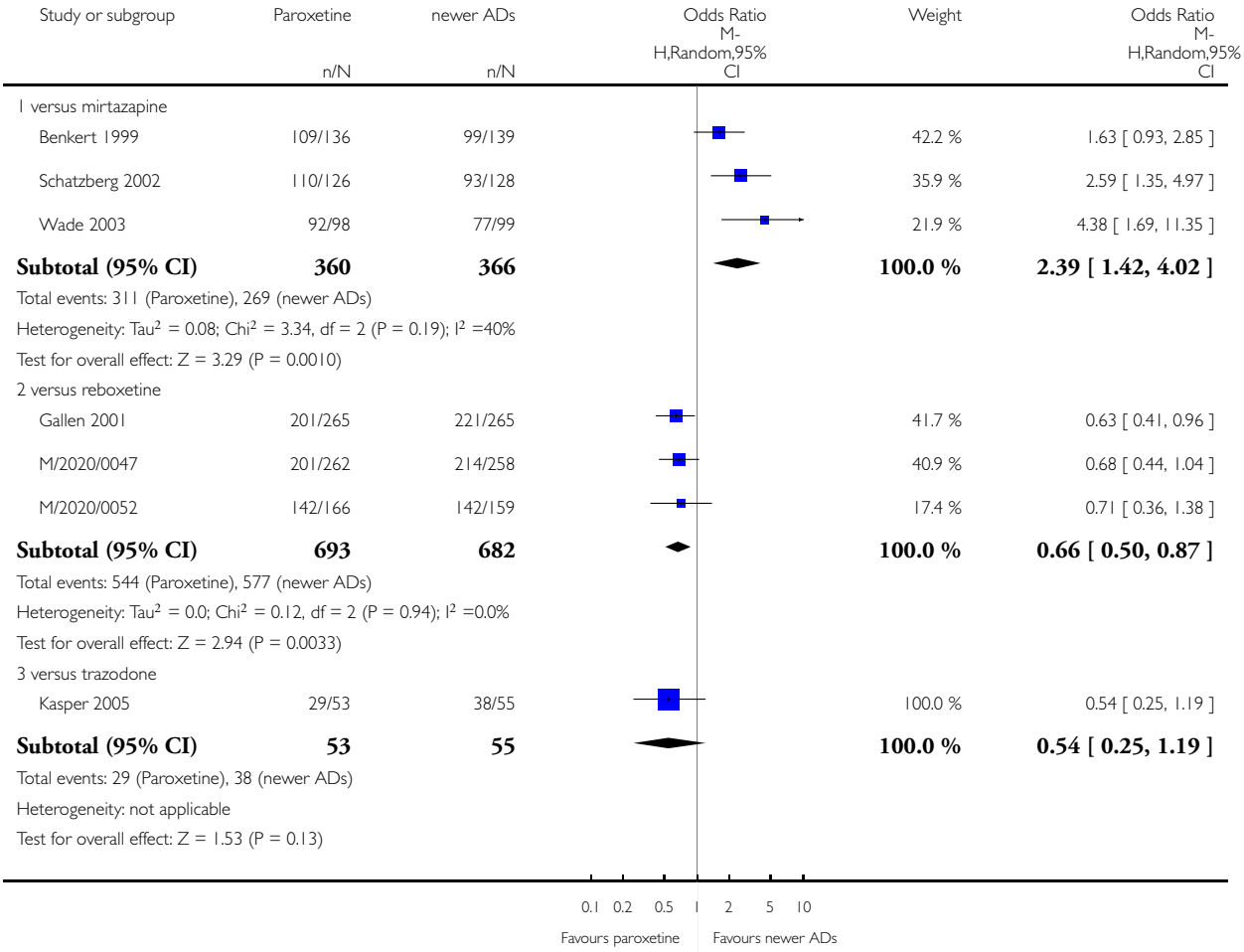
Analysis 2.3. Comparison 2 Failure to respond (at 1 - 4 weeks), Outcome 3 Paroxetine versus newer or non-conventional ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 2 Failure to respond (at 1 - 4 weeks)

Outcome: 3 Paroxetine versus newer or non-conventional ADs



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Analysis 3.1. Comparison 3 Failure to respond (at 16 - 24 weeks), Outcome 1 Paroxetine versus SSRIs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 3 Failure to respond (at 16 - 24 weeks)

Outcome: 1 Paroxetine versus SSRIs

Study or subgroup	Paroxetine n/N	newer ADs n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
1 versus escitalopram					
Boulenger 2006	56/227	45/232		100.0 %	1.36 [0.87, 2.12]
Subtotal (95% CI)	**227**	**232**		**100.0 %**	**1.36 [0.87, 2.12]**
Total events: 56 (Paroxetine), 45 (newer ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.36 (P = 0.17)					
Test for subgroup differences: Not applicable					

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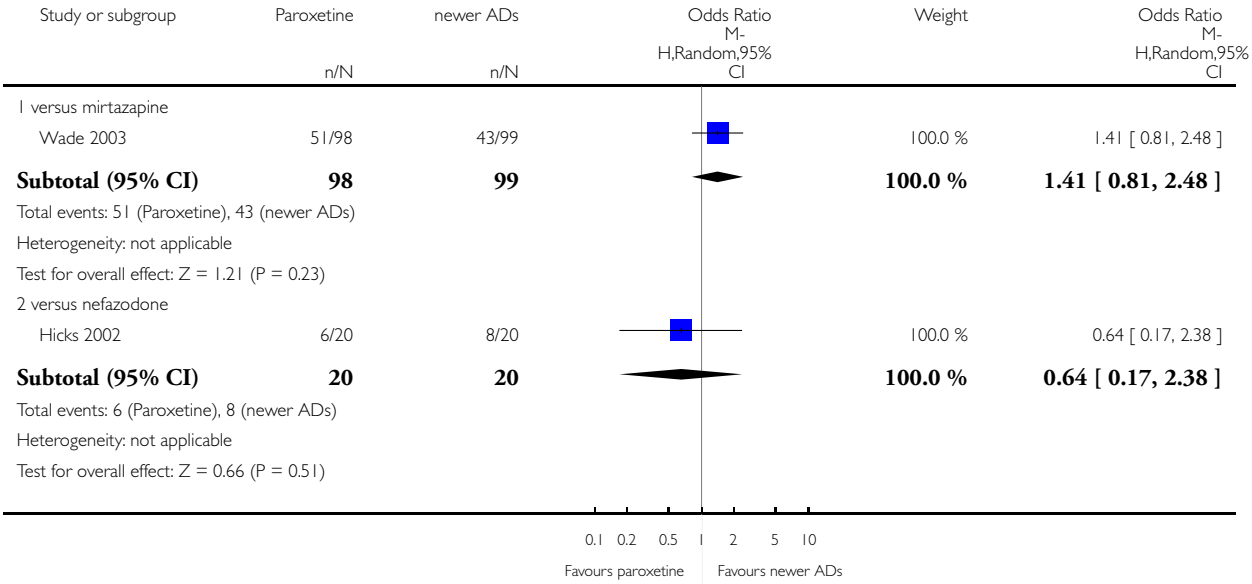
Analysis 3.2. Comparison 3 Failure to respond (at 16 - 24 weeks), Outcome 2 Paroxetine versus newer or non-conventional ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 3 Failure to respond (at 16 - 24 weeks)

Outcome: 2 Paroxetine versus newer or non-conventional ADs



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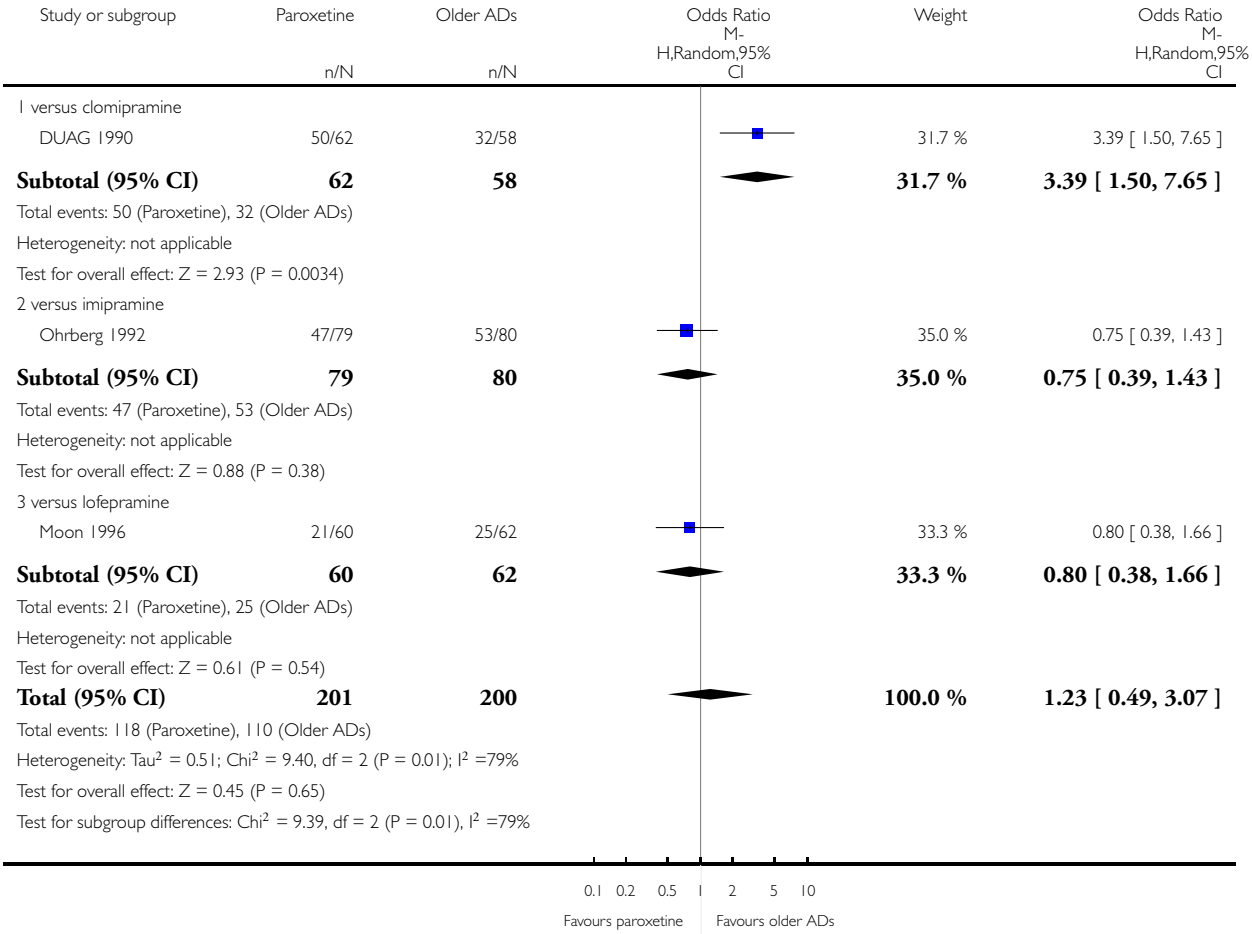
Analysis 4.1. Comparison 4 Failure to remit at endpoint (6 - 12 weeks), Outcome 1 Paroxetine versus older ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 4 Failure to remit at endpoint (6 - 12 weeks)

Outcome: 1 Paroxetine versus older ADs



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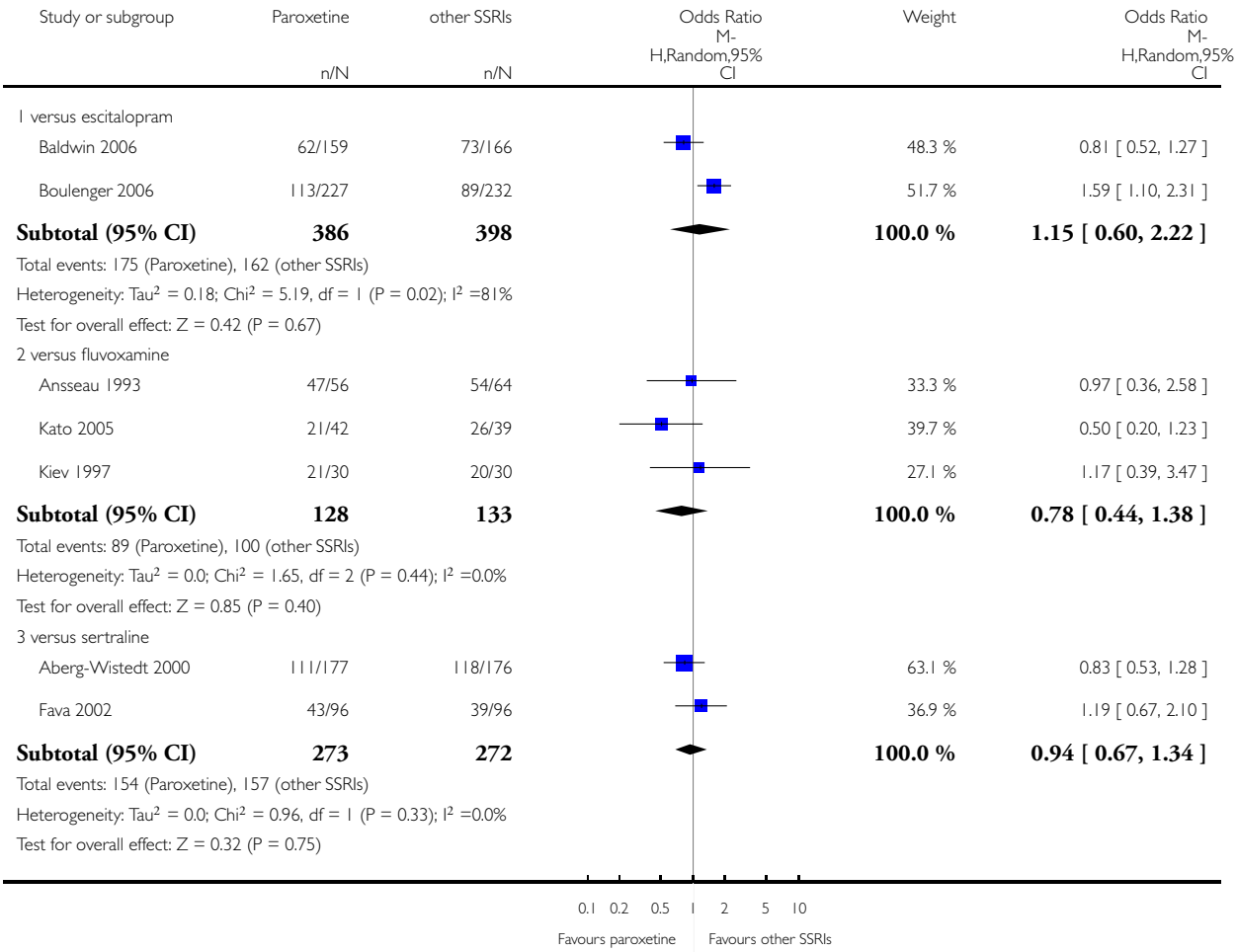
Analysis 4.2. Comparison 4 Failure to remit at endpoint (6 - 12 weeks), Outcome 2 Paroxetine versus other SSRIs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 4 Failure to remit at endpoint (6 - 12 weeks)

Outcome: 2 Paroxetine versus other SSRIs



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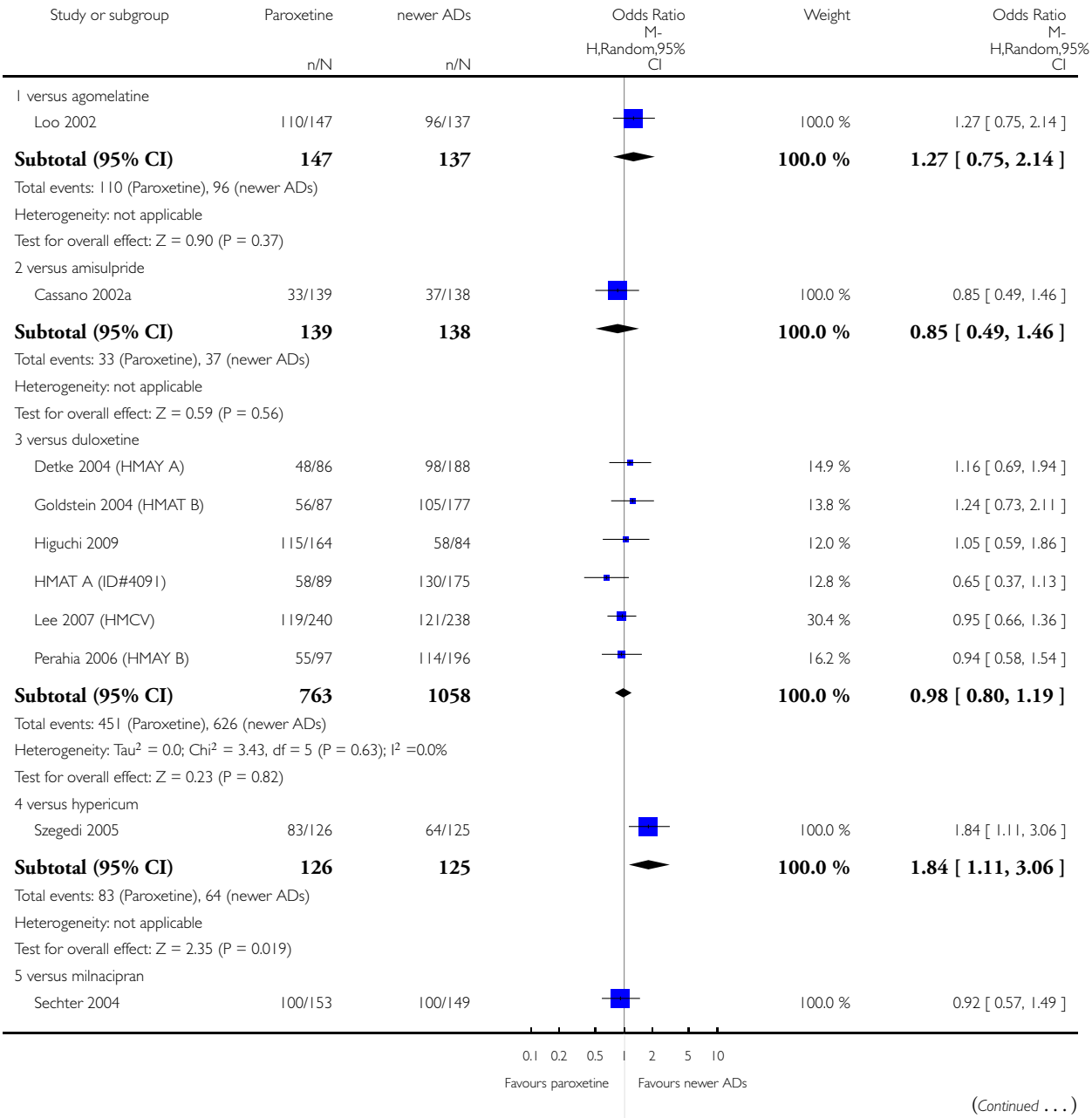
Analysis 4.3. Comparison 4 Failure to remit at endpoint (6 - 12 weeks), Outcome 3 Paroxetine versus newer or non-conventional ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 4 Failure to remit at endpoint (6 - 12 weeks)

Outcome: 3 Paroxetine versus newer or non-conventional ADs



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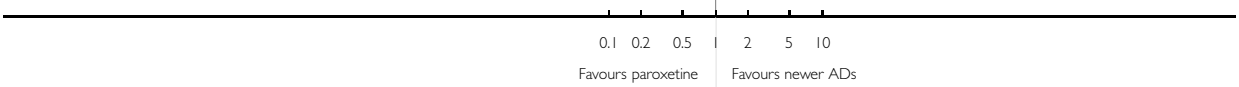
Study or subgroup	Paroxetine n/N	newer ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Subtotal (95% CI)	**153**	**149**		**100.0 %**	**0.92 [0.57, 1.49]**
Total events: 100 (Paroxetine), 100 (newer ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.32 (P = 0.75)					
6 versus mirtazapine					
Benkert 1999	94/136	87/139		36.1 %	1.34 [0.81, 2.21]
Blier 2009	14/19	17/21		4.0 %	0.66 [0.15, 2.93]
Schatzberg 2002	91/126	80/128		32.2 %	1.56 [0.92, 2.65]
Wade 2003	63/98	47/99		27.7 %	1.99 [1.12, 3.53]
Subtotal (95% CI)	**379**	**387**		**100.0 %**	**1.52 [1.13, 2.06]**
Total events: 262 (Paroxetine), 231 (newer ADs)					
Heterogeneity: Tau^2 = 0.0; Chi^2 = 2.32, df = 3 (P = 0.51); I^2 =0.0%					
Test for overall effect: Z = 2.75 (P = 0.0059)					
7 versus tianeptine					
Nickel 2003	14/22	16/22		100.0 %	0.66 [0.18, 2.36]
Subtotal (95% CI)	**22**	**22**		**100.0 %**	**0.66 [0.18, 2.36]**
Total events: 14 (Paroxetine), 16 (newer ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.65 (P = 0.52)					
8 versus trazodone					
Kasper 2005	17/53	17/55		100.0 %	1.06 [0.47, 2.38]
Subtotal (95% CI)	**53**	**55**		**100.0 %**	**1.06 [0.47, 2.38]**
Total events: 17 (Paroxetine), 17 (newer ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.13 (P = 0.90)					
9 versus venlafaxine					
0600B 428	24/56	11/58		15.7 %	3.20 [1.38, 7.45]
0600B1-367	47/81	80/165		29.6 %	1.47 [0.86, 2.51]
Mc Partlin 1998	94/178	89/183		39.2 %	1.18 [0.78, 1.79]
Owens 2008	25/42	20/44		15.4 %	1.76 [0.75, 4.15]
Subtotal (95% CI)	**357**	**450**		**100.0 %**	**1.57 [1.08, 2.29]**
Total events: 190 (Paroxetine), 200 (newer ADs)					
Heterogeneity: Tau^2 = 0.05; Chi^2 = 4.53, df = 3 (P = 0.21); I^2 =34%					
Test for overall effect: Z = 2.34 (P = 0.019)					



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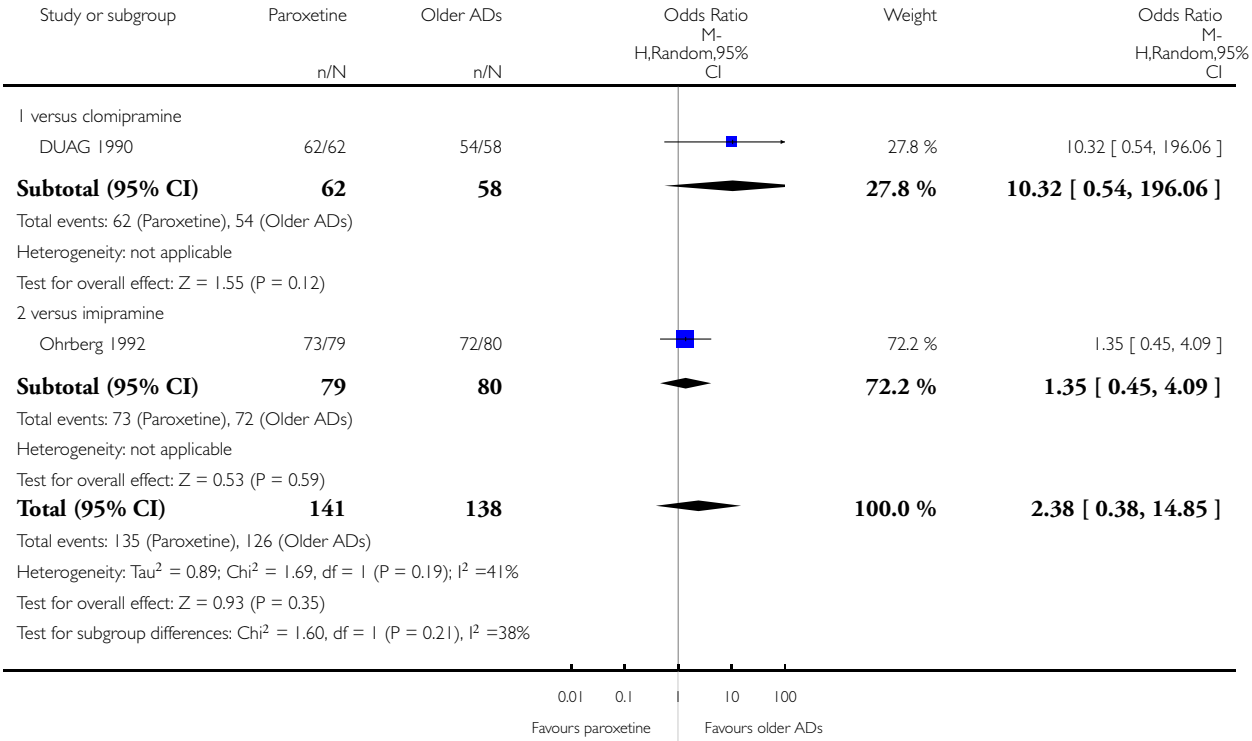
Analysis 5.1. Comparison 5 Failure to remit (at 1 - 4 weeks), Outcome 1 Paroxetine versus older ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 5 Failure to remit (at 1 - 4 weeks)

Outcome: 1 Paroxetine versus older ADs



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Analysis 5.2. Comparison 5 Failure to remit (at 1 - 4 weeks), Outcome 2 Paroxetine versus other SSRIs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 5 Failure to remit (at 1 - 4 weeks)

Outcome: 2 Paroxetine versus other SSRIs

Study or subgroup	Paroxetine n/N	other SSRIs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
1 versus fluvoxamine					
Ansseau 1993	53/56	61/64		40.8 %	0.87 [0.17, 4.49]
Kato 2005	47/49	36/39		32.5 %	1.96 [0.31, 12.34]
Kiev 1997	28/30	28/30		26.7 %	1.00 [0.13, 7.60]
Subtotal (95% CI)	**135**	**133**		**100.0 %**	**1.17 [0.41, 3.35]**
Total events: 128 (Paroxetine), 125 (other SSRIs)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.45$, df = 2 (P = 0.80); $I^2 = 0.0\%$					
Test for overall effect: Z = 0.30 (P = 0.76)					

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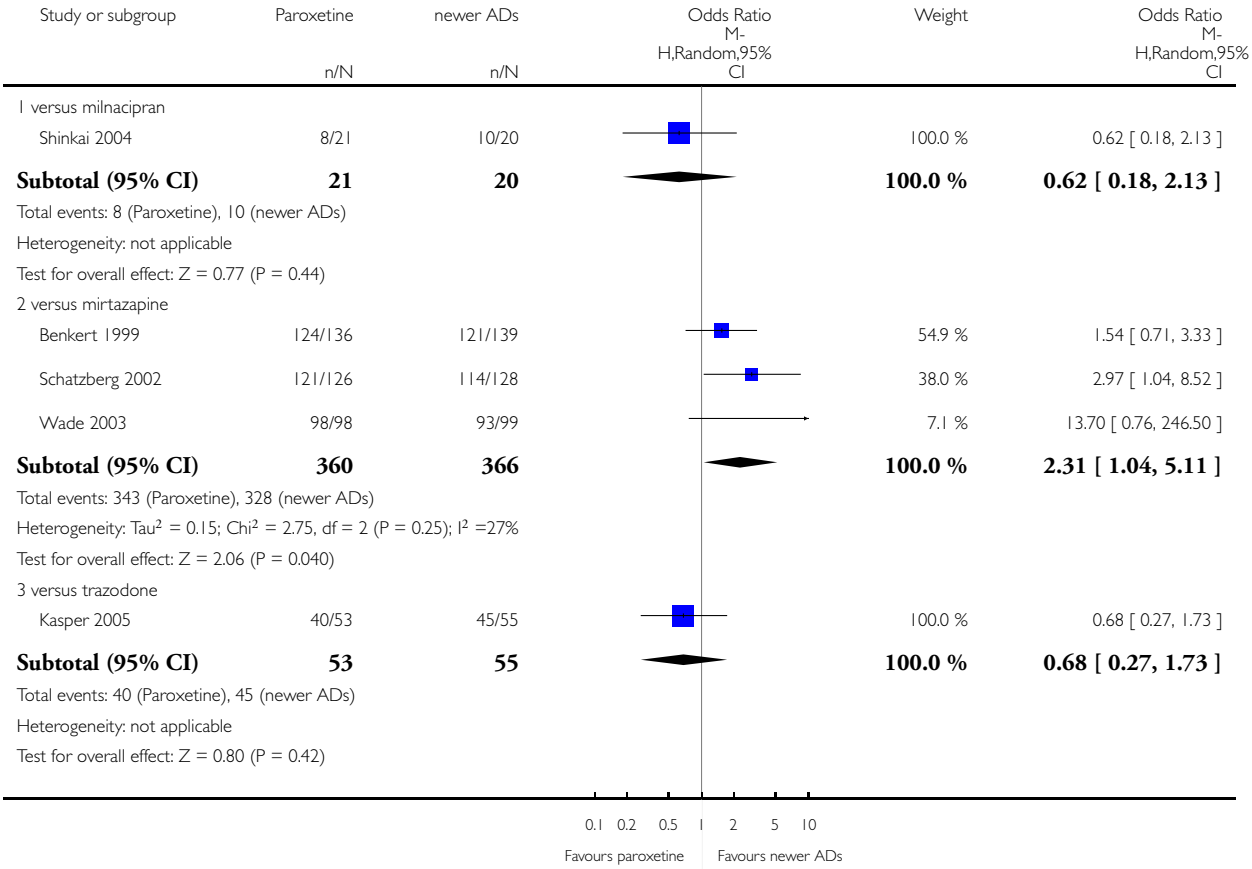
Analysis 5.3. Comparison 5 Failure to remit (at 1 - 4 weeks), Outcome 3 Paroxetine versus newer or non-conventional ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 5 Failure to remit (at 1 - 4 weeks)

Outcome: 3 Paroxetine versus newer or non-conventional ADs



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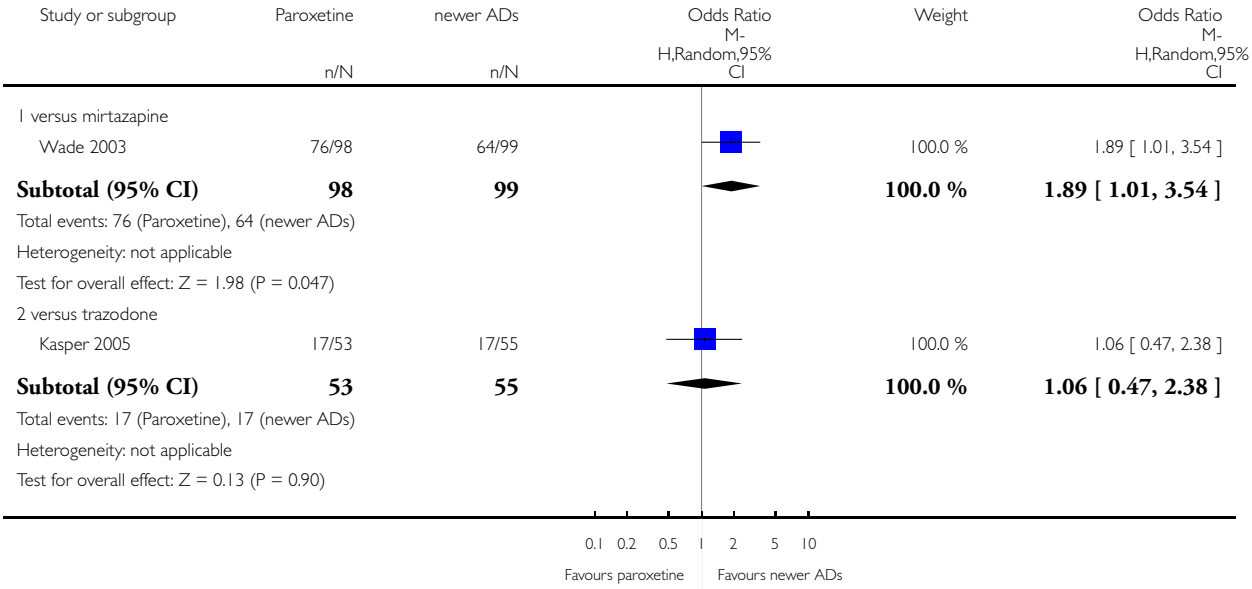
Analysis 6.1. Comparison 6 Failure to remit (at 16 - 24 weeks), Outcome 1 Paroxetine versus newer or non-conventional ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 6 Failure to remit (at 16 - 24 weeks)

Outcome: 1 Paroxetine versus newer or non-conventional ADs



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Analysis 7.1. Comparison 7 Standardized mean difference at endpoint (6 - 12 weeks), Outcome 1 Paroxetine versus older ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 7 Standardized mean difference at endpoint (6 - 12 weeks)

Outcome: 1 Paroxetine versus older ADs

Study or subgroup	Paroxetine N	Mean(SD)	Older ADs N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
1 versus amitriptyline							
29060.07.001	12	-13.08 (10.21)	13	-13.31 (10.2)		1.1 %	0.02 [-0.76, 0.81]
29060/281 PAR	76	16.1 (8.93)	79	12.4 (8.8)		3.9 %	0.42 [0.10, 0.73]
29060/299	102	-14.3 (9.35)	100	-14.39 (8.39)		4.4 %	0.01 [-0.27, 0.29]
Christiansen 1996	56	8.1 (5.9)	57	6.9 (6.2)		3.3 %	0.20 [-0.17, 0.57]
Freed 1996	184	13.7 (10.24)	191	16.58 (10.89)		5.5 %	-0.27 [-0.48, -0.07]
Kuhs 1989	14	7.5 (4.9)	17	7.1 (5)		1.3 %	0.08 [-0.63, 0.79]
Laursen 1985	16	7 (8)	14	6.5 (6.5)		1.3 %	0.07 [-0.65, 0.78]
PAR MDUK 032	29	12 (8.93)	30	12.2 (8.93)		2.1 %	-0.02 [-0.53, 0.49]
Sacchetti 2002	64	-8.7 (7.5)	65	-8.6 (8.3)		3.5 %	-0.01 [-0.36, 0.33]
Staner 1995	21	17.8 (11.3)	19	10.7 (7.9)		1.5 %	0.71 [0.07, 1.35]
Steinmeyer 1992	83	11.1 (8)	80	9.2 (6.7)		4.0 %	0.26 [-0.05, 0.56]
Stott 1993	262	13.9 (10.2)	243	13.8 (10.4)		6.0 %	0.01 [-0.16, 0.18]
Stuppaeck 1994	46	9 (5.9)	46	9.3 (5.8)		2.9 %	-0.05 [-0.46, 0.36]
Subtotal (95% CI)	**965**		**954**			**40.7 %**	**0.07 [-0.06, 0.20]**
Heterogeneity: $Tau^2 = 0.02$; $Chi^2 = 21.56$, df = 12 (P = 0.04); $I^2 = 44\%$							
Test for overall effect: Z = 1.02 (P = 0.31)							
2 versus clomipramine							
029060/1/CPMS 069 1991	20	-17.1 (10.4)	17	-19.7 (6.3)		1.5 %	0.29 [-0.36, 0.94]
DUAG 1990	53	14.3 (6)	43	9.8 (4.8)		2.8 %	0.81 [0.39, 1.23]
Guillibert 1989	40	8.4 (5.9)	39	8.2 (6.6)		2.6 %	0.03 [-0.41, 0.47]
Pelicier 1993	39	10.9 (9.55)	38	13.1 (7.85)		2.6 %	-0.25 [-0.70, 0.20]
Ravindran 1997	479	-17.3 (8.7)	474	-16.6 (9.4)		6.7 %	-0.08 [-0.20, 0.05]
Subtotal (95% CI)	**631**		**611**			**16.2 %**	**0.14 [-0.21, 0.49]**
Heterogeneity: $Tau^2 = 0.12$; $Chi^2 = 17.80$, df = 4 (P = 0.001); $I^2 = 78\%$							
Test for overall effect: Z = 0.79 (P = 0.43)							

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Study or subgroup	Paroxetine N	Mean(SD)	Older ADs N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
3 versus doxepin							
29060/056/UK	57	13.3 (9.55)	61	13.2 (7.85)		3.4 %	0.01 [-0.35, 0.37]
Dunner 1992	92	-13.35 (7.51)	96	-11.84 (7.02)		4.3 %	-0.21 [-0.49, 0.08]
Subtotal (95% CI)	**149**		**157**			**7.6 %**	**-0.12 [-0.35, 0.10]**
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.86$, df = 1 (P = 0.35); $I^2 = 0.0\%$							
Test for overall effect: Z = 1.07 (P = 0.28)							
4 versus imipramine							
029060/1/CPMS-095	129	-15.3 (3.6)	65	-15.8 (5.4)		4.1 %	0.12 [-0.18, 0.41]
29060/409	30	-18 (10.1)	31	-17.2 (8.2)		2.2 %	-0.09 [-0.59, 0.42]
Chiu 1996	15	7.4 (9.6)	15	11.7 (8.1)		1.2 %	-0.47 [-1.20, 0.26]
Fabre 1992	38	-9.13 (8.13)	37	-7.62 (8.69)		2.5 %	-0.18 [-0.63, 0.28]
Feighner 1989	36	-10.67 (7.14)	31	-8.9 (7.18)		2.3 %	-0.24 [-0.73, 0.24]
Peselow 1989	39	-10.26 (9.86)	35	-15.6 (9.87)		2.4 %	0.54 [0.07, 1.00]
Shrivastava 1992	33	-12.03 (8.73)	38	-6.74 (8.75)		2.4 %	-0.60 [-1.08, -0.12]
Subtotal (95% CI)	**320**		**252**			**17.2 %**	**-0.10 [-0.37, 0.17]**
Heterogeneity: $Tau^2 = 0.08$; $Chi^2 = 14.60$, df = 6 (P = 0.02); $I^2 = 59\%$							
Test for overall effect: Z = 0.72 (P = 0.47)							
5 versus lofepramine							
29060/103	49	-17.8 (11.2)	43	-17.1 (10.49)		2.9 %	-0.06 [-0.47, 0.35]
Subtotal (95% CI)	**49**		**43**			**2.9 %**	**-0.06 [-0.47, 0.35]**
Heterogeneity: not applicable							
Test for overall effect: Z = 0.31 (P = 0.76)							
6 versus maprolitine							
29060.065.BE	25	-13.1 (9.1)	28	-12.5 (6.2)		2.0 %	-0.08 [-0.62, 0.46]
Szegedi 1995	137	-2 (1.5)	146	-2 (1.5)		5.0 %	0.0 [-0.23, 0.23]
Subtotal (95% CI)	**162**		**174**			**7.0 %**	**-0.01 [-0.23, 0.20]**
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.07$, df = 1 (P = 0.80); $I^2 = 0.0\%$							
Test for overall effect: Z = 0.11 (P = 0.91)							
7 versus nortriptyline							
Mulsant 1999	29	9.6 (4.6)	27	8.8 (3)		2.1 %	0.20 [-0.32, 0.73]
Subtotal (95% CI)	**29**		**27**			**2.1 %**	**0.20 [-0.32, 0.73]**
Heterogeneity: not applicable							
Test for overall effect: Z = 0.75 (P = 0.45)							
8 versus mianserin							
29060/III/85/030	18	15.6 (10.25)	15	16.7 (10.21)		1.4 %	-0.10 [-0.79, 0.58]
29060III/85/038	29	-15.8 (6.2)	26	-12.9 (7.2)		2.0 %	-0.43 [-0.96, 0.11]
Dalery 2001	46	10.6 (9.8)	55	11.8 (8.2)		3.0 %	-0.13 [-0.52, 0.26]

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Favours paroxetine Favours older ADs

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Study or subgroup	Paroxetine N	Mean(SD)	Older ADs N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
Subtotal (95% CI)	**93**		**96**			**6.4 %**	**-0.21 [-0.50, 0.07]**
Heterogeneity: Tau^2 = 0.0; Chi^2 = 0.87, df = 2 (P = 0.65); I^2 =0.0%							
Test for overall effect: Z = 1.45 (P = 0.15)							
Total (95% CI)	**2398**		**2314**			**100.0 %**	**0.01 [-0.08, 0.10]**
Heterogeneity: Tau^2 = 0.03; Chi^2 = 60.35, df = 33 (P = 0.003); I^2 =45%							
Test for overall effect: Z = 0.21 (P = 0.83)							
Test for subgroup differences: Chi^2 = 6.05, df = 7 (P = 0.53), I^2 =0.0%							

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Favours paroxetine Favours older ADs

Analysis 7.2. Comparison 7 Standardized mean difference at endpoint (6 - 12 weeks), Outcome 2 Paroxetine versus other SSRIs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 7 Standardized mean difference at endpoint (6 - 12 weeks)

Outcome: 2 Paroxetine versus other SSRIs

Study or subgroup	Paroxetine N	Mean(SD)	other SSRIs N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
1 versus citalopram							
Jefferson 2001 29060/785	97	-138 (1083)	104	-15 (102)		100.0 %	-0.16 [-0.44, 0.11]
Subtotal (95% CI)	**97**		**104**			**100.0 %**	**-0.16 [-0.44, 0.11]**
Heterogeneity: not applicable							
Test for overall effect: Z = 1.15 (P = 0.25)							
2 versus escitalopram							
Baldwin 2006	156	-18.31 (10.03)	165	-17.16 (10.03)		48.2 %	-0.11 [-0.33, 0.10]
Boulenger 2006	223	-21.2 (10.03)	228	-23.2 (10.03)		51.8 %	0.20 [0.01, 0.38]
Subtotal (95% CI)	**379**		**393**			**100.0 %**	**0.05 [-0.26, 0.36]**
Heterogeneity: Tau^2 = 0.04; Chi^2 = 4.59, df = 1 (P = 0.03); I^2 =78%							
Test for overall effect: Z = 0.31 (P = 0.76)							

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Favours paroxetine Favours other SSRIs

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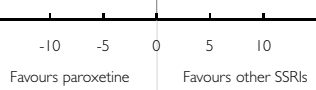
Study or subgroup	Paroxetine N	Mean(SD)	other SSRIs N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
3 versus fluoxetine							
29060/356	64	12 (9.6)	68	12.6 (9.07)		6.5 %	-0.06 [-0.41, 0.28]
Ansseau 1993	38	-12.9 (6.5)	43	-12.4 (7.1)		4.0 %	-0.07 [-0.51, 0.36]
Fava 1998	55	12.1 (10)	54	13.1 (10.3)		5.3 %	-0.10 [-0.47, 0.28]
Fava 2002	93	8.3 (6.8)	88	8.73 (7.1)		8.9 %	-0.06 [-0.35, 0.23]
MY-1045/BRL-029060/1	350	-11.8 (8.79)	344	-13 (8.71)		33.9 %	0.14 [-0.01, 0.29]
Ontiveros 1994	60	-16.4 (8.4)	61	-15.7 (9.5)		5.9 %	-0.08 [-0.43, 0.28]
SBK-115 1998	272	-10.6 (8.25)	278	-11 (8.16)		26.9 %	0.05 [-0.12, 0.22]
Tignol 1993	89	-16.76 (10.92)	87	-16.85 (11.1)		8.6 %	0.01 [-0.29, 0.30]
Subtotal (95% CI)	**1021**		**1023**			**100.0 %**	**0.04 [-0.05, 0.12]**
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 3.69$, df = 7 (P = 0.81); $I^2 = 0.0\%$							
Test for overall effect: Z = 0.86 (P = 0.39)							
4 versus fluvoxamine							
Kiev 1997	29	-12.86 (6.85)	29	-13.45 (6.75)		100.0 %	0.09 [-0.43, 0.60]
Subtotal (95% CI)	**29**		**29**			**100.0 %**	**0.09 [-0.43, 0.60]**
Heterogeneity: not applicable							
Test for overall effect: Z = 0.33 (P = 0.74)							
5 versus sertraline							
Aberg-Wistedt 2000	177	-18.3 (10.5)	176	-16.9 (10.2)		100.0 %	-0.13 [-0.34, 0.07]
Subtotal (95% CI)	**177**		**176**			**100.0 %**	**-0.13 [-0.34, 0.07]**
Heterogeneity: not applicable							
Test for overall effect: Z = 1.27 (P = 0.21)							



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Analysis 7.3. Comparison 7 Standardized mean difference at endpoint (6 - 12 weeks), Outcome 3 Paroxetine versus newer or non-conventional ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 7 Standardized mean difference at endpoint (6 - 12 weeks)

Outcome: 3 Paroxetine versus newer or non-conventional ADs

Study or subgroup	Paroxetine N	Mean(SD)	newer ADs N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
1 versus agomelatine							
CL3-023	137	12.2 (8.1)	141	13 (8)		25.6 %	-0.10 [-0.33, 0.14]
Loo 2002	144	13.09 (8.37)	135	12.77 (8.23)		25.6 %	0.04 [-0.20, 0.27]
Montgomery 2004	104	5.2 (3.2)	88	6.1 (3.5)		21.9 %	-0.27 [-0.55, 0.02]
NCT00463242	163	14 (7.68)	162	17.1 (7.62)		26.8 %	-0.40 [-0.62, -0.18]
Subtotal (95% CI)	**548**		**526**			**100.0 %**	**-0.18 [-0.38, 0.02]**
Heterogeneity: $Tau^2 = 0.03$; $Chi^2 = 8.15$, df = 3 (P = 0.04); $I^2 = 63\%$							
Test for overall effect: Z = 1.80 (P = 0.073)							
2 versus amisulpride							
Cassano 2002a	136	7.4 (5.9)	136	8.3 (7.4)		100.0 %	-0.13 [-0.37, 0.10]
Subtotal (95% CI)	**136**		**136**			**100.0 %**	**-0.13 [-0.37, 0.10]**
Heterogeneity: not applicable							
Test for overall effect: Z = 1.10 (P = 0.27)							
3 versus aprepitant (MK-869)							
Kramer 1998	47	-15.34 (7.94)	55	-15.33 (8.07)		100.0 %	0.00 [-0.39, 0.39]
Subtotal (95% CI)	**47**		**55**			**100.0 %**	**0.00 [-0.39, 0.39]**
Heterogeneity: not applicable							
Test for overall effect: Z = 0.01 (P = 1.0)							
4 versus bupropion							
Kennedy 2004	66	9.3 (7.3)	66	9.6 (6.4)		100.0 %	-0.04 [-0.38, 0.30]
Subtotal (95% CI)	**66**		**66**			**100.0 %**	**-0.04 [-0.38, 0.30]**
Heterogeneity: not applicable							
Test for overall effect: Z = 0.25 (P = 0.80)							
5 versus duloxetine							
Detke 2004 (HMAY A)	85	-11.06 (5.93)	93	-11.32 (6.29)		12.5 %	0.04 [-0.25, 0.34]
Goldstein 2004 (HMAT B)	84	-6.06 (8.12)	86	-7.72 (7.67)		11.9 %	0.21 [-0.09, 0.51]
Higuchi 2009	128	9.6 (6.3)	66	9.8 (5.8)		12.2 %	-0.03 [-0.33, 0.26]
HMAT A (ID#4091)	87	-6.2 (6.97)	81	-5.54 (6.68)		11.8 %	-0.10 [-0.40, 0.21]
Lee 2007 (HMCV)	240	11.94 (4.33)	238	11.73 (4.62)		33.5 %	0.05 [-0.13, 0.23]

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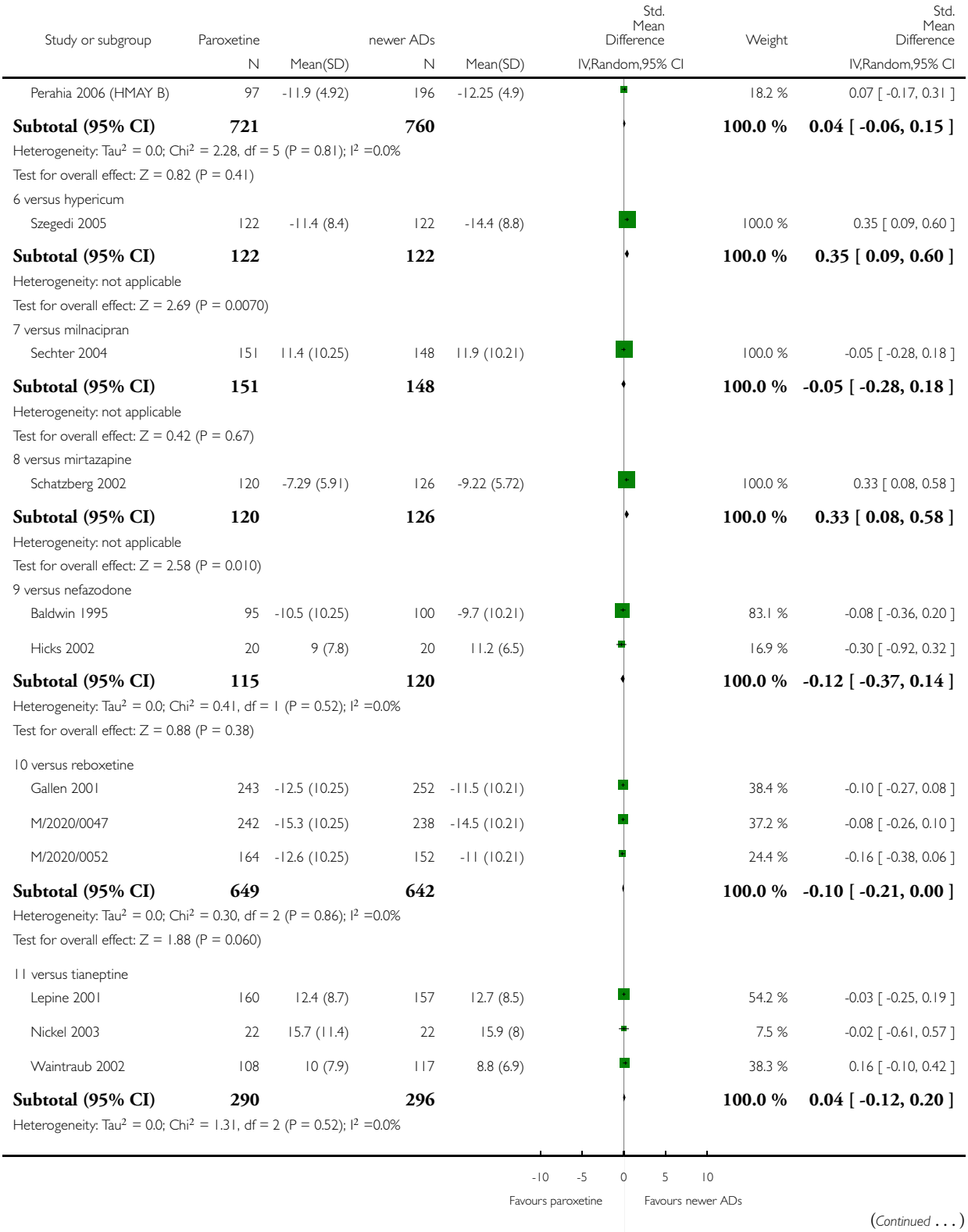

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Study or subgroup	Paroxetine N	Mean(SD)	newer ADs N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
Test for overall effect: Z = 0.50 (P = 0.62)							
12 versus trazodone							
Kasper 2005	53	-15 (4.95)	55	-14.6 (4.89)		100.0 %	-0.08 [-0.46, 0.30]
Subtotal (95% CI)	**53**		**55**			**100.0 %**	**-0.08 [-0.46, 0.30]**
Heterogeneity: not applicable							
Test for overall effect: Z = 0.42 (P = 0.68)							
13 versus venlafaxine							
Mc Partlin 1998	161	-14.1 (7.6)	175	-14.7 (7.6)		81.7 %	0.08 [-0.14, 0.29]
Owens 2008	37	-16.7 (52.25)	38	-17.3 (55.41)		18.3 %	0.01 [-0.44, 0.46]
Subtotal (95% CI)	**198**		**213**			**100.0 %**	**0.07 [-0.13, 0.26]**
Heterogeneity: Tau^2 = 0.0; Chi^2 = 0.07, df = 1 (P = 0.79); I^2 =0.0%							
Test for overall effect: Z = 0.67 (P = 0.50)							

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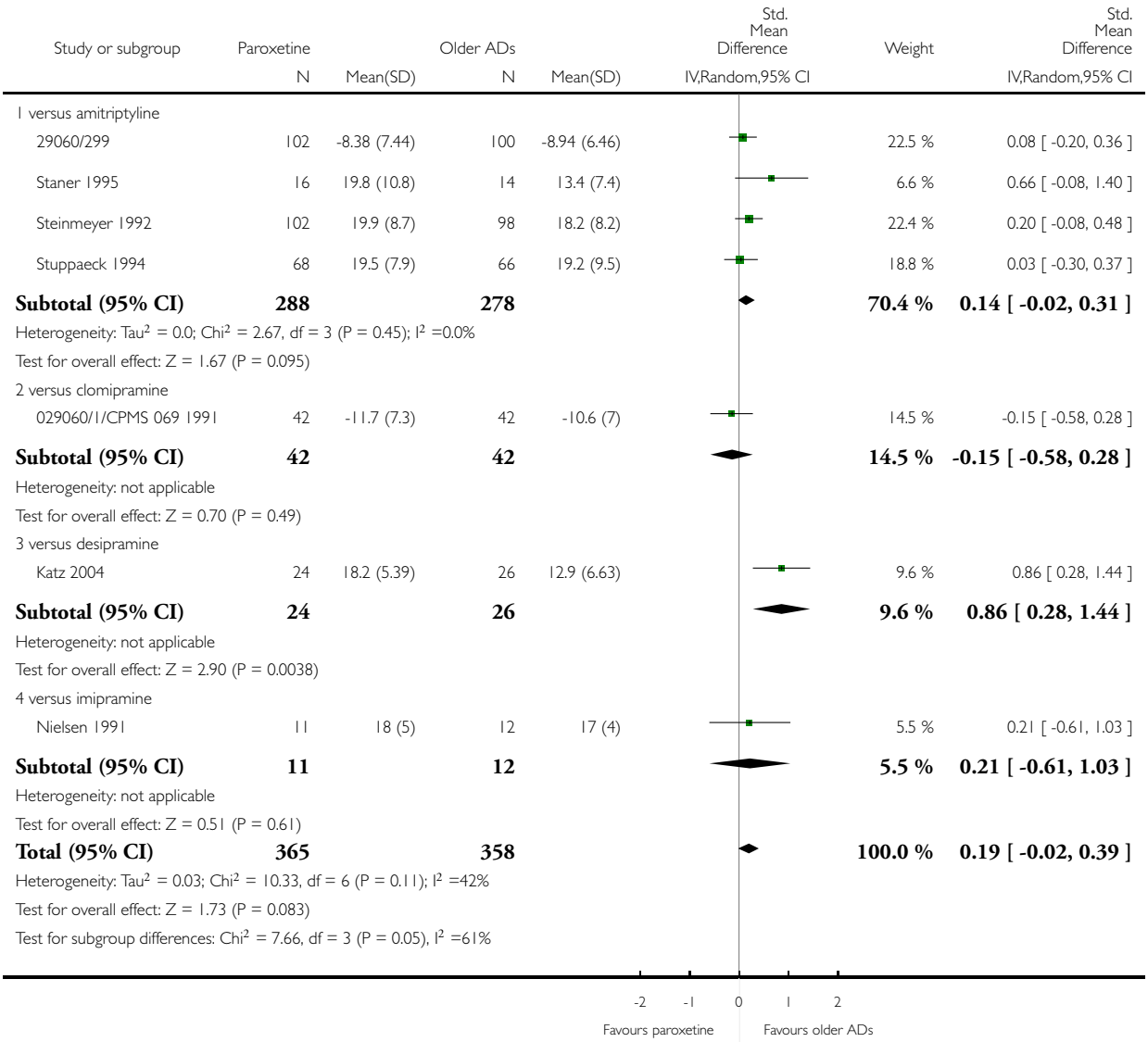
Analysis 8.1. Comparison 8 Standardized mean difference (at 1 - 4 weeks), Outcome 1 Paroxetine versus older ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 8 Standardized mean difference (at 1 - 4 weeks)

Outcome: 1 Paroxetine versus older ADs



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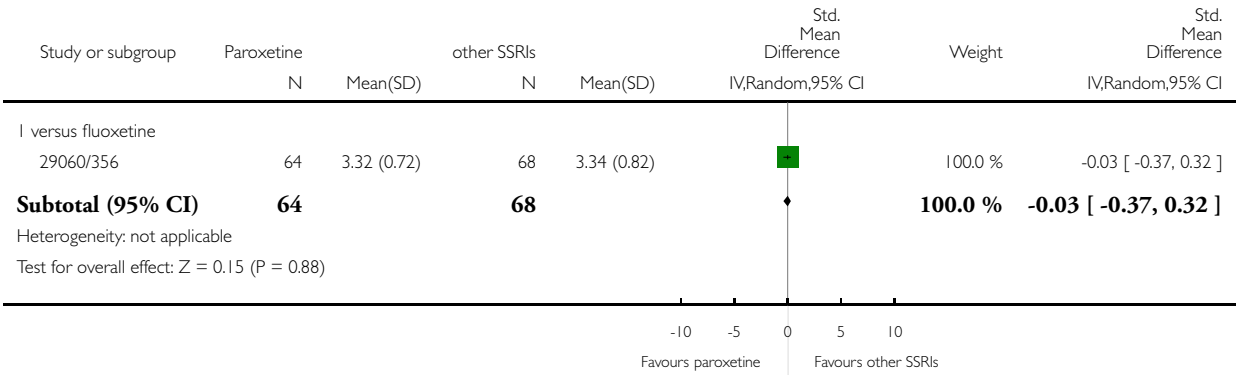
Analysis 8.2. Comparison 8 Standardized mean difference (at 1 - 4 weeks), Outcome 2 Paroxetine versus other SSRIs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 8 Standardized mean difference (at 1 - 4 weeks)

Outcome: 2 Paroxetine versus other SSRIs



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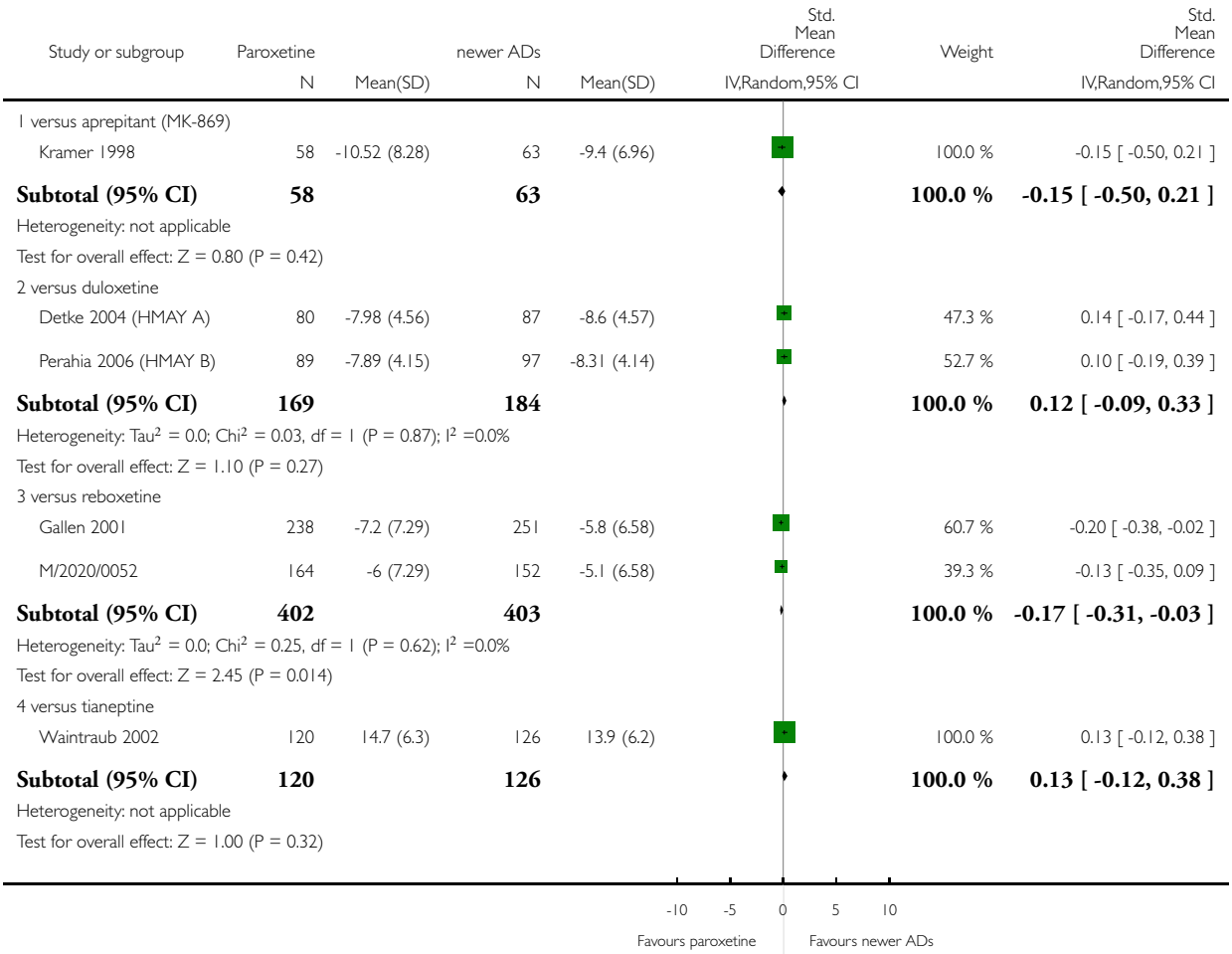
Analysis 8.3. Comparison 8 Standardized mean difference (at 1 - 4 weeks), Outcome 3 Paroxetine versus newer or non-conventional ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 8 Standardized mean difference (at 1 - 4 weeks)

Outcome: 3 Paroxetine versus newer or non-conventional ADs



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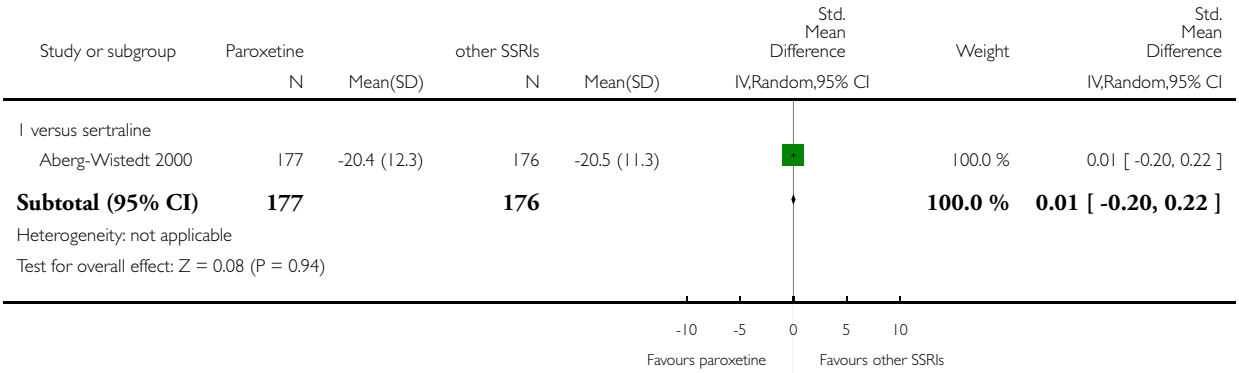
Analysis 9.1. Comparison 9 Standardized mean difference (at 16 - 24 weeks), Outcome 1 Paroxetine versus SSRIs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 9 Standardized mean difference (at 16 - 24 weeks)

Outcome: 1 Paroxetine versus SSRIs

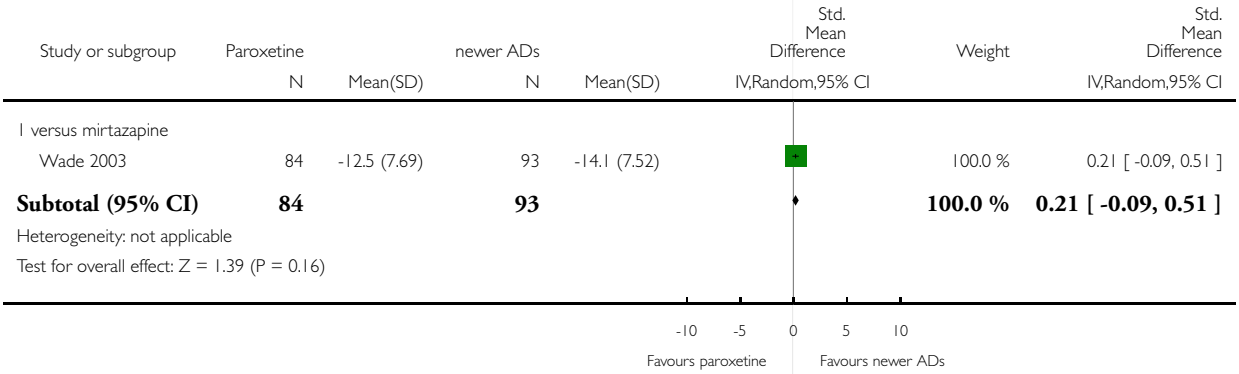


Analysis 9.2. Comparison 9 Standardized mean difference (at 16 - 24 weeks), Outcome 2 Paroxetine versus newer or non-conventional ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 9 Standardized mean difference (at 16 - 24 weeks)

Outcome: 2 Paroxetine versus newer or non-conventional ADs



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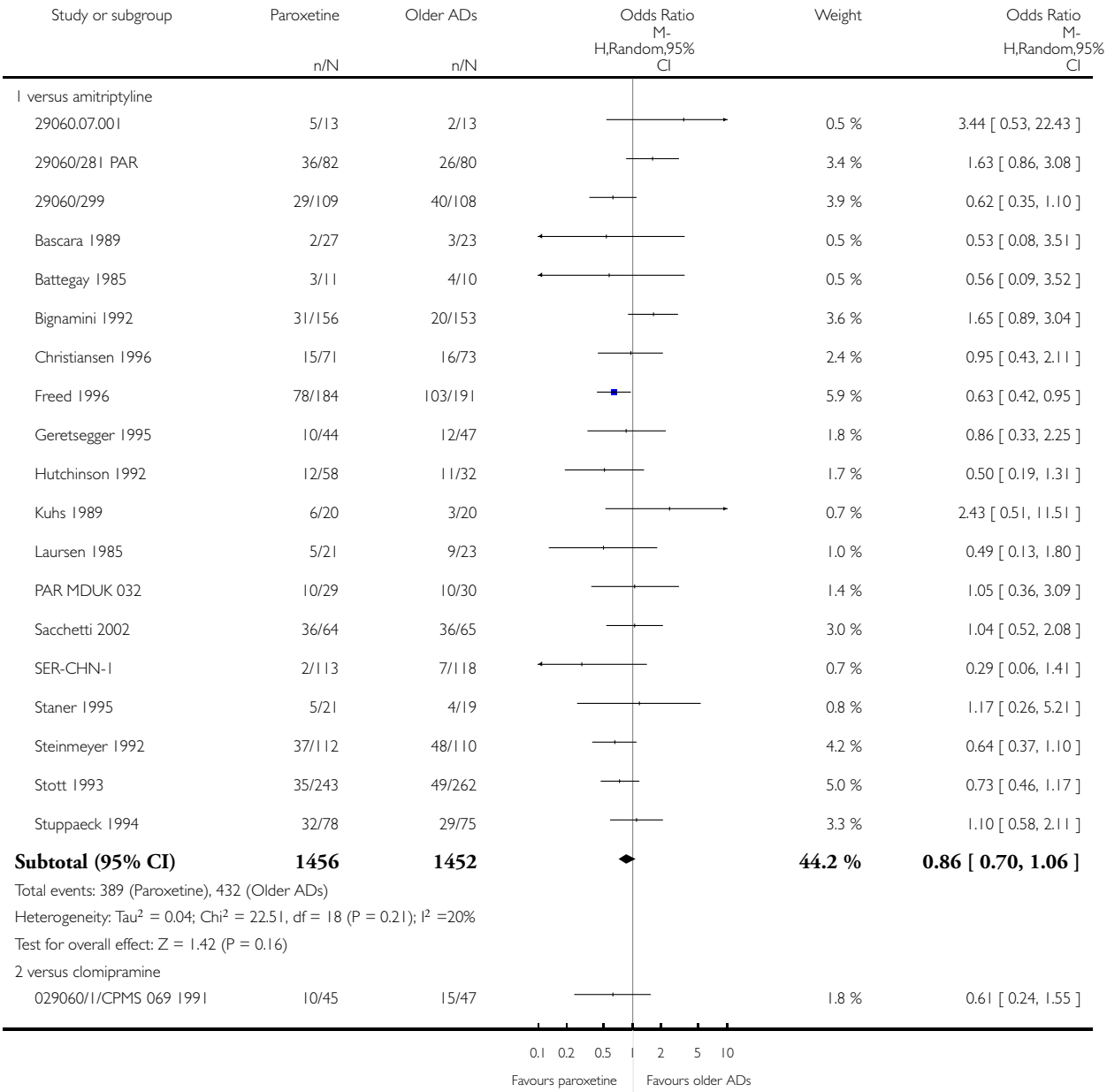
Analysis 10.1. Comparison 10 Failure to complete (any cause), Outcome 1 Paroxetine versus older ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 10 Failure to complete (any cause)

Outcome: 1 Paroxetine versus older ADs



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Study or subgroup	Paroxetine n/N	Older ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Guillibert 1989	9/40	12/39		1.6 %	0.65 [0.24, 1.79]
Pelicier 1993	12/41	10/42		1.7 %	1.32 [0.50, 3.52]
Ravindran 1997	103/513	142/506		7.8 %	0.64 [0.48, 0.86]
Subtotal (95% CI)	**639**	**634**		**13.0 %**	**0.67 [0.52, 0.87]**
Total events: 134 (Paroxetine), 179 (Older ADs)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 1.97$, df = 3 (P = 0.58); $I^2 = 0.0\%$					
Test for overall effect: Z = 2.99 (P = 0.0028)					
3 versus dothiepin					
29060/056/UK	20/67	13/67		2.4 %	1.77 [0.79, 3.93]
Dunner 1992	45/136	39/135		4.5 %	1.22 [0.73, 2.04]
Shillingford 1990	8/46	10/48		1.6 %	0.80 [0.28, 2.25]
Subtotal (95% CI)	**249**	**250**		**8.4 %**	**1.25 [0.84, 1.87]**
Total events: 73 (Paroxetine), 62 (Older ADs)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 1.45$, df = 2 (P = 0.48); $I^2 = 0.0\%$					
Test for overall effect: Z = 1.11 (P = 0.27)					
4 versus imipramine					
029060/1/CPMS-095	7/134	6/68		1.3 %	0.57 [0.18, 1.77]
29060/409	15/38	14/37		1.9 %	1.07 [0.42, 2.72]
Dunbar 1991	103/241	131/241		6.6 %	0.63 [0.44, 0.90]
Fabre 1992	24/40	24/40		2.0 %	1.00 [0.41, 2.45]
Feighner 1989	19/40	26/40		2.0 %	0.49 [0.20, 1.20]
Nielsen 1991	7/16	9/15		0.9 %	0.52 [0.12, 2.17]
Ohrberg 1992	18/79	22/80		2.8 %	0.78 [0.38, 1.60]
Peselow 1989	12/40	11/39		1.7 %	1.09 [0.41, 2.88]
Shrivastava 1992	16/40	30/40		1.8 %	0.22 [0.09, 0.58]
Subtotal (95% CI)	**668**	**600**		**20.9 %**	**0.65 [0.50, 0.85]**
Total events: 221 (Paroxetine), 273 (Older ADs)					
Heterogeneity: $Tau^2 = 0.02$; $Chi^2 = 8.77$, df = 8 (P = 0.36); $I^2 = 9\%$					
Test for overall effect: Z = 3.10 (P = 0.0020)					
5 versus lofepramine					
29060/103	9/57	13/49		1.8 %	0.52 [0.20, 1.35]
Moon 1996	19/60	14/62		2.4 %	1.59 [0.71, 3.56]
Subtotal (95% CI)	**117**	**111**		**4.1 %**	**0.94 [0.31, 2.80]**
Total events: 28 (Paroxetine), 27 (Older ADs)					
Heterogeneity: $Tau^2 = 0.42$; $Chi^2 = 3.08$, df = 1 (P = 0.08); $I^2 = 68\%$					
Test for overall effect: Z = 0.12 (P = 0.91)					
6 versus maprolitine					

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Study or subgroup	Paroxetine n/N	Older ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
29060.065.BE	6/28	2/32		0.6 %	4.09 [0.75, 22.22]
Schnyder 1996	6/37	8/34		1.2 %	0.63 [0.19, 2.05]
Szegedi 1995	40/145	45/153		4.6 %	0.91 [0.55, 1.51]
Subtotal (95% CI)	**210**	**219**		**6.5 %**	**1.05 [0.49, 2.25]**
Total events: 52 (Paroxetine), 55 (Older ADs)					
Heterogeneity: $Tau^2 = 0.20$; $Chi^2 = 3.36$, df = 2 (P = 0.19); $I^2 = 40\%$					
Test for overall effect: Z = 0.13 (P = 0.90)					
7 versus mianserin					
29060/III/85/030	6/18	4/15		0.8 %	1.38 [0.30, 6.20]
29060III/85/038	1/30	3/29		0.3 %	0.30 [0.03, 3.05]
Subtotal (95% CI)	**48**	**44**		**1.1 %**	**0.84 [0.21, 3.41]**
Total events: 7 (Paroxetine), 7 (Older ADs)					
Heterogeneity: $Tau^2 = 0.17$; $Chi^2 = 1.17$, df = 1 (P = 0.28); $I^2 = 15\%$					
Test for overall effect: Z = 0.25 (P = 0.80)					
8 versus nortriptyline					
Mulsant 1999	14/43	10/37		1.7 %	1.30 [0.50, 3.42]
Subtotal (95% CI)	**43**	**37**		**1.7 %**	**1.30 [0.50, 3.42]**
Total events: 14 (Paroxetine), 10 (Older ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.54 (P = 0.59)					
Total (95% CI)	**3430**	**3347**		**100.0 %**	**0.84 [0.73, 0.96]**
Total events: 918 (Paroxetine), 1045 (Older ADs)					
Heterogeneity: $Tau^2 = 0.04$; $Chi^2 = 54.12$, df = 42 (P = 0.10); $I^2 = 22\%$					
Test for overall effect: Z = 2.56 (P = 0.010)					
Test for subgroup differences: $Chi^2 = 10.79$, df = 7 (P = 0.15), $I^2 = 35\%$					

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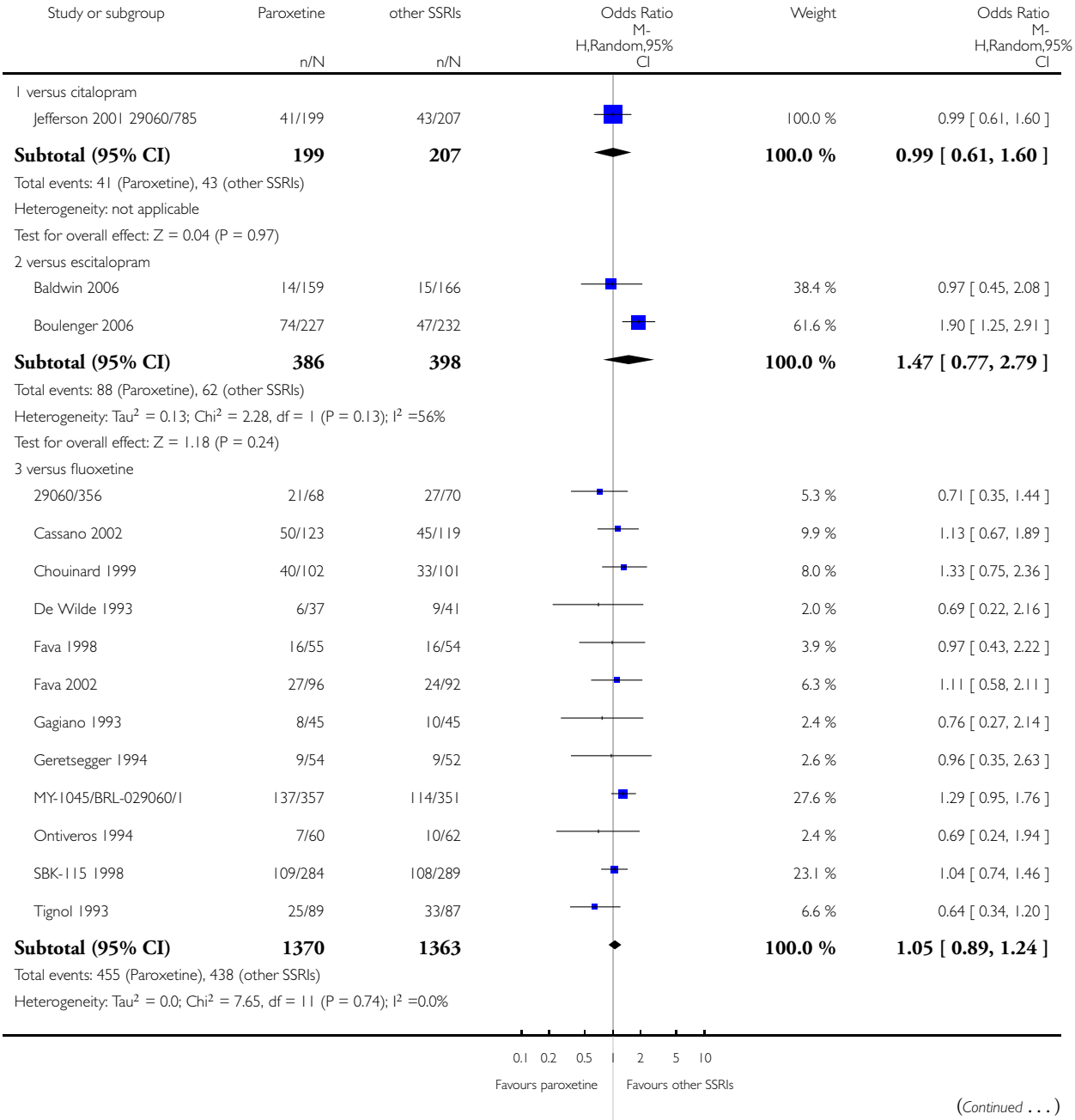
Analysis 10.2. Comparison 10 Failure to complete (any cause), Outcome 2 Paroxetine versus other SSRIs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 10 Failure to complete (any cause)

Outcome: 2 Paroxetine versus other SSRIs



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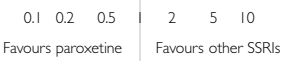
Study or subgroup	Paroxetine n/N	other SSRIs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Test for overall effect: Z = 0.59 (P = 0.55)					
4 versus fluvoxamine					
Ansseau 1993	16/56	23/64		48.6 %	0.71 [0.33, 1.54]
Kato 2005	11/42	6/39		25.3 %	1.95 [0.64, 5.92]
Kiev 1997	9/30	10/30		26.1 %	0.86 [0.29, 2.55]
Subtotal (95% CI)	**128**	**133**		**100.0 %**	**0.96 [0.54, 1.72]**
Total events: 36 (Paroxetine), 39 (other SSRIs)					
Heterogeneity: Tau^2 = 0.02; Chi^2 = 2.18, df = 2 (P = 0.34); I^2 =8%					
Test for overall effect: Z = 0.12 (P = 0.90)					
5 versus sertraline					
Aberg-Wistedt 2000	61/177	64/176		60.6 %	0.92 [0.59, 1.42]
Fava 2002	13/30	10/43		39.4 %	2.52 [0.92, 6.94]
Subtotal (95% CI)	**207**	**219**		**100.0 %**	**1.37 [0.52, 3.60]**
Total events: 74 (Paroxetine), 74 (other SSRIs)					
Heterogeneity: Tau^2 = 0.35; Chi^2 = 3.22, df = 1 (P = 0.07); I^2 =69%					
Test for overall effect: Z = 0.64 (P = 0.52)					



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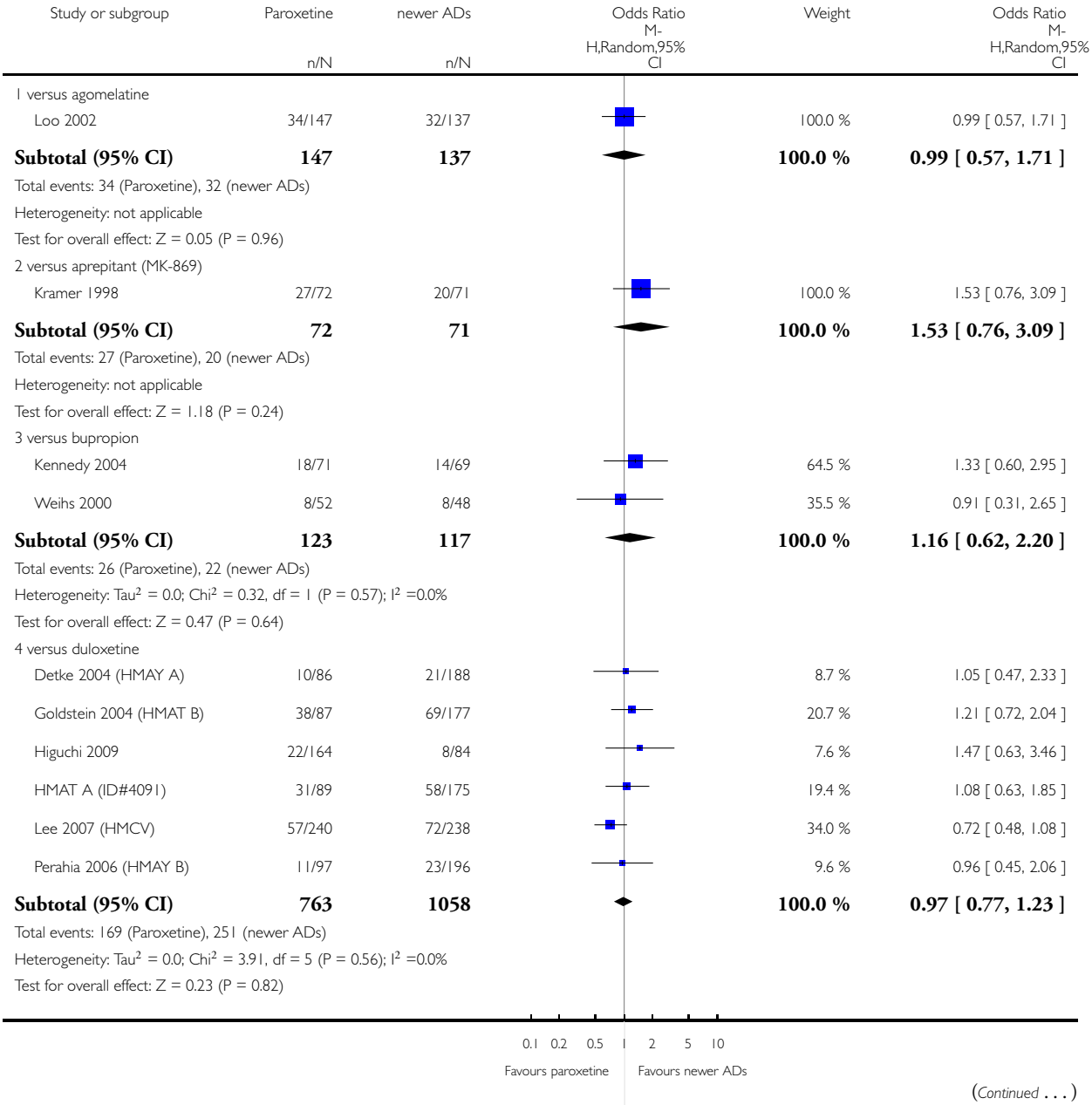
Analysis 10.3. Comparison 10 Failure to complete (any cause), Outcome 3 Paroxetine versus newer or non-conventional ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 10 Failure to complete (any cause)

Outcome: 3 Paroxetine versus newer or non-conventional ADs



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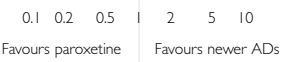
Study or subgroup	Paroxetine n/N	newer ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
5 versus hypericum					
Szegedi 2005	29/126	17/125		100.0 %	1.90 [0.98, 3.67]
Subtotal (95% CI)	**126**	**125**		**100.0 %**	**1.90 [0.98, 3.67]**
Total events: 29 (Paroxetine), 17 (newer ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.91 (P = 0.056)					
6 versus mirtazapine					
Benkert 1999	33/136	30/139		33.2 %	1.16 [0.66, 2.04]
Schatzberg 2002	39/126	29/128		33.5 %	1.53 [0.87, 2.68]
Wade 2003	55/98	53/99		33.4 %	1.11 [0.63, 1.95]
Subtotal (95% CI)	**360**	**366**		**100.0 %**	**1.26 [0.91, 1.74]**
Total events: 127 (Paroxetine), 112 (newer ADs)					
Heterogeneity: Tau^2 = 0.0; Chi^2 = 0.73, df = 2 (P = 0.69); I^2 =0.0%					
Test for overall effect: Z = 1.38 (P = 0.17)					
7 versus milnacipram					
Sechter 2004	33/153	29/149		97.1 %	1.14 [0.65, 1.99]
Shinkai 2004	1/21	0/20		2.9 %	3.00 [0.12, 78.04]
Subtotal (95% CI)	**174**	**169**		**100.0 %**	**1.17 [0.67, 2.03]**
Total events: 34 (Paroxetine), 29 (newer ADs)					
Heterogeneity: Tau^2 = 0.0; Chi^2 = 0.33, df = 1 (P = 0.57); I^2 =0.0%					
Test for overall effect: Z = 0.56 (P = 0.58)					
8 versus nefazodone					
Hicks 2002	3/20	5/20		100.0 %	0.53 [0.11, 2.60]
Subtotal (95% CI)	**20**	**20**		**100.0 %**	**0.53 [0.11, 2.60]**
Total events: 3 (Paroxetine), 5 (newer ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.78 (P = 0.43)					
9 versus reboxetine					
Gallen 2001	58/265	67/265		34.8 %	0.83 [0.55, 1.24]
M/2020/0047	74/262	69/258		35.8 %	1.08 [0.73, 1.58]
M/2020/0052	33/166	53/159		29.4 %	0.50 [0.30, 0.82]
Subtotal (95% CI)	**693**	**682**		**100.0 %**	**0.78 [0.51, 1.19]**
Total events: 165 (Paroxetine), 189 (newer ADs)					
Heterogeneity: Tau^2 = 0.09; Chi^2 = 5.76, df = 2 (P = 0.06); I^2 =65%					
Test for overall effect: Z = 1.15 (P = 0.25)					
10 versus tianeptine					
Lepine 2001	29/165	29/162		47.3 %	0.98 [0.55, 1.72]
Nickel 2003	4/22	0/22		4.7 %	10.95 [0.55, 216.75]



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Study or subgroup	Paroxetine n/N	newer ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Waintraub 2002	42/139	27/138		48.0 %	1.78 [1.02, 3.10]
Subtotal (95% CI)	**326**	**322**		**100.0 %**	**1.46 [0.75, 2.85]**
Total events: 75 (Paroxetine), 56 (newer ADs)					
Heterogeneity: Tau^2 = 0.16; Chi^2 = 4.09, df = 2 (P = 0.13); I^2 =51%					
Test for overall effect: Z = 1.11 (P = 0.27)					
11 versus venlafaxine					
0600A-349	24/85	28/82		18.5 %	0.76 [0.39, 1.46]
0600B 428	10/56	10/58		8.5 %	1.04 [0.40, 2.74]
0600B1-367	28/81	46/165		24.5 %	1.37 [0.77, 2.42]
Hwang 2004	3/53	3/52		2.9 %	0.98 [0.19, 5.09]
Mc Partlin 1998	52/178	47/183		37.2 %	1.19 [0.75, 1.90]
Owens 2008	10/42	12/44		8.4 %	0.83 [0.32, 2.20]
Subtotal (95% CI)	**495**	**584**		**100.0 %**	**1.08 [0.82, 1.44]**
Total events: 127 (Paroxetine), 146 (newer ADs)					
Heterogeneity: Tau^2 = 0.0; Chi^2 = 2.24, df = 5 (P = 0.82); I^2 =0.0%					
Test for overall effect: Z = 0.55 (P = 0.58)					

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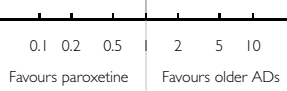
Analysis 11.1. Comparison 11 Failure to complete (due to inefficacy), Outcome 1 Paroxetine versus older ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 11 Failure to complete (due to inefficacy)

Outcome: 1 Paroxetine versus older ADs

Study or subgroup	Paroxetine n/N	Older ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
1 versus amitriptyline					
29060.07.001	4/13	0/13		0.8 %	12.79 [0.61, 266.66]
29060/281 PAR	1/82	1/80		1.0 %	0.98 [0.06, 15.86]
Freed 1996	2/184	7/191		3.1 %	0.29 [0.06, 1.41]
Kuhs 1989	2/20	2/20		1.8 %	1.00 [0.13, 7.89]
Laursen 1985	0/21	1/23		0.7 %	0.35 [0.01, 9.04]
Sacchetti 2002	6/64	3/65		3.8 %	2.14 [0.51, 8.95]
Staner 1995	2/21	1/19		1.2 %	1.89 [0.16, 22.75]
Steinmeyer 1992	16/112	14/110		12.9 %	1.14 [0.53, 2.47]
Stuppaeck 1994	22/78	17/75		14.4 %	1.34 [0.64, 2.79]
Subtotal (95% CI)	**595**	**596**		**39.7 %**	**1.20 [0.77, 1.86]**
Total events: 55 (Paroxetine), 46 (Older ADs)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 6.90$, df = 8 (P = 0.55); $I^2 = 0.0\%$					
Test for overall effect: Z = 0.80 (P = 0.42)					
2 versus clomipramine					
029060/1/CPMS 069 1991	4/45	3/47		3.2 %	1.43 [0.30, 6.78]
Guillibert 1989	4/40	3/39		3.1 %	1.33 [0.28, 6.39]
Pelicier 1993	1/41	0/42		0.7 %	3.15 [0.12, 79.54]
Ravindran 1997	12/513	8/506		9.4 %	1.49 [0.60, 3.68]
Subtotal (95% CI)	**639**	**634**		**16.5 %**	**1.50 [0.76, 2.97]**
Total events: 21 (Paroxetine), 14 (Older ADs)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.23$, df = 3 (P = 0.97); $I^2 = 0.0\%$					
Test for overall effect: Z = 1.16 (P = 0.25)					
3 versus dothiepin					
29060/056/UK	0/67	1/67		0.7 %	0.33 [0.01, 8.21]
Dunner 1992	4/136	6/135		4.6 %	0.65 [0.18, 2.36]
Subtotal (95% CI)	**203**	**202**		**5.4 %**	**0.59 [0.18, 1.96]**
Total events: 4 (Paroxetine), 7 (Older ADs)					



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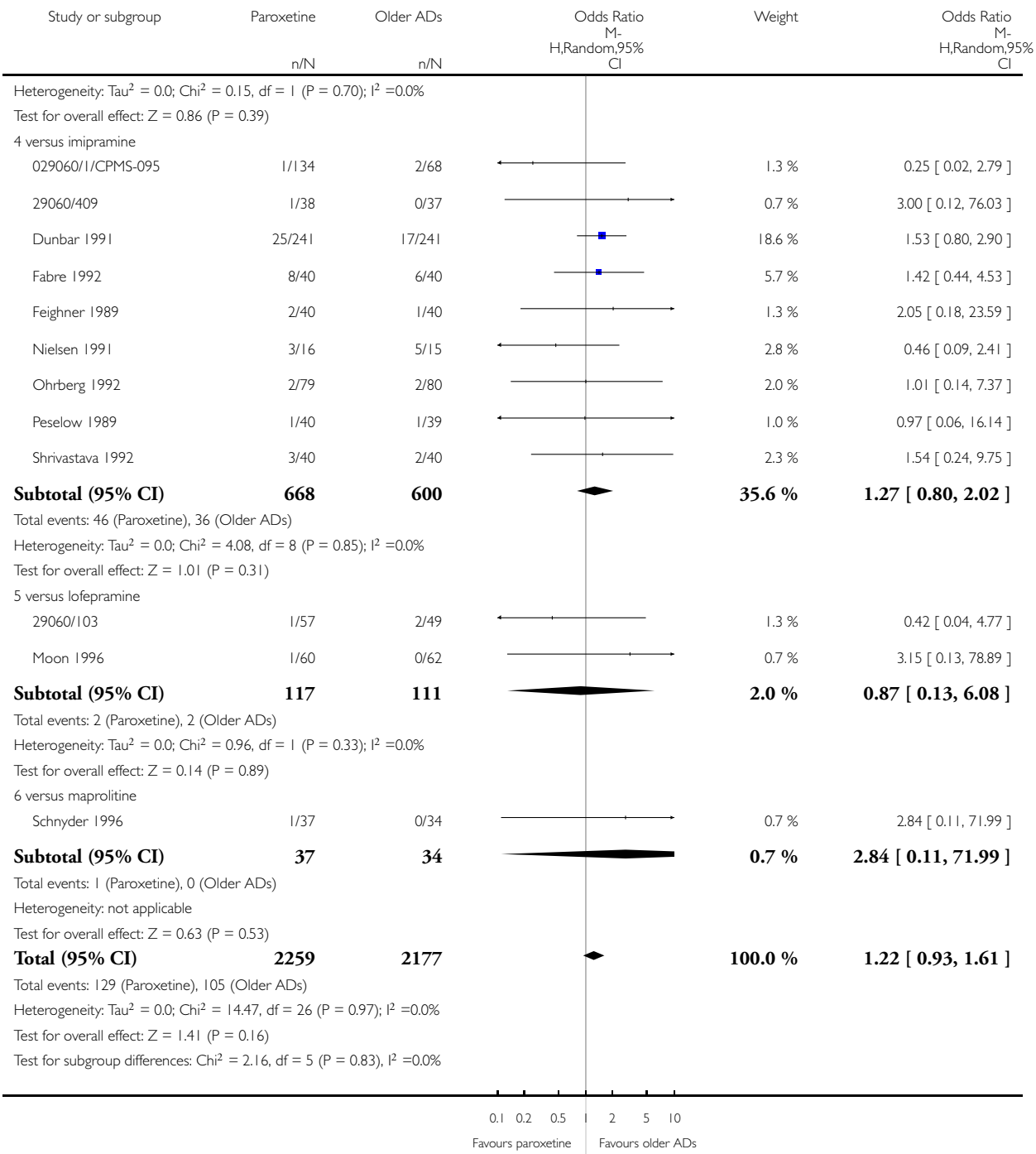

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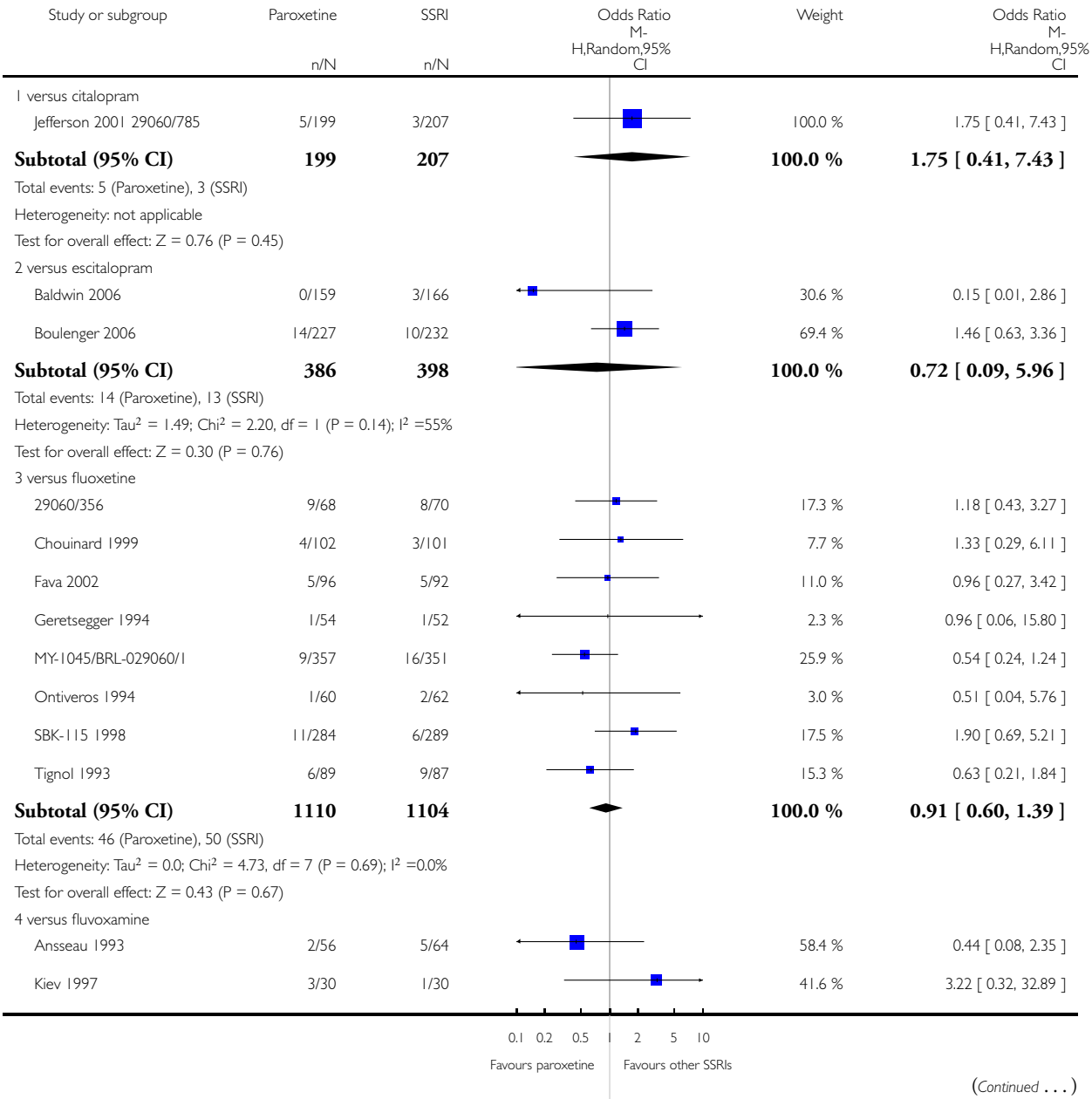
Analysis 11.2. Comparison 11 Failure to complete (due to inefficacy), Outcome 2 Paroxetine versus other SSRIs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 11 Failure to complete (due to inefficacy)

Outcome: 2 Paroxetine versus other SSRIs



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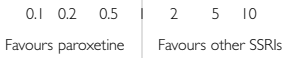
Study or subgroup	Paroxetine n/N	SSRI n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Subtotal (95% CI)	**86**	**94**		**100.0 %**	**1.00 [0.15, 6.93]**
Total events: 5 (Paroxetine), 6 (SSRI)					
Heterogeneity: $Tau^2 = 0.93$; $Chi^2 = 1.87$, df = 1 (P = 0.17); $I^2 = 46\%$					
Test for overall effect: Z = 0.00 (P = 1.0)					
5 versus sertraline					
Fava 2002	5/96	9/96		100.0 %	0.53 [0.17, 1.65]
Subtotal (95% CI)	**96**	**96**		**100.0 %**	**0.53 [0.17, 1.65]**
Total events: 5 (Paroxetine), 9 (SSRI)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.10 (P = 0.27)					



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Analysis 11.3. Comparison 11 Failure to complete (due to inefficacy), Outcome 3 Paroxetine versus newer or non-conventional ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 11 Failure to complete (due to inefficacy)

Outcome: 3 Paroxetine versus newer or non-conventional ADs

Study or subgroup	Paroxetine n/N	newer ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
1 versus agomelatine					
Loo 2002	11/147	9/137		100.0 %	1.15 [0.46, 2.87]
Subtotal (95% CI)	**147**	**137**		**100.0 %**	**1.15 [0.46, 2.87]**
Total events: 11 (Paroxetine), 9 (newer ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.30 (P = 0.76)					
2 versus aprepitant (MK-869)					
Kramer 1998	0/72	1/71		100.0 %	0.32 [0.01, 8.09]
Subtotal (95% CI)	**72**	**71**		**100.0 %**	**0.32 [0.01, 8.09]**
Total events: 0 (Paroxetine), 1 (newer ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.69 (P = 0.49)					
3 versus duloxetine					
Detke 2004 (HMAY A)	1/86	5/188		9.0 %	0.43 [0.05, 3.74]
Goldstein 2004 (HMAT B)	11/87	16/177		63.6 %	1.46 [0.64, 3.29]
Higuchi 2009	3/164	2/84		12.9 %	0.76 [0.13, 4.66]
Lee 2007 (HMCV)	1/240	1/238		5.5 %	0.99 [0.06, 15.95]
Perahia 2006 (HMAY B)	1/97	5/196		9.0 %	0.40 [0.05, 3.45]
Subtotal (95% CI)	**674**	**883**		**100.0 %**	**1.05 [0.55, 2.00]**
Total events: 17 (Paroxetine), 29 (newer ADs)					
Heterogeneity: Tau^2 = 0.0; Chi^2 = 2.19, df = 4 (P = 0.70); I^2 =0.0%					
Test for overall effect: Z = 0.13 (P = 0.89)					
4 versus hypericum					
Szegedi 2005	3/126	6/125		100.0 %	0.48 [0.12, 1.98]
Subtotal (95% CI)	**126**	**125**		**100.0 %**	**0.48 [0.12, 1.98]**
Total events: 3 (Paroxetine), 6 (newer ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.01 (P = 0.31)					
5 versus milnacipran					
Sechter 2004	6/153	9/149		100.0 %	0.63 [0.22, 1.83]
Subtotal (95% CI)	**153**	**149**		**100.0 %**	**0.63 [0.22, 1.83]**

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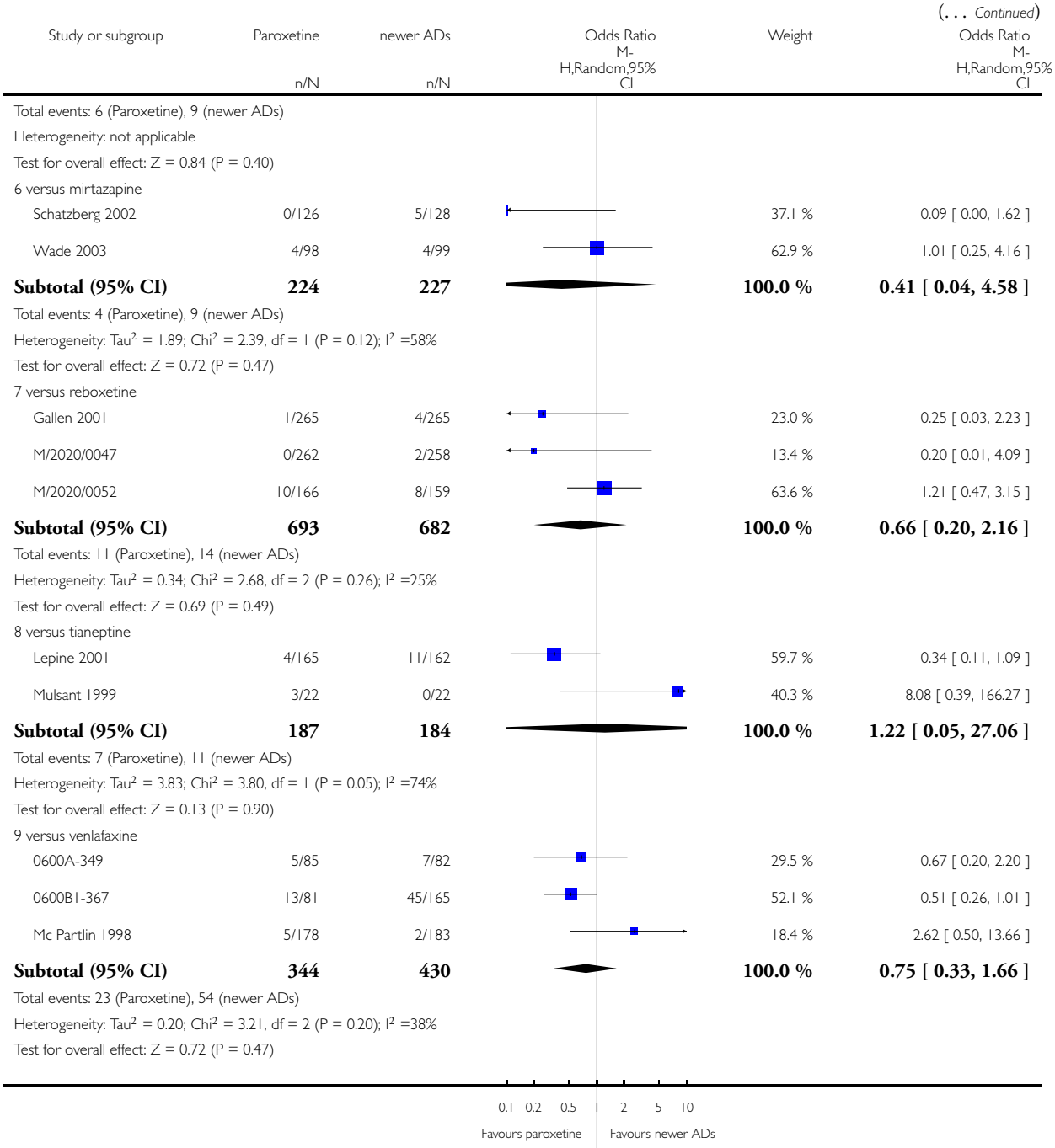

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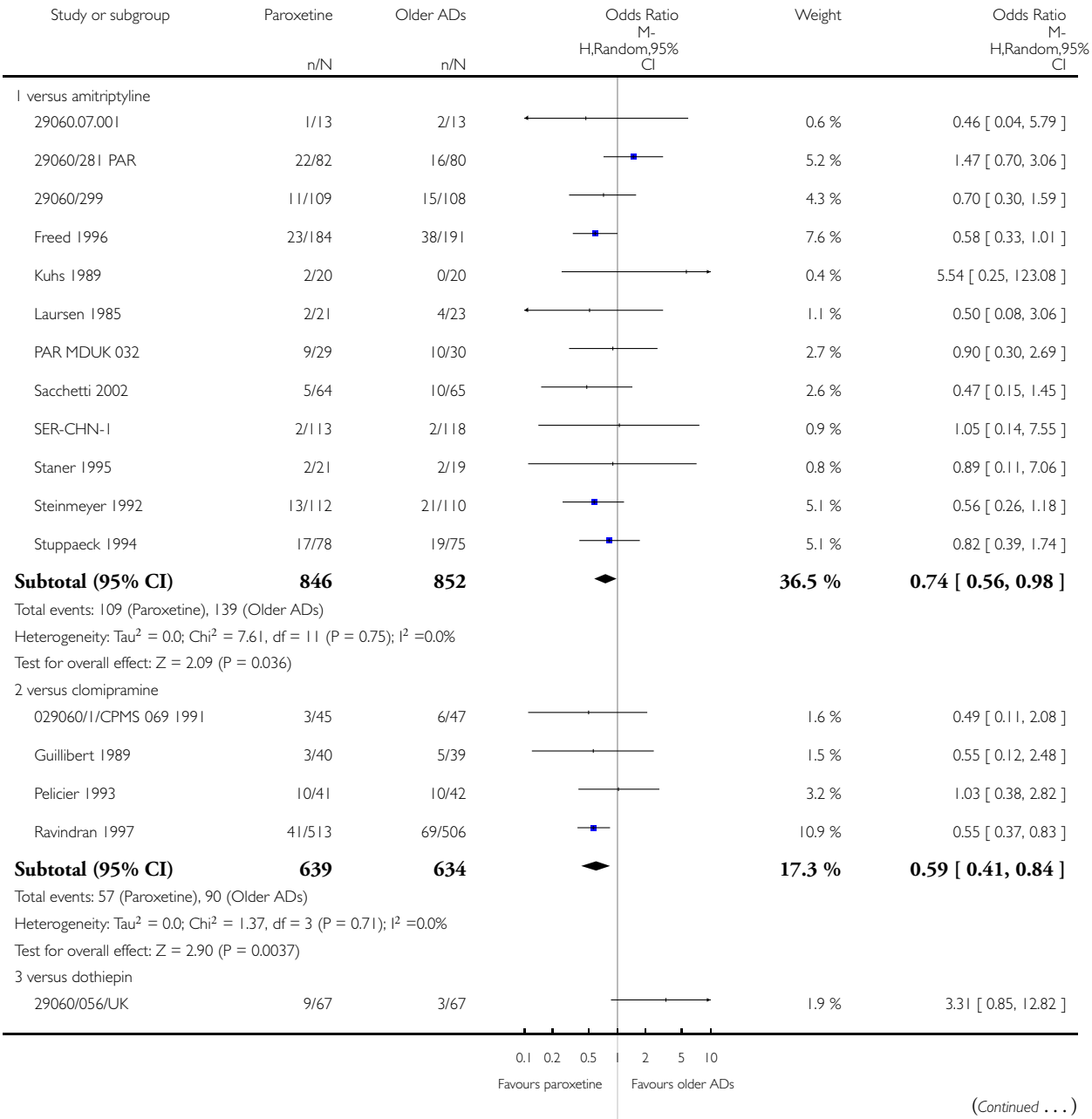
Analysis 12.1. Comparison 12 Failure to complete (due to side effects), Outcome 1 Paroxetine versus older ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 12 Failure to complete (due to side effects)

Outcome: 1 Paroxetine versus older ADs



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Study or subgroup	Paroxetine n/N	Older ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Dunner 1992	33/136	26/135		7.3 %	1.34 [0.75, 2.40]
Subtotal (95% CI)	**203**	**202**		**9.2 %**	**1.70 [0.78, 3.70]**
Total events: 42 (Paroxetine), 29 (Older ADs)					
Heterogeneity: Tau^2 = 0.13; Chi^2 = 1.44, df = 1 (P = 0.23); I^2 =31%					
Test for overall effect: Z = 1.34 (P = 0.18)					
4 versus imipramine					
029060/1/CPMS-095	3/134	1/68		0.7 %	1.53 [0.16, 15.03]
29060/409	4/38	5/37		1.8 %	0.75 [0.19, 3.06]
Dunbar 1991	55/241	85/241		11.1 %	0.54 [0.36, 0.81]
Fabre 1992	9/40	9/40		2.9 %	1.00 [0.35, 2.86]
Feighner 1989	11/40	15/40		3.5 %	0.63 [0.25, 1.63]
Nielsen 1991	1/16	3/15		0.6 %	0.27 [0.02, 2.90]
Ohrberg 1992	10/79	14/80		4.0 %	0.68 [0.28, 1.65]
Peselow 1989	4/40	4/39		1.6 %	0.97 [0.23, 4.19]
Shrivastava 1992	5/40	17/40		2.6 %	0.19 [0.06, 0.60]
Subtotal (95% CI)	**668**	**600**		**28.8 %**	**0.58 [0.43, 0.77]**
Total events: 102 (Paroxetine), 153 (Older ADs)					
Heterogeneity: Tau^2 = 0.0; Chi^2 = 6.68, df = 8 (P = 0.57); I^2 =0.0%					
Test for overall effect: Z = 3.68 (P = 0.00023)					
5 versus lofepramine					
29060/103	5/57	4/49		1.8 %	1.08 [0.27, 4.27]
Moon 1996	5/60	4/62		1.8 %	1.32 [0.34, 5.16]
Subtotal (95% CI)	**117**	**111**		**3.7 %**	**1.19 [0.45, 3.15]**
Total events: 10 (Paroxetine), 8 (Older ADs)					
Heterogeneity: Tau^2 = 0.0; Chi^2 = 0.04, df = 1 (P = 0.84); I^2 =0.0%					
Test for overall effect: Z = 0.36 (P = 0.72)					
6 versus maprolitine					
29060.065.BE	5/28	1/32		0.7 %	6.74 [0.74, 61.66]
Schnyder 1996	0/37	5/34		0.4 %	0.07 [0.00, 1.35]
Subtotal (95% CI)	**65**	**66**		**1.2 %**	**0.77 [0.01, 70.98]**
Total events: 5 (Paroxetine), 6 (Older ADs)					
Heterogeneity: Tau^2 = 8.92; Chi^2 = 6.07, df = 1 (P = 0.01); I^2 =84%					
Test for overall effect: Z = 0.11 (P = 0.91)					
7 versus mianserin					
29060/III/85/030	4/18	1/15		0.7 %	4.00 [0.40, 40.42]
29060III/85/038	1/30	1/29		0.5 %	0.97 [0.06, 16.20]
Subtotal (95% CI)	**48**	**44**		**1.1 %**	**2.26 [0.38, 13.50]**

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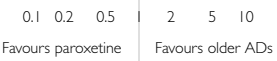
Study or subgroup	Paroxetine n/N	Older ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Total events: 5 (Paroxetine), 2 (Older ADs)					
Heterogeneity: Tau^2 = 0.0; Chi^2 = 0.59, df = 1 (P = 0.44); I^2 =0.0%					
Test for overall effect: Z = 0.89 (P = 0.37)					
8 versus nortriptyline					
Mulsant 1999	8/43	5/37		2.3 %	1.46 [0.43, 4.93]
Subtotal (95% CI)	**43**	**37**		**2.3 %**	**1.46 [0.43, 4.93]**
Total events: 8 (Paroxetine), 5 (Older ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.61 (P = 0.54)					
Total (95% CI)	**2629**	**2546**		**100.0 %**	**0.76 [0.63, 0.92]**
Total events: 338 (Paroxetine), 432 (Older ADs)					
Heterogeneity: Tau^2 = 0.05; Chi^2 = 39.20, df = 33 (P = 0.21); I^2 =16%					
Test for overall effect: Z = 2.76 (P = 0.0057)					
Test for subgroup differences: Chi^2 = 11.93, df = 7 (P = 0.10), I^2 =41%					



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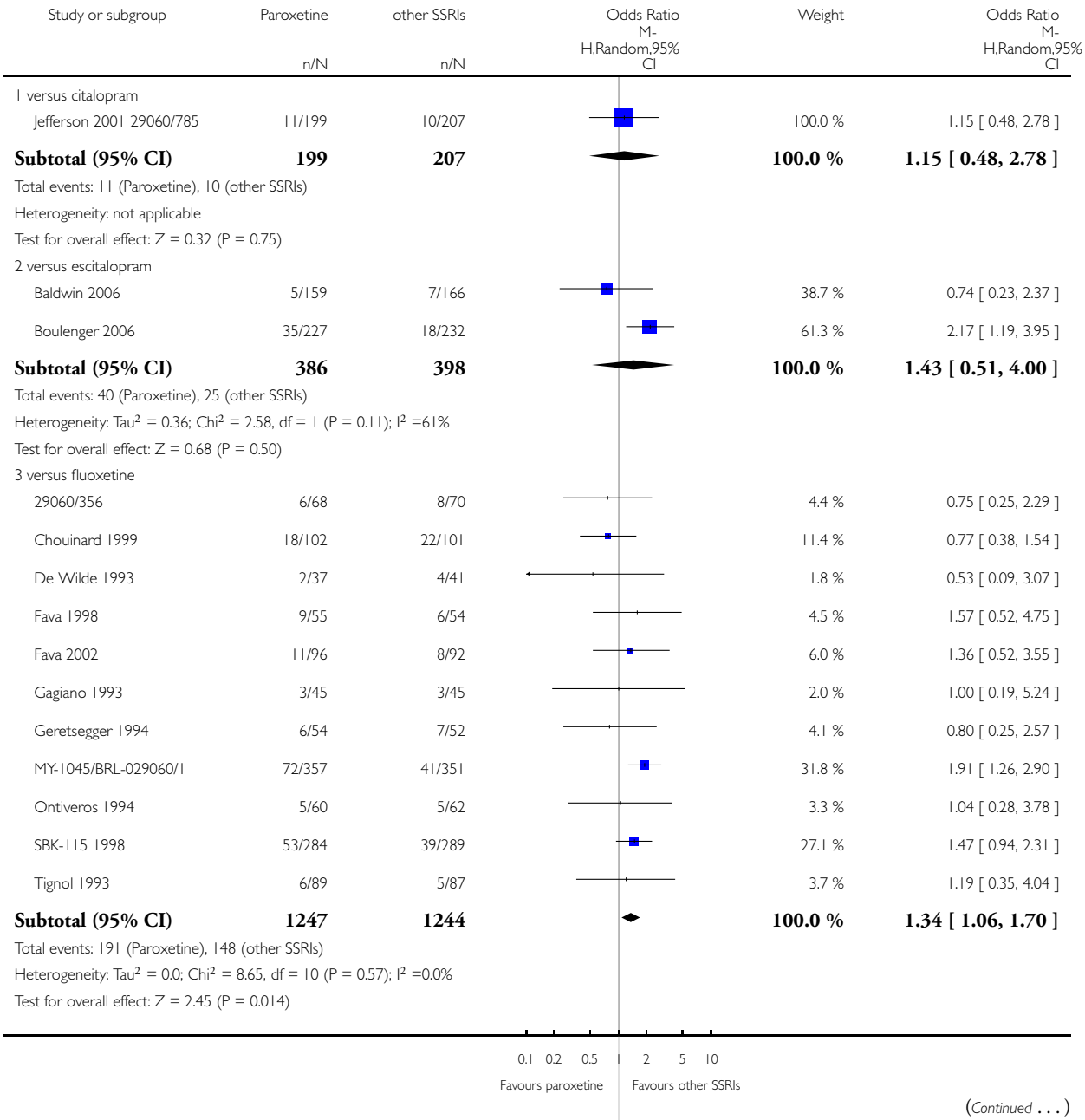
Analysis 12.2. Comparison 12 Failure to complete (due to side effects), Outcome 2 Paroxetine versus other SSRIs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 12 Failure to complete (due to side effects)

Outcome: 2 Paroxetine versus other SSRIs



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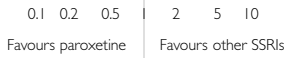
Study or subgroup	Paroxetine n/N	other SSRIs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
4 versus fluvoxamine					
Ansseau 1993	3/56	13/64		36.0 %	0.22 [0.06, 0.83]
Kato 2005	6/42	2/39		32.3 %	3.08 [0.58, 16.29]
Kiev 1997	5/30	2/30		31.7 %	2.80 [0.50, 15.73]
Subtotal (95% CI)	**128**	**133**		**100.0 %**	**1.16 [0.19, 7.16]**
Total events: 14 (Paroxetine), 17 (other SSRIs)					
Heterogeneity: Tau^2 = 1.95; Chi^2 = 8.15, df = 2 (P = 0.02); I^2 =75%					
Test for overall effect: Z = 0.16 (P = 0.87)					
5 versus sertraline					
Fava 2002	11/96	6/96		100.0 %	1.94 [0.69, 5.48]
Subtotal (95% CI)	**96**	**96**		**100.0 %**	**1.94 [0.69, 5.48]**
Total events: 11 (Paroxetine), 6 (other SSRIs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.25 (P = 0.21)					



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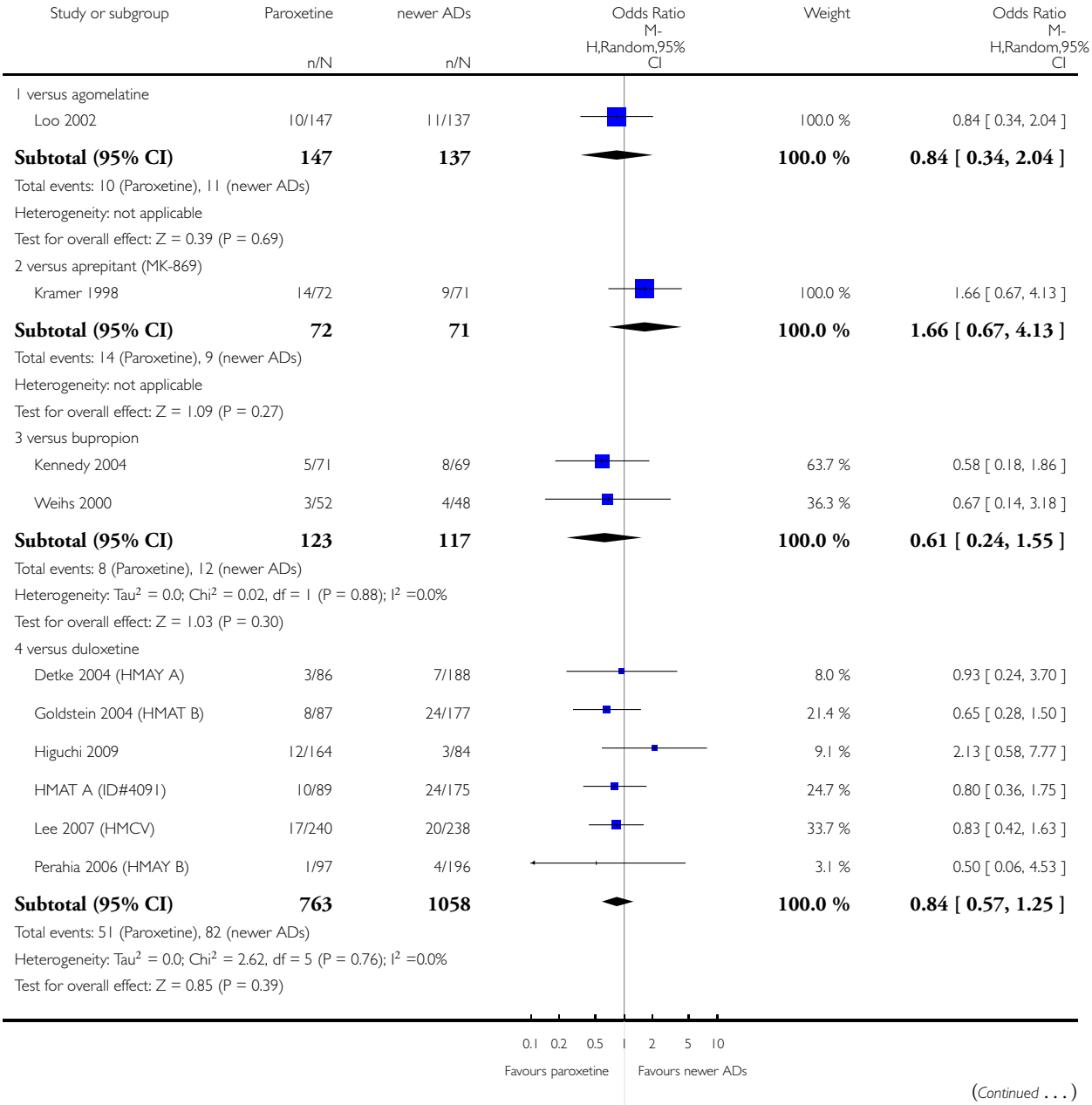
Analysis 12.3. Comparison 12 Failure to complete (due to side effects), Outcome 3 Paroxetine versus newer or non-conventional ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 12 Failure to complete (due to side effects)

Outcome: 3 Paroxetine versus newer or non-conventional ADs



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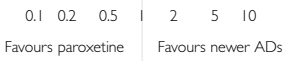
Study or subgroup	Paroxetine n/N	newer ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
5 versus hypericum					
Szegedi 2005	8/126	4/125		100.0 %	2.05 [0.60, 6.99]
Subtotal (95% CI)	**126**	**125**		**100.0 %**	**2.05 [0.60, 6.99]**
Total events: 8 (Paroxetine), 4 (newer ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.15 (P = 0.25)					
6 versus milnacipran					
Sechter 2004	20/153	17/149		100.0 %	1.17 [0.59, 2.33]
Subtotal (95% CI)	**153**	**149**		**100.0 %**	**1.17 [0.59, 2.33]**
Total events: 20 (Paroxetine), 17 (newer ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.44 (P = 0.66)					
7 versus mirtazapine					
Benkert 1999	10/136	12/139		24.5 %	0.84 [0.35, 2.01]
Schatzberg 2002	33/126	19/128		39.2 %	2.04 [1.09, 3.82]
Wade 2003	24/98	21/99		36.3 %	1.20 [0.62, 2.35]
Subtotal (95% CI)	**360**	**366**		**100.0 %**	**1.35 [0.83, 2.21]**
Total events: 67 (Paroxetine), 52 (newer ADs)					
Heterogeneity: Tau^2 = 0.06; Chi^2 = 2.87, df = 2 (P = 0.24); I^2 =30%					
Test for overall effect: Z = 1.21 (P = 0.23)					
8 versus reboxetine					
Gallen 2001	22/265	28/265		38.2 %	0.77 [0.43, 1.38]
M/2020/0047	5/262	20/258		27.8 %	0.23 [0.09, 0.63]
M/2020/0052	10/166	31/159		33.9 %	0.26 [0.13, 0.56]
Subtotal (95% CI)	**693**	**682**		**100.0 %**	**0.38 [0.17, 0.86]**
Total events: 37 (Paroxetine), 79 (newer ADs)					
Heterogeneity: Tau^2 = 0.36; Chi^2 = 6.83, df = 2 (P = 0.03); I^2 =71%					
Test for overall effect: Z = 2.31 (P = 0.021)					
9 versus tianeptine					
Lepine 2001	19/165	6/162		100.0 %	3.38 [1.31, 8.71]
Subtotal (95% CI)	**165**	**162**		**100.0 %**	**3.38 [1.31, 8.71]**
Total events: 19 (Paroxetine), 6 (newer ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 2.53 (P = 0.011)					
10 versus venlafaxine					
0600A-349	8/85	17/82		23.9 %	0.40 [0.16, 0.98]
0600B 428	3/56	2/58		8.4 %	1.58 [0.25, 9.86]
0600B1-367	7/81	15/165		22.8 %	0.95 [0.37, 2.42]



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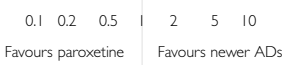
Study or subgroup	Paroxetine n/N	newer ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Mc Partlin 1998	29/178	22/183		35.9 %	1.42 [0.78, 2.59]
Owens 2008	2/42	4/44		9.0 %	0.50 [0.09, 2.89]
Subtotal (95% CI)	**442**	**532**		**100.0 %**	**0.88 [0.50, 1.56]**
Total events: 49 (Paroxetine), 60 (newer ADs)					
Heterogeneity: $Tau^2 = 0.14$; $Chi^2 = 6.17$, df = 4 (P = 0.19); $I^2 = 35\%$					
Test for overall effect: Z = 0.45 (P = 0.66)					



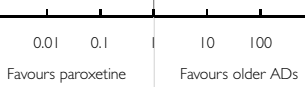
Analysis 13.1. Comparison 13 SE - Participants with at least one TEAE, Outcome 1 Paroxetine versus older ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 13 SE - Participants with at least one TEAE

Outcome: 1 Paroxetine versus older ADs

Study or subgroup	Paroxetine n/N	Older ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
1 versus amitriptyline					
29060.07.001	12/13	12/13		0.4 %	1.00 [0.06, 17.90]
29060/281 PAR	71/82	74/80		2.1 %	0.52 [0.18, 1.49]
29060/299	70/109	81/108		4.2 %	0.60 [0.33, 1.07]
Battegay 1985	6/11	6/10		1.0 %	0.80 [0.14, 4.53]
Bignamini 1992	59/156	96/153		5.0 %	0.36 [0.23, 0.57]
Freed 1996	72/184	91/191		5.3 %	0.71 [0.47, 1.06]
Geretsegger 1995	26/44	30/47		2.8 %	0.82 [0.35, 1.91]
Hutchinson 1992	20/58	20/32		2.6 %	0.32 [0.13, 0.77]
Kuhs 1989	9/20	16/20		1.4 %	0.20 [0.05, 0.83]



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Study or subgroup	Paroxetine n/N	Older ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Laursen 1985	16/21	14/23		1.5 %	2.06 [0.56, 7.61]
PAR MDUK 032	23/29	26/30		1.4 %	0.59 [0.15, 2.35]
Sacchetti 2002	18/64	26/65		3.3 %	0.59 [0.28, 1.23]
SER-CHN-1	51/113	101/118		3.9 %	0.14 [0.07, 0.26]
Staner 1995	14/21	16/19		1.2 %	0.38 [0.08, 1.73]
Stott 1993	161/243	185/262		5.6 %	0.82 [0.56, 1.19]
Stuppaeck 1994	41/78	44/75		3.8 %	0.78 [0.41, 1.48]
Subtotal (95% CI)	**1246**	**1246**		**45.6 %**	**0.53 [0.39, 0.72]**
Total events: 669 (Paroxetine), 838 (Older ADs)					
Heterogeneity: $Tau^2 = 0.20$; $Chi^2 = 37.12$, df = 15 (P = 0.001); I^2 =60%					
Test for overall effect: Z = 3.99 (P = 0.000066)					
2 versus clomipramine					
029060/1/CPMS 069 1991	27/45	33/47		2.8 %	0.64 [0.27, 1.51]
Guillibert 1989	23/40	38/39		0.7 %	0.04 [0.00, 0.29]
Pelicier 1993	26/41	28/42		2.6 %	0.87 [0.35, 2.14]
Ravindran 1997	334/513	368/506		6.3 %	0.70 [0.54, 0.91]
Subtotal (95% CI)	**639**	**634**		**12.4 %**	**0.56 [0.28, 1.10]**
Total events: 410 (Paroxetine), 467 (Older ADs)					
Heterogeneity: $Tau^2 = 0.28$; $Chi^2 = 8.25$, df = 3 (P = 0.04); I^2 =64%					
Test for overall effect: Z = 1.68 (P = 0.093)					
3 versus dothiepin					
29060/056/UK	37/67	34/67		3.6 %	1.20 [0.61, 2.36]
Dunner 1992	123/136	124/135		2.9 %	0.84 [0.36, 1.95]
Subtotal (95% CI)	**203**	**202**		**6.5 %**	**1.04 [0.61, 1.76]**
Total events: 160 (Paroxetine), 158 (Older ADs)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.41$, df = 1 (P = 0.52); I^2 =0.0%					
Test for overall effect: Z = 0.15 (P = 0.88)					
4 versus imipramine					
029060/1/CPMS-095	56/134	27/68		4.1 %	1.09 [0.60, 1.98]
29060/409	23/38	28/37		2.3 %	0.49 [0.18, 1.33]
Cohn 1990	37/40	36/40		1.1 %	1.37 [0.29, 6.56]
Dunbar 1991	211/241	224/241		3.9 %	0.53 [0.29, 1.00]
Fabre 1992	33/40	38/40		1.1 %	0.25 [0.05, 1.28]
Feighner 1989	39/40	40/40		0.3 %	0.33 [0.01, 8.22]
Nielsen 1991	9/16	14/15		0.6 %	0.09 [0.01, 0.88]

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Study or subgroup	Paroxetine n/N	Older ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Peselow 1989	34/40	34/39		1.6 %	0.83 [0.23, 2.99]
Shrivastava 1992	33/40	37/40		1.3 %	0.38 [0.09, 1.60]
Subtotal (95% CI)	**629**	**560**		**16.4 %**	**0.62 [0.42, 0.94]**
Total events: 475 (Paroxetine), 478 (Older ADs)					
Heterogeneity: Tau² = 0.06; Chi² = 9.55, df = 8 (P = 0.30); I² =16%					
Test for overall effect: Z = 2.28 (P = 0.023)					
5 versus lofepramine					
29060/103	36/57	29/49		3.1 %	1.18 [0.54, 2.59]
Moon 1996	35/60	32/62		3.4 %	1.31 [0.64, 2.68]
Subtotal (95% CI)	**117**	**111**		**6.6 %**	**1.25 [0.74, 2.12]**
Total events: 71 (Paroxetine), 61 (Older ADs)					
Heterogeneity: Tau² = 0.0; Chi² = 0.04, df = 1 (P = 0.85); I² =0.0%					
Test for overall effect: Z = 0.83 (P = 0.41)					
6 versus maprolitine					
29060.065.BE	25/28	30/32		0.8 %	0.56 [0.09, 3.59]
Schnyder 1996	12/37	14/34		2.4 %	0.69 [0.26, 1.81]
Subtotal (95% CI)	**65**	**66**		**3.2 %**	**0.66 [0.28, 1.55]**
Total events: 37 (Paroxetine), 44 (Older ADs)					
Heterogeneity: Tau² = 0.0; Chi² = 0.04, df = 1 (P = 0.84); I² =0.0%					
Test for overall effect: Z = 0.96 (P = 0.34)					
7 versus mianserin					
29060/III/83/022	15/18	16/18		0.8 %	0.63 [0.09, 4.28]
29060/III/85/030	14/18	12/15		1.0 %	0.88 [0.16, 4.71]
29060III/85/038	2/30	1/29		0.5 %	2.00 [0.17, 23.34]
Dalery 2001	17/54	26/62		3.2 %	0.64 [0.30, 1.37]
Dorman 1992	16/29	18/28		2.1 %	0.68 [0.24, 1.98]
Subtotal (95% CI)	**149**	**152**		**7.6 %**	**0.71 [0.41, 1.22]**
Total events: 64 (Paroxetine), 73 (Older ADs)					
Heterogeneity: Tau² = 0.0; Chi² = 0.84, df = 4 (P = 0.93); I² =0.0%					
Test for overall effect: Z = 1.25 (P = 0.21)					
8 versus nortriptyline					
Mulsant 1999	8/43	5/37		1.7 %	1.46 [0.43, 4.93]
Subtotal (95% CI)	**43**	**37**		**1.7 %**	**1.46 [0.43, 4.93]**
Total events: 8 (Paroxetine), 5 (Older ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.61 (P = 0.54)					
Total (95% CI)	**3091**	**3008**		**100.0 %**	**0.64 [0.53, 0.77]**
Total events: 1894 (Paroxetine), 2124 (Older ADs)					
Heterogeneity: Tau² = 0.12; Chi² = 70.30, df = 40 (P = 0.002); I² =43%					

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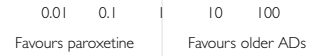
Study or subgroup	Paroxetine n/N	Older ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Test for overall effect: Z = 4.80 (P < 0.00001)					
Test for subgroup differences: Chi² = 12.01, df = 7 (P = 0.10), I² =42%					



Analysis 13.2. Comparison 13 SE - Participants with at least one TEAE, Outcome 2 Paroxetine versus other SSRIs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 13 SE - Participants with at least one TEAE

Outcome: 2 Paroxetine versus other SSRIs

Study or subgroup	Paroxetine n/N	SSRIs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
1 versus citalopram					
Jefferson 2001 29060/785	154/199	170/207		100.0 %	0.74 [0.46, 1.21]
Subtotal (95% CI)	**199**	**207**		**100.0 %**	**0.74 [0.46, 1.21]**
Total events: 154 (Paroxetine), 170 (SSRIs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.19 (P = 0.24)					
2 versus escitalopram					
Boulenger 2006	162/225	153/229		100.0 %	1.28 [0.86, 1.91]
Subtotal (95% CI)	**225**	**229**		**100.0 %**	**1.28 [0.86, 1.91]**
Total events: 162 (Paroxetine), 153 (SSRIs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.20 (P = 0.23)					
3 versus fluoxetine					
29060/356	59/68	62/70		7.1 %	0.85 [0.31, 2.34]
Cassano 2002	34/123	39/119		15.2 %	0.78 [0.45, 1.36]
De Wilde 1993	21/50	29/50		10.1 %	0.52 [0.24, 1.16]

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Study or subgroup	Paroxetine n/N	SSRIs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Gagiano 1993	43/45	39/45		3.1 %	3.31 [0.63, 17.36]
Geretsegger 1994	33/54	40/52		9.2 %	0.47 [0.20, 1.10]
MY-1045/BRL-029060/I	330/357	323/351		15.2 %	1.06 [0.61, 1.84]
Ontiveros 1994	35/60	32/62		11.5 %	1.31 [0.64, 2.68]
SBK-115 1998	264/284	255/289		14.5 %	1.76 [0.99, 3.14]
Tignol 1993	47/89	52/87		14.0 %	0.75 [0.41, 1.37]
Subtotal (95% CI)	**1130**	**1125**		**100.0 %**	**0.94 [0.69, 1.28]**
Total events: 866 (Paroxetine), 871 (SSRIs)					
Heterogeneity: Tau^2 = 0.09; Chi^2 = 13.36, df = 8 (P = 0.10); I^2 =40%					
Test for overall effect: Z = 0.40 (P = 0.69)					
4 versus fluvoxamine					
Ansseau 1993	29/56	41/64		49.6 %	0.60 [0.29, 1.25]
Kato 2005	18/42	11/39		42.4 %	1.91 [0.76, 4.83]
Kiev 1997	30/30	29/30		8.0 %	3.10 [0.12, 79.23]
Subtotal (95% CI)	**128**	**133**		**100.0 %**	**1.12 [0.42, 2.97]**
Total events: 77 (Paroxetine), 81 (SSRIs)					
Heterogeneity: Tau^2 = 0.36; Chi^2 = 4.17, df = 2 (P = 0.12); I^2 =52%					
Test for overall effect: Z = 0.23 (P = 0.82)					

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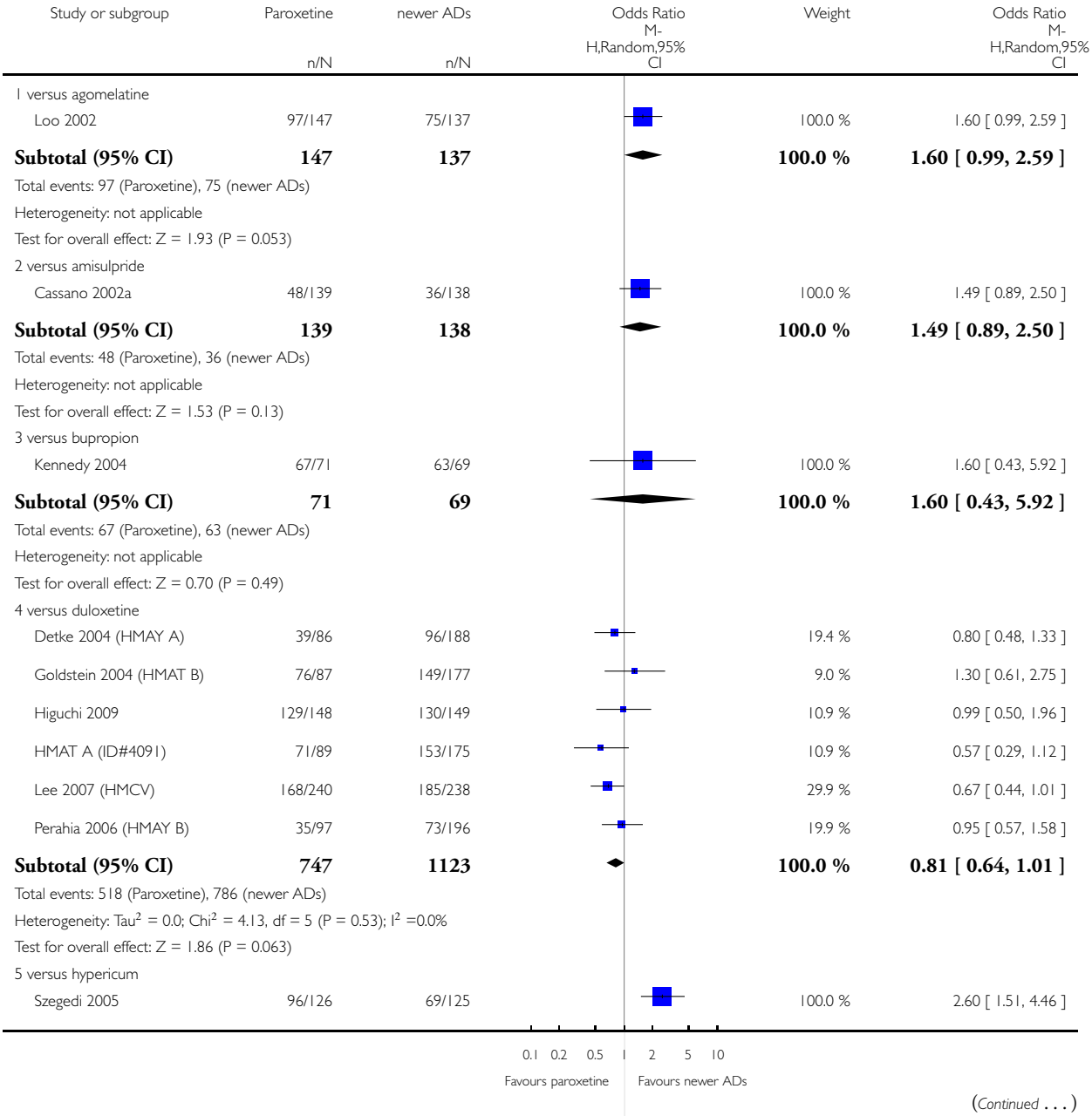
Analysis 13.3. Comparison 13 SE - Participants with at least one TEAE, Outcome 3 Paroxetine versus newer or non-conventional ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 13 SE - Participants with at least one TEAE

Outcome: 3 Paroxetine versus newer or non-conventional ADs



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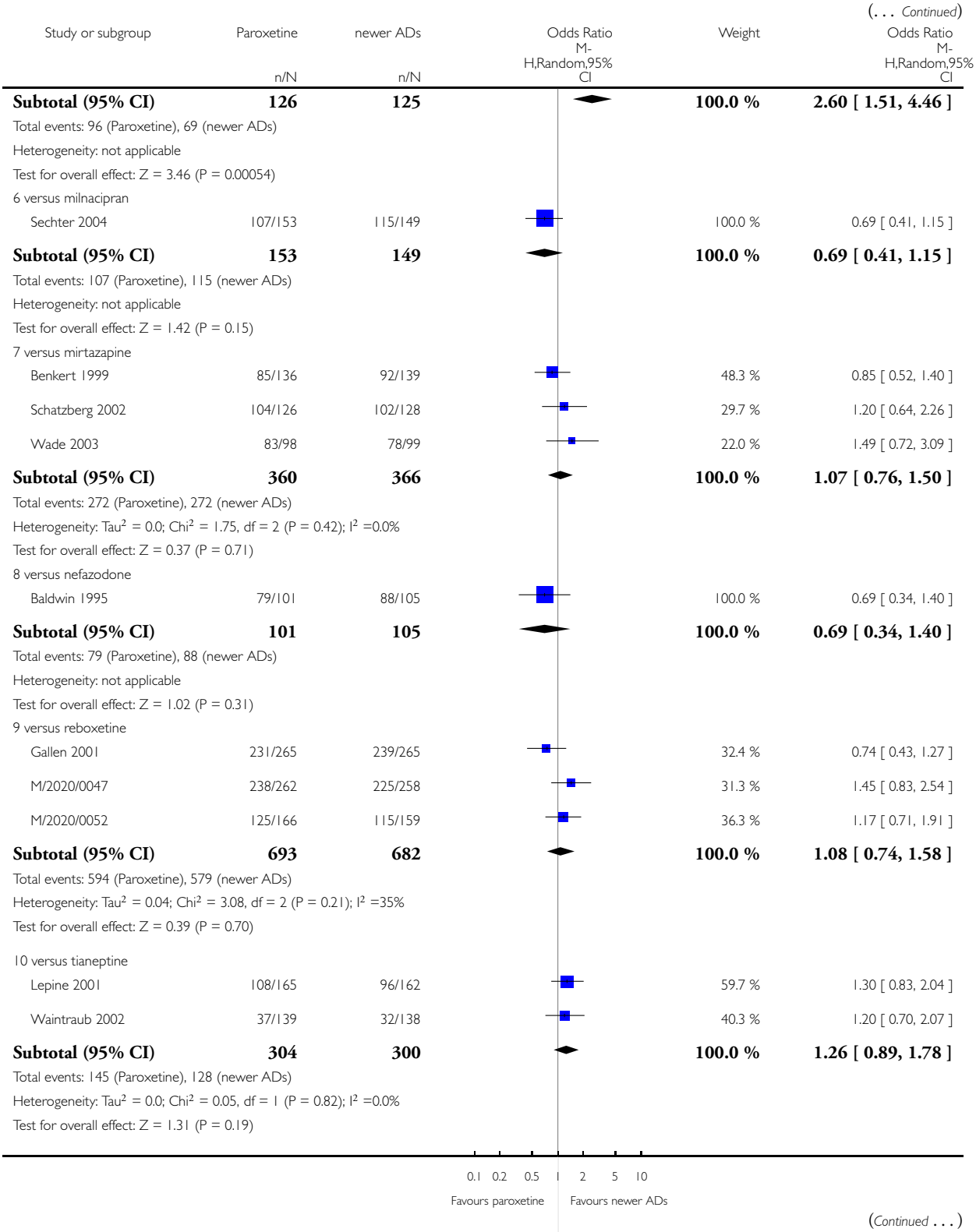

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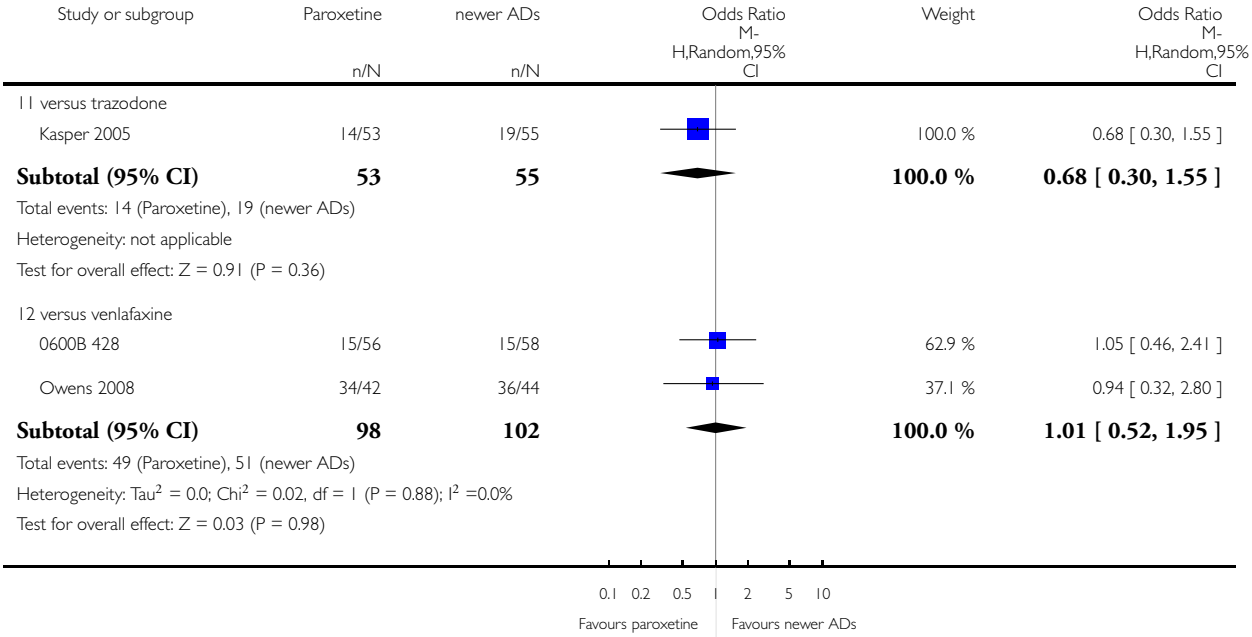
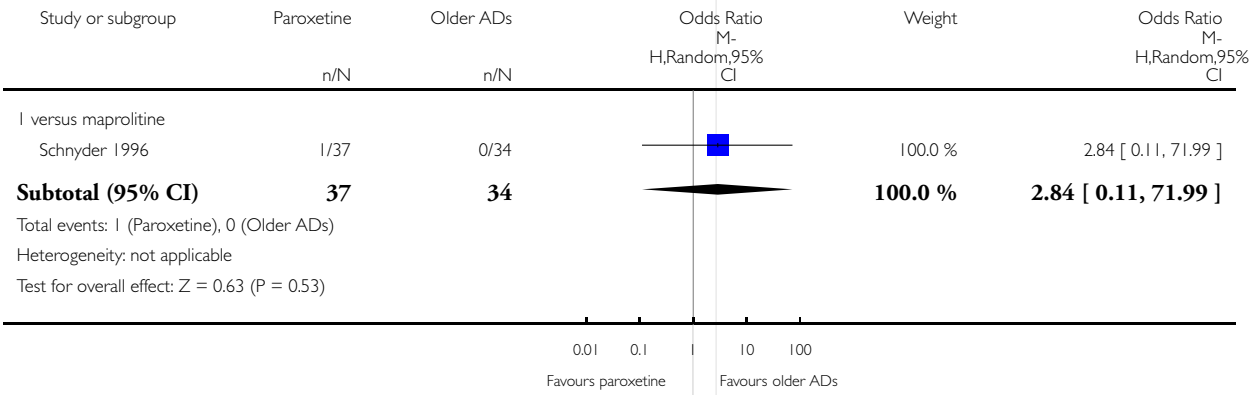


Analysis 14.1. Comparison 14 SE - Abnormal dreams, Outcome 1 Paroxetine versus older ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 14 SE - Abnormal dreams

Outcome: 1 Paroxetine versus older ADs



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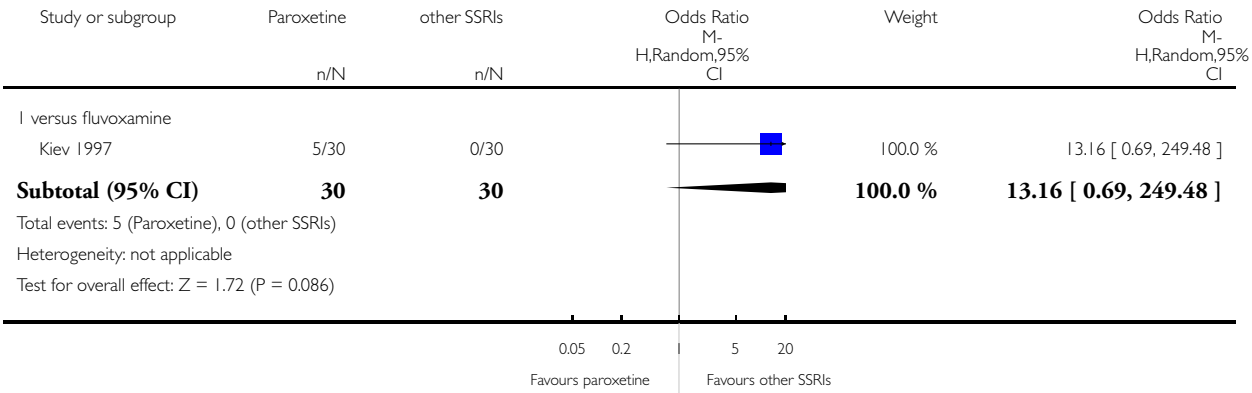
Analysis 14.2. Comparison 14 SE - Abnormal dreams, Outcome 2 Paroxetine versus other SSRIs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 14 SE - Abnormal dreams

Outcome: 2 Paroxetine versus other SSRIs



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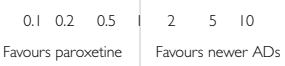
Analysis 14.3. Comparison 14 SE - Abnormal dreams, Outcome 3 Paroxetine versus newer or non-conventional ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 14 SE - Abnormal dreams

Outcome: 3 Paroxetine versus newer or non-conventional ADs

Study or subgroup	Paroxetine n/N	newer ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
1 versus milnacipran					
Sechter 2004	2/153	0/149		100.0 %	4.93 [0.23, 103.64]
Subtotal (95% CI)	**153**	**149**		**100.0 %**	**4.93 [0.23, 103.64]**
Total events: 2 (Paroxetine), 0 (newer ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.03 (P = 0.30)					
2 versus reboxetine					
Gallen 2001	4/265	7/265		50.0 %	0.56 [0.16, 1.95]
M/2020/0047	7/262	4/258		50.0 %	1.74 [0.50, 6.03]
Subtotal (95% CI)	**527**	**523**		**100.0 %**	**0.99 [0.33, 2.99]**
Total events: 11 (Paroxetine), 11 (newer ADs)					
Heterogeneity: $Tau^2 = 0.23$; $Chi^2 = 1.58$, df = 1 (P = 0.21); $I^2 = 37\%$					
Test for overall effect: Z = 0.01 (P = 0.99)					



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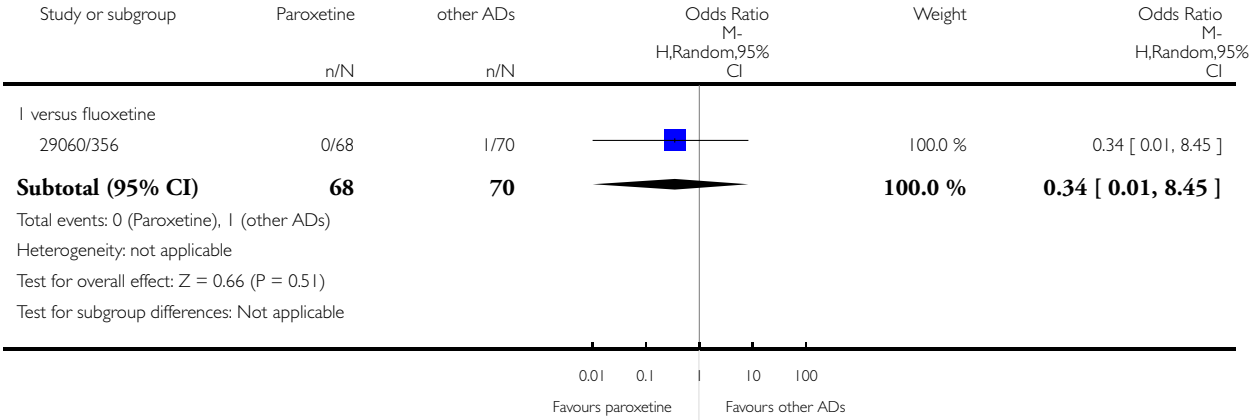
Analysis 15.1. Comparison 15 SE - Abnormal laboratory values, Outcome 1 Abnormal white blood cells.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 15 SE - Abnormal laboratory values

Outcome: 1 Abnormal white blood cells

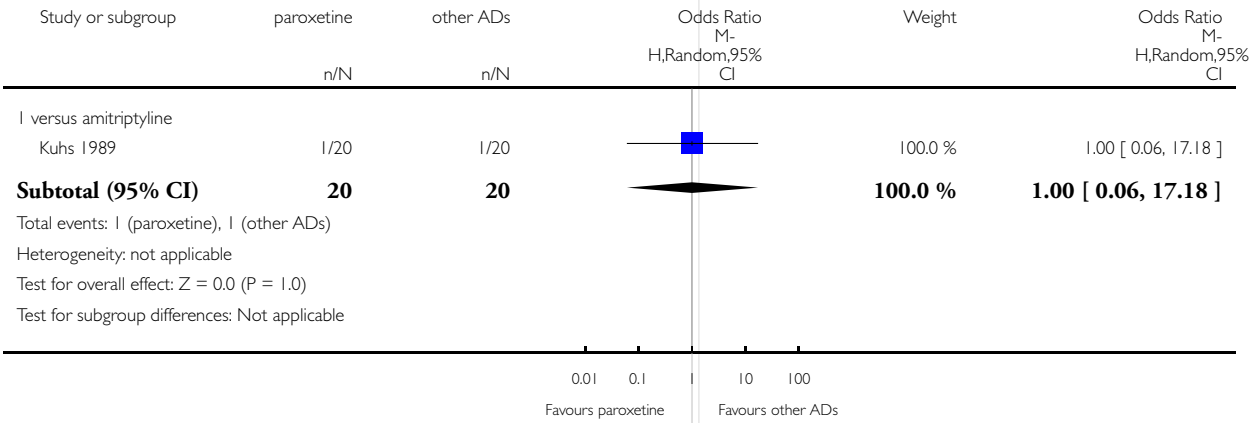


Analysis 15.2. Comparison 15 SE - Abnormal laboratory values, Outcome 2 Leucocytosis.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 15 SE - Abnormal laboratory values

Outcome: 2 Leucocytosis



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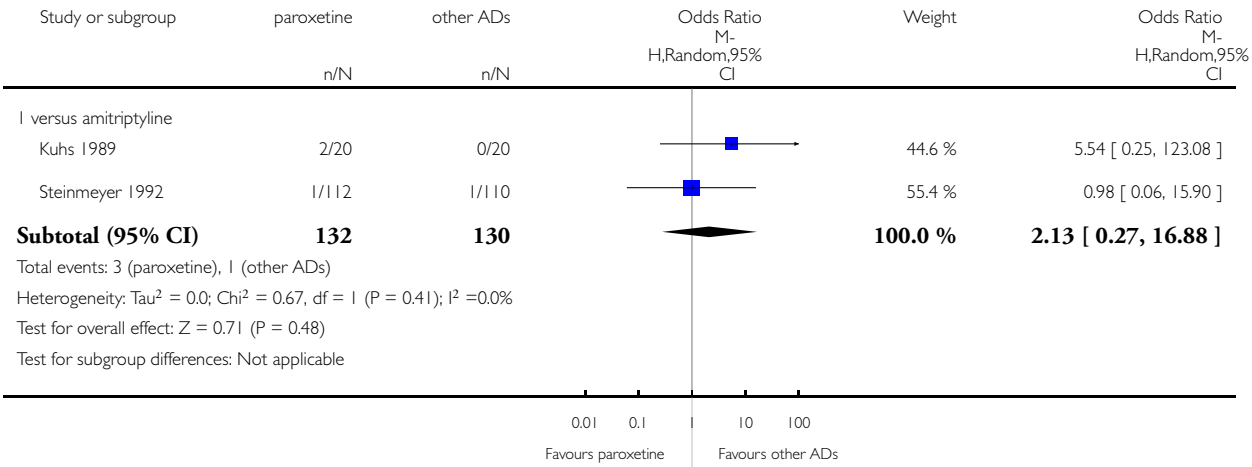
Analysis 15.3. Comparison 15 SE - Abnormal laboratory values, Outcome 3 ALT/AST increase.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 15 SE - Abnormal laboratory values

Outcome: 3 ALT/AST increase



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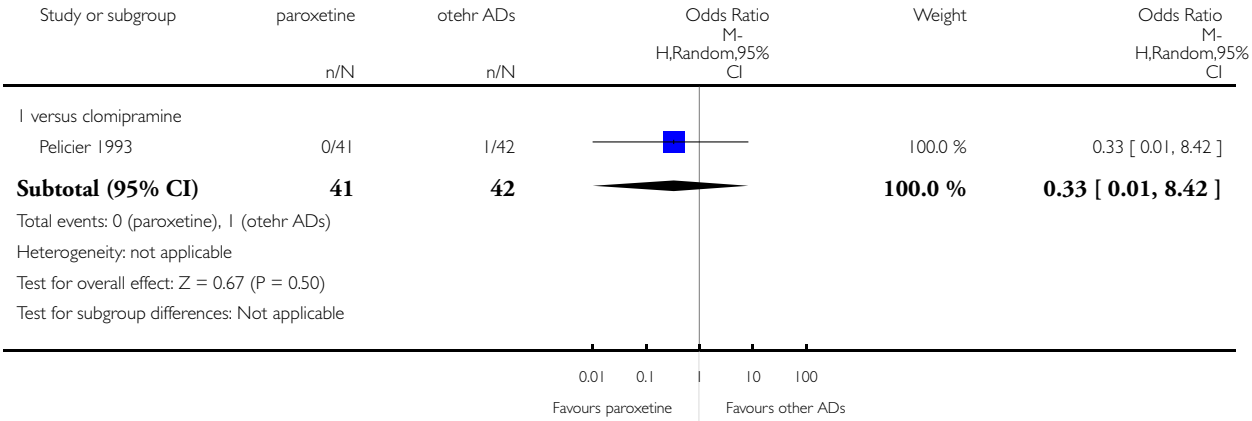
Analysis 15.4. Comparison 15 SE - Abnormal laboratory values, Outcome 4 NOS.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 15 SE - Abnormal laboratory values

Outcome: 4 NOS



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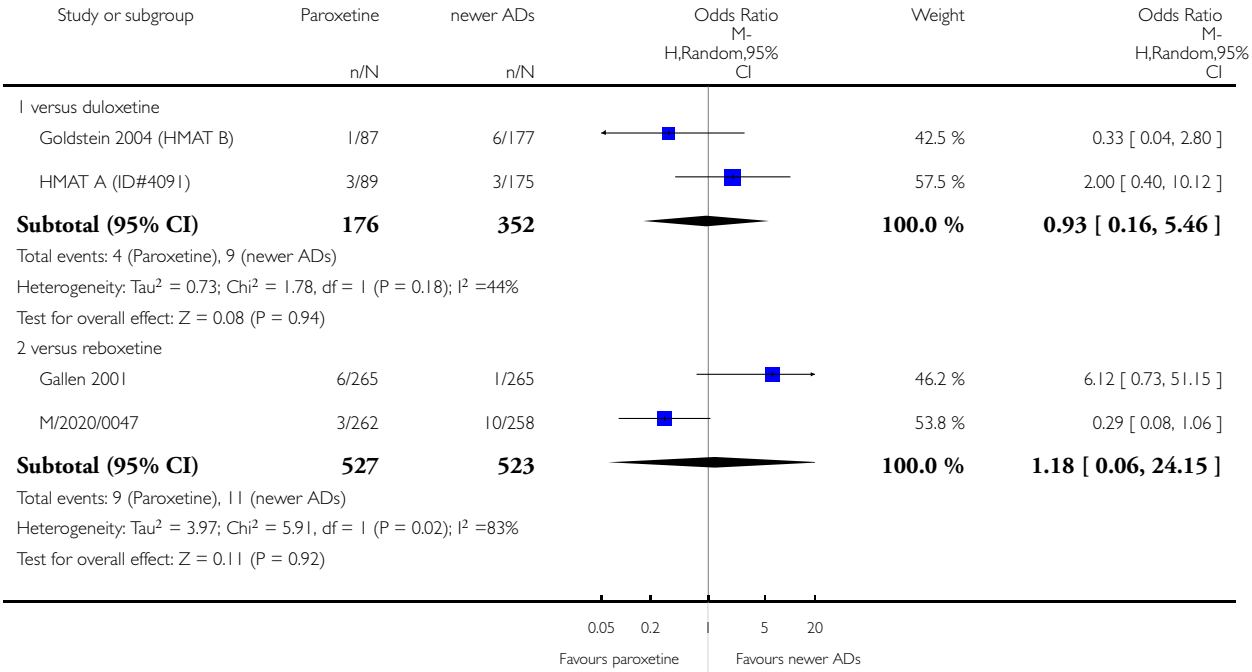
Analysis 16.1. Comparison 16 SE - Abnormal thinking, Outcome 1 Paroxetine versus newer or non-conventional ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 16 SE - Abnormal thinking

Outcome: 1 Paroxetine versus newer or non-conventional ADs



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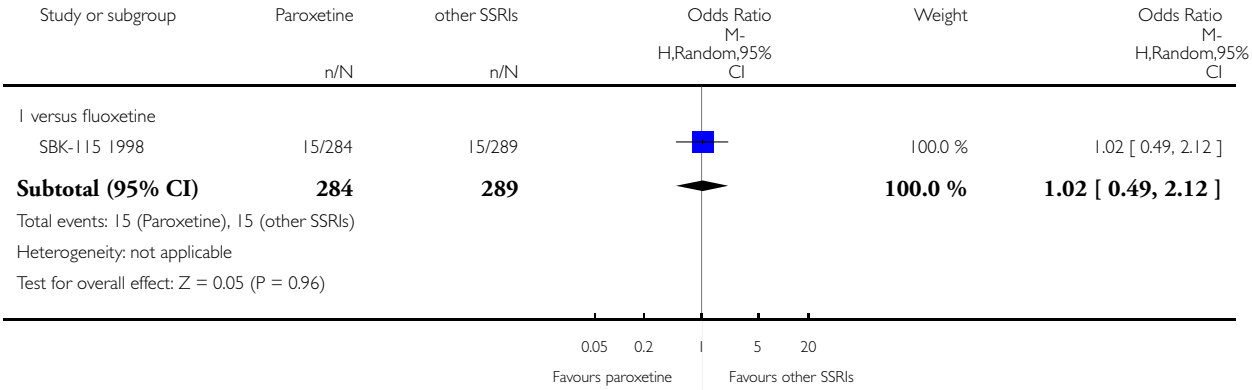
Analysis 17.1. Comparison 17 SE - Accidental injury, Outcome 1 Paroxetine versus other SSRIs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 17 SE - Accidental injury

Outcome: 1 Paroxetine versus other SSRIs



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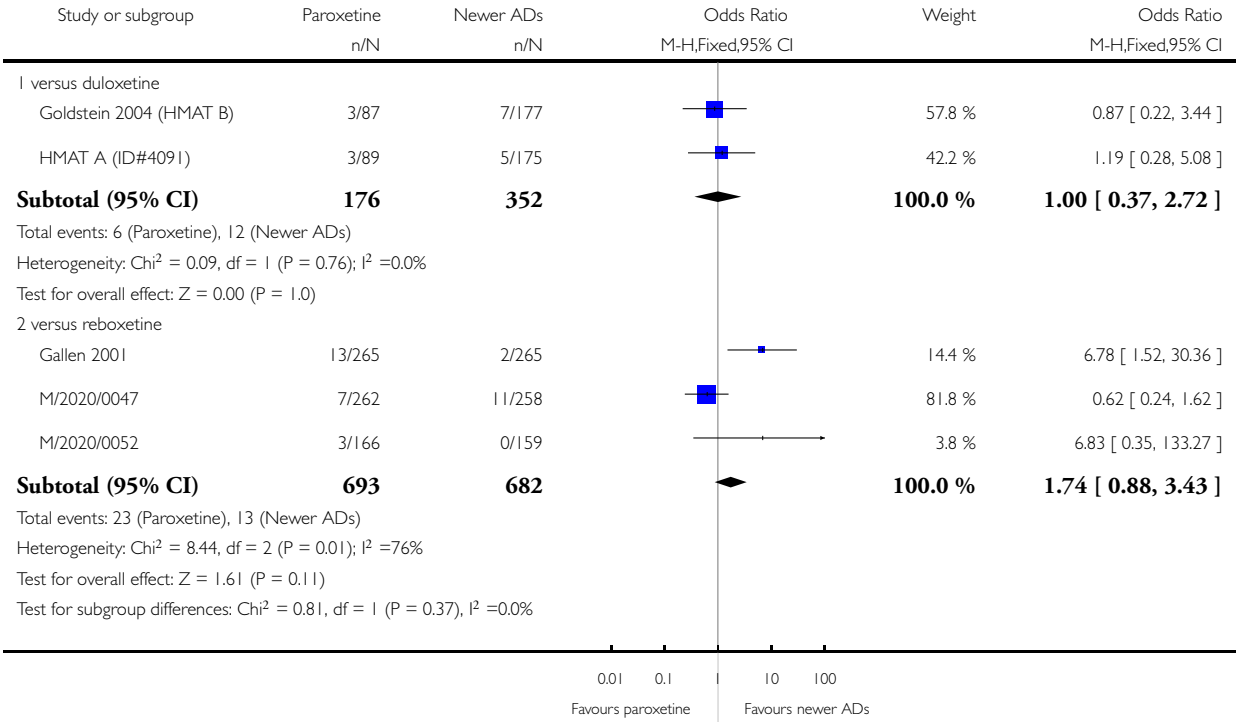
Analysis 17.2. Comparison 17 SE - Accidental injury, Outcome 2 Paroxetine versus newer or non-conventional ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 17 SE - Accidental injury

Outcome: 2 Paroxetine versus newer or non-conventional ADs



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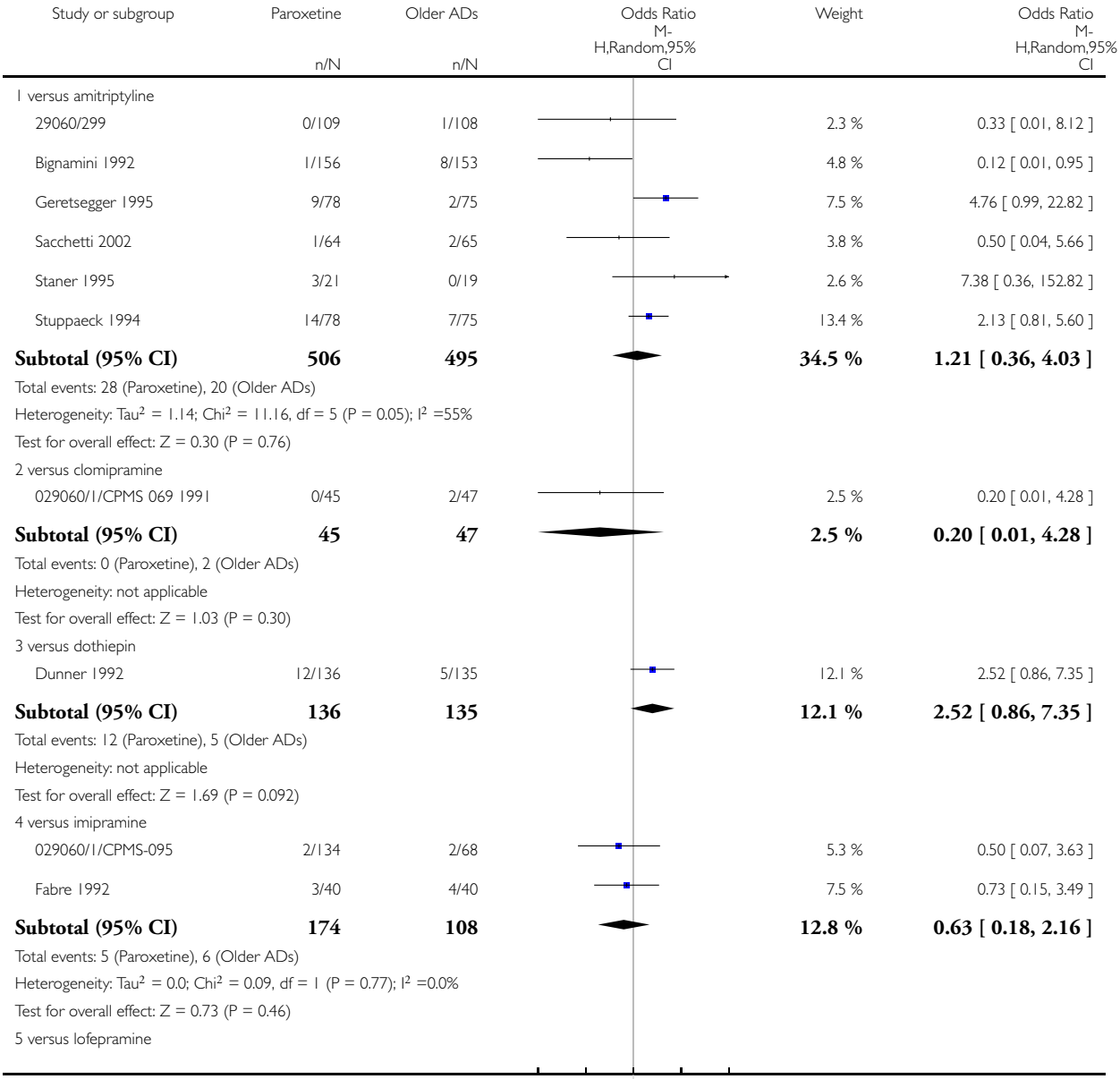
Analysis 18.1. Comparison 18 SE - Agitation/anxiety, Outcome 1 Paroxetine versus older ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 18 SE - Agitation/anxiety

Outcome: 1 Paroxetine versus older ADs



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Study or subgroup	Paroxetine n/N	Older ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
29060/103	0/57	1/49		2.3 %	0.28 [0.01, 7.06]
Subtotal (95% CI)	**57**	**49**		**2.3 %**	**0.28 [0.01, 7.06]**
Total events: 0 (Paroxetine), 1 (Older ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.77 (P = 0.44)					
6 versus maprolitine					
29060.065.BE	4/28	7/32		9.2 %	0.60 [0.15, 2.30]
Schnyder 1996	1/37	3/34		4.1 %	0.29 [0.03, 2.90]
Szegedi 1995	28/145	20/153		18.8 %	1.59 [0.85, 2.97]
Subtotal (95% CI)	**210**	**219**		**32.1 %**	**0.95 [0.38, 2.39]**
Total events: 33 (Paroxetine), 30 (Older ADs)					
Heterogeneity: Tau^2 = 0.28; Chi^2 = 3.29, df = 2 (P = 0.19); I^2 =39%					
Test for overall effect: Z = 0.10 (P = 0.92)					
7 versus mianserin					
29060III/85/038	2/30	1/29		3.7 %	2.00 [0.17, 23.34]
Subtotal (95% CI)	**30**	**29**		**3.7 %**	**2.00 [0.17, 23.34]**
Total events: 2 (Paroxetine), 1 (Older ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.55 (P = 0.58)					
Total (95% CI)	**1158**	**1082**		**100.0 %**	**1.12 [0.67, 1.86]**
Total events: 80 (Paroxetine), 65 (Older ADs)					
Heterogeneity: Tau^2 = 0.26; Chi^2 = 19.97, df = 14 (P = 0.13); I^2 =30%					
Test for overall effect: Z = 0.42 (P = 0.67)					
Test for subgroup differences: Chi^2 = 5.29, df = 6 (P = 0.51), I^2 =0.0%					

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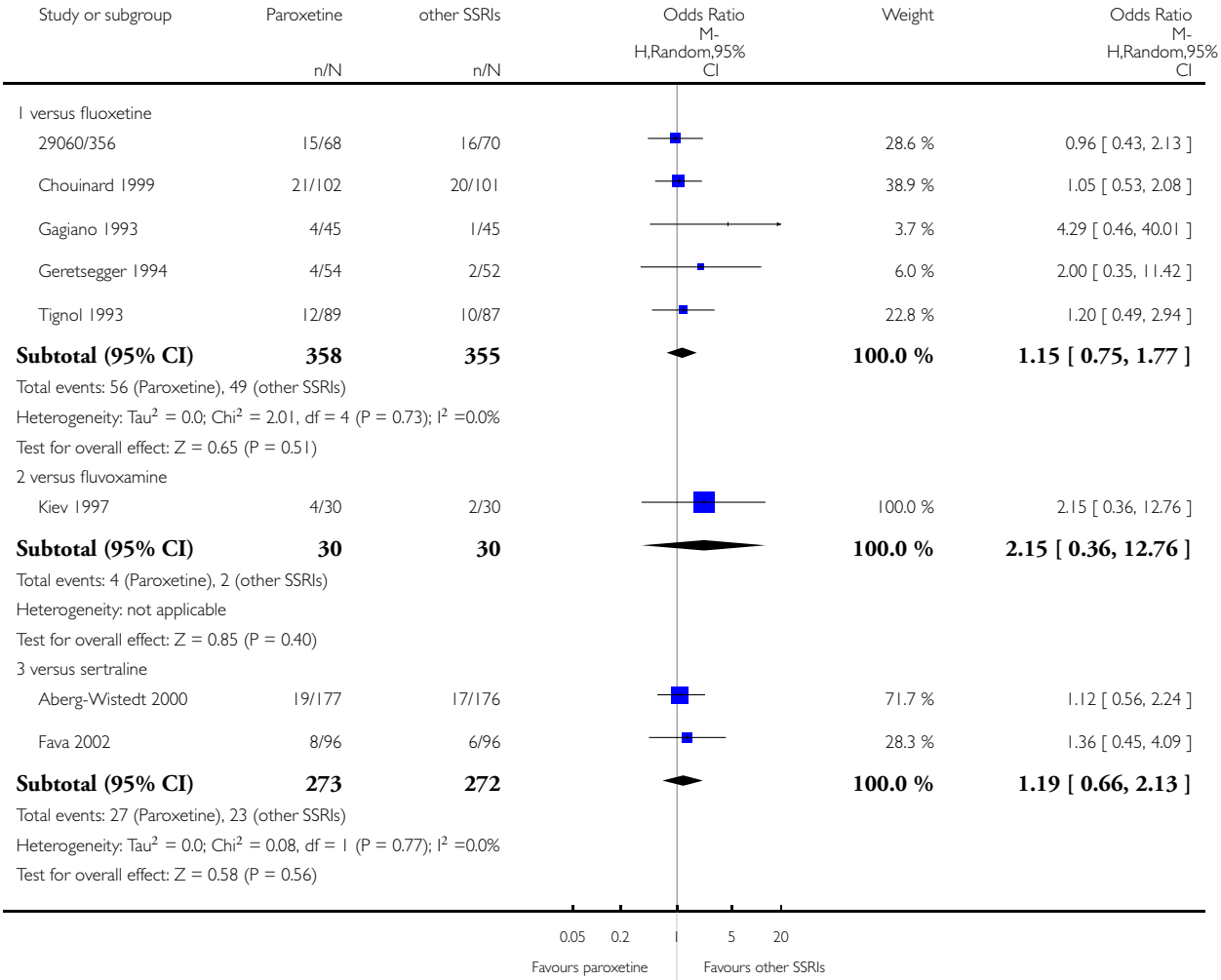
Analysis 18.2. Comparison 18 SE - Agitation/anxiety, Outcome 2 Paroxetine versus other SSRIs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 18 SE - Agitation/anxiety

Outcome: 2 Paroxetine versus other SSRIs



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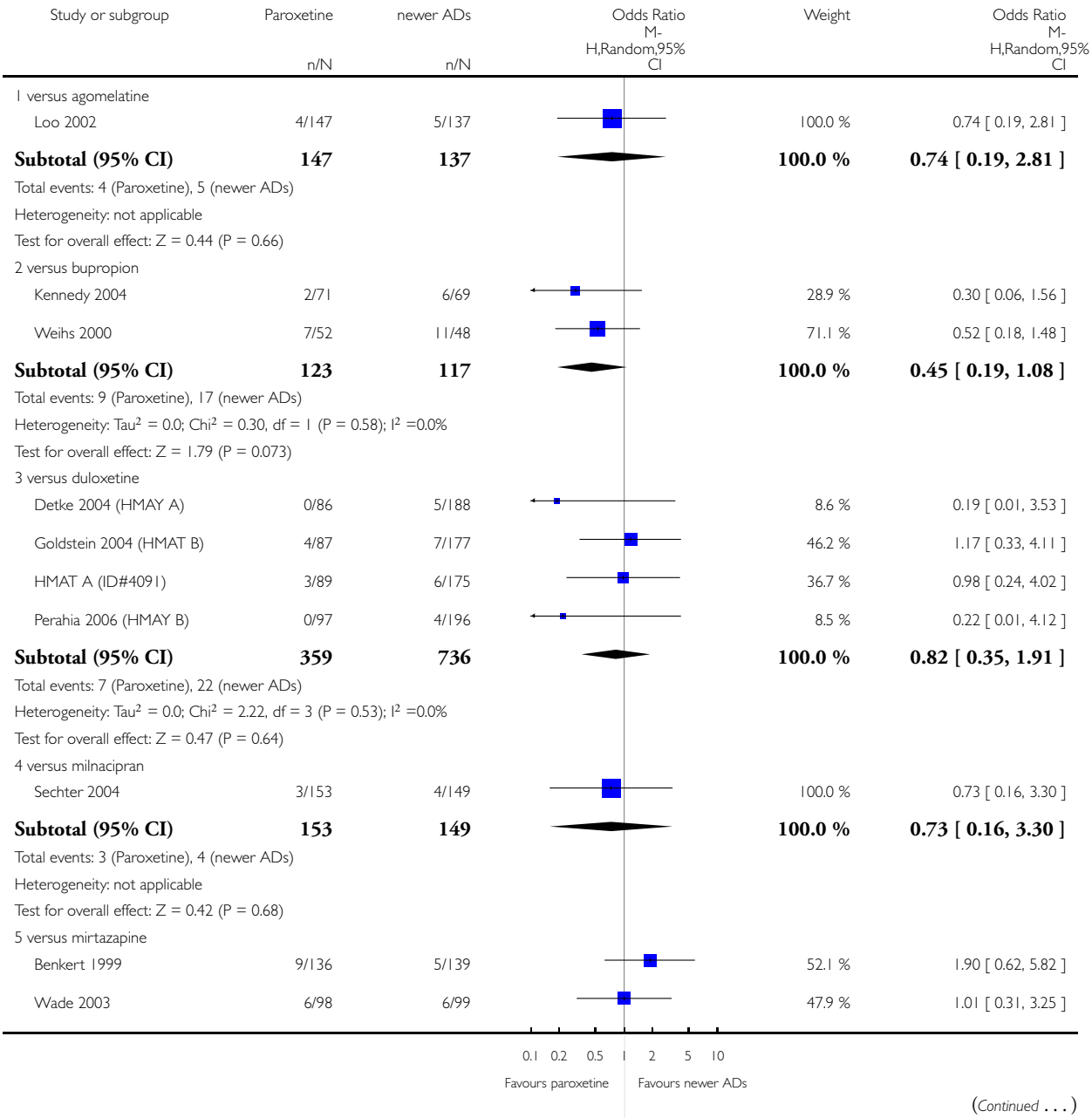
Analysis 18.3. Comparison 18 SE - Agitation/anxiety, Outcome 3 Paroxetine versus newer or non-conventional ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 18 SE - Agitation/anxiety

Outcome: 3 Paroxetine versus newer or non-conventional ADs



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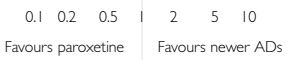
Study or subgroup	Paroxetine n/N	newer ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Subtotal (95% CI)	**234**	**238**		**100.0 %**	**1.40 [0.63, 3.15]**
Total events: 15 (Paroxetine), 11 (newer ADs)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.58$, df = 1 (P = 0.44); $I^2 = 0.0\%$					
Test for overall effect: Z = 0.82 (P = 0.41)					
6 versus reboxetine					
Gallen 2001	9/265	19/265		30.0 %	0.46 [0.20, 1.03]
M/2020/0047	19/262	22/258		46.8 %	0.84 [0.44, 1.59]
M/2020/0052	10/166	9/159		23.3 %	1.07 [0.42, 2.70]
Subtotal (95% CI)	**693**	**682**		**100.0 %**	**0.74 [0.47, 1.17]**
Total events: 38 (Paroxetine), 50 (newer ADs)					
Heterogeneity: $Tau^2 = 0.01$; $Chi^2 = 2.13$, df = 2 (P = 0.35); $I^2 = 6\%$					
Test for overall effect: Z = 1.30 (P = 0.19)					
7 versus tianeptine					
Waintraub 2002	0/139	1/138		100.0 %	0.33 [0.01, 8.14]
Subtotal (95% CI)	**139**	**138**		**100.0 %**	**0.33 [0.01, 8.14]**
Total events: 0 (Paroxetine), 1 (newer ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.68 (P = 0.50)					



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Analysis 19.1. Comparison 19 SE - Akathisia, Outcome 1 Paroxetine versus older ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 19 SE - Akathisia

Outcome: 1 Paroxetine versus older ADs

Study or subgroup	Paroxetine n/N	older ADs n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
1 versus amitriptyline					
Battegay 1985	0/11	1/10		100.0 %	0.28 [0.01, 7.57]
Subtotal (95% CI)	**11**	**10**		**100.0 %**	**0.28 [0.01, 7.57]**
Total events: 0 (Paroxetine), 1 (older ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.76 (P = 0.45)					
Test for subgroup differences: Not applicable					

Analysis 19.2. Comparison 19 SE - Akathisia, Outcome 2 Paroxetine versus newer or non-conventional ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 19 SE - Akathisia

Outcome: 2 Paroxetine versus newer or non-conventional ADs

Study or subgroup	Paroxetine n/N	newer ADs n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
1 versus reboxetine					
Gallen 2001	4/265	4/265		50.1 %	1.00 [0.25, 4.04]
M/2020/0047	7/262	4/258		49.9 %	1.74 [0.50, 6.03]
Subtotal (95% CI)	**527**	**523**		**100.0 %**	**1.37 [0.55, 3.44]**
Total events: 11 (Paroxetine), 8 (newer ADs)					
Heterogeneity: Chi^2 = 0.34, df = 1 (P = 0.56); I^2 =0.0%					
Test for overall effect: Z = 0.67 (P = 0.50)					
Test for subgroup differences: Not applicable					

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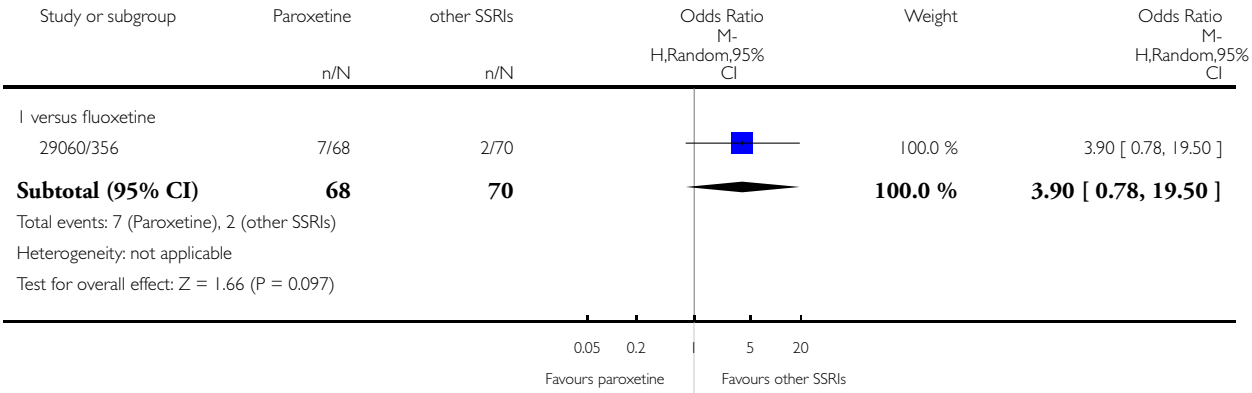
Analysis 20.1. Comparison 20 SE - Anorexia, Outcome 1 Paroxetine versus other SSRIs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 20 SE - Anorexia

Outcome: 1 Paroxetine versus other SSRIs



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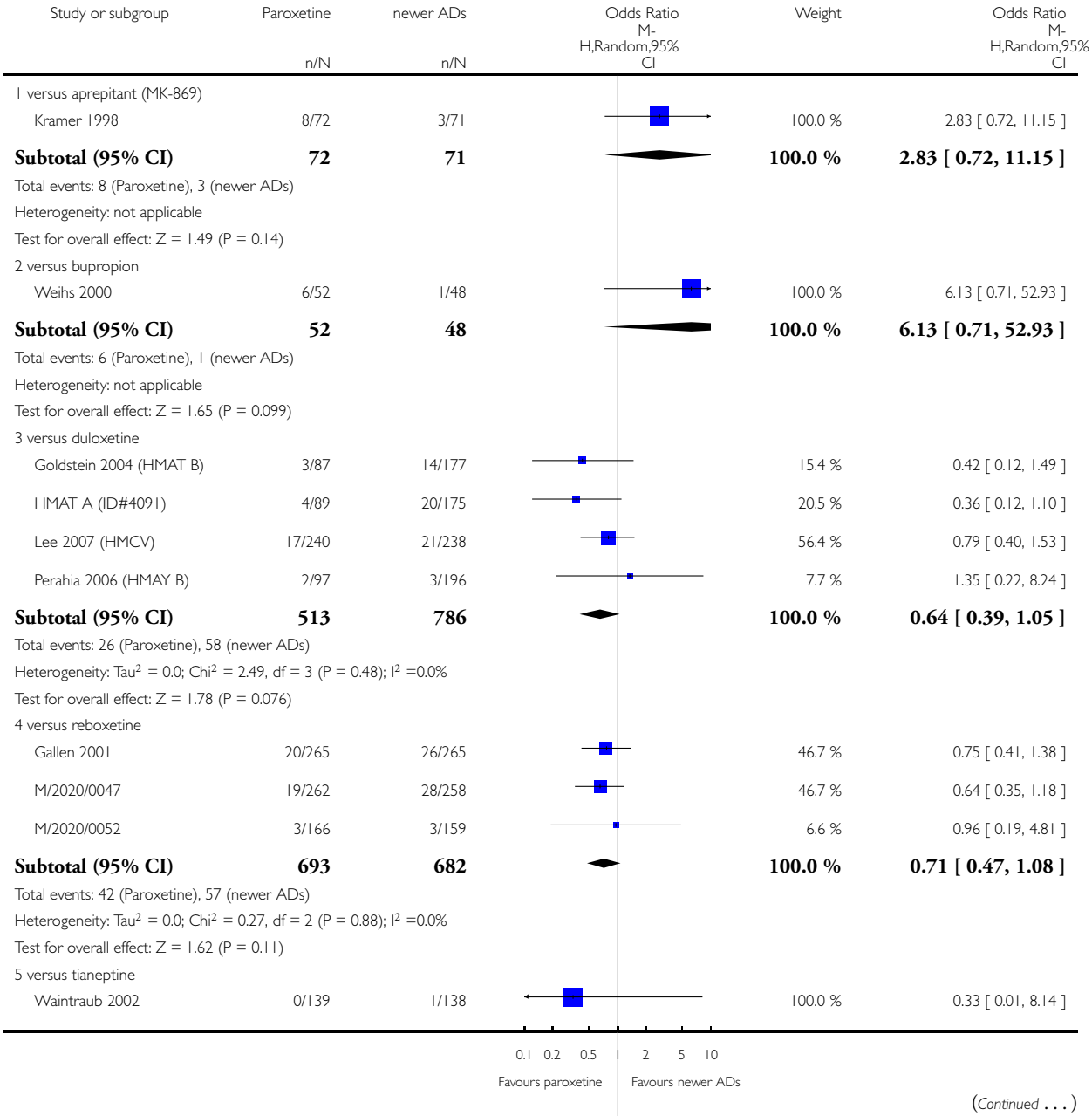
Analysis 20.2. Comparison 20 SE - Anorexia, Outcome 2 Paroxetine versus newer or non-conventional ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 20 SE - Anorexia

Outcome: 2 Paroxetine versus newer or non-conventional ADs



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Study or subgroup	Paroxetine n/N	newer ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Subtotal (95% CI)	**139**	**138**		**100.0 %**	**0.33 [0.01, 8.14]**
Total events: 0 (Paroxetine), 1 (newer ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.68 (P = 0.50)					

0.1 0.2 0.5 1 2 5 10

Favours paroxetine Favours newer ADs

Analysis 21.1. Comparison 21 SE - Anticholinergic, Outcome 1 paroxetine versus older ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 21 SE - Anticholinergic

Outcome: 1 paroxetine versus older ADs

Study or subgroup	paroxetine n/N	older ADs n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
1 versus amitriptyline					
Hutchinson 1992	1/58	2/32		23.0 %	0.26 [0.02, 3.02]
Staner 1995	4/21	10/19		77.0 %	0.21 [0.05, 0.87]
Subtotal (95% CI)	**79**	**51**		**100.0 %**	**0.22 [0.07, 0.76]**
Total events: 5 (paroxetine), 12 (older ADs)					
Heterogeneity: Chi^2 = 0.02, df = 1 (P = 0.88); I^2 =0.0%					
Test for overall effect: Z = 2.40 (P = 0.016)					
2 versus clomipramine					
Guillibert 1989	7/40	16/39		100.0 %	0.30 [0.11, 0.86]
Subtotal (95% CI)	**40**	**39**		**100.0 %**	**0.30 [0.11, 0.86]**
Total events: 7 (paroxetine), 16 (older ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 2.25 (P = 0.025)					
Test for subgroup differences: Chi^2 = 0.14, df = 1 (P = 0.70), I^2 =0.0%					

0.01 0.1 1 10 100

Favours paroxetine Favours older ADs

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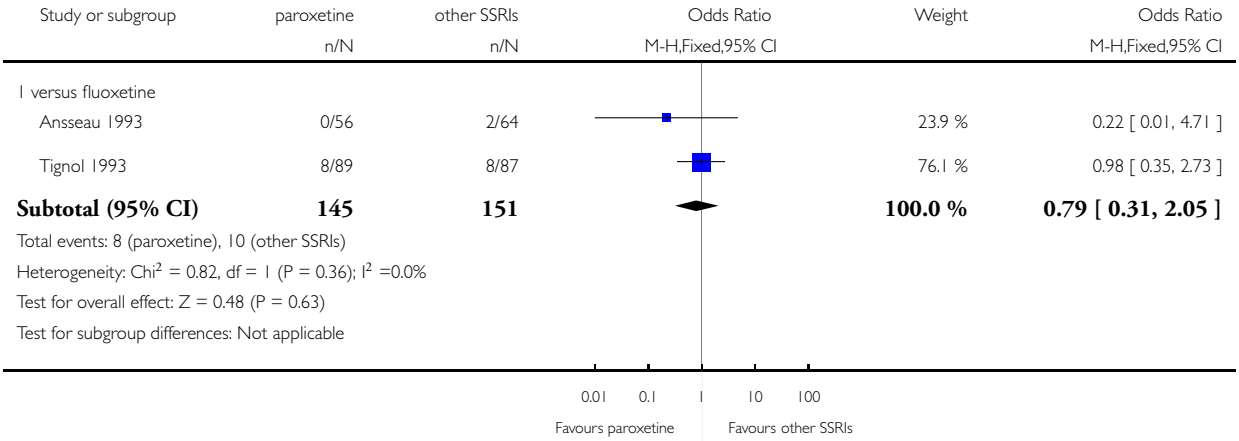
Analysis 21.2. Comparison 21 SE - Anticholinergic, Outcome 2 paroxerine versus other SSRIs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 21 SE - Anticholinergic

Outcome: 2 paroxerine versus other SSRIs



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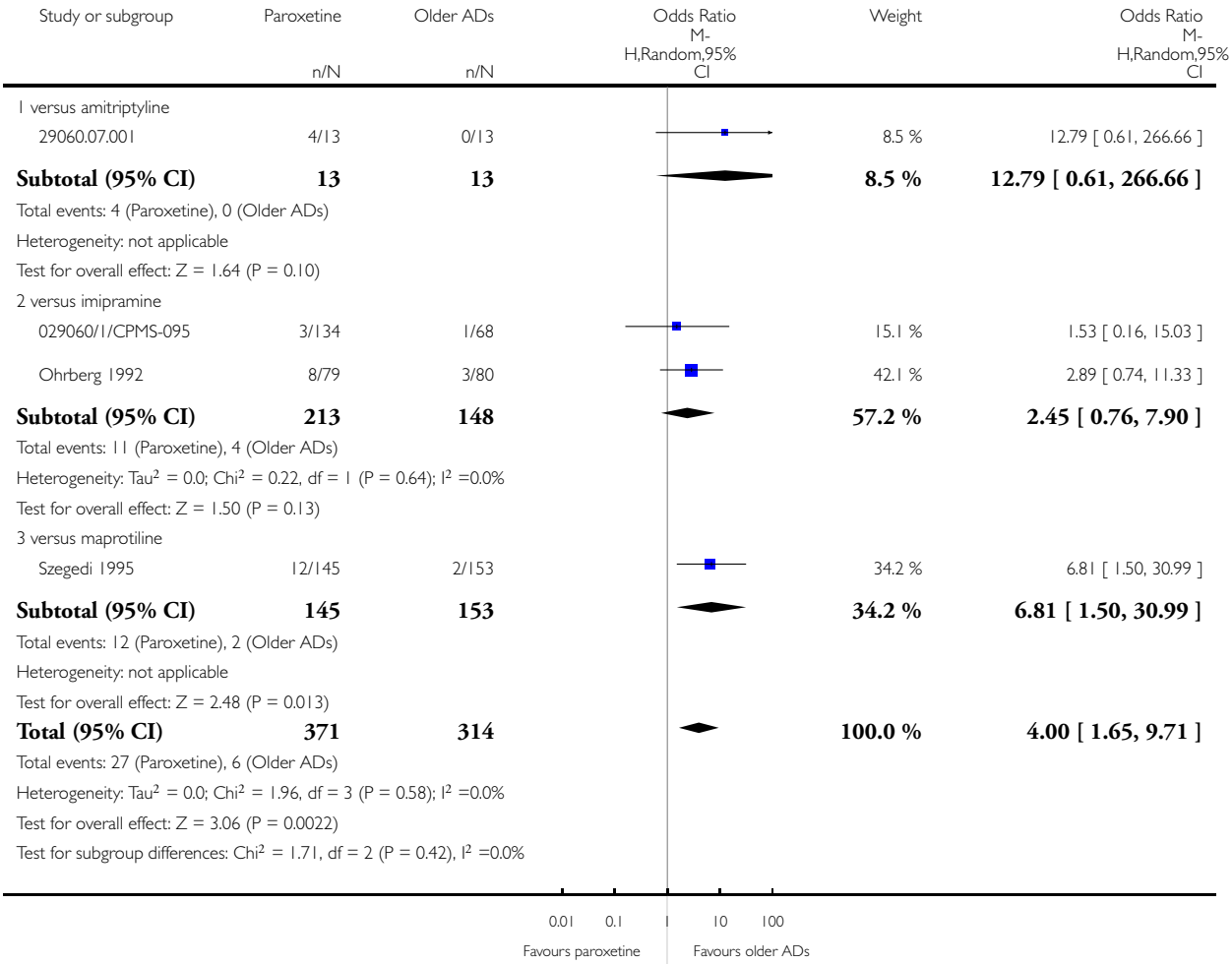
Analysis 22.1. Comparison 22 SE - Appetite decreased, Outcome 1 Paroxetine versus older ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 22 SE - Appetite decreased

Outcome: 1 Paroxetine versus older ADs



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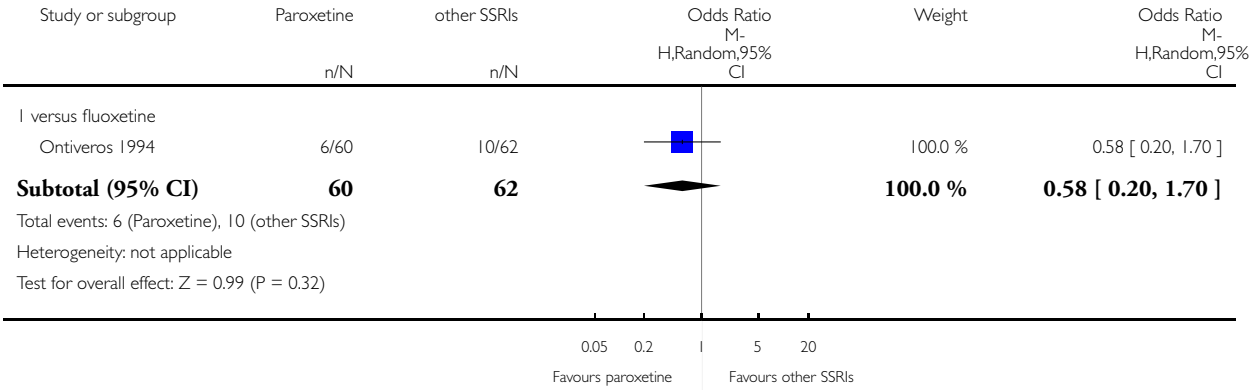
Analysis 22.2. Comparison 22 SE - Appetite decreased, Outcome 2 Paroxetine versus other SSRIs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 22 SE - Appetite decreased

Outcome: 2 Paroxetine versus other SSRIs



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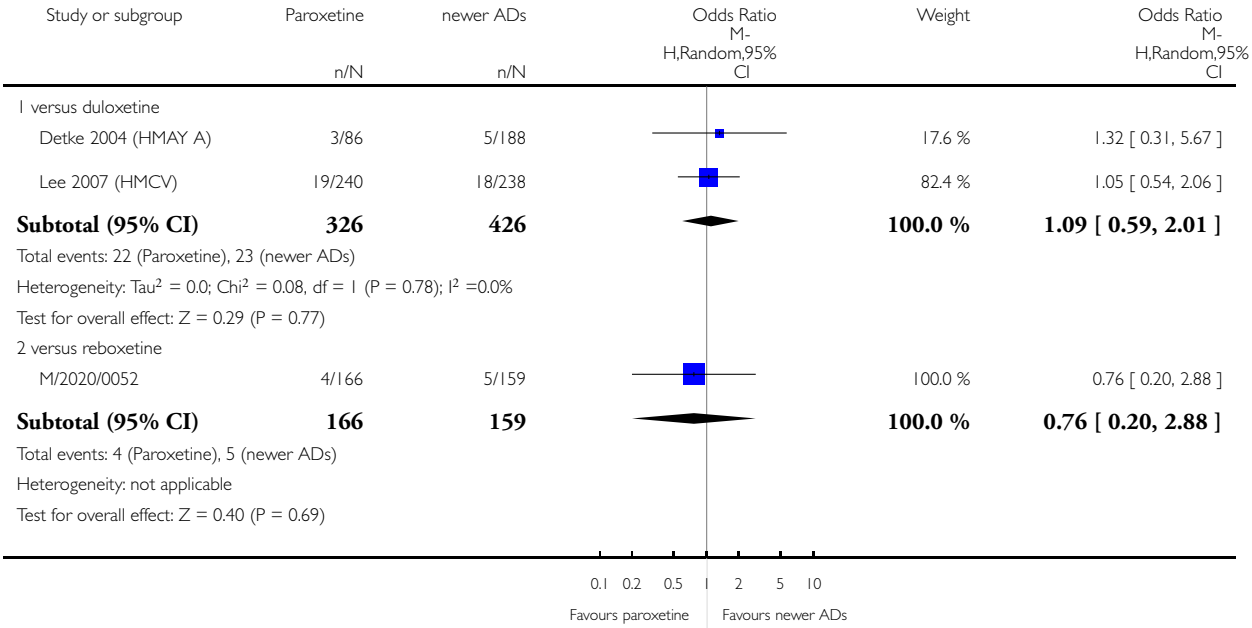
Analysis 22.3. Comparison 22 SE - Appetite decreased, Outcome 3 Paroxetine versus newer or non-conventional ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 22 SE - Appetite decreased

Outcome: 3 Paroxetine versus newer or non-conventional ADs



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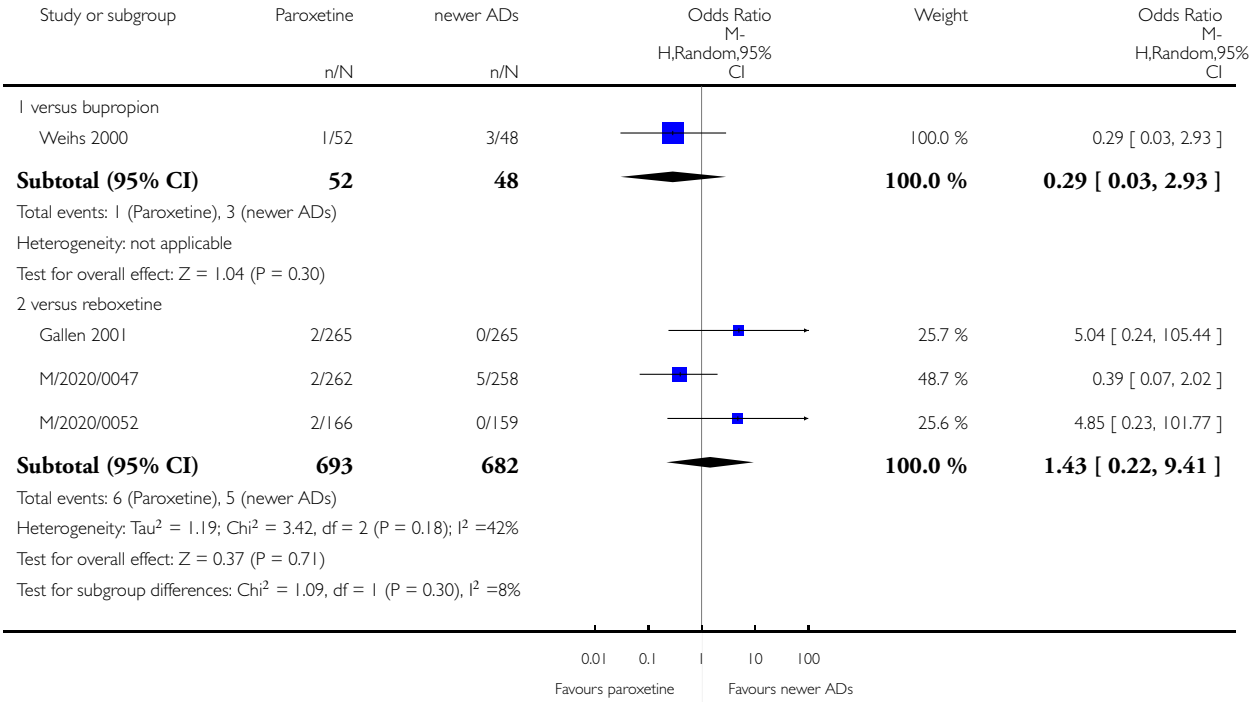
Analysis 23.1. Comparison 23 SE - Appetite increased, Outcome 1 Paroxetine versus newer or non-conventional ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 23 SE - Appetite increased

Outcome: 1 Paroxetine versus newer or non-conventional ADs



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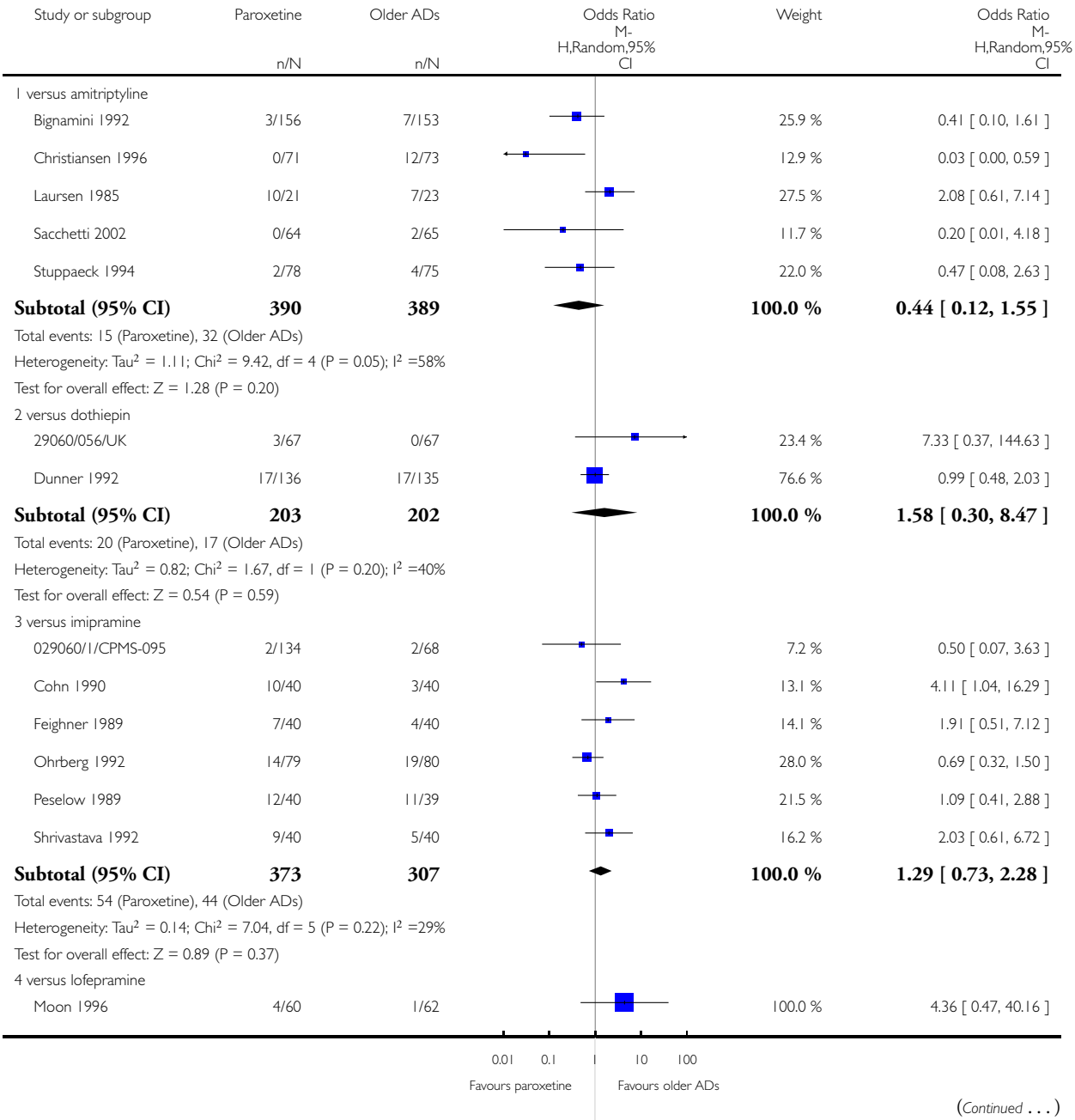
Analysis 24.1. Comparison 24 SE - Asthenia, Outcome 1 Paroxetine versus older ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 24 SE - Asthenia

Outcome: 1 Paroxetine versus older ADs



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Study or subgroup	Paroxetine n/N	Older ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Subtotal (95% CI)	**60**	**62**		**100.0 %**	**4.36 [0.47, 40.16]**
Total events: 4 (Paroxetine), 1 (Older ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.30 (P = 0.19)					
5 versus maprolitine					
29060.065.BE	3/28	3/32		6.6 %	1.16 [0.21, 6.27]
Schnyder 1996	4/37	2/34		6.0 %	1.94 [0.33, 11.34]
Szegedi 1995	54/145	71/153		87.4 %	0.69 [0.43, 1.09]
Subtotal (95% CI)	**210**	**219**		**100.0 %**	**0.76 [0.49, 1.16]**
Total events: 61 (Paroxetine), 76 (Older ADs)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 1.51$, df = 2 (P = 0.47); $I^2 = 0.0\%$					
Test for overall effect: Z = 1.27 (P = 0.20)					

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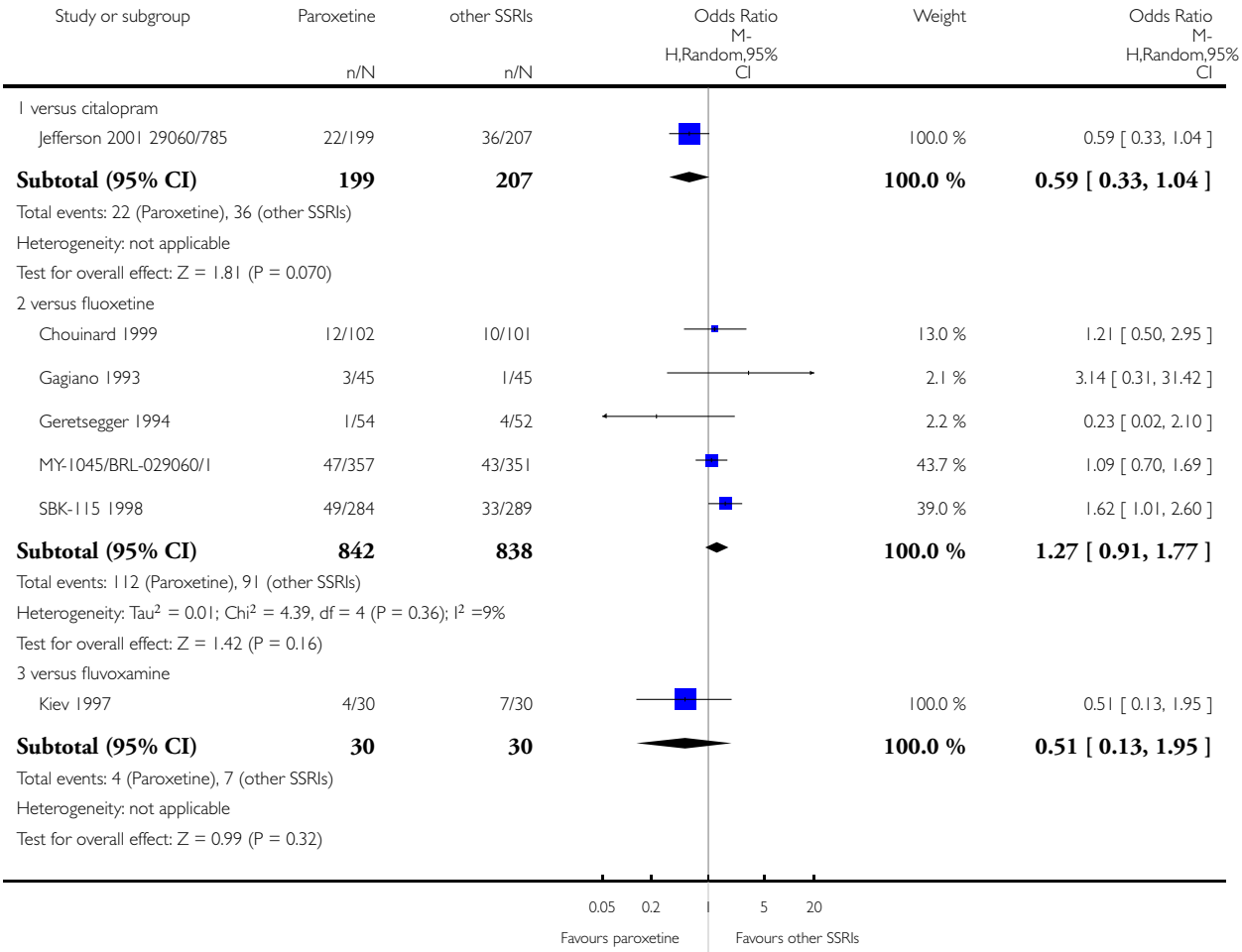
Analysis 24.2. Comparison 24 SE - Asthenia, Outcome 2 Paroxetine versus other SSRIs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 24 SE - Asthenia

Outcome: 2 Paroxetine versus other SSRIs



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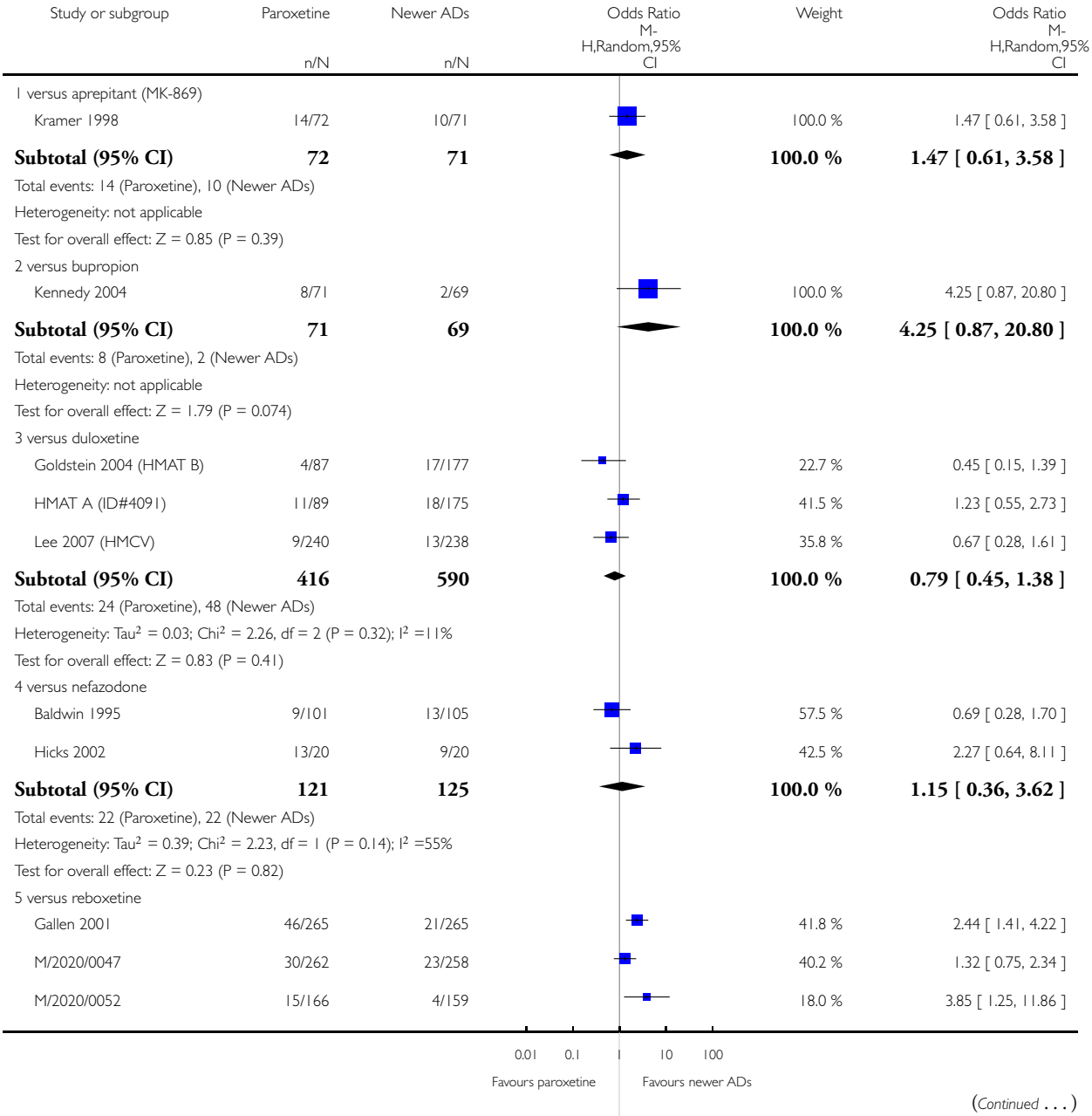
Analysis 24.3. Comparison 24 SE - Asthenia, Outcome 3 Paroxetine versus newer ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 24 SE - Asthenia

Outcome: 3 Paroxetine versus newer ADs



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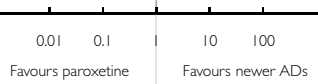
Study or subgroup	Paroxetine n/N	Newer ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Subtotal (95% CI)	**693**	**682**		**100.0 %**	**2.07 [1.19, 3.60]**
Total events: 91 (Paroxetine), 48 (Newer ADs)					
Heterogeneity: $Tau^2 = 0.11$; $Chi^2 = 3.83$, df = 2 (P = 0.15); $I^2 = 48\%$					
Test for overall effect: Z = 2.58 (P = 0.0099)					
6 versus tianeptine					
Waintraub 2002	1/139	1/138		100.0 %	0.99 [0.06, 16.03]
Subtotal (95% CI)	**139**	**138**		**100.0 %**	**0.99 [0.06, 16.03]**
Total events: 1 (Paroxetine), 1 (Newer ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.01 (P = 1.0)					
7 versus venlafaxine					
Mc Partlin 1998	6/178	13/183		100.0 %	0.46 [0.17, 1.23]
Subtotal (95% CI)	**178**	**183**		**100.0 %**	**0.46 [0.17, 1.23]**
Total events: 6 (Paroxetine), 13 (Newer ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.55 (P = 0.12)					
8 versus trazodone					
Kasper 2005	1/53	0/55		100.0 %	3.17 [0.13, 79.60]
Subtotal (95% CI)	**53**	**55**		**100.0 %**	**3.17 [0.13, 79.60]**
Total events: 1 (Paroxetine), 0 (Newer ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.70 (P = 0.48)					
Test for subgroup differences: $Chi^2 = 12.55$, df = 7 (P = 0.08), $I^2 = 44\%$					



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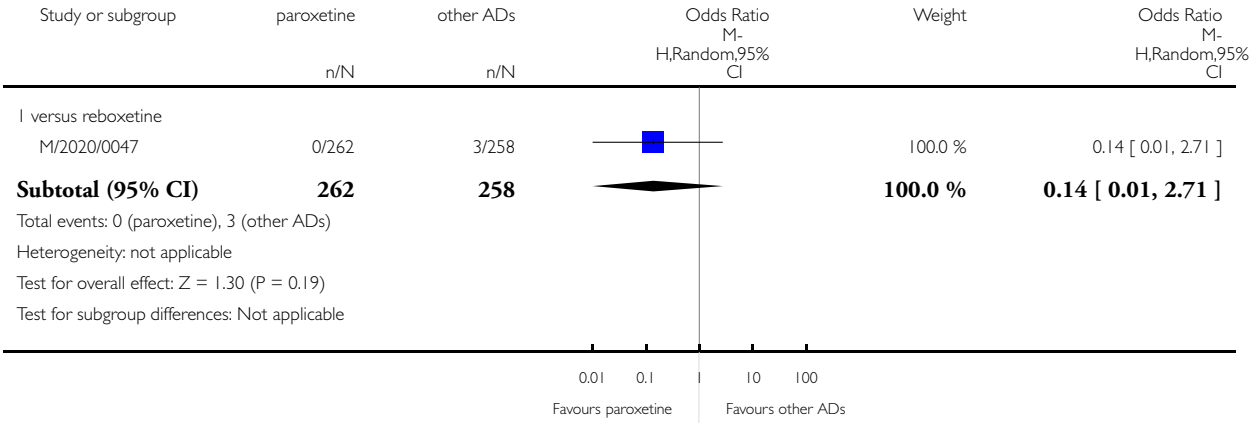
Analysis 25.1. Comparison 25 SE - Behaviour, Outcome 1 Euphoria.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 25 SE - Behaviour

Outcome: 1 Euphoria

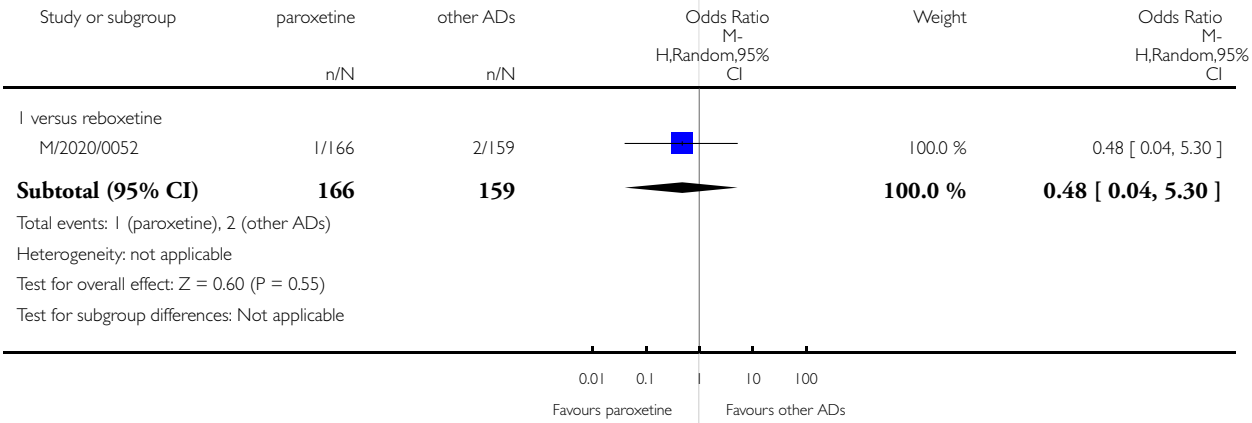


Analysis 25.2. Comparison 25 SE - Behaviour, Outcome 2 Hostility.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 25 SE - Behaviour

Outcome: 2 Hostility



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Analysis 25.3. Comparison 25 SE - Behaviour, Outcome 3 Impulsive.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 25 SE - Behaviour

Outcome: 3 Impulsive

Study or subgroup	paroxetine n/N	other ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
1 versus tianeptine					
Waintraub 2002	0/139	1/138		100.0 %	0.33 [0.01, 8.14]
Subtotal (95% CI)	**139**	**138**		**100.0 %**	**0.33 [0.01, 8.14]**
Total events: 0 (paroxetine), 1 (other ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.68 (P = 0.50)					
Test for subgroup differences: Not applicable					

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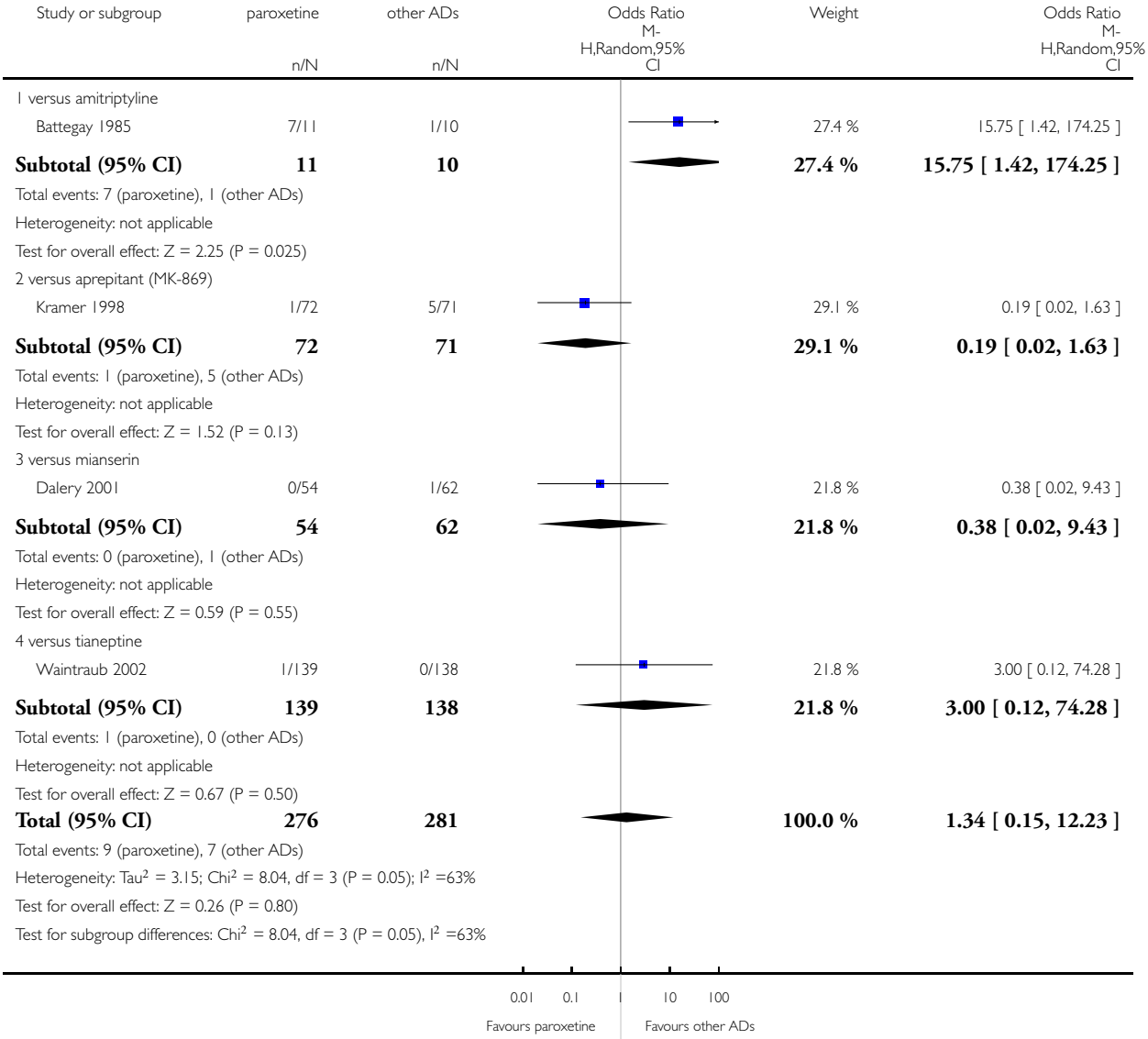
Analysis 25.4. Comparison 25 SE - Behaviour, Outcome 4 Irritability.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 25 SE - Behaviour

Outcome: 4 Irritability



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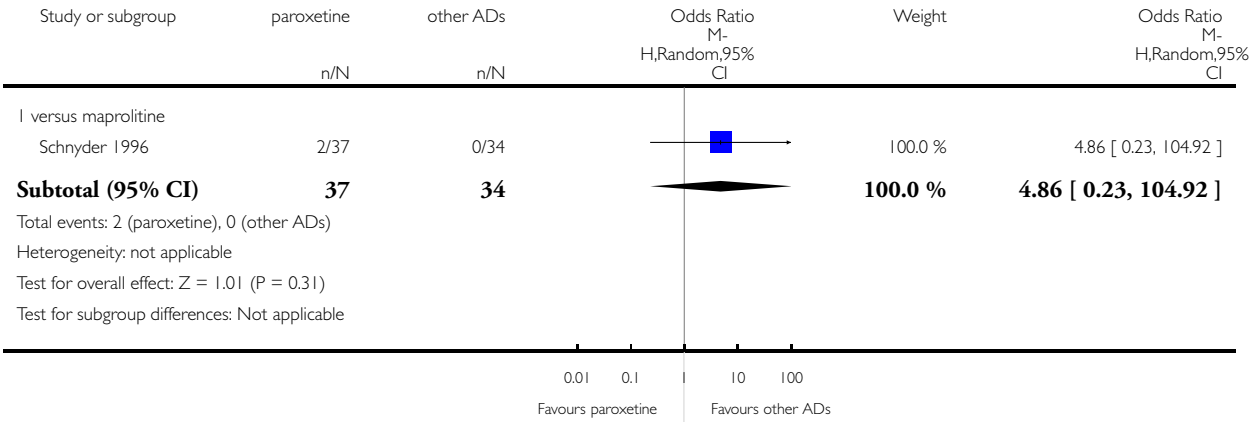
Analysis 25.5. Comparison 25 SE - Behaviour, Outcome 5 Paranoid reaction.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 25 SE - Behaviour

Outcome: 5 Paranoid reaction

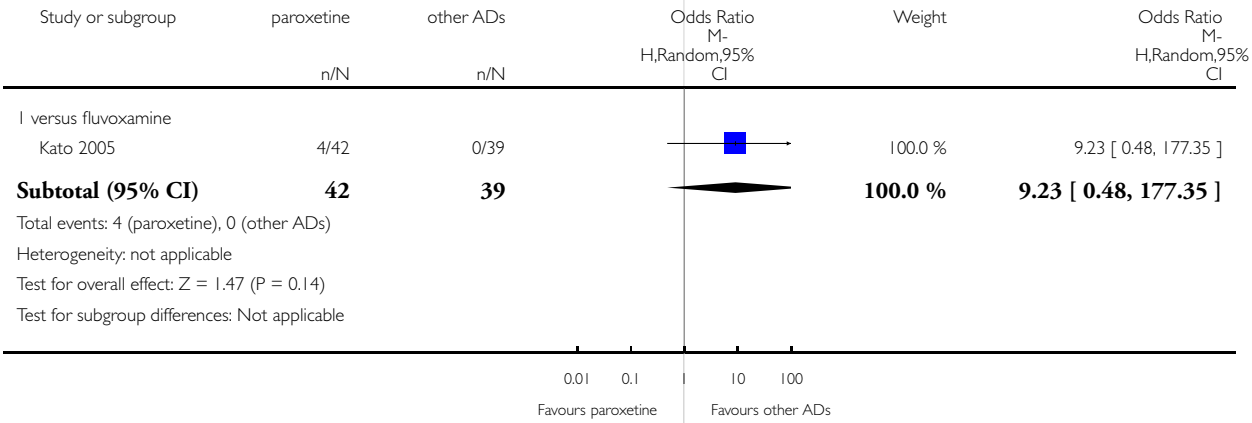


Analysis 25.6. Comparison 25 SE - Behaviour, Outcome 6 Psychotic symptoms.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 25 SE - Behaviour

Outcome: 6 Psychotic symptoms



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Analysis 26.1. Comparison 26 SE - Body as a whole, Outcome 1 Paroxetine versus older ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 26 SE - Body as a whole

Outcome: 1 Paroxetine versus older ADs

Study or subgroup	Paroxetine n/N	Older ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
1 versus amitriptyline					
29060/281 PAR	43/82	29/80		36.7 %	1.94 [1.03, 3.64]
PAR MDUK 032	11/29	8/30		17.4 %	1.68 [0.56, 5.07]
Subtotal (95% CI)	**111**	**110**		**54.1 %**	**1.87 [1.08, 3.23]**
Total events: 54 (Paroxetine), 37 (Older ADs)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.05$, df = 1 (P = 0.83); $I^2 = 0.0\%$					
Test for overall effect: Z = 2.25 (P = 0.024)					
2 versus clomipramine					
Pelicier 1993	4/41	9/42		13.9 %	0.40 [0.11, 1.41]
Subtotal (95% CI)	**41**	**42**		**13.9 %**	**0.40 [0.11, 1.41]**
Total events: 4 (Paroxetine), 9 (Older ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.43 (P = 0.15)					
3 versus mianserin					
29060/III/85/030	5/18	2/15		7.5 %	2.50 [0.41, 15.29]
Subtotal (95% CI)	**18**	**15**		**7.5 %**	**2.50 [0.41, 15.29]**
Total events: 5 (Paroxetine), 2 (Older ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.99 (P = 0.32)					
4 versus mianserin					
29060/III/83/022	3/18	5/18		9.2 %	0.52 [0.10, 2.61]
29060/III/85/030	5/18	2/15		7.5 %	2.50 [0.41, 15.29]
Dorman 1992	4/29	2/28		7.7 %	2.08 [0.35, 12.38]
Subtotal (95% CI)	**65**	**61**		**24.5 %**	**1.29 [0.48, 3.52]**
Total events: 12 (Paroxetine), 9 (Older ADs)					
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 2.01$, df = 2 (P = 0.37); $I^2 = 0\%$					
Test for overall effect: Z = 0.50 (P = 0.61)					

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Study or subgroup	Paroxetine n/N	Older ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Total (95% CI)	**235**	**228**		**100.0 %**	**1.40 [0.83, 2.36]**
Total events: 75 (Paroxetine), 57 (Older ADs)					
Heterogeneity: $Tau^2 = 0.09$; $Chi^2 = 7.31$, df = 6 (P = 0.29); $I^2 = 18\%$					
Test for overall effect: Z = 1.27 (P = 0.20)					
Test for subgroup differences: $Chi^2 = 5.25$, df = 3 (P = 0.15), $I^2 = 43\%$					

Analysis 26.2. Comparison 26 SE - Body as a whole, Outcome 2 Paroxetine versus other SSRIs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 26 SE - Body as a whole

Outcome: 2 Paroxetine versus other SSRIs

Study or subgroup	Paroxetine n/N	other SSRIs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
1 versus fluoxetine					
Cassano 2002	14/123	9/119		100.0 %	1.57 [0.65, 3.78]
Subtotal (95% CI)	**123**	**119**		**100.0 %**	**1.57 [0.65, 3.78]**
Total events: 14 (Paroxetine), 9 (other SSRIs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.01 (P = 0.31)					
Test for subgroup differences: Not applicable					

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Analysis 27.1. Comparison 27 SE - Bronchitis, Outcome 1 Paroxetine versus other SSRIs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 27 SE - Bronchitis

Outcome: 1 Paroxetine versus other SSRIs

Study or subgroup	Paroxetine n/N	other SSRIs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
1 versus fluoxetine					
29060/356	1/68	5/70		100.0 %	0.19 [0.02, 1.71]
Subtotal (95% CI)	**68**	**70**		**100.0 %**	**0.19 [0.02, 1.71]**
Total events: 1 (Paroxetine), 5 (other SSRIs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.48 (P = 0.14)					

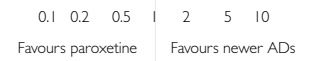
Analysis 27.2. Comparison 27 SE - Bronchitis, Outcome 2 Paroxetine versus newer or non-conventional ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 27 SE - Bronchitis

Outcome: 2 Paroxetine versus newer or non-conventional ADs

Study or subgroup	Paroxetine n/N	newer ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
1 versus reboxetine					
M/2020/0047	0/262	1/258		36.1 %	0.33 [0.01, 8.06]
M/2020/0052	1/166	2/159		63.9 %	0.48 [0.04, 5.30]
Subtotal (95% CI)	**428**	**417**		**100.0 %**	**0.42 [0.06, 2.85]**
Total events: 1 (Paroxetine), 3 (newer ADs)					
Heterogeneity: Tau^2 = 0.0; Chi^2 = 0.03, df = 1 (P = 0.85); I^2 =0.0%					
Test for overall effect: Z = 0.89 (P = 0.37)					



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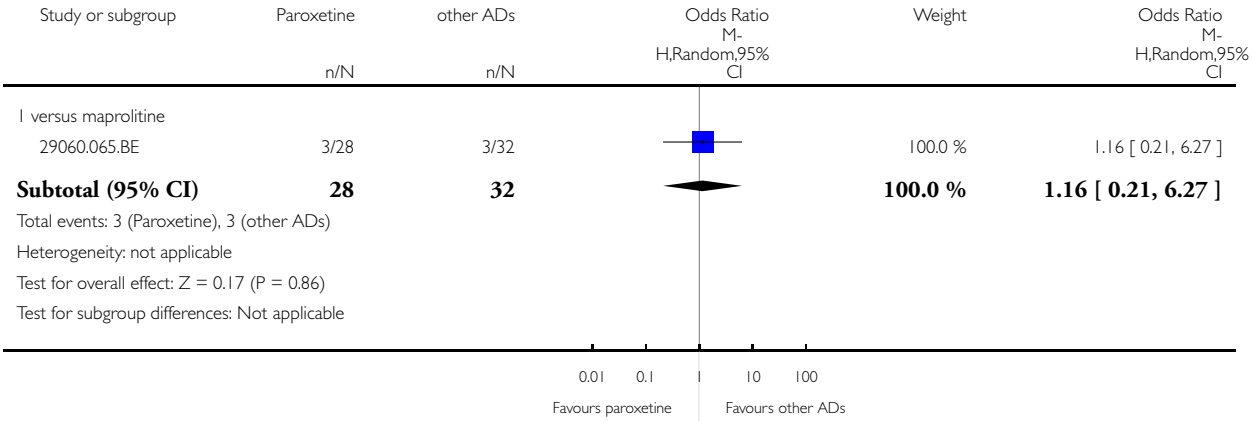
Analysis 28.1. Comparison 28 SE - Cardiovascular system, Outcome 1 Syncope.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 28 SE - Cardiovascular system

Outcome: 1 Syncope



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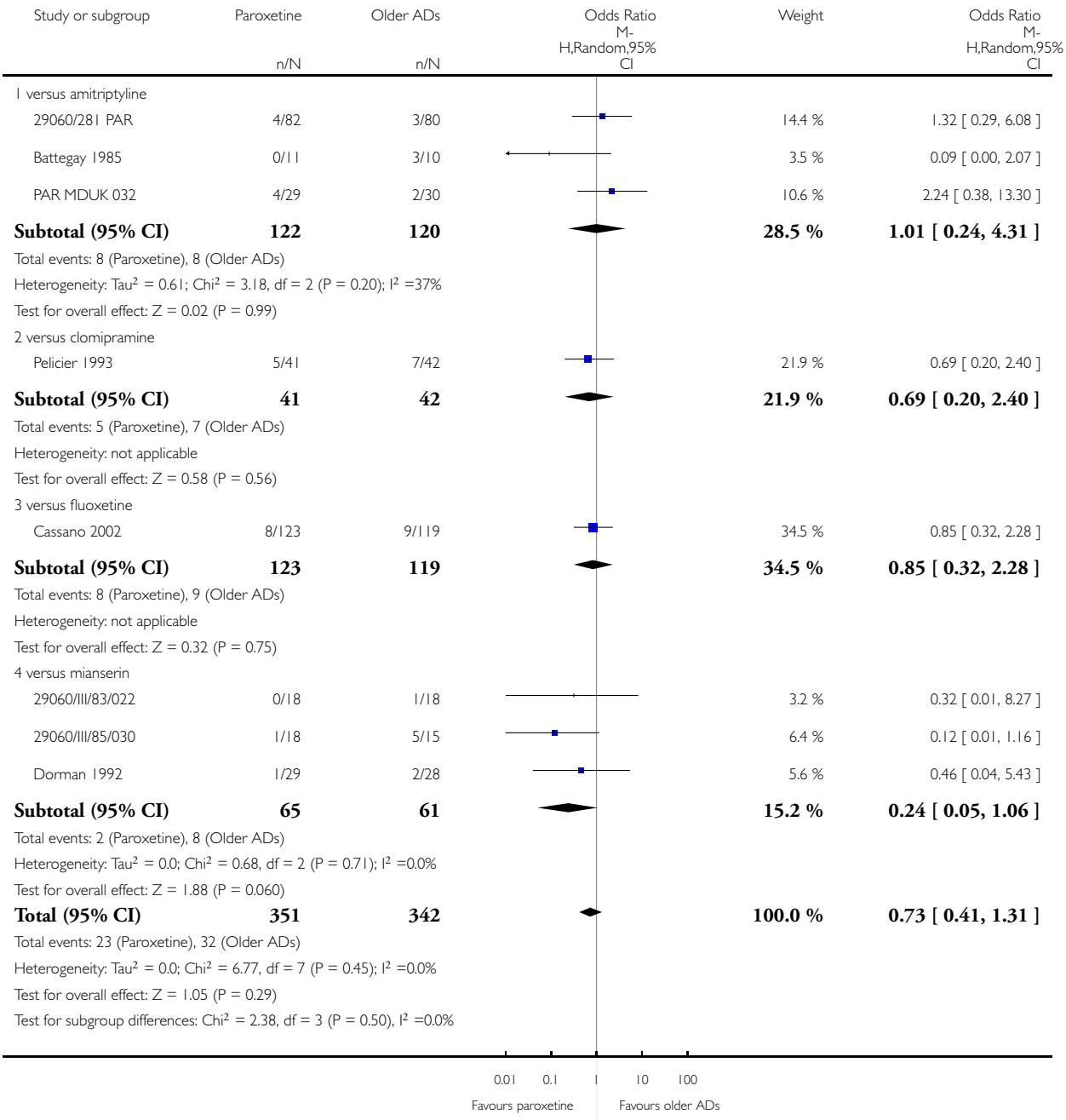
Analysis 28.2. Comparison 28 SE - Cardiovascular system, Outcome 2 NOS.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 28 SE - Cardiovascular system

Outcome: 2 NOS



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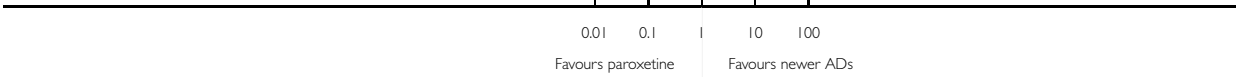
Analysis 29.1. Comparison 29 SE - Chills, Outcome 1 Paroxetine versus newer or non-conventional ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 29 SE - Chills

Outcome: 1 Paroxetine versus newer or non-conventional ADs

Study or subgroup	Paroxetine n/N	newer ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
1 versus reboxetine					
Gallen 2001	2/265	14/265		20.8 %	0.14 [0.03, 0.61]
M/2020/0047	7/262	14/258		49.1 %	0.48 [0.19, 1.21]
M/2020/0052	4/166	8/159		30.1 %	0.47 [0.14, 1.58]
Subtotal (95% CI)	**693**	**682**		**100.0 %**	**0.37 [0.18, 0.74]**
Total events: 13 (Paroxetine), 36 (newer ADs)					
Heterogeneity: $Tau^2 = 0.04$; $Chi^2 = 2.21$, df = 2 (P = 0.33); $I^2 = 10\%$					
Test for overall effect: Z = 2.81 (P = 0.0050)					
Test for subgroup differences: Not applicable					



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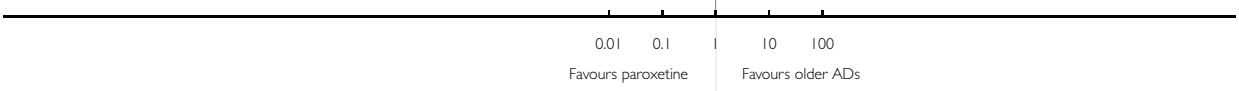
Analysis 30.1. Comparison 30 SE - Confusion, Outcome 1 Paroxetine versus older ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 30 SE - Confusion

Outcome: 1 Paroxetine versus older ADs

Study or subgroup	Paroxetine n/N	Older ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
1 versus amitriptyline					
Geretsegger 1995	2/78	2/75		25.3 %	0.96 [0.13, 7.00]
Subtotal (95% CI)	**78**	**75**		**25.3 %**	**0.96 [0.13, 7.00]**
Total events: 2 (Paroxetine), 2 (Older ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.04 (P = 0.97)					
2 versus clomipramine					
029060/1/CPMS 069 1991	2/45	2/47		24.8 %	1.05 [0.14, 7.76]
Subtotal (95% CI)	**45**	**47**		**24.8 %**	**1.05 [0.14, 7.76]**
Total events: 2 (Paroxetine), 2 (Older ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.04 (P = 0.96)					
3 versus dothiepin					
Dunner 1992	1/136	7/135		22.4 %	0.14 [0.02, 1.12]
Subtotal (95% CI)	**136**	**135**		**22.4 %**	**0.14 [0.02, 1.12]**
Total events: 1 (Paroxetine), 7 (Older ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.86 (P = 0.063)					
4 versus lofepramine					
29060/103	0/57	2/49		10.6 %	0.17 [0.01, 3.53]
Subtotal (95% CI)	**57**	**49**		**10.6 %**	**0.17 [0.01, 3.53]**
Total events: 0 (Paroxetine), 2 (Older ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.15 (P = 0.25)					
5 versus mianserin					
Dalery 2001	1/54	2/62		16.9 %	0.57 [0.05, 6.42]
Subtotal (95% CI)	**54**	**62**		**16.9 %**	**0.57 [0.05, 6.42]**
Total events: 1 (Paroxetine), 2 (Older ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.46 (P = 0.65)					
Total (95% CI)	**370**	**368**		**100.0 %**	**0.48 [0.18, 1.30]**
Total events: 6 (Paroxetine), 15 (Older ADs)					
Heterogeneity: Tau² = 0.0; Chi² = 3.01, df = 4 (P = 0.56); I² =0.0%					
Test for overall effect: Z = 1.44 (P = 0.15)					
Test for subgroup differences: Chi² = 2.92, df = 4 (P = 0.57), I² =0.0%					



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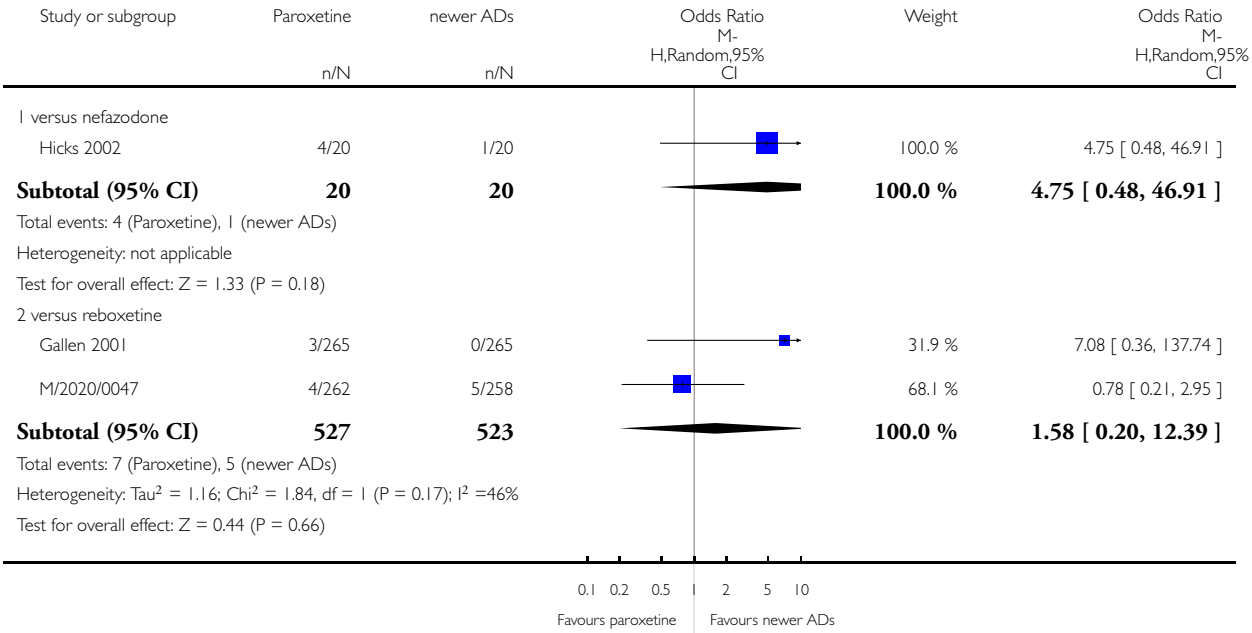
Analysis 30.2. Comparison 30 SE - Confusion, Outcome 2 Paroxetine versus newer or non-conventional ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 30 SE - Confusion

Outcome: 2 Paroxetine versus newer or non-conventional ADs



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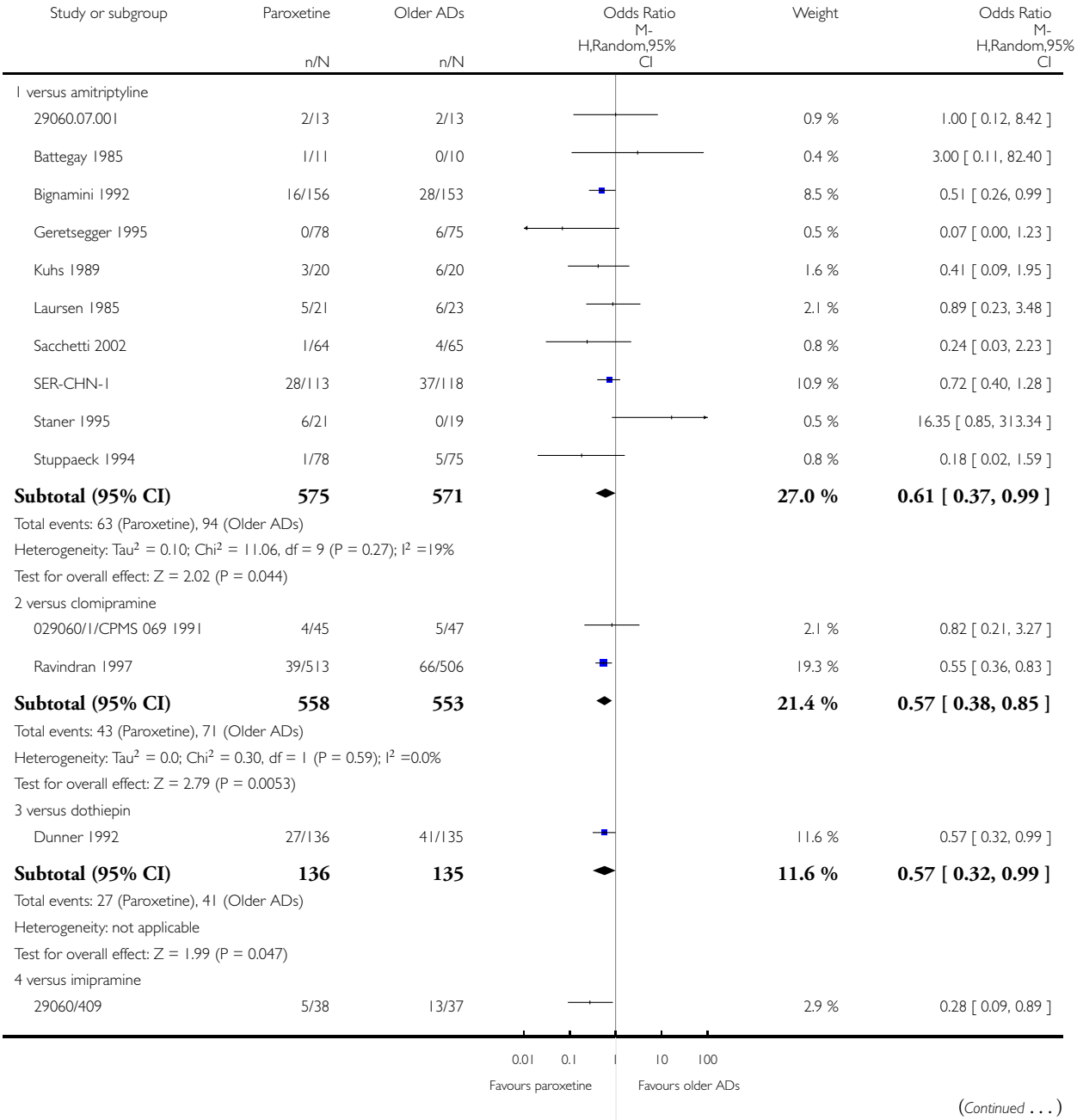
Analysis 31.1. Comparison 31 SE - Constipation, Outcome 1 Paroxetine versus older ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 31 SE - Constipation

Outcome: 1 Paroxetine versus older ADs



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Study or subgroup	Paroxetine n/N	Older ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Cohn 1990	3/40	14/40		2.2 %	0.15 [0.04, 0.58]
Fabre 1992	8/40	8/40		3.2 %	1.00 [0.33, 2.99]
Feighner 1989	5/40	15/40		3.0 %	0.24 [0.08, 0.74]
Ohrberg 1992	9/79	16/80		4.9 %	0.51 [0.21, 1.25]
Peselow 1989	10/40	21/39		4.2 %	0.29 [0.11, 0.74]
Shrivastava 1992	7/40	9/40		3.2 %	0.73 [0.24, 2.20]
Subtotal (95% CI)	**317**	**316**		**23.7 %**	**0.40 [0.25, 0.63]**
Total events: 47 (Paroxetine), 96 (Older ADs)					
Heterogeneity: $Tau^2 = 0.09$; $Chi^2 = 7.83$, df = 6 (P = 0.25); $I^2 = 23\%$					
Test for overall effect: Z = 3.91 (P = 0.000094)					
5 versus lofepramine					
29060/103	5/57	8/49		2.8 %	0.49 [0.15, 1.62]
Moon 1996	3/60	6/62		1.9 %	0.49 [0.12, 2.06]
Subtotal (95% CI)	**117**	**111**		**4.7 %**	**0.49 [0.20, 1.23]**
Total events: 8 (Paroxetine), 14 (Older ADs)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.00$, df = 1 (P = 1.00); $I^2 = 0.0\%$					
Test for overall effect: Z = 1.52 (P = 0.13)					
6 versus maprolitine					
29060.065.BE	6/28	14/32		3.0 %	0.35 [0.11, 1.10]
Schnyder 1996	1/37	1/34		0.5 %	0.92 [0.06, 15.25]
Szegedi 1995	12/145	38/153		7.7 %	0.27 [0.14, 0.55]
Subtotal (95% CI)	**210**	**219**		**11.2 %**	**0.31 [0.17, 0.55]**
Total events: 19 (Paroxetine), 53 (Older ADs)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.74$, df = 2 (P = 0.69); $I^2 = 0.0\%$					
Test for overall effect: Z = 3.99 (P = 0.000067)					
7 versus mianserin					
Dalery 2001	0/54	2/62		0.4 %	0.22 [0.01, 4.73]
Subtotal (95% CI)	**54**	**62**		**0.4 %**	**0.22 [0.01, 4.73]**
Total events: 0 (Paroxetine), 2 (Older ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.96 (P = 0.33)					
Total (95% CI)	**1967**	**1967**		**100.0 %**	**0.49 [0.40, 0.60]**
Total events: 207 (Paroxetine), 371 (Older ADs)					
Heterogeneity: $Tau^2 = 0.01$; $Chi^2 = 25.83$, df = 25 (P = 0.42); $I^2 = 3\%$					
Test for overall effect: Z = 6.93 (P < 0.00001)					
Test for subgroup differences: $Chi^2 = 5.09$, df = 6 (P = 0.53), $I^2 = 0.0\%$					

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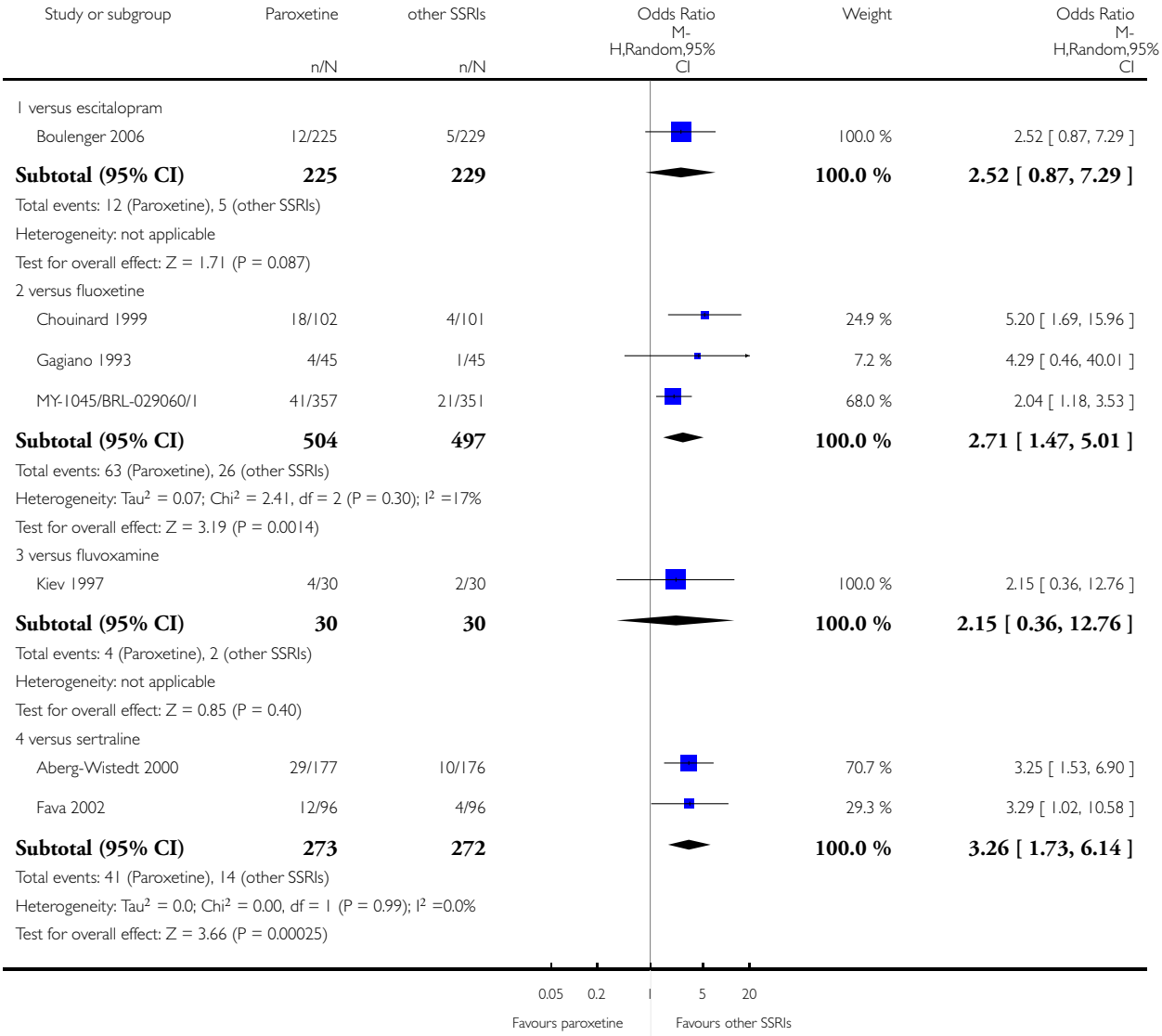
Analysis 31.2. Comparison 31 SE - Constipation, Outcome 2 Paroxetine versus other SSRIs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 31 SE - Constipation

Outcome: 2 Paroxetine versus other SSRIs



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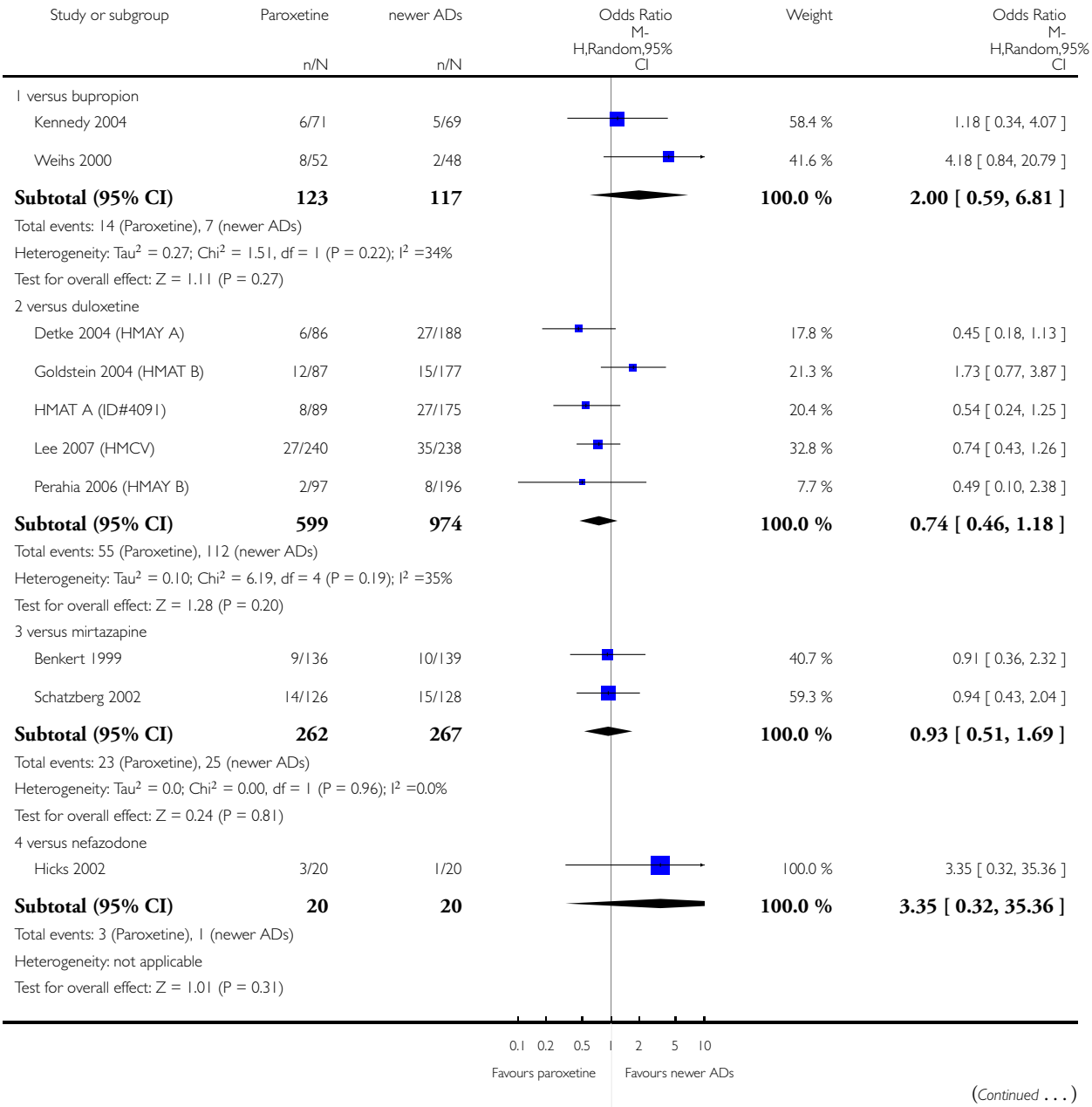
Analysis 31.3. Comparison 31 SE - Constipation, Outcome 3 Paroxetine versus newer or non-conventional ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 31 SE - Constipation

Outcome: 3 Paroxetine versus newer or non-conventional ADs



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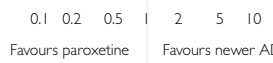
Study or subgroup	Paroxetine n/N	newer ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
5 versus reboxetine					
Gallen 2001	38/265	66/265		41.8 %	0.50 [0.32, 0.79]
M/2020/0047	31/262	65/258		37.2 %	0.40 [0.25, 0.64]
M/2020/0052	19/166	29/159		20.9 %	0.58 [0.31, 1.08]
Subtotal (95% CI)	**693**	**682**		**100.0 %**	**0.48 [0.36, 0.63]**
Total events: 88 (Paroxetine), 160 (newer ADs)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 1.00$, df = 2 (P = 0.61); $I^2 = 0.0\%$					
Test for overall effect: Z = 5.09 (P < 0.00001)					
6 versus tianeptine					
Waintraub 2002	3/139	0/138		100.0 %	7.10 [0.36, 138.80]
Subtotal (95% CI)	**139**	**138**		**100.0 %**	**7.10 [0.36, 138.80]**
Total events: 3 (Paroxetine), 0 (newer ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.29 (P = 0.20)					
7 versus venlafaxine					
Hwang 2004	9/53	4/52		42.6 %	2.45 [0.71, 8.54]
Mc Partlin 1998	12/178	18/183		57.4 %	0.66 [0.31, 1.42]
Subtotal (95% CI)	**231**	**235**		**100.0 %**	**1.16 [0.33, 4.12]**
Total events: 21 (Paroxetine), 22 (newer ADs)					
Heterogeneity: $Tau^2 = 0.58$; $Chi^2 = 3.09$, df = 1 (P = 0.08); $I^2 = 68\%$					
Test for overall effect: Z = 0.23 (P = 0.82)					



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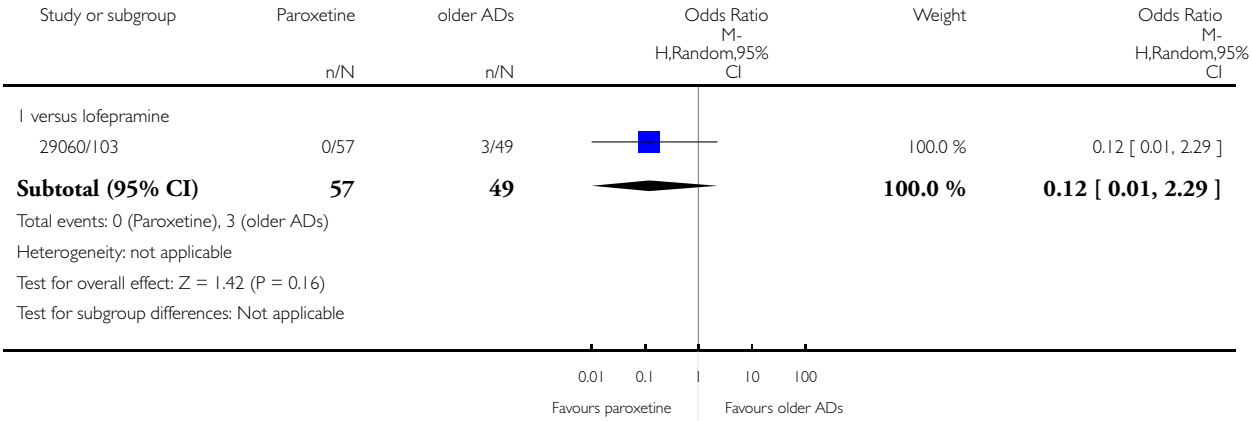
Analysis 32.1. Comparison 32 SE - Cough, Outcome 1 Paroxetine versus older ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 32 SE - Cough

Outcome: 1 Paroxetine versus older ADs



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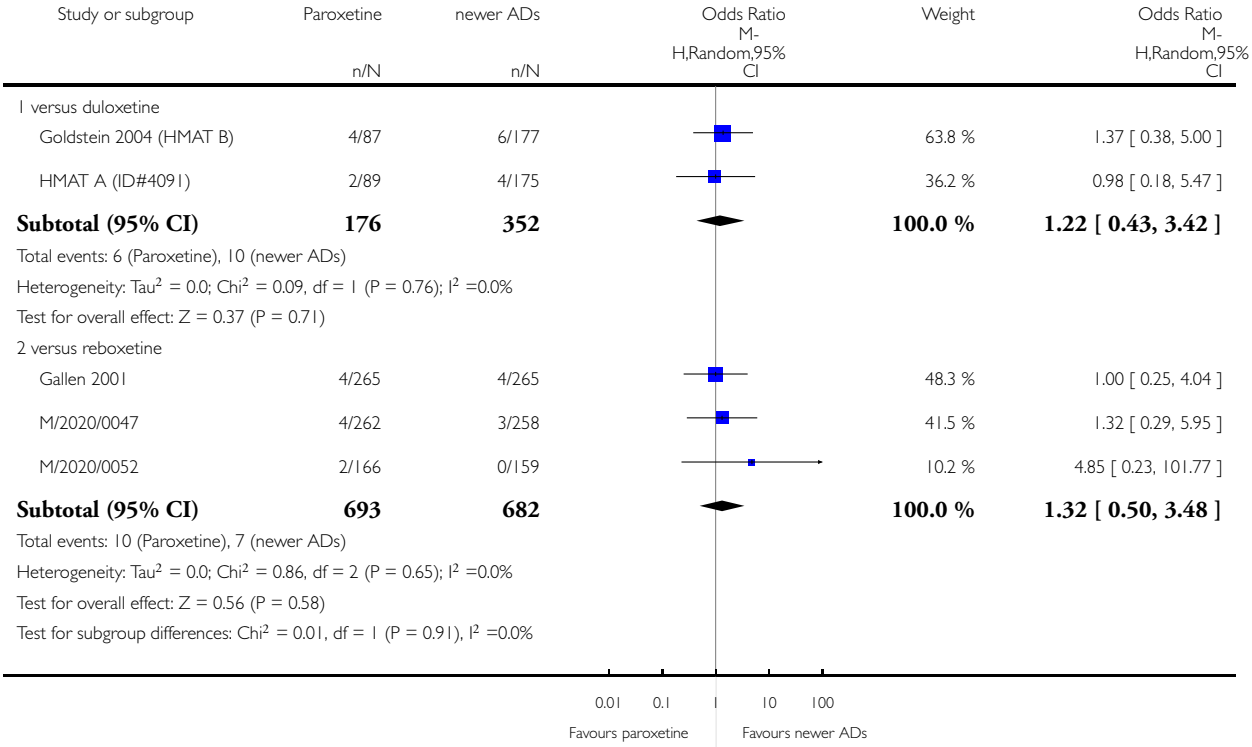
Analysis 32.2. Comparison 32 SE - Cough, Outcome 2 Paroxetine versus newer or non-conventional ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 32 SE - Cough

Outcome: 2 Paroxetine versus newer or non-conventional ADs



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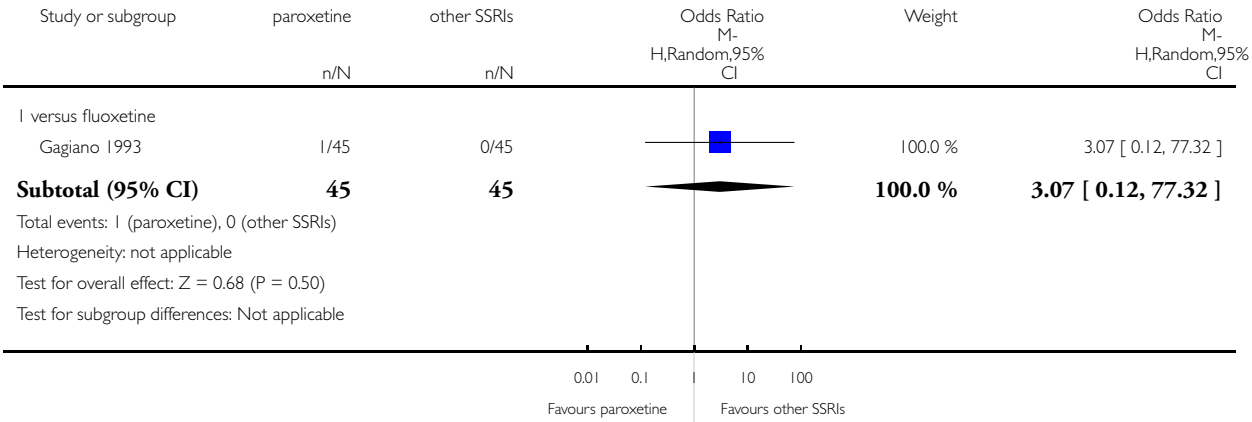
Analysis 33.1. Comparison 33 SE - Delirium, Outcome 1 Paroxetine versus other SSRIs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 33 SE - Delirium

Outcome: 1 Paroxetine versus other SSRIs

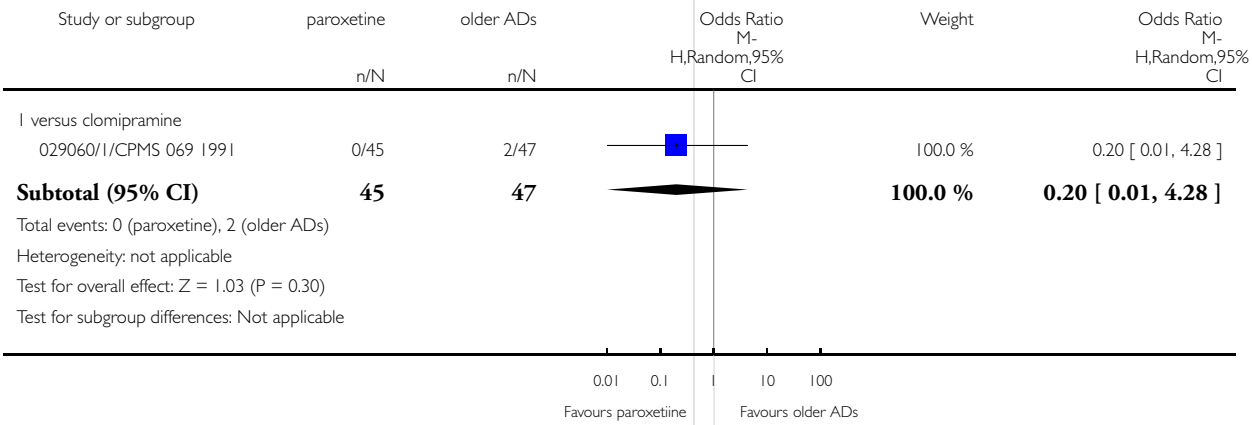


Analysis 33.2. Comparison 33 SE - Delirium, Outcome 2 Paroxetine versus older ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 33 SE - Delirium

Outcome: 2 Paroxetine versus older ADs



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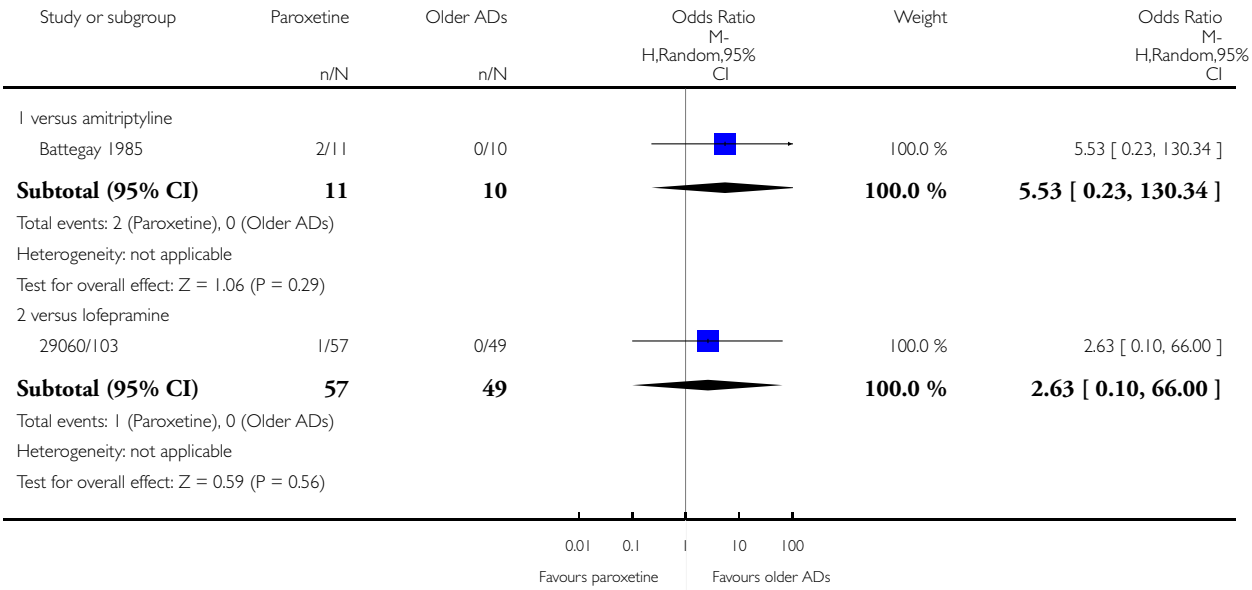
Analysis 34.1. Comparison 34 SE - Depersonalization, Outcome 1 Paroxetine versus older ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 34 SE - Depersonalization

Outcome: 1 Paroxetine versus older ADs



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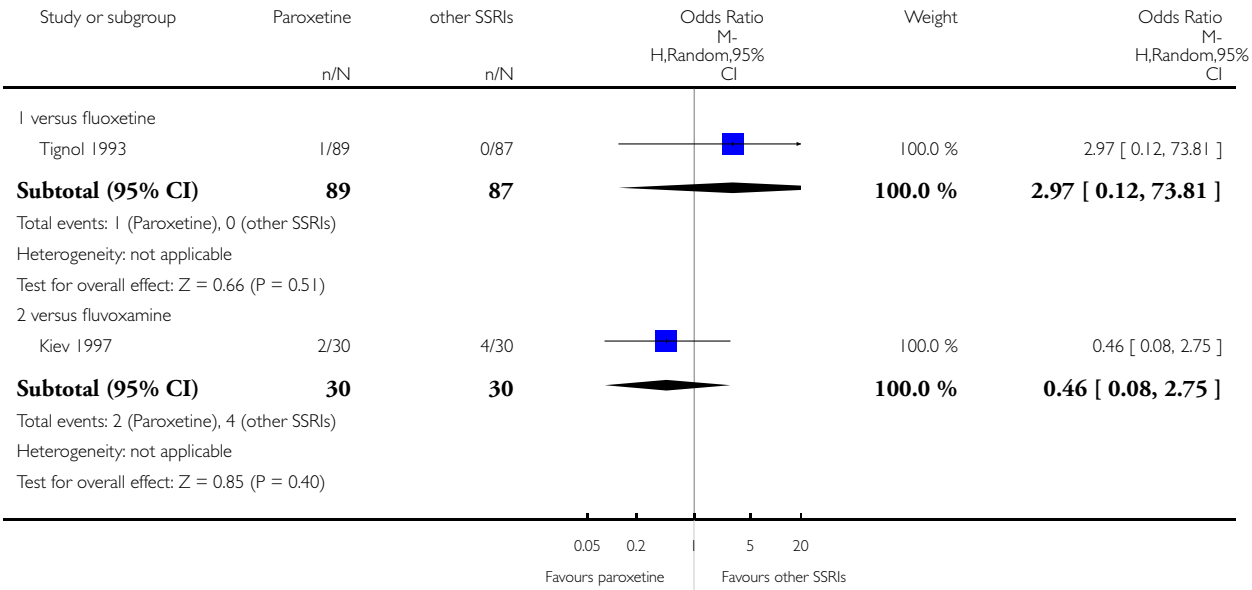
Analysis 34.2. Comparison 34 SE - Depersonalization, Outcome 2 Paroxetine versus other SSRIs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 34 SE - Depersonalization

Outcome: 2 Paroxetine versus other SSRIs



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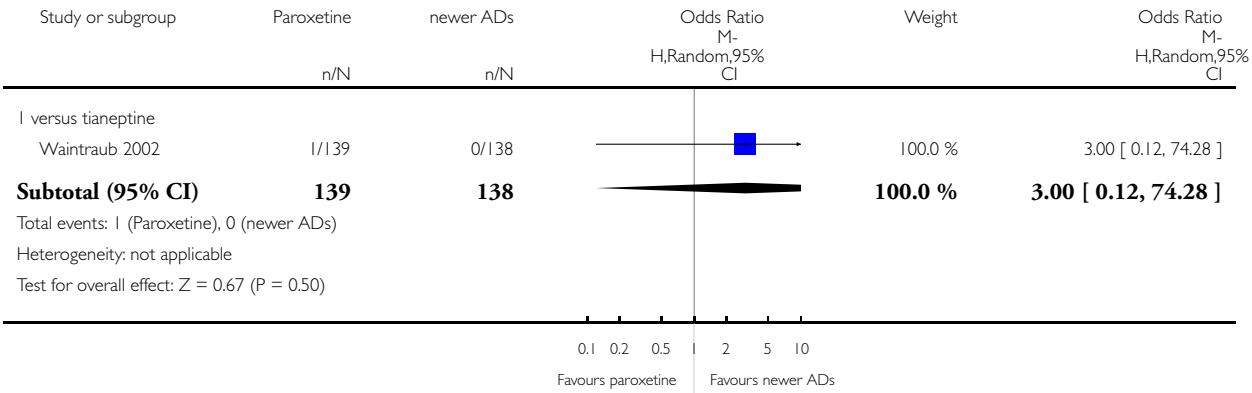
Analysis 34.3. Comparison 34 SE - Depersonalization, Outcome 3 Paroxetine versus newer or non-conventional ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 34 SE - Depersonalization

Outcome: 3 Paroxetine versus newer or non-conventional ADs



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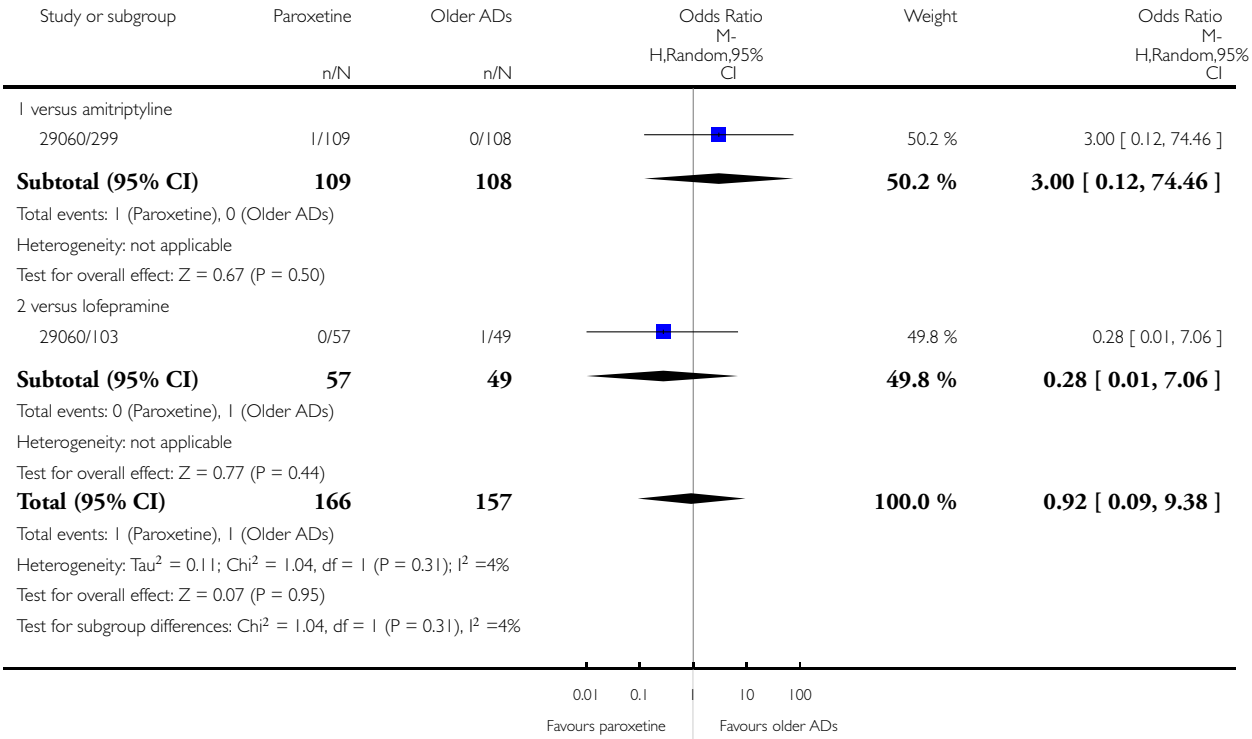
Analysis 35.1. Comparison 35 SE - Depression, Outcome 1 Paroxetine versus older ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 35 SE - Depression

Outcome: 1 Paroxetine versus older ADs



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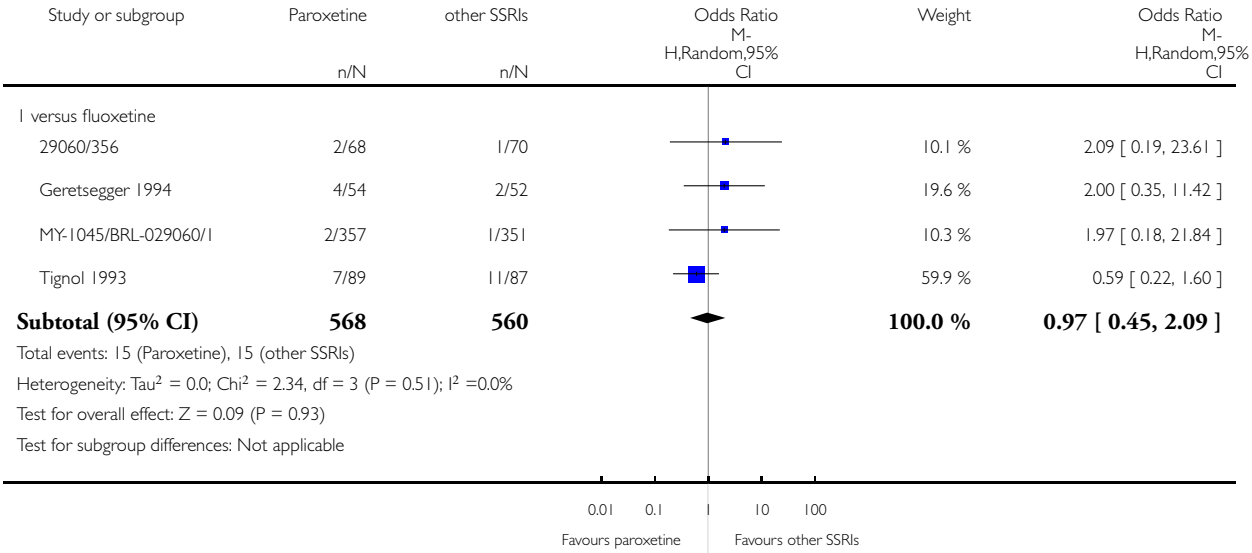
Analysis 35.2. Comparison 35 SE - Depression, Outcome 2 Paroxetine versus other SSRIs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 35 SE - Depression

Outcome: 2 Paroxetine versus other SSRIs



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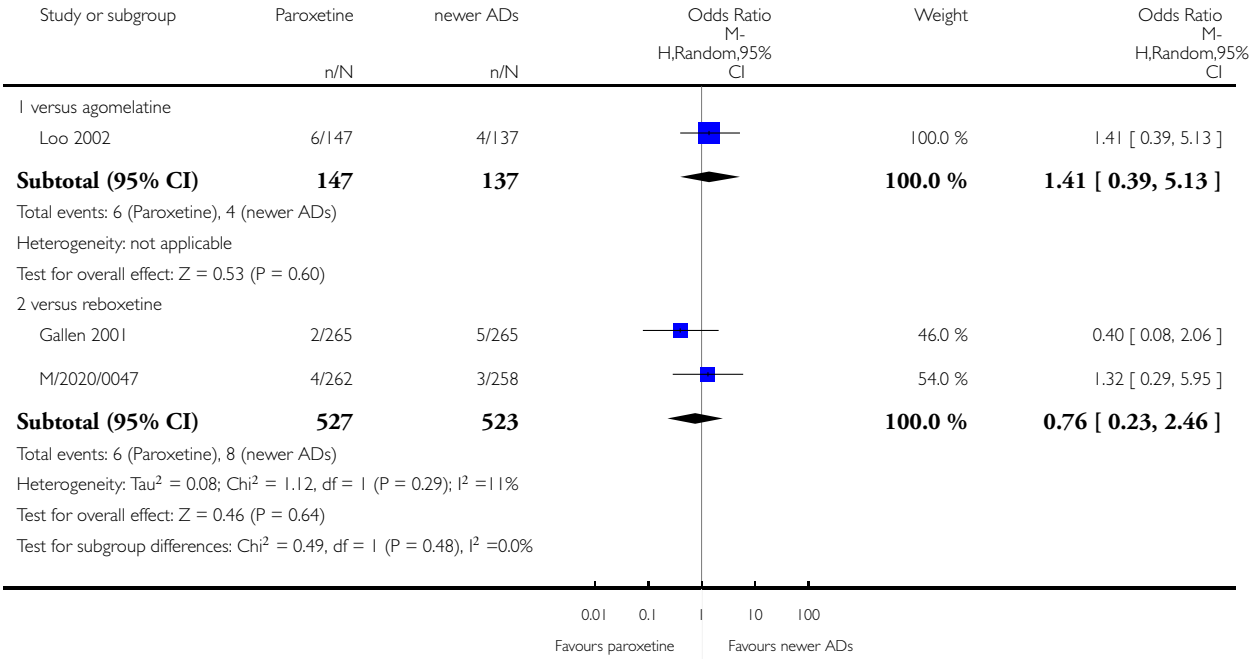
Analysis 35.3. Comparison 35 SE - Depression, Outcome 3 Paroxetine versus newer or non-conventional ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 35 SE - Depression

Outcome: 3 Paroxetine versus newer or non-conventional ADs



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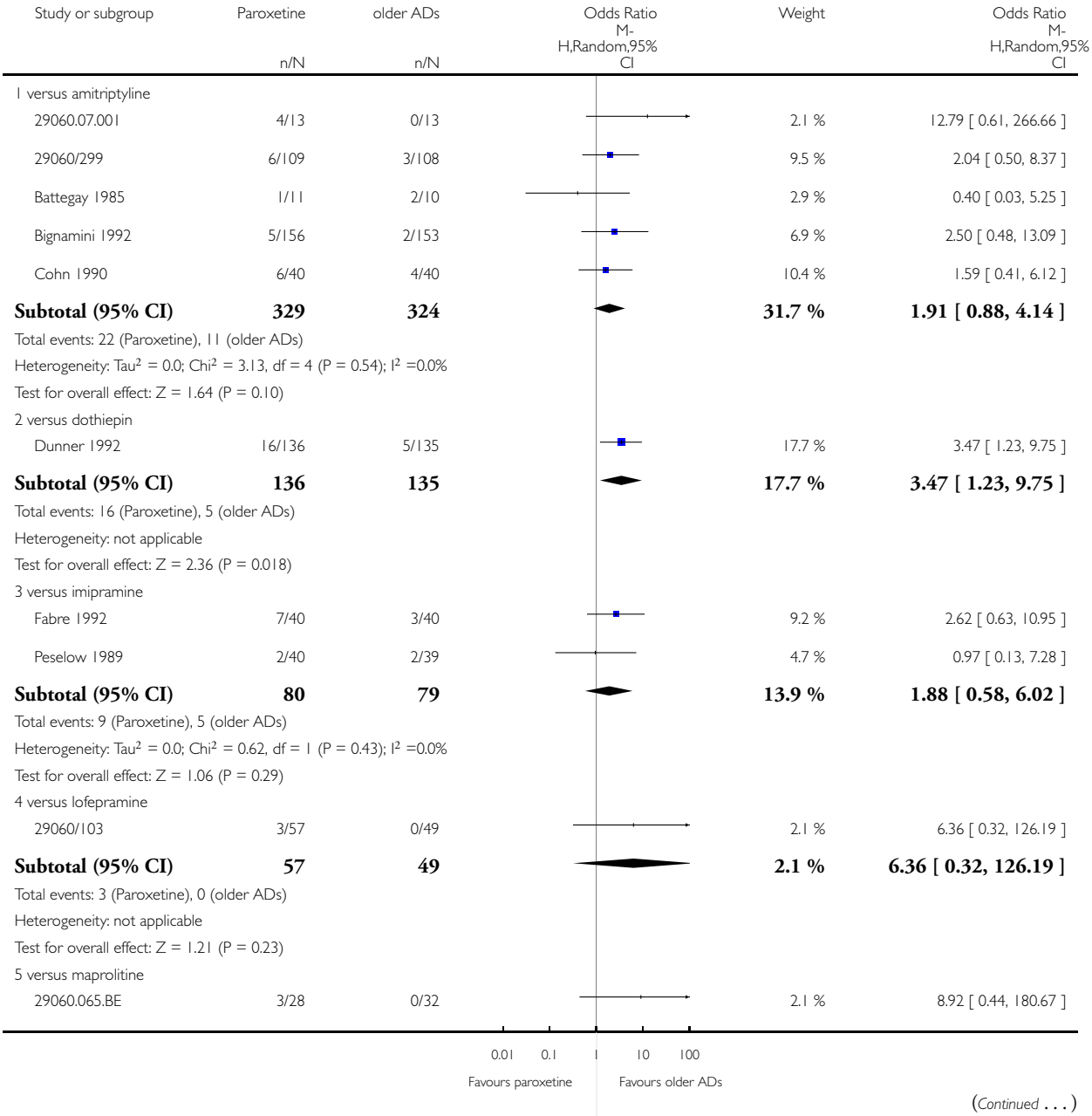
Analysis 36.1. Comparison 36 SE - Diarrhoea, Outcome 1 Paroxetine versus older ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 36 SE - Diarrhoea

Outcome: 1 Paroxetine versus older ADs



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Study or subgroup	Paroxetine n/N	older ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Szegedi 1995	21/145	9/153		28.4 %	2.71 [1.20, 6.13]
Subtotal (95% CI)	**173**	**185**		**30.5 %**	**2.94 [1.34, 6.47]**
Total events: 24 (Paroxetine), 9 (older ADs)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.57$, df = 1 (P = 0.45); $I^2 = 0.0\%$					
Test for overall effect: Z = 2.68 (P = 0.0073)					
6 versus nortriptyline					
Mulsant 1999	2/43	0/37		2.0 %	4.52 [0.21, 97.16]
Subtotal (95% CI)	**43**	**37**		**2.0 %**	**4.52 [0.21, 97.16]**
Total events: 2 (Paroxetine), 0 (older ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.96 (P = 0.34)					
7 versus mianserin					
Dalery 2001	0/54	2/62		2.0 %	0.22 [0.01, 4.73]
Subtotal (95% CI)	**54**	**62**		**2.0 %**	**0.22 [0.01, 4.73]**
Total events: 0 (Paroxetine), 2 (older ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.96 (P = 0.33)					
Total (95% CI)	**872**	**871**		**100.0 %**	**2.41 [1.56, 3.73]**
Total events: 76 (Paroxetine), 32 (older ADs)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 8.43$, df = 12 (P = 0.75); $I^2 = 0.0\%$					
Test for overall effect: Z = 3.97 (P = 0.000073)					
Test for subgroup differences: $Chi^2 = 4.15$, df = 6 (P = 0.66), $I^2 = 0.0\%$					

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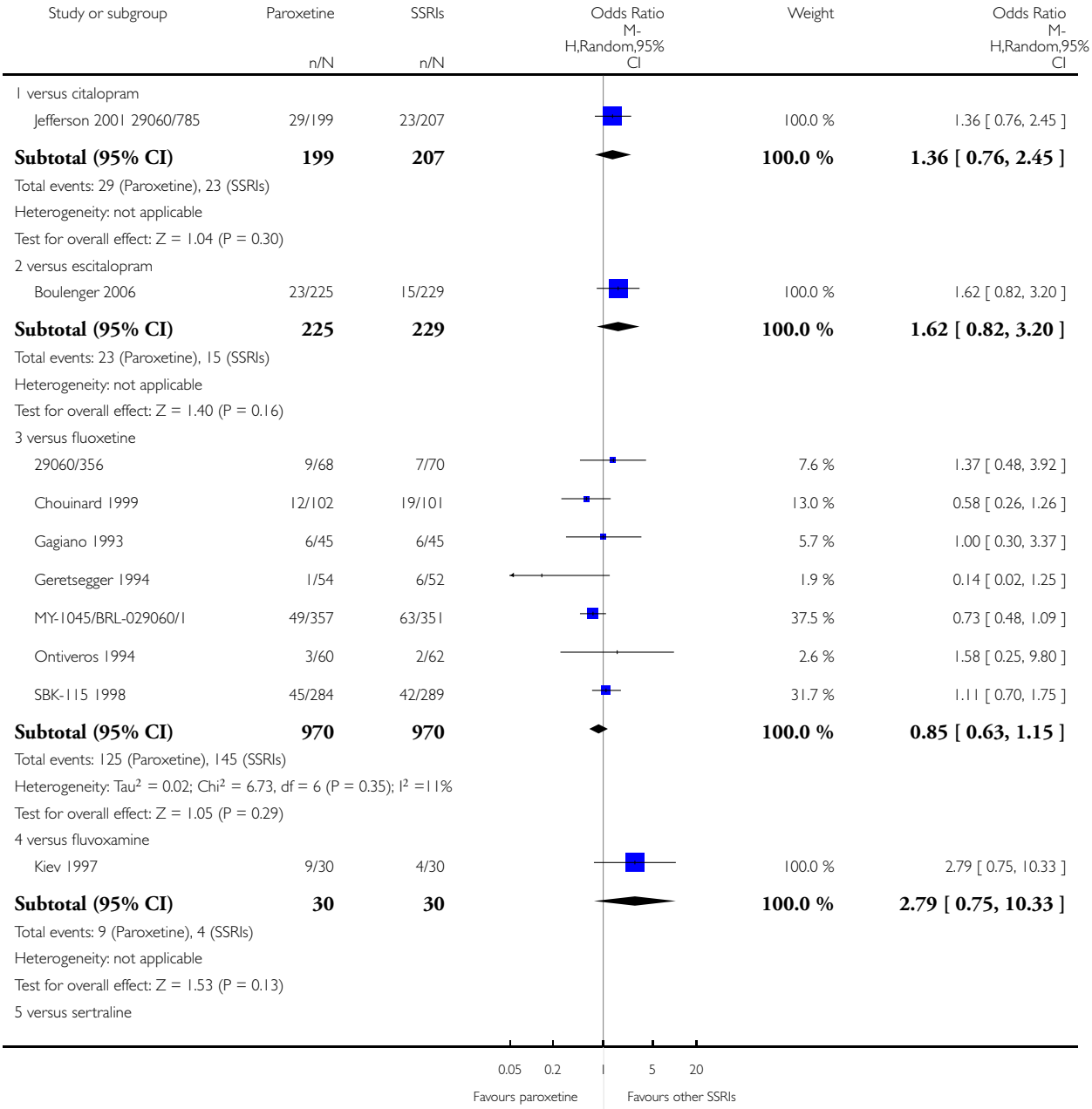
Analysis 36.2. Comparison 36 SE - Diarrhoea, Outcome 2 Paroxetine versus other SSRIs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 36 SE - Diarrhoea

Outcome: 2 Paroxetine versus other SSRIs



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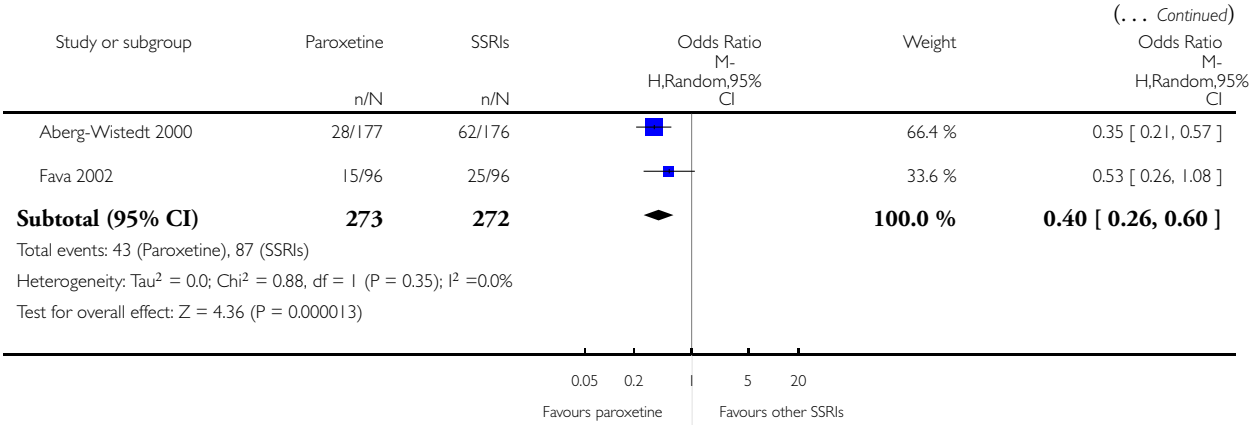
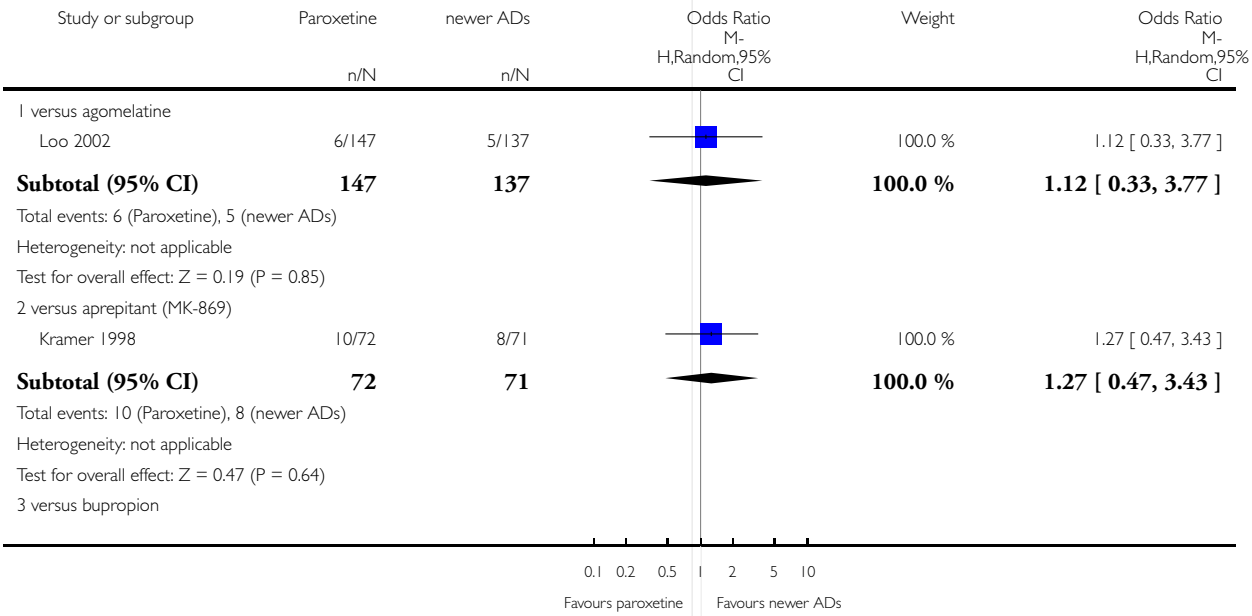


Analysis 36.3. Comparison 36 SE - Diarrhoea, Outcome 3 Paroxetine versus newer or non-conventional ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 36 SE - Diarrhoea

Outcome: 3 Paroxetine versus newer or non-conventional ADs



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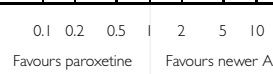
Study or subgroup	Paroxetine n/N	newer ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Kennedy 2004	14/71	6/69		63.4 %	2.58 [0.93, 7.16]
Weihs 2000	11/52	3/48		36.6 %	4.02 [1.05, 15.44]
Subtotal (95% CI)	**123**	**117**		**100.0 %**	**3.03 [1.35, 6.84]**
Total events: 25 (Paroxetine), 9 (newer ADs)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.27$, df = 1 (P = 0.61); $I^2 = 0.0\%$					
Test for overall effect: Z = 2.68 (P = 0.0075)					
4 versus duloxetine					
Detke 2004 (HMAY A)	3/86	5/188		16.3 %	1.32 [0.31, 5.67]
Goldstein 2004 (HMAT B)	10/87	15/177		30.6 %	1.40 [0.60, 3.26]
HMAT A (ID#40911)	8/89	22/175		30.3 %	0.69 [0.29, 1.61]
Lee 2007 (HMCV)	12/240	2/238		15.5 %	6.21 [1.37, 28.06]
Perahia 2006 (HMAY B)	1/97	2/196		7.3 %	1.01 [0.09, 11.28]
Subtotal (95% CI)	**599**	**974**		**100.0 %**	**1.38 [0.68, 2.77]**
Total events: 34 (Paroxetine), 46 (newer ADs)					
Heterogeneity: $Tau^2 = 0.23$; $Chi^2 = 6.42$, df = 4 (P = 0.17); $I^2 = 38\%$					
Test for overall effect: Z = 0.89 (P = 0.37)					
5 versus hypericum					
Szegedi 2005	23/126	12/125		100.0 %	2.10 [1.00, 4.44]
Subtotal (95% CI)	**126**	**125**		**100.0 %**	**2.10 [1.00, 4.44]**
Total events: 23 (Paroxetine), 12 (newer ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.95 (P = 0.051)					
6 versus mirtazapine					
Benkert 1999	11/136	11/139		31.6 %	1.02 [0.43, 2.45]
Schatzberg 2002	22/126	19/128		53.5 %	1.21 [0.62, 2.37]
Wade 2003	5/98	5/99		14.8 %	1.01 [0.28, 3.61]
Subtotal (95% CI)	**360**	**366**		**100.0 %**	**1.12 [0.69, 1.83]**
Total events: 38 (Paroxetine), 35 (newer ADs)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.12$, df = 2 (P = 0.94); $I^2 = 0.0\%$					
Test for overall effect: Z = 0.45 (P = 0.65)					
7 versus reboxetine					
Gallen 2001	53/265	18/265		50.3 %	3.43 [1.95, 6.04]
M/2020/0047	38/262	14/258		39.3 %	2.96 [1.56, 5.60]
M/2020/0052	18/166	3/159		10.4 %	6.32 [1.83, 21.92]
Subtotal (95% CI)	**693**	**682**		**100.0 %**	**3.45 [2.31, 5.15]**
Total events: 109 (Paroxetine), 35 (newer ADs)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 1.14$, df = 2 (P = 0.56); $I^2 = 0.0\%$					
Test for overall effect: Z = 6.05 (P < 0.00001)					



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Study or subgroup	Paroxetine n/N	newer ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
8 versus tianeptine					
Waintraub 2002	3/139	0/138		100.0 %	7.10 [0.36, 138.80]
Subtotal (95% CI)	**139**	**138**		**100.0 %**	**7.10 [0.36, 138.80]**
Total events: 3 (Paroxetine), 0 (newer ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.29 (P = 0.20)					
9 versus venlafaxine					
Mc Partlin 1998	9/178	8/183		100.0 %	1.16 [0.44, 3.09]
Subtotal (95% CI)	**178**	**183**		**100.0 %**	**1.16 [0.44, 3.09]**
Total events: 9 (Paroxetine), 8 (newer ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.31 (P = 0.76)					
10 versus trazodone					
Kasper 2005	1/53	0/55		100.0 %	3.17 [0.13, 79.60]
Subtotal (95% CI)	**53**	**55**		**100.0 %**	**3.17 [0.13, 79.60]**
Total events: 1 (Paroxetine), 0 (newer ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.70 (P = 0.48)					

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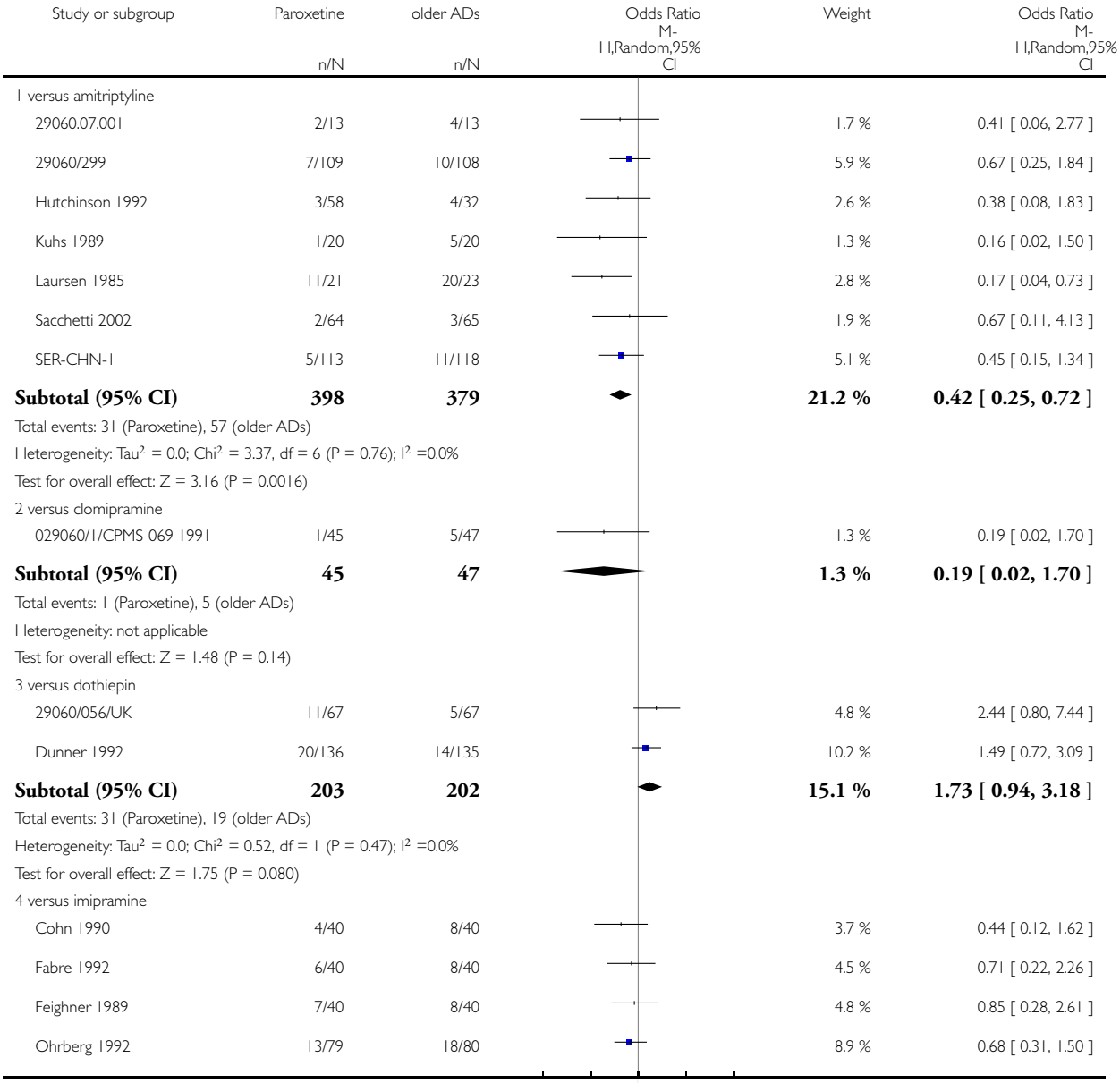
Analysis 37.1. Comparison 37 SE - Dizziness, Outcome 1 Paroxetine versus older ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 37 SE - Dizziness

Outcome: 1 Paroxetine versus older ADs



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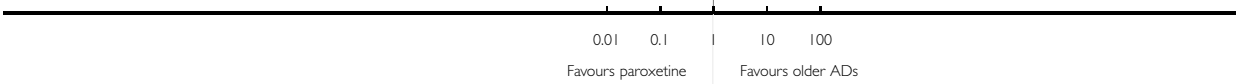
Study or subgroup	Paroxetine n/N	older ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Peselow 1989	16/40	13/39		6.9 %	1.33 [0.53, 3.34]
Shrivastava 1992	9/40	10/40		5.6 %	0.87 [0.31, 2.44]
Subtotal (95% CI)	**279**	**279**		**34.3 %**	**0.80 [0.53, 1.22]**
Total events: 55 (Paroxetine), 65 (older ADs)					
Heterogeneity: Tau^2 = 0.0; Chi^2 = 2.23, df = 5 (P = 0.82); I^2 =0.0%					
Test for overall effect: Z = 1.04 (P = 0.30)					
5 versus lofepramine					
29060/103	8/57	7/49		5.0 %	0.98 [0.33, 2.93]
Moon 1996	3/60	6/62		3.0 %	0.49 [0.12, 2.06]
Subtotal (95% CI)	**117**	**111**		**8.0 %**	**0.76 [0.32, 1.81]**
Total events: 11 (Paroxetine), 13 (older ADs)					
Heterogeneity: Tau^2 = 0.0; Chi^2 = 0.56, df = 1 (P = 0.45); I^2 =0.0%					
Test for overall effect: Z = 0.62 (P = 0.54)					
6 versus maprotiline					
Szegedi 1995	44/145	44/153		18.3 %	1.08 [0.66, 1.78]
Subtotal (95% CI)	**145**	**153**		**18.3 %**	**1.08 [0.66, 1.78]**
Total events: 44 (Paroxetine), 44 (older ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.30 (P = 0.76)					
7 versus mianserin					
Dalery 2001	1/54	2/62		1.1 %	0.57 [0.05, 6.42]
Subtotal (95% CI)	**54**	**62**		**1.1 %**	**0.57 [0.05, 6.42]**
Total events: 1 (Paroxetine), 2 (older ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.46 (P = 0.65)					
8 versus nortriptyline					
Mulsant 1999	0/43	1/37		0.6 %	0.28 [0.01, 7.08]
Subtotal (95% CI)	**43**	**37**		**0.6 %**	**0.28 [0.01, 7.08]**
Total events: 0 (Paroxetine), 1 (older ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.77 (P = 0.44)					
Total (95% CI)	**1284**	**1270**		**100.0 %**	**0.80 [0.62, 1.03]**
Total events: 174 (Paroxetine), 206 (older ADs)					
Heterogeneity: Tau^2 = 0.03; Chi^2 = 21.79, df = 20 (P = 0.35); I^2 =8%					
Test for overall effect: Z = 1.71 (P = 0.088)					
Test for subgroup differences: Chi^2 = 15.08, df = 7 (P = 0.03), I^2 =54%					



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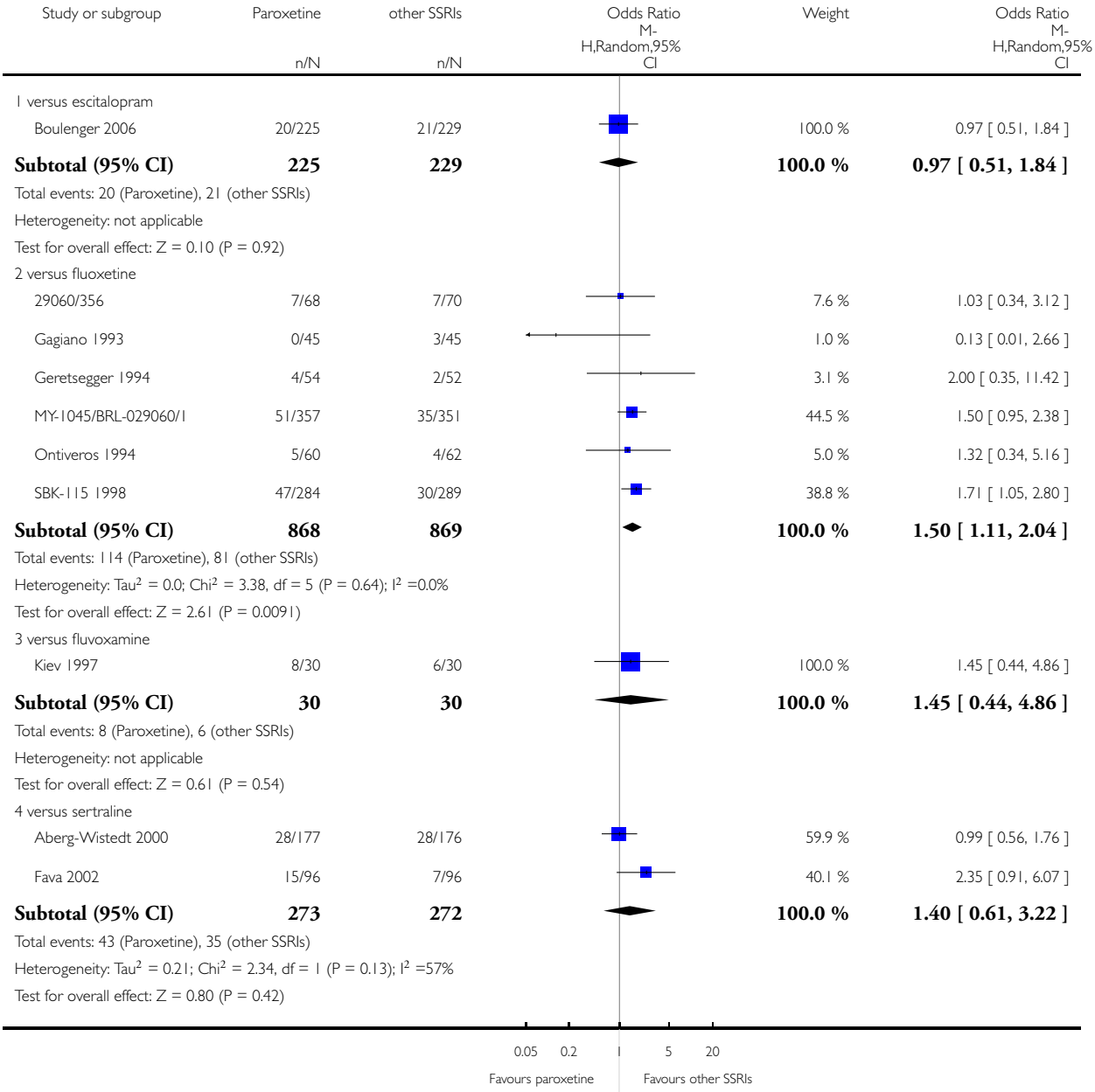
Analysis 37.2. Comparison 37 SE - Dizziness, Outcome 2 Paroxetine versus other SSRIs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 37 SE - Dizziness

Outcome: 2 Paroxetine versus other SSRIs



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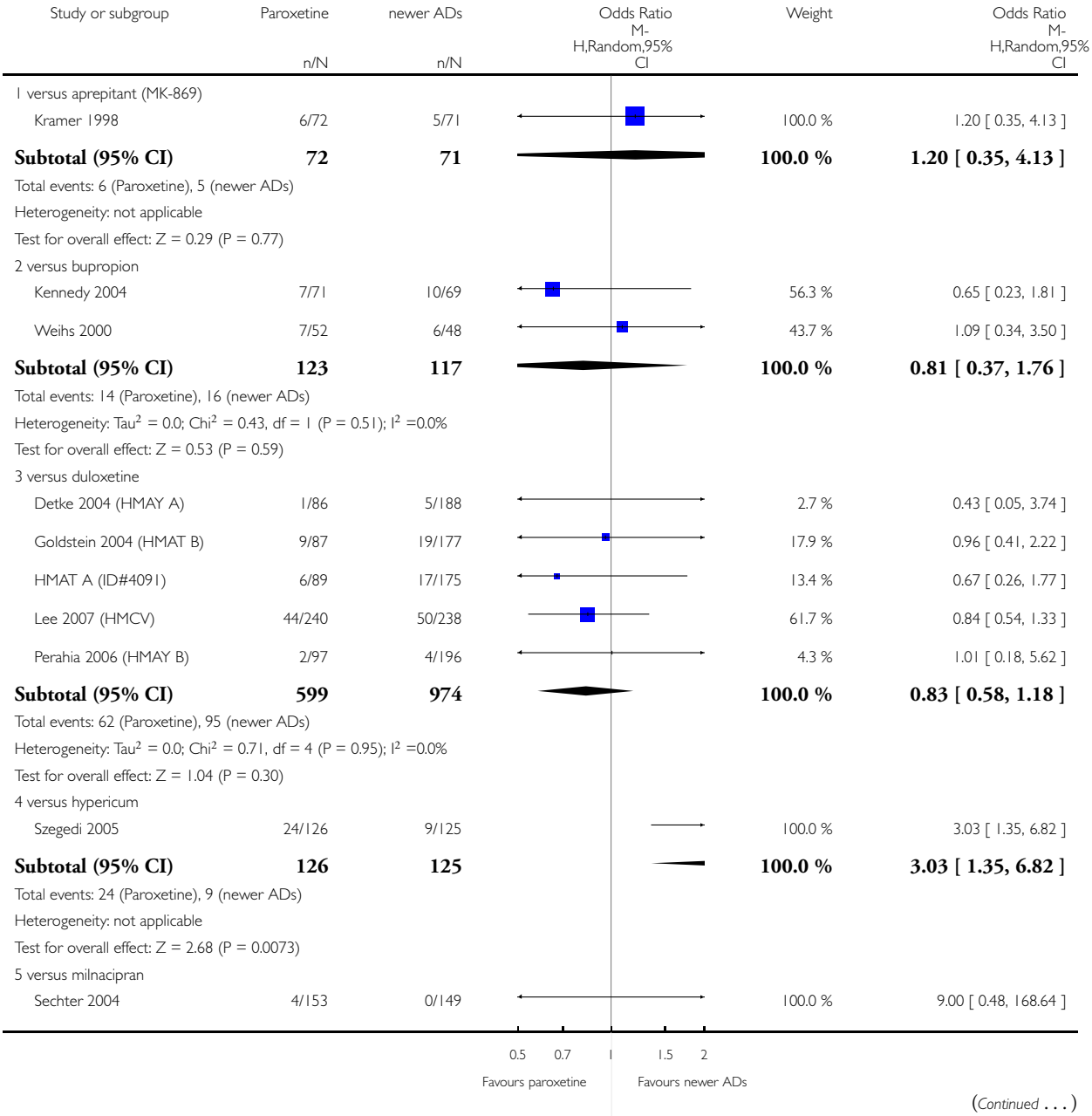
Analysis 37.3. Comparison 37 SE - Dizziness, Outcome 3 Paroxetine versus newer or non-conventional ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 37 SE - Dizziness

Outcome: 3 Paroxetine versus newer or non-conventional ADs



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Study or subgroup	Paroxetine n/N	newer ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Subtotal (95% CI)	**153**	**149**		**100.0 %**	**9.00 [0.48, 168.64]**
Total events: 4 (Paroxetine), 0 (newer ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.47 (P = 0.14)					
6 versus mirtazapine					
Benkert 1999	11/136	12/139		31.4 %	0.93 [0.40, 2.19]
Schatzberg 2002	18/126	20/128		41.3 %	0.90 [0.45, 1.80]
Wade 2003	15/98	7/99		27.3 %	2.38 [0.92, 6.11]
Subtotal (95% CI)	**360**	**366**		**100.0 %**	**1.19 [0.66, 2.11]**
Total events: 44 (Paroxetine), 39 (newer ADs)					
Heterogeneity: Tau^2 = 0.09; Chi^2 = 2.98, df = 2 (P = 0.22); I^2 =33%					
Test for overall effect: Z = 0.58 (P = 0.56)					
7 versus nefazodone					
Baldwin 1995	9/101	18/105		77.7 %	0.47 [0.20, 1.11]
Hicks 2002	3/20	5/20		22.3 %	0.53 [0.11, 2.60]
Subtotal (95% CI)	**121**	**125**		**100.0 %**	**0.48 [0.23, 1.03]**
Total events: 12 (Paroxetine), 23 (newer ADs)					
Heterogeneity: Tau^2 = 0.0; Chi^2 = 0.02, df = 1 (P = 0.90); I^2 =0.0%					
Test for overall effect: Z = 1.89 (P = 0.059)					
8 versus reboxetine					
Gallen 2001	28/265	41/265		40.9 %	0.65 [0.39, 1.08]
M/2020/0047	34/262	30/258		39.6 %	1.13 [0.67, 1.91]
M/2020/0052	13/166	15/159		19.6 %	0.82 [0.38, 1.77]
Subtotal (95% CI)	**693**	**682**		**100.0 %**	**0.84 [0.59, 1.21]**
Total events: 75 (Paroxetine), 86 (newer ADs)					
Heterogeneity: Tau^2 = 0.01; Chi^2 = 2.27, df = 2 (P = 0.32); I^2 =12%					
Test for overall effect: Z = 0.93 (P = 0.35)					
9 versus tianeptine					
Lepine 2001	8/165	1/162		68.0 %	8.20 [1.01, 66.36]
Waintraub 2002	2/139	0/138		32.0 %	5.04 [0.24, 105.87]
Subtotal (95% CI)	**304**	**300**		**100.0 %**	**7.02 [1.25, 39.32]**
Total events: 10 (Paroxetine), 1 (newer ADs)					
Heterogeneity: Tau^2 = 0.0; Chi^2 = 0.07, df = 1 (P = 0.80); I^2 =0.0%					
Test for overall effect: Z = 2.22 (P = 0.027)					
10 versus trazodone					
Kasper 2005	1/53	2/55		100.0 %	0.51 [0.04, 5.79]
Subtotal (95% CI)	**53**	**55**		**100.0 %**	**0.51 [0.04, 5.79]**
Total events: 1 (Paroxetine), 2 (newer ADs)					
Heterogeneity: not applicable					

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Study or subgroup	Paroxetine n/N	newer ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Test for overall effect: Z = 0.54 (P = 0.59)					
11 versus venlafaxine					
Hwang 2004	11/53	3/52		45.8 %	4.28 [1.12, 16.36]
Mc Partlin 1998	17/178	30/183		54.2 %	0.54 [0.29, 1.02]
Subtotal (95% CI)	**231**	**235**		**100.0 %**	**1.39 [0.18, 10.62]**
Total events: 28 (Paroxetine), 33 (newer ADs)					
Heterogeneity: Tau^2 = 1.88; Chi^2 = 7.55, df = 1 (P = 0.01); I^2 =87%					
Test for overall effect: Z = 0.32 (P = 0.75)					

Analysis 38.1. Comparison 38 SE - Dry mouth, Outcome 1 Paroxetine versus older ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 38 SE - Dry mouth

Outcome: 1 Paroxetine versus older ADs

Study or subgroup	Paroxetine n/N	Control n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
1 versus amitriptyline					
29060.07.001	1/13	10/13		1.1 %	0.03 [0.00, 0.28]
29060/299	14/109	36/108		5.1 %	0.29 [0.15, 0.59]
Bignamini 1992	20/156	54/153		5.7 %	0.27 [0.15, 0.48]
Christiansen 1996	23/71	58/73		4.8 %	0.12 [0.06, 0.26]
Geretsegger 1995	4/78	7/75		2.8 %	0.53 [0.15, 1.87]
Hutchinson 1992	3/58	6/32		2.4 %	0.24 [0.05, 1.02]
Kuhs 1989	8/20	10/20		2.9 %	0.67 [0.19, 2.33]
Laursen 1985	7/21	14/23		3.0 %	0.32 [0.09, 1.10]

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Study or subgroup	Paroxetine n/N	Control n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Sacchetti 2002	0/64	16/65		0.8 %	0.02 [0.00, 0.40]
SER-CHN-1	34/113	65/118		5.9 %	0.35 [0.20, 0.60]
Staner 1995	8/21	0/19		0.8 %	24.56 [1.30, 462.34]
Stuppaeck 1994	3/78	19/75		2.9 %	0.12 [0.03, 0.42]
Subtotal (95% CI)	**802**	**774**		**38.2 %**	**0.27 [0.17, 0.43]**
Total events: 125 (Paroxetine), 295 (Control)					
Heterogeneity: $Tau^2 = 0.33$; $Chi^2 = 25.56$, df = 11 (P = 0.01); $I^2 = 57\%$					
Test for overall effect: Z = 5.47 (P < 0.00001)					
2 versus clomipramine					
029060/1/CPMS 069 1991	6/45	17/47		3.6 %	0.27 [0.10, 0.77]
Ravindran 1997	65/513	146/506		7.0 %	0.36 [0.26, 0.49]
Subtotal (95% CI)	**558**	**553**		**10.5 %**	**0.35 [0.26, 0.48]**
Total events: 71 (Paroxetine), 163 (Control)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.24$, df = 1 (P = 0.62); $I^2 = 0.0\%$					
Test for overall effect: Z = 6.67 (P < 0.00001)					
3 versus dothiepin					
29060/056/UK	4/67	9/67		3.0 %	0.41 [0.12, 1.40]
Dunner 1992	32/136	88/135		5.9 %	0.16 [0.10, 0.28]
Subtotal (95% CI)	**203**	**202**		**8.9 %**	**0.22 [0.10, 0.50]**
Total events: 36 (Paroxetine), 97 (Control)					
Heterogeneity: $Tau^2 = 0.18$; $Chi^2 = 1.78$, df = 1 (P = 0.18); $I^2 = 44\%$					
Test for overall effect: Z = 3.62 (P = 0.00029)					
4 versus imipramine					
029060/1/CPMS-095	7/134	7/68		3.4 %	0.48 [0.16, 1.43]
29060/409	5/38	23/37		3.2 %	0.09 [0.03, 0.29]
Cohn 1990	10/40	25/40		3.9 %	0.20 [0.08, 0.52]
Fabre 1992	8/40	25/40		3.7 %	0.15 [0.05, 0.41]
Feighner 1989	11/40	32/40		3.6 %	0.09 [0.03, 0.27]
Ohrberg 1992	24/79	53/80		5.3 %	0.22 [0.11, 0.43]
Peselow 1989	12/40	26/39		4.0 %	0.21 [0.08, 0.55]
Shrivastava 1992	1/40	26/40		1.4 %	0.01 [0.00, 0.11]
Subtotal (95% CI)	**451**	**384**		**28.4 %**	**0.16 [0.10, 0.26]**
Total events: 78 (Paroxetine), 217 (Control)					
Heterogeneity: $Tau^2 = 0.21$; $Chi^2 = 12.54$, df = 7 (P = 0.08); $I^2 = 44\%$					
Test for overall effect: Z = 7.30 (P < 0.00001)					
5 versus lofepramine					
29060/103	4/57	3/49		2.2 %	1.16 [0.25, 5.44]

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Study or subgroup	Paroxetine n/N	Control n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Subtotal (95% CI)	**57**	**49**		**2.2 %**	**1.16 [0.25, 5.44]**
Total events: 4 (Paroxetine), 3 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.18 (P = 0.85)					
6 versus maprolitine					
29060.065.BE	6/28	16/32		3.3 %	0.27 [0.09, 0.85]
Schnyder 1996	1/37	6/34		1.3 %	0.13 [0.01, 1.14]
Szegedi 1995	69/145	137/153		5.5 %	0.11 [0.06, 0.20]
Subtotal (95% CI)	**210**	**219**		**10.1 %**	**0.13 [0.08, 0.23]**
Total events: 76 (Paroxetine), 159 (Control)					
Heterogeneity: Tau^2 = 0.01; Chi^2 = 2.05, df = 2 (P = 0.36); I^2 =3%					
Test for overall effect: Z = 7.31 (P < 0.00001)					
7 versus mianserin					
Dalery 2001	2/54	3/62		1.7 %	0.76 [0.12, 4.70]
Subtotal (95% CI)	**54**	**62**		**1.7 %**	**0.76 [0.12, 4.70]**
Total events: 2 (Paroxetine), 3 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.30 (P = 0.76)					
Total (95% CI)	**2335**	**2243**		**100.0 %**	**0.23 [0.18, 0.30]**
Total events: 392 (Paroxetine), 937 (Control)					
Heterogeneity: Tau^2 = 0.25; Chi^2 = 63.05, df = 28 (P = 0.00016); I^2 =56%					
Test for overall effect: Z = 10.67 (P < 0.00001)					
Test for subgroup differences: Chi^2 = 18.07, df = 6 (P = 0.01), I^2 =67%					

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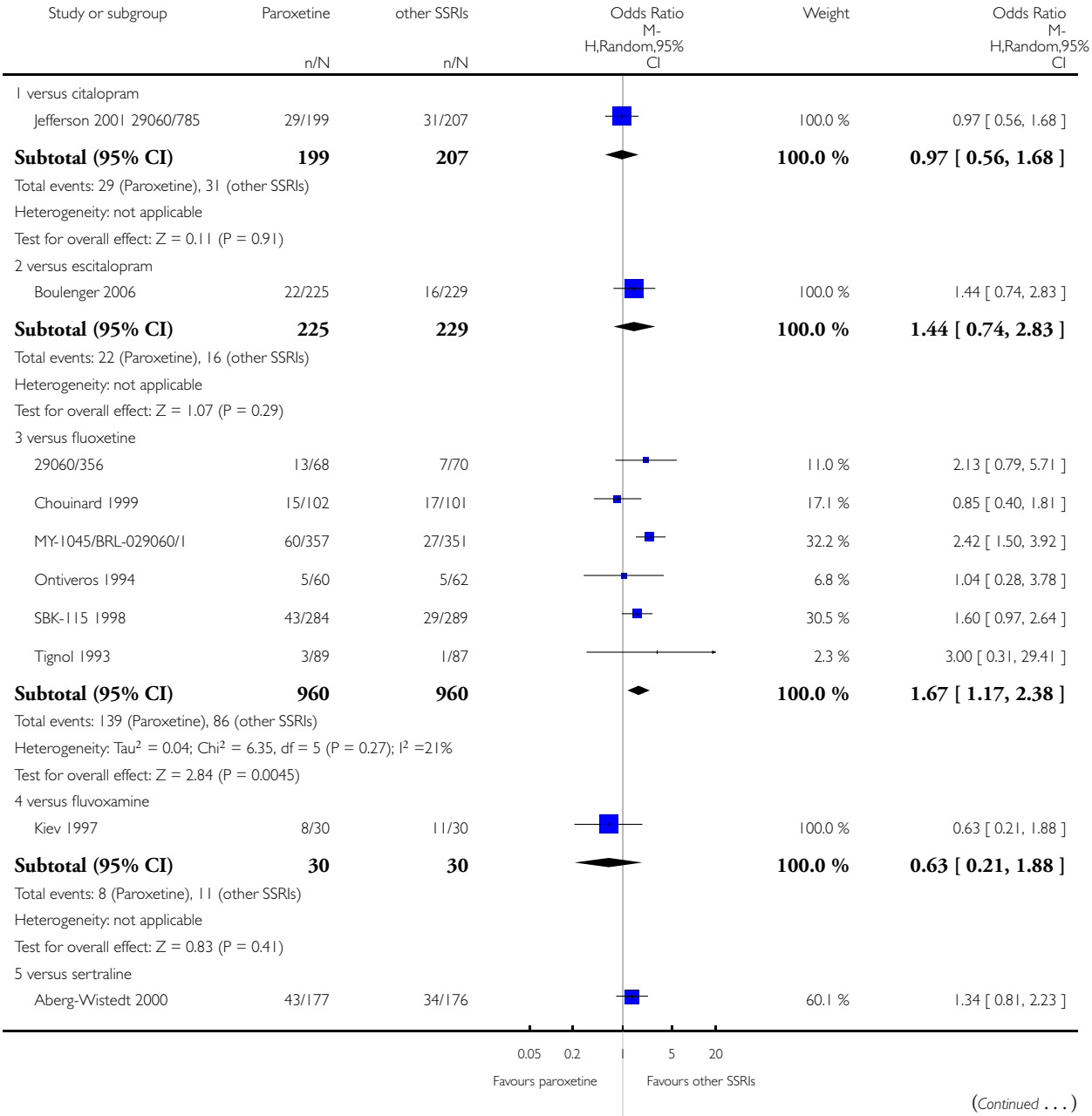
Analysis 38.2. Comparison 38 SE - Dry mouth, Outcome 2 Paroxetine versus other SSRIs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 38 SE - Dry mouth

Outcome: 2 Paroxetine versus other SSRIs



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Study or subgroup	Paroxetine n/N	other SSRIs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Fava 2002	12/96	17/96		39.9 %	0.66 [0.30, 1.48]
Subtotal (95% CI)	**273**	**272**		**100.0 %**	**1.01 [0.52, 1.99]**
Total events: 55 (Paroxetine), 51 (other SSRIs)					
Heterogeneity: $Tau^2 = 0.13$; $Chi^2 = 2.11$, df = 1 (P = 0.15); $I^2 = 53\%$					
Test for overall effect: Z = 0.04 (P = 0.97)					

Analysis 38.3. Comparison 38 SE - Dry mouth, Outcome 3 Paroxetine versus newer or non-conventional ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 38 SE - Dry mouth

Outcome: 3 Paroxetine versus newer or non-conventional ADs

Study or subgroup	Paroxetine n/N	newer ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
1 versus agomelatine					
Loo 2002	5/147	1/137		100.0 %	4.79 [0.55, 41.52]
Subtotal (95% CI)	**147**	**137**		**100.0 %**	**4.79 [0.55, 41.52]**
Total events: 5 (Paroxetine), 1 (newer ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.42 (P = 0.16)					
2 versus aprepitant (MK-869)					
Kramer 1998	6/72	6/71		100.0 %	0.98 [0.30, 3.21]
Subtotal (95% CI)	**72**	**71**		**100.0 %**	**0.98 [0.30, 3.21]**
Total events: 6 (Paroxetine), 6 (newer ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.03 (P = 0.98)					
3 versus bupropion					
Kennedy 2004	12/71	21/69		58.4 %	0.46 [0.21, 1.04]

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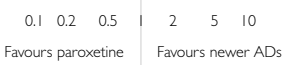
Study or subgroup	Paroxetine n/N	newer ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Weihs 2000	8/52	6/48		41.6 %	1.27 [0.41, 3.98]
Subtotal (95% CI)	**123**	**117**		**100.0 %**	**0.71 [0.27, 1.87]**
Total events: 20 (Paroxetine), 27 (newer ADs)					
Heterogeneity: Tau² = 0.25; Chi² = 2.00, df = 1 (P = 0.16); I² =50%					
Test for overall effect: Z = 0.70 (P = 0.49)					
4 versus duloxetine					
Detke 2004 (HMAY A)	6/86	11/186		11.4 %	1.19 [0.43, 3.34]
Goldstein 2004 (HMAT B)	7/87	23/177		15.3 %	0.59 [0.24, 1.42]
HMAT A (ID#40911)	12/89	24/175		21.7 %	0.98 [0.47, 2.07]
Lee 2007 (HMCV)	29/240	41/238		45.6 %	0.66 [0.40, 1.10]
Perahia 2006 (HMAY B)	3/97	6/196		6.1 %	1.01 [0.25, 4.13]
Subtotal (95% CI)	**599**	**972**		**100.0 %**	**0.78 [0.55, 1.10]**
Total events: 57 (Paroxetine), 105 (newer ADs)					
Heterogeneity: Tau² = 0.0; Chi² = 1.95, df = 4 (P = 0.75); I² =0.0%					
Test for overall effect: Z = 1.44 (P = 0.15)					
5 versus hypericum					
Szegedi 2005	35/126	16/125		100.0 %	2.62 [1.36, 5.04]
Subtotal (95% CI)	**126**	**125**		**100.0 %**	**2.62 [1.36, 5.04]**
Total events: 35 (Paroxetine), 16 (newer ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 2.89 (P = 0.0039)					
6 versus mirtazapine					
Benkert 1999	11/136	19/139		33.8 %	0.56 [0.25, 1.22]
Schatzberg 2002	13/126	34/128		36.6 %	0.32 [0.16, 0.64]
Wade 2003	11/98	9/99		29.5 %	1.26 [0.50, 3.20]
Subtotal (95% CI)	**360**	**366**		**100.0 %**	**0.58 [0.27, 1.24]**
Total events: 35 (Paroxetine), 62 (newer ADs)					
Heterogeneity: Tau² = 0.29; Chi² = 5.45, df = 2 (P = 0.07); I² =63%					
Test for overall effect: Z = 1.42 (P = 0.16)					
7 versus nefazodone					
Baldwin 1995	6/101	10/105		61.4 %	0.60 [0.21, 1.72]
Hicks 2002	7/20	6/20		38.6 %	1.26 [0.33, 4.73]
Subtotal (95% CI)	**121**	**125**		**100.0 %**	**0.80 [0.35, 1.82]**
Total events: 13 (Paroxetine), 16 (newer ADs)					
Heterogeneity: Tau² = 0.0; Chi² = 0.73, df = 1 (P = 0.39); I² =0.0%					
Test for overall effect: Z = 0.54 (P = 0.59)					
8 versus reboxetine					
Gallen 2001	62/265	120/265		44.3 %	0.37 [0.25, 0.54]



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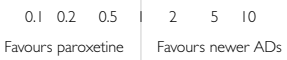
Study or subgroup	Paroxetine n/N	newer ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
M/2020/0047	53/262	110/258		40.7 %	0.34 [0.23, 0.50]
M/2020/0052	15/166	38/159		14.9 %	0.32 [0.17, 0.60]
Subtotal (95% CI)	**693**	**682**		**100.0 %**	**0.35 [0.27, 0.45]**
Total events: 130 (Paroxetine), 268 (newer ADs)					
Heterogeneity: Tau² = 0.0; Chi² = 0.19, df = 2 (P = 0.91); I² =0.0%					
Test for overall effect: Z = 8.29 (P < 0.00001)					
9 versus tianeptine					
Waintraub 2002	5/139	7/138		100.0 %	0.70 [0.22, 2.26]
Subtotal (95% CI)	**139**	**138**		**100.0 %**	**0.70 [0.22, 2.26]**
Total events: 5 (Paroxetine), 7 (newer ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.60 (P = 0.55)					
10 versus trazodone					
Kasper 2005	4/53	0/55		100.0 %	10.09 [0.53, 192.17]
Subtotal (95% CI)	**53**	**55**		**100.0 %**	**10.09 [0.53, 192.17]**
Total events: 4 (Paroxetine), 0 (newer ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.54 (P = 0.12)					
11 versus venlafaxine					
Hwang 2004	1/53	1/52		12.1 %	0.98 [0.06, 16.11]
Mc Partlin 1998	8/178	7/183		87.9 %	1.18 [0.42, 3.33]
Subtotal (95% CI)	**231**	**235**		**100.0 %**	**1.16 [0.44, 3.06]**
Total events: 9 (Paroxetine), 8 (newer ADs)					
Heterogeneity: Tau² = 0.0; Chi² = 0.02, df = 1 (P = 0.90); I² =0.0%					
Test for overall effect: Z = 0.29 (P = 0.77)					



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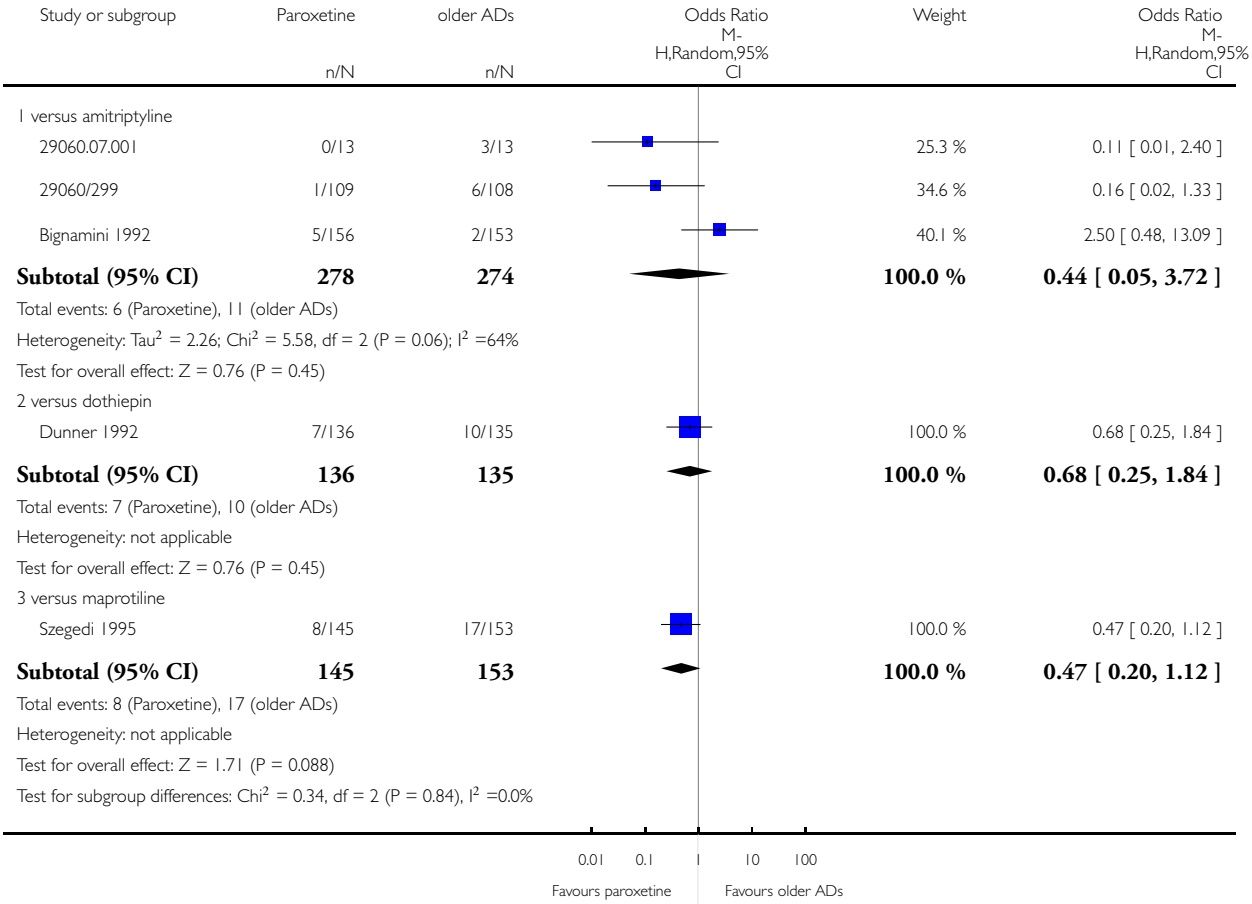
Analysis 39.1. Comparison 39 SE - Dyspepsia, Outcome 1 Paroxetine versus older ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 39 SE - Dyspepsia

Outcome: 1 Paroxetine versus older ADs



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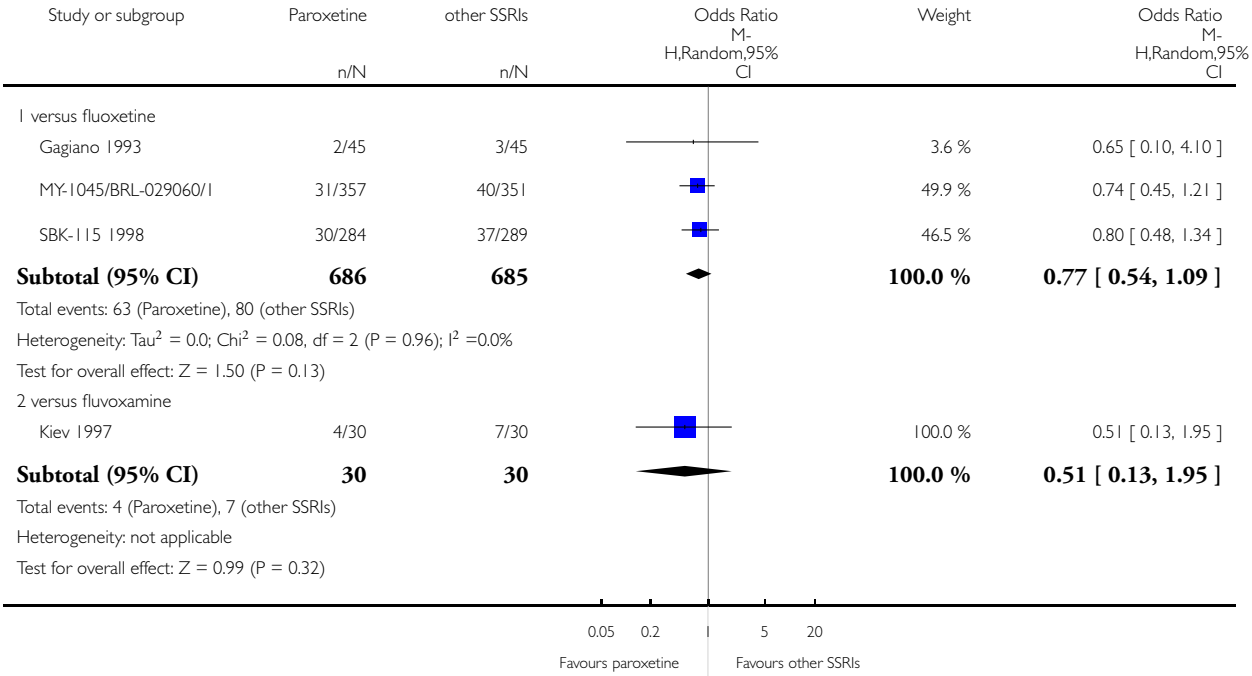
Analysis 39.2. Comparison 39 SE - Dyspepsia, Outcome 2 Paroxetine versus other SSRIs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 39 SE - Dyspepsia

Outcome: 2 Paroxetine versus other SSRIs



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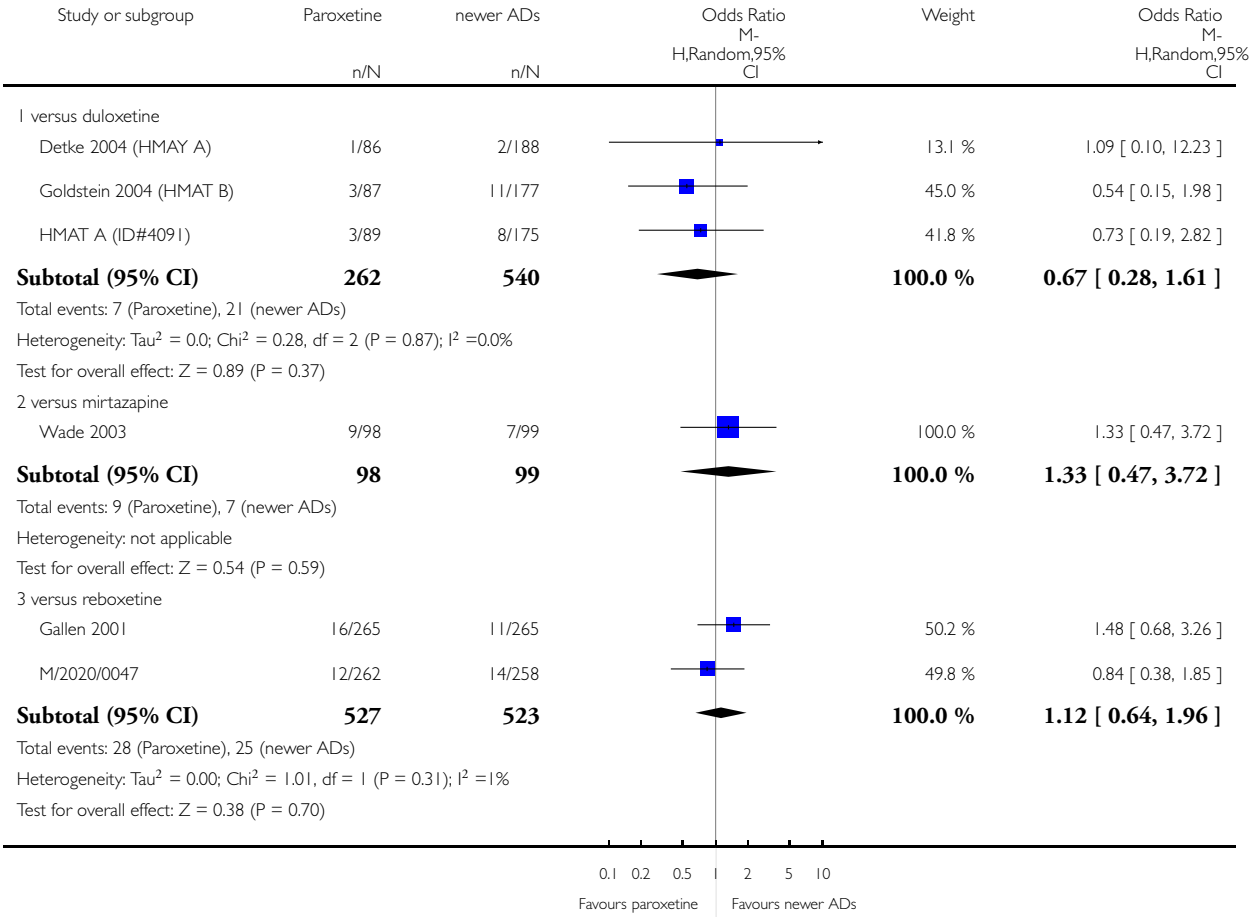
Analysis 39.3. Comparison 39 SE - Dyspepsia, Outcome 3 Paroxetine versus newer or non-conventional ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 39 SE - Dyspepsia

Outcome: 3 Paroxetine versus newer or non-conventional ADs



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Analysis 40.1. Comparison 40 SE - Dyspnea, Outcome 1 Paroxetine versus older ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 40 SE - Dyspnea

Outcome: 1 Paroxetine versus older ADs

Study or subgroup	Paroxetine n/N	older ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
1 versus imipramine					
29060/409	4/38	12/37		100.0 %	0.25 [0.07, 0.85]
Subtotal (95% CI)	**38**	**37**		**100.0 %**	**0.25 [0.07, 0.85]**
Total events: 4 (Paroxetine), 12 (older ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 2.22 (P = 0.027)					
Test for subgroup differences: Not applicable					

Analysis 40.2. Comparison 40 SE - Dyspnea, Outcome 2 Paroxetine versus other SSRIs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 40 SE - Dyspnea

Outcome: 2 Paroxetine versus other SSRIs

Study or subgroup	Paroxetine n/N	other SSRIs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
1 versus fluoxetine					
Chouinard 1999	13/102	6/101		100.0 %	2.31 [0.84, 6.35]
Subtotal (95% CI)	**102**	**101**		**100.0 %**	**2.31 [0.84, 6.35]**
Total events: 13 (Paroxetine), 6 (other SSRIs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.63 (P = 0.10)					
Test for subgroup differences: Not applicable					

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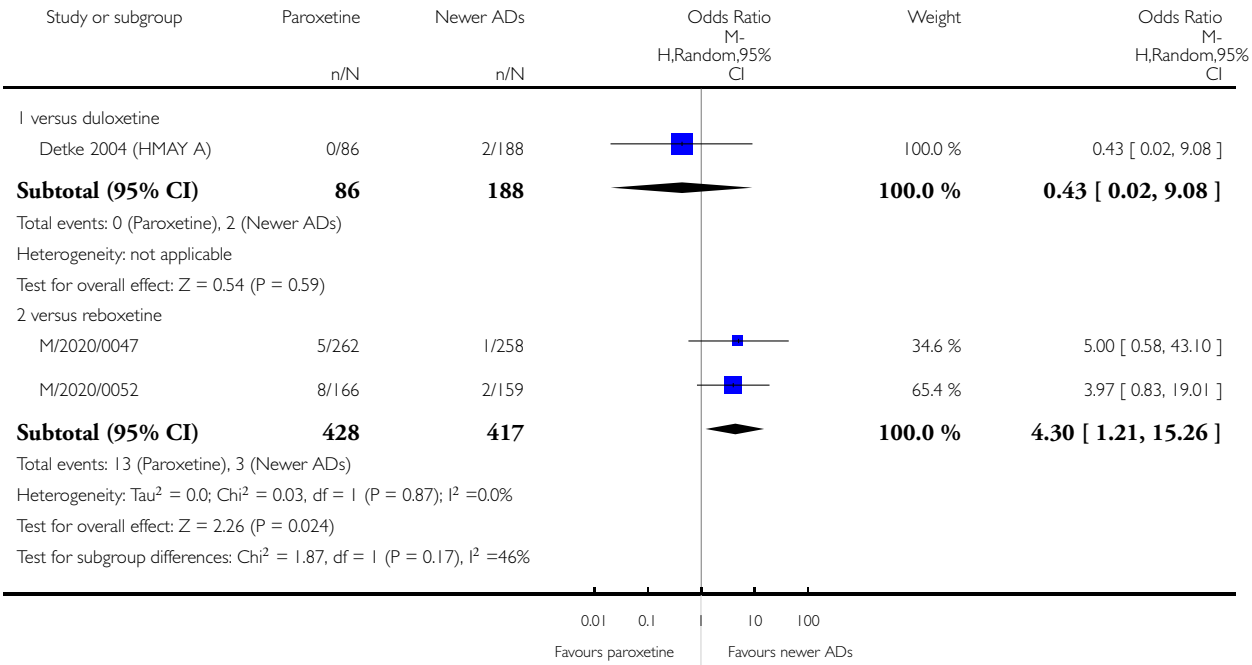
Analysis 40.3. Comparison 40 SE - Dyspnea, Outcome 3 Paroxetine versus newer or non-conventional ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 40 SE - Dyspnea

Outcome: 3 Paroxetine versus newer or non-conventional ADs



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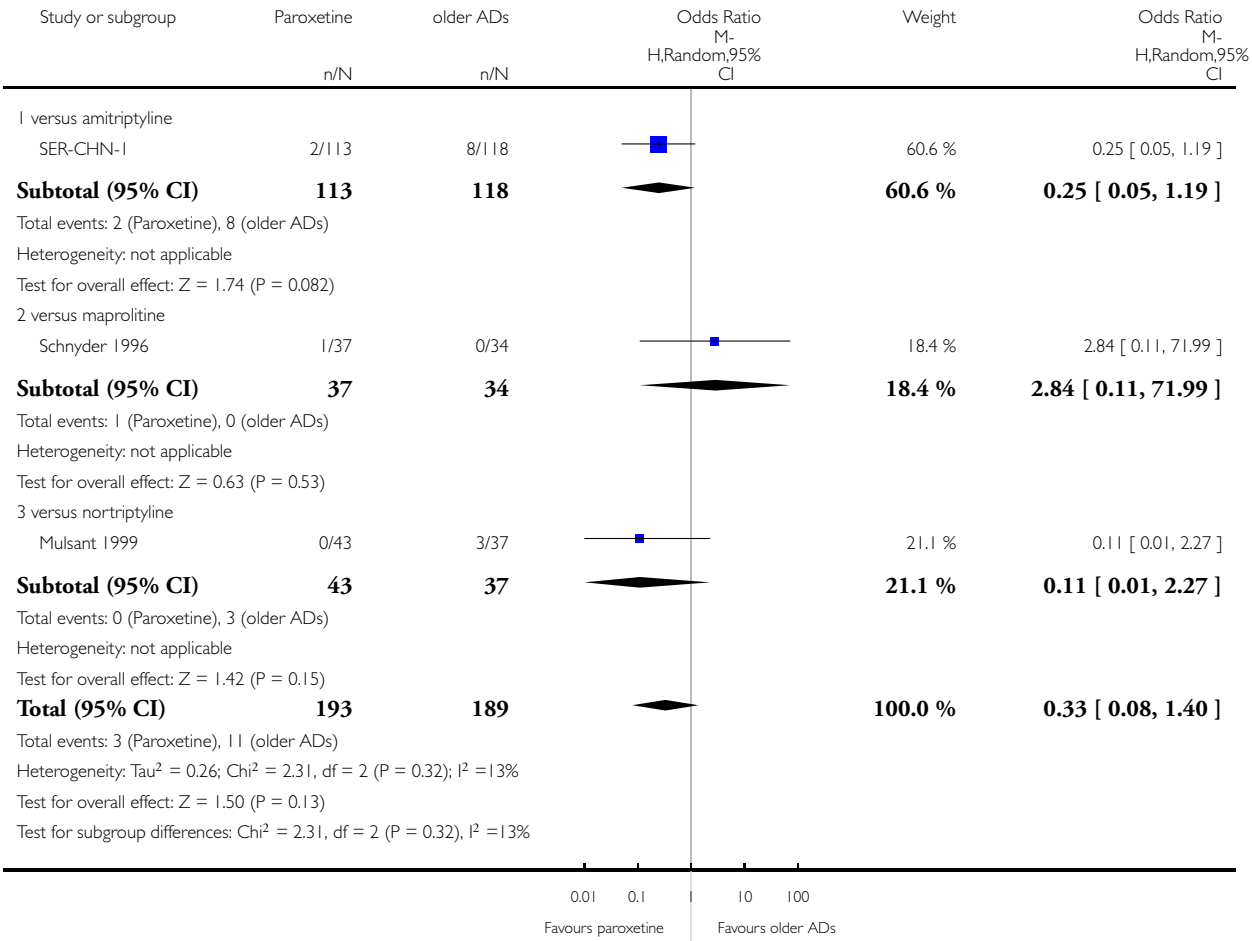
Analysis 41.1. Comparison 41 SE - ECG abnormailities, Outcome 1 Paroxetine versus older ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 41 SE - ECG abnormailities

Outcome: 1 Paroxetine versus older ADs



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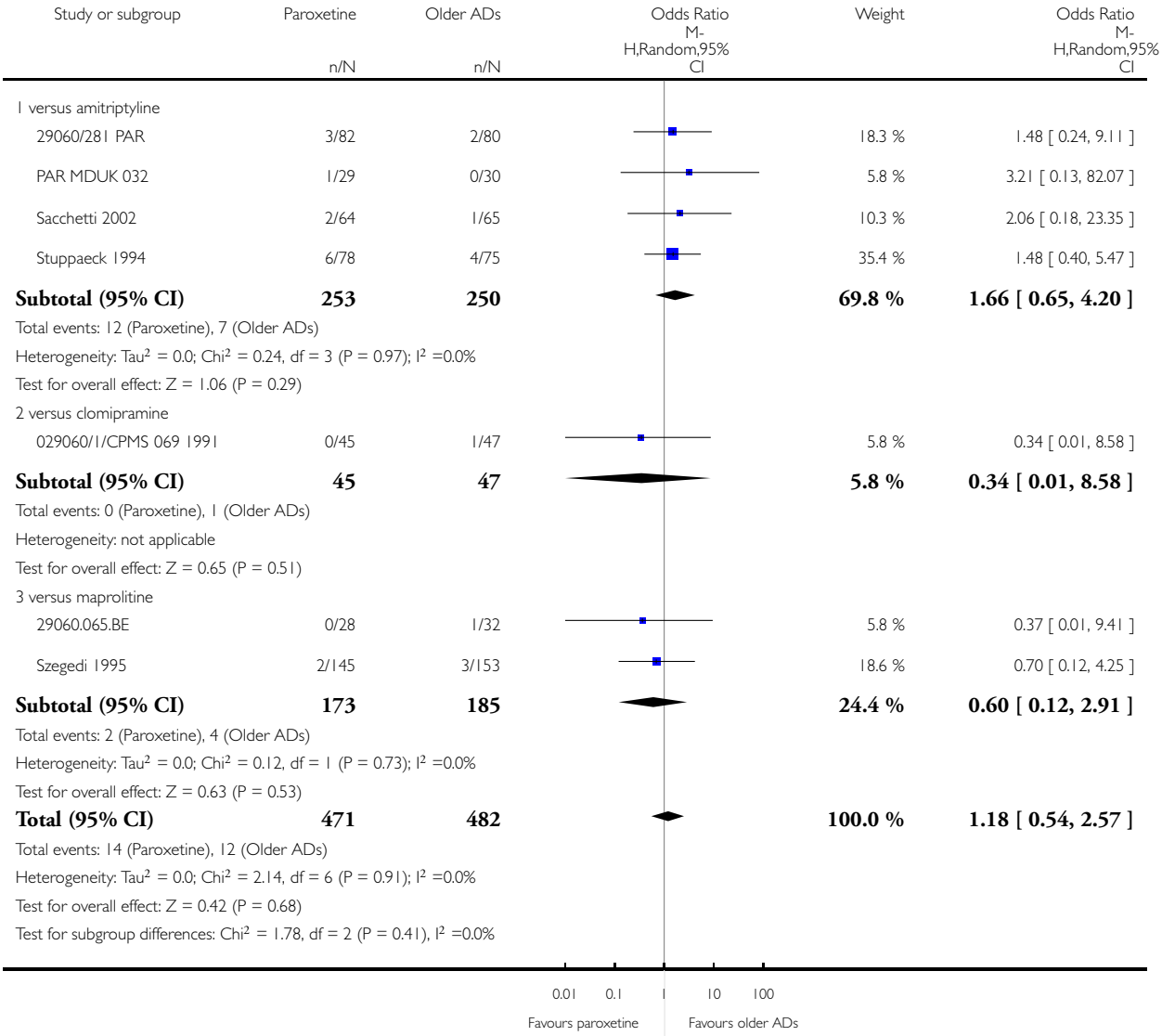
Analysis 42.1. Comparison 42 SE - Emotional lability, Outcome 1 Paroxetine versus older ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 42 SE - Emotional lability

Outcome: 1 Paroxetine versus older ADs



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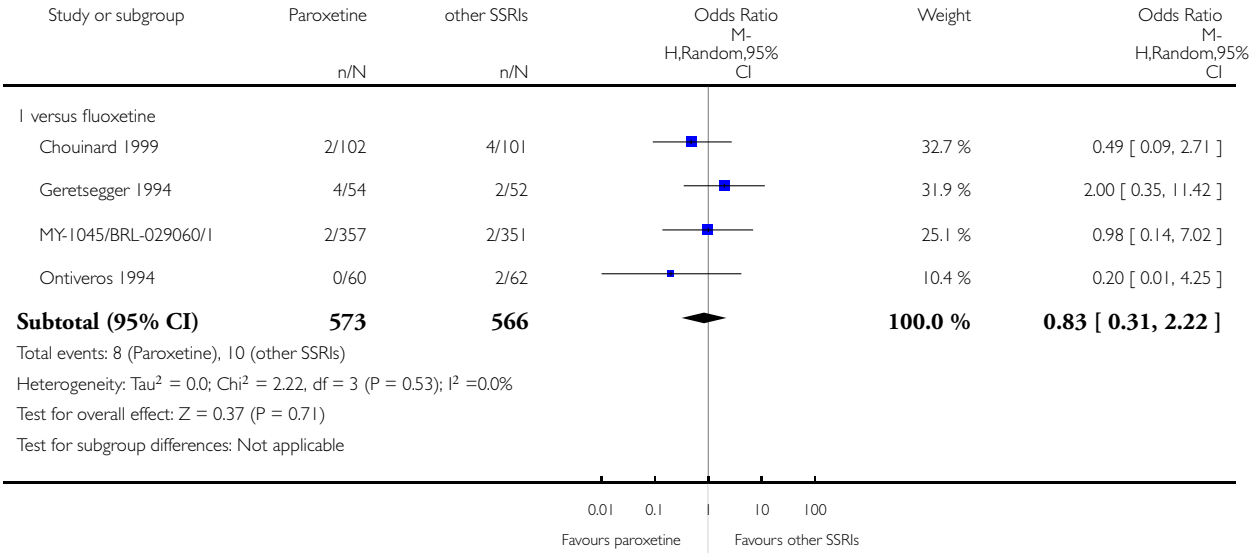
Analysis 42.2. Comparison 42 SE - Emotional lability, Outcome 2 Paroxetine versus other SSRIs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 42 SE - Emotional lability

Outcome: 2 Paroxetine versus other SSRIs



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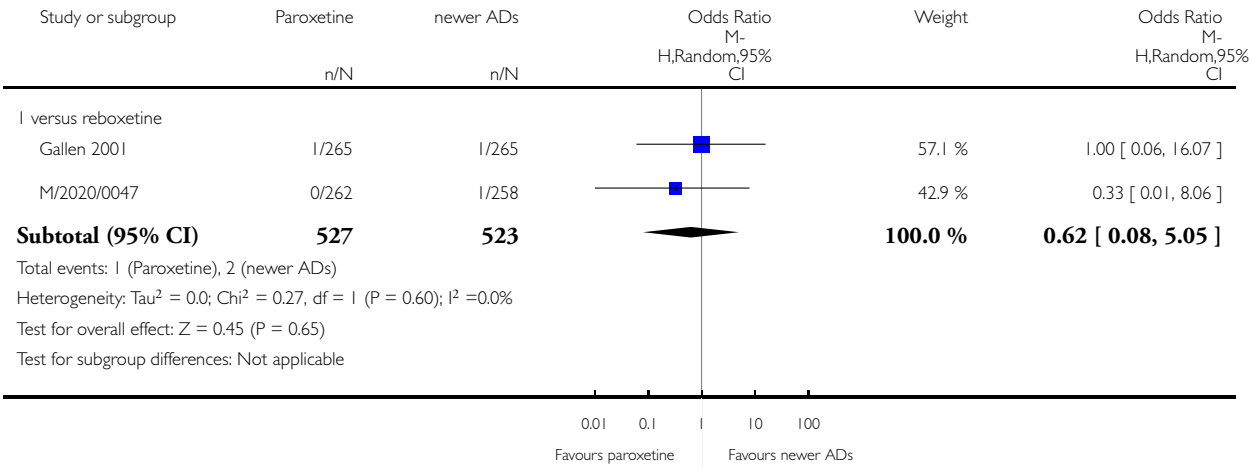
Analysis 42.3. Comparison 42 SE - Emotional lability, Outcome 3 Paroxetine versus newer or non-conventional ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 42 SE - Emotional lability

Outcome: 3 Paroxetine versus newer or non-conventional ADs



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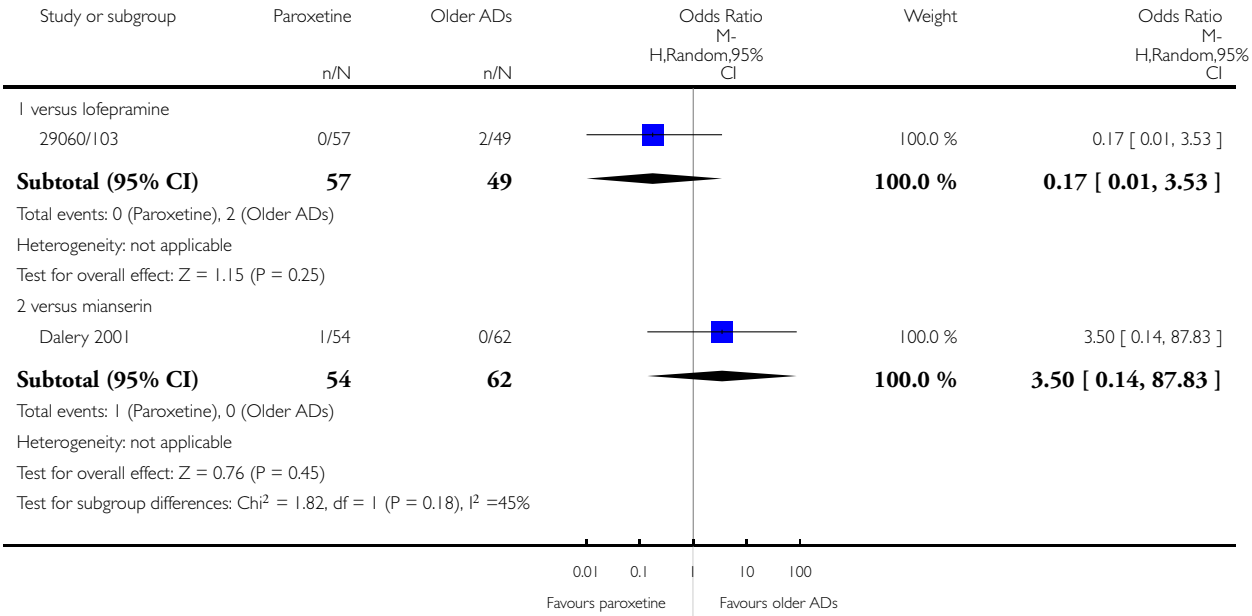
Analysis 43.1. Comparison 43 SE - Fatigue, Outcome 1 Paroxetine versus older ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 43 SE - Fatigue

Outcome: 1 Paroxetine versus older ADs



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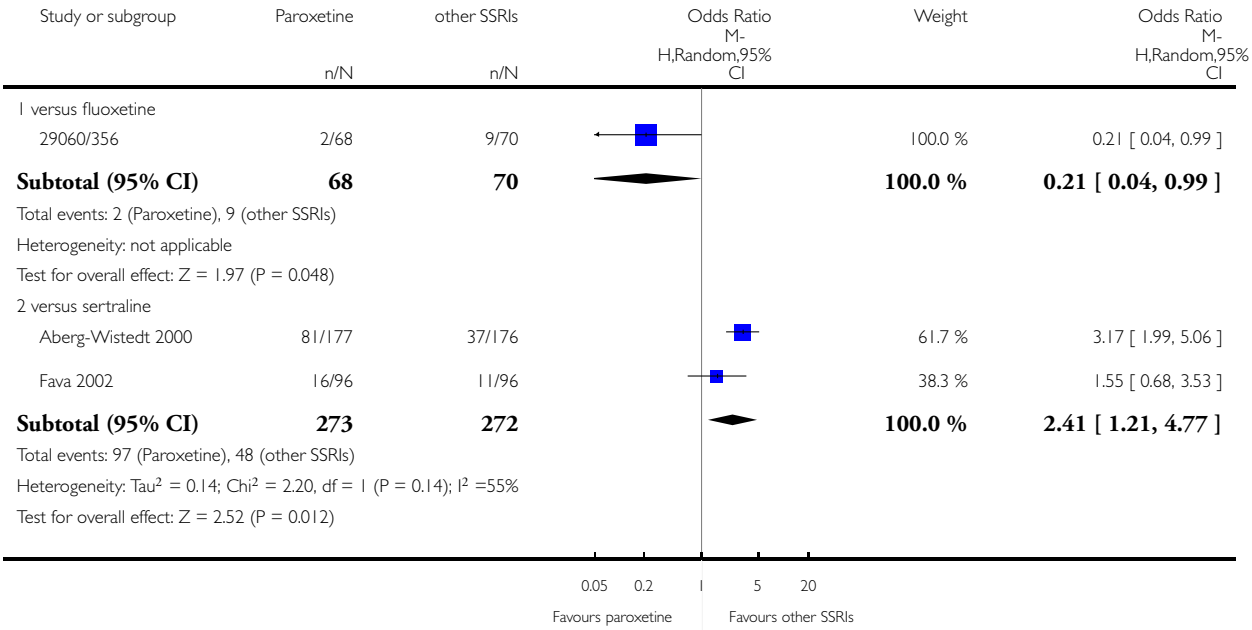
Analysis 43.2. Comparison 43 SE - Fatigue, Outcome 2 Paroxetine versus other SSRIs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 43 SE - Fatigue

Outcome: 2 Paroxetine versus other SSRIs



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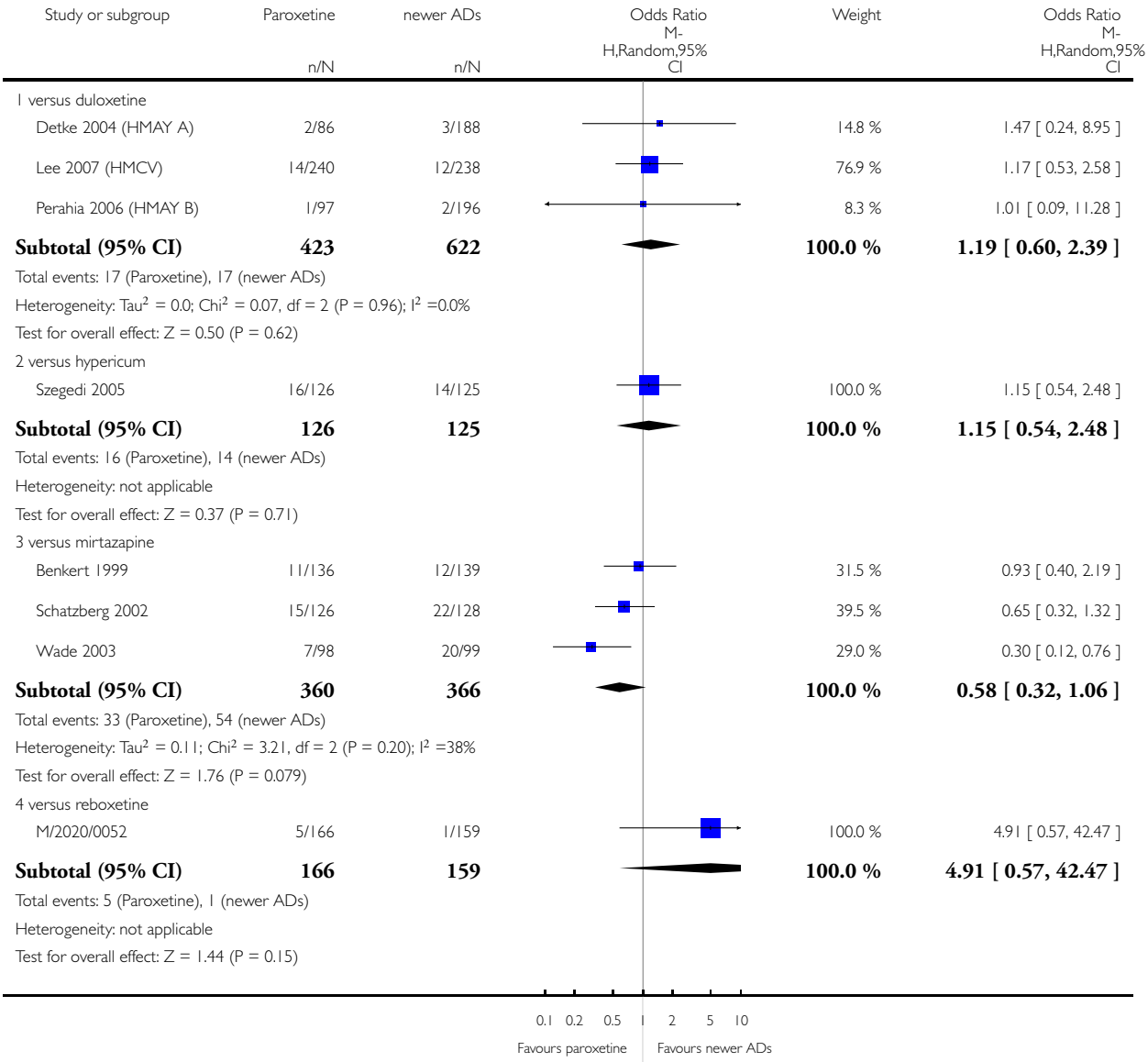
Analysis 43.3. Comparison 43 SE - Fatigue, Outcome 3 Paroxetine versus newer or non-conventional ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 43 SE - Fatigue

Outcome: 3 Paroxetine versus newer or non-conventional ADs



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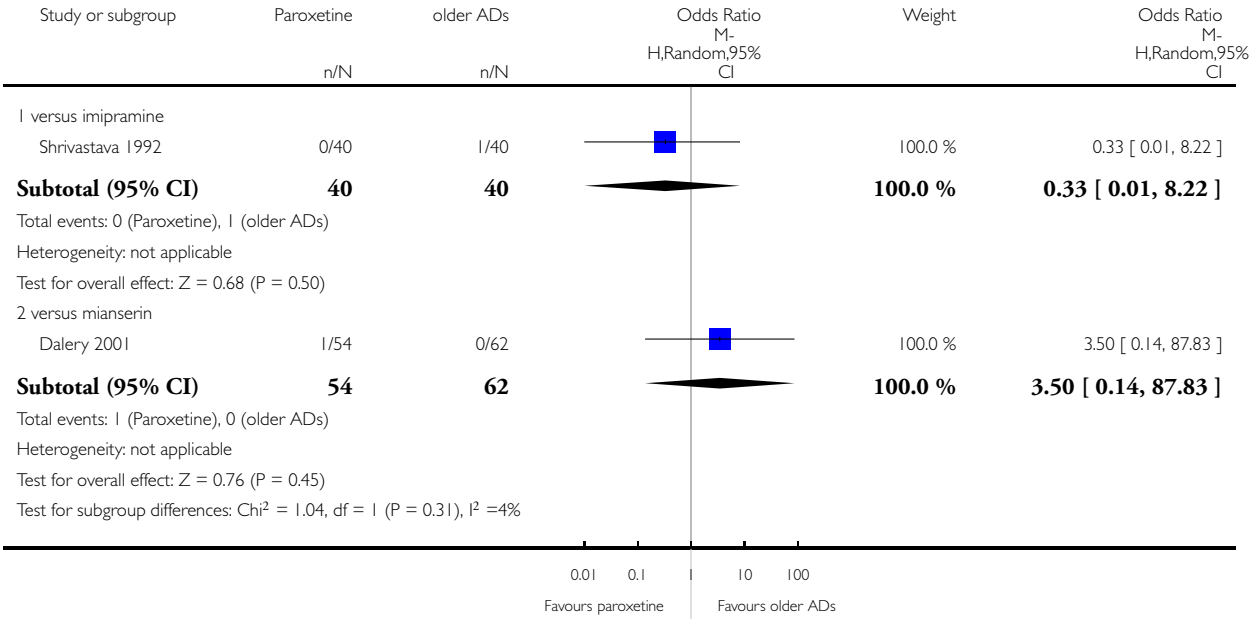
Analysis 44.1. Comparison 44 SE - Fever, Outcome 1 Paroxetine versus older ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 44 SE - Fever

Outcome: 1 Paroxetine versus older ADs



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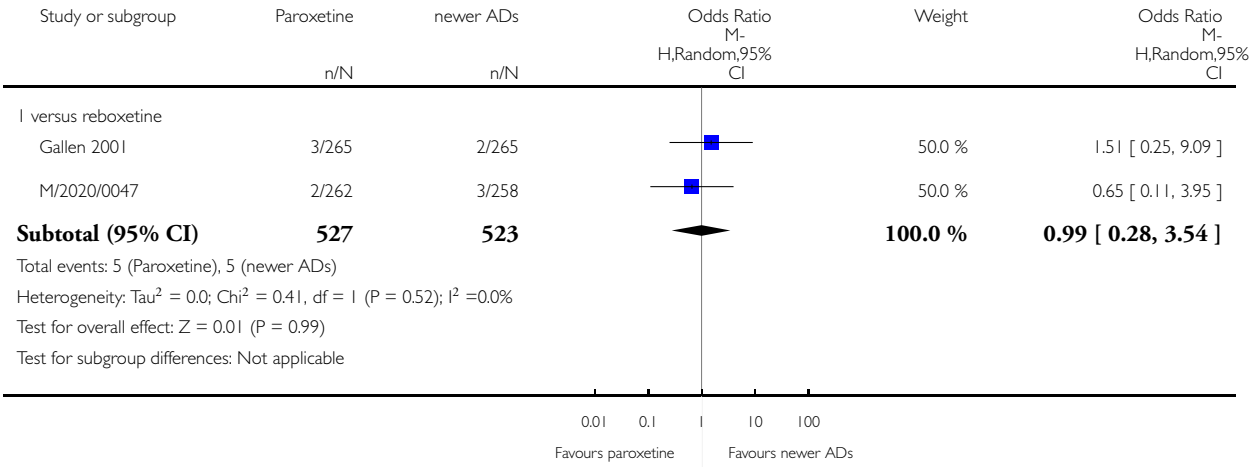
Analysis 44.2. Comparison 44 SE - Fever, Outcome 2 Paroxetine versus newer or non-conventional ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 44 SE - Fever

Outcome: 2 Paroxetine versus newer or non-conventional ADs

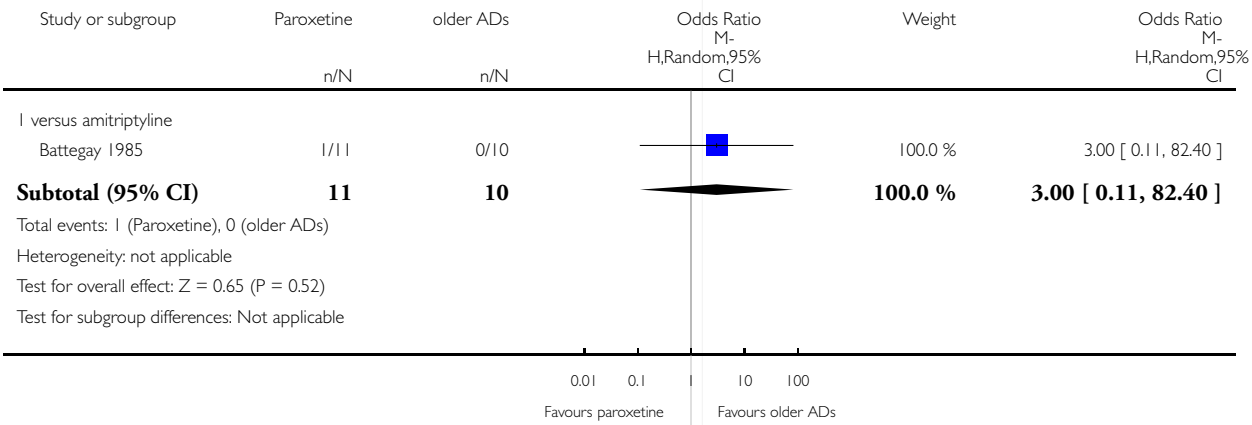


Analysis 45.1. Comparison 45 SE - Flatulence, Outcome 1 Paroxetine versus older ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 45 SE - Flatulence

Outcome: 1 Paroxetine versus older ADs



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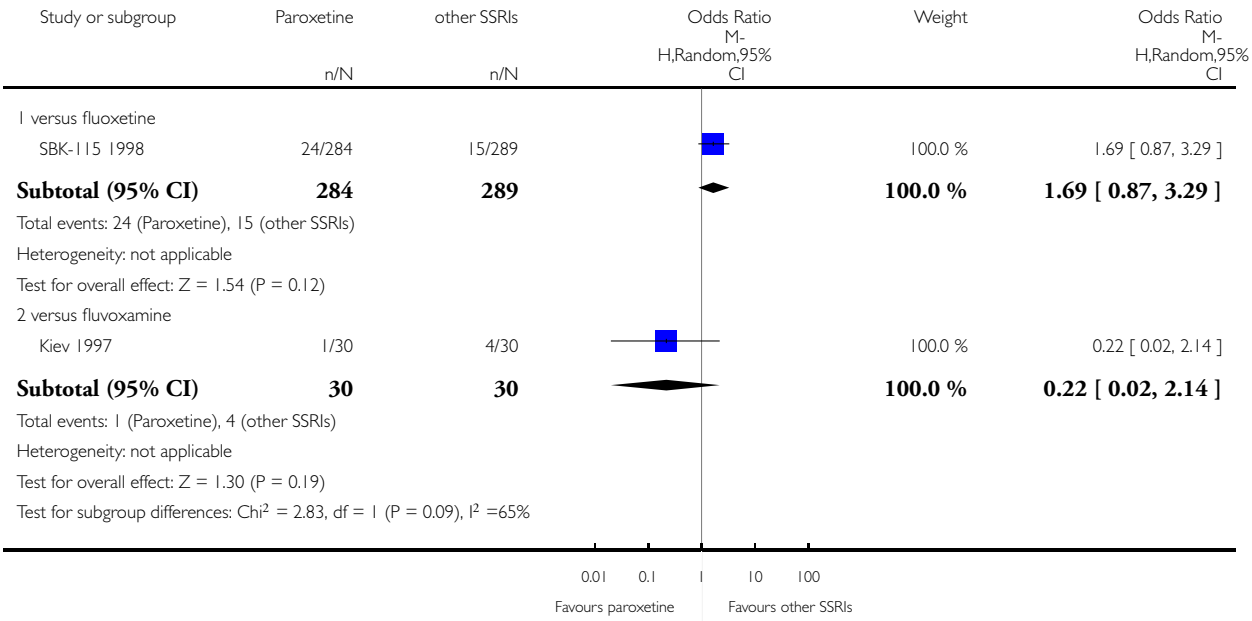
Analysis 45.2. Comparison 45 SE - Flatulence, Outcome 2 Paroxetine versus other SSRIs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 45 SE - Flatulence

Outcome: 2 Paroxetine versus other SSRIs



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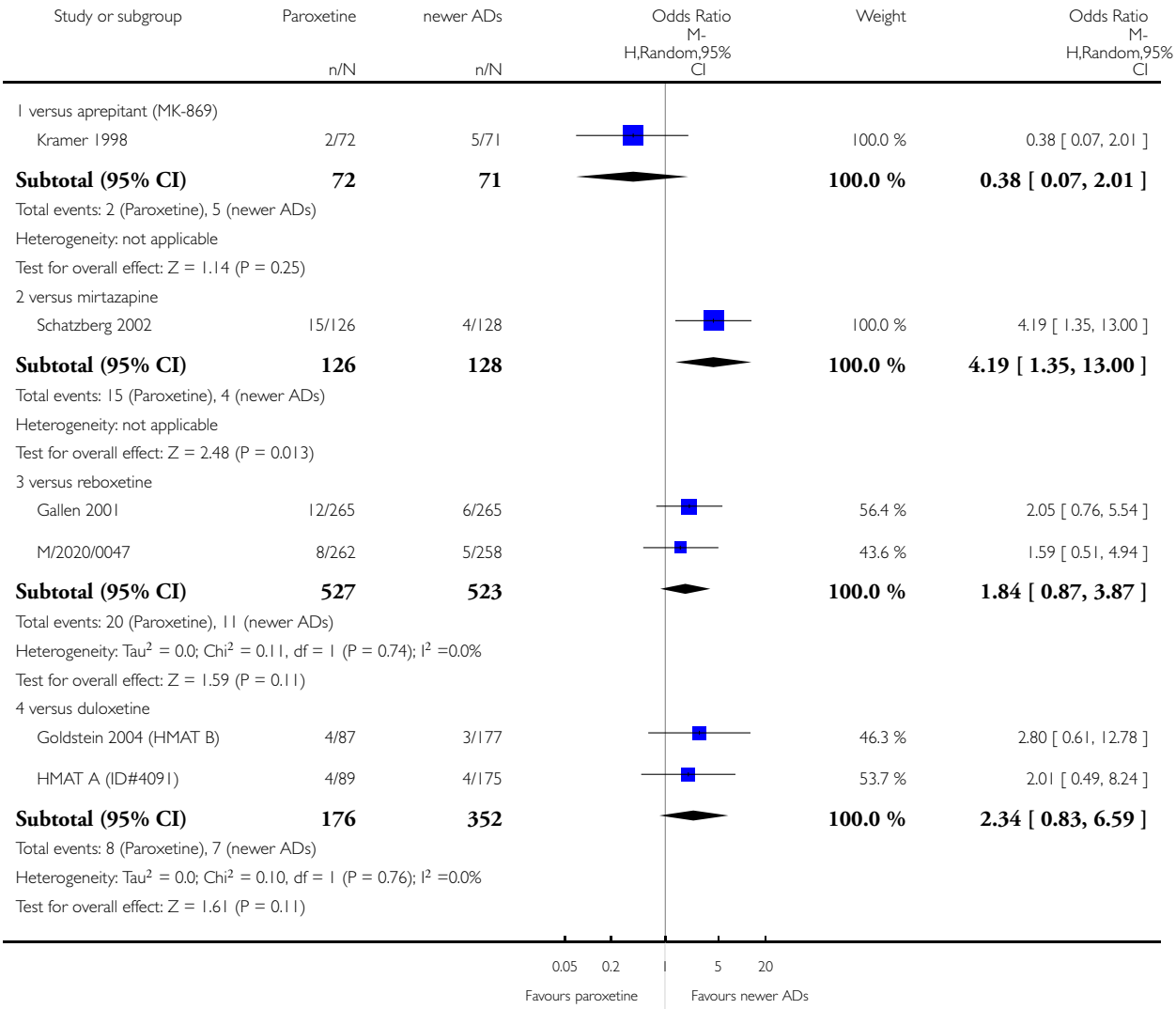
Analysis 45.3. Comparison 45 SE - Flatulence, Outcome 3 Paroxetine versus newer or non-conventional ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 45 SE - Flatulence

Outcome: 3 Paroxetine versus newer or non-conventional ADs



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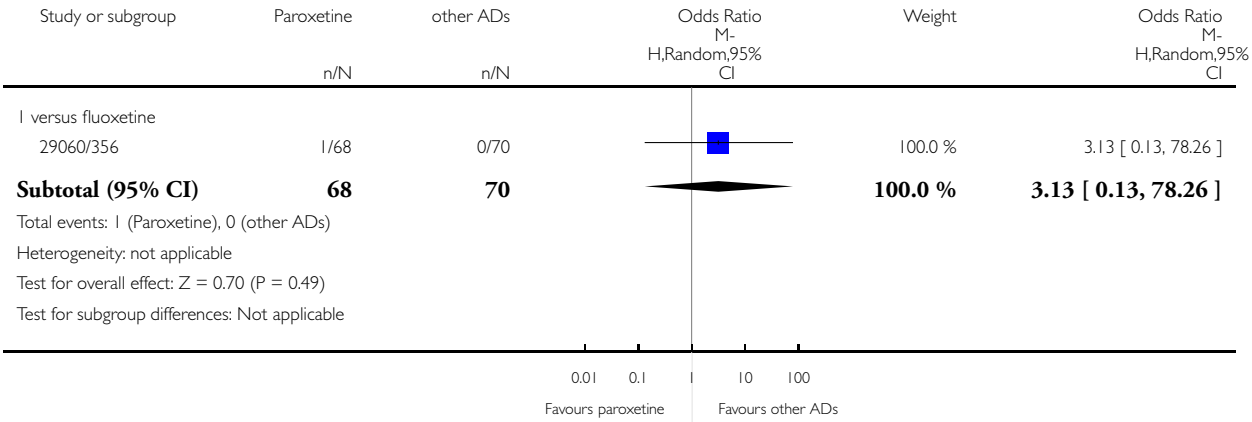
Analysis 46.1. Comparison 46 SE - Gastrointestinal disorder, Outcome 1 Appendicitis.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 46 SE - Gastrointestinal disorder

Outcome: 1 Appendicitis

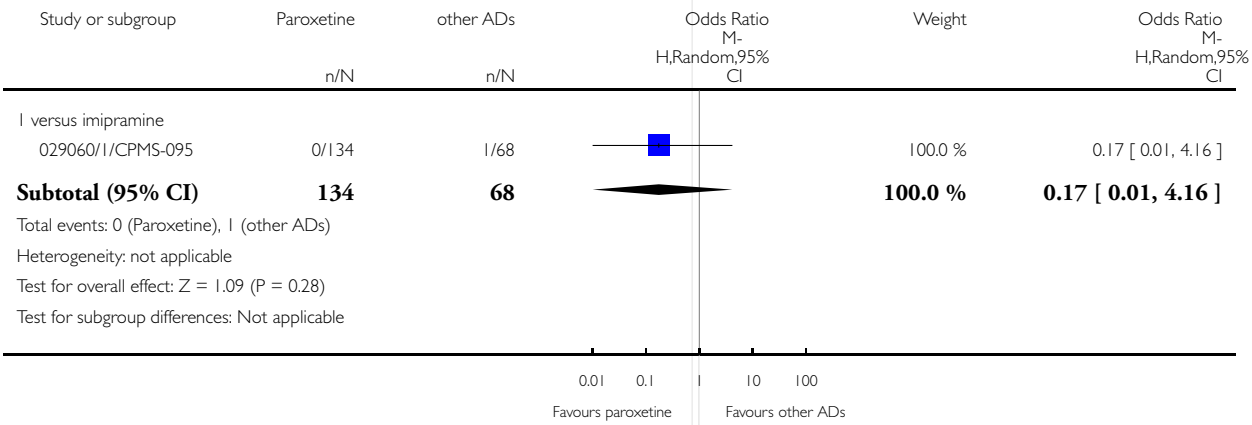


Analysis 46.2. Comparison 46 SE - Gastrointestinal disorder, Outcome 2 Cholelithiasis.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 46 SE - Gastrointestinal disorder

Outcome: 2 Cholelithiasis



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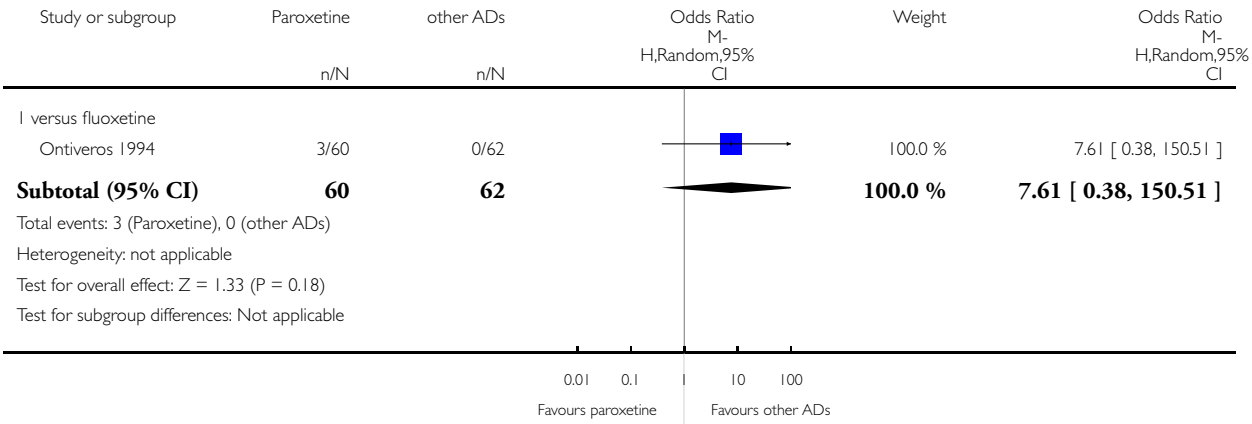
Analysis 46.3. Comparison 46 SE - Gastrointestinal disorder, Outcome 3 Colitis.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 46 SE - Gastrointestinal disorder

Outcome: 3 Colitis



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Analysis 46.4. Comparison 46 SE - Gastrointestinal disorder, Outcome 4 Eructation.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 46 SE - Gastrointestinal disorder

Outcome: 4 Eructation

Study or subgroup	Paroxetine n/N	other ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
1 versus reboxetine					
M/2020/0047	0/262	3/258		100.0 %	0.14 [0.01, 2.71]
Subtotal (95% CI)	**262**	**258**		**100.0 %**	**0.14 [0.01, 2.71]**
Total events: 0 (Paroxetine), 3 (other ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.30 (P = 0.19)					
Test for subgroup differences: Not applicable					

Analysis 46.5. Comparison 46 SE - Gastrointestinal disorder, Outcome 5 Melena.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 46 SE - Gastrointestinal disorder

Outcome: 5 Melena

Study or subgroup	Paroxetine n/N	other ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
1 versus maprolitine					
29060.065.BE	1/28	0/32		100.0 %	3.55 [0.14, 90.59]
Subtotal (95% CI)	**28**	**32**		**100.0 %**	**3.55 [0.14, 90.59]**
Total events: 1 (Paroxetine), 0 (other ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.77 (P = 0.44)					
Test for subgroup differences: Not applicable					

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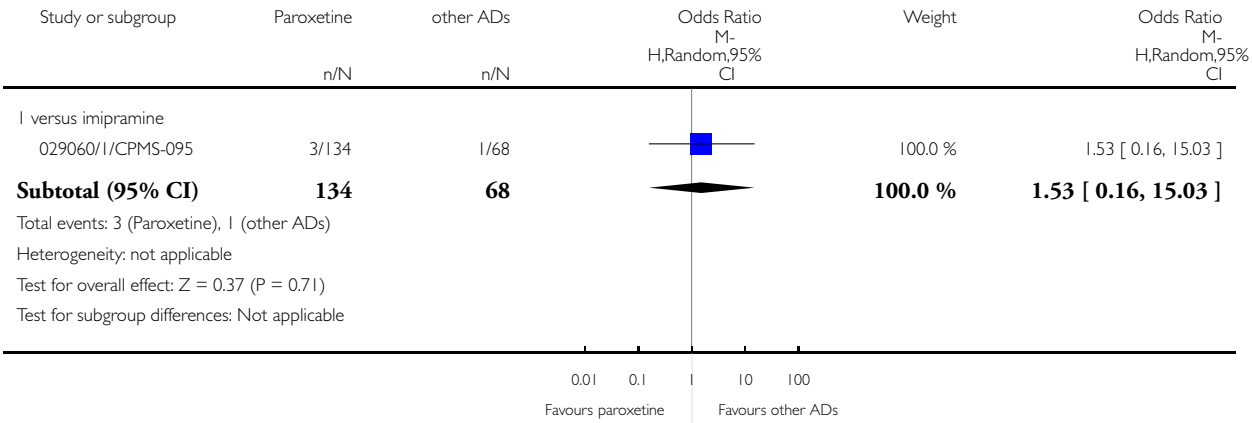
Analysis 46.6. Comparison 46 SE - Gastrointestinal disorder, Outcome 6 Gastritis.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 46 SE - Gastrointestinal disorder

Outcome: 6 Gastritis



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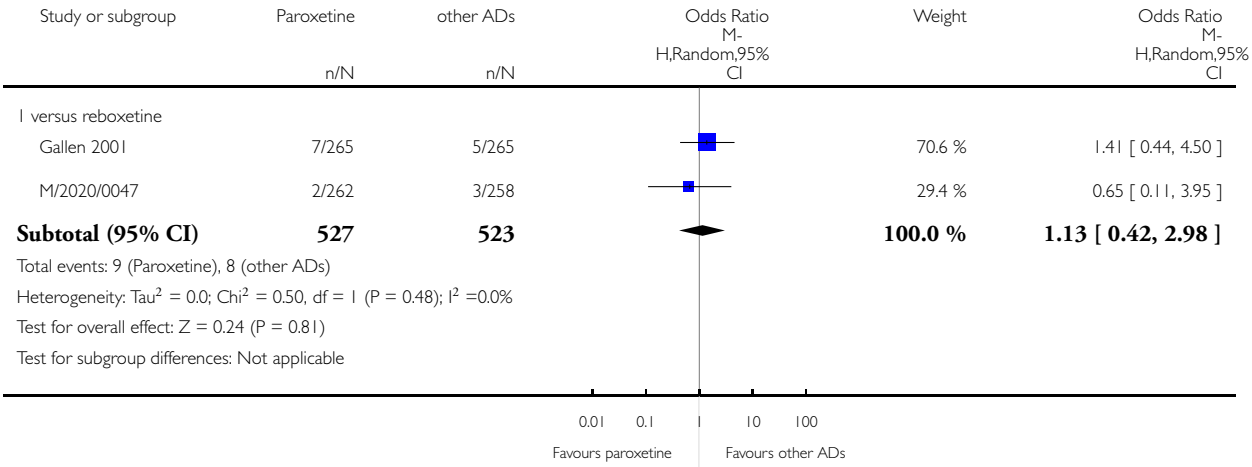
Analysis 46.7. Comparison 46 SE - Gastrointestinal disorder, Outcome 7 Gastroenteritis.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 46 SE - Gastrointestinal disorder

Outcome: 7 Gastroenteritis

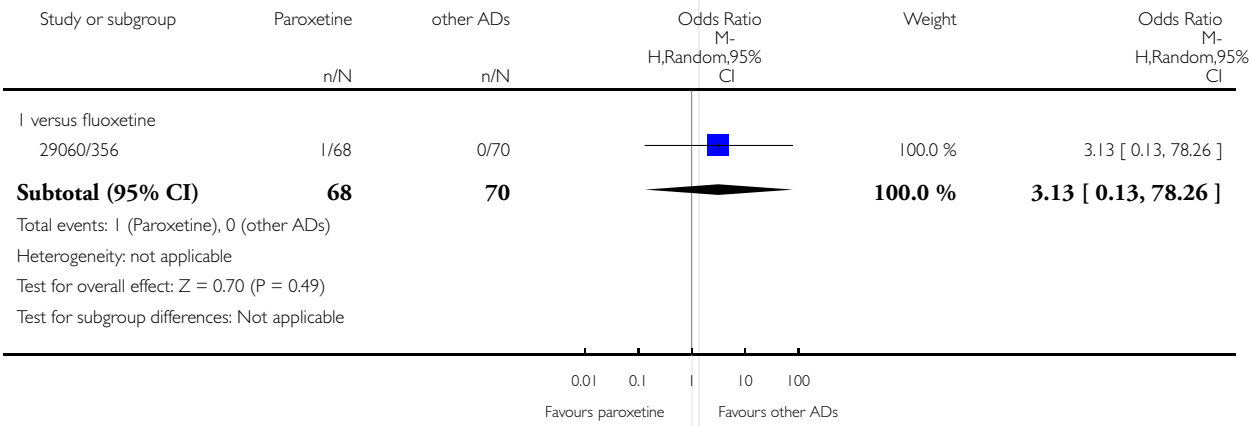


Analysis 46.8. Comparison 46 SE - Gastrointestinal disorder, Outcome 8 Intestinal obstruction.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 46 SE - Gastrointestinal disorder

Outcome: 8 Intestinal obstruction



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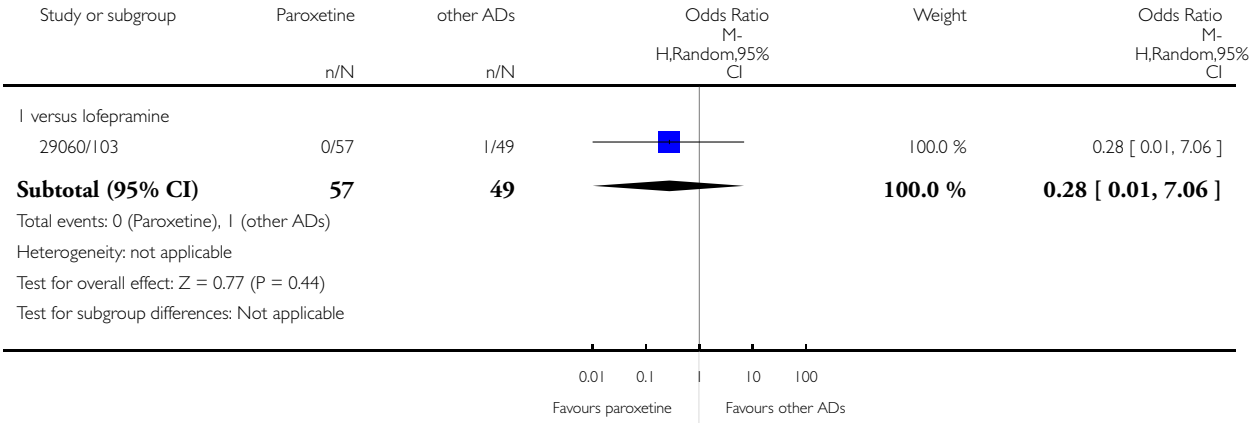
Analysis 46.9. Comparison 46 SE - Gastrointestinal disorder, Outcome 9 Intestinal perforation.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 46 SE - Gastrointestinal disorder

Outcome: 9 Intestinal perforation



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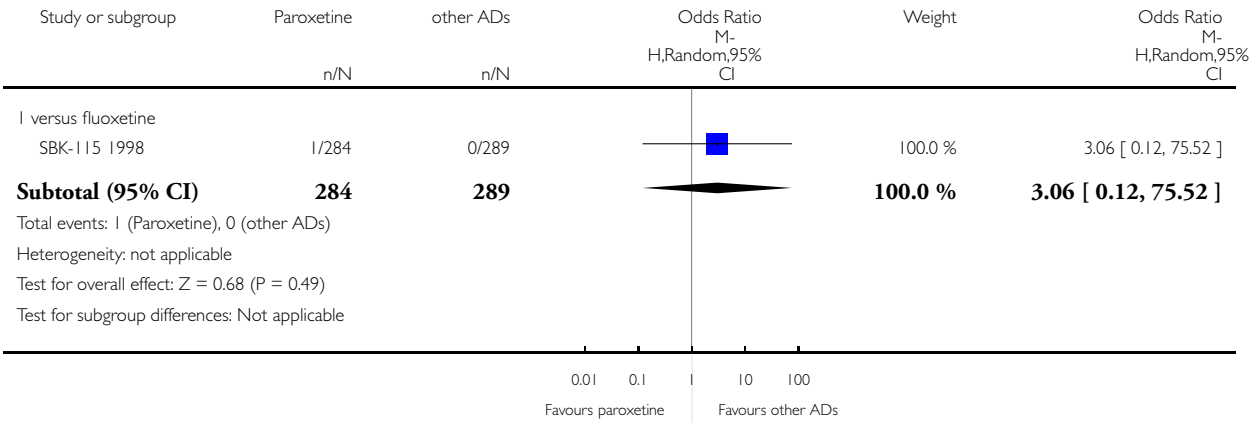
Analysis 46.10. Comparison 46 SE - Gastrointestinal disorder, Outcome 10 Peptic ulcer hemorrhage.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 46 SE - Gastrointestinal disorder

Outcome: 10 Peptic ulcer hemorrhage



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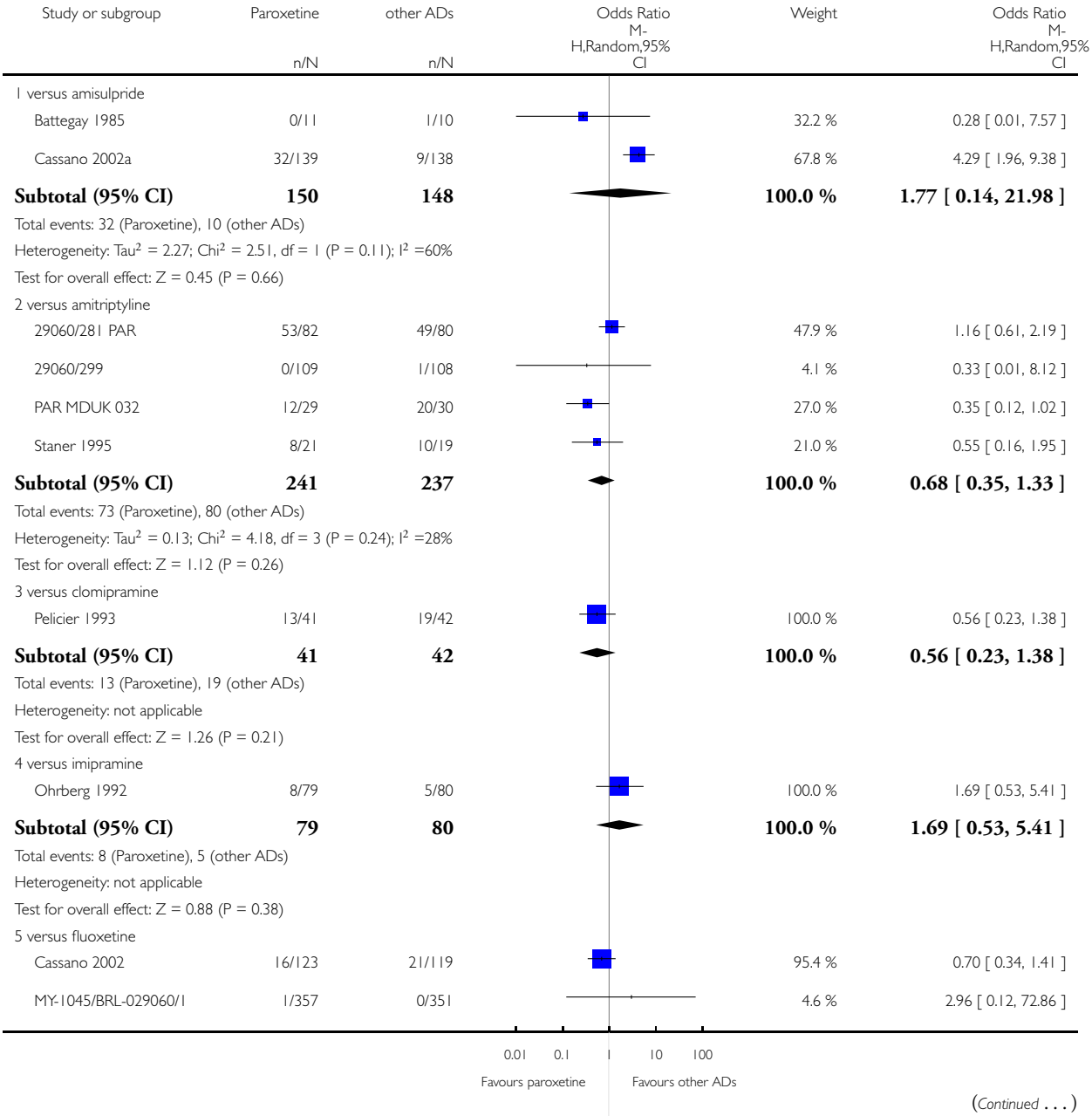
Analysis 46.11. Comparison 46 SE - Gastrointestinal disorder, Outcome 11 NOS.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 46 SE - Gastrointestinal disorder

Outcome: 11 NOS



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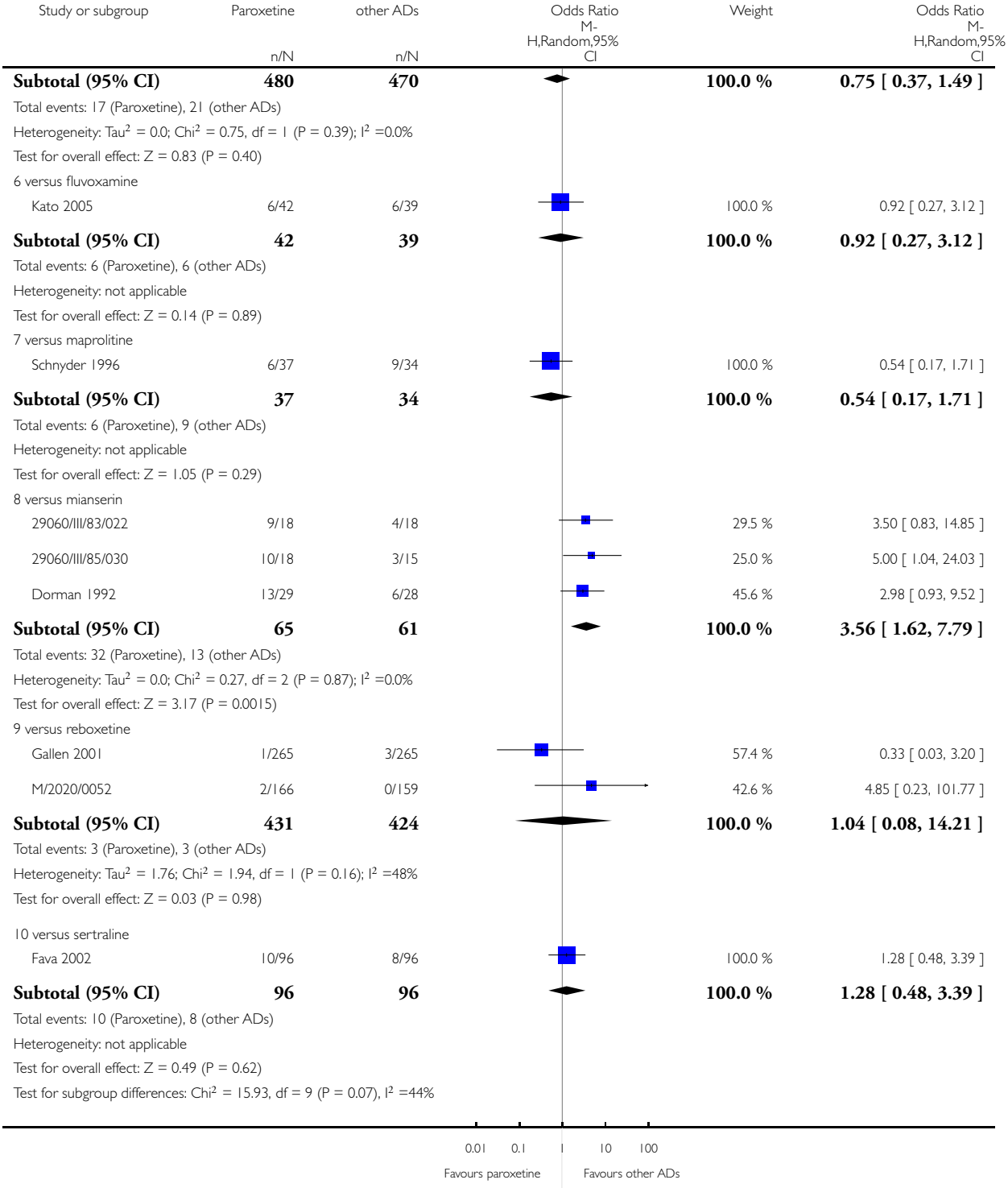

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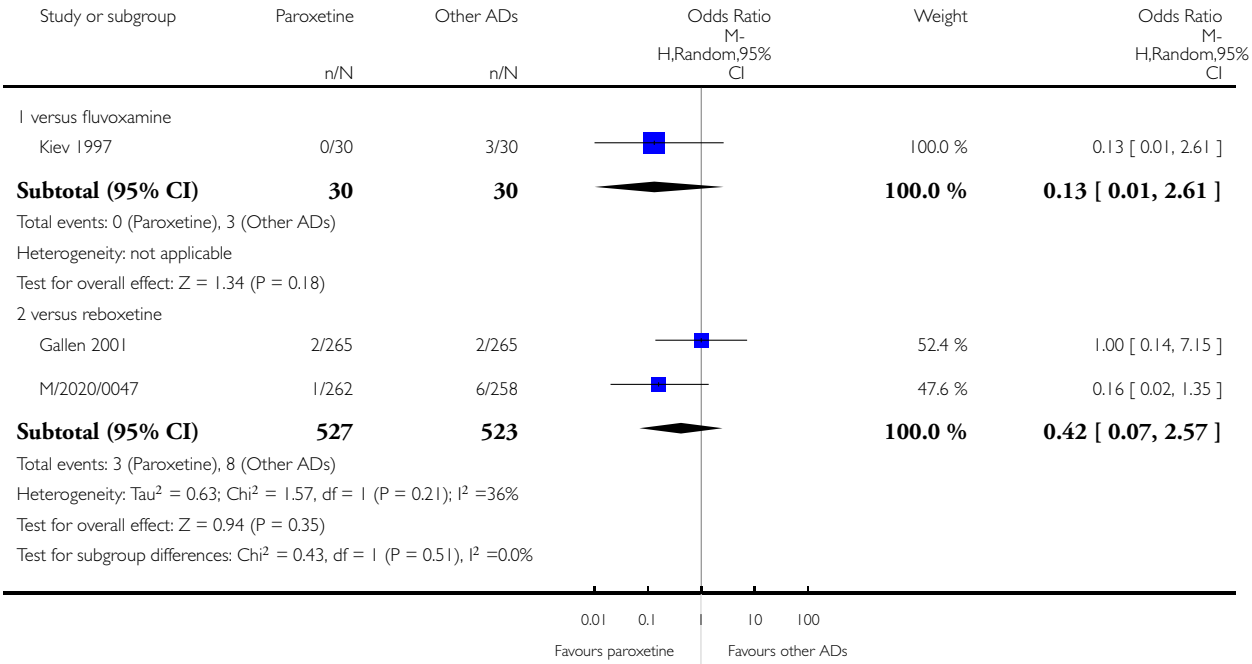
Analysis 47.1. Comparison 47 SE - Gynecological, Outcome 1 Dysmenorrhea.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 47 SE - Gynecological

Outcome: 1 Dysmenorrhea



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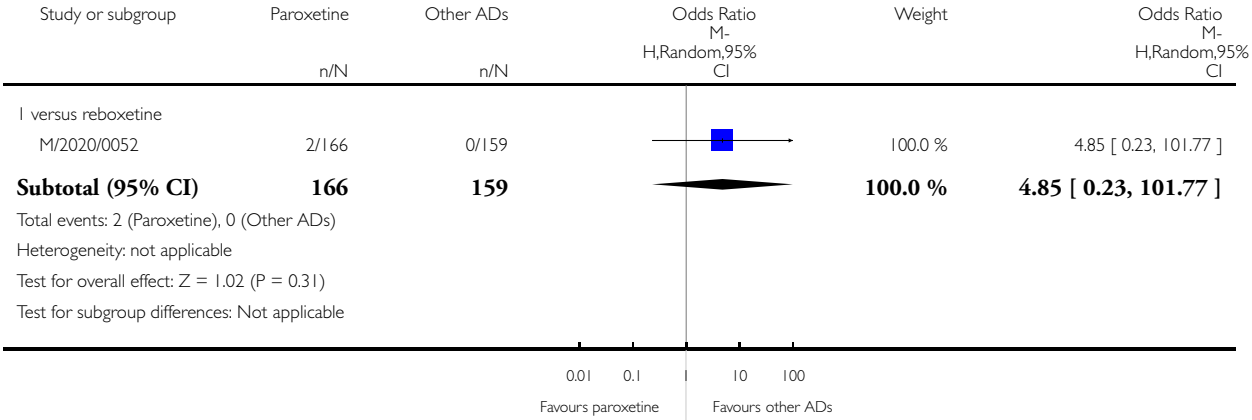
Analysis 47.2. Comparison 47 SE - Gynecological, Outcome 2 Mestrual disorder.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 47 SE - Gynecological

Outcome: 2 Mestrual disorder

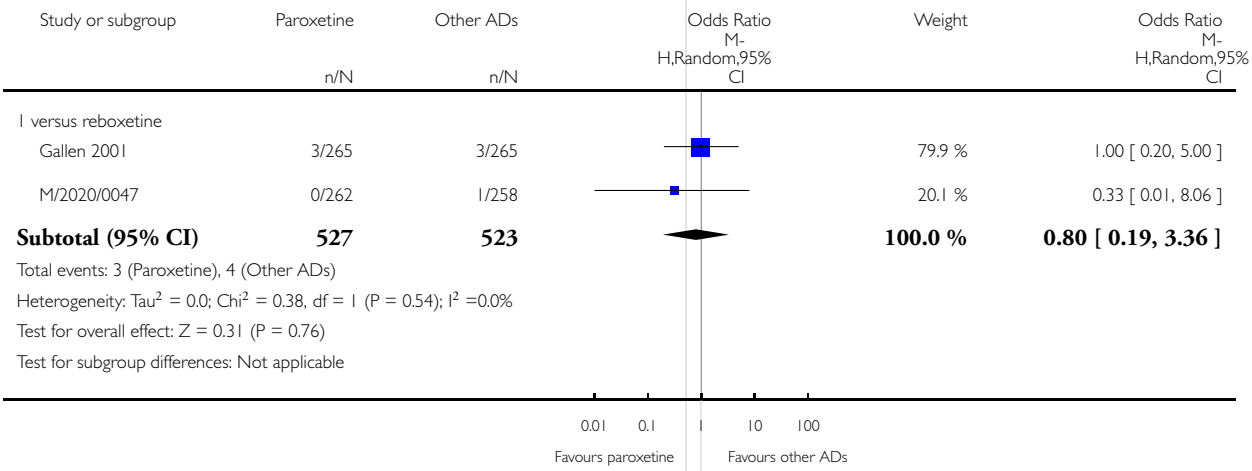


Analysis 47.3. Comparison 47 SE - Gynecological, Outcome 3 Vaginal moniliasis.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 47 SE - Gynecological

Outcome: 3 Vaginal moniliasis



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Analysis 47.4. Comparison 47 SE - Gynecological, Outcome 4 Ectopic pregnancy.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 47 SE - Gynecological

Outcome: 4 Ectopic pregnancy

Study or subgroup	Paroxetine n/N	Other ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
1 versus fluoxetine					
SBK-115 1998	0/284	2/289		100.0 %	0.20 [0.01, 4.23]
Subtotal (95% CI)	**284**	**289**		**100.0 %**	**0.20 [0.01, 4.23]**
Total events: 0 (Paroxetine), 2 (Other ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.03 (P = 0.30)					
Test for subgroup differences: Not applicable					

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Analysis 47.5. Comparison 47 SE - Gynecological, Outcome 5 Polycystic granuloma.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 47 SE - Gynecological

Outcome: 5 Polycystic granuloma

Study or subgroup	Paroxetine n/N	Other ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
1 versus fluoxetine					
SBK-115 1998	0/284	1/289		100.0 %	0.34 [0.01, 8.33]
Subtotal (95% CI)	**284**	**289**		**100.0 %**	**0.34 [0.01, 8.33]**
Total events: 0 (Paroxetine), 1 (Other ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.66 (P = 0.51)					
Test for subgroup differences: Not applicable					

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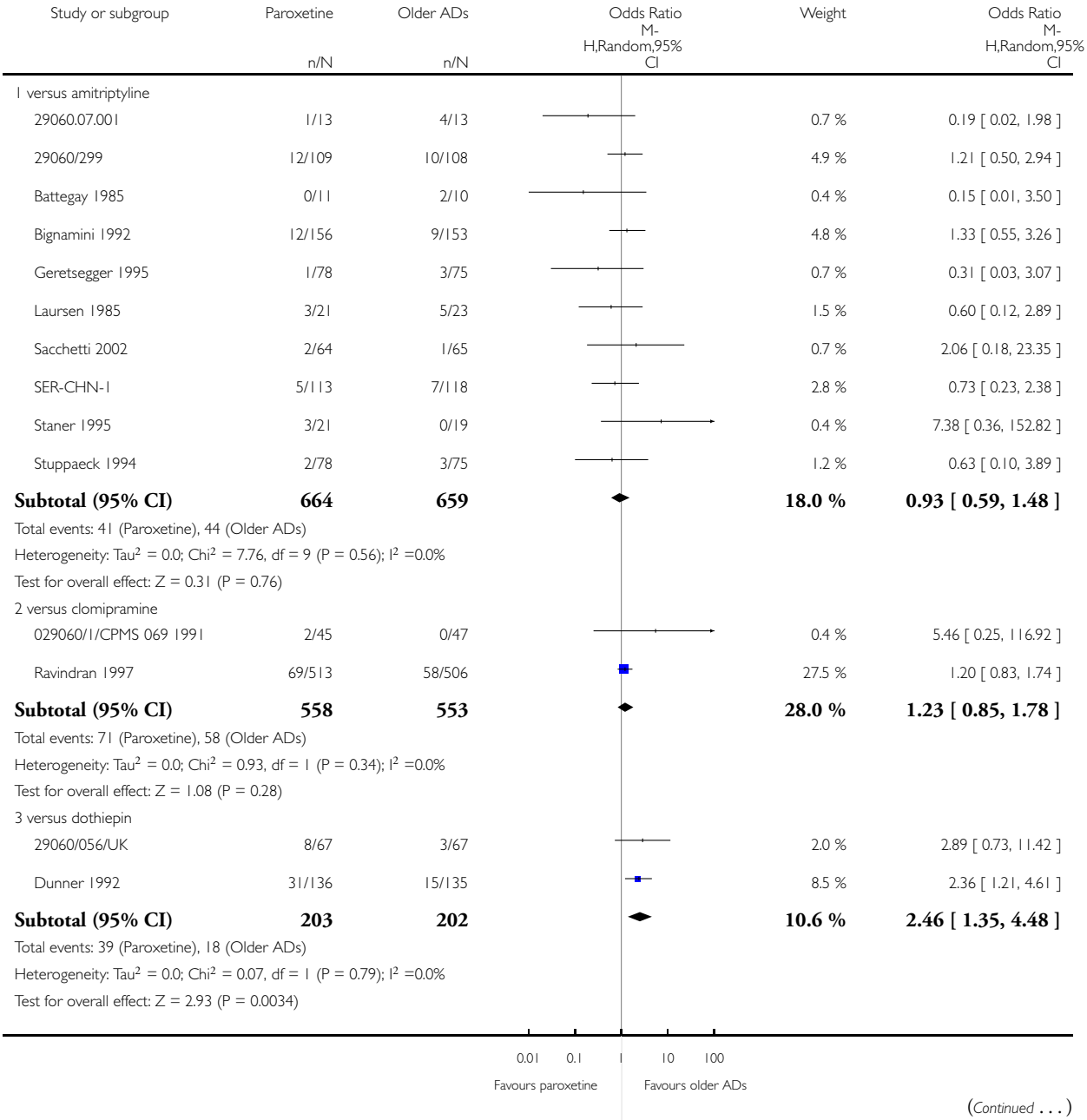
Analysis 48.1. Comparison 48 SE - Headache, Outcome 1 Paroxetine versus older ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 48 SE - Headache

Outcome: 1 Paroxetine versus older ADs



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Study or subgroup	Paroxetine n/N	Older ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
4 versus imipramine					
029060/1/CPMS-095	12/134	5/68		3.2 %	1.24 [0.42, 3.67]
29060/409	7/38	1/37		0.8 %	8.13 [0.95, 69.76]
Cohn 1990	4/40	7/40		2.2 %	0.52 [0.14, 1.95]
Fabre 1992	12/40	11/40		4.1 %	1.13 [0.43, 2.98]
Feighner 1989	12/40	10/40		4.0 %	1.29 [0.48, 3.44]
Ohrberg 1992	14/79	9/80		4.7 %	1.70 [0.69, 4.19]
Peselow 1989	8/40	4/39		2.3 %	2.19 [0.60, 7.97]
Shrivastava 1992	7/40	8/40		3.0 %	0.85 [0.28, 2.61]
Subtotal (95% CI)	**451**	**384**		**24.4 %**	**1.29 [0.87, 1.93]**
Total events: 76 (Paroxetine), 55 (Older ADs)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 6.26$, df = 7 (P = 0.51); $I^2 = 0.0\%$					
Test for overall effect: Z = 1.28 (P = 0.20)					
5 versus lofepramine					
29060/103	6/57	4/49		2.2 %	1.32 [0.35, 4.99]
Moon 1996	4/60	2/62		1.3 %	2.14 [0.38, 12.16]
Subtotal (95% CI)	**117**	**111**		**3.4 %**	**1.58 [0.55, 4.54]**
Total events: 10 (Paroxetine), 6 (Older ADs)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.19$, df = 1 (P = 0.67); $I^2 = 0.0\%$					
Test for overall effect: Z = 0.85 (P = 0.39)					
6 versus maprolitine					
29060.065.BE	10/28	8/32		3.1 %	1.67 [0.55, 5.07]
Schnyder 1996	2/37	3/34		1.1 %	0.59 [0.09, 3.77]
Szegedi 1995	39/145	19/143		10.4 %	2.40 [1.31, 4.40]
Subtotal (95% CI)	**210**	**209**		**14.6 %**	**1.96 [1.13, 3.39]**
Total events: 51 (Paroxetine), 30 (Older ADs)					
Heterogeneity: $Tau^2 = 0.02$; $Chi^2 = 2.12$, df = 2 (P = 0.35); $I^2 = 6\%$					
Test for overall effect: Z = 2.41 (P = 0.016)					
7 versus mianserin					
29060III/85/038	0/30	1/29		0.4 %	0.31 [0.01, 7.96]
Dalery 2001	2/54	1/62		0.6 %	2.35 [0.21, 26.62]
Subtotal (95% CI)	**84**	**91**		**1.0 %**	**1.14 [0.16, 7.93]**
Total events: 2 (Paroxetine), 2 (Older ADs)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.96$, df = 1 (P = 0.33); $I^2 = 0.0\%$					
Test for overall effect: Z = 0.13 (P = 0.90)					
Total (95% CI)	**2287**	**2209**		**100.0 %**	**1.38 [1.13, 1.68]**
Total events: 290 (Paroxetine), 213 (Older ADs)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 27.16$, df = 28 (P = 0.51); $I^2 = 0.0\%$					

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Study or subgroup	Paroxetine n/N	Older ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Test for overall effect: Z = 3.21 (P = 0.0013)					
Test for subgroup differences: Chi² = 8.47, df = 6 (P = 0.21), I² =29%					

Analysis 48.2. Comparison 48 SE - Headache, Outcome 2 Paroxetine versus other SSRIs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 48 SE - Headache

Outcome: 2 Paroxetine versus other SSRIs

Study or subgroup	Paroxetine n/N	other SSRIs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
1 versus citalopram					
Jefferson 2001 29060/785	44/199	54/207		100.0 %	0.80 [0.51, 1.27]
Subtotal (95% CI)	**199**	**207**		**100.0 %**	**0.80 [0.51, 1.27]**
Total events: 44 (Paroxetine), 54 (other SSRIs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.94 (P = 0.35)					
2 versus escitalopram					
Boulenger 2006	46/225	56/229		100.0 %	0.79 [0.51, 1.24]
Subtotal (95% CI)	**225**	**229**		**100.0 %**	**0.79 [0.51, 1.24]**
Total events: 46 (Paroxetine), 56 (other SSRIs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.02 (P = 0.31)					
3 versus fluoxetine					
29060/356	32/68	32/70		8.0 %	1.06 [0.54, 2.06]
Chouinard 1999	37/102	37/101		11.0 %	0.98 [0.56, 1.74]
Gagiano 1993	24/45	21/45		5.2 %	1.31 [0.57, 2.99]
Geretsegger 1994	4/54	3/52		1.5 %	1.31 [0.28, 6.14]

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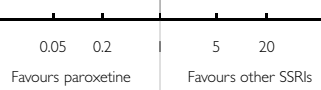
Study or subgroup	Paroxetine n/N	other SSRIs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
MY-1045/BRL-029060/1	137/357	130/351		38.7 %	1.06 [0.78, 1.43]
Ontiveros 1994	6/60	13/62		3.3 %	0.42 [0.15, 1.19]
SBK-115 1998	104/284	105/289		30.9 %	1.01 [0.72, 1.42]
Tignol 1993	3/89	3/87		1.4 %	0.98 [0.19, 4.98]
Subtotal (95% CI)	**1059**	**1057**		**100.0 %**	**1.02 [0.84, 1.23]**
Total events: 347 (Paroxetine), 344 (other SSRIs)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 3.33$, df = 7 (P = 0.85); $I^2 = 0.0\%$					
Test for overall effect: Z = 0.18 (P = 0.86)					
4 versus fluvoxamine					
Kato 2005	0/42	2/39		31.7 %	0.18 [0.01, 3.79]
Kiev 1997	17/30	12/30		68.3 %	1.96 [0.70, 5.48]
Subtotal (95% CI)	**72**	**69**		**100.0 %**	**0.91 [0.10, 8.45]**
Total events: 17 (Paroxetine), 14 (other SSRIs)					
Heterogeneity: $Tau^2 = 1.61$; $Chi^2 = 2.18$, df = 1 (P = 0.14); $I^2 = 54\%$					
Test for overall effect: Z = 0.08 (P = 0.94)					
5 versus sertraline					
Aberg-Wistedt 2000	61/177	68/176		69.7 %	0.84 [0.54, 1.29]
Fava 2002	21/96	27/96		30.3 %	0.72 [0.37, 1.38]
Subtotal (95% CI)	**273**	**272**		**100.0 %**	**0.80 [0.55, 1.14]**
Total events: 82 (Paroxetine), 95 (other SSRIs)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.15$, df = 1 (P = 0.70); $I^2 = 0.0\%$					
Test for overall effect: Z = 1.23 (P = 0.22)					



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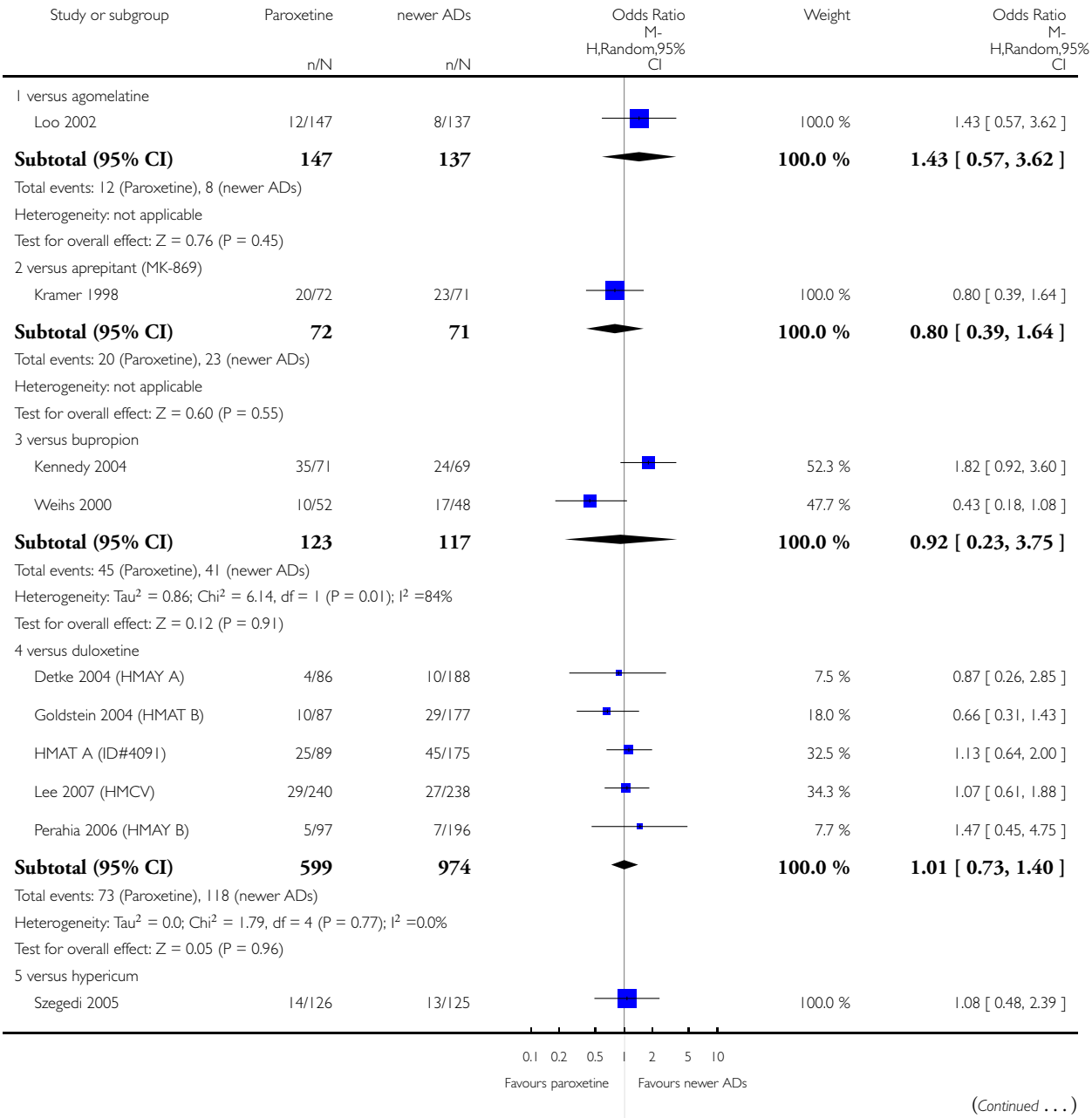
Analysis 48.3. Comparison 48 SE - Headache, Outcome 3 Paroxetine versus newer or non-conventional ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 48 SE - Headache

Outcome: 3 Paroxetine versus newer or non-conventional ADs



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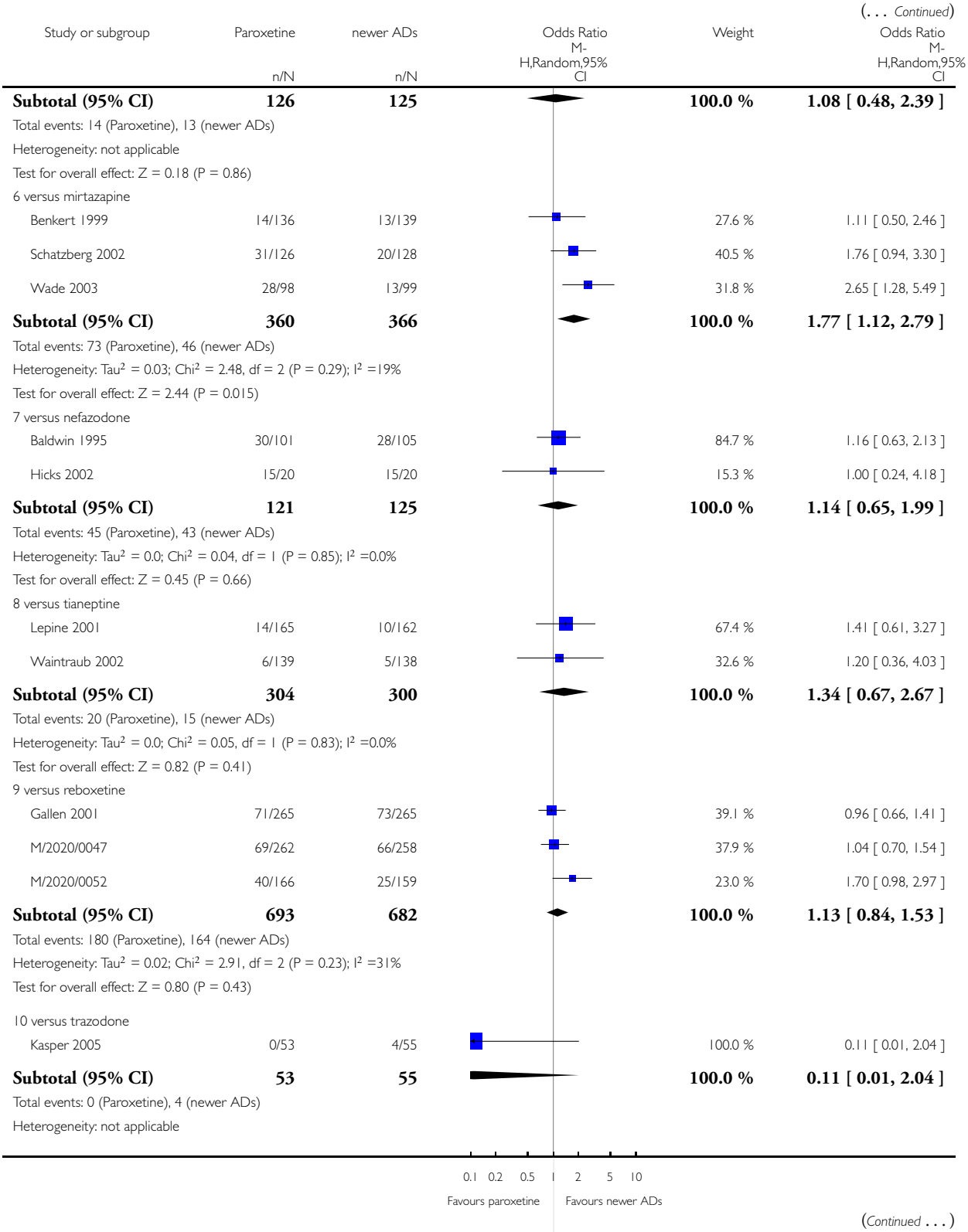

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Study or subgroup	Paroxetine n/N	newer ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Test for overall effect: Z = 1.49 (P = 0.14)					
11 versus venlafaxine					
Hwang 2004	1/53	1/52		5.7 %	0.98 [0.06, 16.11]
Mc Partlin 1998	21/178	16/183		94.3 %	1.40 [0.70, 2.77]
Subtotal (95% CI)	**231**	**235**		**100.0 %**	**1.37 [0.70, 2.66]**
Total events: 22 (Paroxetine), 17 (newer ADs)					
Heterogeneity: Tau^2 = 0.0; Chi^2 = 0.06, df = 1 (P = 0.81); I^2 =0.0%					
Test for overall effect: Z = 0.92 (P = 0.36)					

Analysis 49.1. Comparison 49 SE - Hypertension, Outcome 1 Paroxetine versus older ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 49 SE - Hypertension

Outcome: 1 Paroxetine versus older ADs

Study or subgroup	Paroxetine n/N	older ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
1 versus amitriptyline					
29060.07.001	0/13	2/13		18.2 %	0.17 [0.01, 3.92]
Subtotal (95% CI)	**13**	**13**		**18.2 %**	**0.17 [0.01, 3.92]**
Total events: 0 (Paroxetine), 2 (older ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.11 (P = 0.27)					
2 versus maprolitine					
29060.065.BE	3/28	2/32		51.4 %	1.80 [0.28, 11.64]
Subtotal (95% CI)	**28**	**32**		**51.4 %**	**1.80 [0.28, 11.64]**
Total events: 3 (Paroxetine), 2 (older ADs)					
Heterogeneity: not applicable					

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Study or subgroup	Paroxetine n/N	older ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Test for overall effect: Z = 0.62 (P = 0.54)					
3 versus mianserin					
Dalery 2001	1/54	2/62		30.4 %	0.57 [0.05, 6.42]
Subtotal (95% CI)	**54**	**62**		**30.4 %**	**0.57 [0.05, 6.42]**
Total events: 1 (Paroxetine), 2 (older ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.46 (P = 0.65)					
Total (95% CI)	**95**	**107**		**100.0 %**	**0.82 [0.22, 3.14]**
Total events: 4 (Paroxetine), 6 (older ADs)					
Heterogeneity: Tau^2 = 0.0; Chi^2 = 1.75, df = 2 (P = 0.42); I^2 =0.0%					
Test for overall effect: Z = 0.28 (P = 0.78)					
Test for subgroup differences: Chi^2 = 1.74, df = 2 (P = 0.42), I^2 =0.0%					

Analysis 49.2. Comparison 49 SE - Hypertension, Outcome 2 Paroxetine versus other SSRIs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 49 SE - Hypertension

Outcome: 2 Paroxetine versus other SSRIs

Study or subgroup	Paroxetine n/N	other SSRIs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
1 versus fluoxetine					
SBK-115 1998	1/284	0/289		100.0 %	3.06 [0.12, 75.52]
Subtotal (95% CI)	**284**	**289**		**100.0 %**	**3.06 [0.12, 75.52]**
Total events: 1 (Paroxetine), 0 (other SSRIs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.68 (P = 0.49)					

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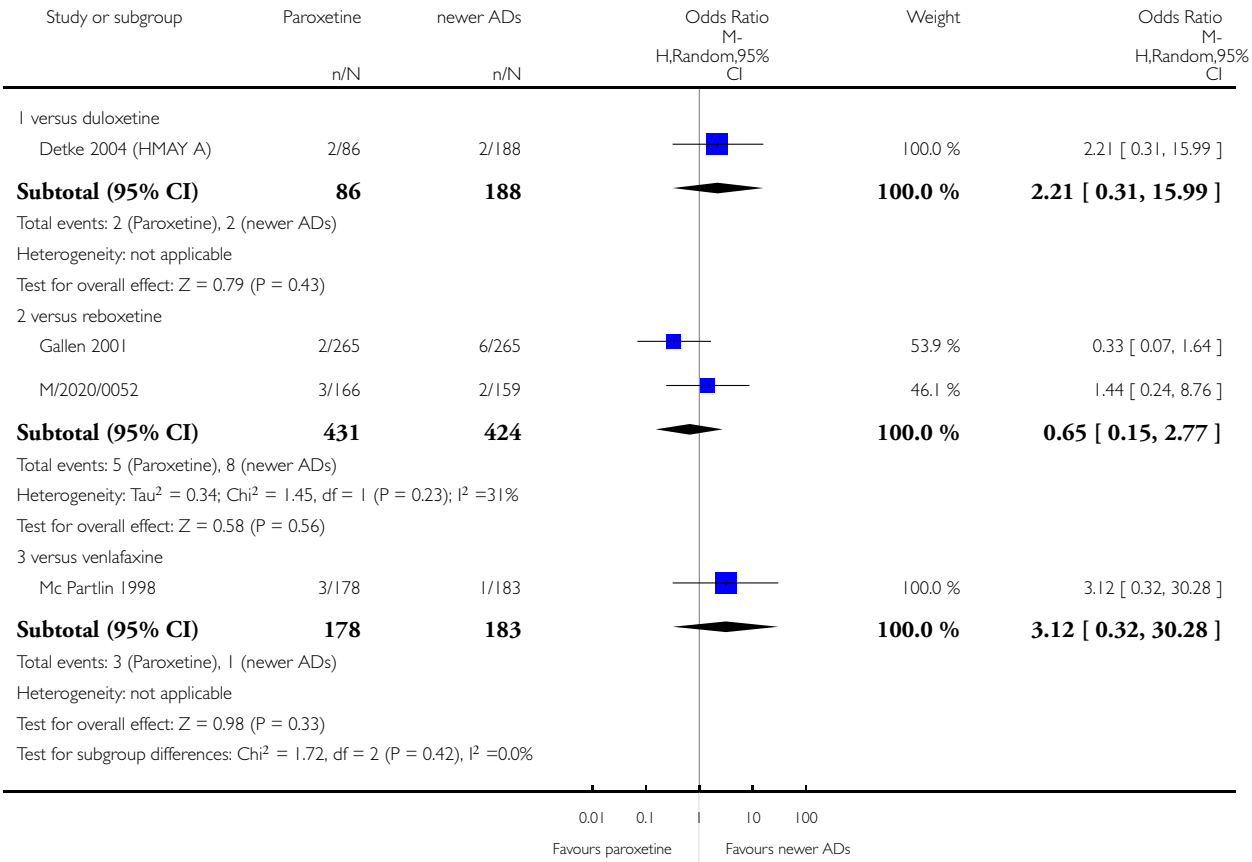
Analysis 49.3. Comparison 49 SE - Hypertension, Outcome 3 Paroxetine versus newer or non-conventional ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 49 SE - Hypertension

Outcome: 3 Paroxetine versus newer or non-conventional ADs



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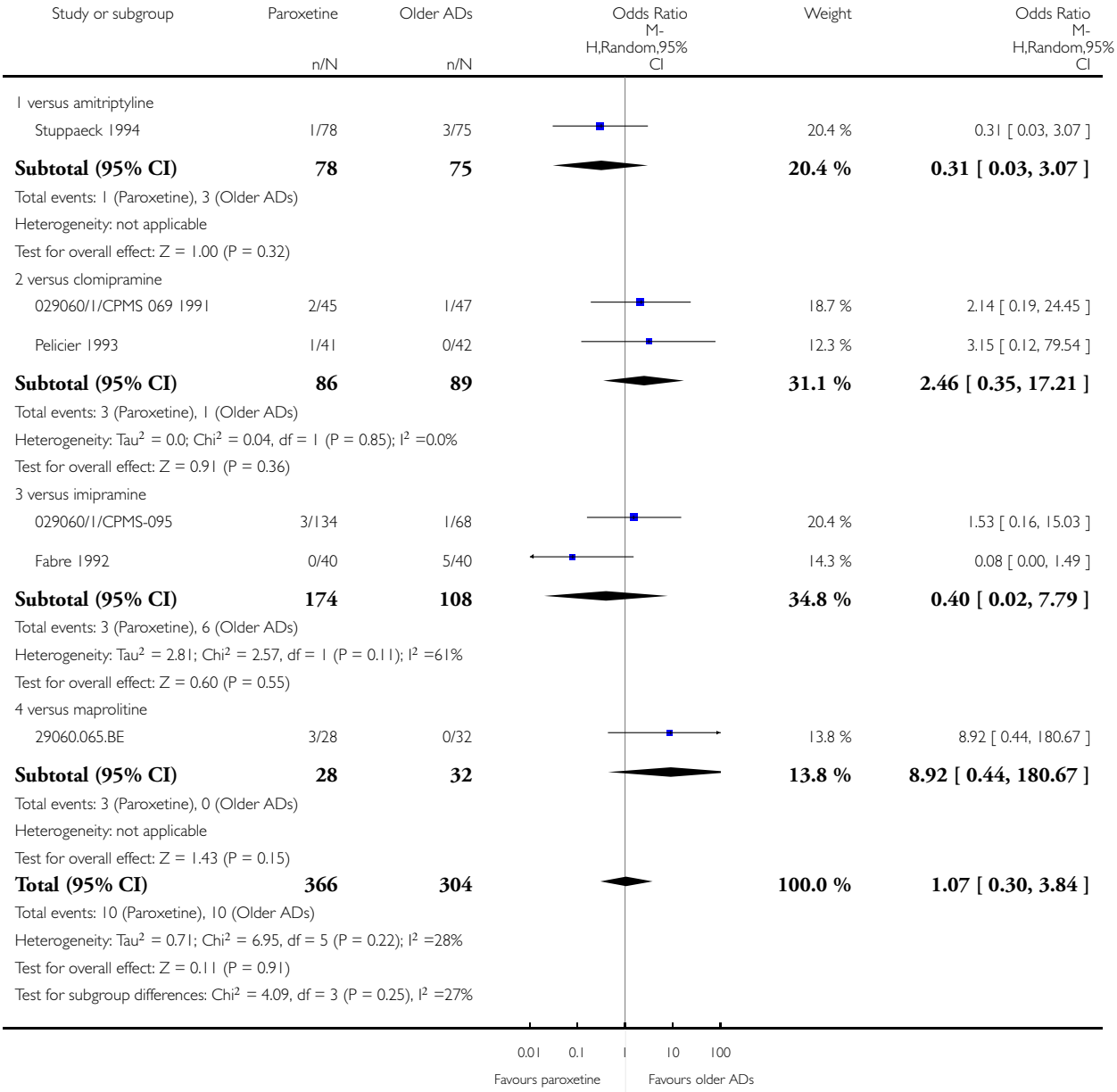
Analysis 50.1. Comparison 50 SE - Hypotension, Outcome 1 Paroxetine versus older ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 50 SE - Hypotension

Outcome: 1 Paroxetine versus older ADs



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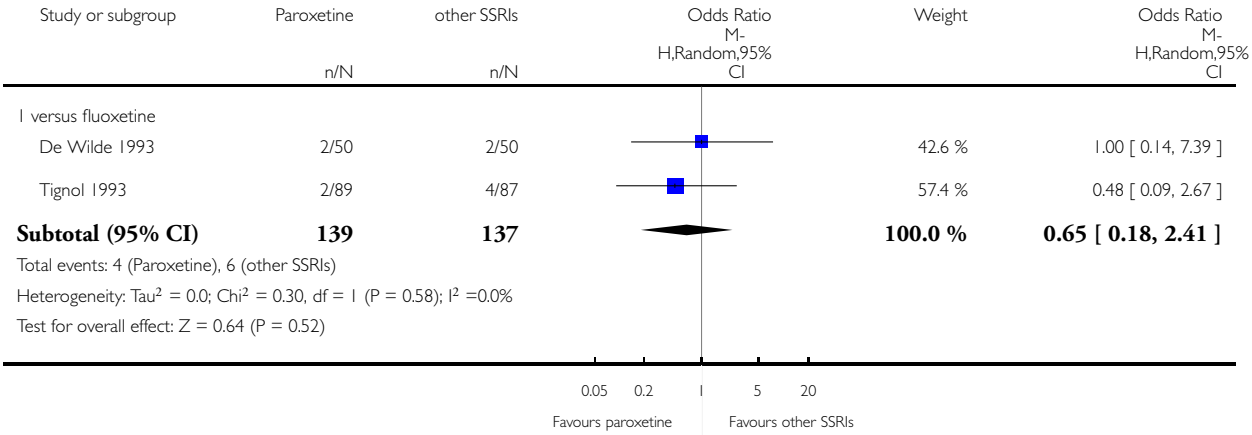
Analysis 50.2. Comparison 50 SE - Hypotension, Outcome 2 Paroxetine versus other SSRIs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 50 SE - Hypotension

Outcome: 2 Paroxetine versus other SSRIs



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Analysis 50.3. Comparison 50 SE - Hypotension, Outcome 3 Paroxetine versus newer or non-conventional ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 50 SE - Hypotension

Outcome: 3 Paroxetine versus newer or non-conventional ADs

Study or subgroup	Paroxetine n/N	Newer ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
1 versus reboxetine					
Gallen 2001	6/265	29/265		34.2 %	0.19 [0.08, 0.46]
M/2020/0047	9/262	18/258		37.7 %	0.47 [0.21, 1.08]
M/2020/0052	6/166	9/159		28.1 %	0.63 [0.22, 1.80]
Subtotal (95% CI)	**693**	**682**		**100.0 %**	**0.37 [0.19, 0.75]**
Total events: 21 (Paroxetine), 56 (Newer ADs)					
Heterogeneity: $Tau^2 = 0.17$; $Chi^2 = 3.51$, df = 2 (P = 0.17); $I^2 = 43\%$					
Test for overall effect: Z = 2.75 (P = 0.0060)					
2 versus trazodone					
Kasper 2005	1/53	0/55		100.0 %	3.17 [0.13, 79.60]
Subtotal (95% CI)	**53**	**55**		**100.0 %**	**3.17 [0.13, 79.60]**
Total events: 1 (Paroxetine), 0 (Newer ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.70 (P = 0.48)					
Test for subgroup differences: $Chi^2 = 1.61$, df = 1 (P = 0.20), $I^2 = 38\%$					

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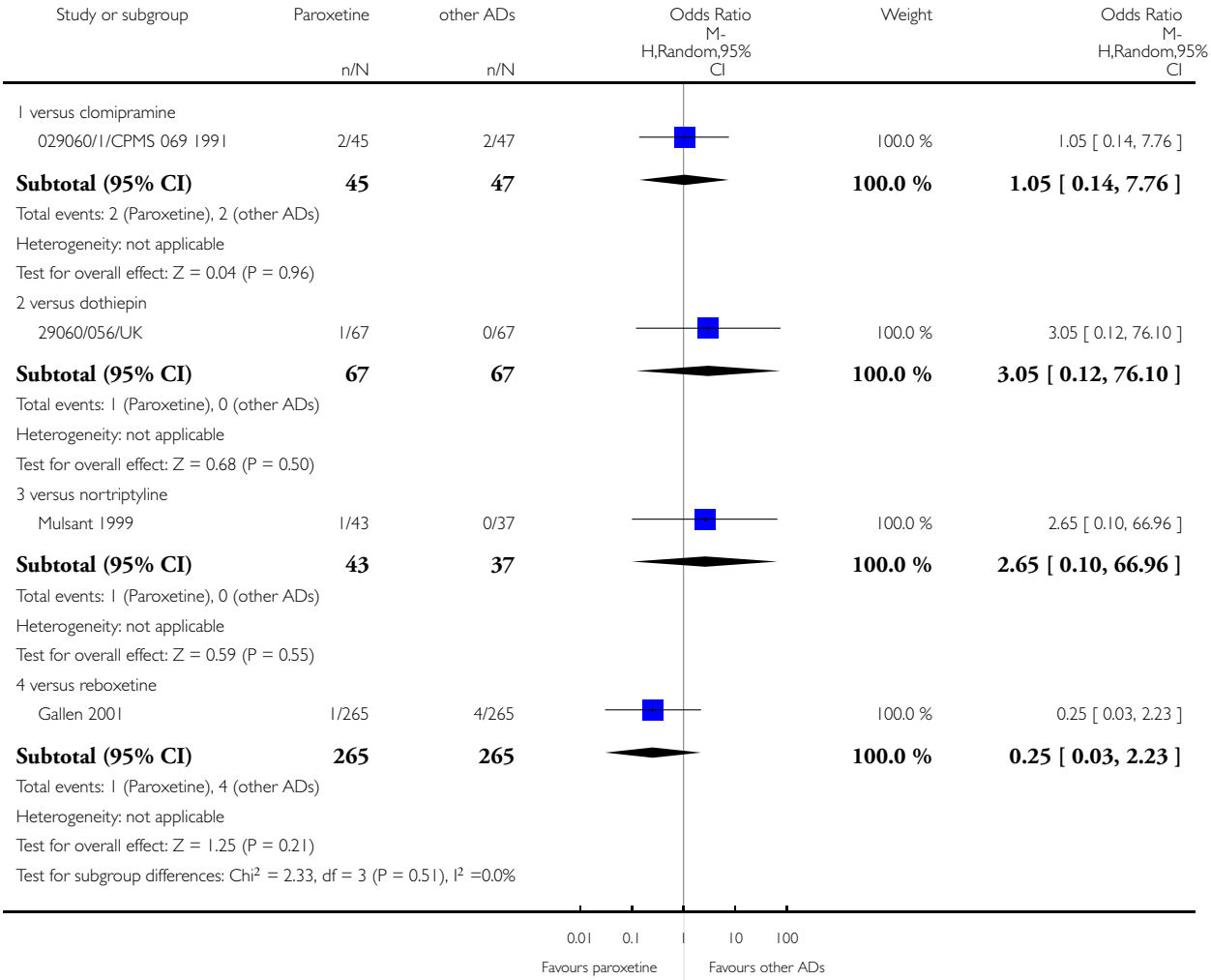
Analysis 50.4. Comparison 50 SE - Hypotension, Outcome 4 Postural hypotension.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 50 SE - Hypotension

Outcome: 4 Postural hypotension



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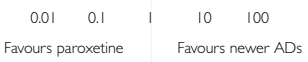
Analysis 51.1. Comparison 51 SE - Hypertonia, Outcome 1 Paroxetine versus newer or non-conventional ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 51 SE - Hypertonia

Outcome: 1 Paroxetine versus newer or non-conventional ADs

Study or subgroup	Paroxetine n/N	newer ADs n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
1 versus reboxetine					
Gallen 2001	6/265	4/265		28.2 %	1.51 [0.42, 5.42]
M/2020/0047	4/262	9/258		64.5 %	0.43 [0.13, 1.41]
M/2020/0052	2/166	1/159		7.3 %	1.93 [0.17, 21.46]
Subtotal (95% CI)	**693**	**682**		**100.0 %**	**0.84 [0.39, 1.84]**
Total events: 12 (Paroxetine), 14 (newer ADs)					
Heterogeneity: Chi^2 = 2.49, df = 2 (P = 0.29); I^2 =20%					
Test for overall effect: Z = 0.43 (P = 0.67)					
Test for subgroup differences: Not applicable					



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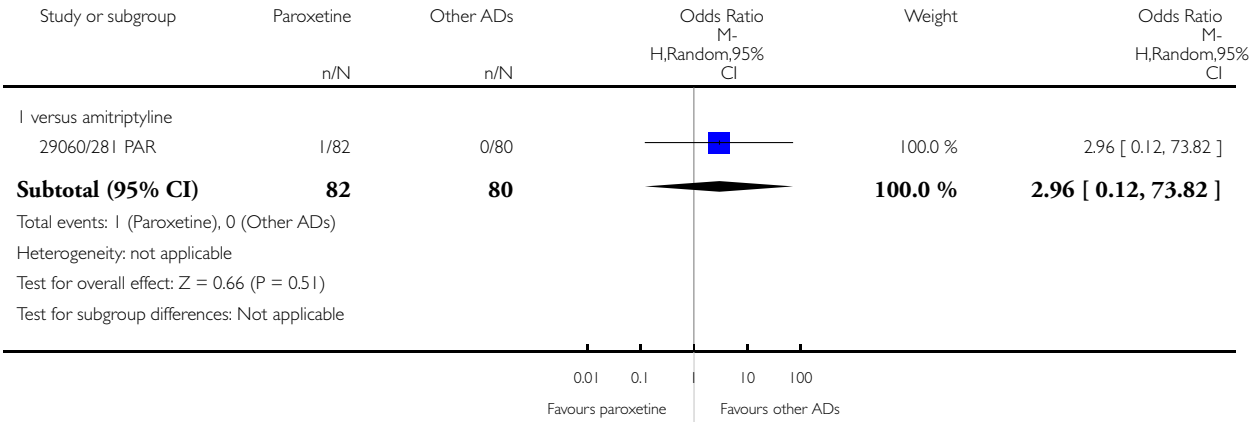
Analysis 52.1. Comparison 52 SE - Infection, Outcome 1 Meningitis.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 52 SE - Infection

Outcome: 1 Meningitis

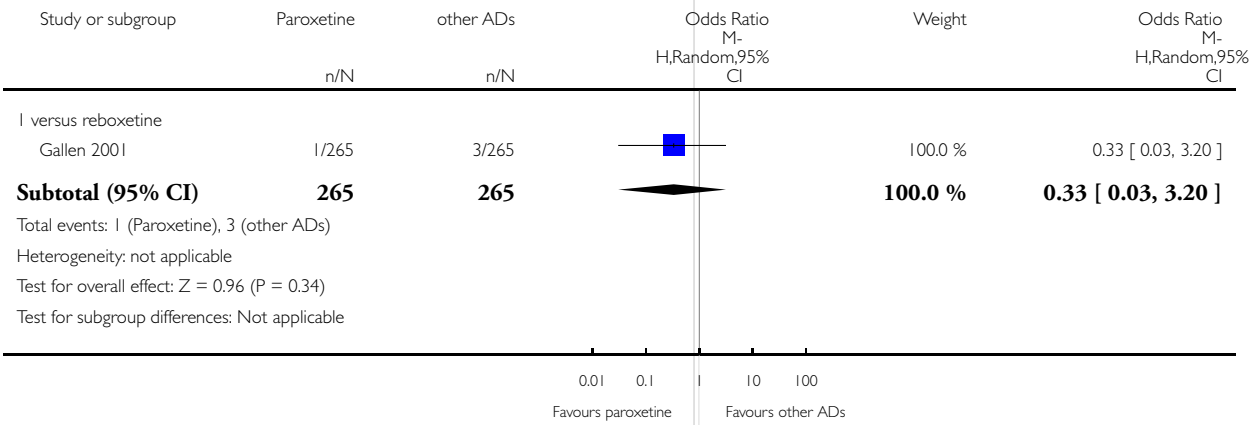


Analysis 52.2. Comparison 52 SE - Infection, Outcome 2 Otitis media.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 52 SE - Infection

Outcome: 2 Otitis media



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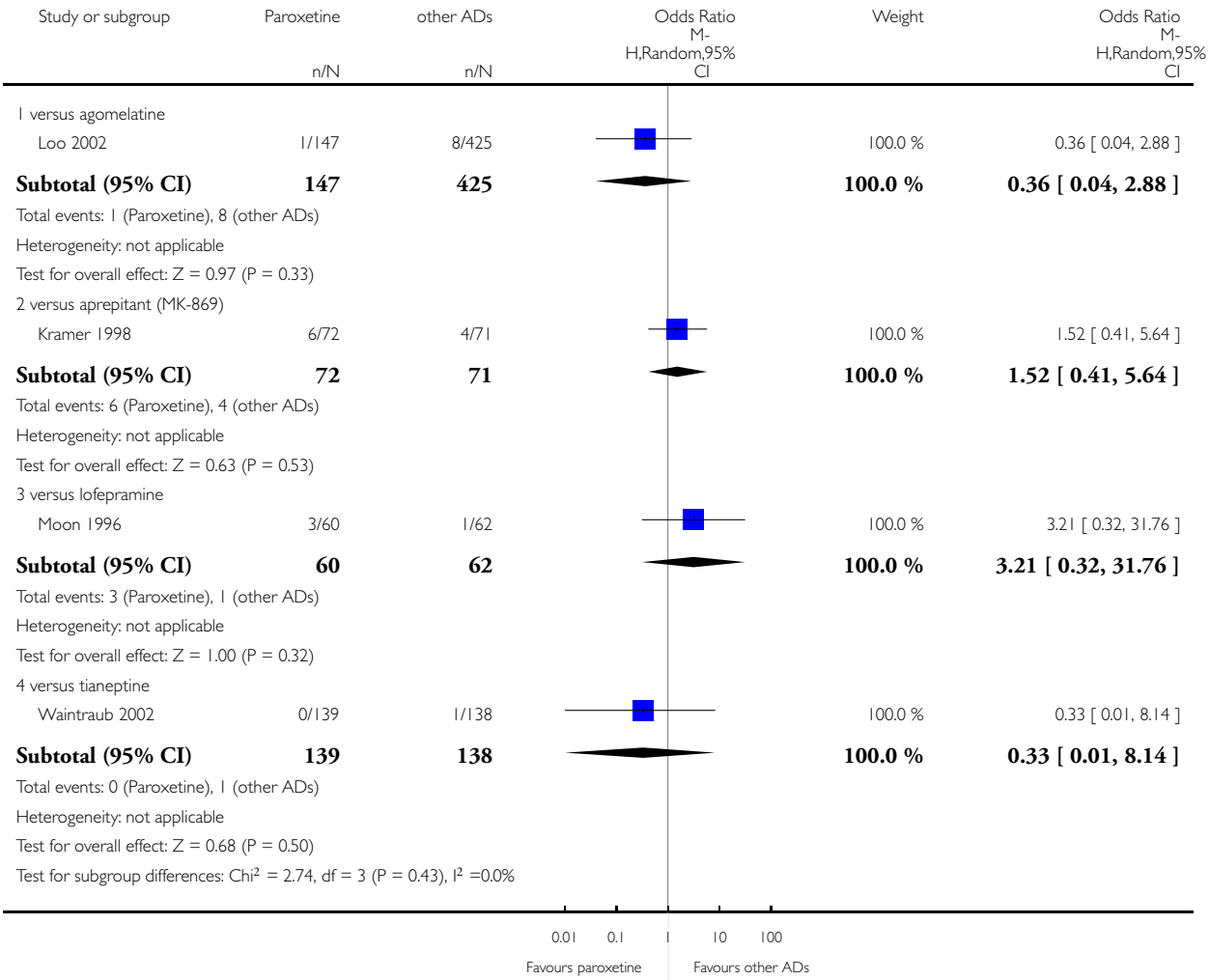
Analysis 52.3. Comparison 52 SE - Infection, Outcome 3 Respiratory upper.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 52 SE - Infection

Outcome: 3 Respiratory upper



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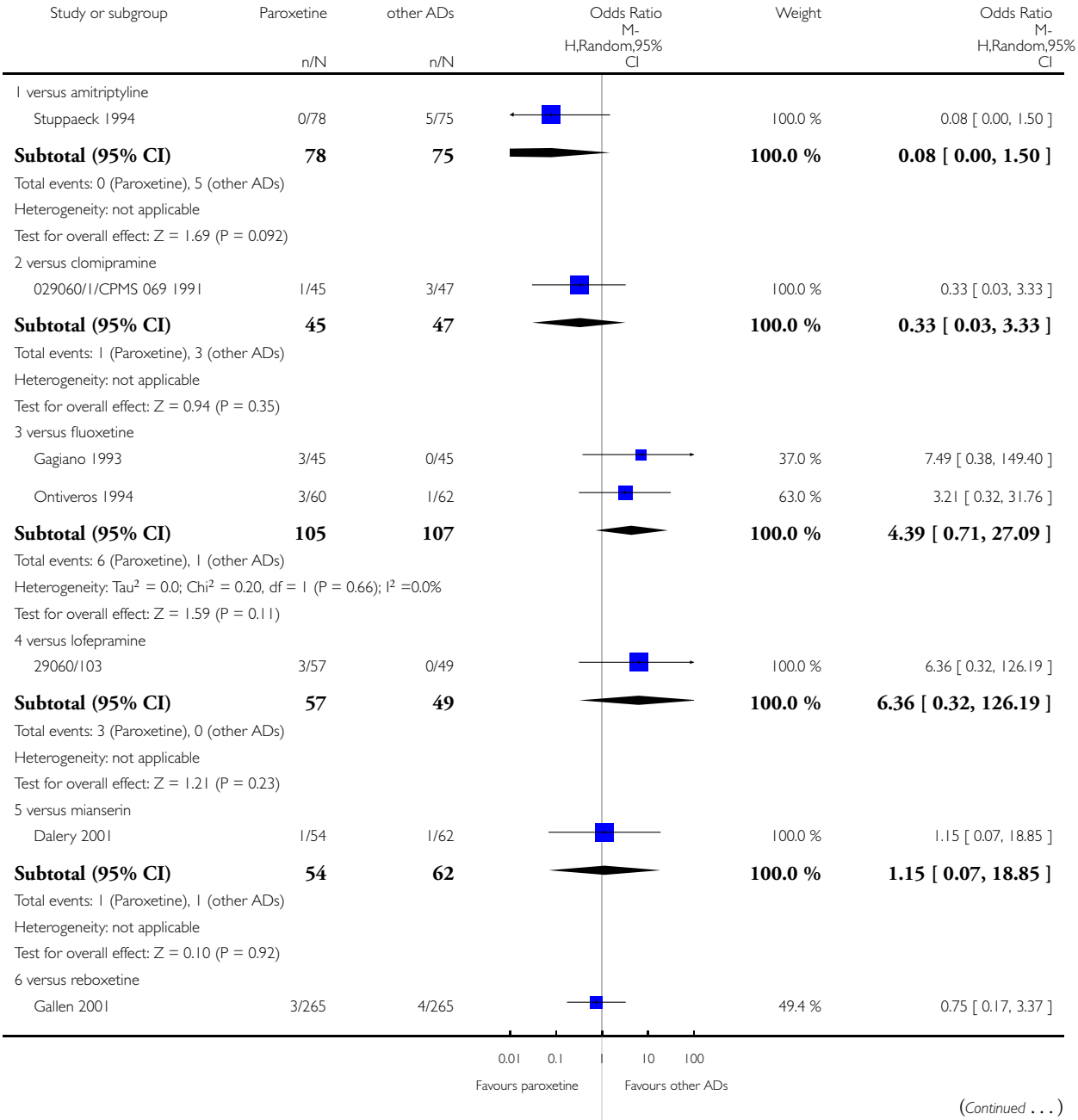
Analysis 52.4. Comparison 52 SE - Infection, Outcome 4 Urinary.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 52 SE - Infection

Outcome: 4 Urinary



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Study or subgroup	Paroxetine n/N	other ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
M/2020/0047	2/262	4/258		38.5 %	0.49 [0.09, 2.69]
M/2020/0052	0/166	2/159		12.1 %	0.19 [0.01, 3.97]
Subtotal (95% CI)	**693**	**682**		**100.0 %**	**0.54 [0.19, 1.55]**
Total events: 5 (Paroxetine), 10 (other ADs)					
Heterogeneity: Tau² = 0.0; Chi² = 0.65, df = 2 (P = 0.72); I² =0.0%					
Test for overall effect: Z = 1.15 (P = 0.25)					
Test for subgroup differences: Chi² = 8.74, df = 5 (P = 0.12), I² =43%					

Analysis 52.5. Comparison 52 SE - Infection, Outcome 5 NOS.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 52 SE - Infection

Outcome: 5 NOS

Study or subgroup	Paroxetine n/N	other ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
1 versus amitriptyline					
29060/299	5/109	0/108		100.0 %	11.42 [0.62, 209.13]
Subtotal (95% CI)	**109**	**108**		**100.0 %**	**11.42 [0.62, 209.13]**
Total events: 5 (Paroxetine), 0 (other ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.64 (P = 0.10)					
2 versus bupropion					
Weihs 2000	1/52	3/48		100.0 %	0.29 [0.03, 2.93]
Subtotal (95% CI)	**52**	**48**		**100.0 %**	**0.29 [0.03, 2.93]**
Total events: 1 (Paroxetine), 3 (other ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.04 (P = 0.30)					
3 versus mirtazapine					

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Study or subgroup	Paroxetine n/N	other ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Wade 2003	6/98	9/99		100.0 %	0.65 [0.22, 1.91]
Subtotal (95% CI)	**98**	**99**		**100.0 %**	**0.65 [0.22, 1.91]**
Total events: 6 (Paroxetine), 9 (other ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.78 (P = 0.43)					
4 versus reboxetine					
Gallen 2001	13/265	18/265		50.0 %	0.71 [0.34, 1.48]
M/2020/0047	11/262	18/258		45.4 %	0.58 [0.27, 1.26]
M/2020/0052	1/166	2/159		4.6 %	0.48 [0.04, 5.30]
Subtotal (95% CI)	**693**	**682**		**100.0 %**	**0.64 [0.38, 1.07]**
Total events: 25 (Paroxetine), 38 (other ADs)					
Heterogeneity: Tau^2 = 0.0; Chi^2 = 0.18, df = 2 (P = 0.91); I^2 =0.0%					
Test for overall effect: Z = 1.70 (P = 0.089)					
Test for subgroup differences: Chi^2 = 4.19, df = 3 (P = 0.24), I^2 =28%					

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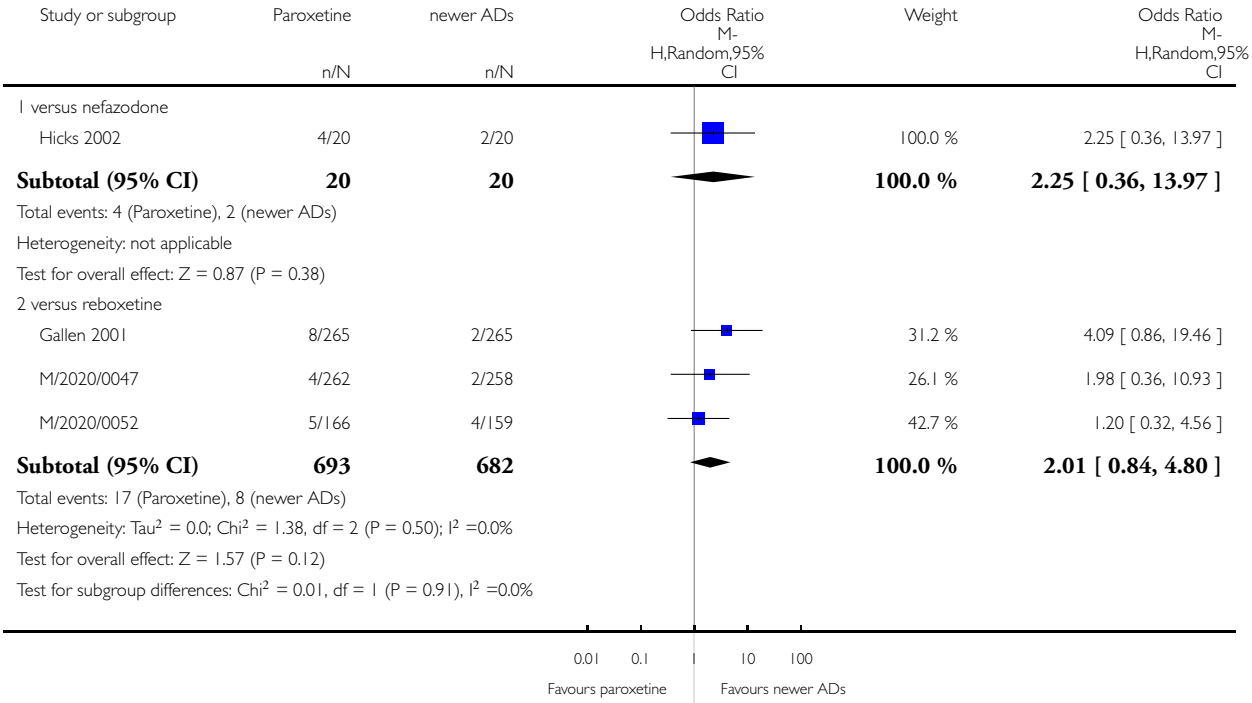
Analysis 53.1. Comparison 53 SE - Influenza-like symptoms, Outcome 1 Paroxetine versus newer or non-conventional ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 53 SE - Influenza-like symptoms

Outcome: 1 Paroxetine versus newer or non-conventional ADs



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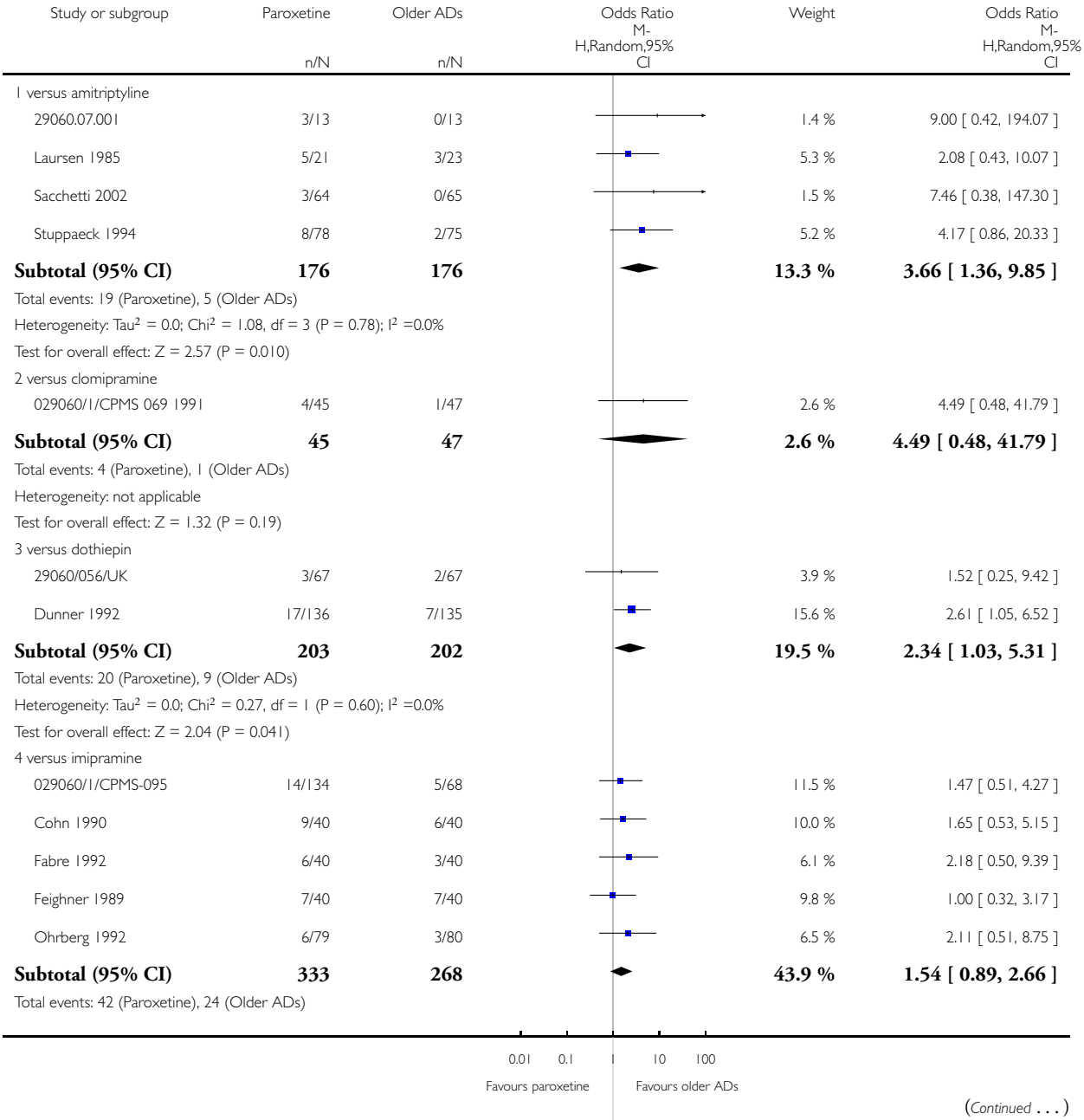
Analysis 54.1. Comparison 54 SE - Insomnia, Outcome 1 Paroxetine versus older ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 54 SE - Insomnia

Outcome: 1 Paroxetine versus older ADs



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Study or subgroup	Paroxetine n/N	Older ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Heterogeneity: Tau^2 = 0.0; Chi^2 = 0.96, df = 4 (P = 0.92); I^2 =0.0%					
Test for overall effect: Z = 1.55 (P = 0.12)					
5 versus lofepramine					
Moon 1996	2/60	4/62		4.3 %	0.50 [0.09, 2.84]
Subtotal (95% CI)	**60**	**62**		**4.3 %**	**0.50 [0.09, 2.84]**
Total events: 2 (Paroxetine), 4 (Older ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.78 (P = 0.43)					
6 versus maprotiline					
Szegedi 1995	22/145	6/153		15.0 %	4.38 [1.72, 11.15]
Subtotal (95% CI)	**145**	**153**		**15.0 %**	**4.38 [1.72, 11.15]**
Total events: 22 (Paroxetine), 6 (Older ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 3.10 (P = 0.0019)					
7 versus mianserin					
Dalery 2001	1/54	0/62		1.3 %	3.50 [0.14, 87.83]
Subtotal (95% CI)	**54**	**62**		**1.3 %**	**3.50 [0.14, 87.83]**
Total events: 1 (Paroxetine), 0 (Older ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.76 (P = 0.45)					
Total (95% CI)	**1016**	**970**		**100.0 %**	**2.17 [1.51, 3.12]**
Total events: 110 (Paroxetine), 49 (Older ADs)					
Heterogeneity: Tau^2 = 0.0; Chi^2 = 10.37, df = 14 (P = 0.73); I^2 =0.0%					
Test for overall effect: Z = 4.21 (P = 0.000026)					
Test for subgroup differences: Chi^2 = 8.03, df = 6 (P = 0.24), I^2 =25%					

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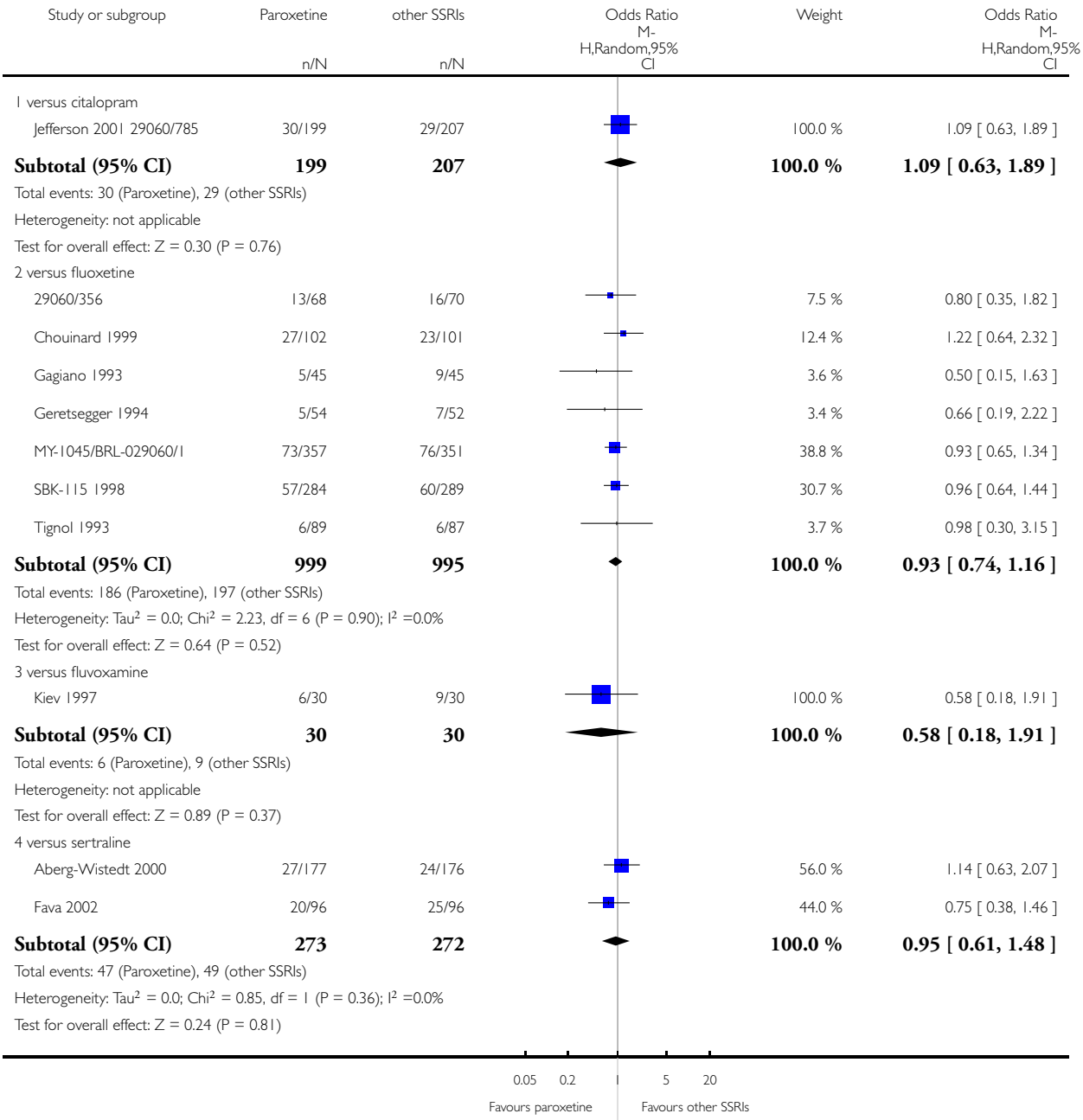
Analysis 54.2. Comparison 54 SE - Insomnia, Outcome 2 Paroxetine versus other SSRIs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 54 SE - Insomnia

Outcome: 2 Paroxetine versus other SSRIs



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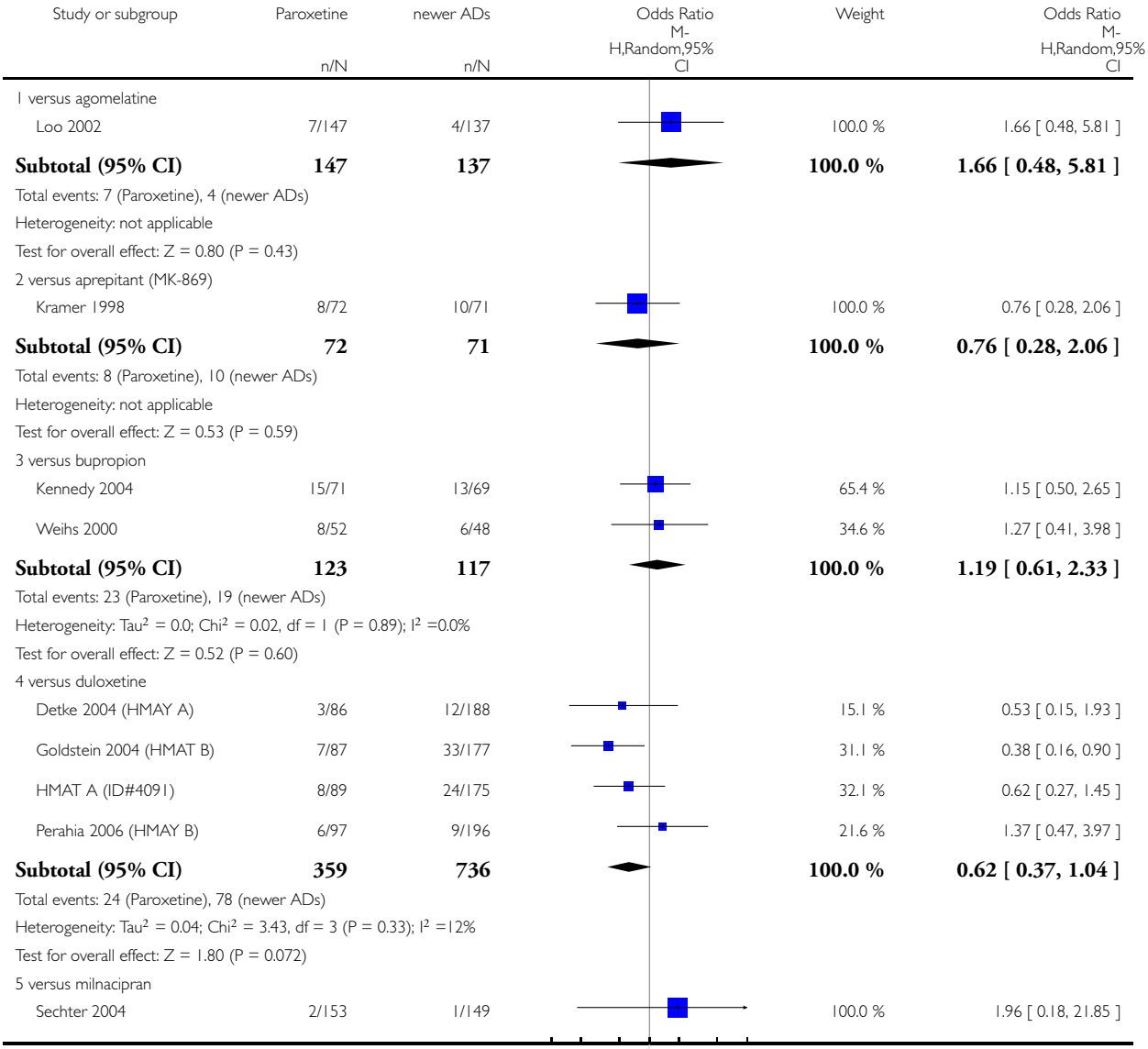
Analysis 54.3. Comparison 54 SE - Insomnia, Outcome 3 Paroxetine versus newer or non-conventional ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 54 SE - Insomnia

Outcome: 3 Paroxetine versus newer or non-conventional ADs



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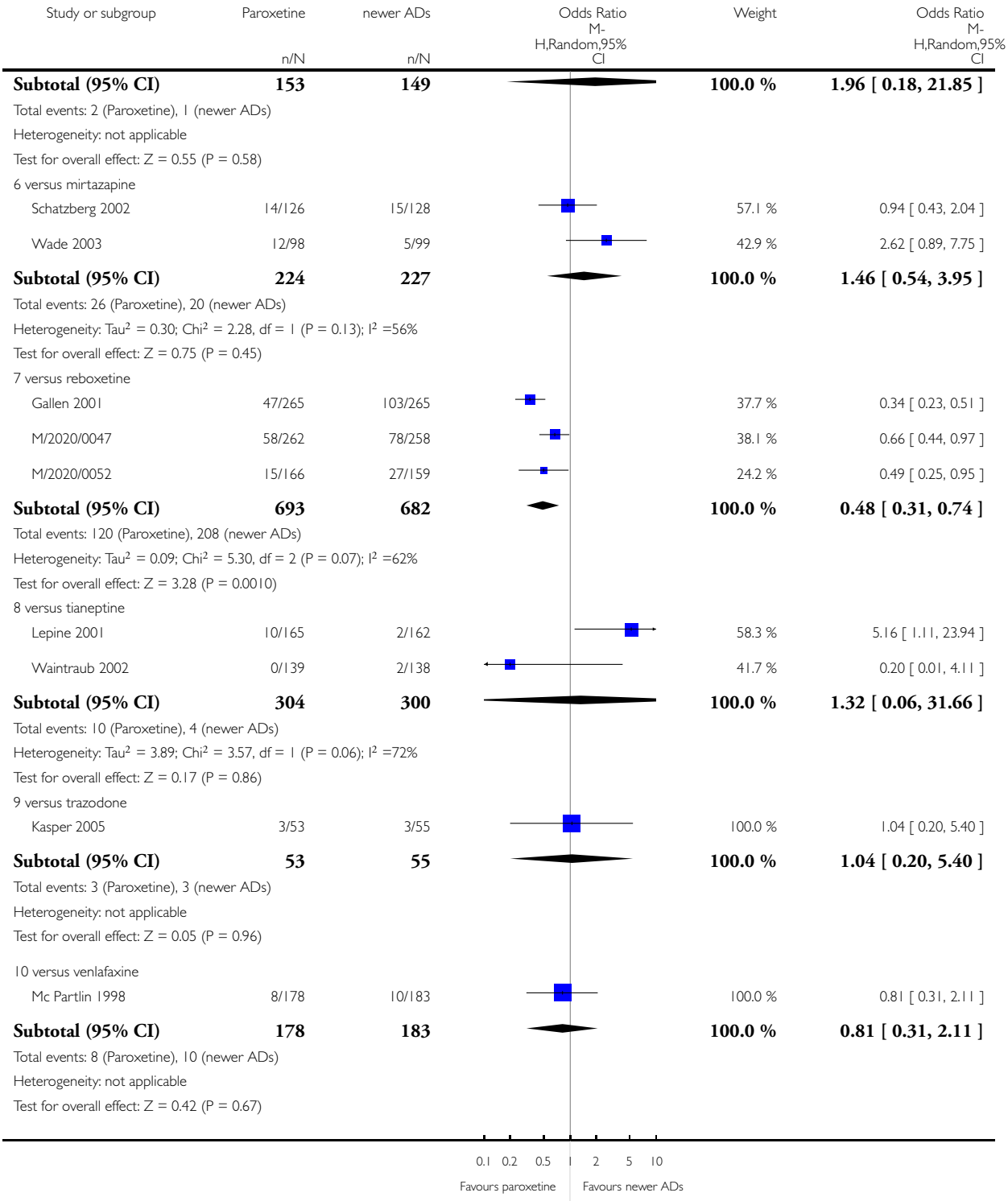

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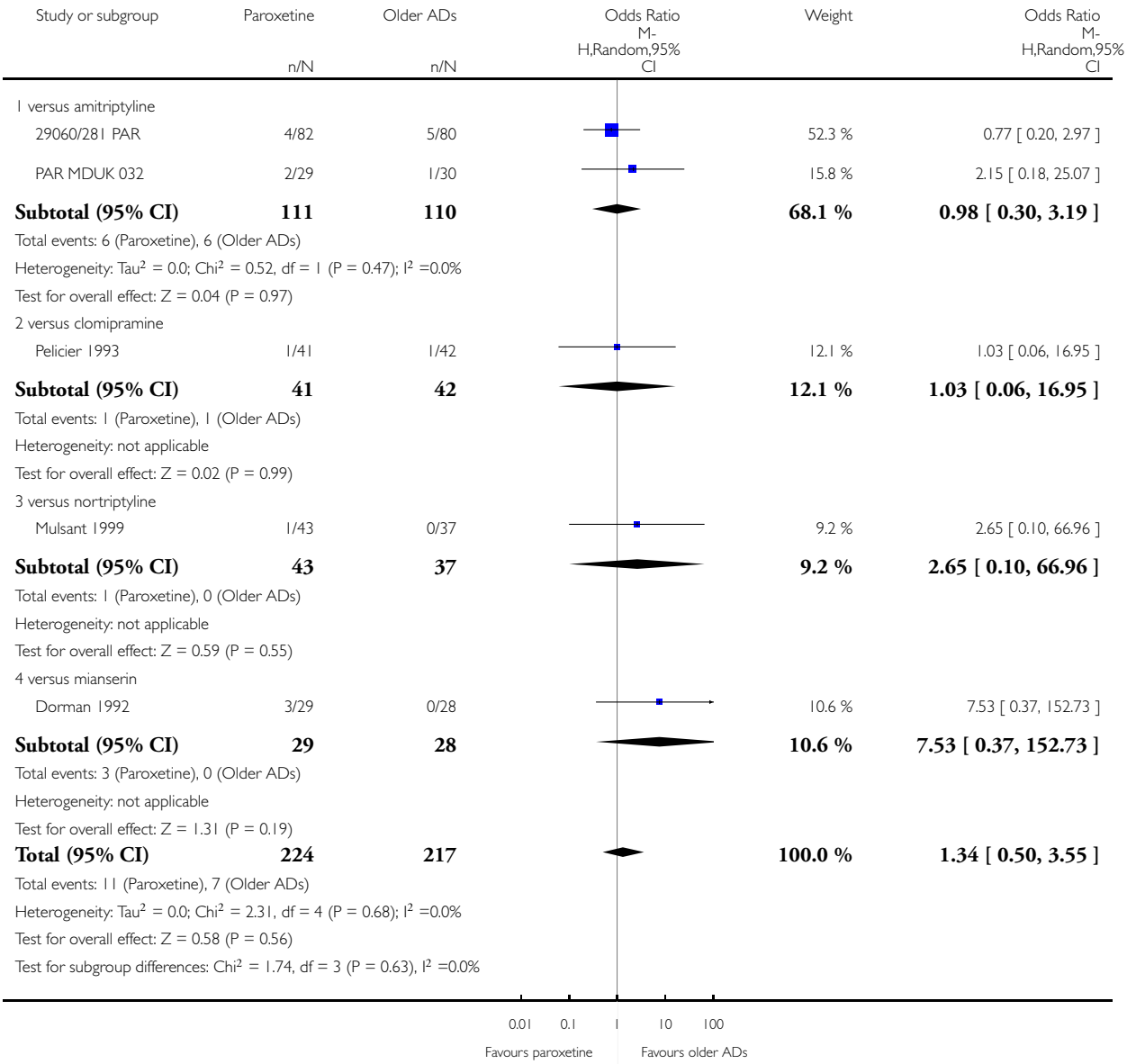
Analysis 55.1. Comparison 55 SE - Metabolic and nutritional system, Outcome 1 Paroxetine versus older ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 55 SE - Metabolic and nutritional system

Outcome: 1 Paroxetine versus older ADs



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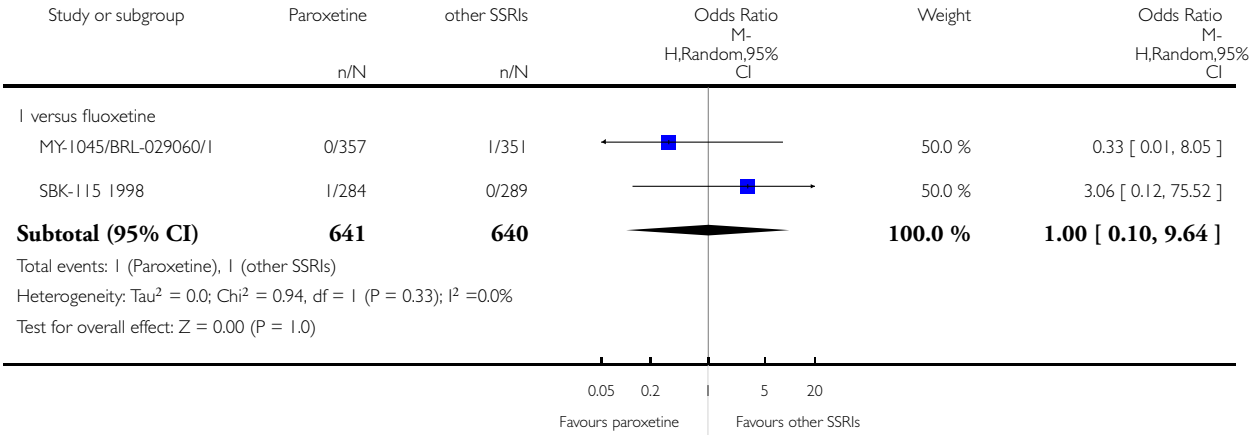
Analysis 55.2. Comparison 55 SE - Metabolic and nutritional system, Outcome 2 Paroxetine versus other SSRIs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 55 SE - Metabolic and nutritional system

Outcome: 2 Paroxetine versus other SSRIs



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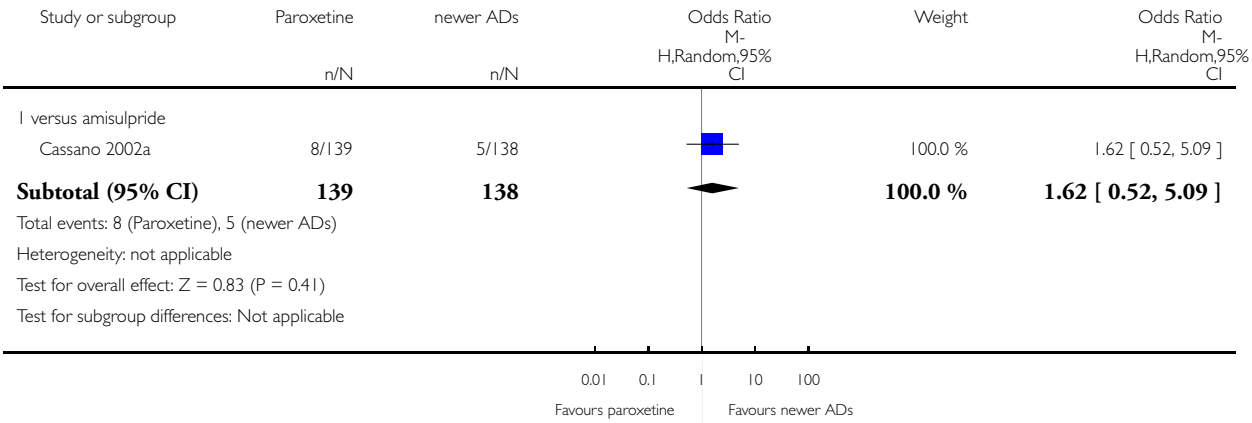
Analysis 55.3. Comparison 55 SE - Metabolic and nutritional system, Outcome 3 Paroxetine versus newer or non-conventional ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 55 SE - Metabolic and nutritional system

Outcome: 3 Paroxetine versus newer or non-conventional ADs



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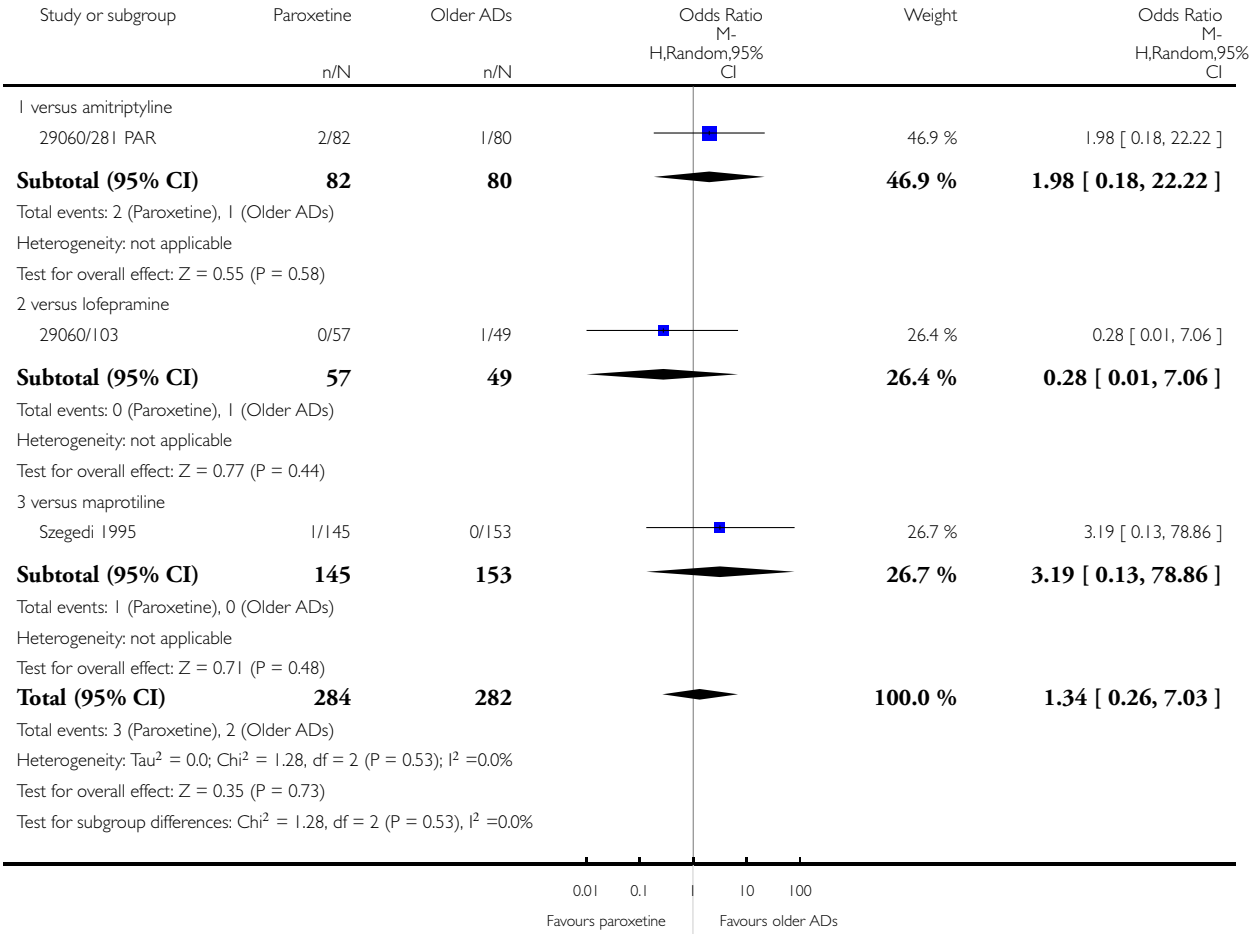
Analysis 56.1. Comparison 56 SE - Musculoskeletal and connective tissue disorders, Outcome 1 Paroxetine versus older ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 56 SE - Musculoskeletal and connective tissue disorders

Outcome: 1 Paroxetine versus older ADs



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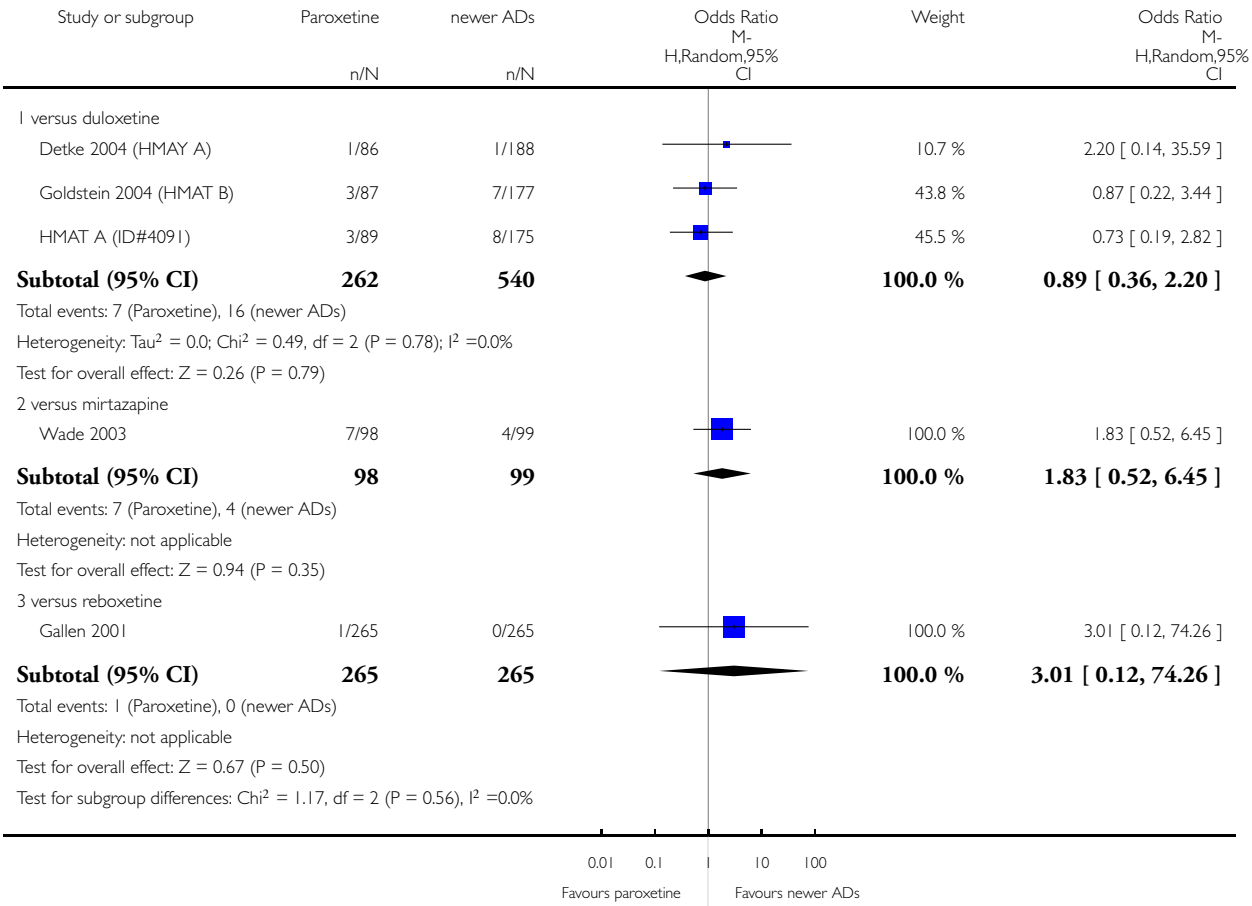
Analysis 56.2. Comparison 56 SE - Musculoskeletal and connective tissue disorders, Outcome 2 Paroxetine versus newer or non-conventional ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 56 SE - Musculoskeletal and connective tissue disorders

Outcome: 2 Paroxetine versus newer or non-conventional ADs



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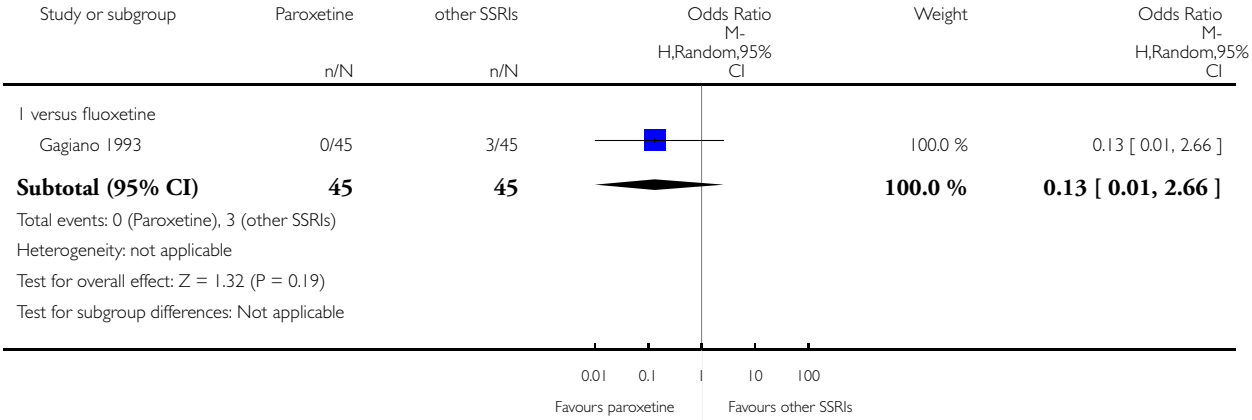
Analysis 57.1. Comparison 57 SE - Myalgia, Outcome 1 Paroxetine versus other SSRIs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 57 SE - Myalgia

Outcome: 1 Paroxetine versus other SSRIs

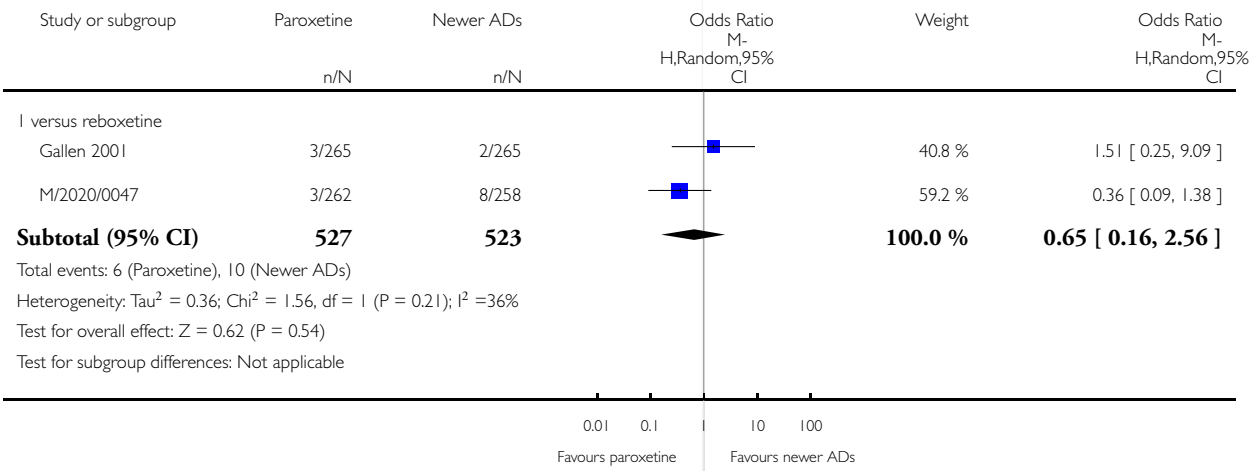


Analysis 57.2. Comparison 57 SE - Myalgia, Outcome 2 Paroxetine versus newer or non-conventional ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 57 SE - Myalgia

Outcome: 2 Paroxetine versus newer or non-conventional ADs



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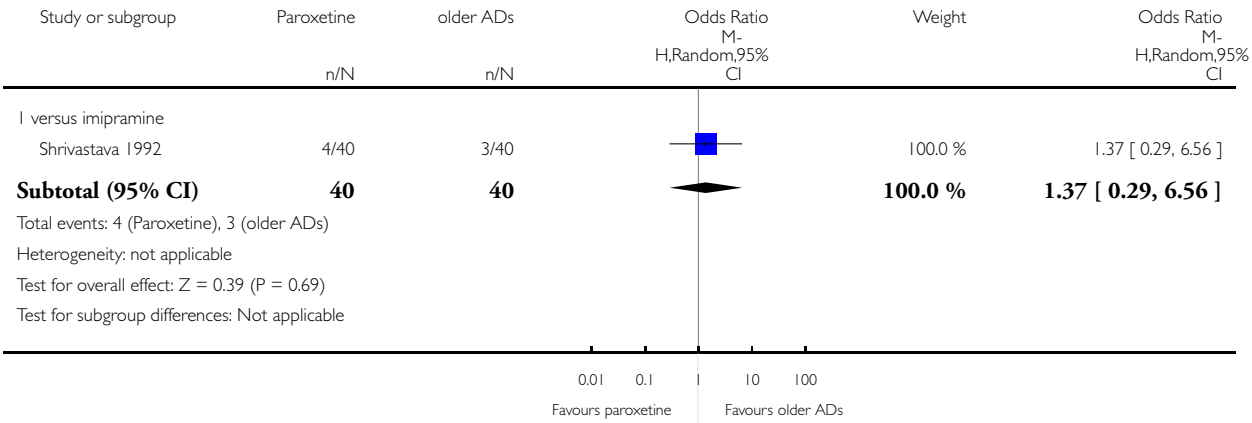
Analysis 58.1. Comparison 58 SE - Nervousness, Outcome 1 Paroxetine versus older ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 58 SE - Nervousness

Outcome: 1 Paroxetine versus older ADs



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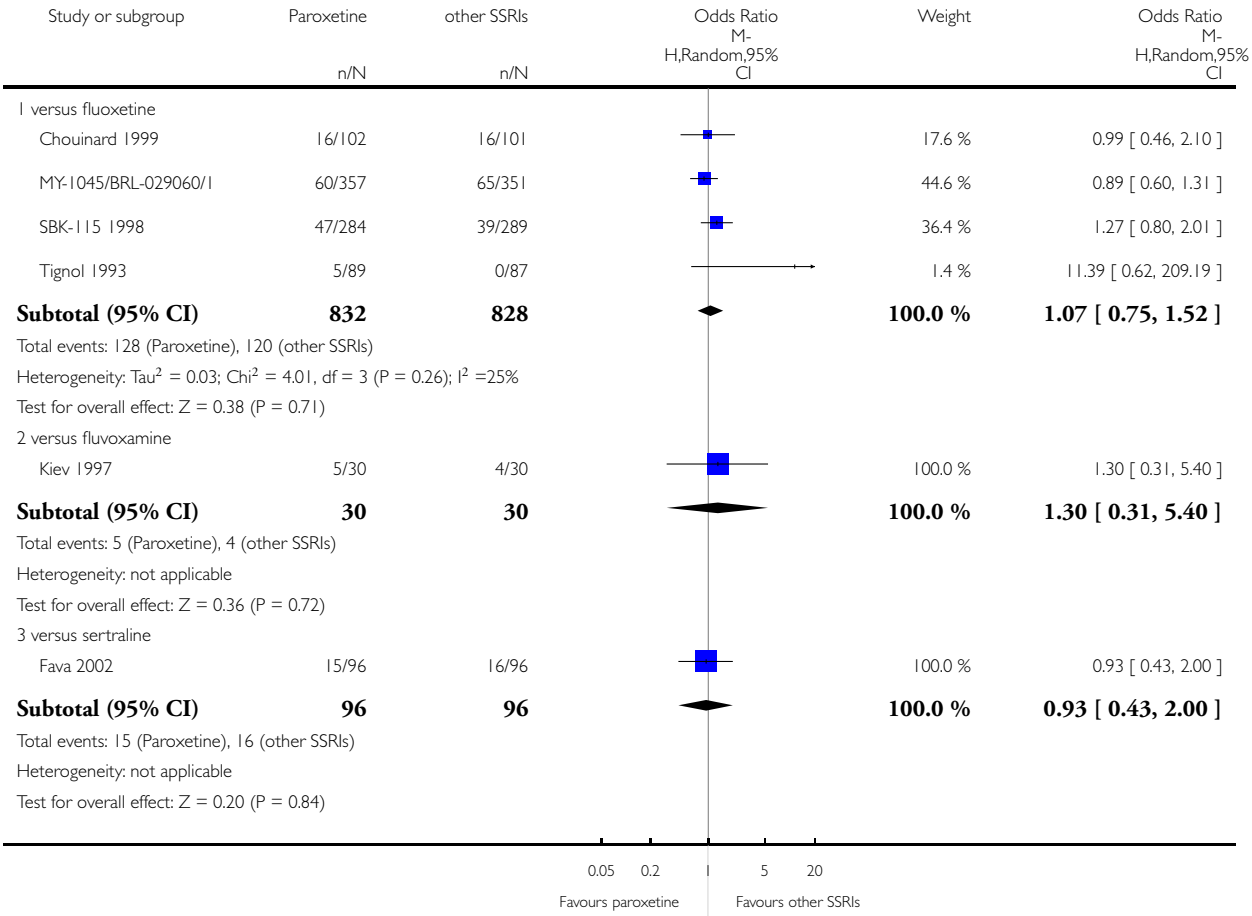
Analysis 58.2. Comparison 58 SE - Nervousness, Outcome 2 Paroxetine versus other SSRIs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 58 SE - Nervousness

Outcome: 2 Paroxetine versus other SSRIs



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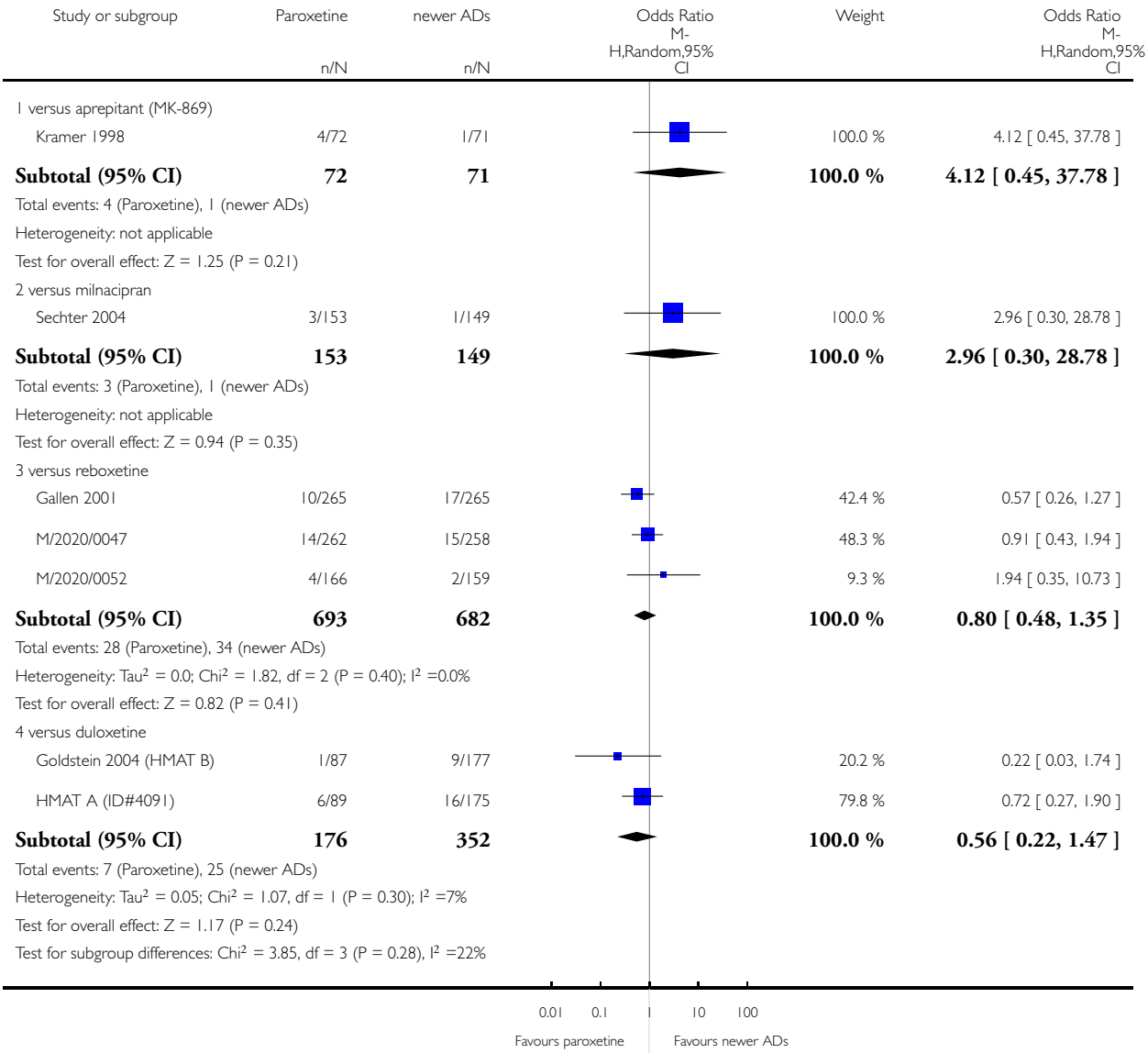
Analysis 58.3. Comparison 58 SE - Nervousness, Outcome 3 Paroxetine versus newer or non-conventional ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 58 SE - Nervousness

Outcome: 3 Paroxetine versus newer or non-conventional ADs



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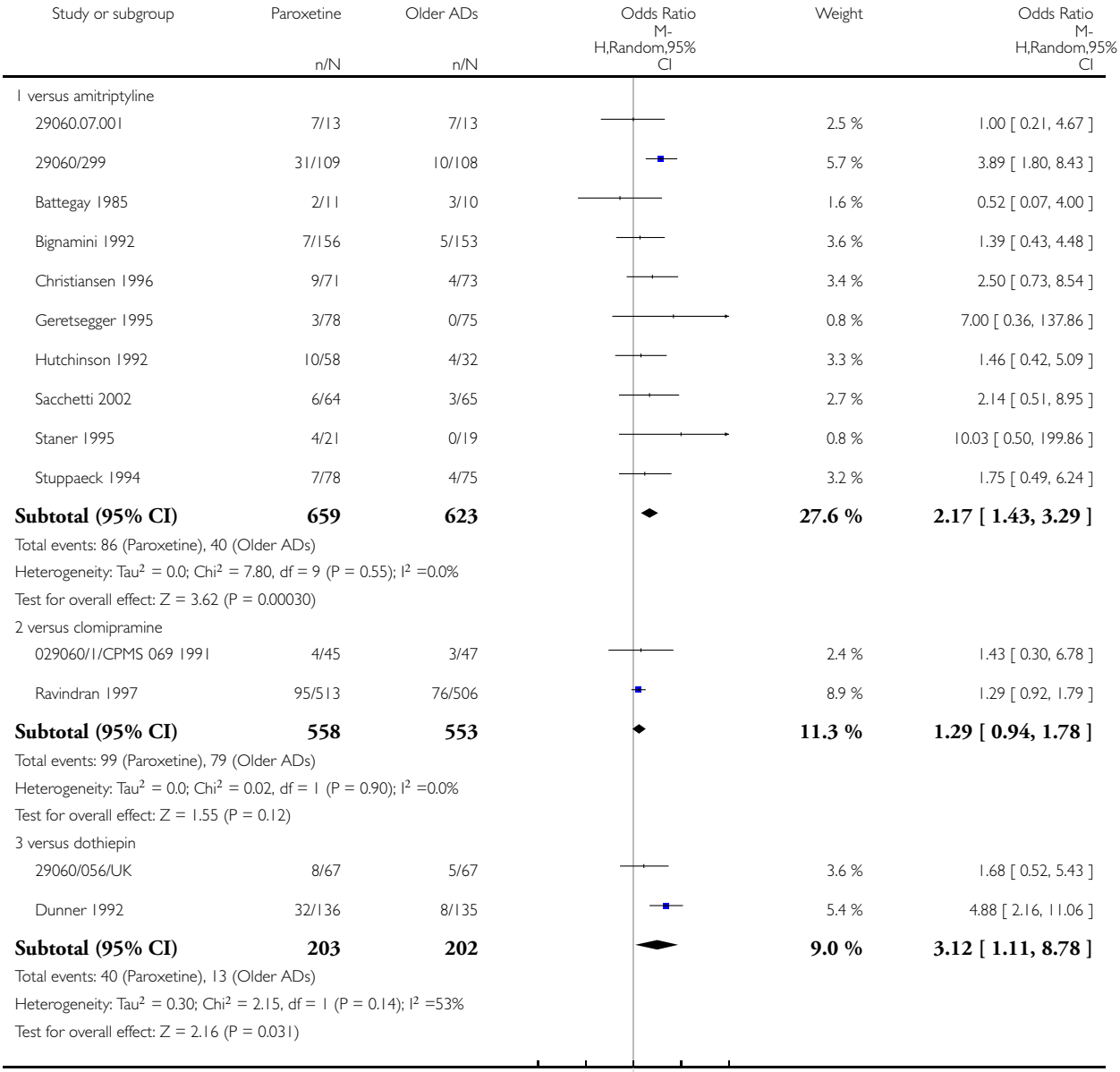
Analysis 59.1. Comparison 59 SE - Nausea/vomiting, Outcome 1 Paroxetine versus older ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 59 SE - Nausea/vomiting

Outcome: 1 Paroxetine versus older ADs



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Study or subgroup	Paroxetine n/N	Older ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
4 versus imipramine					
029060/1/CPMS-095	11/134	4/68		3.6 %	1.43 [0.44, 4.67]
29060/409	7/38	4/37		3.1 %	1.86 [0.50, 6.99]
Cohn 1990	13/40	6/40		4.0 %	2.73 [0.92, 8.13]
Fabre 1992	13/40	4/40		3.4 %	4.33 [1.27, 14.78]
Feighner 1989	11/40	3/40		2.9 %	4.68 [1.19, 18.34]
Ohrberg 1992	43/79	21/80		6.4 %	3.36 [1.72, 6.53]
Peselow 1989	8/40	7/39		3.8 %	1.14 [0.37, 3.53]
Shrivastava 1992	9/40	13/40		4.4 %	0.60 [0.22, 1.63]
Subtotal (95% CI)	**451**	**384**		**31.5 %**	**2.05 [1.23, 3.42]**
Total events: 115 (Paroxetine), 62 (Older ADs)					
Heterogeneity: $Tau^2 = 0.23$; $Chi^2 = 12.38$, df = 7 (P = 0.09); $I^2 = 43\%$					
Test for overall effect: Z = 2.77 (P = 0.0057)					
5 versus lofepramine					
29060/103	15/57	6/49		4.2 %	2.56 [0.91, 7.23]
Moon 1996	4/60	0/62		0.8 %	9.96 [0.52, 189.04]
Subtotal (95% CI)	**117**	**111**		**5.0 %**	**2.97 [1.12, 7.92]**
Total events: 19 (Paroxetine), 6 (Older ADs)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.75$, df = 1 (P = 0.39); $I^2 = 0.0\%$					
Test for overall effect: Z = 2.18 (P = 0.029)					
6 versus maprolitine					
29060.065.BE	8/28	3/32		2.7 %	3.87 [0.91, 16.39]
Schnyder 1996	4/37	5/34		2.8 %	0.70 [0.17, 2.87]
Szegedi 1995	58/145	20/153		7.1 %	4.43 [2.49, 7.88]
Subtotal (95% CI)	**210**	**219**		**12.6 %**	**2.56 [0.86, 7.60]**
Total events: 70 (Paroxetine), 28 (Older ADs)					
Heterogeneity: $Tau^2 = 0.59$; $Chi^2 = 5.67$, df = 2 (P = 0.06); $I^2 = 65\%$					
Test for overall effect: Z = 1.70 (P = 0.090)					
7 versus mianserin					
29060III/85/038	1/30	0/29		0.7 %	3.00 [0.12, 76.68]
Dalery 2001	1/54	6/62		1.4 %	0.18 [0.02, 1.51]
Subtotal (95% CI)	**84**	**91**		**2.1 %**	**0.55 [0.04, 8.50]**
Total events: 2 (Paroxetine), 6 (Older ADs)					
Heterogeneity: $Tau^2 = 2.05$; $Chi^2 = 2.04$, df = 1 (P = 0.15); $I^2 = 51\%$					
Test for overall effect: Z = 0.42 (P = 0.67)					
8 versus nortriptyline					
Mulsant 1999	2/43	0/37		0.8 %	4.52 [0.21, 97.16]

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Study or subgroup	Paroxetine n/N	Older ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Subtotal (95% CI)	**43**	**37**		**0.8 %**	**4.52 [0.21, 97.16]**
Total events: 2 (Paroxetine), 0 (Older ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.96 (P = 0.34)					
Total (95% CI)	**2325**	**2220**		**100.0 %**	**2.10 [1.59, 2.77]**
Total events: 433 (Paroxetine), 234 (Older ADs)					
Heterogeneity: Tau^2 = 0.20; Chi^2 = 49.02, df = 29 (P = 0.01); I^2 =41%					
Test for overall effect: Z = 5.26 (P < 0.00001)					
Test for subgroup differences: Chi^2 = 8.61, df = 7 (P = 0.28), I^2 =19%					

0.01 0.1 1 10 100

Favours paroxetine Favours older ADs

Analysis 59.2. Comparison 59 SE - Nausea/vomiting, Outcome 2 Paroxetine versus other SSRIs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 59 SE - Nausea/vomiting

Outcome: 2 Paroxetine versus other SSRIs

Study or subgroup	Paroxetine n/N	other SSRIs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
1 versus citalopram					
Jefferson 2001 29060/785	30/199	35/207		100.0 %	0.87 [0.51, 1.48]
Subtotal (95% CI)	**199**	**207**		**100.0 %**	**0.87 [0.51, 1.48]**
Total events: 30 (Paroxetine), 35 (other SSRIs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.50 (P = 0.61)					
2 versus escitalopram					
Boulenger 2006	58/225	57/229		100.0 %	1.05 [0.69, 1.60]
Subtotal (95% CI)	**225**	**229**		**100.0 %**	**1.05 [0.69, 1.60]**
Total events: 58 (Paroxetine), 57 (other SSRIs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.22 (P = 0.83)					

0.05 0.2 1 5 20

Favours paroxetine Favours other SSRIs

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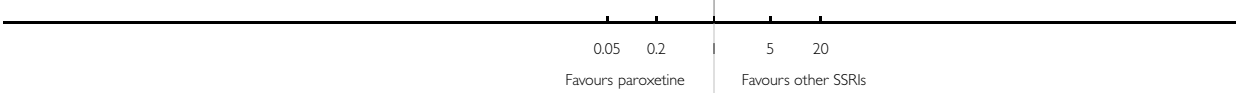
Study or subgroup	Paroxetine n/N	other SSRIs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
3 versus fluoxetine					
29060/356	26/68	22/70		7.7 %	1.35 [0.67, 2.73]
Ansseau 1993	11/56	12/64		4.6 %	1.06 [0.43, 2.63]
Chouinard 1999	38/102	32/101		11.3 %	1.28 [0.72, 2.29]
De Wilde 1993	10/50	10/50		4.0 %	1.00 [0.38, 2.66]
Gagiano 1993	18/45	18/45		5.3 %	1.00 [0.43, 2.32]
Geretsegger 1994	8/54	4/52		2.4 %	2.09 [0.59, 7.41]
MY-1045/BRL-029060/1	107/357	81/351		33.6 %	1.43 [1.02, 2.00]
Ontiveros 1994	6/60	3/62		1.8 %	2.19 [0.52, 9.17]
SBK-115 1998	76/284	70/289		26.8 %	1.14 [0.78, 1.67]
Tignol 1993	4/89	9/87		2.6 %	0.41 [0.12, 1.38]
Subtotal (95% CI)	**1165**	**1171**		**100.0 %**	**1.24 [1.02, 1.51]**
Total events: 304 (Paroxetine), 261 (other SSRIs)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 5.92$, df = 9 (P = 0.75); $I^2 = 0.0\%$					
Test for overall effect: Z = 2.19 (P = 0.028)					
4 versus fluvoxamine					
Kiev 1997	14/30	11/30		100.0 %	1.51 [0.54, 4.24]
Subtotal (95% CI)	**30**	**30**		**100.0 %**	**1.51 [0.54, 4.24]**
Total events: 14 (Paroxetine), 11 (other SSRIs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.78 (P = 0.43)					
5 versus sertraline					
Aberg-Wistedt 2000	78/177	92/176		61.4 %	0.72 [0.47, 1.09]
Fava 2002	24/96	20/96		38.6 %	1.27 [0.64, 2.49]
Subtotal (95% CI)	**273**	**272**		**100.0 %**	**0.89 [0.52, 1.54]**
Total events: 102 (Paroxetine), 112 (other SSRIs)					
Heterogeneity: $Tau^2 = 0.08$; $Chi^2 = 1.95$, df = 1 (P = 0.16); $I^2 = 49\%$					
Test for overall effect: Z = 0.40 (P = 0.69)					



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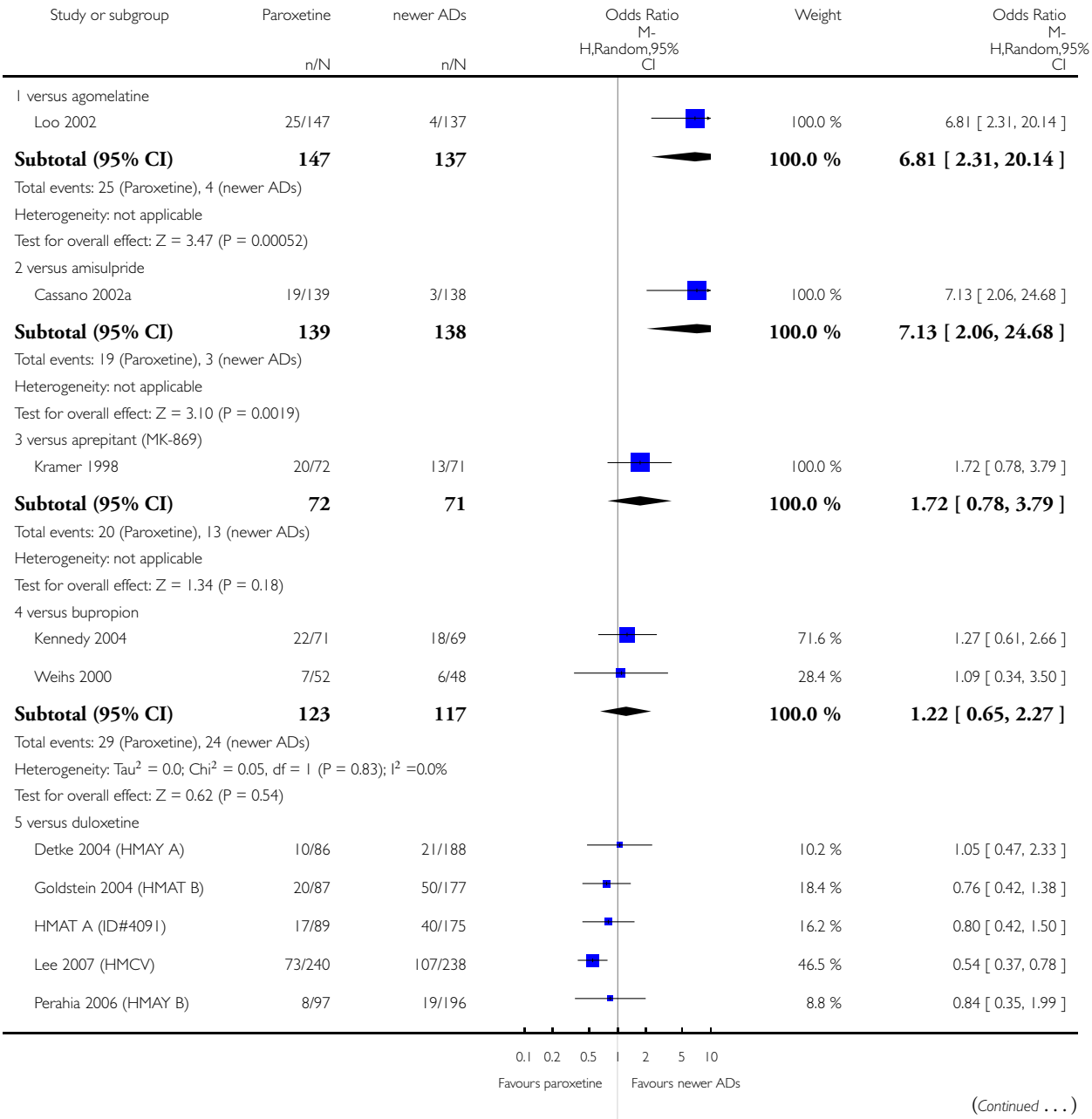
Analysis 59.3. Comparison 59 SE - Nausea/vomiting, Outcome 3 Paroxetine versus newer or non-conventional ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 59 SE - Nausea/vomiting

Outcome: 3 Paroxetine versus newer or non-conventional ADs



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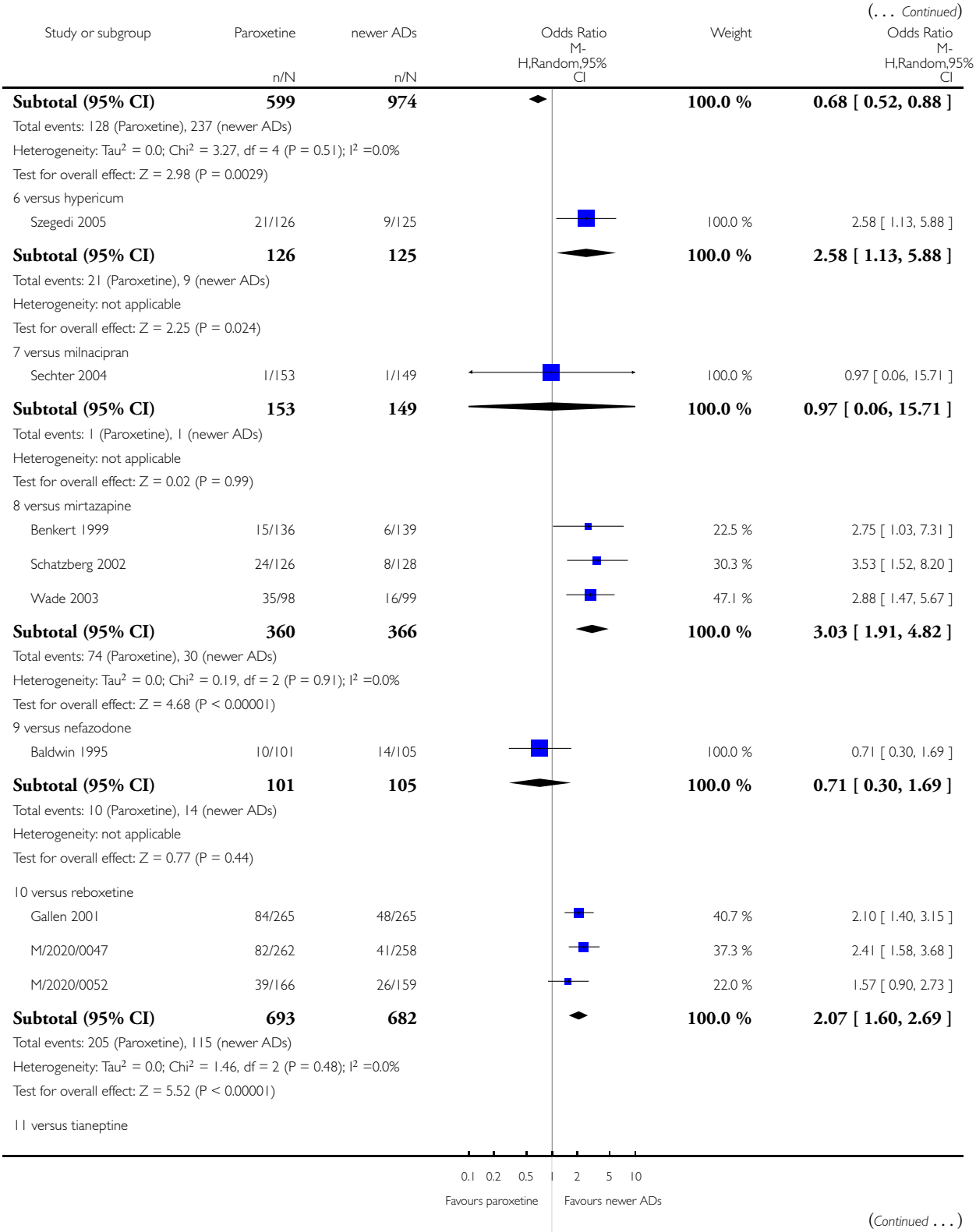

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Study or subgroup	Paroxetine n/N	newer ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Lepine 2001	24/165	11/162		66.2 %	2.34 [1.10, 4.94]
Waintraub 2002	14/139	5/138		33.8 %	2.98 [1.04, 8.51]
Subtotal (95% CI)	**304**	**300**		**100.0 %**	**2.54 [1.38, 4.67]**
Total events: 38 (Paroxetine), 16 (newer ADs)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.14$, df = 1 (P = 0.71); $I^2 = 0.0\%$					
Test for overall effect: Z = 2.99 (P = 0.0028)					
12 versus trazodone					
Kasper 2005	6/53	1/55		100.0 %	6.89 [0.80, 59.35]
Subtotal (95% CI)	**53**	**55**		**100.0 %**	**6.89 [0.80, 59.35]**
Total events: 6 (Paroxetine), 1 (newer ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.76 (P = 0.079)					
13 versus venlafaxine					
Mc Partlin 1998	56/178	56/183		100.0 %	1.04 [0.67, 1.63]
Subtotal (95% CI)	**178**	**183**		**100.0 %**	**1.04 [0.67, 1.63]**
Total events: 56 (Paroxetine), 56 (newer ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.18 (P = 0.86)					

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Analysis 60.1. Comparison 60 SE - Neoplasm, Outcome 1 Basal cell carcinoma.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 60 SE - Neoplasm

Outcome: 1 Basal cell carcinoma

Study or subgroup	Paroxetine n/N	other ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
1 versus fluoxetine					
SBK-115 1998	0/284	2/289		100.0 %	0.20 [0.01, 4.23]
Subtotal (95% CI)	**284**	**289**		**100.0 %**	**0.20 [0.01, 4.23]**
Total events: 0 (Paroxetine), 2 (other ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.03 (P = 0.30)					
Test for subgroup differences: Not applicable					

Analysis 60.2. Comparison 60 SE - Neoplasm, Outcome 2 Bone.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 60 SE - Neoplasm

Outcome: 2 Bone

Study or subgroup	Paroxetine n/N	Newer ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
1 versus amitriptyline					
29060/299	0/109	1/108		100.0 %	0.33 [0.01, 8.12]
Subtotal (95% CI)	**109**	**108**		**100.0 %**	**0.33 [0.01, 8.12]**
Total events: 0 (Paroxetine), 1 (Newer ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.68 (P = 0.50)					
Test for subgroup differences: Not applicable					

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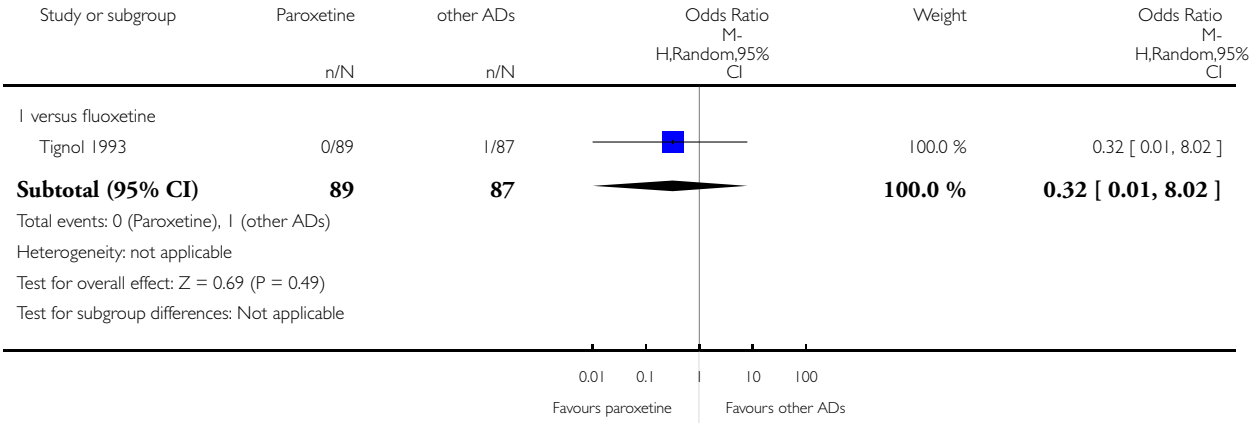
Analysis 60.3. Comparison 60 SE - Neoplasm, Outcome 3 Meningioma.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 60 SE - Neoplasm

Outcome: 3 Meningioma



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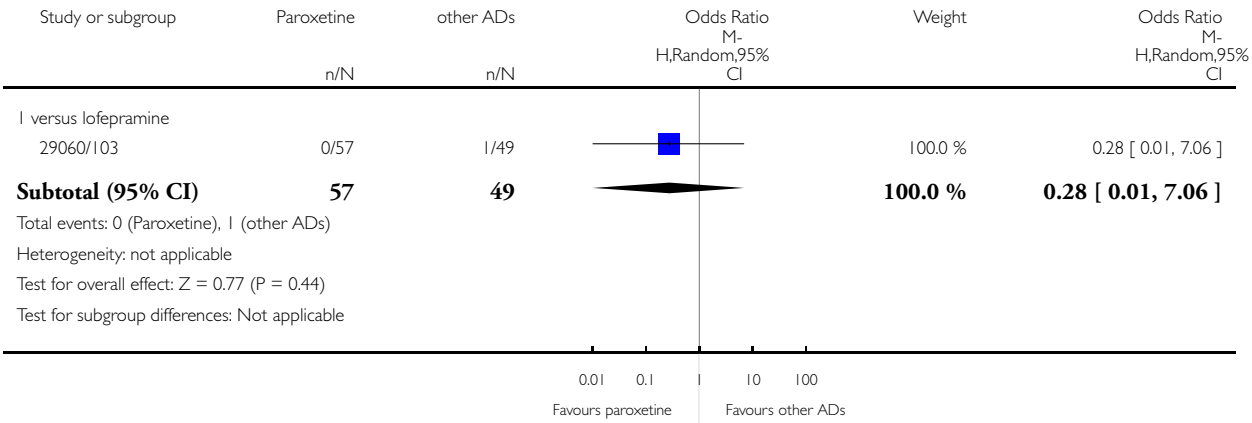
Analysis 60.4. Comparison 60 SE - Neoplasm, Outcome 4 Pulmonary.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 60 SE - Neoplasm

Outcome: 4 Pulmonary



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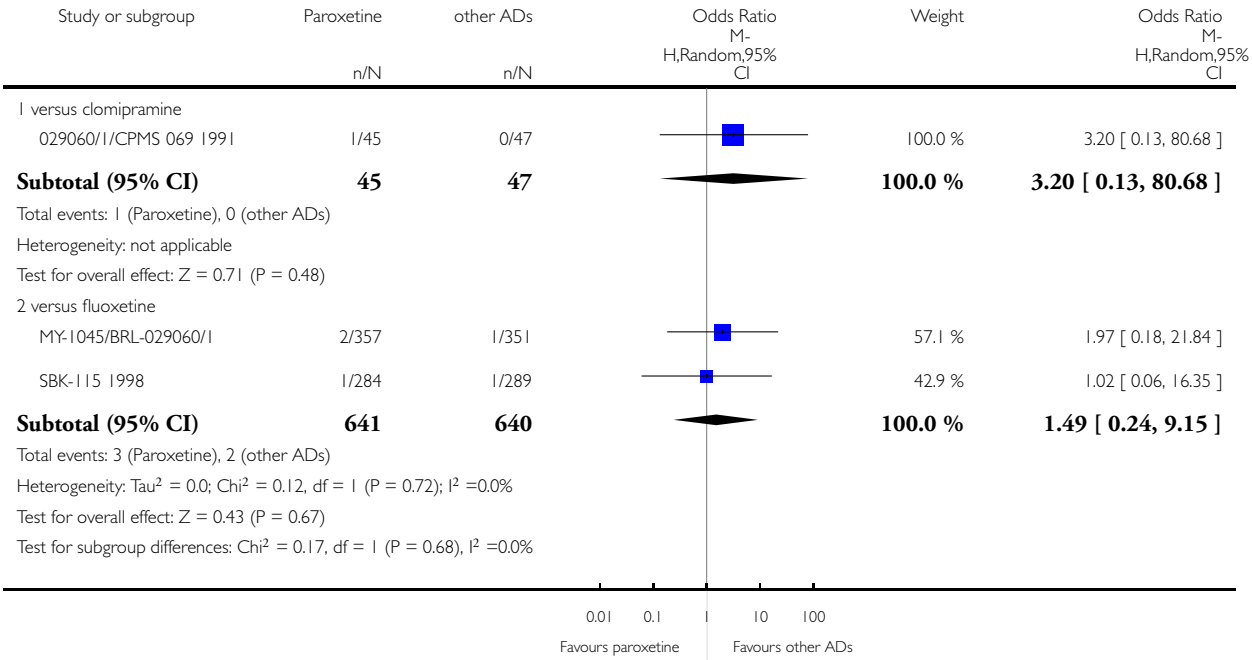
Analysis 60.5. Comparison 60 SE - Neoplasm, Outcome 5 NOS.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 60 SE - Neoplasm

Outcome: 5 NOS



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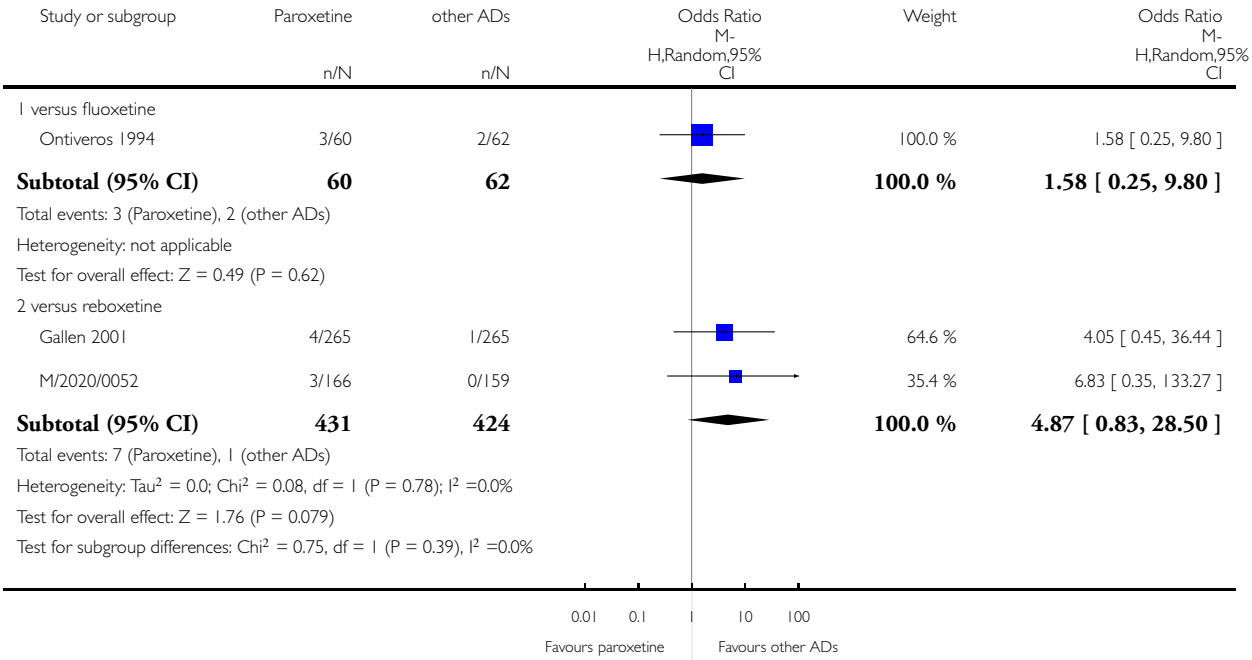
Analysis 61.1. Comparison 61 SE - Nervous system, Outcome 1 Amnesia.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 61 SE - Nervous system

Outcome: 1 Amnesia



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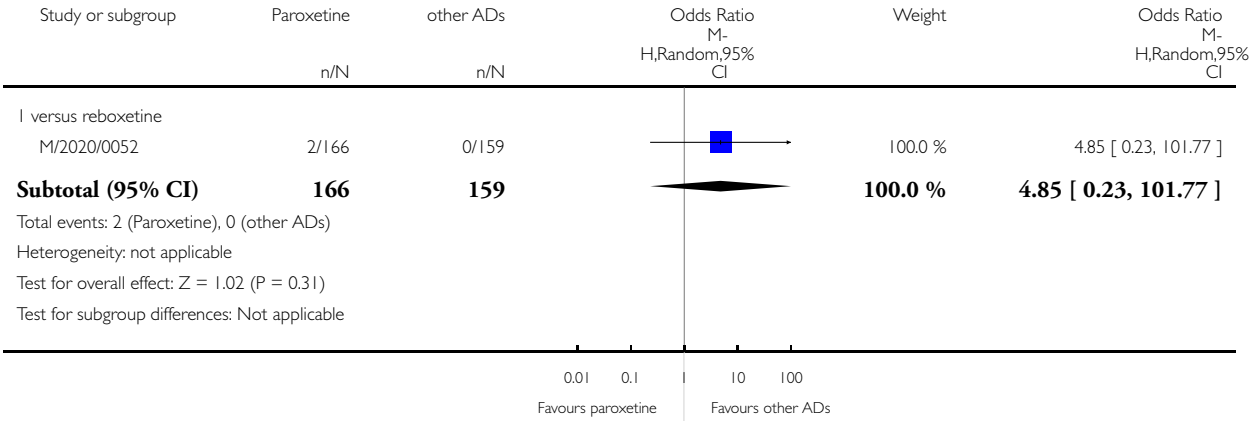
Analysis 61.2. Comparison 61 SE - Nervous system, Outcome 2 Concentration impaired.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 61 SE - Nervous system

Outcome: 2 Concentration impaired

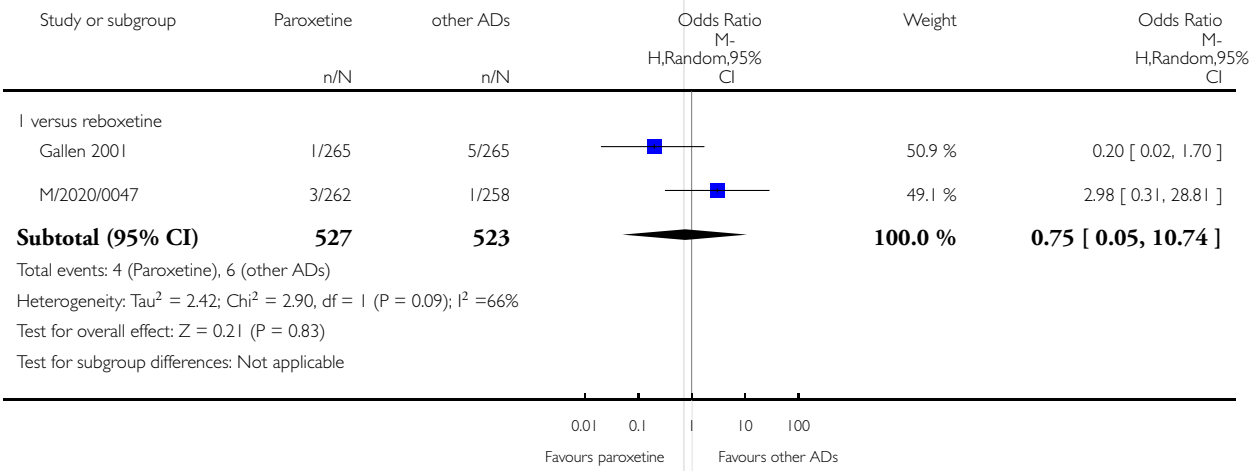


Analysis 61.3. Comparison 61 SE - Nervous system, Outcome 3 Hyperesthesia.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 61 SE - Nervous system

Outcome: 3 Hyperesthesia



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Analysis 61.4. Comparison 61 SE - Nervous system, Outcome 4 Parkinsonism.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 61 SE - Nervous system

Outcome: 4 Parkinsonism

Study or subgroup	Paroxetine n/N	other ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
1 versus nortriptyline					
Mulsant 1999	0/43	1/37		100.0 %	0.28 [0.01, 7.08]
Subtotal (95% CI)	**43**	**37**		**100.0 %**	**0.28 [0.01, 7.08]**
Total events: 0 (Paroxetine), 1 (other ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.77 (P = 0.44)					
Test for subgroup differences: Not applicable					

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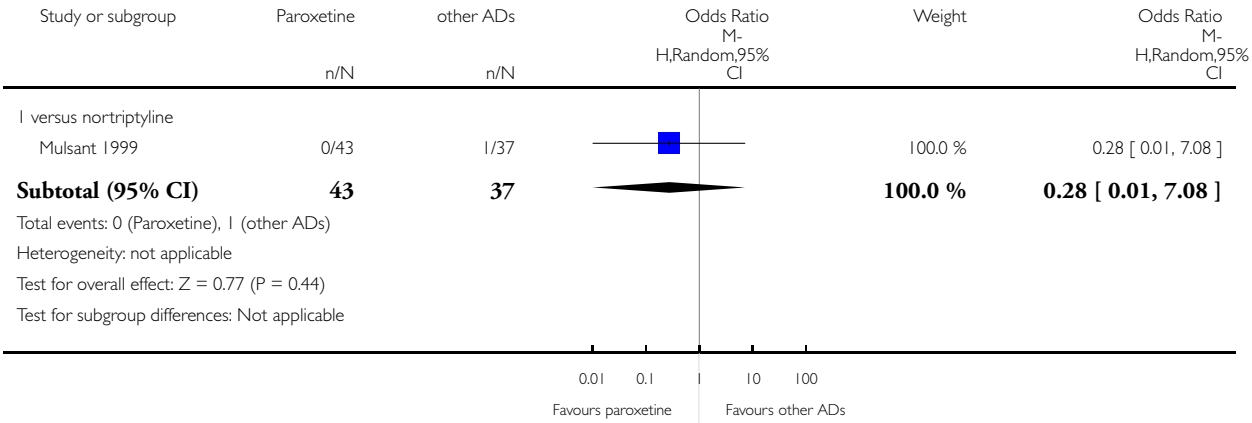
Analysis 61.5. Comparison 61 SE - Nervous system, Outcome 5 Seizure.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 61 SE - Nervous system

Outcome: 5 Seizure

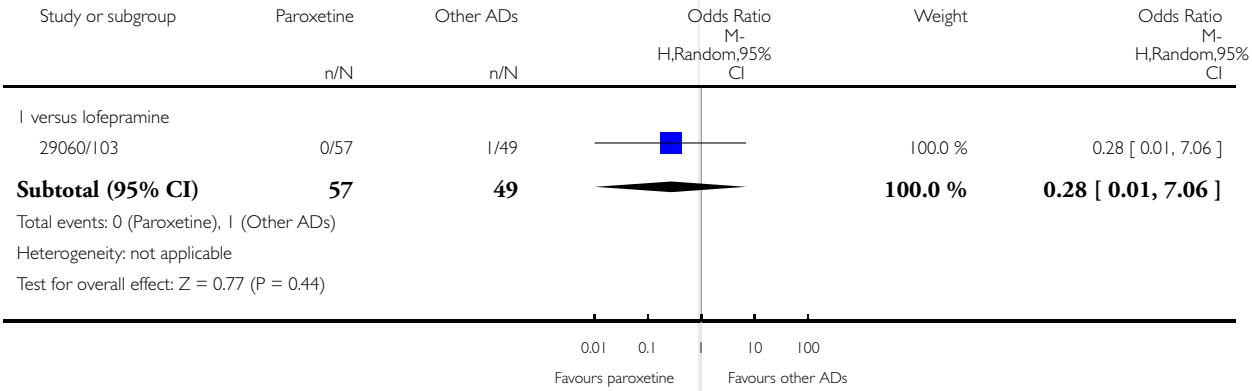


Analysis 61.6. Comparison 61 SE - Nervous system, Outcome 6 Stroke.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 61 SE - Nervous system

Outcome: 6 Stroke



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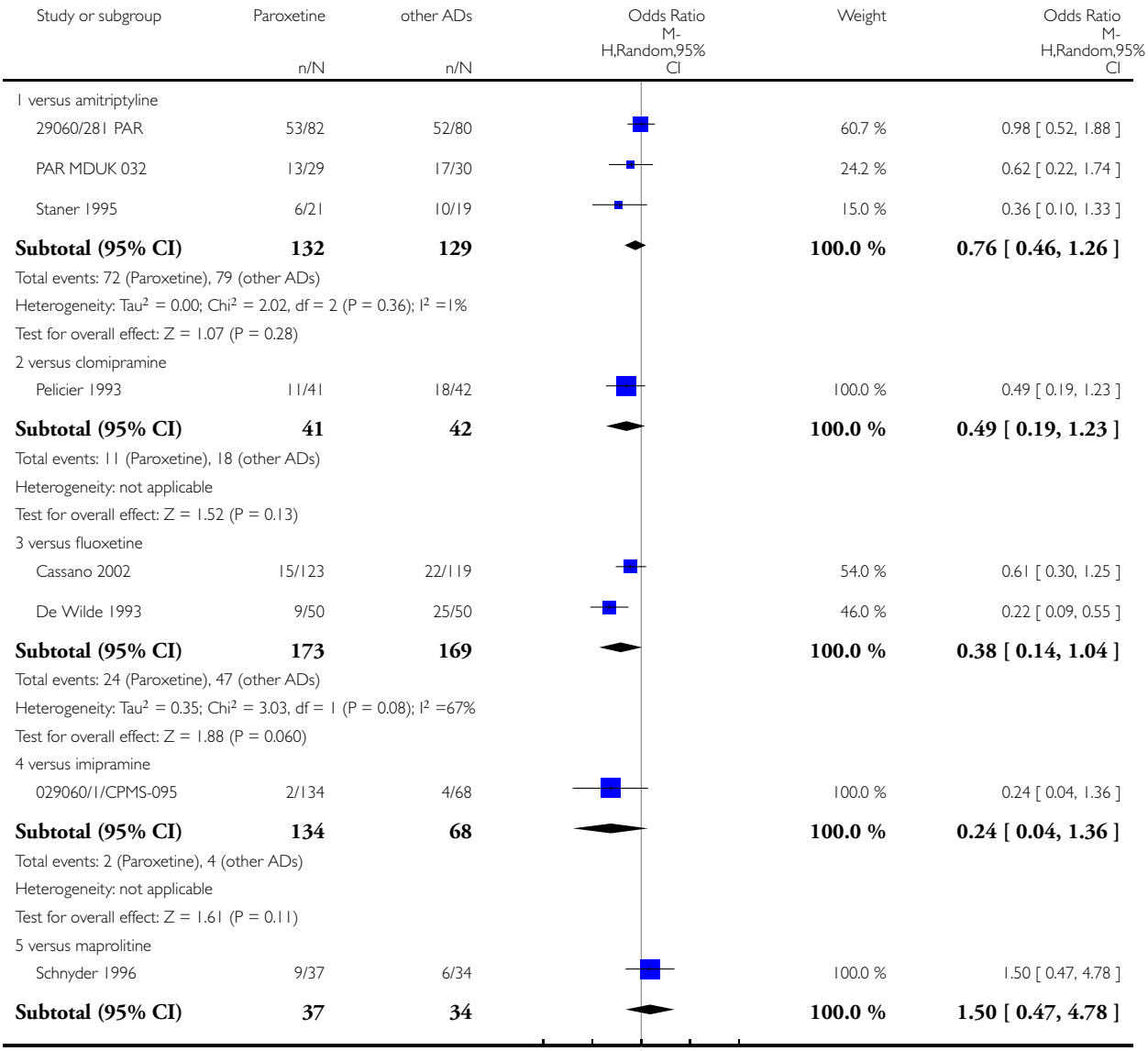
Analysis 61.7. Comparison 61 SE - Nervous system, Outcome 7 NOS.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 61 SE - Nervous system

Outcome: 7 NOS



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Study or subgroup	Paroxetine n/N	other ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Total events: 9 (Paroxetine), 6 (other ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.69 (P = 0.49)					
6 versus mianserin					
29060/III/85/030	11/18	12/15		40.0 %	0.39 [0.08, 1.91]
Dorman 1992	4/29	13/28		60.0 %	0.18 [0.05, 0.67]
Subtotal (95% CI)	**47**	**43**		**100.0 %**	**0.25 [0.09, 0.68]**
Total events: 15 (Paroxetine), 25 (other ADs)					
Heterogeneity: Tau^2 = 0.0; Chi^2 = 0.53, df = 1 (P = 0.47); I^2 =0.0%					
Test for overall effect: Z = 2.72 (P = 0.0065)					
7 versus sertraline					
Aberg-Wistedt 2000	7/177	11/176		100.0 %	0.62 [0.23, 1.63]
Subtotal (95% CI)	**177**	**176**		**100.0 %**	**0.62 [0.23, 1.63]**
Total events: 7 (Paroxetine), 11 (other ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.97 (P = 0.33)					
Test for subgroup differences: Chi^2 = 8.17, df = 6 (P = 0.23), I^2 =27%					

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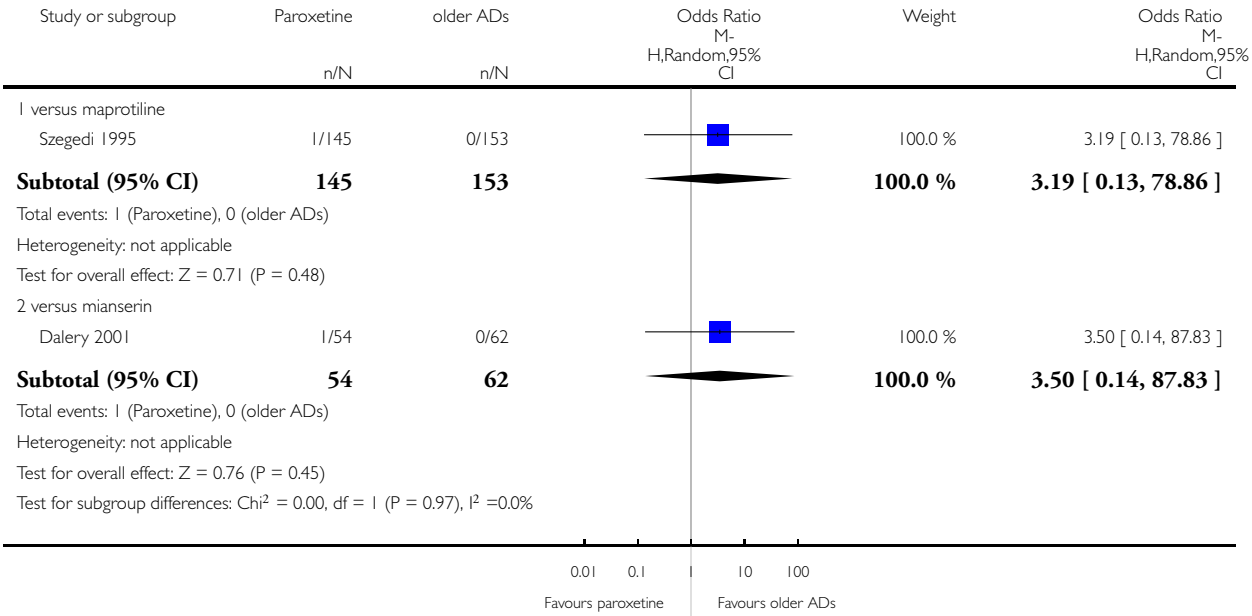
Analysis 62.1. Comparison 62 SE - Pain (back), Outcome 1 Paroxetine versus older ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 62 SE - Pain (back)

Outcome: 1 Paroxetine versus older ADs



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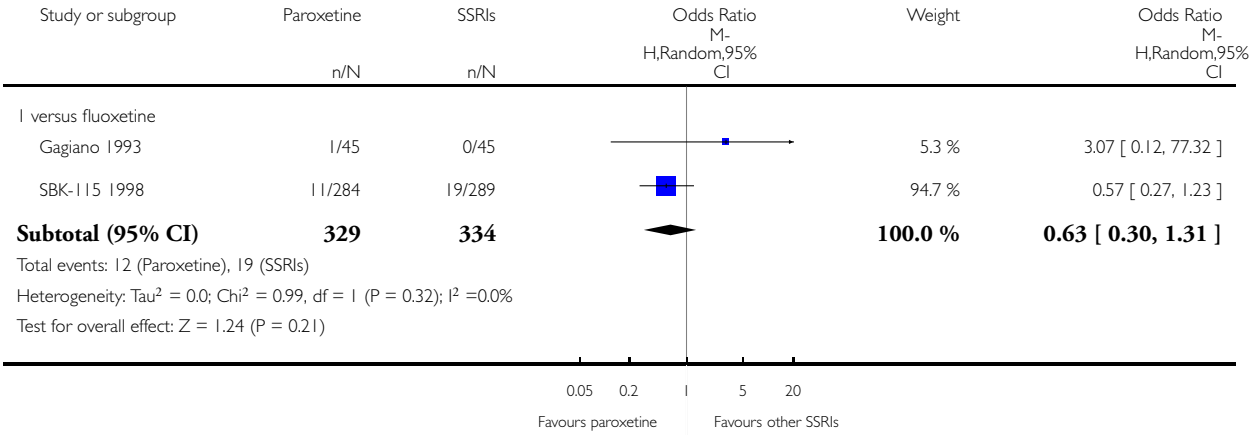
Analysis 62.2. Comparison 62 SE - Pain (back), Outcome 2 Paroxetine versus other SSRIs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 62 SE - Pain (back)

Outcome: 2 Paroxetine versus other SSRIs



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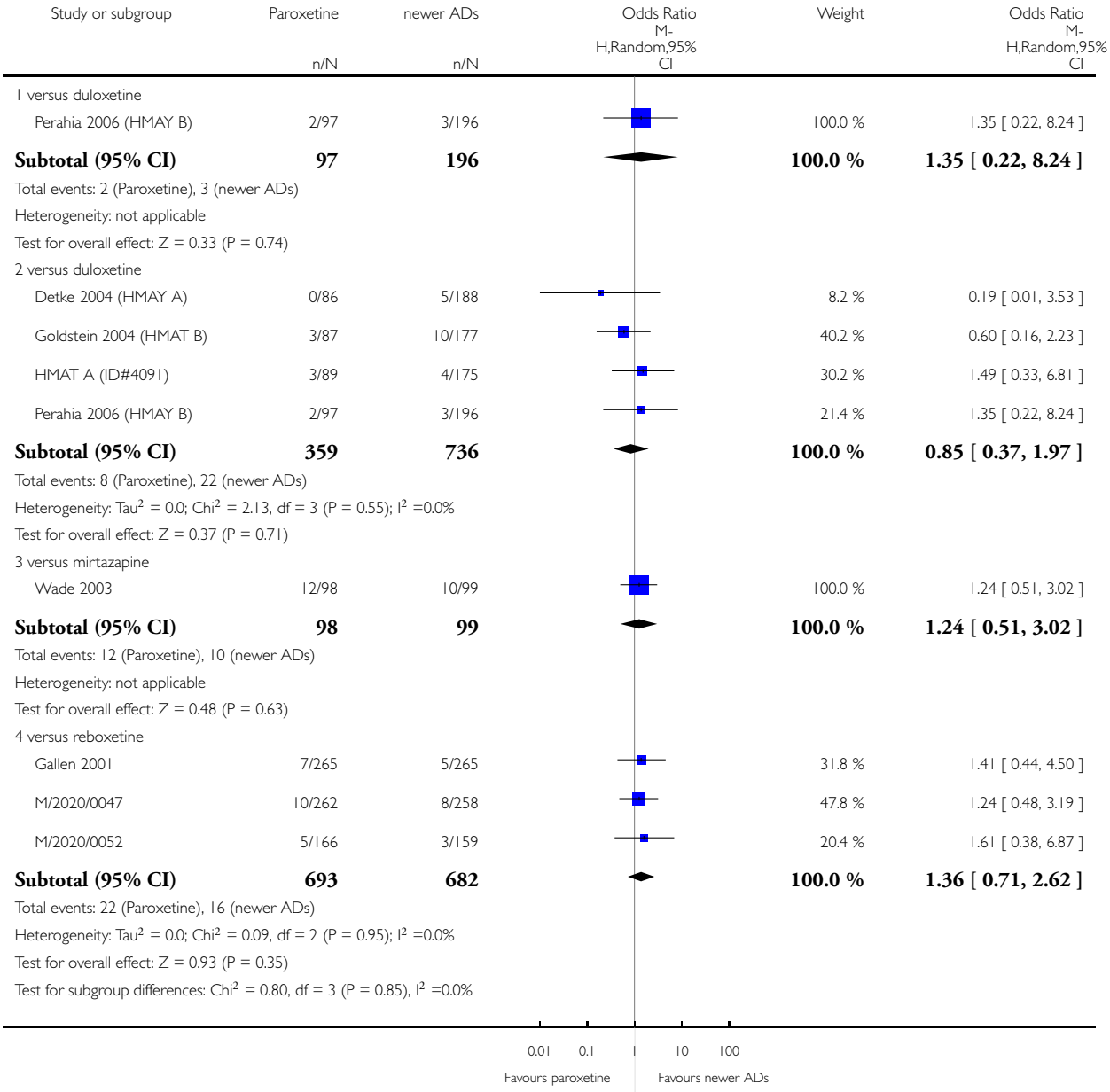
Analysis 62.3. Comparison 62 SE - Pain (back), Outcome 3 Paroxetine versus newer or non-conventional ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 62 SE - Pain (back)

Outcome: 3 Paroxetine versus newer or non-conventional ADs



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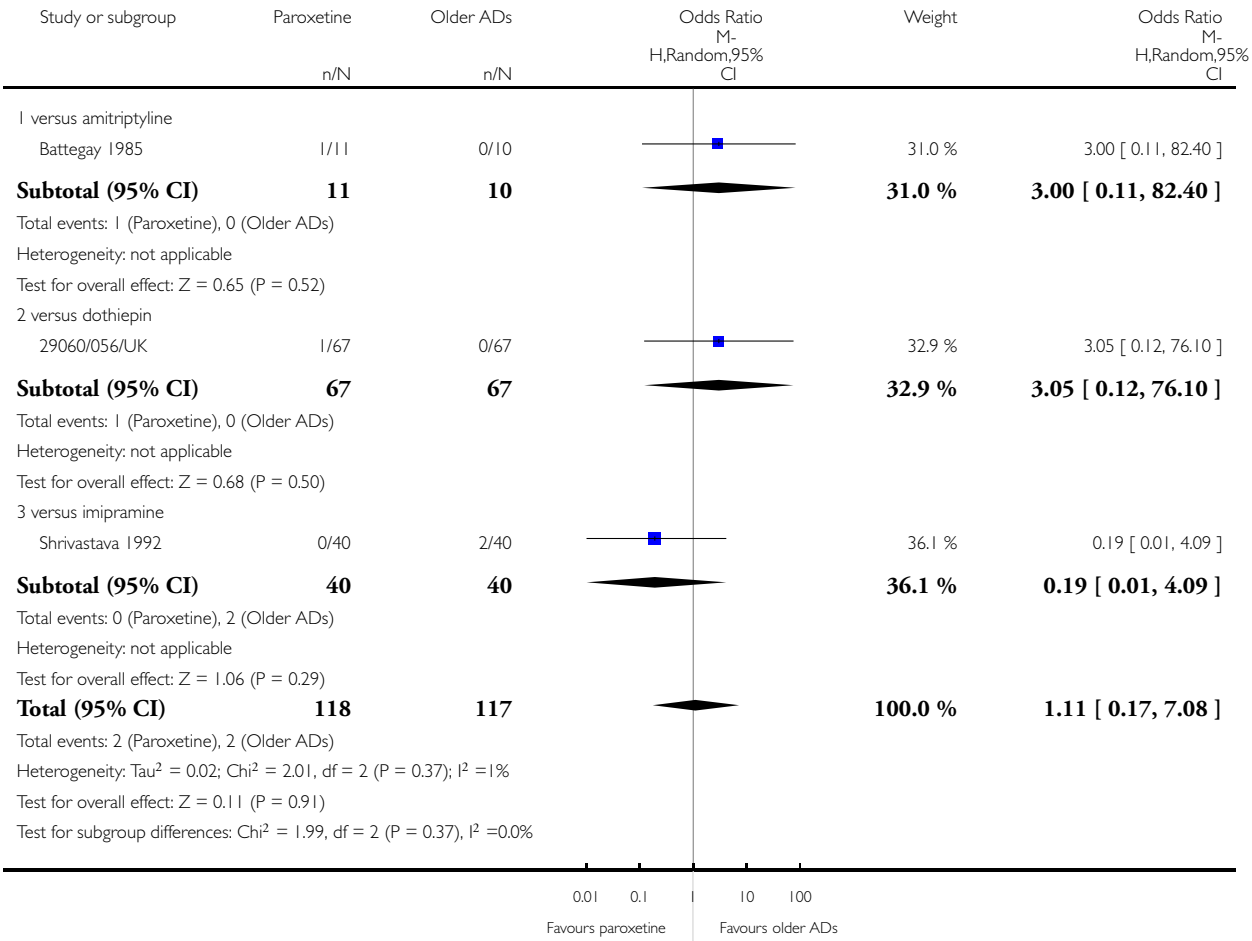
Analysis 63.1. Comparison 63 SE - Pain (chest), Outcome 1 Paroxetine versus older ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 63 SE - Pain (chest)

Outcome: 1 Paroxetine versus older ADs



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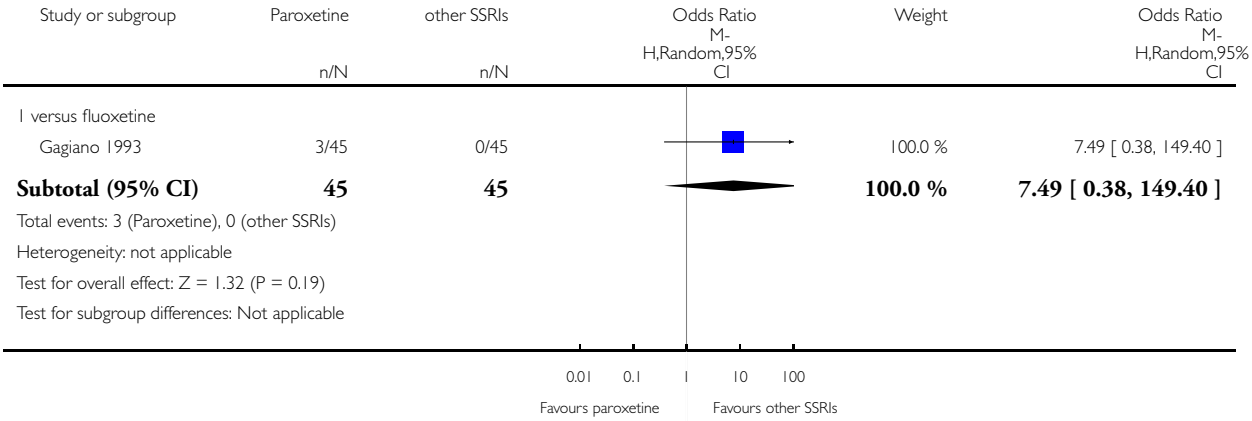
Analysis 63.2. Comparison 63 SE - Pain (chest), Outcome 2 Paroxetine versus other SSRIs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 63 SE - Pain (chest)

Outcome: 2 Paroxetine versus other SSRIs



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Analysis 63.3. Comparison 63 SE - Pain (chest), Outcome 3 Paroxetine versus newer or non-conventional ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 63 SE - Pain (chest)

Outcome: 3 Paroxetine versus newer or non-conventional ADs

Study or subgroup	Paroxetine n/N	newer ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
1 versus duloxetine					
HMAT A (ID#4091)	3/89	4/175		100.0 %	1.49 [0.33, 6.81]
Subtotal (95% CI)	**89**	**175**		**100.0 %**	**1.49 [0.33, 6.81]**
Total events: 3 (Paroxetine), 4 (newer ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.52 (P = 0.61)					
2 versus reboxetine					
Gallen 2001	2/265	2/265		27.1 %	1.00 [0.14, 7.15]
M/2020/0047	5/262	6/258		72.9 %	0.82 [0.25, 2.71]
Subtotal (95% CI)	**527**	**523**		**100.0 %**	**0.86 [0.31, 2.40]**
Total events: 7 (Paroxetine), 8 (newer ADs)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.03$, df = 1 (P = 0.86); $I^2 = 0.0\%$					
Test for overall effect: Z = 0.28 (P = 0.78)					
Test for subgroup differences: $Chi^2 = 0.34$, df = 1 (P = 0.56), $I^2 = 0.0\%$					

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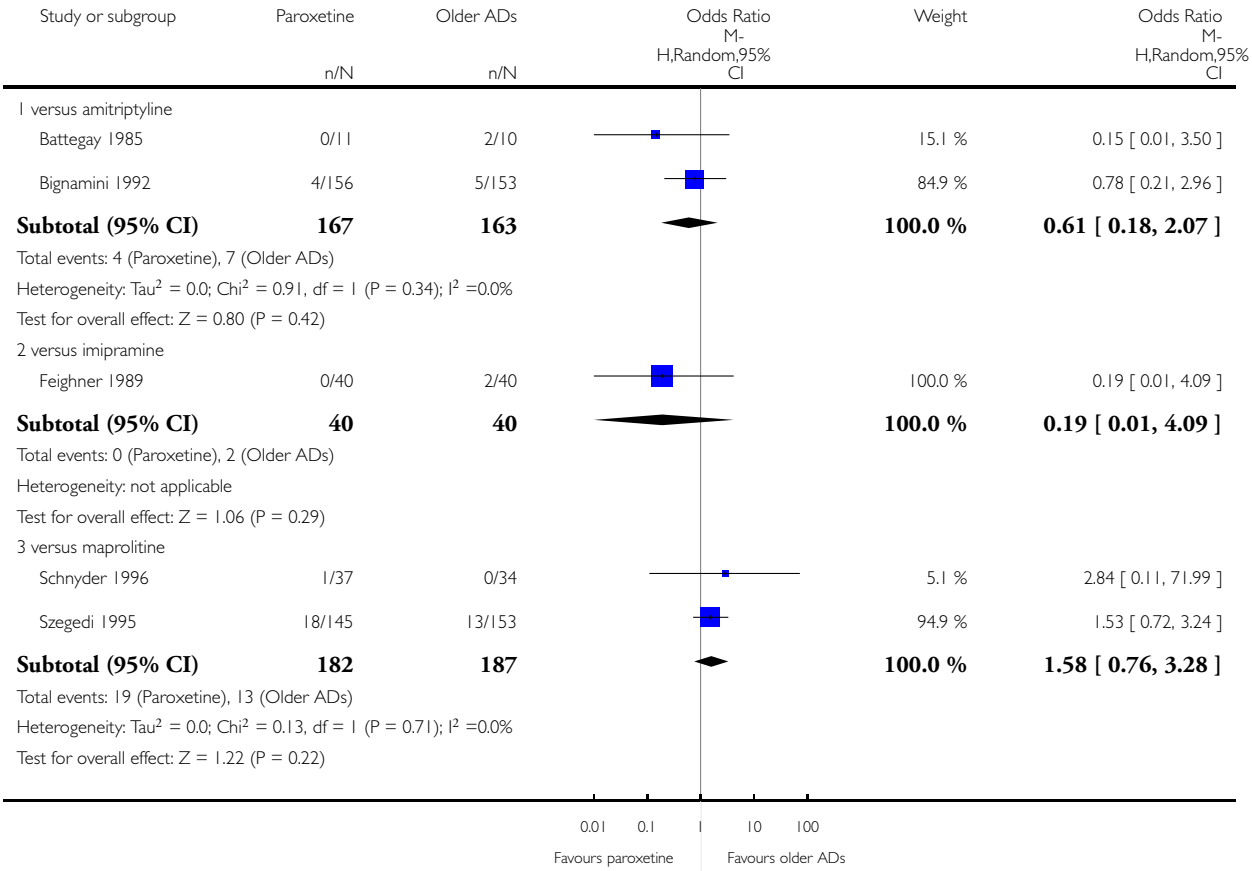
Analysis 64.1. Comparison 64 SE - Pain (abdominal), Outcome 1 Paroxetine versus older ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 64 SE - Pain (abdominal)

Outcome: 1 Paroxetine versus older ADs



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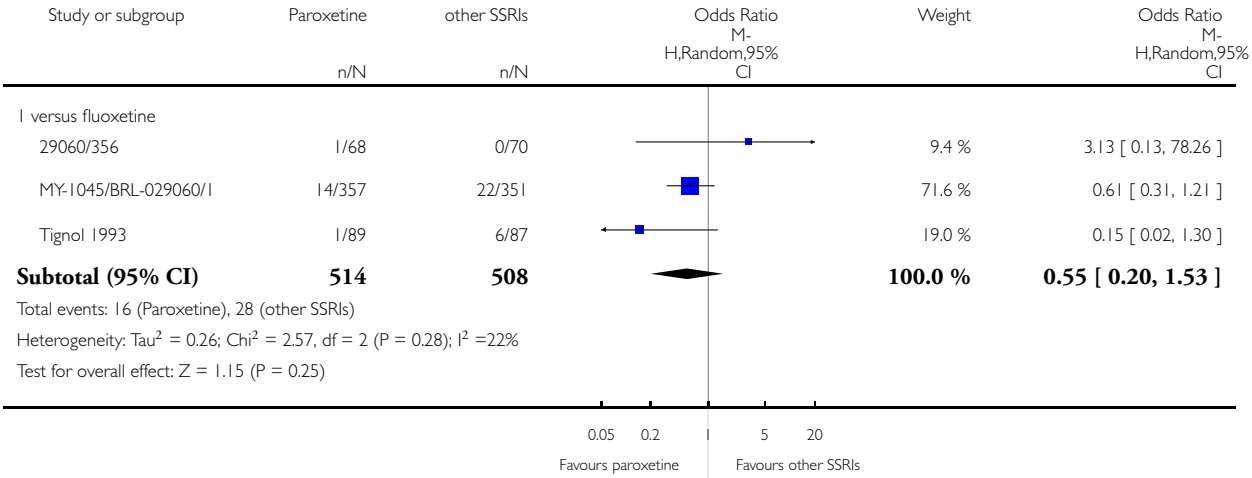
Analysis 64.2. Comparison 64 SE - Pain (abdominal), Outcome 2 Paroxetine versus other SSRIs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 64 SE - Pain (abdominal)

Outcome: 2 Paroxetine versus other SSRIs



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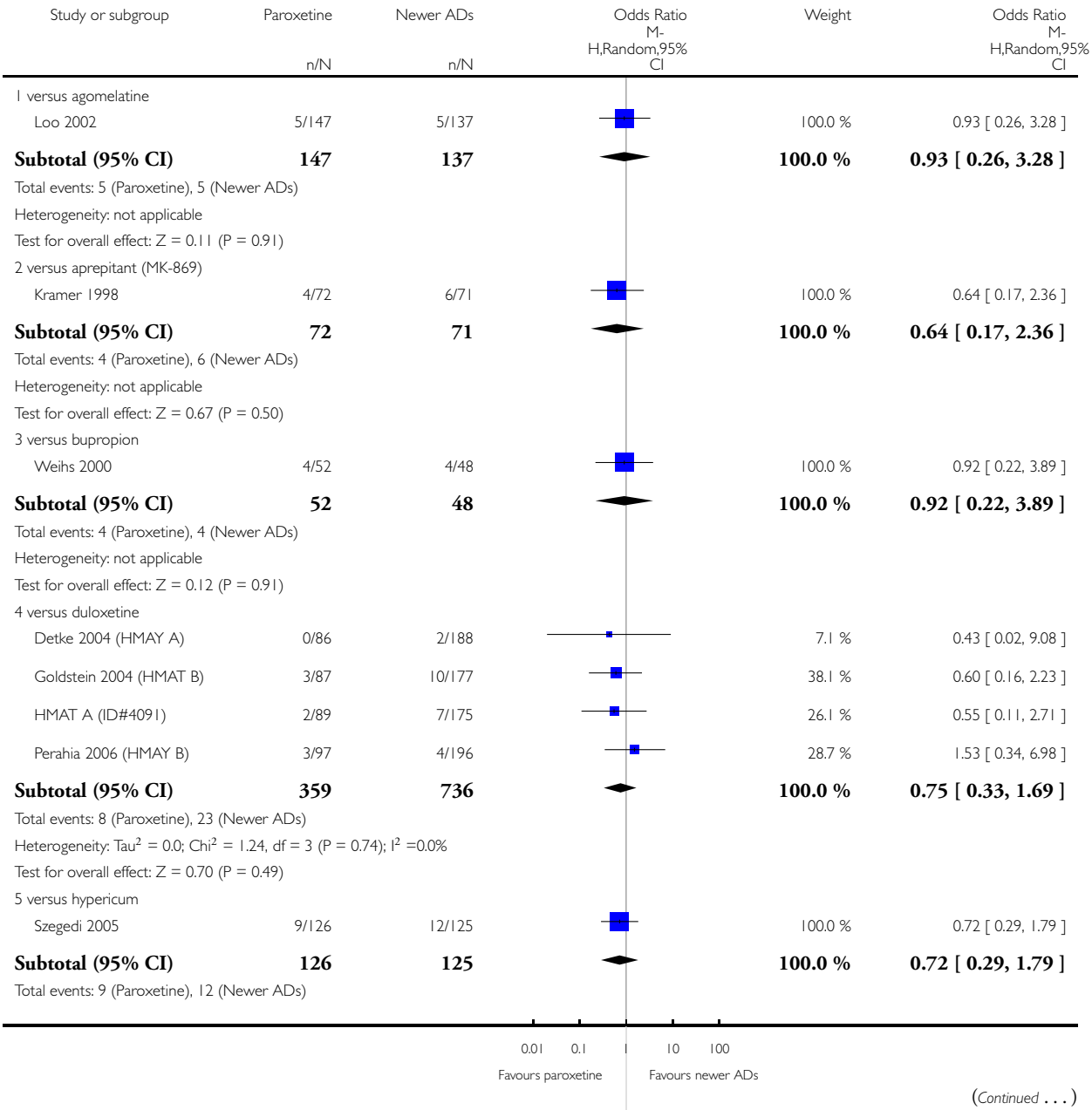
Analysis 64.3. Comparison 64 SE - Pain (abdominal), Outcome 3 Paroxetine versus newer or non-conventional ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 64 SE - Pain (abdominal)

Outcome: 3 Paroxetine versus newer or non-conventional ADs



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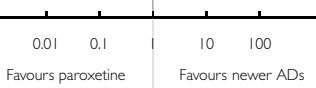
Study or subgroup	Paroxetine n/N	Newer ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Heterogeneity: not applicable					
Test for overall effect: Z = 0.70 (P = 0.48)					
6 versus mirtazapine					
Wade 2003	7/98	7/99		100.0 %	1.01 [0.34, 3.00]
Subtotal (95% CI)	**98**	**99**		**100.0 %**	**1.01 [0.34, 3.00]**
Total events: 7 (Paroxetine), 7 (Newer ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.02 (P = 0.98)					
7 versus reboxetine					
Gallen 2001	10/265	8/265		36.0 %	1.26 [0.49, 3.24]
M/2020/0047	13/262	11/258		47.7 %	1.17 [0.52, 2.67]
M/2020/0052	3/166	6/159		16.3 %	0.47 [0.12, 1.91]
Subtotal (95% CI)	**693**	**682**		**100.0 %**	**1.04 [0.59, 1.83]**
Total events: 26 (Paroxetine), 25 (Newer ADs)					
Heterogeneity: Tau^2 = 0.0; Chi^2 = 1.48, df = 2 (P = 0.48); I^2 =0.0%					
Test for overall effect: Z = 0.12 (P = 0.90)					
8 versus tianeptine					
Waintraub 2002	2/139	5/138		100.0 %	0.39 [0.07, 2.04]
Subtotal (95% CI)	**139**	**138**		**100.0 %**	**0.39 [0.07, 2.04]**
Total events: 2 (Paroxetine), 5 (Newer ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.12 (P = 0.26)					
Test for subgroup differences: Chi^2 = 1.85, df = 7 (P = 0.97), I^2 =0.0%					



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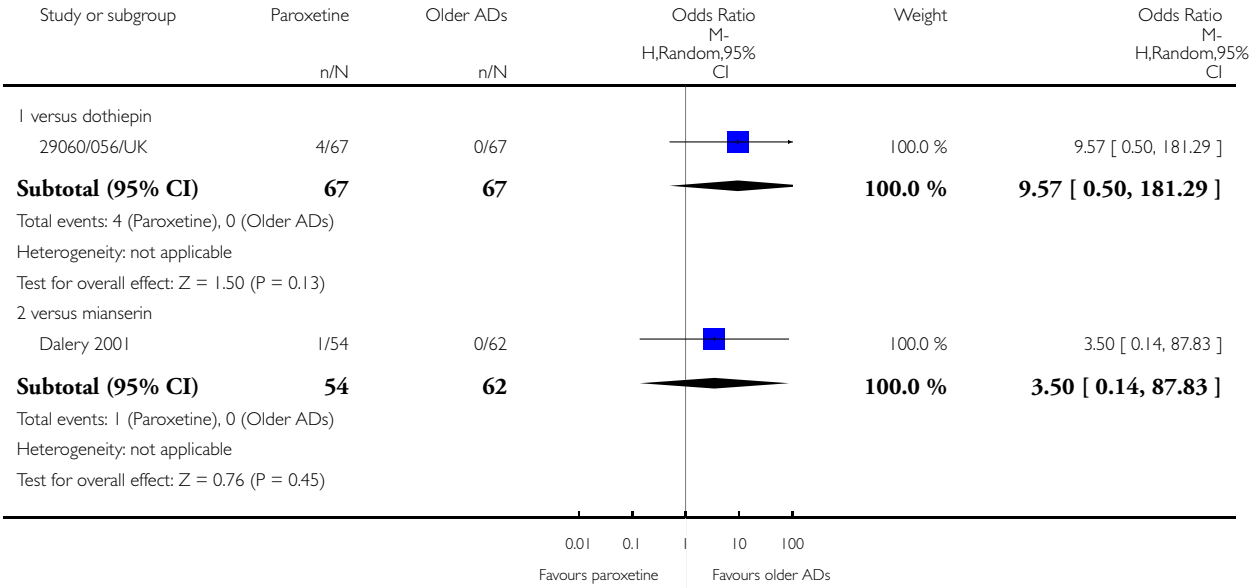
Analysis 65.1. Comparison 65 SE - Pain (general), Outcome 1 Paroxetine versus older ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 65 SE - Pain (general)

Outcome: 1 Paroxetine versus older ADs



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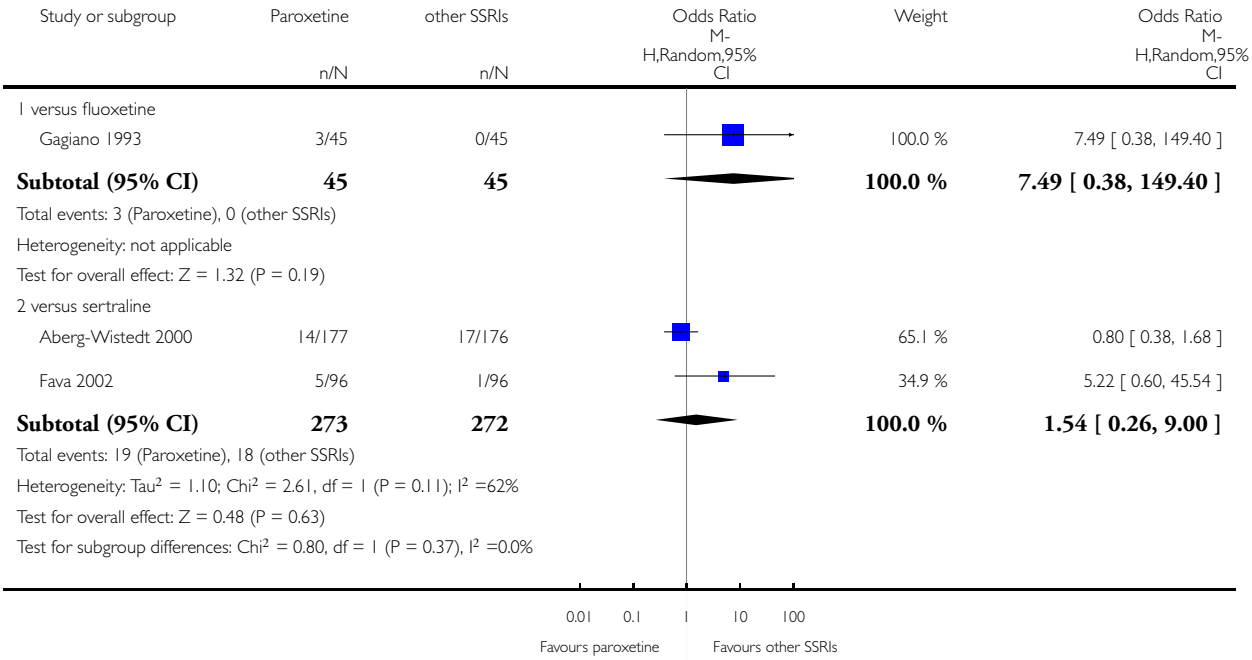
Analysis 65.2. Comparison 65 SE - Pain (general), Outcome 2 Paroxetine versus SSRIs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 65 SE - Pain (general)

Outcome: 2 Paroxetine versus SSRIs



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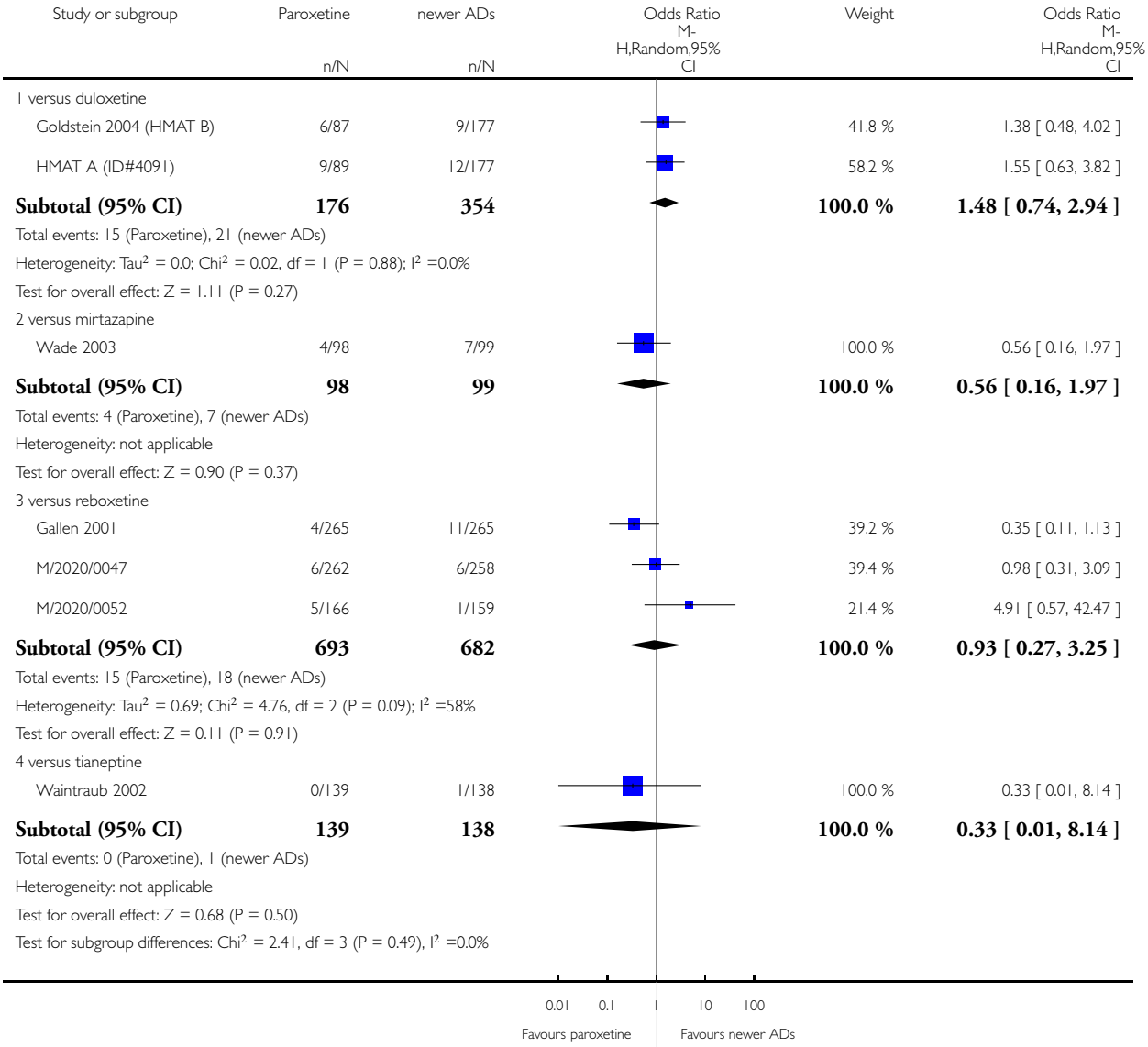
Analysis 65.3. Comparison 65 SE - Pain (general), Outcome 3 Paroxetine versus newer or non-conventional ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 65 SE - Pain (general)

Outcome: 3 Paroxetine versus newer or non-conventional ADs



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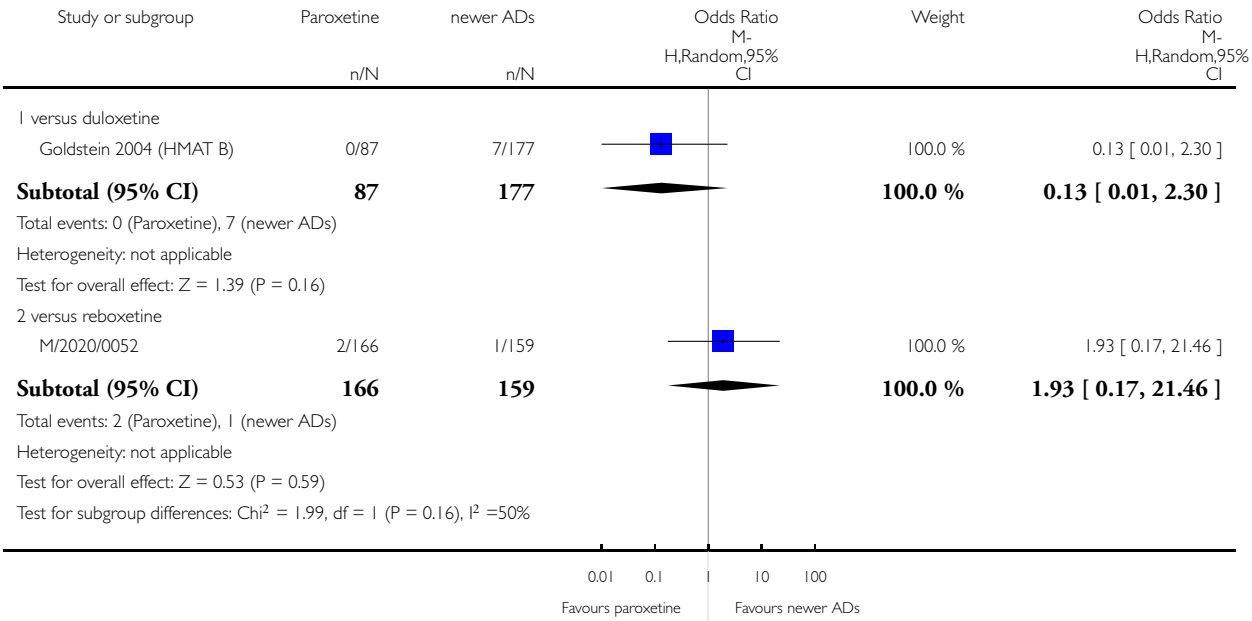
Analysis 66.1. Comparison 66 SE - Pain (neck), Outcome 1 Paroxetine versus newer or non-conventional ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 66 SE - Pain (neck)

Outcome: 1 Paroxetine versus newer or non-conventional ADs



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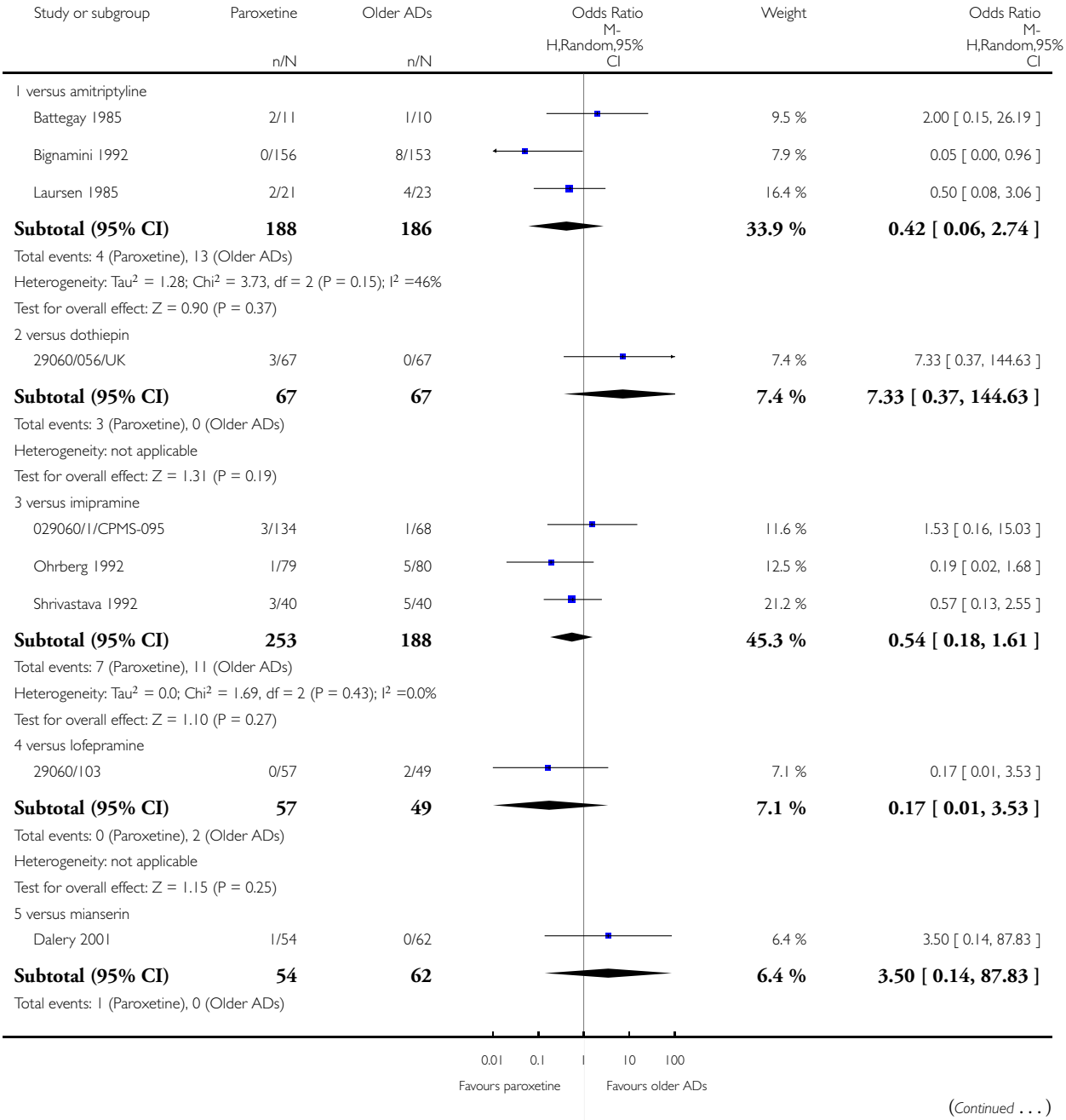
Analysis 67.1. Comparison 67 SE - Palpitations, Outcome 1 Paroxetine versus older ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 67 SE - Palpitations

Outcome: 1 Paroxetine versus older ADs



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Study or subgroup	Paroxetine n/N	Older ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Heterogeneity: not applicable					
Test for overall effect: Z = 0.76 (P = 0.45)					
Total (95% CI)	**619**	**552**		**100.0 %**	**0.63 [0.27, 1.51]**
Total events: 15 (Paroxetine), 26 (Older ADs)					
Heterogeneity: Tau² = 0.34; Chi² = 9.92, df = 8 (P = 0.27); I² =19%					
Test for overall effect: Z = 1.03 (P = 0.30)					
Test for subgroup differences: Chi² = 4.67, df = 4 (P = 0.32), I² =14%					

Analysis 67.2. Comparison 67 SE - Palpitations, Outcome 2 Paroxetine versus other SSRIs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 67 SE - Palpitations

Outcome: 2 Paroxetine versus other SSRIs

Study or subgroup	Paroxetine n/N	other SSRIs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
1 versus fluoxetine					
De Wilde 1993	0/50	1/50		100.0 %	0.33 [0.01, 8.21]
Subtotal (95% CI)	**50**	**50**		**100.0 %**	**0.33 [0.01, 8.21]**
Total events: 0 (Paroxetine), 1 (other SSRIs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.68 (P = 0.50)					
2 versus fluvoxamine					
Kiev 1997	1/30	4/30		100.0 %	0.22 [0.02, 2.14]
Subtotal (95% CI)	**30**	**30**		**100.0 %**	**0.22 [0.02, 2.14]**
Total events: 1 (Paroxetine), 4 (other SSRIs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.30 (P = 0.19)					

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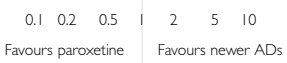
Analysis 67.3. Comparison 67 SE - Palpitations, Outcome 3 Paroxetine versus newer or non-conventional ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 67 SE - Palpitations

Outcome: 3 Paroxetine versus newer or non-conventional ADs

Study or subgroup	Paroxetine n/N	newer ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
1 versus duloxetine					
Detke 2004 (HMAY A)	1/86	3/188		12.9 %	0.73 [0.07, 7.08]
Goldstein 2004 (HMAT B)	2/87	4/177		19.4 %	1.02 [0.18, 5.67]
HMAT A (ID#4091)	5/89	4/175		26.2 %	2.54 [0.67, 9.72]
Lee 2007 (HMCV)	10/240	22/238		41.5 %	0.43 [0.20, 0.92]
Subtotal (95% CI)	**502**	**778**		**100.0 %**	**0.86 [0.34, 2.18]**
Total events: 18 (Paroxetine), 33 (newer ADs)					
Heterogeneity: Tau^2 = 0.38; Chi^2 = 5.33, df = 3 (P = 0.15); I^2 =44%					
Test for overall effect: Z = 0.31 (P = 0.76)					
2 versus reboxetine					
Gallen 2001	12/265	14/265		47.2 %	0.85 [0.39, 1.87]
M/2020/0047	7/262	7/258		30.8 %	0.98 [0.34, 2.85]
M/2020/0052	3/166	10/159		22.0 %	0.27 [0.07, 1.02]
Subtotal (95% CI)	**693**	**682**		**100.0 %**	**0.69 [0.36, 1.35]**
Total events: 22 (Paroxetine), 31 (newer ADs)					
Heterogeneity: Tau^2 = 0.08; Chi^2 = 2.61, df = 2 (P = 0.27); I^2 =23%					
Test for overall effect: Z = 1.07 (P = 0.28)					



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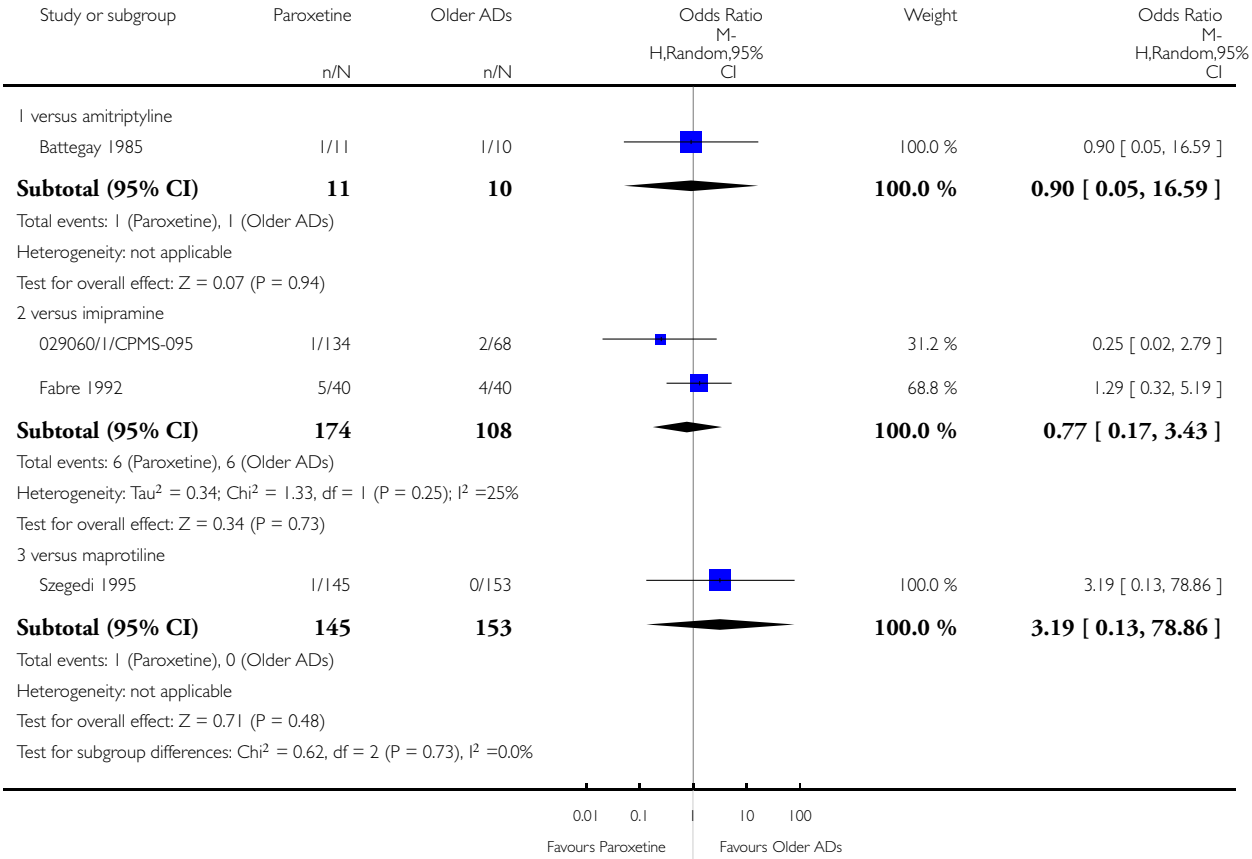
Analysis 68.1. Comparison 68 SE - Paraesthesia, Outcome 1 Paroxetine versus older ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 68 SE - Paraesthesia

Outcome: 1 Paroxetine versus older ADs



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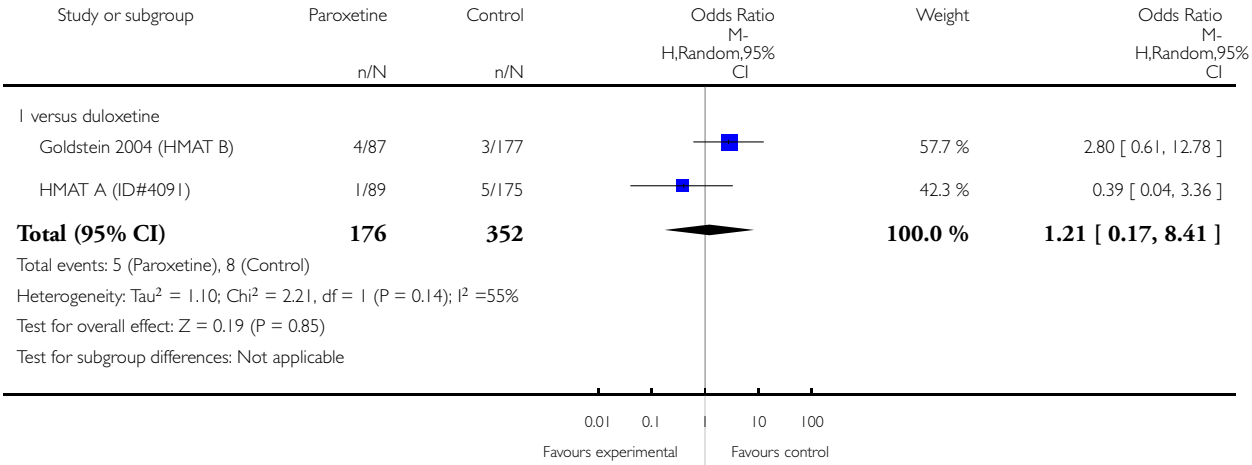
Analysis 68.2. Comparison 68 SE - Paraesthesia, Outcome 2 Paroxetine versus SSRIs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 68 SE - Paraesthesia

Outcome: 2 Paroxetine versus SSRIs



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Analysis 68.3. Comparison 68 SE - Paraesthesia, Outcome 3 Paroxetine versus newer or non-conventional ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 68 SE - Paraesthesia

Outcome: 3 Paroxetine versus newer or non-conventional ADs

Study or subgroup	Paroxetine n/N	newer ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
1 versus reboxetine					
Gallen 2001	4/265	11/265		45.4 %	0.35 [0.11, 1.13]
M/2020/0047	4/262	10/258		44.2 %	0.38 [0.12, 1.24]
M/2020/0052	2/166	1/159		10.5 %	1.93 [0.17, 21.46]
Subtotal (95% CI)	**693**	**682**		**100.0 %**	**0.44 [0.20, 0.96]**
Total events: 10 (Paroxetine), 22 (newer ADs)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 1.63$, df = 2 (P = 0.44); $I^2 = 0.0\%$					
Test for overall effect: Z = 2.07 (P = 0.038)					

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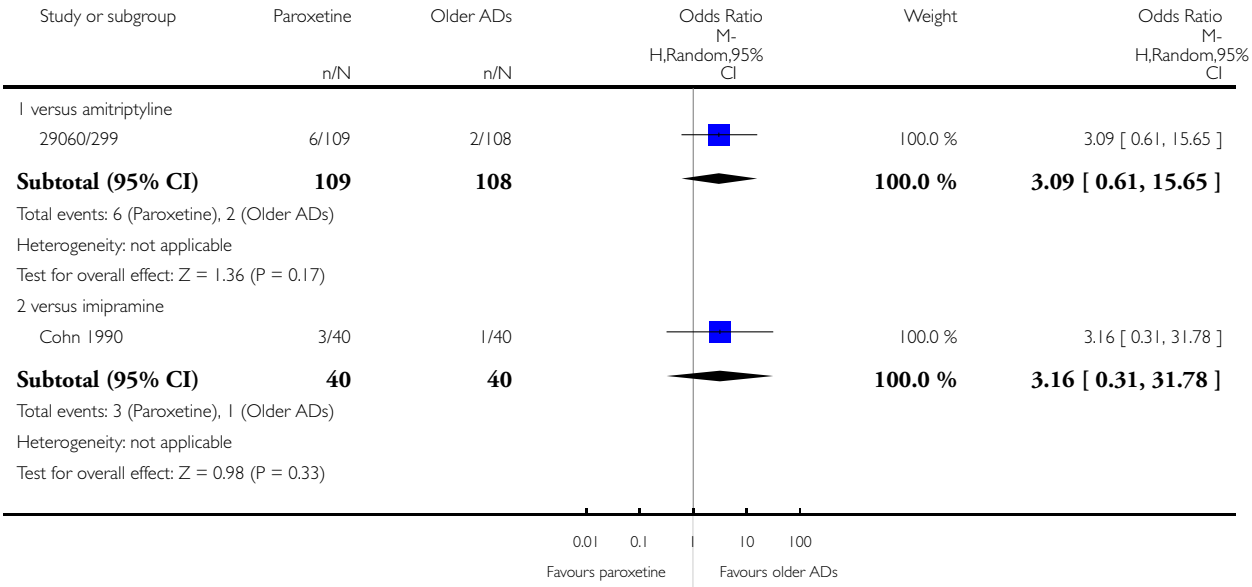
Analysis 69.1. Comparison 69 SE - Pharyngitis, Outcome 1 Paroxetine versus older ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 69 SE - Pharyngitis

Outcome: 1 Paroxetine versus older ADs



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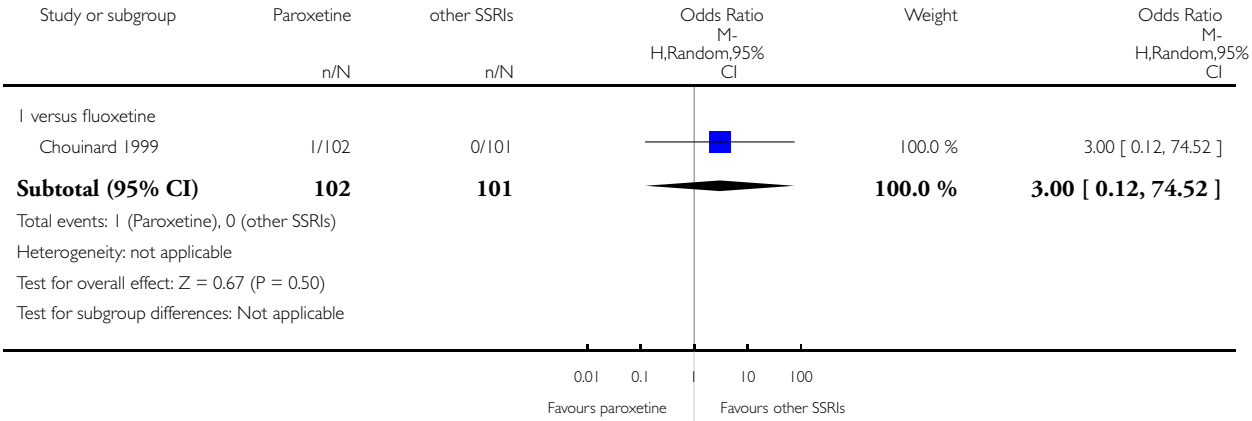
Analysis 69.2. Comparison 69 SE - Pharyngitis, Outcome 2 Paroxetine versus SSRIs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 69 SE - Pharyngitis

Outcome: 2 Paroxetine versus SSRIs



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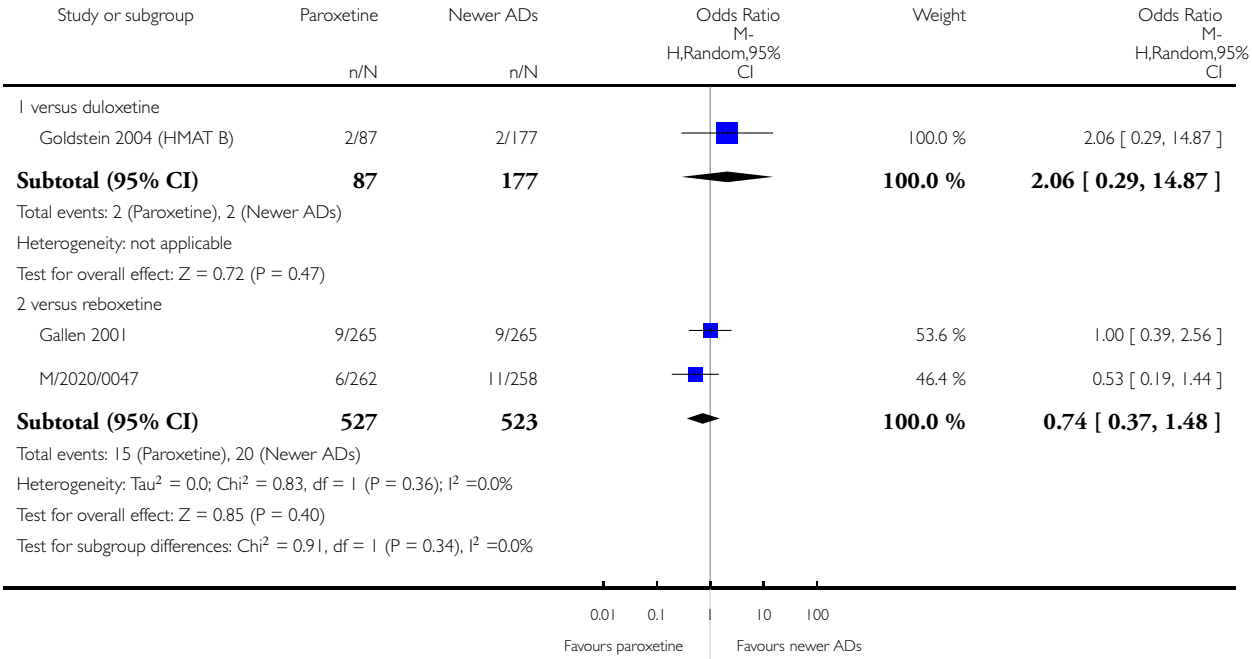
Analysis 69.3. Comparison 69 SE - Pharyngitis, Outcome 3 Paroxetine versus newer or non-conventional ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 69 SE - Pharyngitis

Outcome: 3 Paroxetine versus newer or non-conventional ADs



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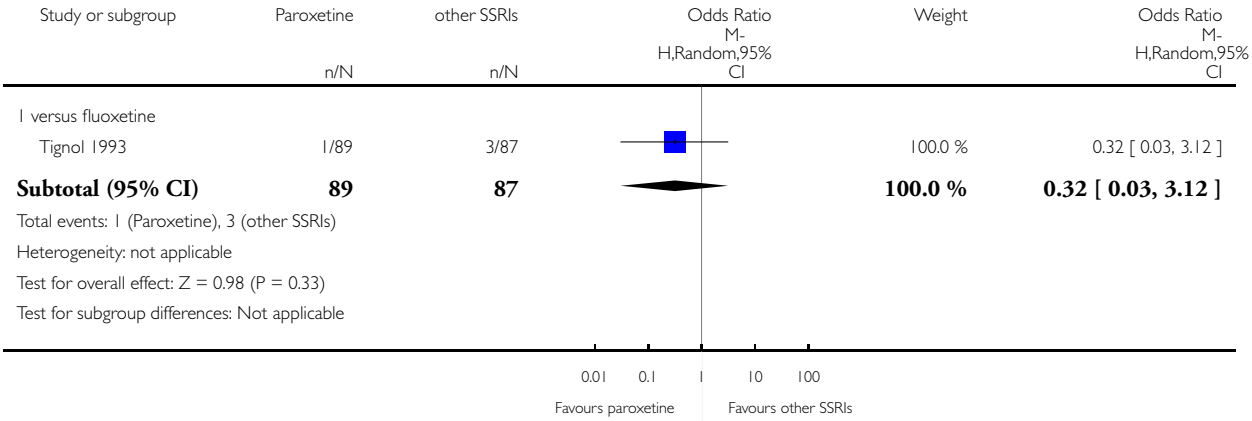
Analysis 70.1. Comparison 70 SE - Pruritus, Outcome 1 Paroxetine versus other SSRIs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 70 SE - Pruritus

Outcome: 1 Paroxetine versus other SSRIs



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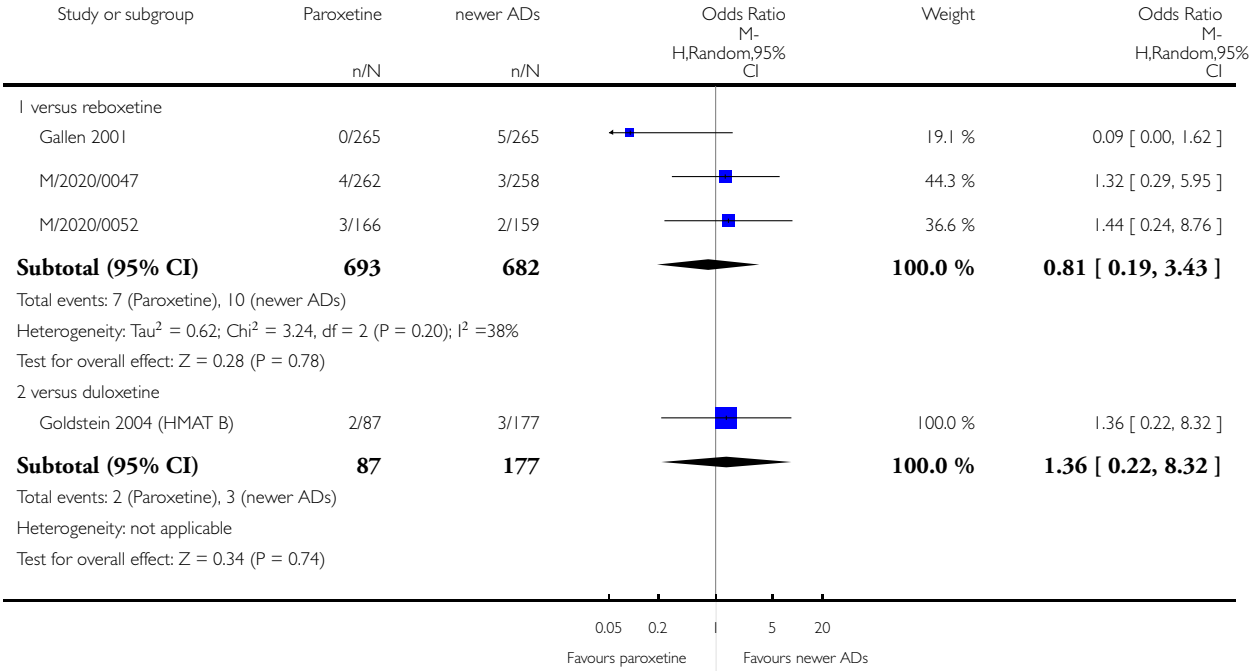
Analysis 70.2. Comparison 70 SE - Pruritus, Outcome 2 Paroxetine versus newer or non-conventional ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 70 SE - Pruritus

Outcome: 2 Paroxetine versus newer or non-conventional ADs



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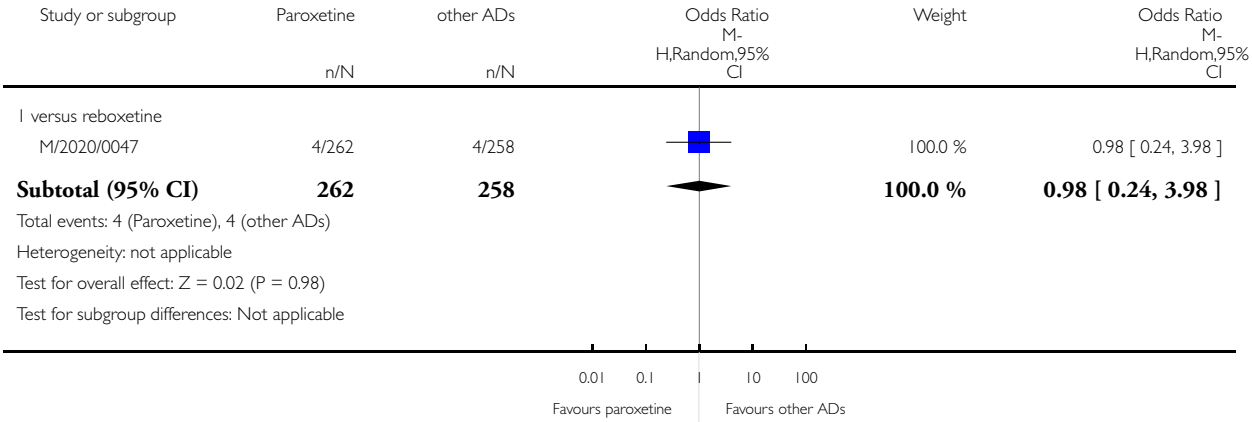
Analysis 71.1. Comparison 71 SE - RARE, Outcome 1 Abdomen enlarged.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 71 SE - RARE

Outcome: 1 Abdomen enlarged

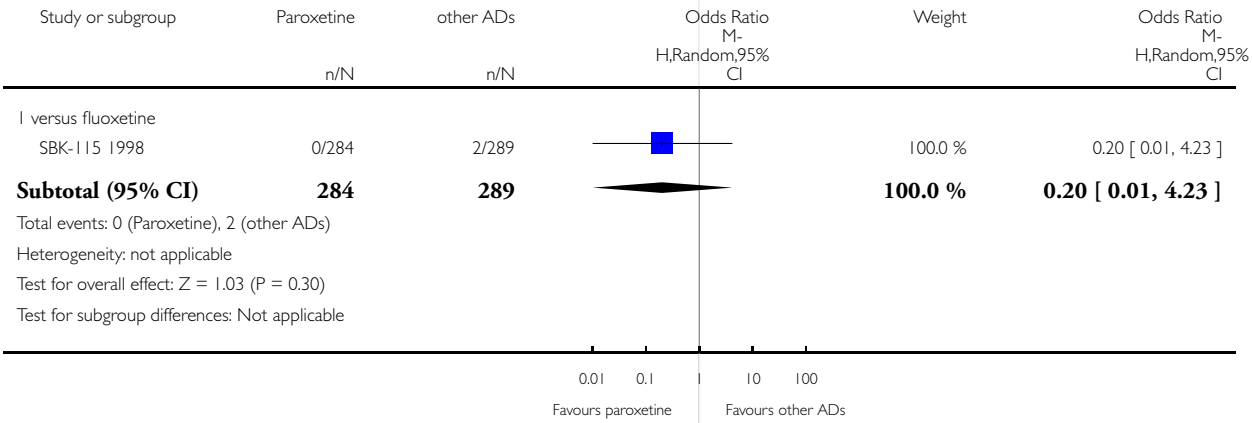


Analysis 71.2. Comparison 71 SE - RARE, Outcome 2 Acute pyelonephritis.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 71 SE - RARE

Outcome: 2 Acute pyelonephritis



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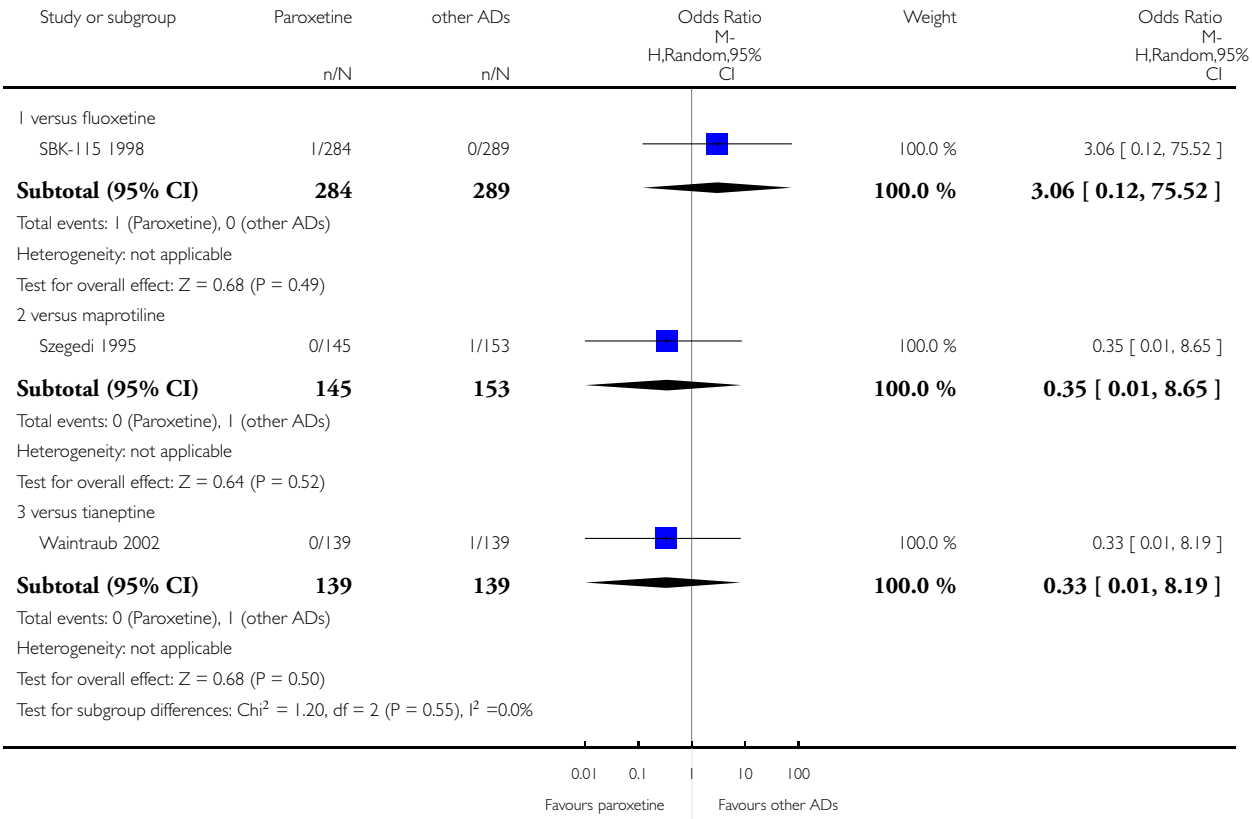
Analysis 71.3. Comparison 71 SE - RARE, Outcome 3 Alcohol abuse.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 71 SE - RARE

Outcome: 3 Alcohol abuse



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Analysis 71.4. Comparison 71 SE - RARE, Outcome 4 Angina attack.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 71 SE - RARE

Outcome: 4 Angina attack

Study or subgroup	Paroxetine n/N	other ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
1 versus dothiepin					
29060/056/UK	0/67	1/67		100.0 %	0.33 [0.01, 8.21]
Subtotal (95% CI)	**67**	**67**		**100.0 %**	**0.33 [0.01, 8.21]**
Total events: 0 (Paroxetine), 1 (other ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.68 (P = 0.50)					
Test for subgroup differences: Not applicable					

Analysis 71.5. Comparison 71 SE - RARE, Outcome 5 Coronary artery disorder.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 71 SE - RARE

Outcome: 5 Coronary artery disorder

Study or subgroup	Paroxetine n/N	other ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
1 versus fluoxetine					
MY-1045/BRL-029060/1	0/357	1/351		100.0 %	0.33 [0.01, 8.05]
Subtotal (95% CI)	**357**	**351**		**100.0 %**	**0.33 [0.01, 8.05]**
Total events: 0 (Paroxetine), 1 (other ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.68 (P = 0.49)					
Test for subgroup differences: Not applicable					

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Analysis 71.6. Comparison 71 SE - RARE, Outcome 6 Deep thrombophlebitis.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 71 SE - RARE

Outcome: 6 Deep thrombophlebitis

Study or subgroup	Paroxetine n/N	other ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
1 versus fluoxetine					
29060/356	0/68	1/70		33.1 %	0.34 [0.01, 8.45]
MY-1045/BRL-029060/1	0/357	1/351		33.4 %	0.33 [0.01, 8.05]
SBK-115 1998	0/284	1/289		33.4 %	0.34 [0.01, 8.33]
Subtotal (95% CI)	**709**	**710**		**100.0 %**	**0.33 [0.05, 2.13]**
Total events: 0 (Paroxetine), 3 (other ADs)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.00$, df = 2 (P = 1.00); $I^2 = 0.0\%$					
Test for overall effect: Z = 1.16 (P = 0.25)					
Test for subgroup differences: Not applicable					

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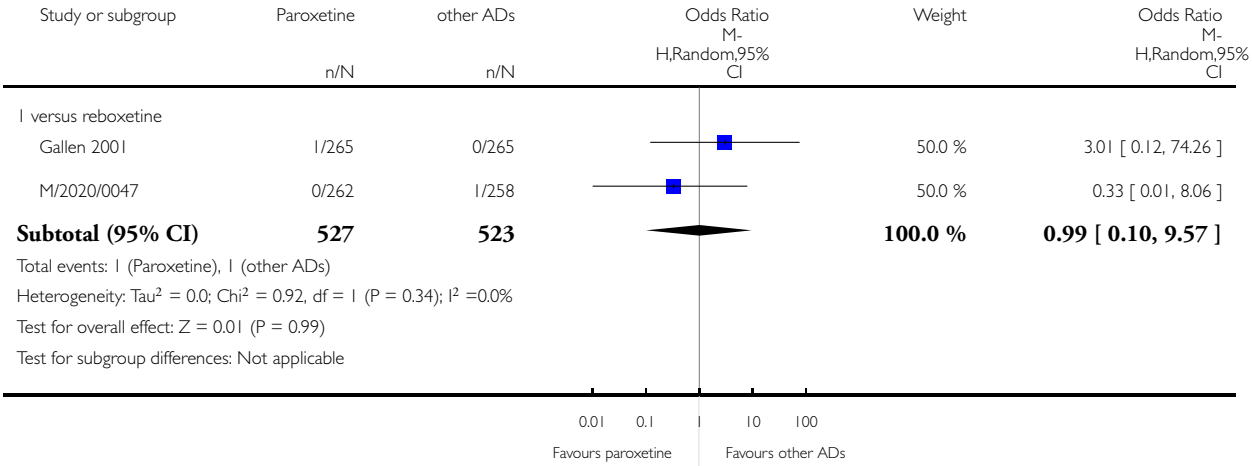
Analysis 71.7. Comparison 71 SE - RARE, Outcome 7 Edema generalized.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 71 SE - RARE

Outcome: 7 Edema generalized

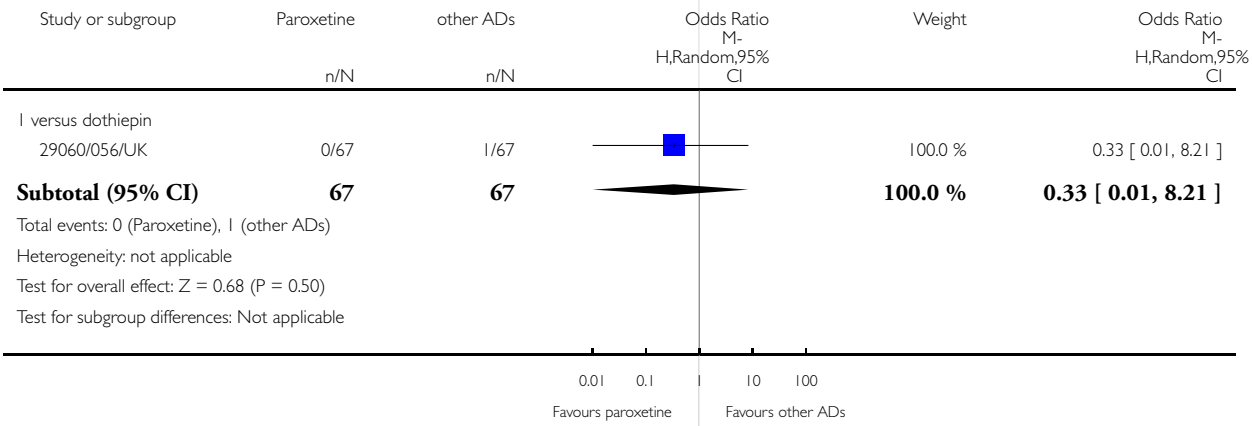


Analysis 71.8. Comparison 71 SE - RARE, Outcome 8 Balance difficulty.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 71 SE - RARE

Outcome: 8 Balance difficulty



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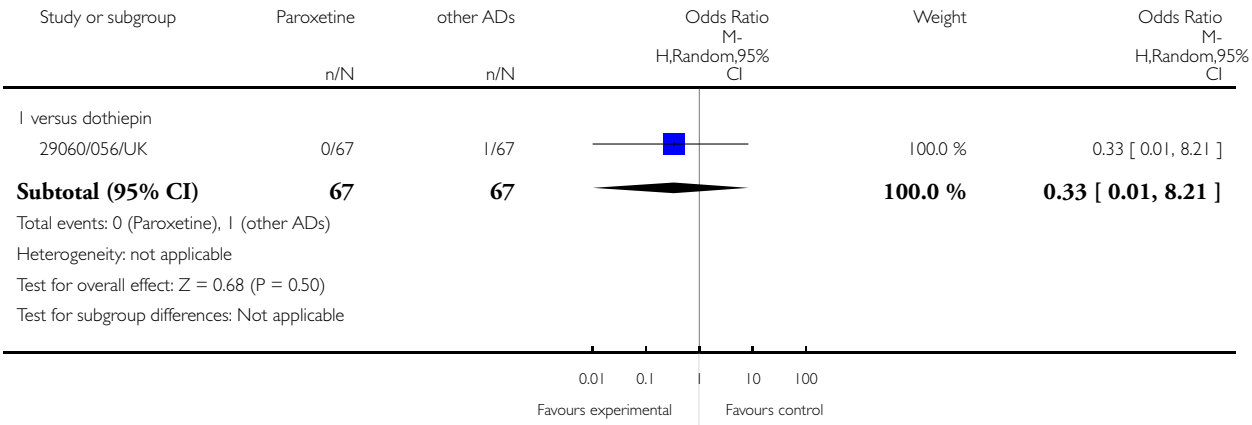
Analysis 71.9. Comparison 71 SE - RARE, Outcome 9 Enucleation of eyeball.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 71 SE - RARE

Outcome: 9 Enucleation of eyeball



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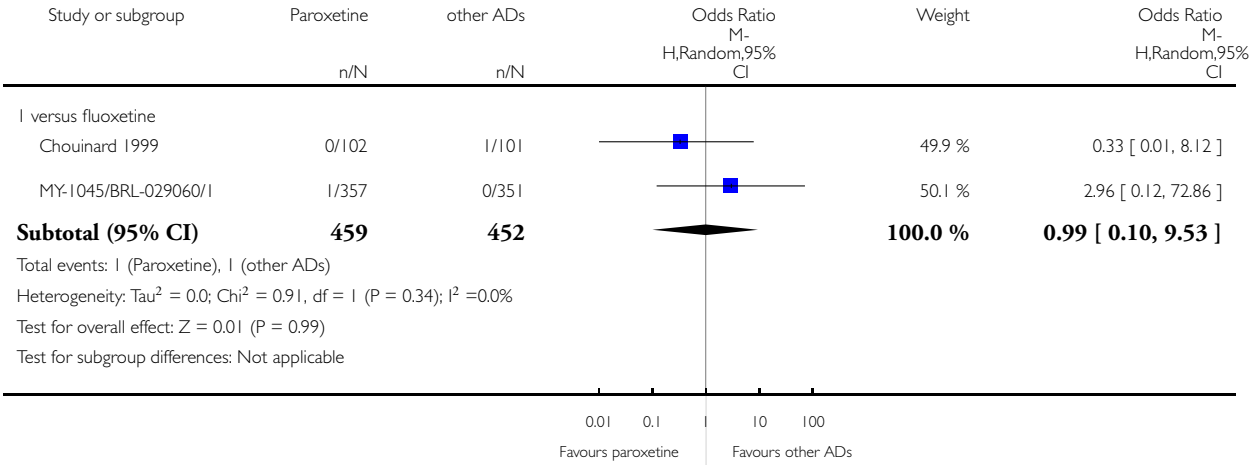
Analysis 71.10. Comparison 71 SE - RARE, Outcome 10 Epistaxis.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 71 SE - RARE

Outcome: 10 Epistaxis



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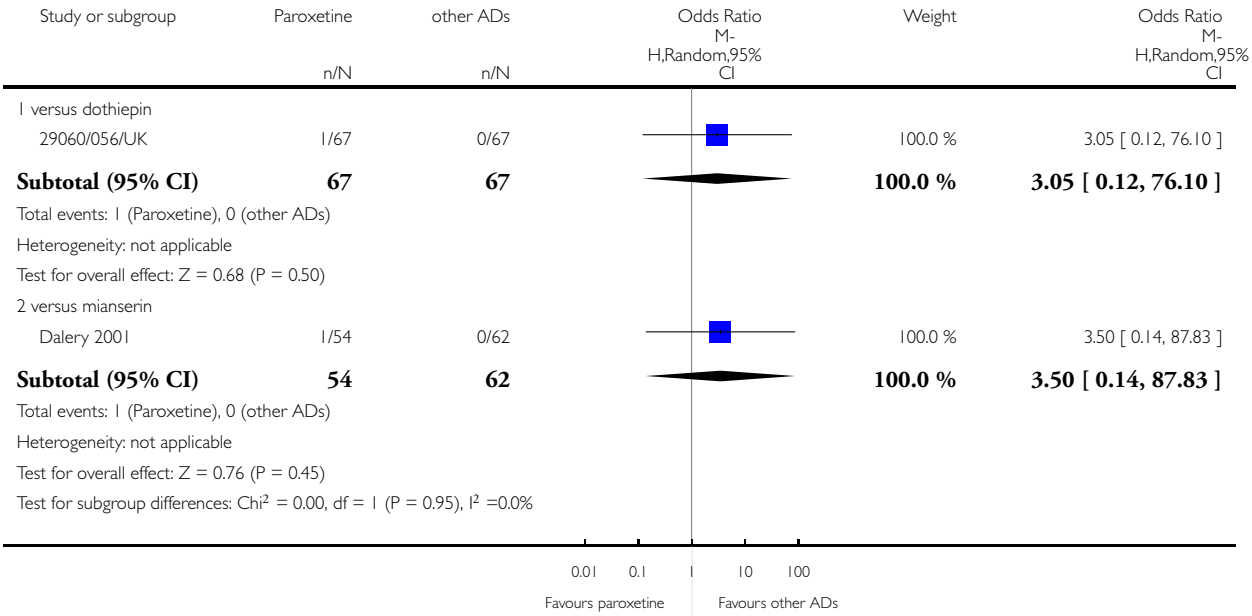
Analysis 71.11. Comparison 71 SE - RARE, Outcome 11 Falls.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 71 SE - RARE

Outcome: 11 Falls



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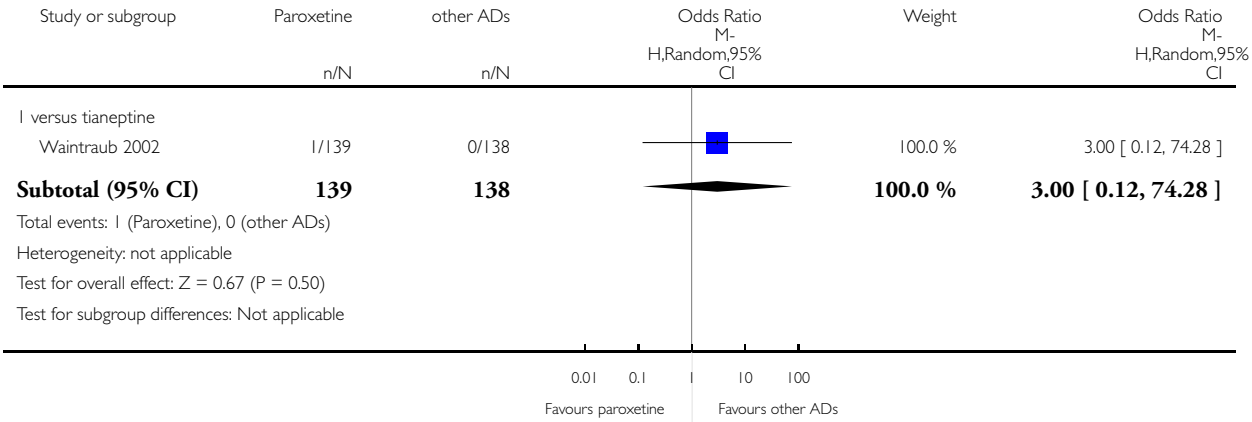
Analysis 71.12. Comparison 71 SE - RARE, Outcome 12 Hiccup.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 71 SE - RARE

Outcome: 12 Hiccup

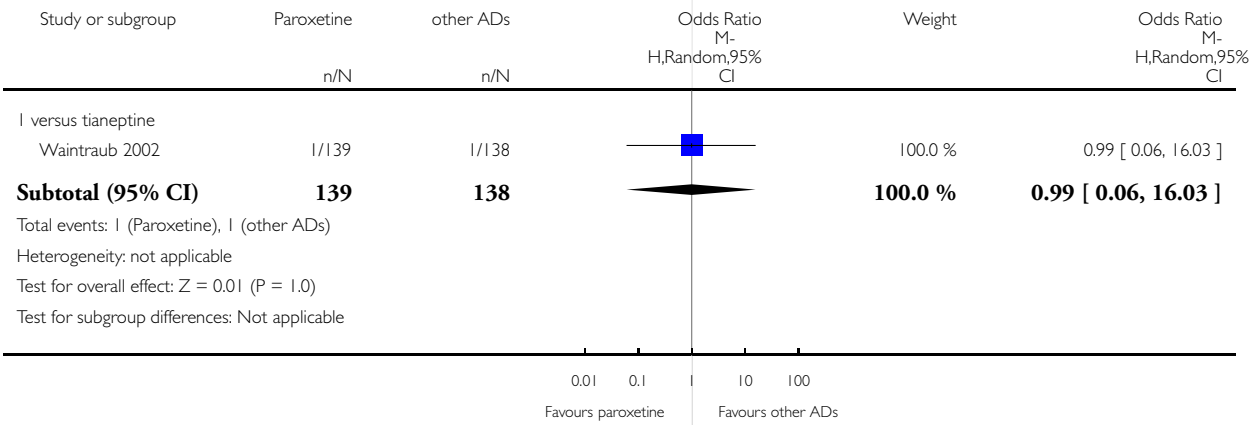


Analysis 71.13. Comparison 71 SE - RARE, Outcome 13 Hot flushes.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 71 SE - RARE

Outcome: 13 Hot flushes



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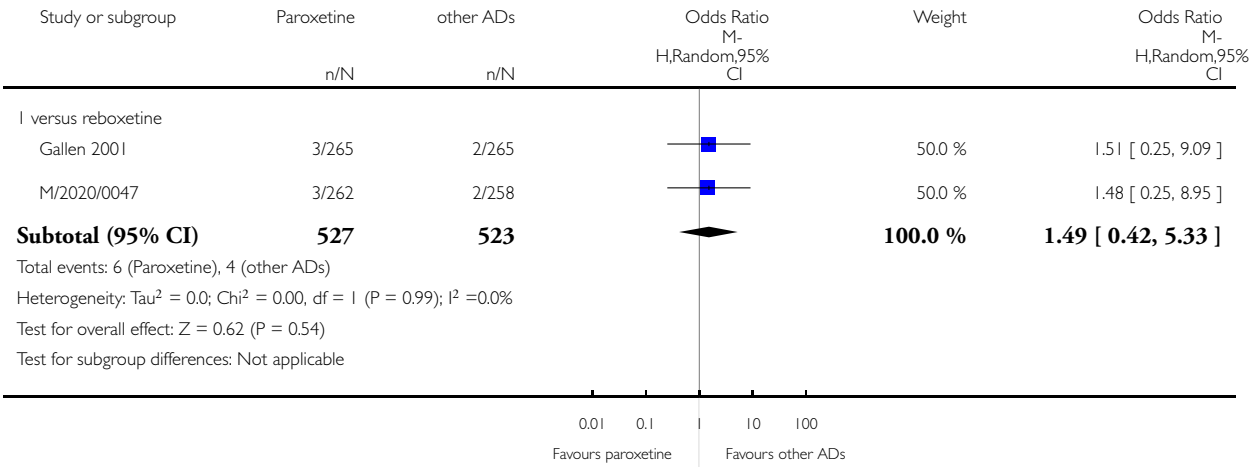
Analysis 71.14. Comparison 71 SE - RARE, Outcome 14 Hyperkinesia.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 71 SE - RARE

Outcome: 14 Hyperkinesia



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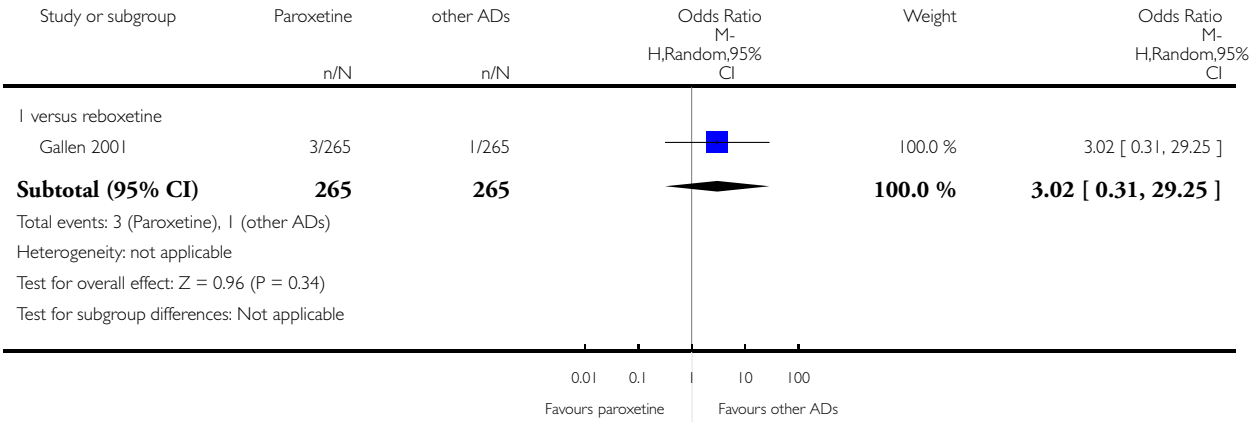
Analysis 71.15. Comparison 71 SE - RARE, Outcome 15 Incoordination.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 71 SE - RARE

Outcome: 15 Incoordination

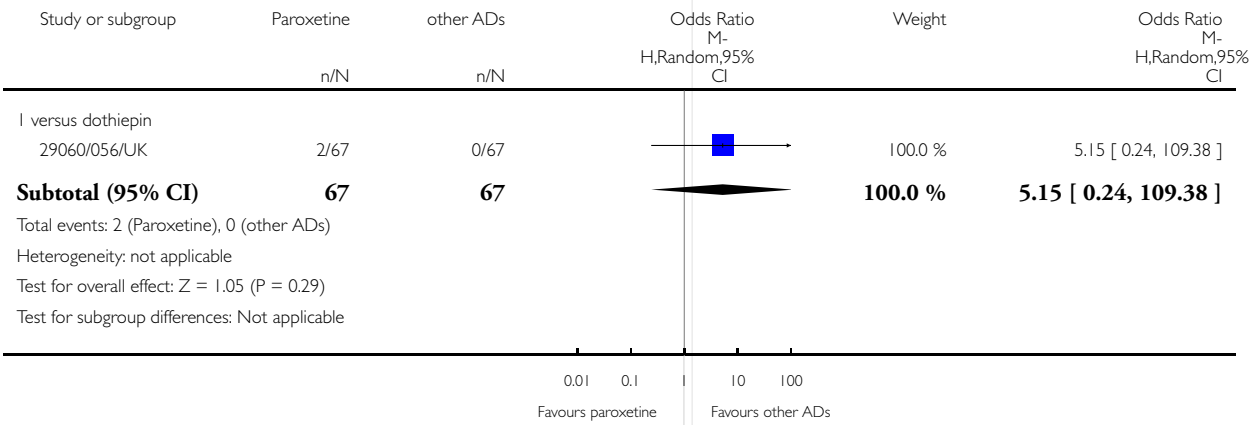


Analysis 71.16. Comparison 71 SE - RARE, Outcome 16 Irregular pulse.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 71 SE - RARE

Outcome: 16 Irregular pulse



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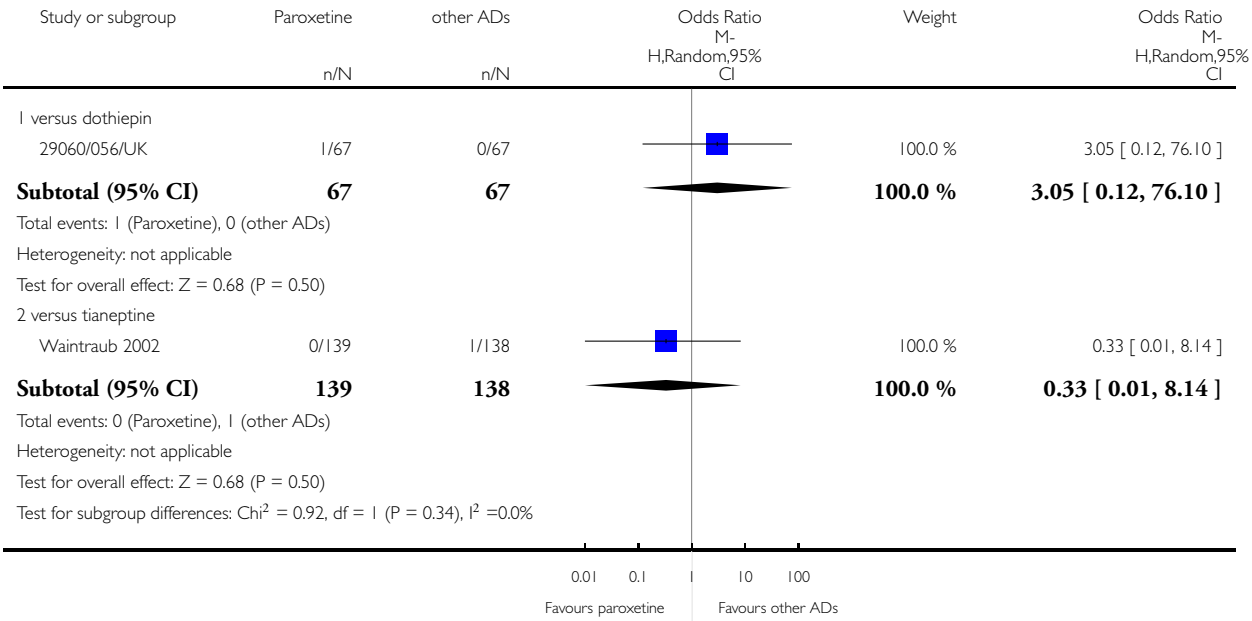
Analysis 71.17. Comparison 71 SE - RARE, Outcome 17 Light headedness.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 71 SE - RARE

Outcome: 17 Light headedness



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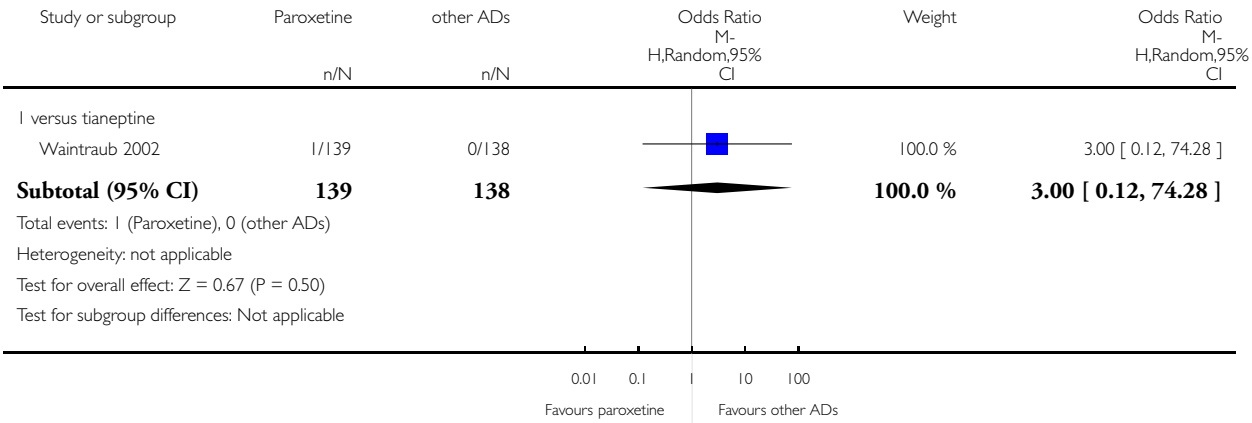
Analysis 71.18. Comparison 71 SE - RARE, Outcome 18 Malaise.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 71 SE - RARE

Outcome: 18 Malaise



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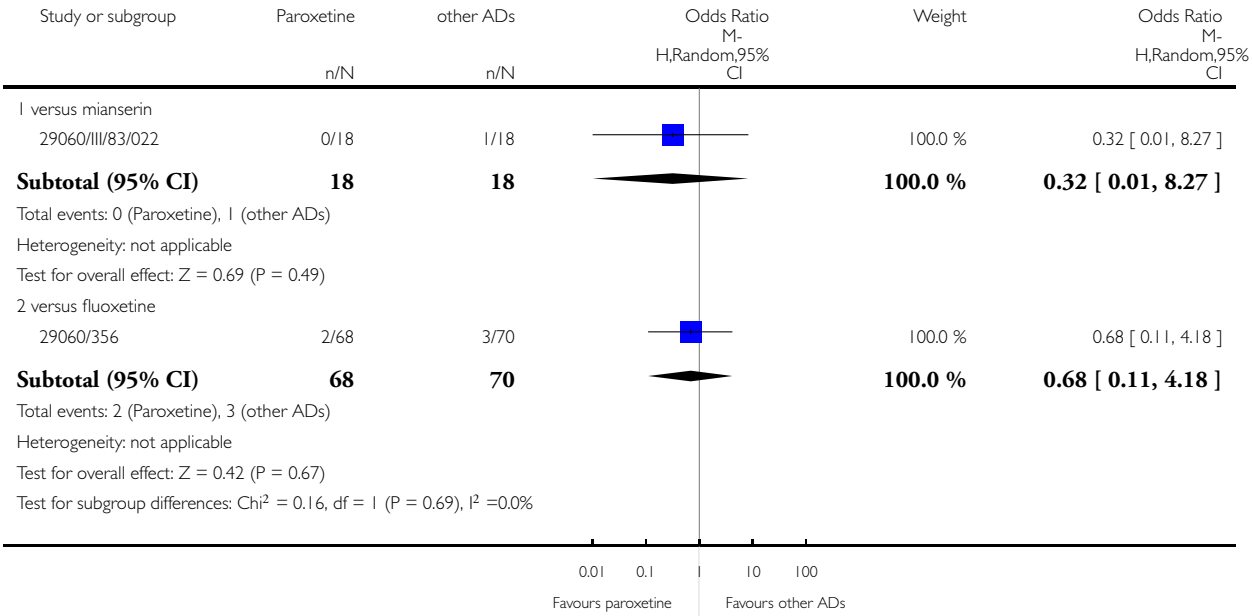
Analysis 71.19. Comparison 71 SE - RARE, Outcome 19 Overdose.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 71 SE - RARE

Outcome: 19 Overdose



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Analysis 71.20. Comparison 71 SE - RARE, Outcome 20 Peripheal vascular disorder.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 71 SE - RARE

Outcome: 20 Peripheal vascular disorder

Study or subgroup	Paroxetine n/N	other ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
1 versus reboxetine					
Gallen 2001	1/265	3/265		100.0 %	0.33 [0.03, 3.20]
Subtotal (95% CI)	**265**	**265**		**100.0 %**	**0.33 [0.03, 3.20]**
Total events: 1 (Paroxetine), 3 (other ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.96 (P = 0.34)					
Test for subgroup differences: Not applicable					

Analysis 71.21. Comparison 71 SE - RARE, Outcome 21 Pregnancy.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 71 SE - RARE

Outcome: 21 Pregnancy

Study or subgroup	Paroxetine n/N	other ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
1 versus amitriptyline					
29060/299	0/109	1/108		100.0 %	0.33 [0.01, 8.12]
Subtotal (95% CI)	**109**	**108**		**100.0 %**	**0.33 [0.01, 8.12]**
Total events: 0 (Paroxetine), 1 (other ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.68 (P = 0.50)					
Test for subgroup differences: Not applicable					

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Analysis 71.22. Comparison 71 SE - RARE, Outcome 22 Psychosomatic disorders.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 71 SE - RARE

Outcome: 22 Psychosomatic disorders

Study or subgroup	Paroxetine n/N	other ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
1 versus fluoxetine					
Tignol 1993	0/89	1/87		100.0 %	0.32 [0.01, 8.02]
Subtotal (95% CI)	**89**	**87**		**100.0 %**	**0.32 [0.01, 8.02]**
Total events: 0 (Paroxetine), 1 (other ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.69 (P = 0.49)					
Test for subgroup differences: Not applicable					

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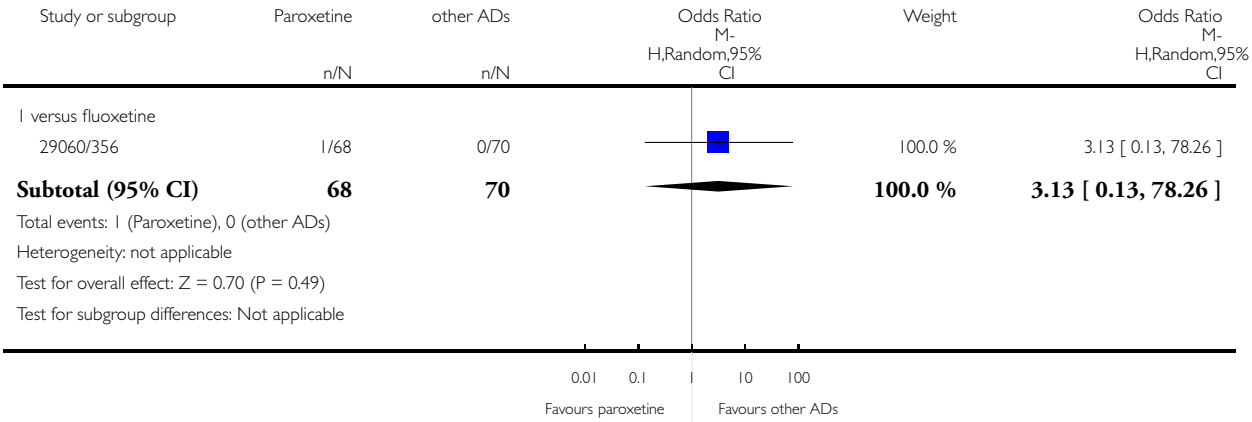
Analysis 71.23. Comparison 71 SE - RARE, Outcome 23 Renal failure.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 71 SE - RARE

Outcome: 23 Renal failure

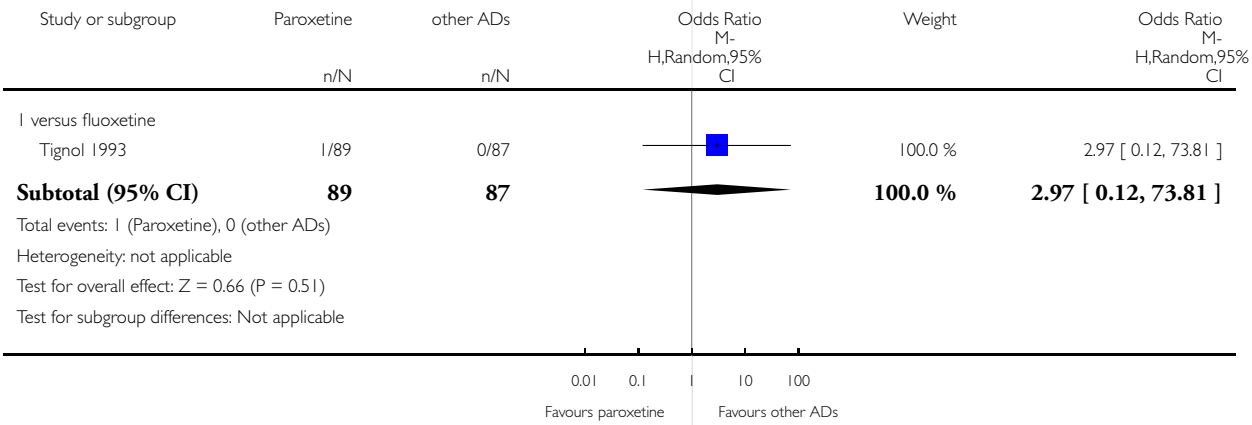


Analysis 71.24. Comparison 71 SE - RARE, Outcome 24 Stage 1 coma.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 71 SE - RARE

Outcome: 24 Stage 1 coma



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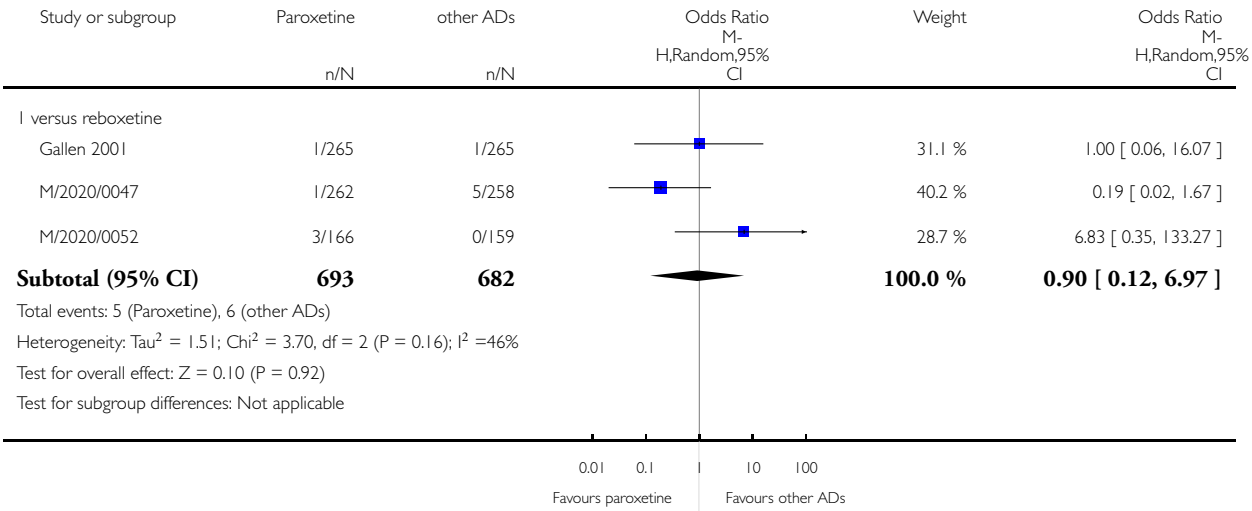
Analysis 71.25. Comparison 71 SE - RARE, Outcome 25 Tooth disorder.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 71 SE - RARE

Outcome: 25 Tooth disorder



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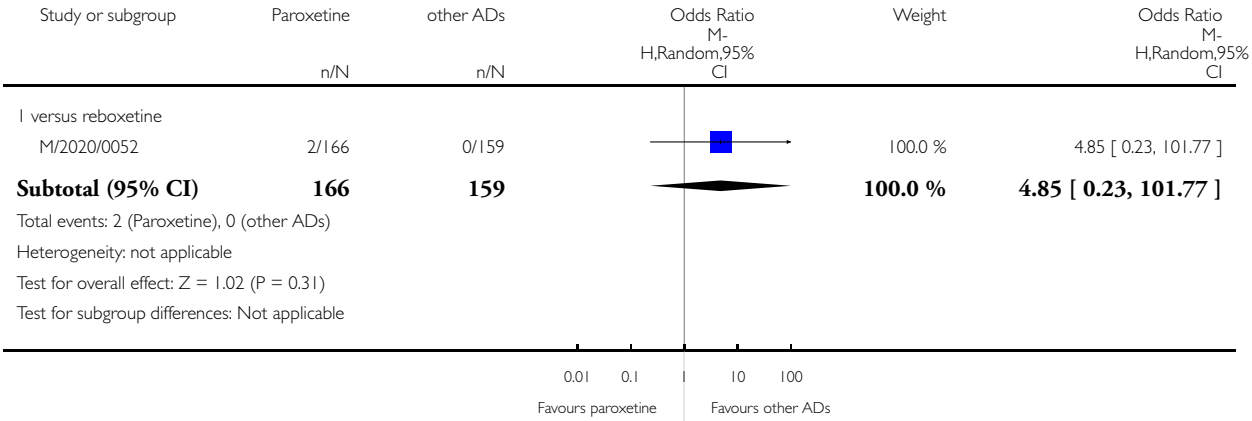
Analysis 71.26. Comparison 71 SE - RARE, Outcome 26 Voice alteration.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 71 SE - RARE

Outcome: 26 Voice alteration



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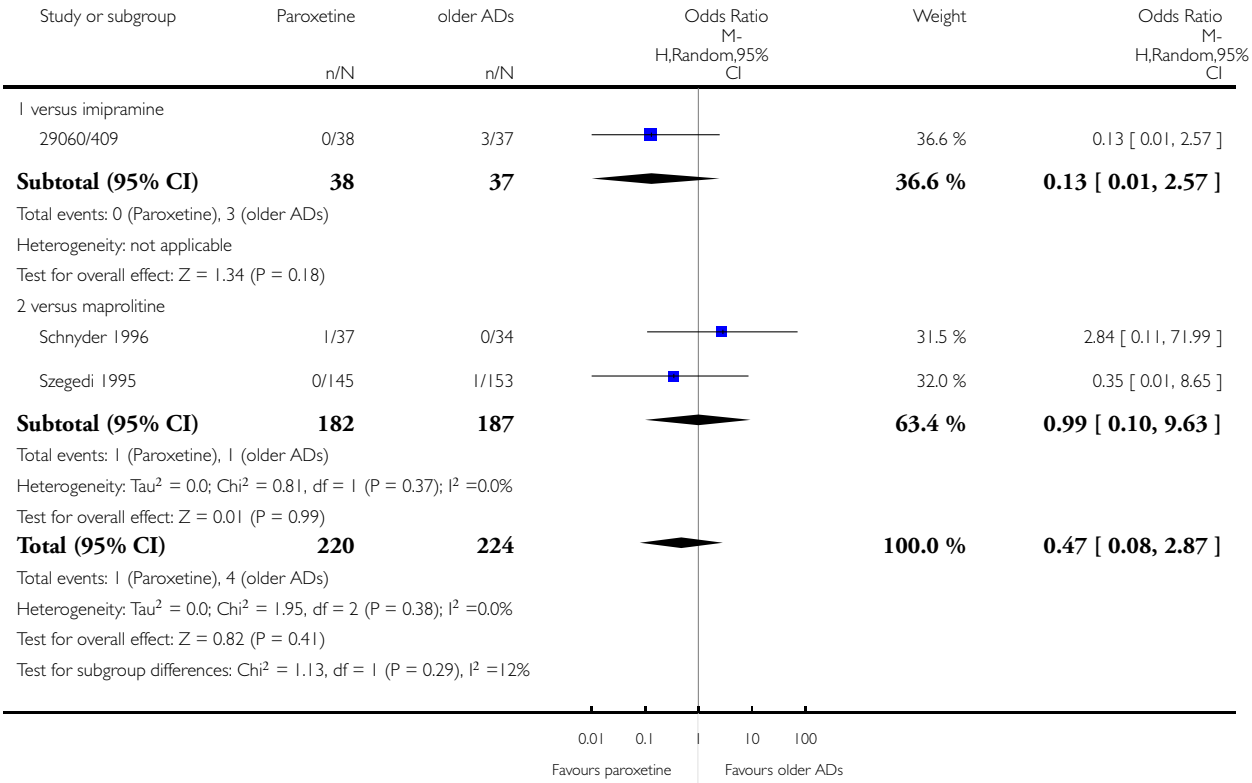
Analysis 72.1. Comparison 72 SE - Rash, itching, allergic reactions, Outcome 1 Paroxetine verus older ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 72 SE - Rash, itching, allergic reactions

Outcome: 1 Paroxetine verus older ADs



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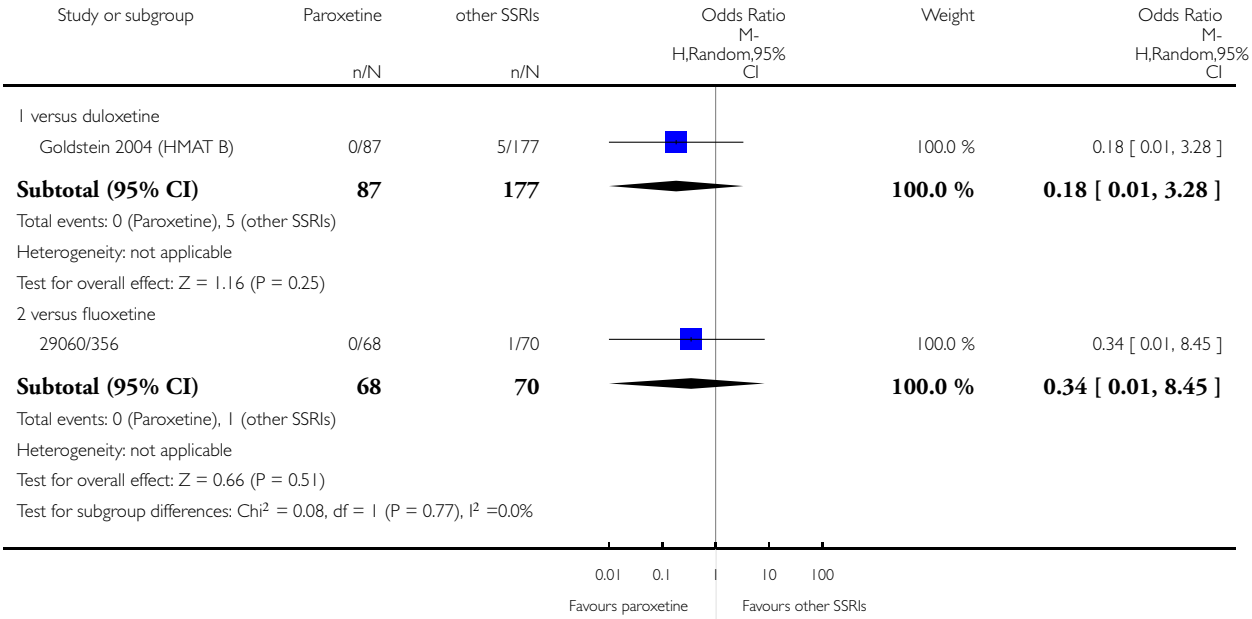
Analysis 72.2. Comparison 72 SE - Rash, itching, allergic reactions, Outcome 2 Paroxetine versus other SSRIs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 72 SE - Rash, itching, allergic reactions

Outcome: 2 Paroxetine versus other SSRIs



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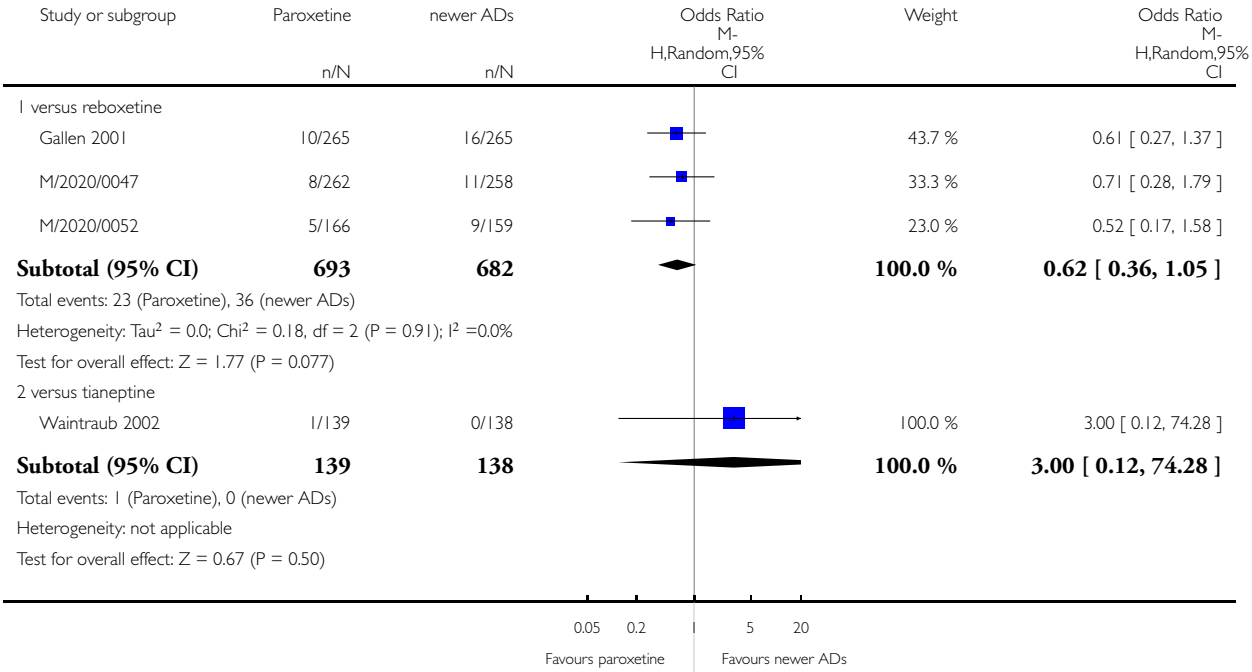
Analysis 72.3. Comparison 72 SE - Rash, itching, allergic reactions, Outcome 3 Paroxetine versus newer or non-conventional ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 72 SE - Rash, itching, allergic reactions

Outcome: 3 Paroxetine versus newer or non-conventional ADs



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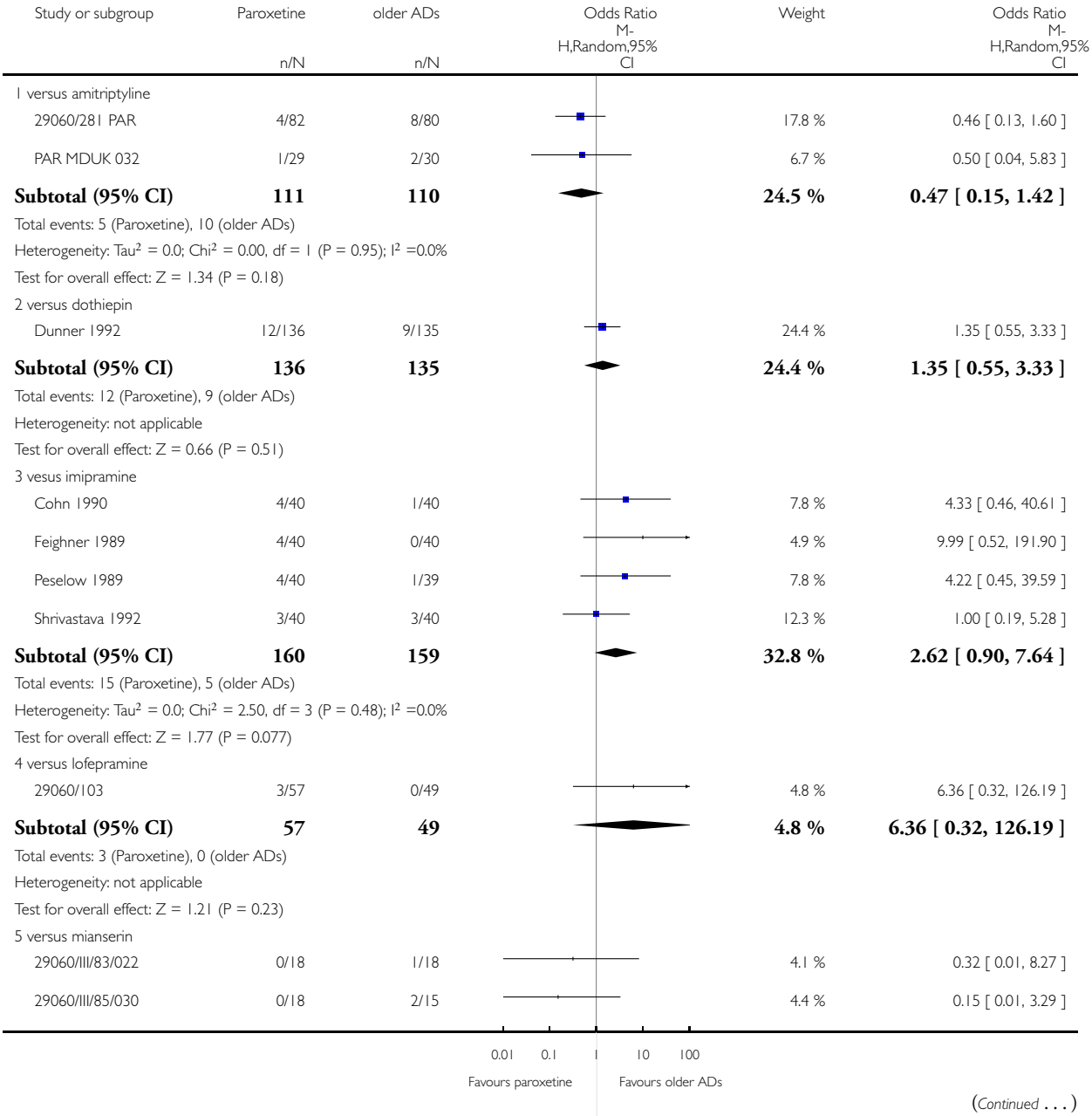
Analysis 73.1. Comparison 73 SE - Respiratory disorder, Outcome 1 Paroxetine versus older ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 73 SE - Respiratory disorder

Outcome: 1 Paroxetine versus older ADs



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Study or subgroup	Paroxetine n/N	older ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Dalery 2001	0/54	4/62		4.9 %	0.12 [0.01, 2.27]
Subtotal (95% CI)	**90**	**95**		**13.5 %**	**0.17 [0.03, 1.02]**
Total events: 0 (Paroxetine), 7 (older ADs)					
Heterogeneity: Tau^2 = 0.0; Chi^2 = 0.21, df = 2 (P = 0.90); I^2 =0.0%					
Test for overall effect: Z = 1.94 (P = 0.053)					
Total (95% CI)	**554**	**548**		**100.0 %**	**1.08 [0.54, 2.18]**
Total events: 35 (Paroxetine), 31 (older ADs)					
Heterogeneity: Tau^2 = 0.31; Chi^2 = 13.15, df = 10 (P = 0.22); I^2 =24%					
Test for overall effect: Z = 0.23 (P = 0.82)					
Test for subgroup differences: Chi^2 = 10.49, df = 4 (P = 0.03), I^2 =62%					

Analysis 73.2. Comparison 73 SE - Respiratory disorder, Outcome 2 Paroxetine versus other SSRIs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 73 SE - Respiratory disorder

Outcome: 2 Paroxetine versus other SSRIs

Study or subgroup	Paroxetine n/N	other SSRIs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
1 versus fluoxetine					
Chouinard 1999	13/102	9/101		16.0 %	1.49 [0.61, 3.67]
De Wilde 1993	0/50	4/50		1.5 %	0.10 [0.01, 1.95]
Gagiano 1993	4/45	3/45		5.3 %	1.37 [0.29, 6.48]
MY-1045/BRL-029060/1	28/357	30/351		44.7 %	0.91 [0.53, 1.56]
SBK-115 1998	19/284	23/289		32.5 %	0.83 [0.44, 1.56]
Subtotal (95% CI)	**838**	**836**		**100.0 %**	**0.95 [0.66, 1.35]**
Total events: 64 (Paroxetine), 69 (other SSRIs)					
Heterogeneity: Tau^2 = 0.0; Chi^2 = 3.60, df = 4 (P = 0.46); I^2 =0.0%					
Test for overall effect: Z = 0.30 (P = 0.76)					
Test for subgroup differences: Not applicable					

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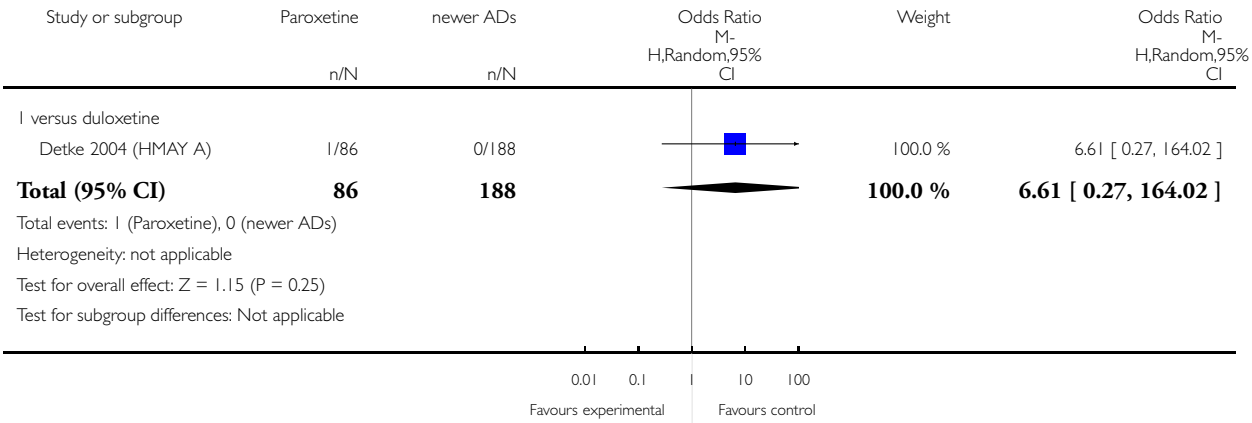
Analysis 74.1. Comparison 74 SE - Restlessness, Outcome 1 Paroxetine versus SSRIs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 74 SE - Restlessness

Outcome: 1 Paroxetine versus SSRIs



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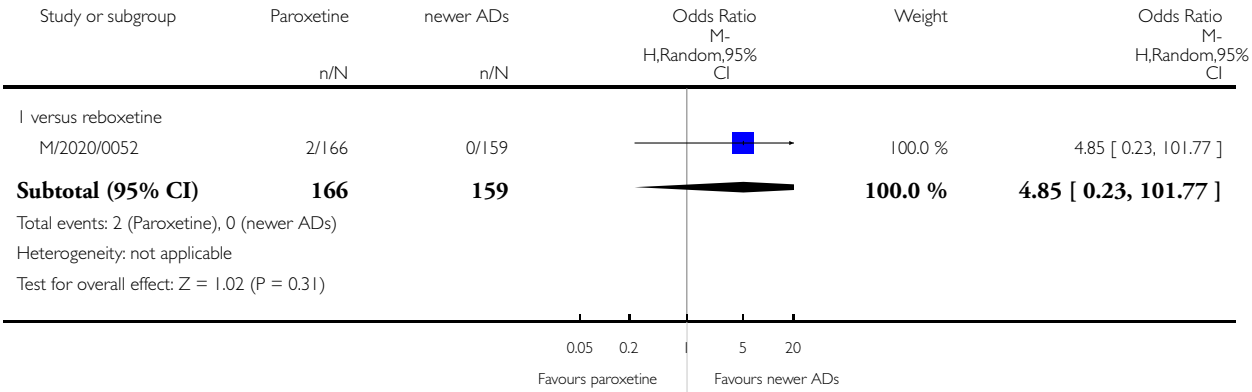
Analysis 74.2. Comparison 74 SE - Restlessness, Outcome 2 Paroxetine versus newer or non-conventional ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 74 SE - Restlessness

Outcome: 2 Paroxetine versus newer or non-conventional ADs

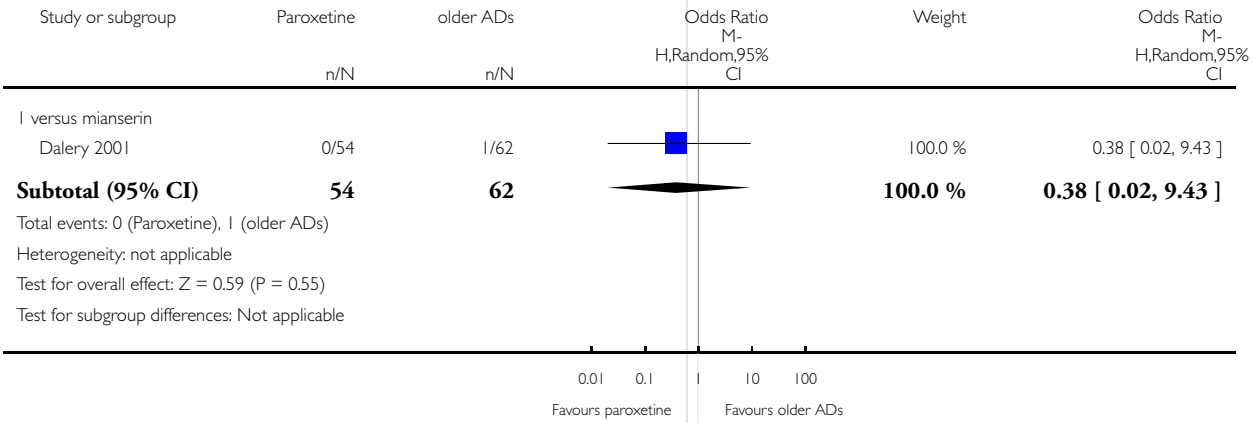


Analysis 75.1. Comparison 75 SE - Rhinitis, Outcome 1 Paroxetine versus older ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 75 SE - Rhinitis

Outcome: 1 Paroxetine versus older ADs



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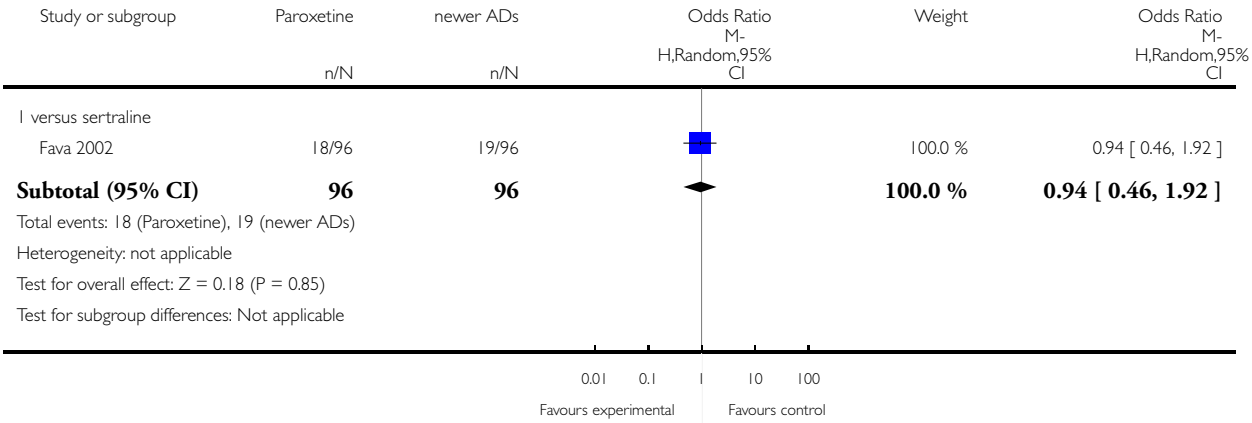
Analysis 75.2. Comparison 75 SE - Rhinitis, Outcome 2 Paroxetine versus SSRIs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 75 SE - Rhinitis

Outcome: 2 Paroxetine versus SSRIs



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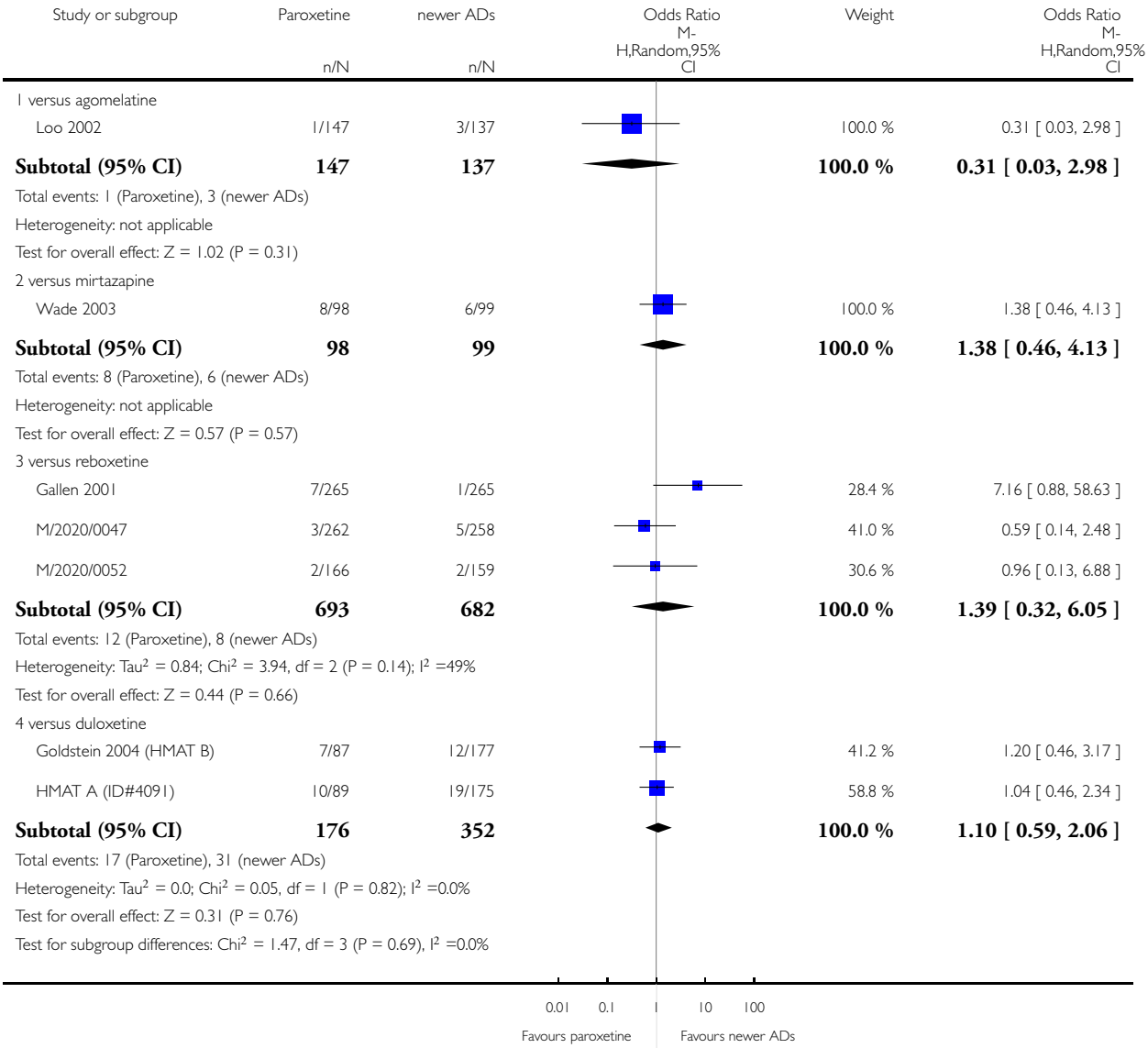
Analysis 75.3. Comparison 75 SE - Rhinitis, Outcome 3 Paroxetine versus newer or non-conventional ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 75 SE - Rhinitis

Outcome: 3 Paroxetine versus newer or non-conventional ADs



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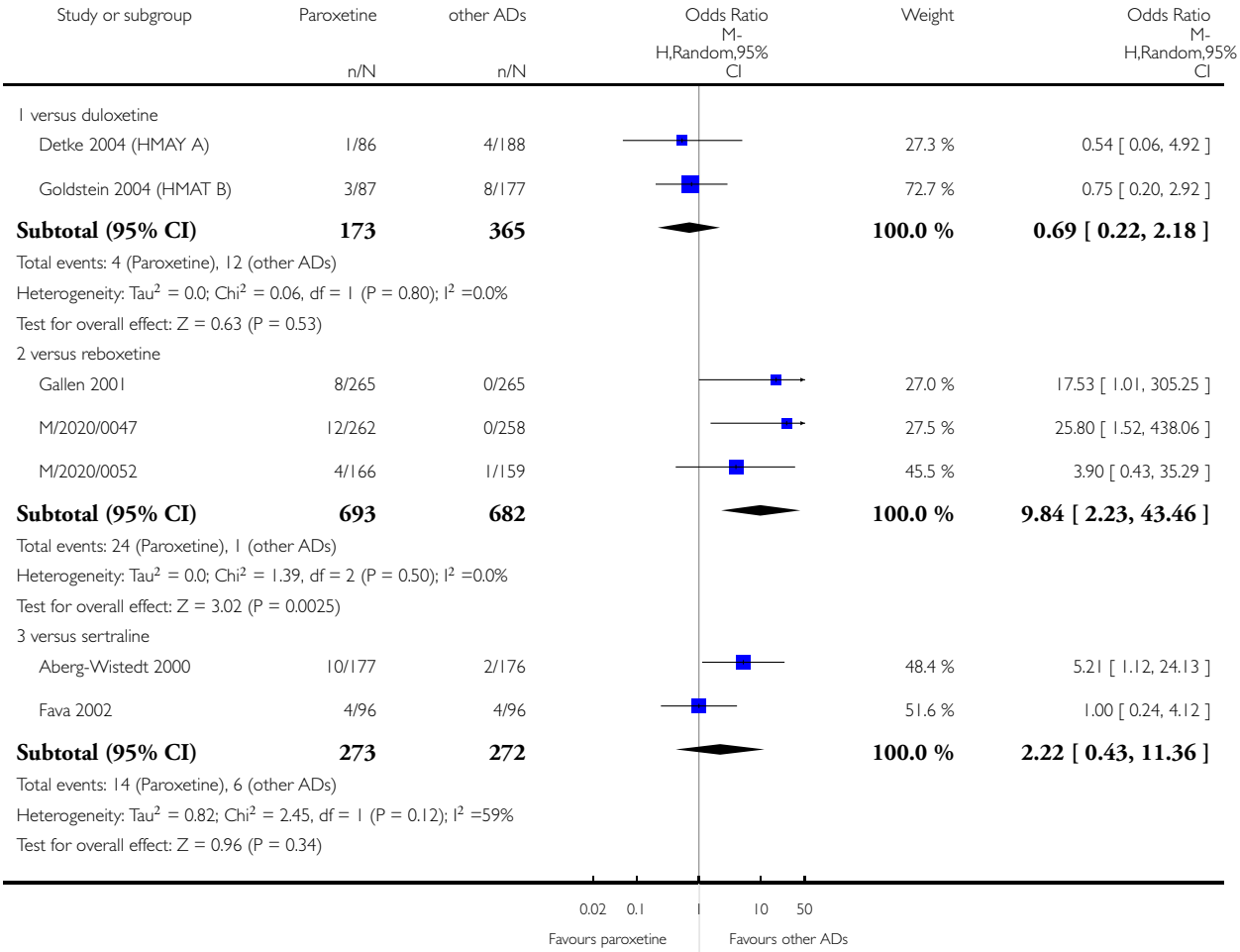
Analysis 76.1. Comparison 76 SE - Sexual problems, Outcome 1 Anorgasmia.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 76 SE - Sexual problems

Outcome: 1 Anorgasmia



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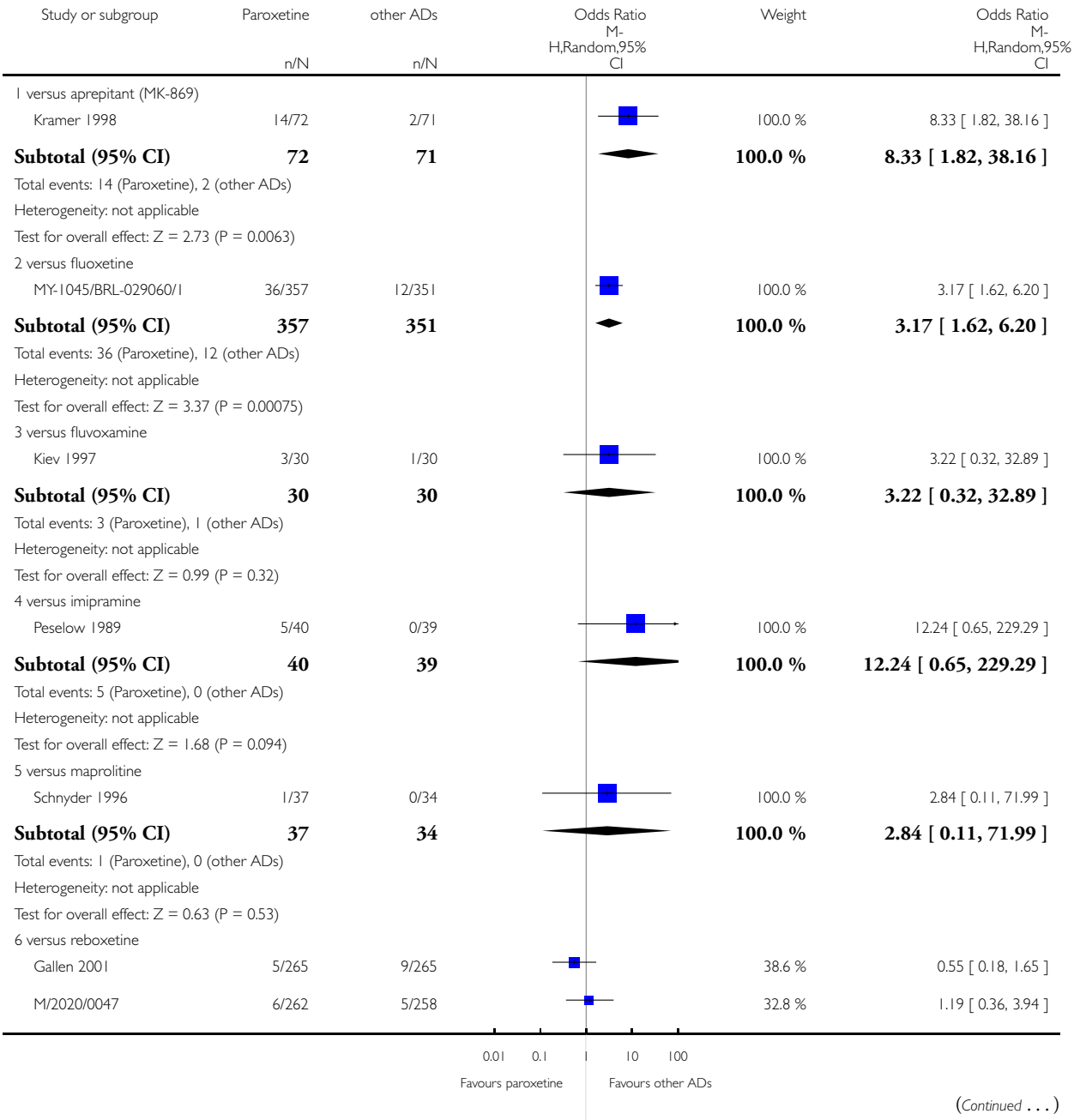
Analysis 76.2. Comparison 76 SE - Sexual problems, Outcome 2 Ejaculation disorder.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 76 SE - Sexual problems

Outcome: 2 Ejaculation disorder



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Study or subgroup	Paroxetine n/N	other ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
M/2020/0052	4/166	6/159		28.6 %	0.63 [0.17, 2.27]
Subtotal (95% CI)	**693**	**682**		**100.0 %**	**0.73 [0.37, 1.46]**
Total events: 15 (Paroxetine), 20 (other ADs)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.94$, df = 2 (P = 0.62); $I^2 = 0.0\%$					
Test for overall effect: Z = 0.88 (P = 0.38)					
7 versus sertraline					
Aberg-Wistedt 2000	24/177	8/176		78.3 %	3.29 [1.44, 7.55]
Fava 2002	8/96	2/96		21.7 %	4.27 [0.88, 20.67]
Subtotal (95% CI)	**273**	**272**		**100.0 %**	**3.49 [1.67, 7.26]**
Total events: 32 (Paroxetine), 10 (other ADs)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.08$, df = 1 (P = 0.77); $I^2 = 0.0\%$					
Test for overall effect: Z = 3.33 (P = 0.00086)					
8 versus tianeptine					
Waintraub 2002	1/139	0/138		100.0 %	3.00 [0.12, 74.28]
Subtotal (95% CI)	**139**	**138**		**100.0 %**	**3.00 [0.12, 74.28]**
Total events: 1 (Paroxetine), 0 (other ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.67 (P = 0.50)					
Test for subgroup differences: $Chi^2 = 16.83$, df = 7 (P = 0.02), $I^2 = 58\%$					

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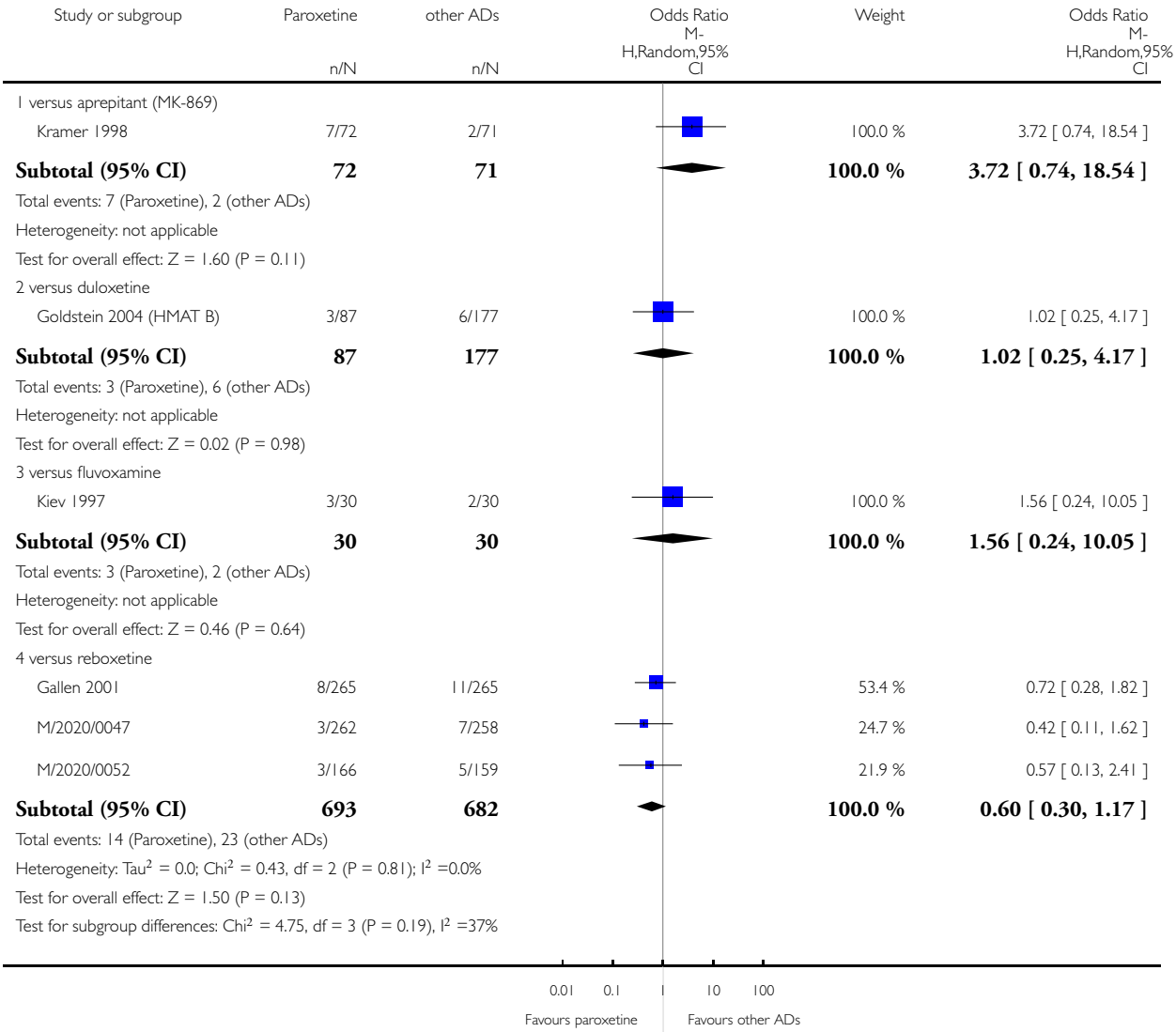
Analysis 76.3. Comparison 76 SE - Sexual problems, Outcome 3 Impotence.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 76 SE - Sexual problems

Outcome: 3 Impotence



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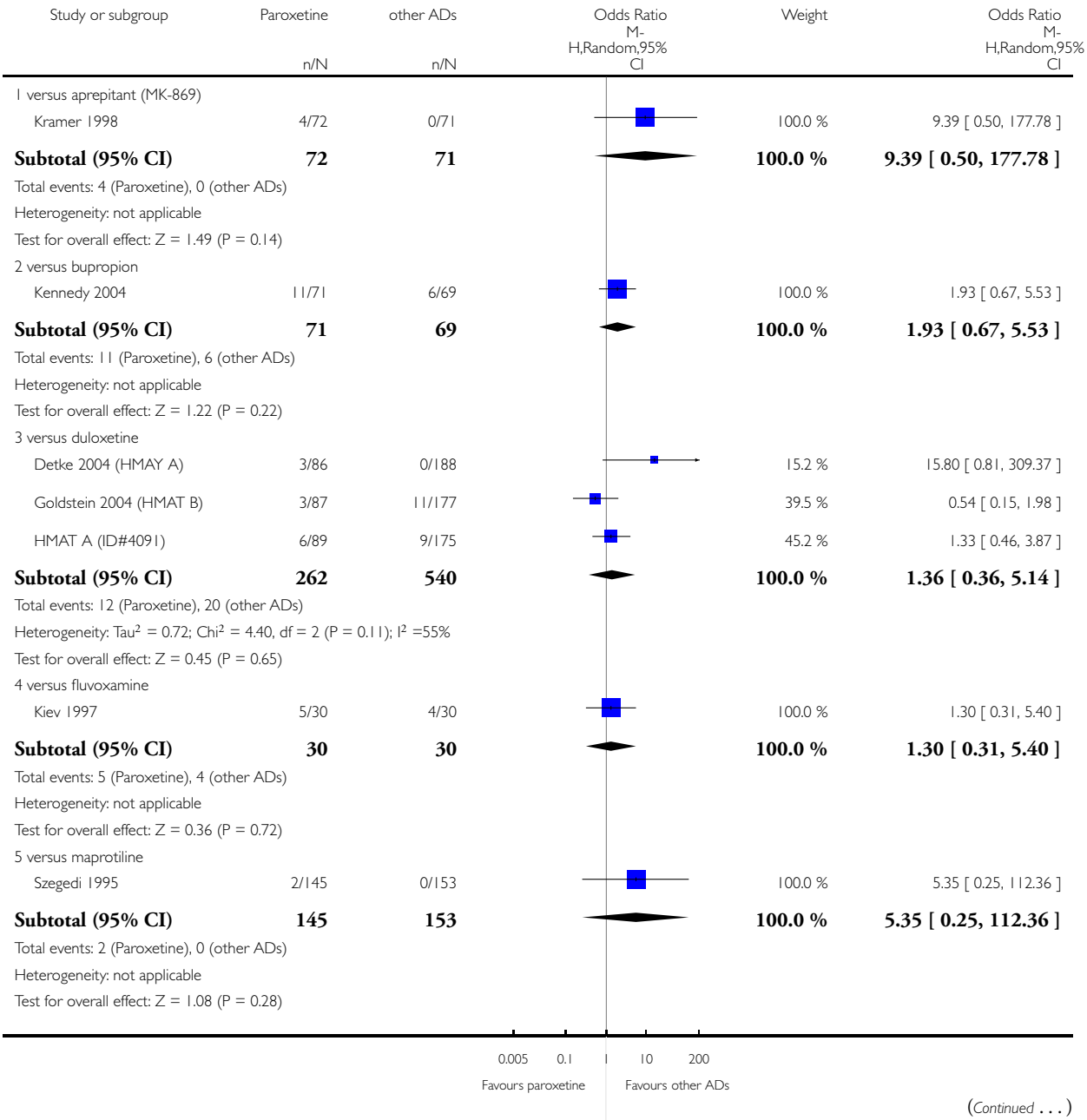
Analysis 76.4. Comparison 76 SE - Sexual problems, Outcome 4 Libido decreased.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 76 SE - Sexual problems

Outcome: 4 Libido decreased



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Study or subgroup	Paroxetine n/N	other ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
6 versus reboxetine					
Gallen 2001	12/265	5/265		46.5 %	2.47 [0.86, 7.10]
M/2020/0047	10/262	3/258		30.7 %	3.37 [0.92, 12.40]
M/2020/0052	4/166	3/159		22.7 %	1.28 [0.28, 5.83]
Subtotal (95% CI)	**693**	**682**		**100.0 %**	**2.34 [1.14, 4.82]**
Total events: 26 (Paroxetine), 11 (other ADs)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.92$, df = 2 (P = 0.63); $I^2 = 0.0\%$					
Test for overall effect: Z = 2.31 (P = 0.021)					
7 versus tianeptine					
Waintraub 2002	1/139	1/138		100.0 %	0.99 [0.06, 16.03]
Subtotal (95% CI)	**139**	**138**		**100.0 %**	**0.99 [0.06, 16.03]**
Total events: 1 (Paroxetine), 1 (other ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.01 (P = 1.0)					

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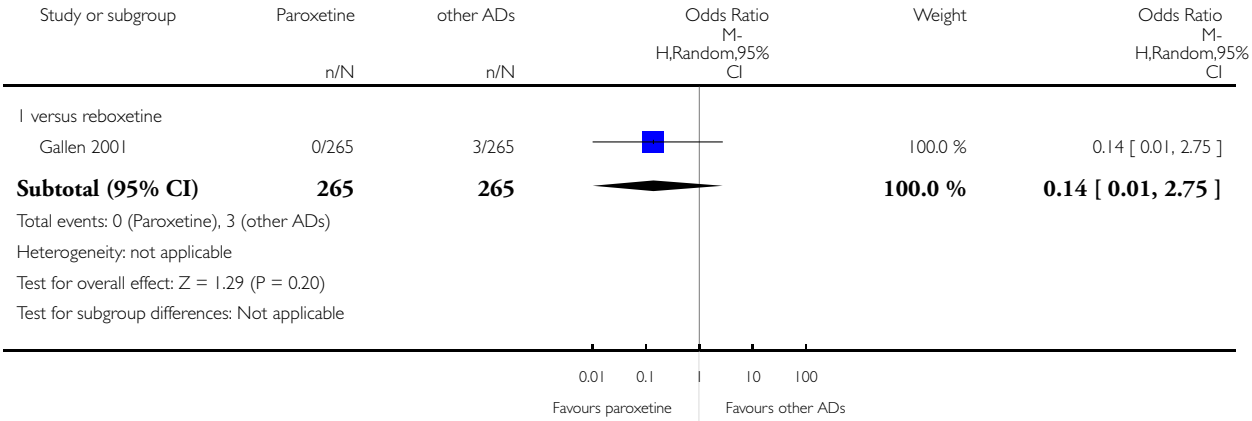
Analysis 76.5. Comparison 76 SE - Sexual problems, Outcome 5 Penis disorder.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 76 SE - Sexual problems

Outcome: 5 Penis disorder



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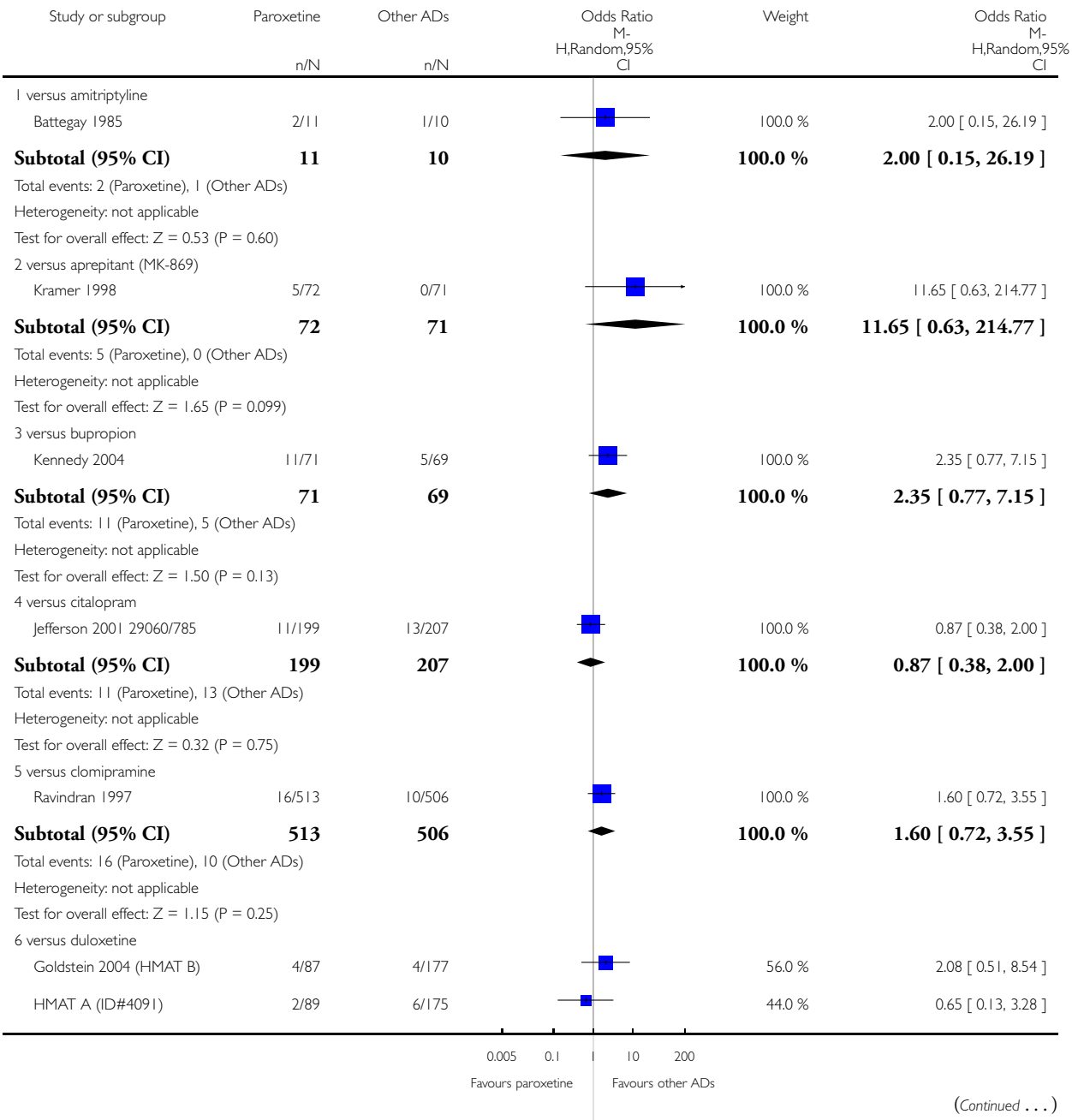
Analysis 76.6. Comparison 76 SE - Sexual problems, Outcome 6 NOS.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 76 SE - Sexual problems

Outcome: 6 NOS



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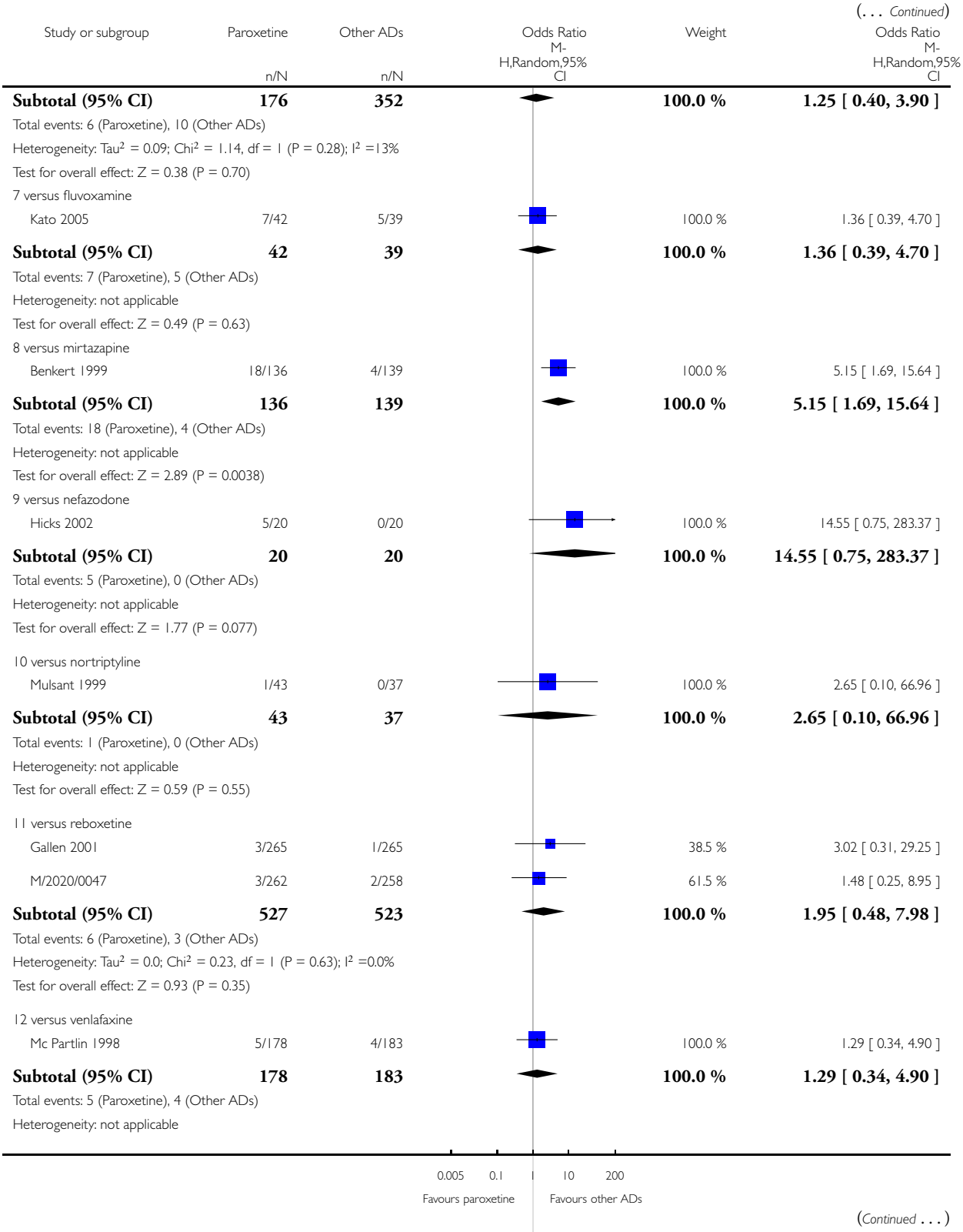

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Study or subgroup	Paroxetine n/N	Other ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Test for overall effect: Z = 0.38 (P = 0.70)					

Analysis 77.1. Comparison 77 SE - Skin and appendages, Outcome 1 Paroxetine versus older ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 77 SE - Skin and appendages

Outcome: 1 Paroxetine versus older ADs

Study or subgroup	Paroxetine n/N	Older ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
1 versus amitriptyline					
29060/281 PAR	12/82	10/80		58.5 %	1.20 [0.49, 2.96]
PAR MDUK 032	4/29	2/30		15.0 %	2.24 [0.38, 13.30]
Subtotal (95% CI)	**111**	**110**		**73.6 %**	**1.36 [0.61, 3.05]**
Total events: 16 (Paroxetine), 12 (Older ADs)					
Heterogeneity: Tau^2 = 0.0; Chi^2 = 0.38, df = 1 (P = 0.54); I^2 =0.0%					
Test for overall effect: Z = 0.75 (P = 0.45)					
2 versus clomipramine					
Pelicier 1993	3/41	3/42		17.3 %	1.03 [0.19, 5.41]
Subtotal (95% CI)	**41**	**42**		**17.3 %**	**1.03 [0.19, 5.41]**
Total events: 3 (Paroxetine), 3 (Older ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.03 (P = 0.98)					
3 versus maprotiline					
Szegedi 1995	1/145	0/153		4.6 %	3.19 [0.13, 78.86]
Subtotal (95% CI)	**145**	**153**		**4.6 %**	**3.19 [0.13, 78.86]**
Total events: 1 (Paroxetine), 0 (Older ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.71 (P = 0.48)					

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Study or subgroup	Paroxetine n/N	Older ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
4 versus mianserin					
Dorman 1992	0/29	1/28		4.5 %	0.31 [0.01, 7.95]
Subtotal (95% CI)	**29**	**28**		**4.5 %**	**0.31 [0.01, 7.95]**
Total events: 0 (Paroxetine), 1 (Older ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.71 (P = 0.48)					
Total (95% CI)	**326**	**333**		**100.0 %**	**1.26 [0.63, 2.52]**
Total events: 20 (Paroxetine), 16 (Older ADs)					
Heterogeneity: Tau^2 = 0.0; Chi^2 = 1.51, df = 4 (P = 0.83); I^2 =0.0%					
Test for overall effect: Z = 0.66 (P = 0.51)					
Test for subgroup differences: Chi^2 = 1.13, df = 3 (P = 0.77), I^2 =0.0%					

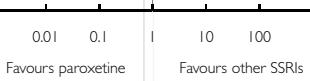
Analysis 77.2. Comparison 77 SE - Skin and appendages, Outcome 2 Paroxetine versus other SSRIs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 77 SE - Skin and appendages

Outcome: 2 Paroxetine versus other SSRIs

Study or subgroup	Paroxetine n/N	other SSRIs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
1 versus fluoxetine					
De Wilde 1993	1/50	7/50		100.0 %	0.13 [0.01, 1.06]
Subtotal (95% CI)	**50**	**50**		**100.0 %**	**0.13 [0.01, 1.06]**
Total events: 1 (Paroxetine), 7 (other SSRIs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.91 (P = 0.057)					
Test for subgroup differences: Not applicable					



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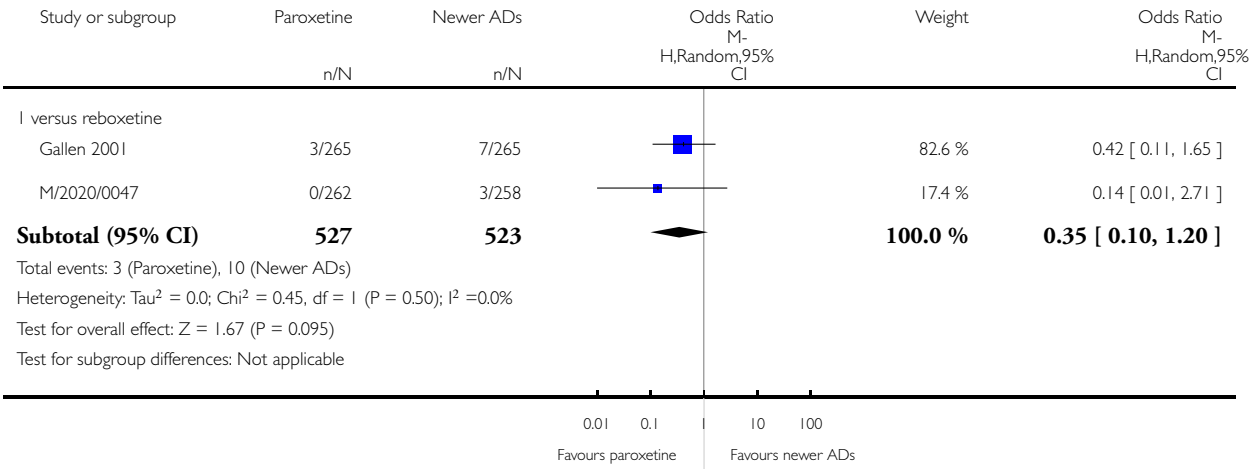
Analysis 77.3. Comparison 77 SE - Skin and appendages, Outcome 3 Paroxetine versus newer or non-conventional ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 77 SE - Skin and appendages

Outcome: 3 Paroxetine versus newer or non-conventional ADs



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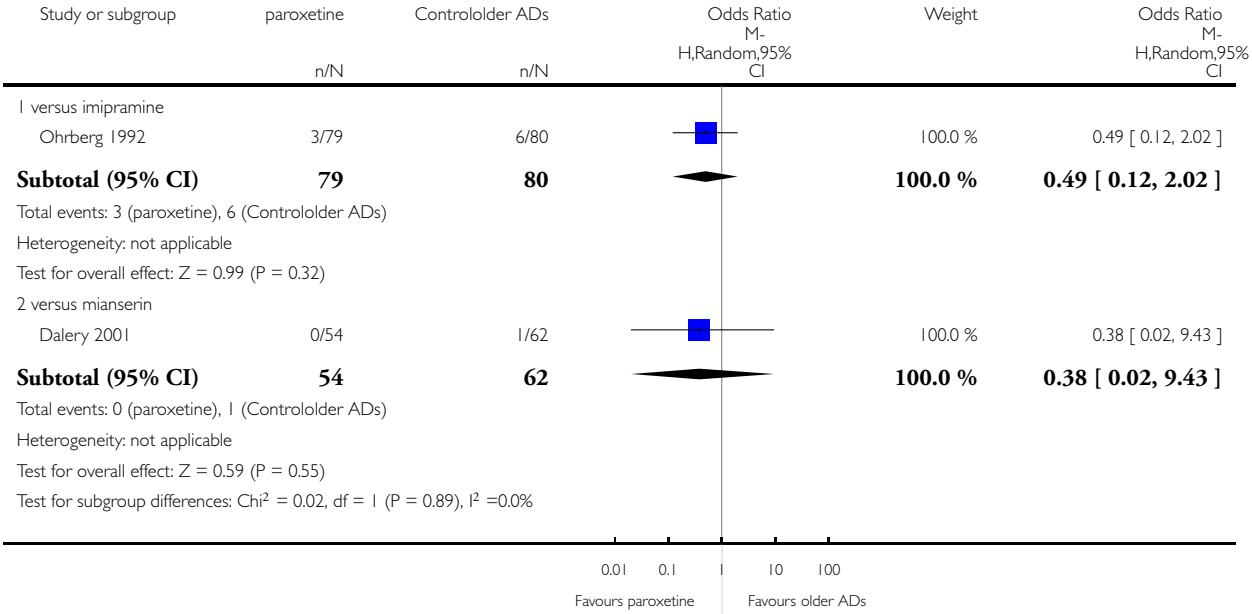
Analysis 78.1. Comparison 78 SE - Sleep disorders, Outcome 1 Paroxetine versus older ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 78 SE - Sleep disorders

Outcome: 1 Paroxetine versus older ADs



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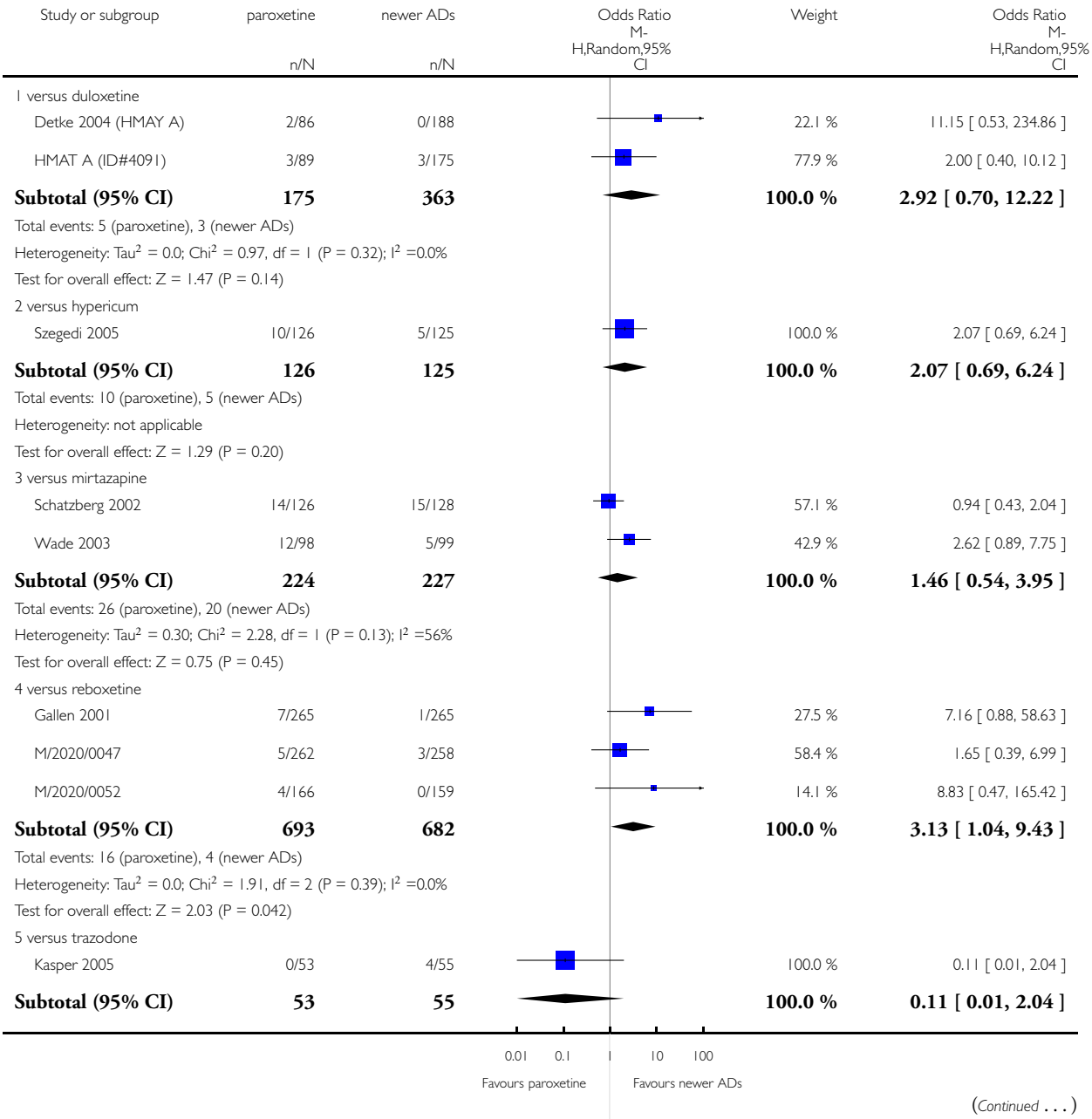
Analysis 78.2. Comparison 78 SE - Sleep disorders, Outcome 2 Paroxetine versus newer or non-conventional ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 78 SE - Sleep disorders

Outcome: 2 Paroxetine versus newer or non-conventional ADs



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Study or subgroup	paroxetine n/N	newer ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Total events: 0 (paroxetine), 4 (newer ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.49 (P = 0.14)					
Test for subgroup differences: Chi² = 5.08, df = 4 (P = 0.28), I² =21%					

Analysis 79.1. Comparison 79 SE - Sleepiness/drowsiness, Outcome 1 Paroxetine versus older ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 79 SE - Sleepiness/drowsiness

Outcome: 1 Paroxetine versus older ADs

Study or subgroup	Paroxetine n/N	Older ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
1 versus amitriptyline					
29060.07.001	5/13	5/13		3.6 %	1.00 [0.21, 4.86]
29060/299	9/109	16/108		7.1 %	0.52 [0.22, 1.23]
Battegay 1985	0/11	4/10		1.2 %	0.06 [0.00, 1.36]
Bignamini 1992	10/156	11/153		7.0 %	0.88 [0.36, 2.15]
Hutchinson 1992	2/58	4/32		3.0 %	0.25 [0.04, 1.45]
Sacchetti 2002	3/64	5/65		3.9 %	0.59 [0.14, 2.58]
Staner 1995	5/21	0/19		1.3 %	13.00 [0.67, 252.98]
Stuppaeck 1994	3/78	0/75		1.3 %	7.00 [0.36, 137.86]
Subtotal (95% CI)	**510**	**475**		**28.3 %**	**0.72 [0.36, 1.43]**
Total events: 37 (Paroxetine), 45 (Older ADs)					
Heterogeneity: Tau² = 0.31; Chi² = 10.79, df = 7 (P = 0.15); I² =35%					
Test for overall effect: Z = 0.93 (P = 0.35)					
2 versus clomipramine					

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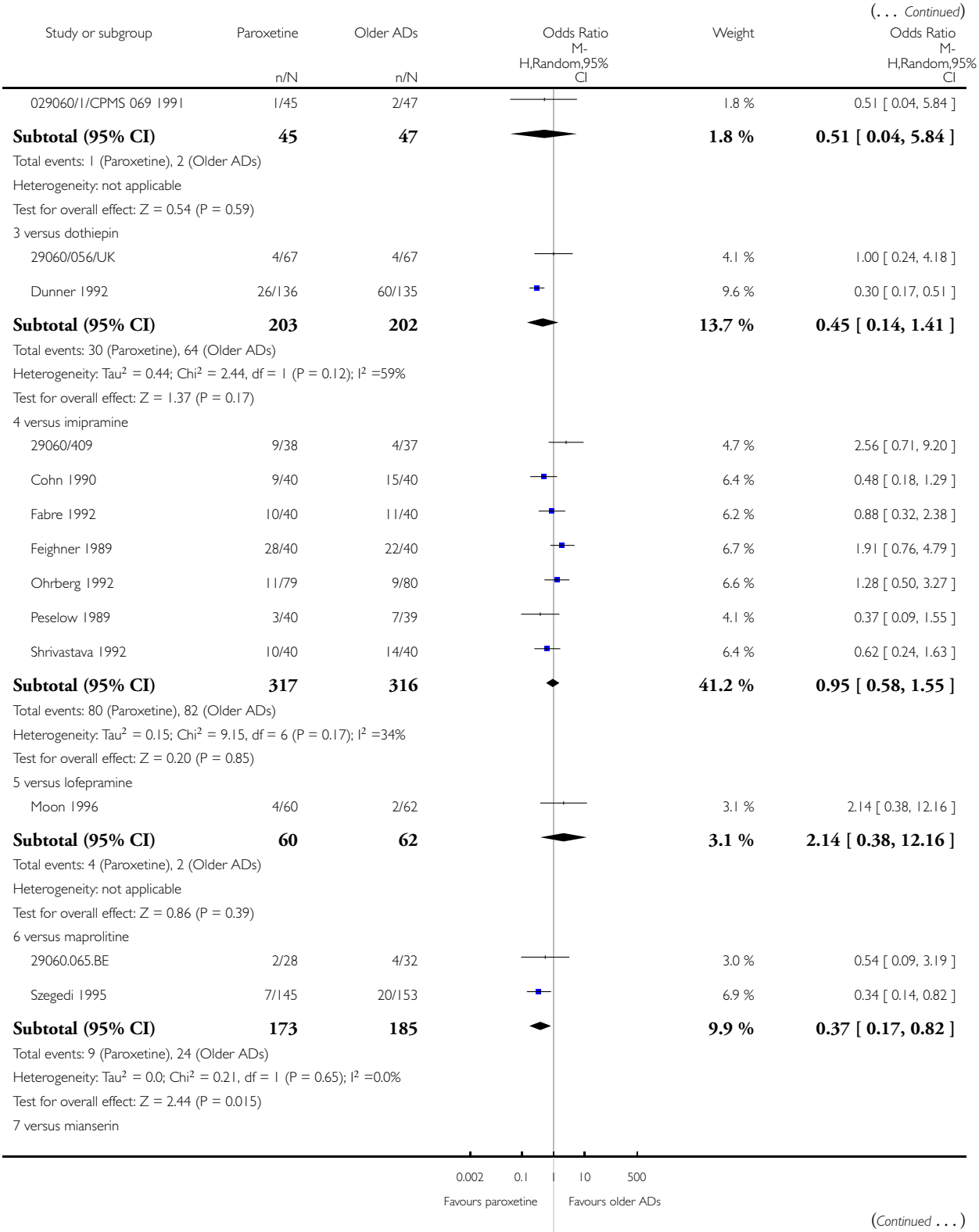

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Study or subgroup	Paroxetine n/N	Older ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Dalery 2001	1/54	3/62		2.0 %	0.37 [0.04, 3.68]
Subtotal (95% CI)	**54**	**62**		**2.0 %**	**0.37 [0.04, 3.68]**
Total events: 1 (Paroxetine), 3 (Older ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.85 (P = 0.40)					
Total (95% CI)	**1362**	**1349**		**100.0 %**	**0.72 [0.50, 1.02]**
Total events: 162 (Paroxetine), 222 (Older ADs)					
Heterogeneity: Tau^2 = 0.26; Chi^2 = 36.28, df = 21 (P = 0.02); I^2 =42%					
Test for overall effect: Z = 1.86 (P = 0.063)					
Test for subgroup differences: Chi^2 = 6.48, df = 6 (P = 0.37), I^2 =7%					

Analysis 79.2. Comparison 79 SE - Sleepiness/drowsiness, Outcome 2 Paroxetine versus other SSRIs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 79 SE - Sleepiness/drowsiness

Outcome: 2 Paroxetine versus other SSRIs

Study or subgroup	Paroxetine n/N	SSRIs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
1 versus citalopram					
Jefferson 2001 29060/785	22/199	35/207		100.0 %	0.61 [0.34, 1.08]
Subtotal (95% CI)	**199**	**207**		**100.0 %**	**0.61 [0.34, 1.08]**
Total events: 22 (Paroxetine), 35 (SSRIs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.69 (P = 0.092)					
2 versus fluoxetine					
29060/356	6/68	5/70		3.8 %	1.26 [0.37, 4.33]
Chouinard 1999	19/102	17/101		11.3 %	1.13 [0.55, 2.33]
Gagiano 1993	4/45	1/45		1.2 %	4.29 [0.46, 40.01]

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Study or subgroup	Paroxetine n/N	SSRIs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Geretsegger 1994	3/54	3/52		2.2 %	0.96 [0.18, 4.99]
MY-1045/BRL-029060/1	84/357	58/351		42.1 %	1.55 [1.07, 2.26]
Ontiveros 1994	6/60	4/62		3.4 %	1.61 [0.43, 6.02]
SBK-115 1998	69/284	51/289		35.5 %	1.50 [1.00, 2.25]
Tignol 1993	1/89	0/87		0.6 %	2.97 [0.12, 73.81]
Subtotal (95% CI)	**1059**	**1057**		**100.0 %**	**1.48 [1.16, 1.88]**
Total events: 192 (Paroxetine), 139 (SSRIs)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 2.00$, df = 7 (P = 0.96); $I^2 = 0.0\%$					
Test for overall effect: Z = 3.16 (P = 0.0016)					
3 versus fluvoxamine					
Kiev 1997	9/30	12/30		100.0 %	0.64 [0.22, 1.87]
Subtotal (95% CI)	**30**	**30**		**100.0 %**	**0.64 [0.22, 1.87]**
Total events: 9 (Paroxetine), 12 (SSRIs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.81 (P = 0.42)					
4 versus sertraline					
Aberg-Wistedt 2000	10/177	4/176		54.0 %	2.57 [0.79, 8.37]
Fava 2002	3/30	7/43		46.0 %	0.57 [0.14, 2.42]
Subtotal (95% CI)	**207**	**219**		**100.0 %**	**1.29 [0.30, 5.60]**
Total events: 13 (Paroxetine), 11 (SSRIs)					
Heterogeneity: $Tau^2 = 0.68$; $Chi^2 = 2.51$, df = 1 (P = 0.11); $I^2 = 60\%$					
Test for overall effect: Z = 0.34 (P = 0.74)					

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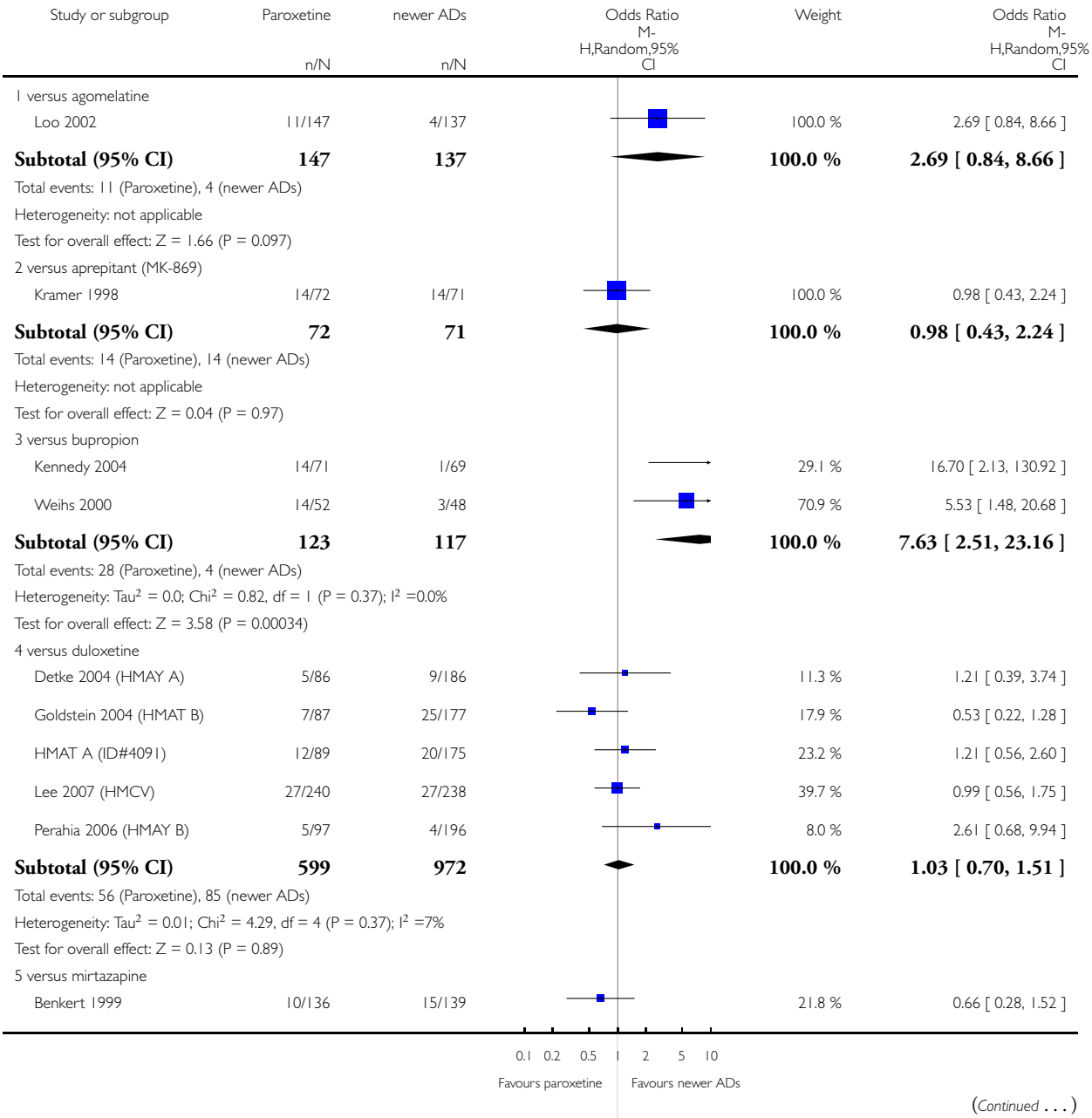
Analysis 79.3. Comparison 79 SE - Sleepiness/drowsiness, Outcome 3 Paroxetine versus newer or non-conventional ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 79 SE - Sleepiness/drowsiness

Outcome: 3 Paroxetine versus newer or non-conventional ADs



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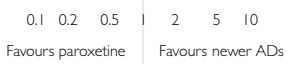
Study or subgroup	Paroxetine n/N	newer ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Schatzberg 2002	37/126	39/128		52.9 %	0.95 [0.55, 1.62]
Wade 2003	13/98	18/99		25.4 %	0.69 [0.32, 1.49]
Subtotal (95% CI)	**360**	**366**		**100.0 %**	**0.81 [0.55, 1.19]**
Total events: 60 (Paroxetine), 72 (newer ADs)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.74$, df = 2 (P = 0.69); $I^2 = 0.0\%$					
Test for overall effect: Z = 1.08 (P = 0.28)					
6 versus nefazodone					
Baldwin 1995	24/101	17/105		55.4 %	1.61 [0.81, 3.22]
Hicks 2002	5/20	11/20		44.6 %	0.27 [0.07, 1.04]
Subtotal (95% CI)	**121**	**125**		**100.0 %**	**0.73 [0.13, 4.13]**
Total events: 29 (Paroxetine), 28 (newer ADs)					
Heterogeneity: $Tau^2 = 1.28$; $Chi^2 = 5.33$, df = 1 (P = 0.02); $I^2 = 81\%$					
Test for overall effect: Z = 0.36 (P = 0.72)					
7 versus reboxetine					
Gallen 2001	46/265	18/265		46.5 %	2.88 [1.62, 5.12]
M/2020/0047	34/262	19/258		45.5 %	1.88 [1.04, 3.38]
M/2020/0052	12/166	1/159		7.9 %	12.31 [1.58, 95.83]
Subtotal (95% CI)	**693**	**682**		**100.0 %**	**2.66 [1.45, 4.89]**
Total events: 92 (Paroxetine), 38 (newer ADs)					
Heterogeneity: $Tau^2 = 0.12$; $Chi^2 = 3.54$, df = 2 (P = 0.17); $I^2 = 44\%$					
Test for overall effect: Z = 3.15 (P = 0.0017)					
8 versus trazodone					
Kasper 2005	1/53	3/55		100.0 %	0.33 [0.03, 3.31]
Subtotal (95% CI)	**53**	**55**		**100.0 %**	**0.33 [0.03, 3.31]**
Total events: 1 (Paroxetine), 3 (newer ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.94 (P = 0.35)					
9 versus venlafaxine					
Mc Partlin 1998	10/178	10/183		100.0 %	1.03 [0.42, 2.54]
Subtotal (95% CI)	**178**	**183**		**100.0 %**	**1.03 [0.42, 2.54]**
Total events: 10 (Paroxetine), 10 (newer ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.06 (P = 0.95)					



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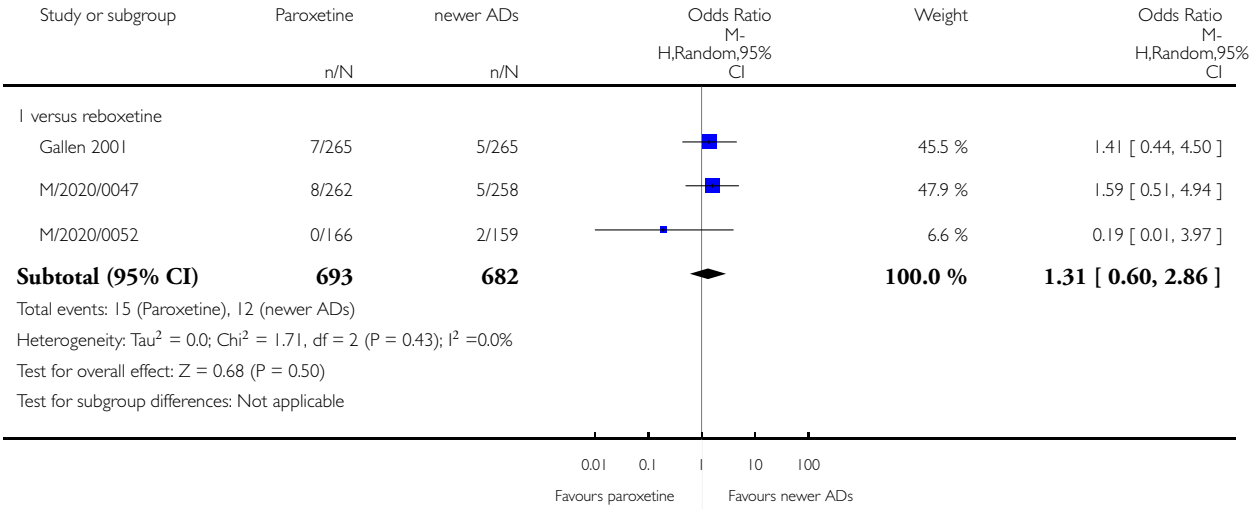
Analysis 80.1. Comparison 80 SE - Sinusitis, Outcome 1 Paroxetine versus newer or non-conventional ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 80 SE - Sinusitis

Outcome: 1 Paroxetine versus newer or non-conventional ADs



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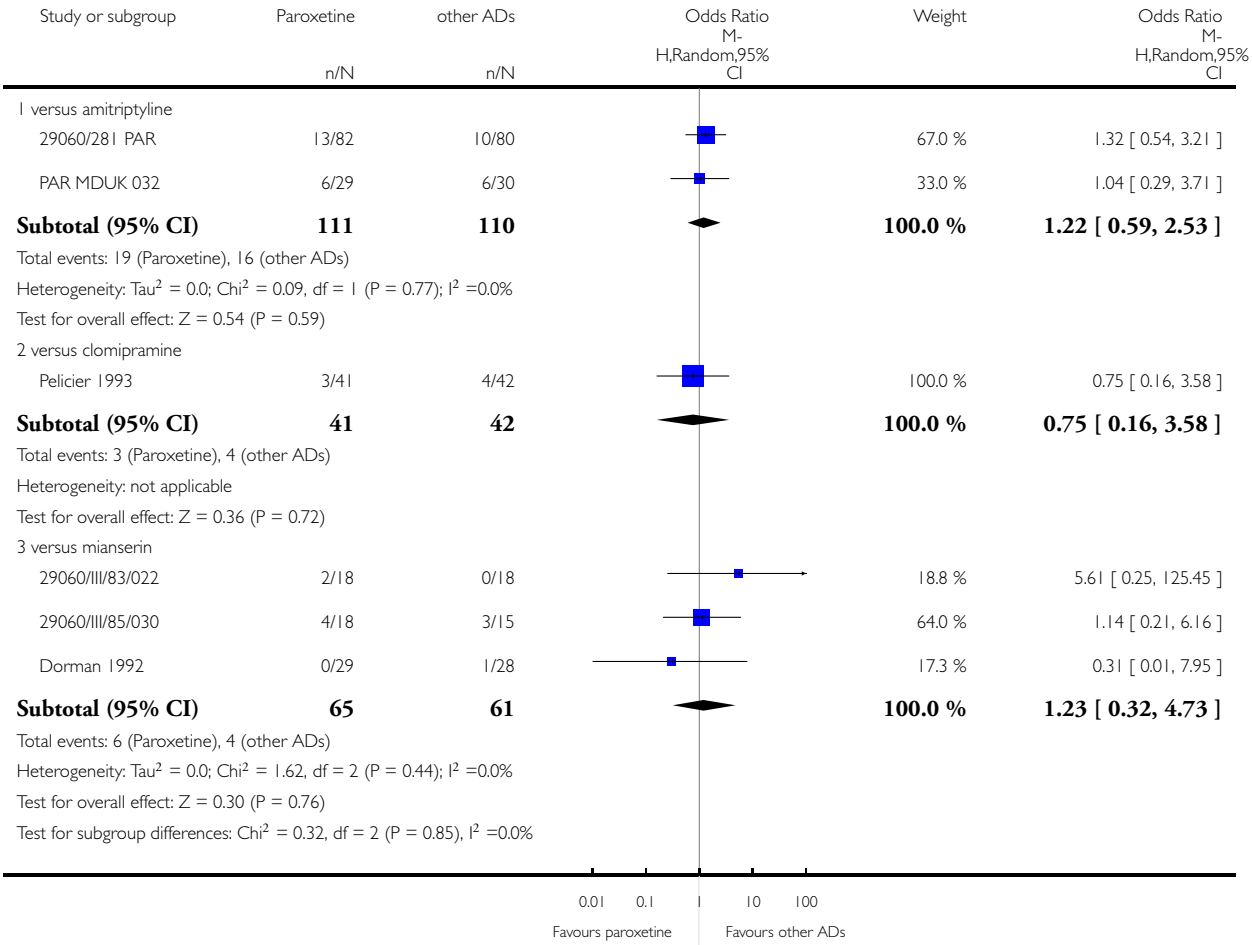
Analysis 81.1. Comparison 81 SE - Special senses, Outcome 1 NOS.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 81 SE - Special senses

Outcome: 1 NOS



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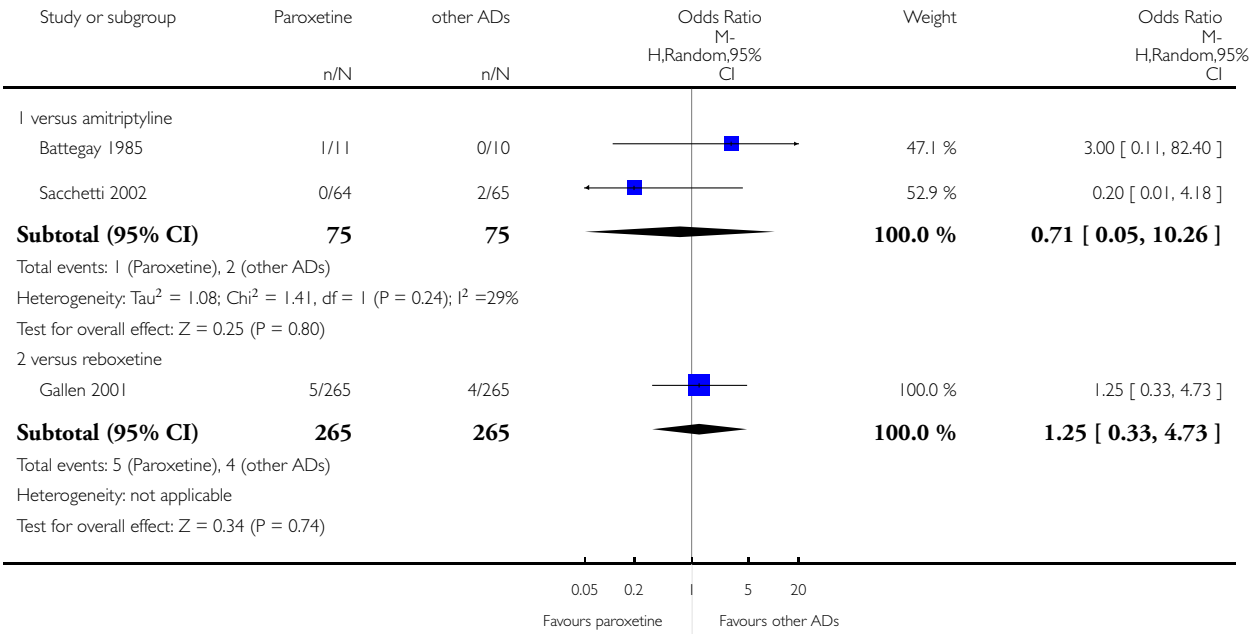
Analysis 81.2. Comparison 81 SE - Special senses, Outcome 2 Taste perversion.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 81 SE - Special senses

Outcome: 2 Taste perversion



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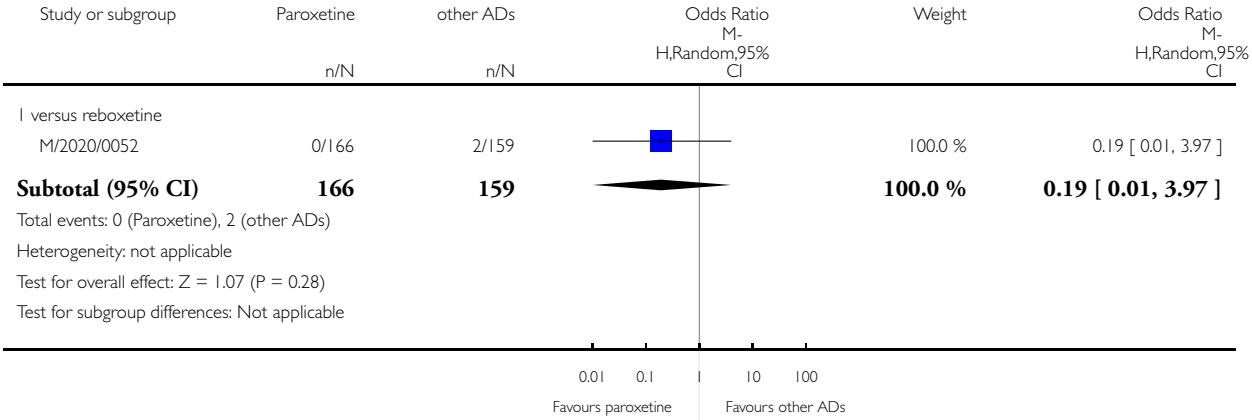
Analysis 81.3. Comparison 81 SE - Special senses, Outcome 3 Auditory disorders.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 81 SE - Special senses

Outcome: 3 Auditory disorders

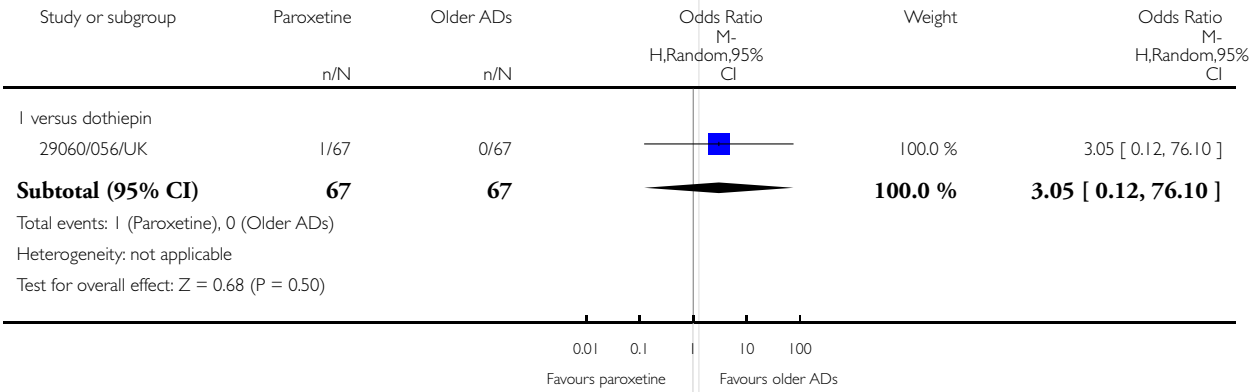


Analysis 82.1. Comparison 82 SE - Surgical procedure, Outcome 1 Paroxetine versus older ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 82 SE - Surgical procedure

Outcome: 1 Paroxetine versus older ADs



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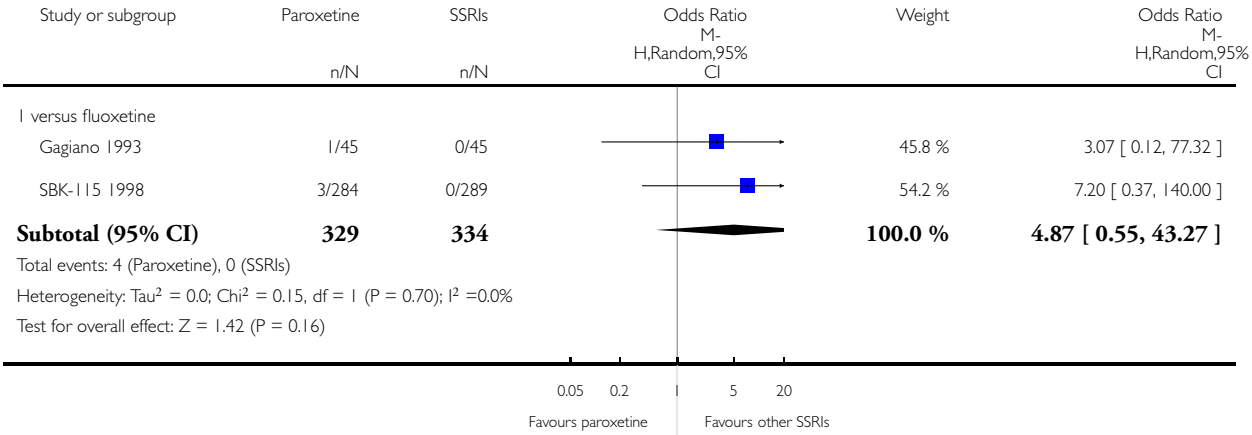
Analysis 82.2. Comparison 82 SE - Surgical procedure, Outcome 2 Paroxetine versus other SSRIs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 82 SE - Surgical procedure

Outcome: 2 Paroxetine versus other SSRIs



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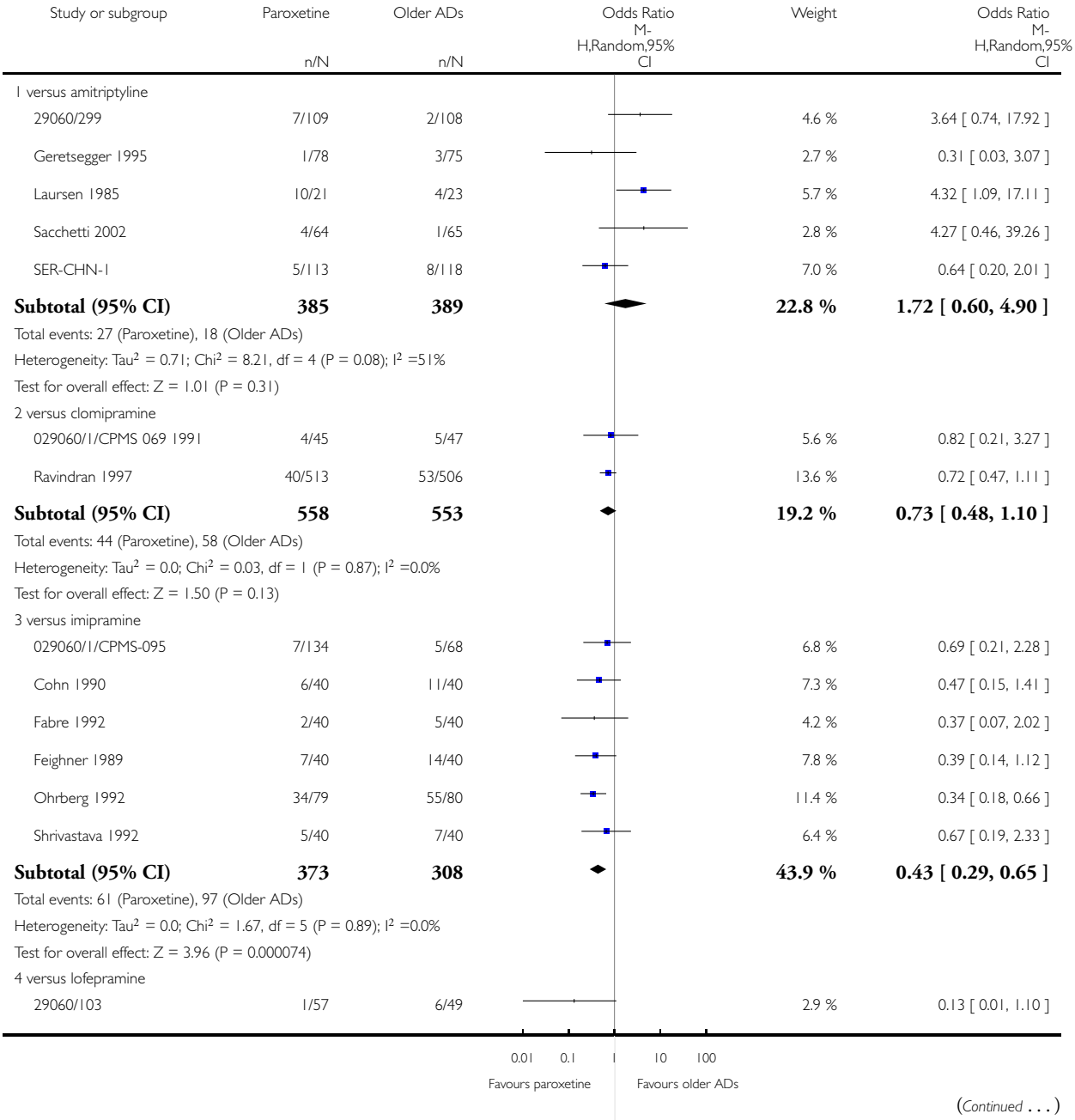
Analysis 83.1. Comparison 83 SE - Sweating, Outcome 1 Paroxetine versus older ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 83 SE - Sweating

Outcome: 1 Paroxetine versus older ADs



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Study or subgroup	Paroxetine n/N	Older ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Subtotal (95% CI)	**57**	**49**		**2.9 %**	**0.13 [0.01, 1.10]**
Total events: 1 (Paroxetine), 6 (Older ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.87 (P = 0.061)					
5 versus maprotiline					
Szegedi 1995	23/145	17/153		11.1 %	1.51 [0.77, 2.96]
Subtotal (95% CI)	**145**	**153**		**11.1 %**	**1.51 [0.77, 2.96]**
Total events: 23 (Paroxetine), 17 (Older ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.20 (P = 0.23)					
Total (95% CI)	**1518**	**1452**		**100.0 %**	**0.75 [0.50, 1.12]**
Total events: 156 (Paroxetine), 196 (Older ADs)					
Heterogeneity: Tau^2 = 0.27; Chi^2 = 28.12, df = 14 (P = 0.01); I^2 =50%					
Test for overall effect: Z = 1.40 (P = 0.16)					
Test for subgroup differences: Chi^2 = 15.41, df = 4 (P = 0.00), I^2 =74%					

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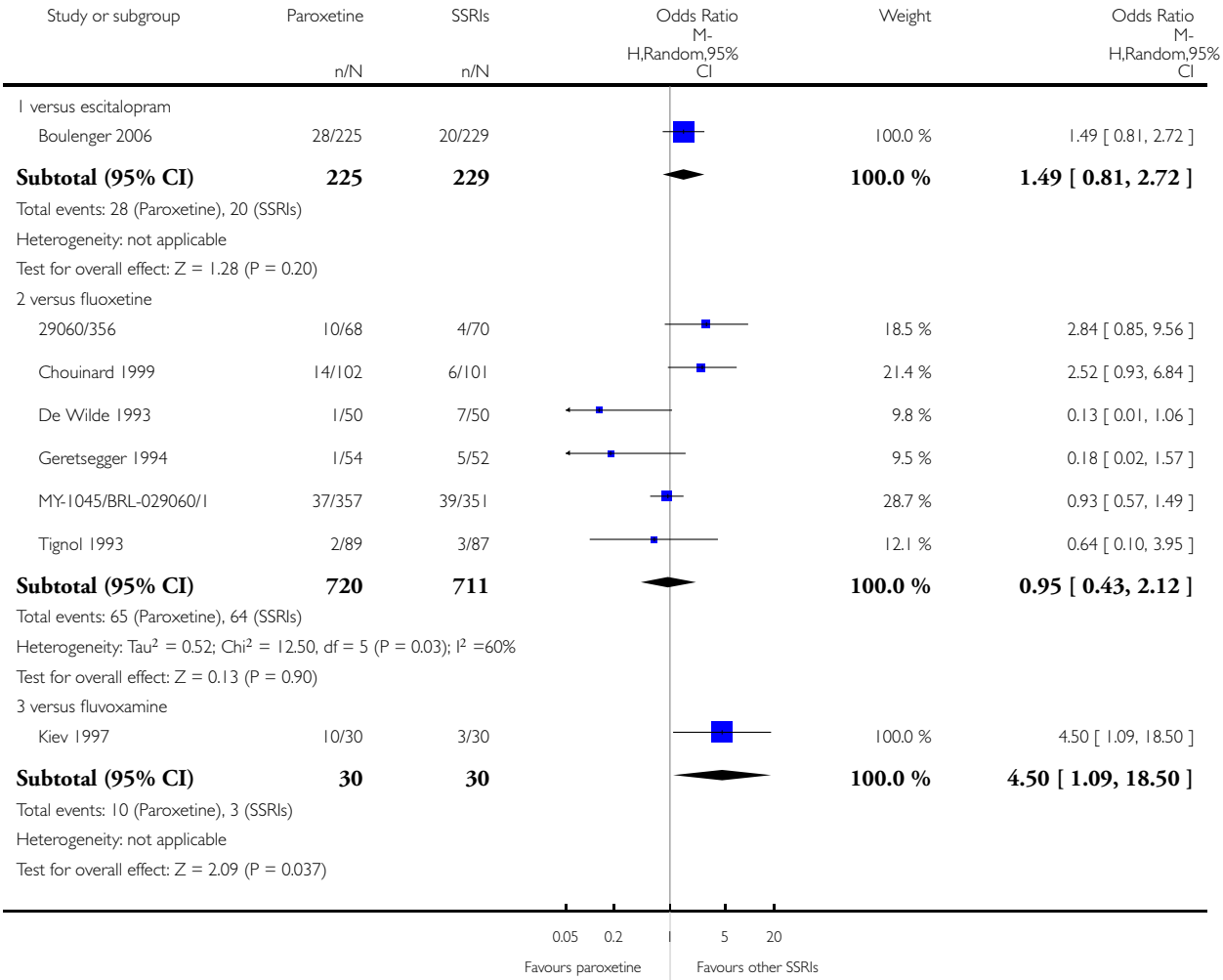
Analysis 83.2. Comparison 83 SE - Sweating, Outcome 2 Paroxetine versus other SSRIs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 83 SE - Sweating

Outcome: 2 Paroxetine versus other SSRIs



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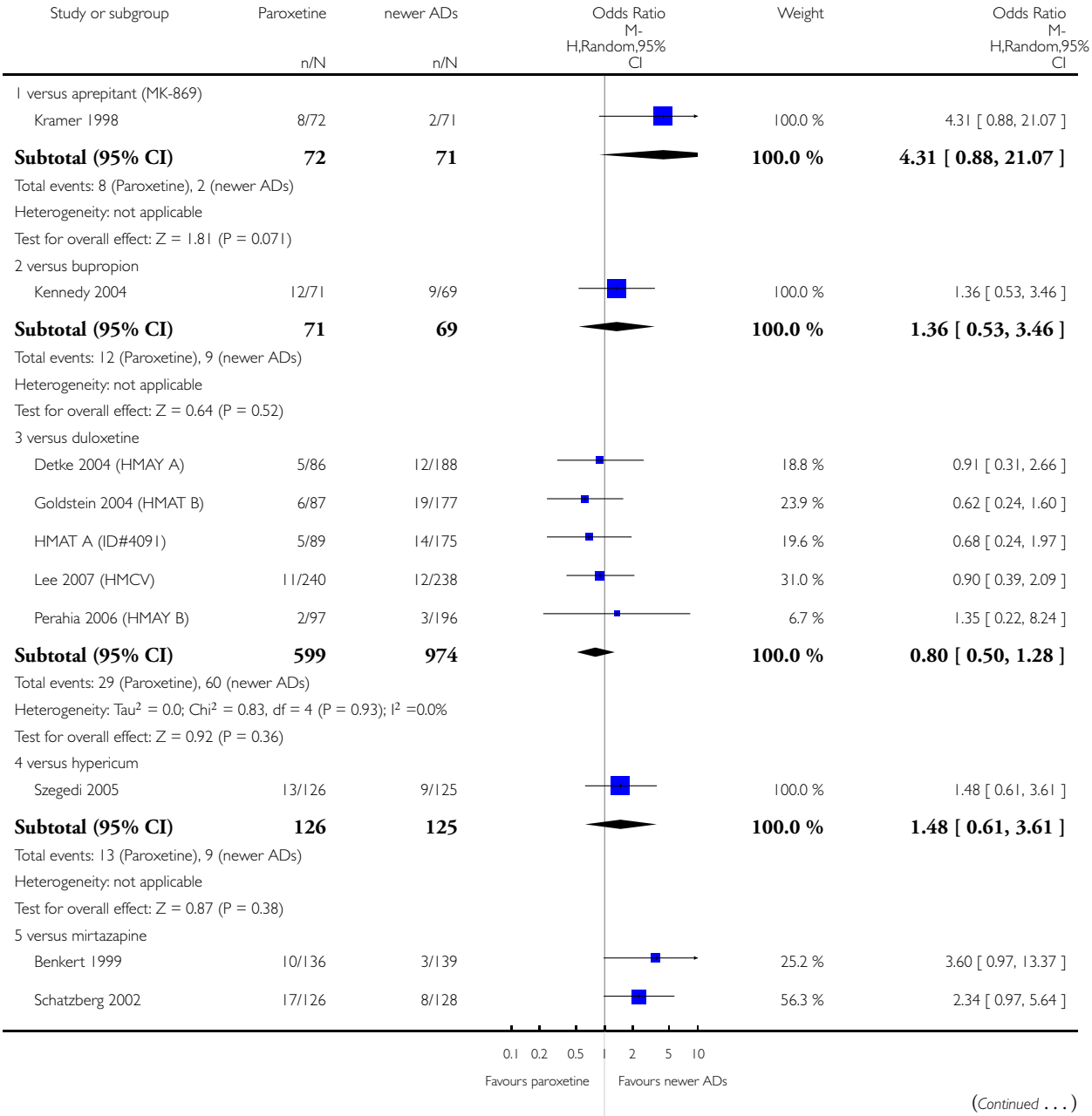
Analysis 83.3. Comparison 83 SE - Sweating, Outcome 3 Paroxetine versus newer or non-conventional ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 83 SE - Sweating

Outcome: 3 Paroxetine versus newer or non-conventional ADs



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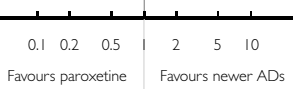
Study or subgroup	Paroxetine n/N	newer ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Wade 2003	11/98	2/99		18.5 %	6.13 [1.32, 28.44]
Subtotal (95% CI)	**360**	**366**		**100.0 %**	**3.12 [1.61, 6.03]**
Total events: 38 (Paroxetine), 13 (newer ADs)					
Heterogeneity: Tau^2 = 0.0; Chi^2 = 1.21, df = 2 (P = 0.55); I^2 =0.0%					
Test for overall effect: Z = 3.38 (P = 0.00073)					
6 versus nefazodone					
Hicks 2002	7/20	0/20		100.0 %	22.78 [1.20, 432.58]
Subtotal (95% CI)	**20**	**20**		**100.0 %**	**22.78 [1.20, 432.58]**
Total events: 7 (Paroxetine), 0 (newer ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 2.08 (P = 0.037)					
7 versus reboxetine					
Gallen 2001	17/265	40/265		34.0 %	0.39 [0.21, 0.70]
M/2020/0047	26/262	40/258		43.4 %	0.60 [0.35, 1.02]
M/2020/0052	12/166	24/159		22.6 %	0.44 [0.21, 0.91]
Subtotal (95% CI)	**693**	**682**		**100.0 %**	**0.48 [0.34, 0.68]**
Total events: 55 (Paroxetine), 104 (newer ADs)					
Heterogeneity: Tau^2 = 0.0; Chi^2 = 1.27, df = 2 (P = 0.53); I^2 =0.0%					
Test for overall effect: Z = 4.13 (P = 0.000036)					
8 versus tianeptine					
Waintraub 2002	6/139	0/138		100.0 %	13.49 [0.75, 241.76]
Subtotal (95% CI)	**139**	**138**		**100.0 %**	**13.49 [0.75, 241.76]**
Total events: 6 (Paroxetine), 0 (newer ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.77 (P = 0.077)					
9 versus trazodone					
Kasper 2005	1/53	0/55		100.0 %	3.17 [0.13, 79.60]
Subtotal (95% CI)	**53**	**55**		**100.0 %**	**3.17 [0.13, 79.60]**
Total events: 1 (Paroxetine), 0 (newer ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.70 (P = 0.48)					
10 versus venlafaxine					
Mc Partlin 1998	11/178	4/183		100.0 %	2.95 [0.92, 9.44]
Subtotal (95% CI)	**178**	**183**		**100.0 %**	**2.95 [0.92, 9.44]**
Total events: 11 (Paroxetine), 4 (newer ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.82 (P = 0.069)					



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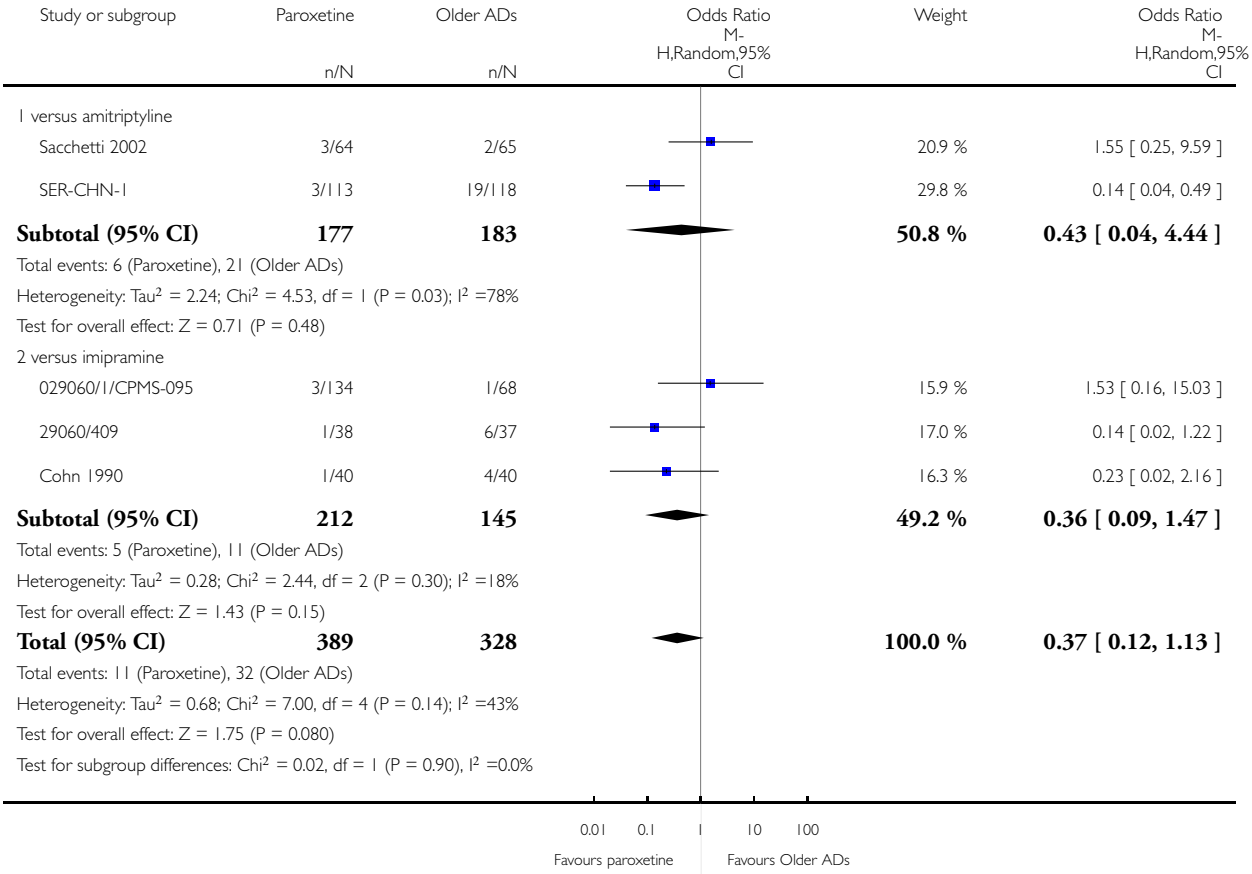
Analysis 84.1. Comparison 84 SE - Tachycardia, Outcome 1 Paroxetine versus older ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 84 SE - Tachycardia

Outcome: 1 Paroxetine versus older ADs



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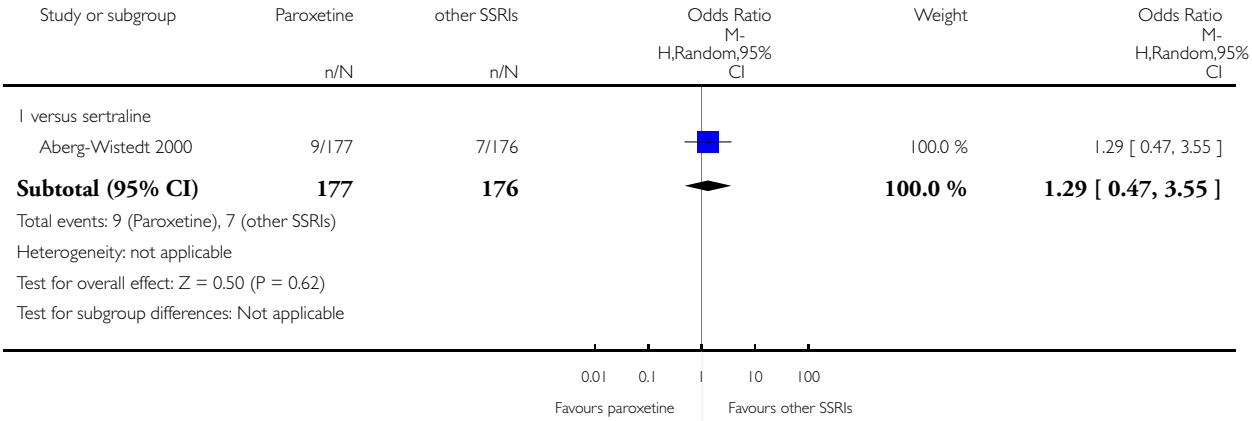
Analysis 84.2. Comparison 84 SE - Tachycardia, Outcome 2 Paroxetine versus SSRIs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 84 SE - Tachycardia

Outcome: 2 Paroxetine versus SSRIs



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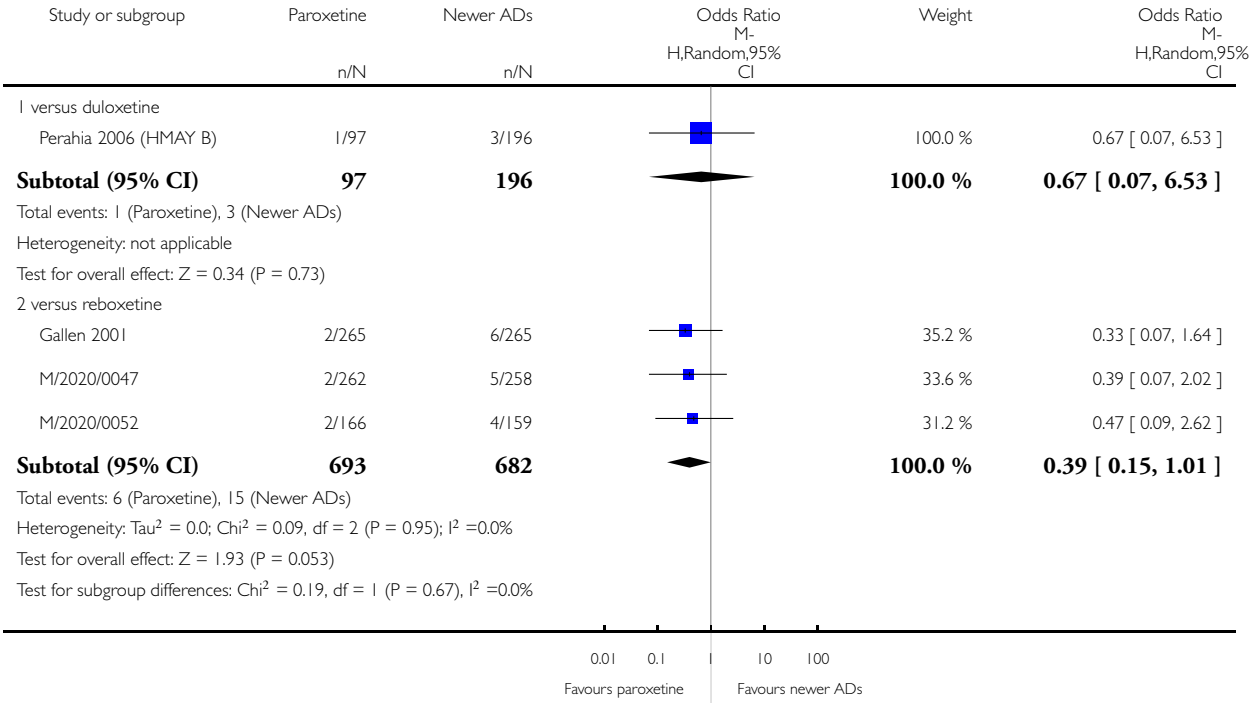
Analysis 84.3. Comparison 84 SE - Tachycardia, Outcome 3 Paroxetine versus newer or non-conventional ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 84 SE - Tachycardia

Outcome: 3 Paroxetine versus newer or non-conventional ADs



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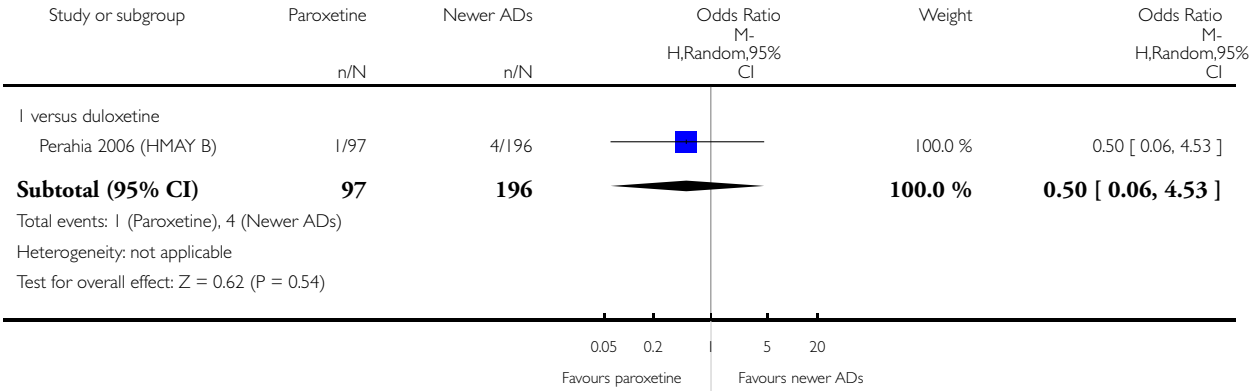
Analysis 85.1. Comparison 85 SE - Tension, Outcome 1 Paroxetine versus newer or non-conventional ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 85 SE - Tension

Outcome: 1 Paroxetine versus newer or non-conventional ADs

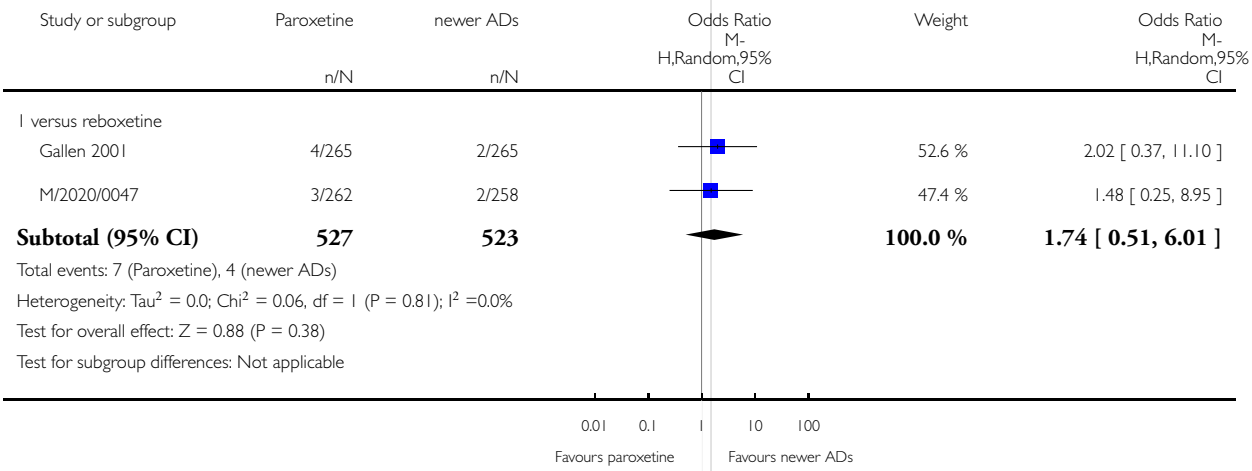


Analysis 86.1. Comparison 86 SE - Thirst, Outcome 1 Paroxetine versus newer or non-conventional ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 86 SE - Thirst

Outcome: 1 Paroxetine versus newer or non-conventional ADs



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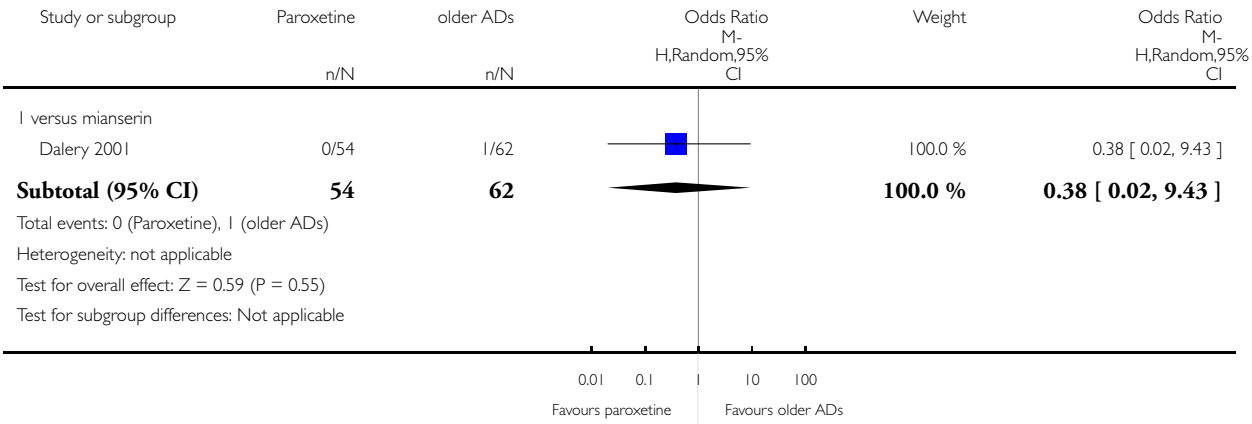
Analysis 87.1. Comparison 87 SE - Tinnitus, Outcome 1 Paroxetine versus older ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 87 SE - Tinnitus

Outcome: 1 Paroxetine versus older ADs



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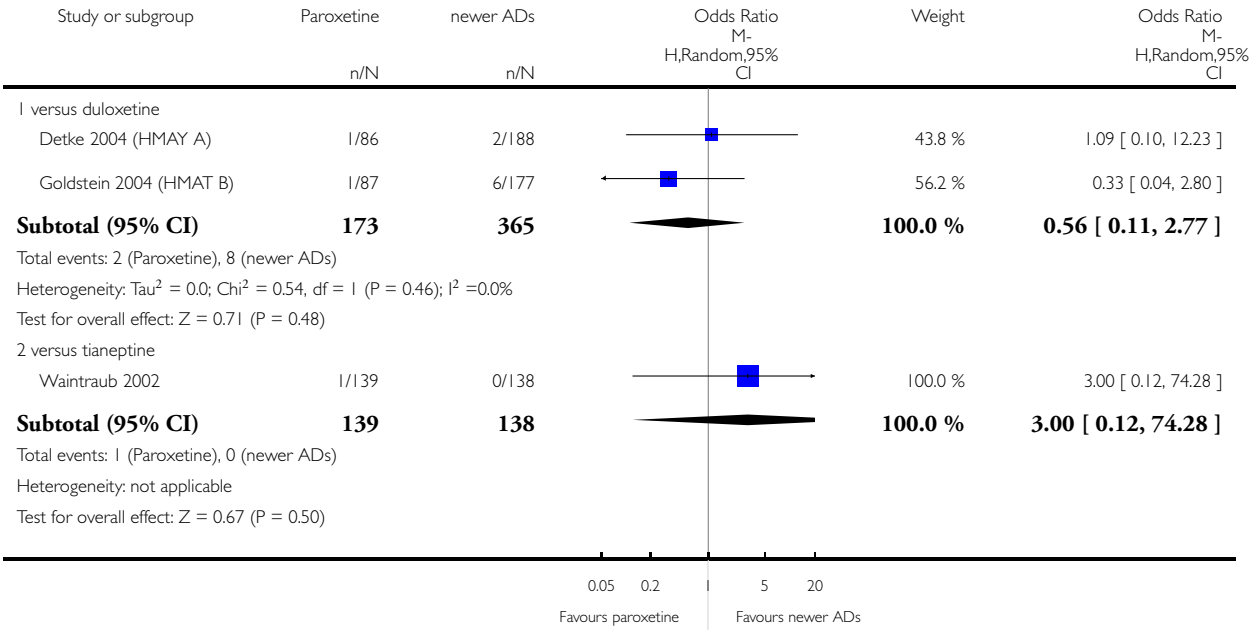
Analysis 87.2. Comparison 87 SE - Tinnitus, Outcome 2 Paroxetine versus newer or non-conventional ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 87 SE - Tinnitus

Outcome: 2 Paroxetine versus newer or non-conventional ADs



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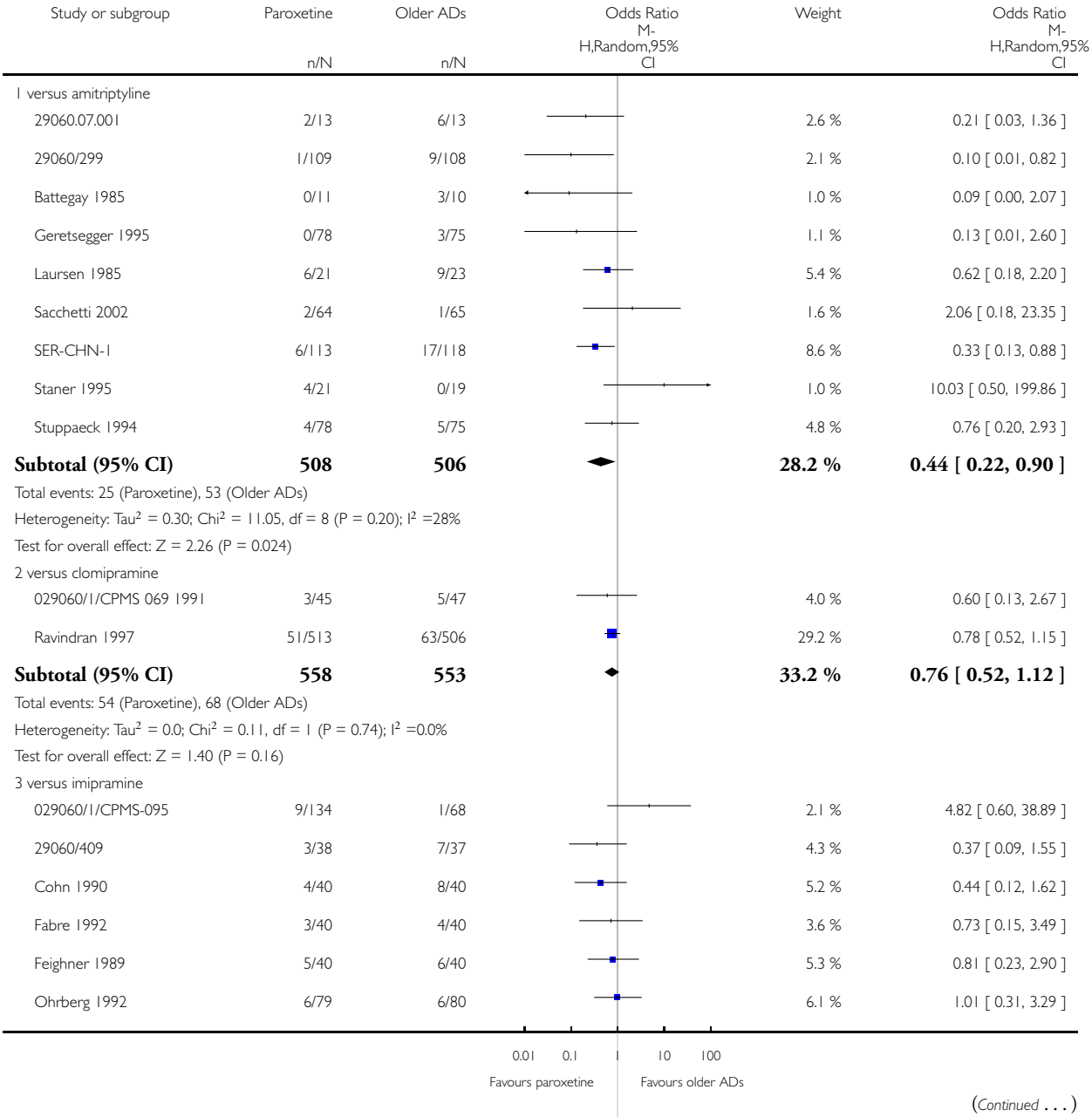
Analysis 88.1. Comparison 88 SE - Tremor, Outcome 1 Paroxetine versus older ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 88 SE - Tremor

Outcome: 1 Paroxetine versus older ADs



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Study or subgroup	Paroxetine n/N	Older ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Peselow 1989	7/40	5/39		5.6 %	1.44 [0.42, 5.00]
Shrivastava 1992	1/40	1/40		1.2 %	1.00 [0.06, 16.56]
Subtotal (95% CI)	**451**	**384**		**33.4 %**	**0.85 [0.51, 1.42]**
Total events: 38 (Paroxetine), 38 (Older ADs)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 5.82$, df = 7 (P = 0.56); $I^2 = 0.0\%$					
Test for overall effect: Z = 0.62 (P = 0.53)					
4 versus lofepramine					
29060/103	2/57	2/49		2.3 %	0.85 [0.12, 6.30]
Subtotal (95% CI)	**57**	**49**		**2.3 %**	**0.85 [0.12, 6.30]**
Total events: 2 (Paroxetine), 2 (Older ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.15 (P = 0.88)					
5 versus maprolitine					
29060.065.BE	0/28	3/32		1.0 %	0.15 [0.01, 2.99]
Schnyder 1996	2/37	0/34		1.0 %	4.86 [0.23, 104.92]
Subtotal (95% CI)	**65**	**66**		**2.0 %**	**0.84 [0.03, 25.65]**
Total events: 2 (Paroxetine), 3 (Older ADs)					
Heterogeneity: $Tau^2 = 3.70$; $Chi^2 = 2.54$, df = 1 (P = 0.11); $I^2 = 61\%$					
Test for overall effect: Z = 0.10 (P = 0.92)					
6 versus mianserin					
Dalery 2001	1/54	0/62		0.9 %	3.50 [0.14, 87.83]
Subtotal (95% CI)	**54**	**62**		**0.9 %**	**3.50 [0.14, 87.83]**
Total events: 1 (Paroxetine), 0 (Older ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.76 (P = 0.45)					
Total (95% CI)	**1693**	**1620**		**100.0 %**	**0.69 [0.50, 0.94]**
Total events: 122 (Paroxetine), 164 (Older ADs)					
Heterogeneity: $Tau^2 = 0.05$; $Chi^2 = 23.99$, df = 22 (P = 0.35); $I^2 = 8\%$					
Test for overall effect: Z = 2.38 (P = 0.017)					
Test for subgroup differences: $Chi^2 = 3.25$, df = 5 (P = 0.66), $I^2 = 0.0\%$					

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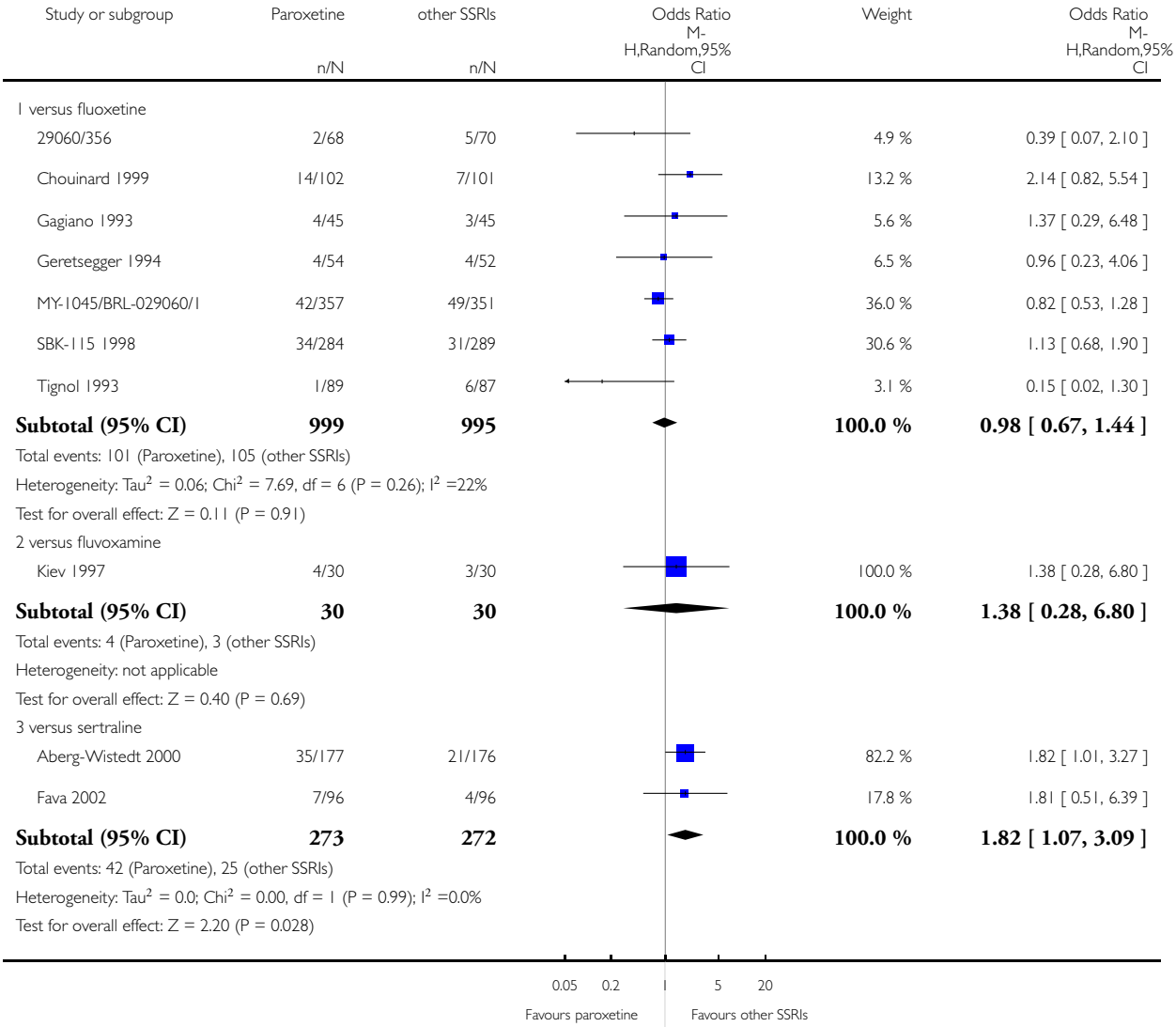
Analysis 88.2. Comparison 88 SE - Tremor, Outcome 2 Paroxetine versus other SSRIs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 88 SE - Tremor

Outcome: 2 Paroxetine versus other SSRIs



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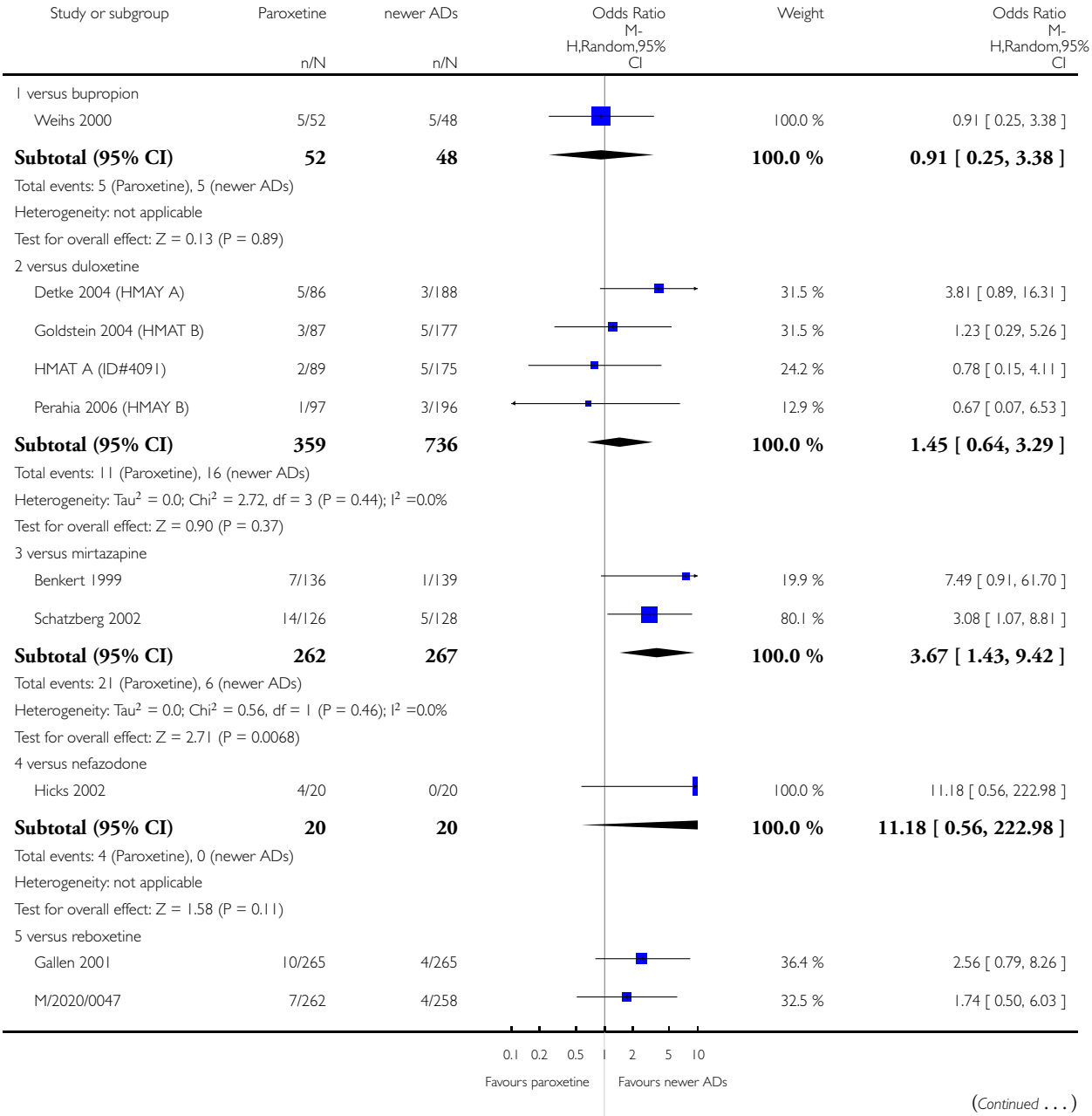
Analysis 88.3. Comparison 88 SE - Tremor, Outcome 3 Paroxetine versus newer or non-conventional ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 88 SE - Tremor

Outcome: 3 Paroxetine versus newer or non-conventional ADs



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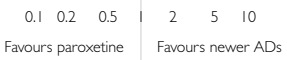
Study or subgroup	Paroxetine n/N	newer ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
M/2020/0052	14/166	3/159		31.2 %	4.79 [1.35, 17.00]
Subtotal (95% CI)	**693**	**682**		**100.0 %**	**2.75 [1.35, 5.57]**
Total events: 31 (Paroxetine), 11 (newer ADs)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 1.28$, df = 2 (P = 0.53); $I^2 = 0.0\%$					
Test for overall effect: Z = 2.80 (P = 0.00051)					
6 versus tianeptine					
Waintraub 2002	2/139	1/138		100.0 %	2.00 [0.18, 22.31]
Subtotal (95% CI)	**139**	**138**		**100.0 %**	**2.00 [0.18, 22.31]**
Total events: 2 (Paroxetine), 1 (newer ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.56 (P = 0.57)					
7 versus trazodone					
Kasper 2005	2/53	2/55		100.0 %	1.04 [0.14, 7.66]
Subtotal (95% CI)	**53**	**55**		**100.0 %**	**1.04 [0.14, 7.66]**
Total events: 2 (Paroxetine), 2 (newer ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.04 (P = 0.97)					



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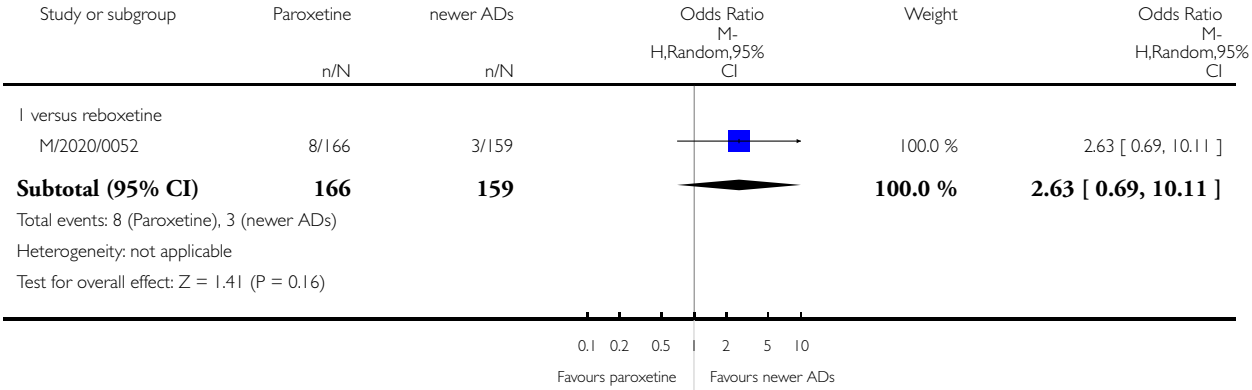
Analysis 89.1. Comparison 89 SE - Upper respiratory tract infection, Outcome 1 Paroxetine versus newer or non-conventional ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 89 SE - Upper respiratory tract infection

Outcome: 1 Paroxetine versus newer or non-conventional ADs

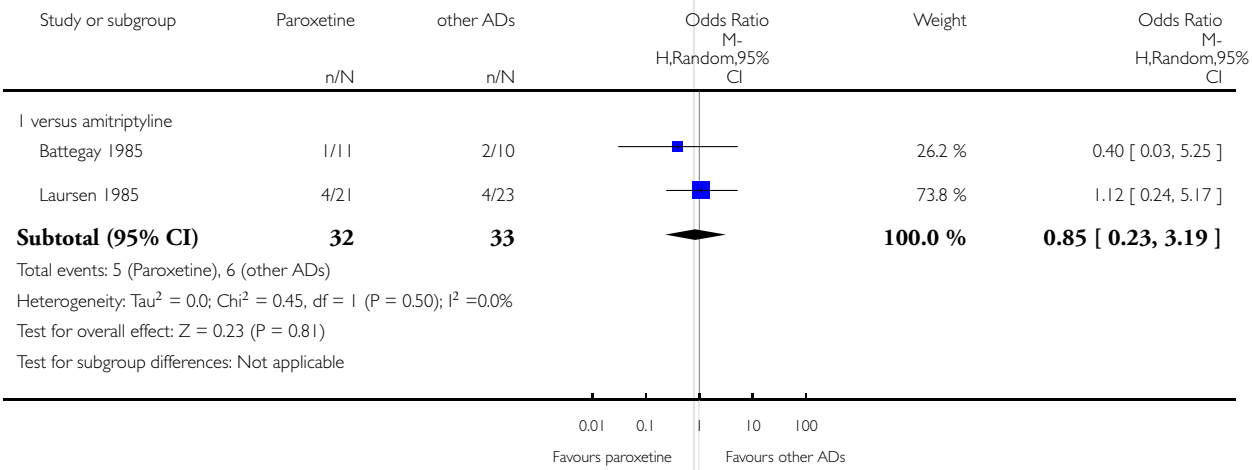


Analysis 90.1. Comparison 90 SE - Urination/Urogenital problems, Outcome 1 Difficulty micturating.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 90 SE - Urination/Urogenital problems

Outcome: 1 Difficulty micturating



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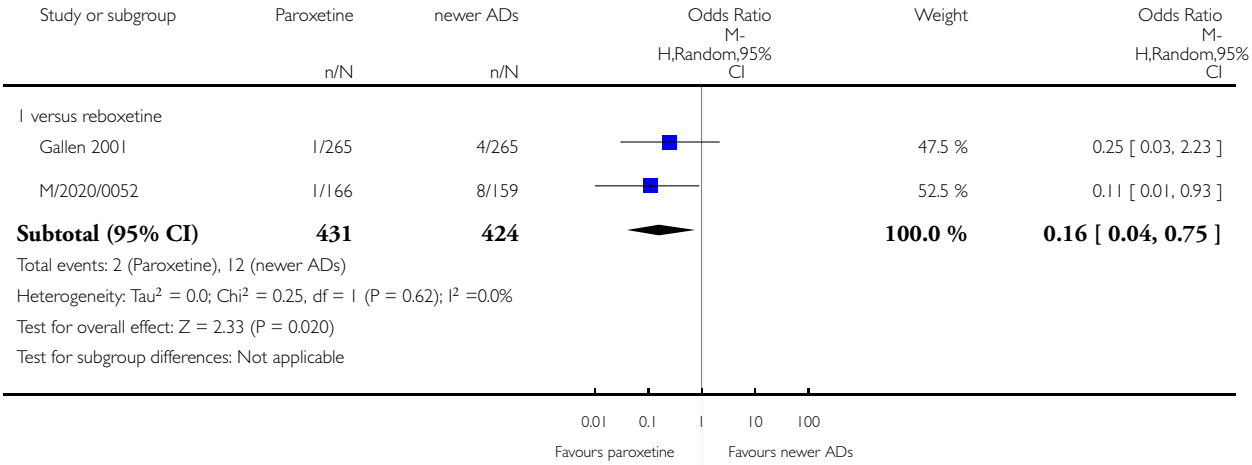
Analysis 90.2. Comparison 90 SE - Urination/Urogenital problems, Outcome 2 Dysuria.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 90 SE - Urination/Urogenital problems

Outcome: 2 Dysuria



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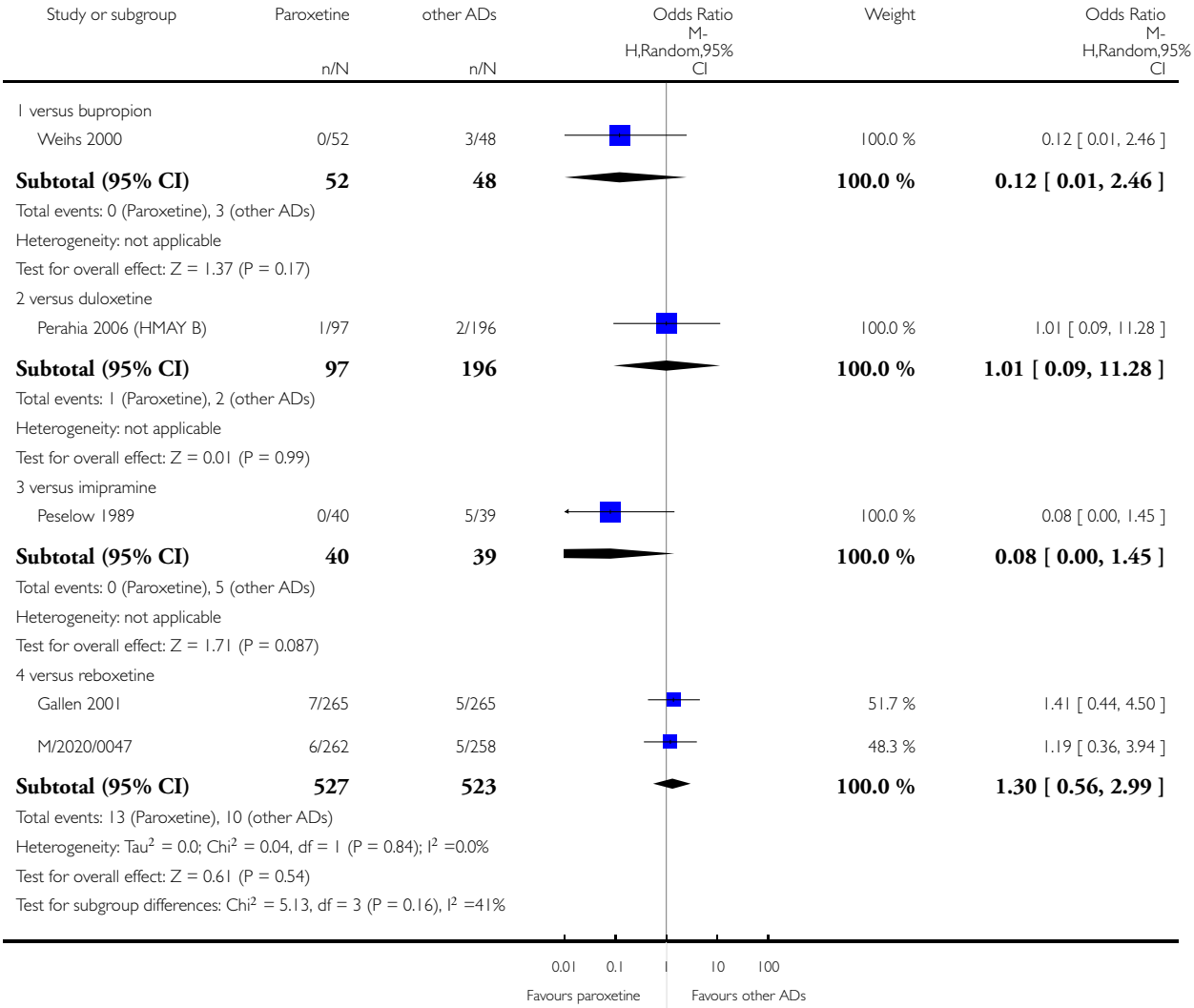
Analysis 90.3. Comparison 90 SE - Urination/Urogenital problems, Outcome 3 Urination frequency.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 90 SE - Urination/Urogenital problems

Outcome: 3 Urination frequency



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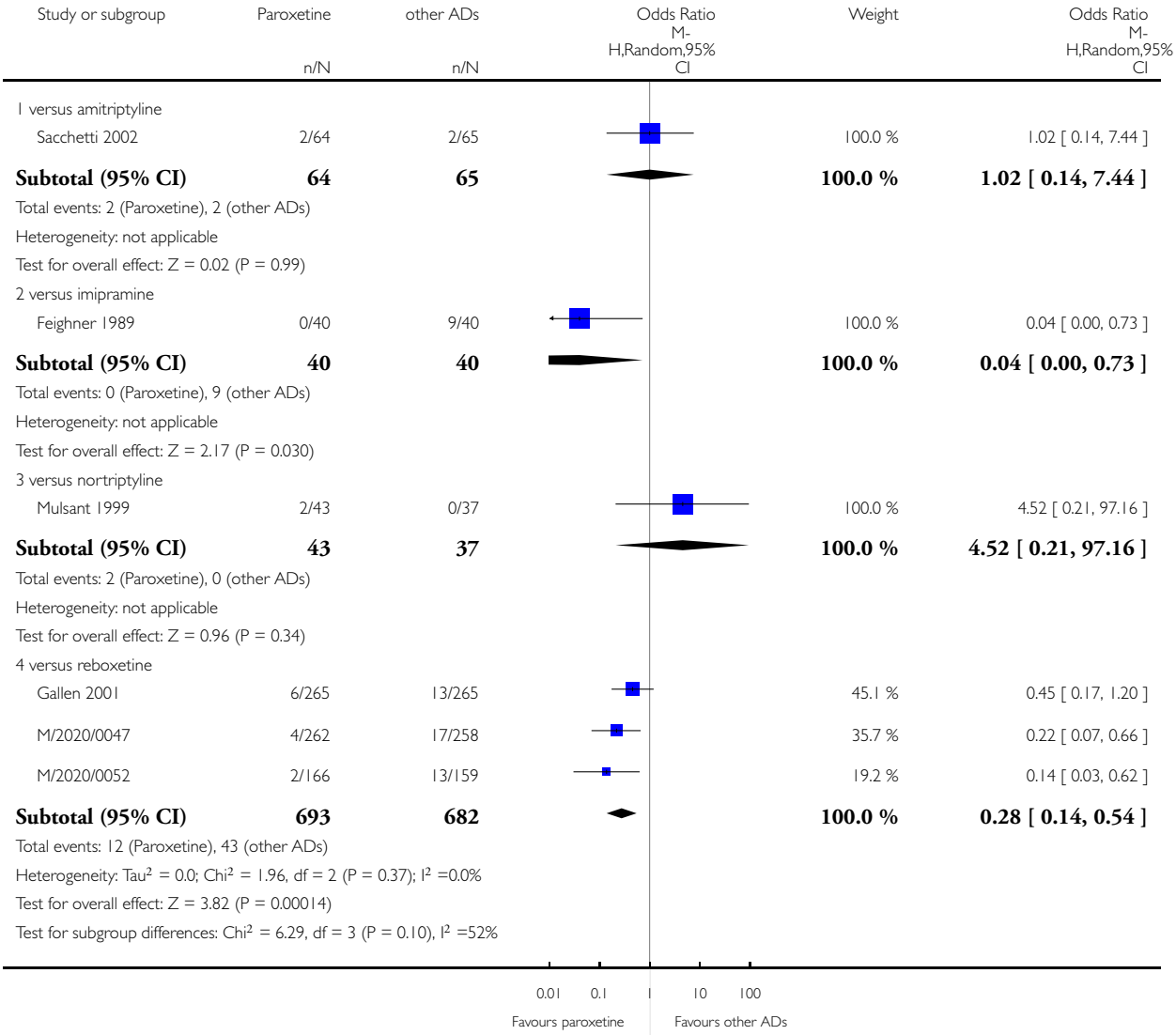
Analysis 90.4. Comparison 90 SE - Urination/Urogenital problems, Outcome 4 Urinary retention.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 90 SE - Urination/Urogenital problems

Outcome: 4 Urinary retention



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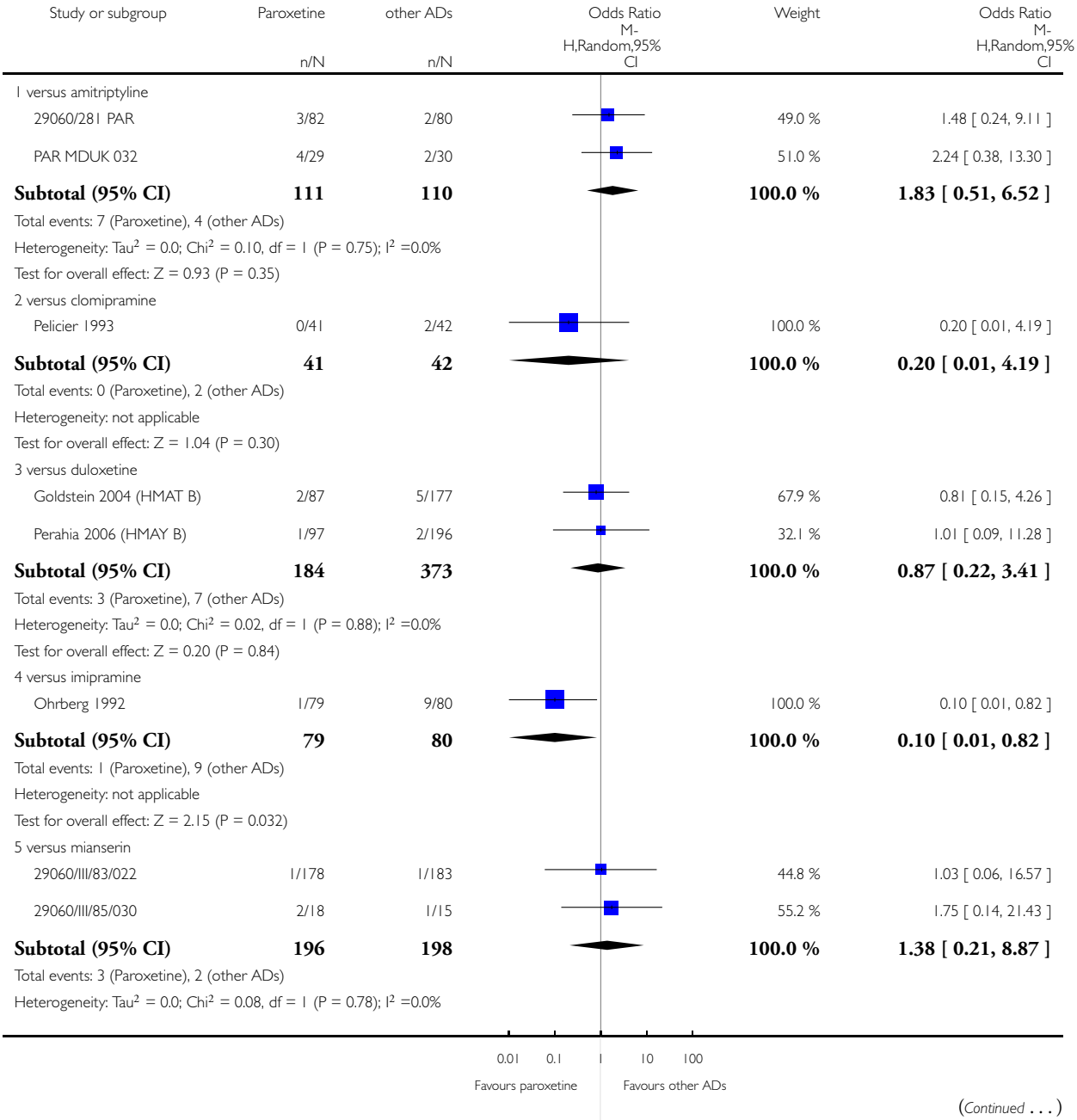
Analysis 90.5. Comparison 90 SE - Urination/Urogenital problems, Outcome 5 Not Otherwise Specified.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 90 SE - Urination/Urogenital problems

Outcome: 5 Not Otherwise Specified



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Study or subgroup	Paroxetine n/N	other ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Test for overall effect: Z = 0.34 (P = 0.74)					
6 versus sertraline					
Aberg-Wistedt 2000	11/177	1/176		100.0 %	11.60 [1.48, 90.81]
Subtotal (95% CI)	**177**	**176**		**100.0 %**	**11.60 [1.48, 90.81]**
Total events: 11 (Paroxetine), 1 (other ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 2.33 (P = 0.020)					
Test for subgroup differences: Chi^2 = 12.03, df = 5 (P = 0.03), I^2 =58%					

Analysis 91.1. Comparison 91 SE - Visual problems (accommodation disorders, amblyopia, blepharoptosis, blurred vision, detached retina, dry eye, eye strain, mydriasis), Outcome 1 Paroxetine versus older ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 91 SE - Visual problems (accommodation disorders, amblyopia, blepharoptosis, blurred vision, detached retina, dry eye, eye strain, mydriasis)

Outcome: 1 Paroxetine versus older ADs

Study or subgroup	Paroxetine n/N	Older ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
1 versus amitriptyline					
29060.07.001	0/13	2/13		2.5 %	0.17 [0.01, 3.92]
Battegay 1985	1/11	0/10		2.2 %	3.00 [0.11, 82.40]
SER-CHN-1	13/113	17/118		40.4 %	0.77 [0.36, 1.67]
Subtotal (95% CI)	**137**	**141**		**45.1 %**	**0.76 [0.37, 1.58]**
Total events: 14 (Paroxetine), 19 (Older ADs)					
Heterogeneity: Tau^2 = 0.0; Chi^2 = 1.54, df = 2 (P = 0.46); I^2 =0.0%					
Test for overall effect: Z = 0.73 (P = 0.46)					
2 versus clomipramine					
029060/1/CPMS 069 1991	4/45	2/47		7.9 %	2.20 [0.38, 12.62]

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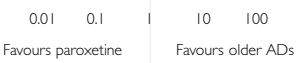
Study or subgroup	Paroxetine n/N	Older ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Subtotal (95% CI)	**45**	**47**		**7.9 %**	**2.20 [0.38, 12.62]**
Total events: 4 (Paroxetine), 2 (Older ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.88 (P = 0.38)					
3 versus imipramine					
Ohrberg 1992	13/79	6/80		23.1 %	2.43 [0.87, 6.75]
Peselow 1989	7/40	7/39		18.1 %	0.97 [0.31, 3.08]
Subtotal (95% CI)	**119**	**119**		**41.2 %**	**1.60 [0.65, 3.92]**
Total events: 20 (Paroxetine), 13 (Older ADs)					
Heterogeneity: Tau^2 = 0.11; Chi^2 = 1.36, df = 1 (P = 0.24); I^2 =27%					
Test for overall effect: Z = 1.03 (P = 0.31)					
4 versus lofepramine					
29060/103	3/57	0/49		2.7 %	6.36 [0.32, 126.19]
Subtotal (95% CI)	**57**	**49**		**2.7 %**	**6.36 [0.32, 126.19]**
Total events: 3 (Paroxetine), 0 (Older ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.21 (P = 0.23)					
5 versus mianserin					
Dalery 2001	1/54	1/62		3.1 %	1.15 [0.07, 18.85]
Subtotal (95% CI)	**54**	**62**		**3.1 %**	**1.15 [0.07, 18.85]**
Total events: 1 (Paroxetine), 1 (Older ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.10 (P = 0.92)					
Total (95% CI)	**412**	**418**		**100.0 %**	**1.21 [0.74, 1.98]**
Total events: 42 (Paroxetine), 35 (Older ADs)					
Heterogeneity: Tau^2 = 0.0; Chi^2 = 6.65, df = 7 (P = 0.47); I^2 =0.0%					
Test for overall effect: Z = 0.77 (P = 0.44)					
Test for subgroup differences: Chi^2 = 3.53, df = 4 (P = 0.47), I^2 =0.0%					



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Analysis 91.2. Comparison 91 SE - Visual problems (accommodation disorders, amblyopia, blepharoptosis, blurred vision, detached retina, dry eye, eye strain, mydriasis), Outcome 2 Paroxetine versus SSRIs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 91 SE - Visual problems (accommodation disorders, amblyopia, blepharoptosis, blurred vision, detached retina, dry eye, eye strain, mydriasis)

Outcome: 2 Paroxetine versus SSRIs

Study or subgroup	Paroxetine n/N	other SSRIs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
1 versus sertraline					
Aberg-Wistedt 2000	12/177	10/176		100.0 %	1.21 [0.51, 2.87]
Subtotal (95% CI)	**177**	**176**		**100.0 %**	**1.21 [0.51, 2.87]**
Total events: 12 (Paroxetine), 10 (other SSRIs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.43 (P = 0.67)					
Test for subgroup differences: Not applicable					

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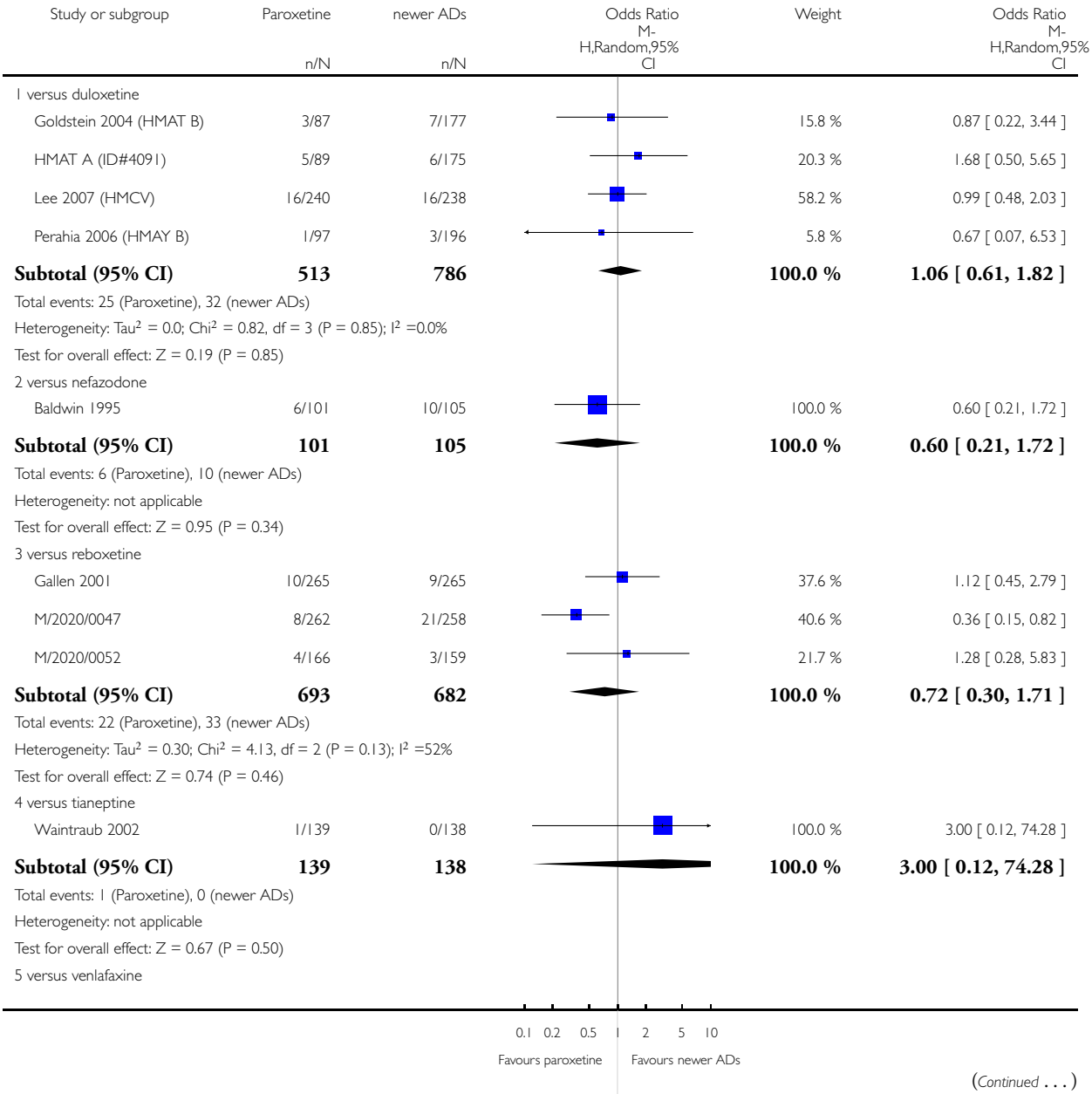
Analysis 91.3. Comparison 91 SE - Visual problems (accommodation disorders, amblyopia, blepharoptosis, blurred vision, detached retina, dry eye, eye strain, mydriasis), Outcome 3 Paroxetine versus newer or non-conventional ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 91 SE - Visual problems (accommodation disorders, amblyopia, blepharoptosis, blurred vision, detached retina, dry eye, eye strain, mydriasis)

Outcome: 3 Paroxetine versus newer or non-conventional ADs



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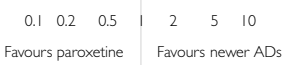
Study or subgroup	Paroxetine n/N	newer ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Hwang 2004	2/53	1/52		100.0 %	2.00 [0.18, 22.75]
Subtotal (95% CI)	**53**	**52**		**100.0 %**	**2.00 [0.18, 22.75]**
Total events: 2 (Paroxetine), 1 (newer ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.56 (P = 0.58)					



Analysis 92.1. Comparison 92 SE - Vertigo, Outcome 1 Paroxetine versus older ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 92 SE - Vertigo

Outcome: 1 Paroxetine versus older ADs

Study or subgroup	Paroxetine n/N	Older ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
1 versus amitriptyline					
Battegay 1985	5/11	4/10		19.6 %	1.25 [0.22, 7.08]
Bignamini 1992	2/156	6/153		22.6 %	0.32 [0.06, 1.60]
Geretsegger 1995	2/78	1/75		10.1 %	1.95 [0.17, 21.94]
Stuppaeck 1994	0/78	5/75		7.0 %	0.08 [0.00, 1.50]
Subtotal (95% CI)	**323**	**313**		**59.2 %**	**0.57 [0.17, 1.91]**
Total events: 9 (Paroxetine), 16 (Older ADs)					
Heterogeneity: Tau^2 = 0.41; Chi^2 = 4.12, df = 3 (P = 0.25); I^2 =27%					
Test for overall effect: Z = 0.91 (P = 0.37)					
2 versus maprolitine					
29060.065.BE	4/28	6/32		30.9 %	0.72 [0.18, 2.87]
Schnyder 1996	2/37	1/34		9.9 %	1.89 [0.16, 21.79]
Subtotal (95% CI)	**65**	**66**		**40.8 %**	**0.91 [0.27, 3.03]**

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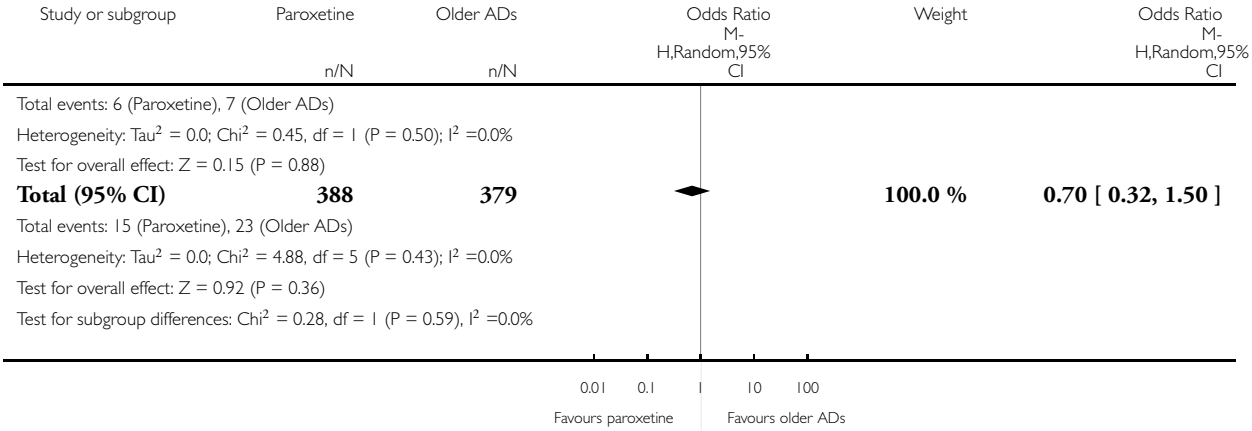
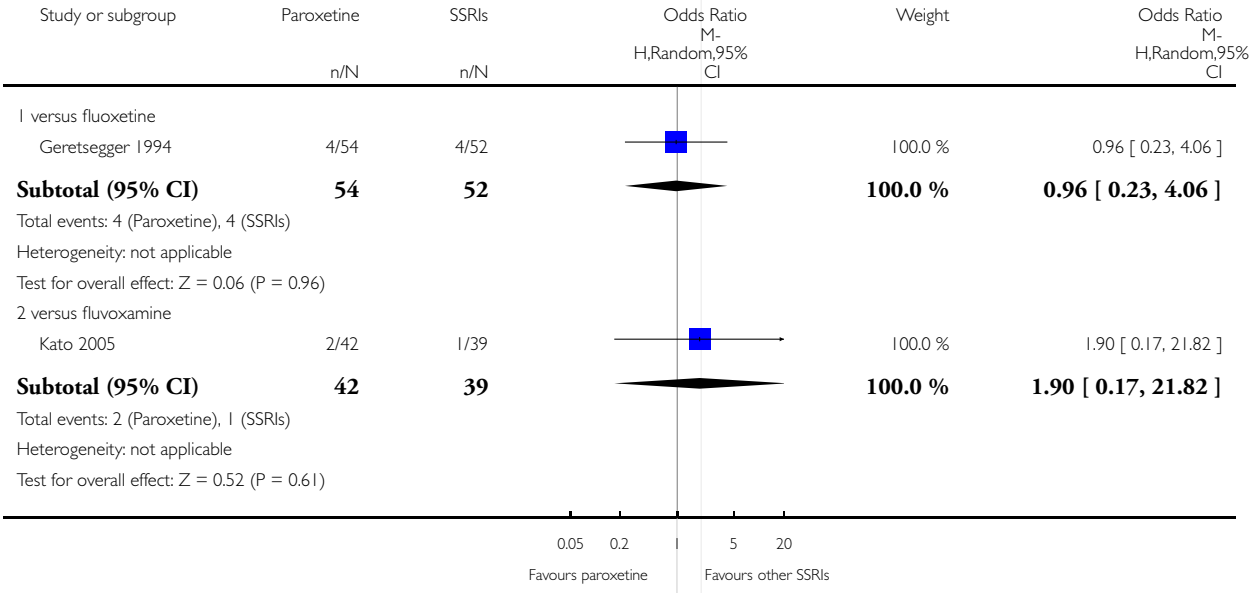


Analysis 92.2. Comparison 92 SE - Vertigo, Outcome 2 Paroxetine versus other SSRIs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 92 SE - Vertigo

Outcome: 2 Paroxetine versus other SSRIs



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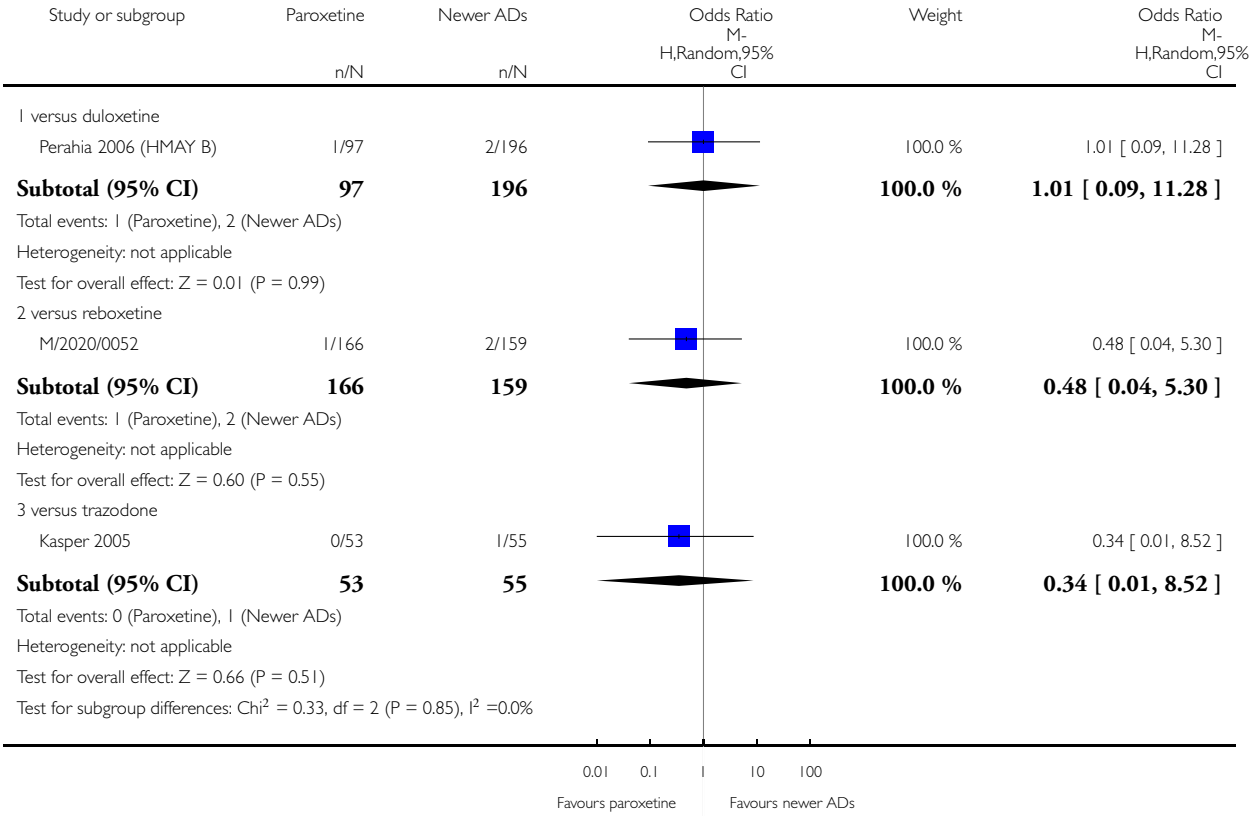
Analysis 92.3. Comparison 92 SE - Vertigo, Outcome 3 Paroxetine versus newer or non-conventional ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 92 SE - Vertigo

Outcome: 3 Paroxetine versus newer or non-conventional ADs



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Analysis 93.1. Comparison 93 SE - Weight gain, Outcome 1 Paroxetine versus older ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 93 SE - Weight gain

Outcome: 1 Paroxetine versus older ADs

Study or subgroup	Paroxetine n/N	Older ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
1 versus amitryptline					
SER-CHN-1	7/113	7/118		30.1 %	1.05 [0.36, 3.09]
Subtotal (95% CI)	**113**	**118**		**30.1 %**	**1.05 [0.36, 3.09]**
Total events: 7 (Paroxetine), 7 (Older ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.08 (P = 0.93)					
2 versus clomipramine					
029060/1/CPMS 069 1991	2/45	0/47		12.6 %	5.46 [0.25, 116.92]
Subtotal (95% CI)	**45**	**47**		**12.6 %**	**5.46 [0.25, 116.92]**
Total events: 2 (Paroxetine), 0 (Older ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.09 (P = 0.28)					
3 versus imipramine					
Ohrberg 1992	1/79	8/80		19.4 %	0.12 [0.01, 0.95]
Subtotal (95% CI)	**79**	**80**		**19.4 %**	**0.12 [0.01, 0.95]**
Total events: 1 (Paroxetine), 8 (Older ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 2.01 (P = 0.044)					
4 versus maprolitine					
29060.065.BE	0/28	4/32		13.1 %	0.11 [0.01, 2.16]
Schnyder 1996	0/37	4/34		13.1 %	0.09 [0.00, 1.74]
Subtotal (95% CI)	**65**	**66**		**26.2 %**	**0.10 [0.01, 0.81]**
Total events: 0 (Paroxetine), 8 (Older ADs)					
Heterogeneity: Tau^2 = 0.0; Chi^2 = 0.01, df = 1 (P = 0.92); I^2 =0.0%					
Test for overall effect: Z = 2.15 (P = 0.031)					
5 versus mianserin					
Dalery 2001	1/54	0/62		11.7 %	3.50 [0.14, 87.83]
Subtotal (95% CI)	**54**	**62**		**11.7 %**	**3.50 [0.14, 87.83]**
Total events: 1 (Paroxetine), 0 (Older ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.76 (P = 0.45)					
Total (95% CI)	**356**	**373**		**100.0 %**	**0.52 [0.14, 1.98]**
Total events: 11 (Paroxetine), 23 (Older ADs)					

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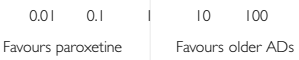
Study or subgroup	Paroxetine n/N	Older ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Heterogeneity: Tau^2 = 1.23; Chi^2 = 9.54, df = 5 (P = 0.09); I^2 =48%					
Test for overall effect: Z = 0.95 (P = 0.34)					
Test for subgroup differences: Chi^2 = 9.30, df = 4 (P = 0.05), I^2 =57%					



Analysis 93.2. Comparison 93 SE - Weight gain, Outcome 2 Paroxetine versus other SSRIs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 93 SE - Weight gain

Outcome: 2 Paroxetine versus other SSRIs

Study or subgroup	Paroxetine n/N	other SSRIs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
1 versus fluoxetine					
De Wilde 1993	3/50	2/50		49.5 %	1.53 [0.24, 9.59]
Tignol 1993	2/89	3/87		50.5 %	0.64 [0.10, 3.95]
Subtotal (95% CI)	**139**	**137**		**100.0 %**	**0.99 [0.27, 3.59]**
Total events: 5 (Paroxetine), 5 (other SSRIs)					
Heterogeneity: Tau^2 = 0.0; Chi^2 = 0.43, df = 1 (P = 0.51); I^2 =0.0%					
Test for overall effect: Z = 0.02 (P = 0.99)					

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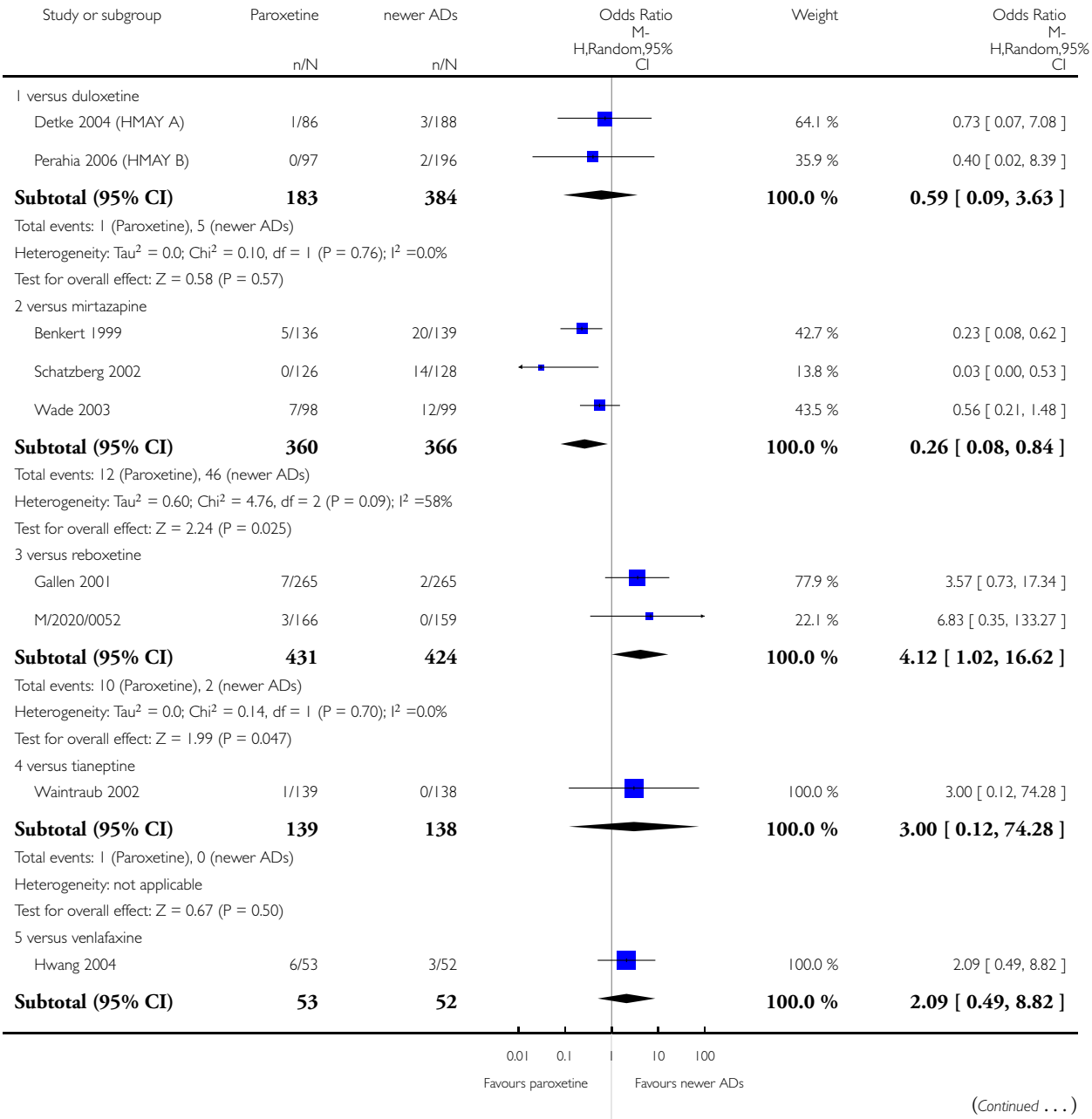
Analysis 93.3. Comparison 93 SE - Weight gain, Outcome 3 Paroxetine versus newer or non-conventional ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 93 SE - Weight gain

Outcome: 3 Paroxetine versus newer or non-conventional ADs



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Study or subgroup	Paroxetine n/N	newer ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Total events: 6 (Paroxetine), 3 (newer ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.00 (P = 0.32)					
Test for subgroup differences: Chi² = 10.74, df = 4 (P = 0.03), I² =63%					

Analysis 94.1. Comparison 94 SE - Weight loss, Outcome 1 Paroxetine versus older ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 94 SE - Weight loss

Outcome: 1 Paroxetine versus older ADs

Study or subgroup	Paroxetine n/N	older ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
1 versus maprolitine					
Schnyder 1996	1/37	0/34		100.0 %	2.84 [0.11, 71.99]
Subtotal (95% CI)	**37**	**34**		**100.0 %**	**2.84 [0.11, 71.99]**
Total events: 1 (Paroxetine), 0 (older ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.63 (P = 0.53)					
Test for subgroup differences: Not applicable					

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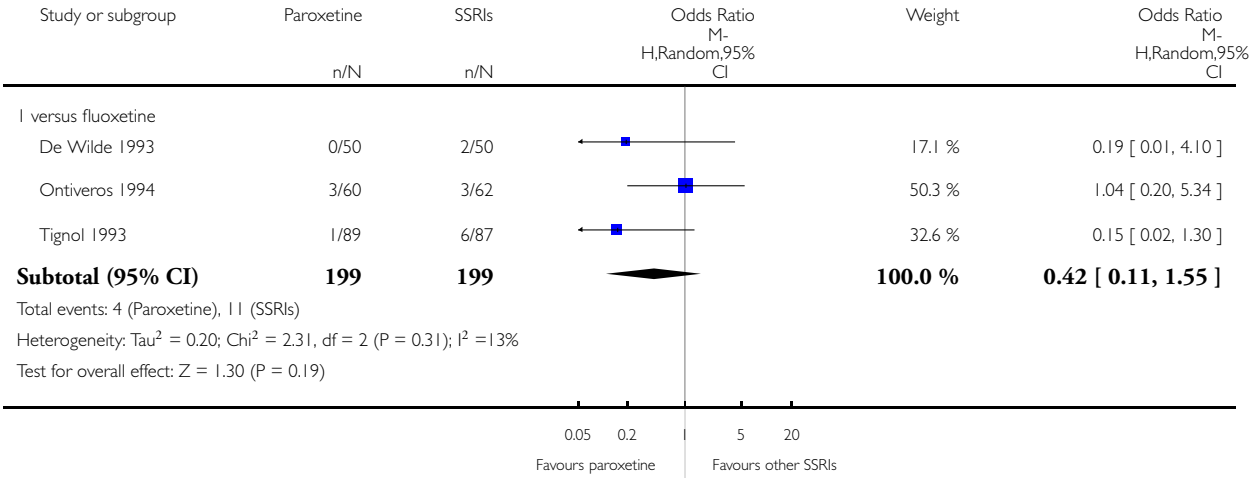
Analysis 94.2. Comparison 94 SE - Weight loss, Outcome 2 Paroxetine versus other SSRIs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 94 SE - Weight loss

Outcome: 2 Paroxetine versus other SSRIs



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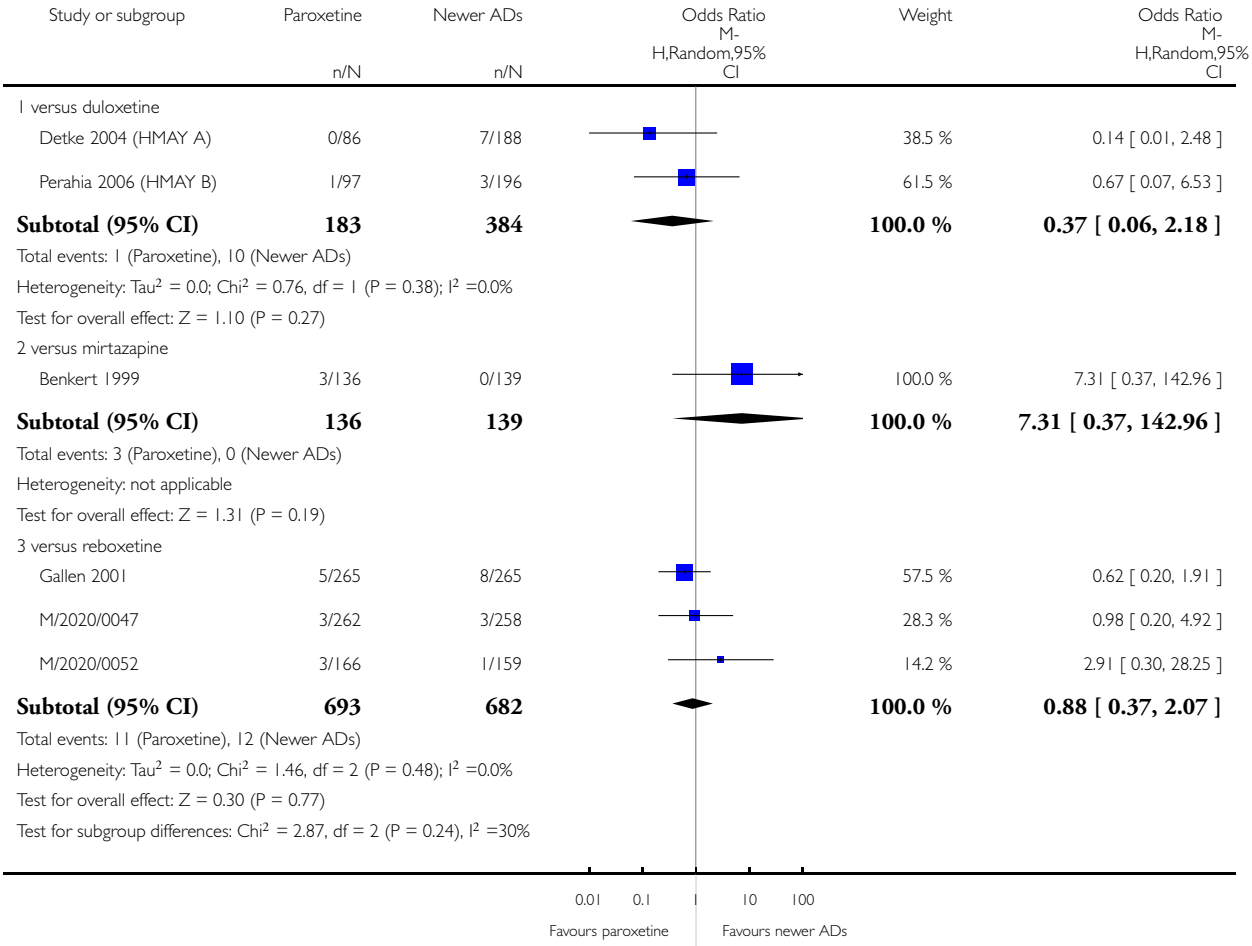
Analysis 94.3. Comparison 94 SE - Weight loss, Outcome 3 Paroxetine versus newer or non-conventional ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 94 SE - Weight loss

Outcome: 3 Paroxetine versus newer or non-conventional ADs



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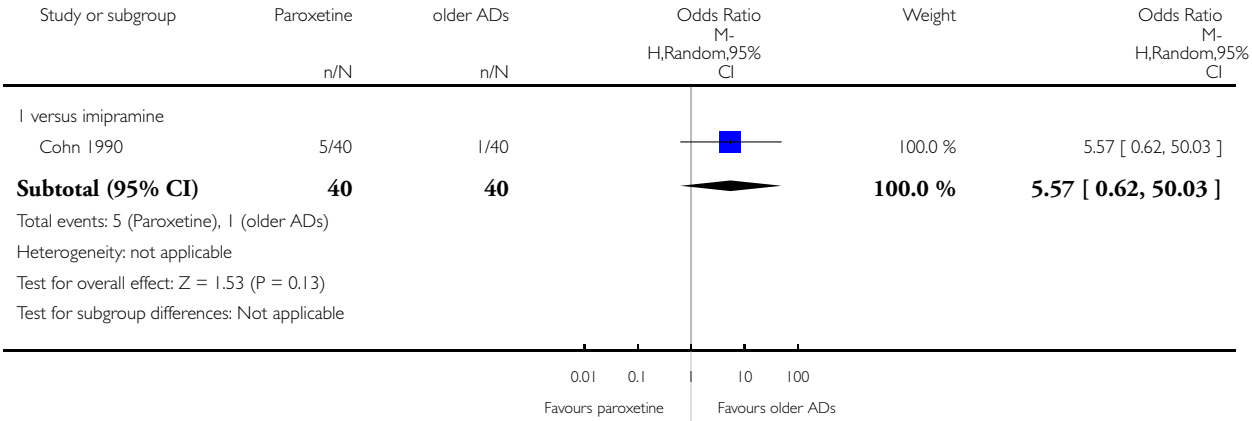
Analysis 95.1. Comparison 95 SE - Yawning, Outcome 1 Paroxetine versus older ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 95 SE - Yawning

Outcome: 1 Paroxetine versus older ADs



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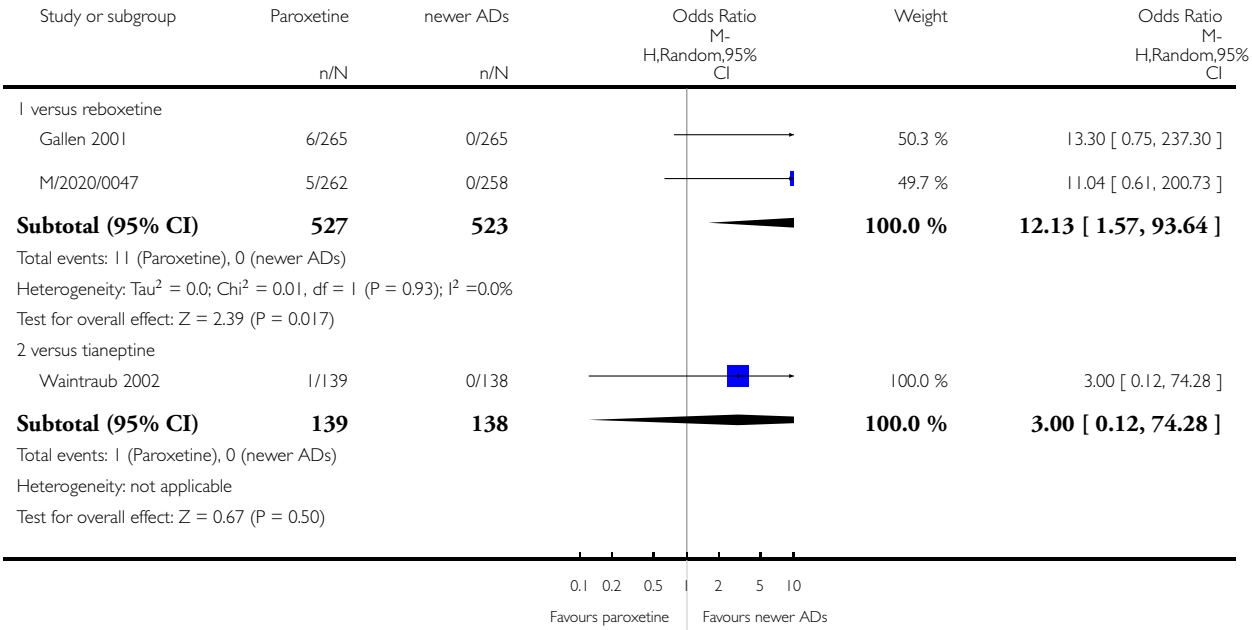
Analysis 95.2. Comparison 95 SE - Yawning, Outcome 2 Paroxetine versus newer or non-conventional ADs.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 95 SE - Yawning

Outcome: 2 Paroxetine versus newer or non-conventional ADs



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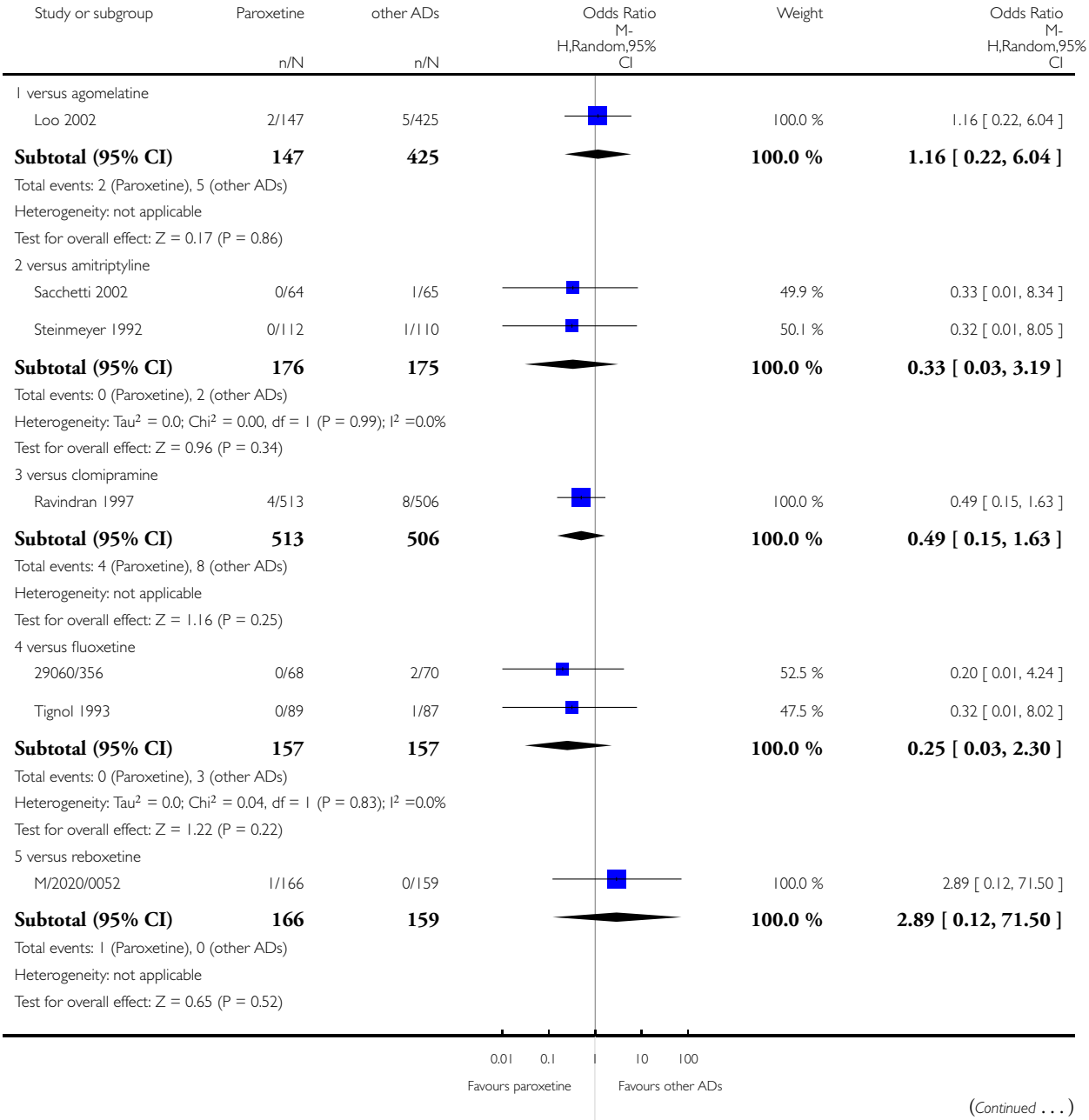
Analysis 96.1. Comparison 96 Deaths, suicide and suicidality, Outcome 1 Suicide - attempted.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 96 Deaths, suicide and suicidality

Outcome: 1 Suicide - attempted



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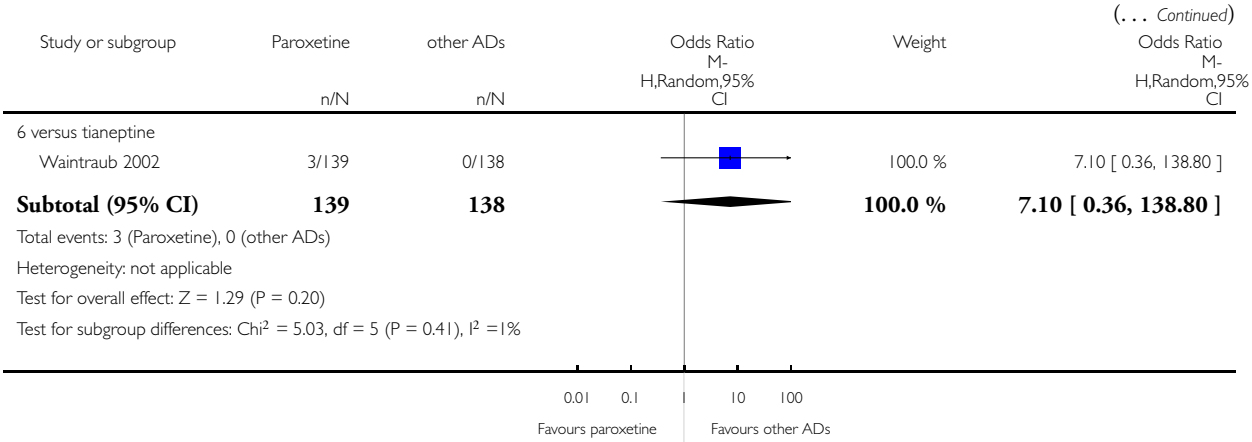
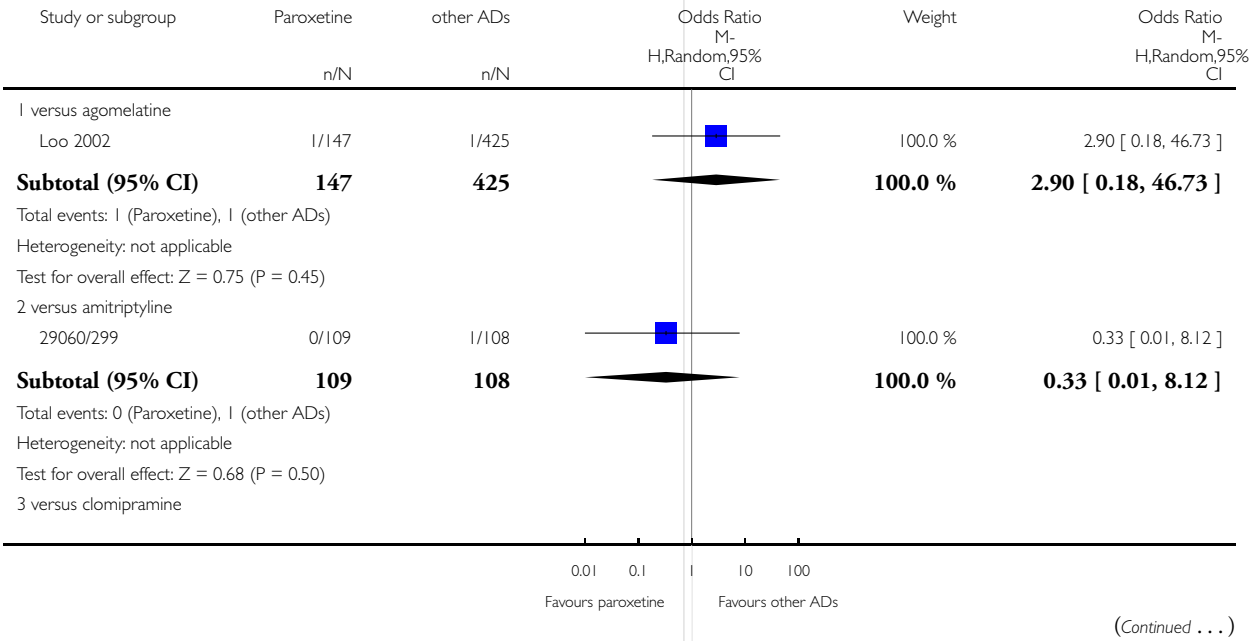


Analysis 96.2. Comparison 96 Deaths, suicide and suicidality, Outcome 2 Suicide - completed.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 96 Deaths, suicide and suicidality

Outcome: 2 Suicide - completed



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Study or subgroup	Paroxetine n/N	other ADs n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Ravindran 1997	1/513	1/506		100.0 %	0.99 [0.06, 15.81]
Subtotal (95% CI)	**513**	**506**		**100.0 %**	**0.99 [0.06, 15.81]**
Total events: 1 (Paroxetine), 1 (other ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.01 (P = 0.99)					
4 versus fluoxetine					
29060/356	1/68	1/70		100.0 %	1.03 [0.06, 16.80]
Subtotal (95% CI)	**68**	**70**		**100.0 %**	**1.03 [0.06, 16.80]**
Total events: 1 (Paroxetine), 1 (other ADs)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.02 (P = 0.98)					
Test for subgroup differences: Chi^2 = 1.02, df = 3 (P = 0.80), I^2 =0.0%					

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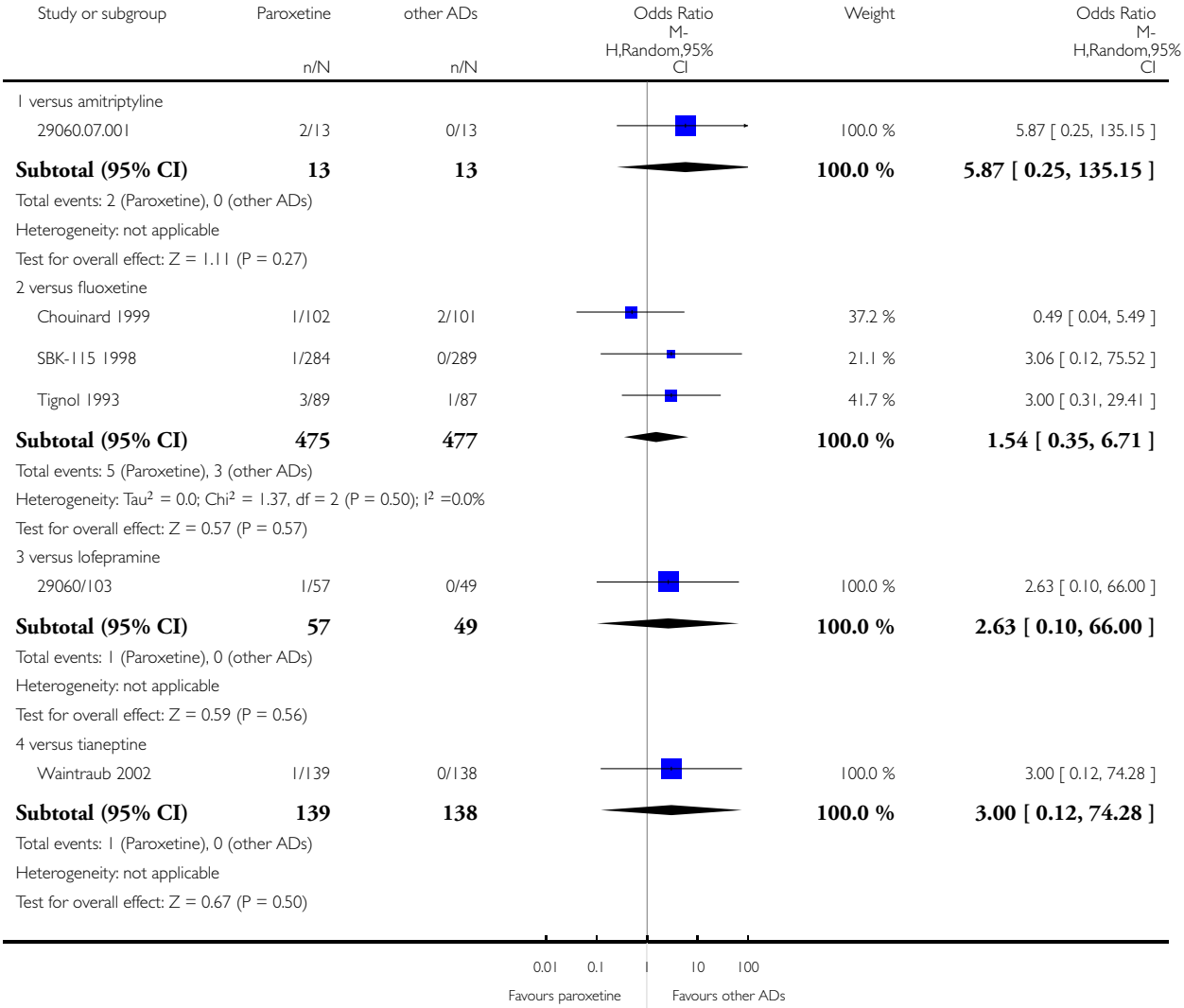
Analysis 96.3. Comparison 96 Deaths, suicide and suicidality, Outcome 3 Suicide - tendency/ideation.

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 96 Deaths, suicide and suicidality

Outcome: 3 Suicide - tendency/ideation



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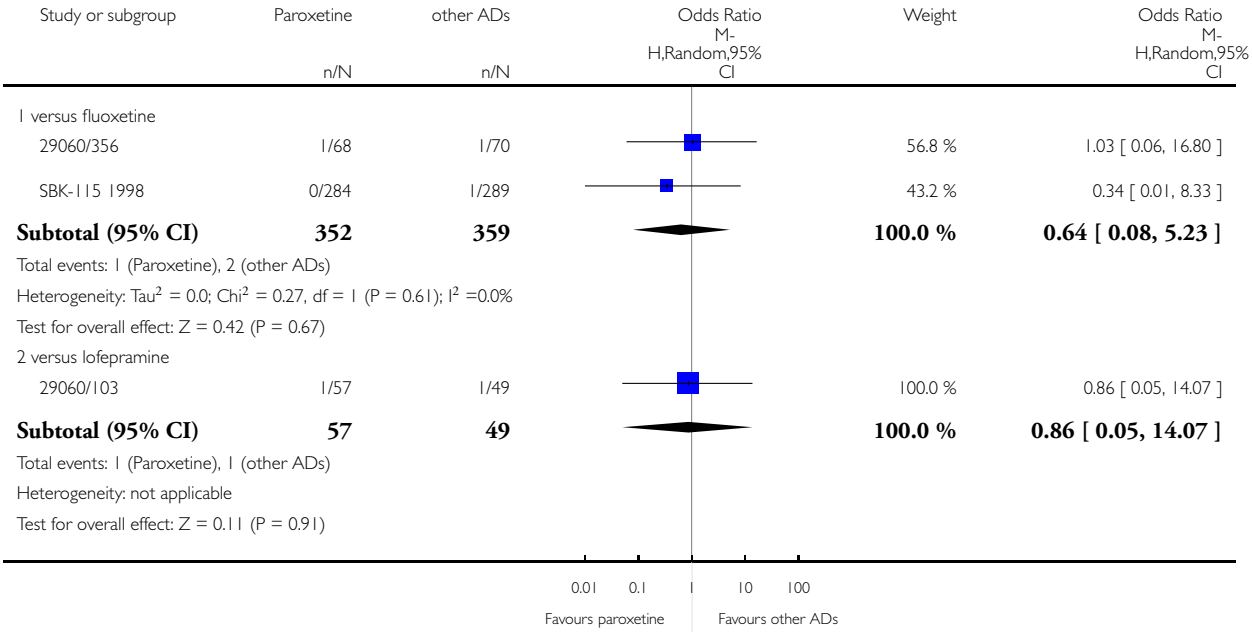
Analysis 96.4. Comparison 96 Deaths, suicide and suicidality, Outcome 4 Deaths (any cause).

Review: Paroxetine versus other anti-depressive agents for depression

Comparison: 96 Deaths, suicide and suicidality

Outcome: 4 Deaths (any cause)



ADDITIONAL TABLES

Table 1. Other significant tolerability outcomes not a priori listed in the protocol

Adverse event	Study	Paroxetine		Comparator		Odds Ratio, Random [95% CI]	NNTh [95% CI]
		Events	Total	Events	Total		
Paroxetine versus older antidepressants							
Paroxetine vs amitriptyline							
Anticholinergic	Hutchinson 1992; Staner 1995	5	79	12	51	0.22 [0.07 to 0.76]	6 [3 to 23]

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Table 1. Other significant tolerability outcomes not a priori listed in the protocol (*Continued*)

Body as a whole	29060/281 PAR; PAR MDUK 032	54	111	37	110	1.87 [1.08 to 3.23]	7 [4 to 46]
Dizziness	29060/299; 29060.07.001; Hutchinson 1992; Kuhs 1989; Laursen 1985; Sacchetti 2002; SER-CHN-1	31	398	57	379	0.42 [0.25 to 0.72]	14 [9 to 36]
Behaviour (irritability)	Battegay 1985	7	11	1	10	15.75 [1.42 to 174.25]	2 [1 to 5]
Palpitations	Battegay 1985; Bignamini 1992; Laursen 1985	4	188	13	186	0.42 [0.06 to 2.74]	21 [11 to 152]
Tachycardia	Sacchetti 2002; SER-CHN-1	6	177	21	183	0.43 [0.04 to 4.44]	12 [7 to 36]
Tremor	29060/299; 29060.07.001; Battegay 1985; Geretsegger 1995; Laursen 1985; Sacchetti 2002; SER-CHN-1; Staner 1995; Stuppaeck 1994	25	508	53	506	0.44 [0.22 to 0.90]	18 [11 to 44]
Paroxetine vs clomipramine							
Anticholinergic	Guillibert 1989	7	40	16	39	0.30 [0.11 to 0.86]	4 [2 to 24]
Paroxetine vs dothiepin							

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Table 1. Other significant tolerability outcomes not a priori listed in the protocol (*Continued*)

Headache	29060/056/UK; Dunner 1992	39	203	18	202	2.46 [1.35 to 4.48]	10 [6 to 28]
Paroxetine vs imipramine							
Dyspnea	29060/409	4	38	12	37	0.25 [0.07 to 0.85]	5 [3 to 25]
Sweating	Cohn 1990; Feighner 1989; Peselow 1989; Shrivastava 1992; 029060/1/CPMS-095; Fabre 1992; Ohrberg 1992	61	373	97	308	0.43 [0.29 to 0.65]	7 [5 to 11]
Weight gain	Ohrberg 1992	1	79	8	80	0.12 [0.01 to 0.95]	11 [6 to 58]
Paroxetine vs maprotiline							
Appetite decreased	Szegedi 1995	12	145	2	153	6.81 [1.50 to 30.99]	14 [8 to 47]
Headache	29060.065.BE; Schnyder 1996; Szegedi 1995	51	210	30	209	1.96 [1.13 to 3.39]	10 [6 to 41]
Weight gain	29060.065.BE; Schnyder 1996	0	65	8	66	0.10 [0.01 to 0.81]	8 [5 to 24]
Paroxetine vs mianserin							
Nervous system	29060/III/85/030; Dorman 1992	15	47	25	43	0.25 [0.09 to 0.67]	4 [2 to 16]
Gastrointestinal	29060/III/83/022; 29060/III/85/030; Dorman 1992	32	65	13	61	3.56 [1.63 to 7.79]	4 [2 to 8]

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Table 1. Other significant tolerability outcomes not a priori listed in the protocol (*Continued*)

Paroxetine versus other SSRIs							
Paroxetine vs fluoxetine							
Dizziness	29060/356; Gagiano 1993; Geretsegger 1994; MY-1045/BRL-029060/1; Ontiveros 1994	114	868	81	869	1.50 [1.11 to 2.04]	26 [15 to 118]
Fatigue	29060/356	2	68	9	70	0.21 [0.04 to 0.99]	10 [5 to 90]
Nervous system	Cassano 2002; De Wilde 1993	24	173	47	169	0.41 [0.24 to 0.72]	7 [4 to 18]
Sexual problems (ejaculation disorders)	MY-1045/BRL-029060/1	36	357	12	351	3.17 [1.62 to 6.20]	15 [10 to 33]
Paroxetine vs fluvoxamine							
Sweating	Kiev 1997	10	30	3	30	4.50 [1.09 to 18.50]	4 [2 to 30]
Paroxetine vs sertraline							
Fatigue	Aberg-Wistedt 2000; Fava 2002	97	273	48	272	2.41 [1.21 to 4.77]	6 [4 to 9]
Sexual problems (ejaculation disorders)	Aberg-Wistedt 2000; Fava 2002	32	273	10	272	3.50 [1.68 to 7.28]	12 [8 to 28]
Tremor	Aberg-Wistedt 2000; Fava 2002	42	273	25	272	1.82 [1.07 to 3.09]	16 [9 to 142]
Paroxetine versus newer or non-conventional **antidepressants and other agents**							
Paroxetine vs aprepitant							
Sexual problems (ejaculation disorders)	Kramer 1998	14	72	2	71	8.33 [1.82 to 38.16]	6 [4 to 15]

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Table 1. Other significant tolerability outcomes not a priori listed in the protocol (*Continued*)

Paroxetine vs hypericum							
Dizziness	Szegedi 2005	24	126	9	125	3.03 [1.35 to 6.82]	8 [5 to 2]8
Paroxetine vs mirtazapine							
Fatigue	Benkert 1999; Schatzberg 2002; Wade 2003	33	360	54	366	0.47 [0.22 to 0.99]	12 [7 to 43]
Flatulence	Schatzberg 2002	15	126	4	128	4.19 [1.35 to 13.00]	11 [7 to 42]
Headache	Benkert 1999; Schatzberg 2002; Wade 2003	73	360	46	366	1.77 [1.12 to 2.79]	11 [7 to 28]
Sexual problems (general)	Benkert 1999	18	136	4	139	5.15 [1.69 to 15.64]	10 [6 to 25]
Sweating	Benkert 1999; Schatzberg 2002; Wade 2003	38	360	13	366	3.12 [1.61 to 6.03]	14 [9 to 30]
Tremor	Benkert 1999; Schatzberg 2002	21	262	6	267	3.67 [1.43 to 9.42]	17 [11 to 49]
Weight gain	Benkert 1999; Schatzberg 2002; Wade 2003	12	360	46	366	0.25 [0.13 to 0.47]	11 [8 to 19]
Paroxetine vs nefazodone							
Sweating	Hicks 2002	7	20	0	20	22.78 [1.20 to 432.58]	3 [2 to 7]
Paroxetine vs reboxetine							
Asthenia	Gallen 2001; M/2020/0047; M/2020/0052	91	693	48	682	2.01 [1.39 to 2.91]	16 [11 to 34]

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Table 1. Other significant tolerability outcomes not a priori listed in the protocol (*Continued*)

Chills	Gallen 2001; M/2020/0047; M/2020/0052	13	693	36	682	0.34 [0.18 to 0.65]	29 [19 to 69]
Dyspnea	M/2020/0047; M/2020/0052	13	428	3	417	4.32 [1.22 to 15.31]	43 [24 to 200]
Paraesthesia	Gallen 2001; M/2020/0047; M/2020/0052	10	693	22	682	0.44 [0.20 to 0.96]	56 [30 to 535]
Sexual problems (anorgasmia)	Gallen 2001; M/2020/0047; M/2020/0052	24	693	1	682	9.84 [2.23 to 43.46]	30 [21 to 52]
Sexual problems (libido decreased)	Gallen 2001; M/2020/0047; M/2020/0052	26	693	11	682	2.34 [1.14 to 4.82]	47 [26 to 229]
Sleep disorders	Gallen 2001; M/2020/0047; M/2020/0052	16	693	4	682	3.67 [1.29 to 10.45]	58 [34 to 215]
Sweating	Gallen 2001; M/2020/0047; M/2020/0052	55	693	104	682	0.48 [0.34 to 0.68]	14 [9 to 25]
Tremor	Gallen 2001; M/2020/0047; M/2020/0052	31	693	11	682	2.75 [1.35 to 5.57]	35 [21 to 95]
Weight gain	Gallen 2001; M/2020/0052	10	431	2	424	4.12 [1.02 to 16.62]	54 [29 to 351]
Yawning	Gallen 2001; M/2020/0047	11	527	0	523	12.13 [1.57 to 93.64]	48 [30 to 115]
Paroxetine vs tianeptine							

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Table 1. Other significant tolerability outcomes not a priori listed in the protocol (*Continued*)

Dizziness	Lepine 2001; Waintraub 2002	10	304	1	300	7.02 [1.25 to 39.32]	34 [20 to 118]

FEEDBACK

June 2007

Summary

Feedback 1. The protocol does not refer to dosage change in the studies that will be included, or how data on the effects of dosage change and its timing will be analysed. A major problem with paroxetine are adverse effects early during treatment and withdrawal symptoms with reduction of dosage, omission of doses, and cessation of treatment. Many RCTs have not examined these aspects, and the review must state how far they have done so.

Feedback 2. Because RCTs are not the main source of information about harmful effects it is important to look at other types of study, including caseseries, in reviewing the evidence. The methods of reviewing adverse effects are discussed in detail in the *Handbook for Reviews of Interventions*, Appendix 6b (which will be updated and incorporated in theforthcoming 5th edition in the body of the Handbook).

Feedback 3. The evidence that treatment with paroxetine and other SSRIs or withdrawal from it can cause violent behaviour, albeit rarely, should also be considered in the protocol. It has been summarised by Healy, Herxheimer and Menkes. *Antidepressants and violence: problems at the interface of medicine and law*. PLoS Medicine 2006; 3(9):e372

Reply

Feedback 1.

We agree with Dr. Herxheimer that all issues relating to dose change are really important clinical questions. Unfortunately, most RCTs have not reported anything about that. However, in order to be able to show all available information about safety/tolerability issues, in the protocol we stated that that "in order not to miss any relatively rare or unexpected yet important side effects, in the extraction phase, we will collect all side effects data reported in literature and will discuss ways to summarize them post hoc."

Feedback 2.

RCTs are not the main source of information especially about side effects, because rare adverse events are unlikely to be observed in clinical trials. Furthermore, a through investigation should require the inclusion of observational evidence (cohort studies, case control and even case series). However, the main aim of the present review is to compare head-to-head paroxetine with other active treatments for depression. Thus, we decided to focus only on randomised evidence to reduce the risk of selection bias.

Feedback 3.

This is an very interesting paper. We were aware of this issue (and other similar issues) related to tolerability profile of antidepressant drugs (and especially paroxetine). This is the reason why we reported in the protocol that we are going to collect and report in the full text review all available information "about rare or unexpected yet important side effects."

Contributors

Andrew Herxheimer

Submitter agrees with default conflict of interest statement:

I certify that I have no affiliations with or involvement in any organization or entity with a financial interest in the subject matter of my feedback.

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WHAT'S NEW

Last assessed as up-to-date: 30 September 2012.

Date	Event	Description
2 November 2008	Amended	Converted to new review format.

CONTRIBUTIONS OF AUTHORS

MP, CG, DP, LRM, CT, CR, TAF, NW, CB, AC collected the data; MP, AC, CB ran the analyses; MP, AC, CB drafted and critically revised the manuscript.

TAF and NW critically revised the manuscript.

DECLARATIONS OF INTEREST

MP, CG, DP, CT, LRM, CR, CB, AC: none.

TAF has received honoraria for speaking at CME meetings sponsored by Asahi Kasei, Eli Lilly, GlaxoSmithKline, Mochida, MSD, Otsuka, Pfizer, Shionogi and Tanabe-Mitsubishi. He is diplomate of the Academy of Cognitive Therapy. He has received royalties from Igaku-Shoin, Seiwa-Shoten and Nihon Bunka Kagaku-sha. He is on advisory board for Sekisui Chemicals and Takeda Science Foundation. The Japanese Ministry of Education, Science, and Technology, the Japanese Ministry of Health, Labor and Welfare, and the Japan Foundation for Neuroscience and Mental Health have funded his research projects.

NW has received research grants from the Japanese Ministry of Education, Science, Sports and Culture; and from the Japanese Ministry of the Health, Labour and Welfare. He has also received speaking fees and research funds from Asahi Kasei, Dai-Nippon Sumitomo, Eli Lilly, GlaxoSmithKline, Janssen, MSD, Otsuka, Pfizer and Schering-Plough.

SOURCES OF SUPPORT

Internal sources

- Department of Public Health and Community Medicine, Section of Psychiatry, University of Verona, Italy.

External sources

- No sources of support supplied

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DIFFERENCES BETWEEN PROTOCOL AND REVIEW

In the present review we added the 'Summary of findings' tables using the GRADE methodology.

NOTES

This review is one of a number of separate reviews examining head-to-head comparisons as part of the multiple Meta-Analyses of New Generation Antidepressants (MANGA) Study . We have up to now completed individual reviews about sertraline (Cipriani 2009a), escitalopram (Cipriani 2009b), milnacipran (Nakagawa 2009), fluvoxamine (Omori 2010), mirtazapine (Watanabe 2011), duloxetine (Cipriani 2012a), citalopram (Cipriani 2012b), fluoxetine (Magni 2013) and a number of other reviews are now underway.

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