Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery (Review)

Mead GE, Hsieh CF, Lee R, Kutlubaev MA, Claxton A, Hankey GJ, Hackett ML

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[Intervention Review]

Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

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ABSTRACT

Background

Stroke is the major cause of adult disability. Selective serotonin reuptake inhibitors (SSRIs) have been used for many years to manage depression. Recently, small trials have demonstrated that SSRIs might improve recovery after stroke, even in people who are not depressed. Systematic reviews and meta-analyses are the least biased way to bring together data from several trials. Given the promising effect of SSRIs on stroke recovery seen in small trials, a systematic review and meta-analysis is needed.

Objectives

To determine whether SSRIs improve recovery after stroke, and whether treatment with SSRIs was associated with adverse effects.

Search methods

We searched the Cochrane Stroke Group Trials Register (August 2011), Cochrane Depression Anxiety and Neurosis Group Trials Register (November 2011), Cochrane Central Register of Controlled Trials (CENTRAL) (*The Cochrane Library* 2011, Issue 8), MEDLINE (from 1948 to August 2011), EMBASE (from 1980 to August 2011), CINAHL (from 1982 to August 2011), AMED (Allied and Complementary Medicine) (from 1985 to August 2011), PsycINFO (from 1967 to August 2011) and PsycBITE (Pyschological Database for Brain Impairment Treatment Efficacy) (March 2012). To identify further published, unpublished and ongoing trials we searched trials registers, pharmaceutical websites, reference lists, contacted experts and performed citation tracking of included studies.

Selection criteria

We included randomised controlled trials that recruited stroke survivors (ischaemic or haemorrhagic) at any time within the first year. The intervention was any SSRI, given at any dose, for any period. We excluded drugs with mixed pharmacological effects. The comparator was usual care or placebo. In order to be included, trials had to collect data on at least one of our primary (dependence and disability) or secondary (impairments, depression, anxiety, quality of life, fatigue, healthcare cost, death, adverse events and leaving the trial early) outcomes.

Data collection and analysis

We extracted data on demographics, type of stroke, time since stroke, our primary and secondary outcomes, and sources of bias. For trials in English, two review authors independently extracted data. For Chinese papers, one review author extracted data. We used standardised mean differences (SMD) to estimate treatment effects for continuous variables, and risk ratios (RR) for dichotomous effects, with their 95% confidence intervals (CIs).

Main results

We identified 56 completed trials of SSRI versus control, of which 52 trials (4060 participants) provided data for meta-analysis. There were statistically significant benefits of SSRI on both of the primary outcomes: RR for reducing dependency at the end of treatment was 0.81 (95% CI 0.68 to 0.97) based on one trial, and for disability score, the SMD was 0.92 (95% CI 0.62 to 1.23) (22 trials involving 1310 participants) with high heterogeneity between trials (I^2 = 85%; P < 0.0001). For neurological deficit, depression and anxiety, there were statistically significant benefits of SSRIs. For neurological deficit score, the SMD was -1.00 (95% CI -1.26 to -0.75) (29 trials involving 2011 participants) with high heterogeneity between trials (I^2 = 86%; P < 0.00001). For dichotomous depression scores, the RR was 0.43 (95% CI 0.24 to 0.77) (eight trials involving 771 participants) with high heterogeneity between trials (I^2 = 77%; P < 0.0001). For continuous depression scores, the SMD was -1.91 (95% CI -2.34 to -1.48) (39 trials involving 2728 participants) with high heterogeneity between trials (I^2 = 95%; P < 0.00001). For anxiety, the SMD was -0.77 (95% CI -1.52 to -0.02) (eight trials involving 413 participants) with high heterogeneity between trials (I^2 = 92%; P < 0.00001). There was no statistically significant benefit of SSRI on cognition, death, motor deficits and leaving the trial early. For cognition, the SMD was 0.32 (95% CI -0.23 to 0.86), (seven trials involving 425 participants) with high heterogeneity between trials (I^2 = 86%; P < 0.00001). The RR for death was 0.76 (95% CI 0.34 to 1.70) (46 trials involving 3344 participants) with no heterogeneity between trials (I^2 = 0%; P = 0.85). For motor deficits, the SMD was -0.33 (95% CI -1.22 to 0.56) (two trials involving 145 participants). The RR for leaving the trial early was 1.02 (95% CI 0.86 to 1.21) in favour of control, with no heterogeneity between trials. There was a non-significant excess of seizures (RR 2.67; 95% CI 0.61 to 11.63) (seven trials involving 444 participants), a non-significant excess of gastrointestinal side effects (RR 1.90; 95% CI 0.94 to 3.85) (14 trials involving 902 participants) and a non-significant excess of bleeding (RR 1.63; 95% CI 0.20 to 13.05) (two trials involving 249 participants) in those allocated SSRIs. Data were not available on quality of life, fatigue or healthcare costs.

There was no clear evidence from subgroup analyses that one SSRI was consistently superior to another, or that time since stroke or depression at baseline had a major influence on effect sizes. Sensitivity analyses suggested that effect sizes were smaller when we excluded trials at high or unclear risk of bias.

Only eight trials provided data on outcomes after treatment had been completed; the effect sizes were generally in favour of SSRIs but CIs were wide.

Authors' conclusions

SSRIs appeared to improve dependence, disability, neurological impairment, anxiety and depression after stroke, but there was heterogeneity between trials and methodological limitations in a substantial proportion of the trials. Large, well-designed trials are now needed to determine whether SSRIs should be given routinely to patients with stroke.

PLAIN LANGUAGE SUMMARY

Selective serotonin reuptake inhibitors for stroke recovery

Selective serotonin reuptake inhibitors (SSRIs) are a class of drugs that have been in use for many years, mainly for the treatment of mood disorders such as depression. Animal studies have shown that SSRIs may have other direct effects on the brain, such as encouraging the development of new brain cells. If this also occurs in humans, recovery from stroke may be improved. This review brought together the results of 52 trials (4060 participants) of SSRIs in people who had had a stroke in the previous year, to find out whether SSRIs might reduce dependency and disability. The review found promising evidence that SSRIs might improve recovery after stroke, even in patients who were not depressed. Large trials are now needed to confirm or refute these findings, and to determine whether SSRIs increase the risk of side effects such as seizures. If effective, SSRIs would be a low-cost, simple and widely applicable treatment for patients with stroke.

BACKGROUND

Description of the condition

Each year, stroke affects about 16 million people for the first time and causes about 5.7 million deaths (Strong 2007). Moreover, survivors of stroke account for about 51 million disability-adjusted life years (DALYs). This is because recovery of functional independence after stroke only occurs in about half of all survivors of stroke, and mainly during the first six months after a stroke (Hankey 2007a; Hankey 2007b). Although major advances in the early reperfusion of ischaemic stroke have been realised in recent years (e.g. by intravenous thrombolysis and prevention of early recurrent stroke), effective, safe and widely accessible and affordable treatments that facilitate early and sustained recovery after stroke are urgently needed to further reduce the burdens of disability and dependency after stroke.

Description of the intervention

Selective serotonin reuptake inhibitors (SSRIs) are a class of drug that have been available for many years. Their main use in clinical practice is for mood disorders, particularly depression. They are sometimes used in stroke to manage emotionalism (Hackett 2010) (i.e. emotional behaviour that the patient reports as being outside normal control and that occurs in situations that previously would not have provoked such behaviour). Small trials have suggested that fluoxetine, one of the SSRIs, might have a favourable effect on motor recovery after stroke (Chollet 2011; Yi 2010). The recently published 'Fluoxetine on Motor Rehabilitation after Ischemic Stroke' (FLAME) trial reported that 15 (26%) of 56 acute stroke patients allocated to receive fluoxetine and five (9%) of 54 allocated to placebo had a modified Rankin score (mRS) of 0 to 2 (no dependency on other people) at three months, and an odds ratio (OR) of 3.8 (95% confidence interval (CI) 1.2 to 10.7) (Chollet 2011).

How the intervention might work

In animal studies, multiple, potentially beneficial effects of SSRIs have been demonstrated in both normal and diseased brains. First, SSRIs have a neurotrophic effect. Neurotrophins are a family of proteins that are involved in embryogenesis (formulation of an embryo) and organogenesis (development of organs). They control neural plasticity (ability to change, or easily changed or shaped) in adults, regulate synaptic activity and neurotransmitter synthesis, and are essential for the regeneration of nerves (Lang 2004). The development of new nerve cells in adults is generally restricted to specific areas of the brain, namely the subependymal cells of the ventricular system and the subgranular zone of the dentate gyrus in the hippocampus (Ming 2005). SSRIs increase neurogenesis and expression of neurotrophic or growth factors in the adult hippocampus (Schmidt 2007) and this is likely to account for the behavioural benefits of antidepressants in animals (Santarelli 2003). Importantly, several studies have shown that migration of new neurones to damaged areas of brain may occur (Wiltrout 2007) and that neurogenesis can also occur within areas of damaged brain, for example in patients with Alzheimer's disease and in animal models of Alzheimer's disease (Taupin 2006).
Second, fluoxetine may have a neuroprotective effect (i.e. protect nerve cells when the brain is damaged, for example, by a stroke). In animals, there may be several mechanisms for neuroprotective effects of SSRIs, such as reducing inflammation (e.g. repression of microglia activation) (Lim 2009) and by enhancement of specific protein expression (hypoxia inducible factor-1 alpha, heme oxygenase-1) (Shin 2009). Third, SSRIs can indirectly affect an important hormonal system in the body, the adrenergic system, through upregulation (i.e. increase a cellular component of a cell, such as ribonucleic acid (RNA) or protein, in response to an external variable) of beta1 receptors (Palvimaki 1994).
In healthy humans, functional magnetic resonance imaging (fMRI) studies have demonstrated that fluoxetine can modulate cerebral motor activity (Loubinoux 1999). Zittel et al investigated the effects of a single dose of citalopram 40 mg in eight chronic stroke patients and reported that dexterity was significantly improved (Zittel 2008).
SSRIs may also improve recovery after stroke simply through their effect on preventing or treating depression and anxiety; and through improving sleep and alertness.

Why it is important to do this review

It is rare for treatments for neurological diseases such as stroke to have a dramatically favourable effect, such as that of fluoxetine on recovery after stroke as suggested by the FLAME trial (Chollet 2011). Treatments for stroke are far more likely to have a modest treatment effect, at best, which can nevertheless be clinically worthwhile. If modest but worthwhile treatment effects are to be reliably detected or refuted, then any errors in the evaluation of their effectiveness need to be much smaller than the effect of the treatment itself, otherwise the errors may nullify the effect of the treatment and lead to a false-negative result. Similarly, if the treatment is not effective, substantial errors could lead to a false-positive result, or an exaggerated positive result.
The common sources of error in trials of interventions are systematic error (bias) and random error. Systematic errors can be minimised by proper randomisation, analysis by allocated treatment, evaluation of outcome evaluation blinded to the allocated treatment, emphasis on the overall primary results, and publication of all studies irrespective of the results; whereas random error can really only be minimised by studying the effect of the treatment compared with a control on a large number of major outcomes, and therefore in all trials. It is therefore important to systemat-

ically review all the relevant trials that have evaluated the effect of SSRIs on recovery after stroke (published and unpublished) to minimise systematic and random error in our estimates of the potential effects of SSRIs on recovery after stroke. Although a review of fluoxetine in stroke has already been undertaken and published (Yi 2010), the searches were done in 2009 and so the review did not include the FLAME trial (Chollet 2011). The review was limited to fluoxetine rather than all SSRIs (Yi 2010). Furthermore, although the authors of the existing review considered some important aspects of study quality, the Cochrane 'Risk of bias' tool was not used, so the review authors may have missed some sources of bias. Thus, there is a need to produce an updated, methodologically robust systematic review incorporating all the relevant trials that have examined the role of all SSRIs for stroke recovery.

If a simple, inexpensive drug such as one of the SSRIs is shown to improve stroke recovery, this would have major implications for patients, carers, health services, social care services and the economy.

There are two previous Cochrane reviews of interventions to treat and prevent depression after stroke (Hackett 2008a; Hackett 2008b). These two reviews focused on depression and included physical measures as secondary outcomes. However, the reviews excluded studies in which there was no placebo. Thus, we decided that a new review focusing on SSRIs for recovery after stroke was needed.

OBJECTIVES

Our objective was to determine whether SSRIs improve recovery after stroke, and whether treatment with SSRIs was associated with adverse effects.

METHODS

Criteria for considering studies for this review

Types of studies

The review was restricted to all relevant randomised controlled trials (RCTs) in patients with a clinical diagnosis of stroke (Hatano 1976) where an SSRI had been given within the first year of stroke onset. Initially we decided to include trials that recruited patients within three months of stroke onset, but for some relevant trials, the study authors did not state the time since stroke. If we had excluded these studies, we would have lost a large amount of potentially relevant information. Thus, we changed our inclusion criteria to include trials (1) that stipulated that patients had to be recruited within 12 months of stroke onset, and (2) trials where the mean (or median) time since stroke was less than 12 months. The searches identified several trials with more than two arms (e.g. SSRI versus another active treatment versus placebo). We included data from the SSRI arm and the placebo arm (or usual care arm if a placebo was not used), and discarded data from the other active treatment arm.

We excluded trials using a cross-over design. We also excluded trials in which two or more active interventions were compared against each other rather than a placebo or standard care group. We included trials in all languages. There was no restriction on the eligibility of RCTs on the basis of sample size or duration of follow-up. We considered unpublished reports, abstracts, brief and preliminary reports for inclusion on the same basis as published reports.

We included published trials that fulfilled our inclusion criteria, even if they provided no data that we could use in our meta-analysis.

We categorised as 'studies awaiting classification' trials for which we identified a protocol, but no published results, and no clear evidence that they were still ongoing (e.g. no response from study author).

We categorised ongoing trials as 'ongoing' if we received confirmation from the author that they were still recruiting or analysing the results.

Types of participants

We included trials that had recruited survivors of a stroke, defined as a sudden-onset focal neurological disturbance, assumed to be vascular in origin, and lasting more than 24 hours (Hatano 1976). Trials had to recruit participants within 12 months of stroke onset or the mean time since stroke had to be less than 12 months. We intended to include trials that recruited patients with subarachnoid haemorrhage and perform subgroup analyses of this type of stroke, though we did not find any such trials. We intended to exclude trials that included mixed populations (such as stroke and head injury or other central nervous system disorders) unless separate results for patients with stroke were available, but we found no such trials.

Types of interventions

We included any drug classified as a SSRI (e.g. fluvoxamine, fluoxetine, sertraline, citalopram and paroxetine). We included any dose or mode of delivery, given for any duration and for any reason (e.g. to aid neurological recovery, to treat depression or anxiety or emotionalism, or to prevent depression or anxiety or other mood disorders). We did not include drugs that have mixed effects that include SSRI actions.

The comparator arm could include usual care, or a placebo. We excluded studies in which fluoxetine was compared with another

active intervention (e.g. another type of drug or herb or acupuncture).

Types of outcome measures

Primary outcomes

Disability and dependence at the end of treatment or at the end of follow-up.

We anticipated that disability would be measured by the Barthel Index and Functional Independence Measure (FIM). However, if disability was measured using other scales, we included these data too.

We anticipated that dependency would be measured by the mRS. If other scales were used, we included these data too.

Secondary outcomes

Impairments, depression, anxiety, quality of life, fatigue, healthcare cost, death, adverse events, leaving the trial early (for any reason, including death). After publication of the protocol for this review, we stipulated that we were particularly interested in gastrointestinal (GI) side effects, bleeding and seizures, as these side effects are either common or potentially serious after stroke, and are known side effects of SSRIs.

Search methods for identification of studies

See the 'Specialized register' section in the Cochrane Stroke Group module. We searched for relevant trials in all languages and arranged for translation of trial reports published in languages other than English.

Electronic searches

We searched the following electronic bibliographic databases:

- Cochrane Stroke Group Trials Register (August 2011);
- Cochrane Depression Anxiety and Neurosis Group Trials Register (November 2011);
- Cochrane Central Register of Controlled Trials (CENTRAL) (*The Cochrane Library* 2011, Issue 8) (Appendix 1);
- MEDLINE (from 1948 to August 2011) (Appendix 2);
- EMBASE (from 1980 to August 2011) (Appendix 3);
- CINAHL (from 1982 to August 2011) (Appendix 4);
- AMED (Allied and Complementary Medicine) (from 1985 to August 2011) (Appendix 5);
- PsycINFO (from 1967 to August 2011) (Appendix 6);
- PsycBITE Pyschological Database for Brain Impairment Treatment Efficacy (www.psycbite.com/) (March 2012).

We developed the MEDLINE search strategy with the help of the Cochrane Stroke Group Trials Search Co-ordinator and adapted it for the other databases. For www.psycbite.com, we used the search terms on the 'drop down' menu (Stroke/CVA (cerebrovascular accident) and RCT and > 18 years).

In addition, we searched:

- the online Clinical Trial Results and Clinical Trial Registries for Bristol-Myers Squibb, Eli Lilly, Forest, GlaxoSmithKline, Novartis, Pfizer, Roche, and Lundbeck (August 2011);
- the following ongoing trials registers:
  - Stroke Trials Registry (www.strokecenter.org/trials) (September 2011);
  - ClinicalTrials.gov (www.ClinicalTrials.gov) (September 2011);
  - Current Controlled Trials (www.controlled-trials.com) (January 2012);
  - EU Clinical Trials Register (www.clinicaltrialsregister.eu) (January 2012).

Searching other resources

In an effort to identify further published, unpublished and ongoing trials, we:

- searched reference lists of included trials and relevant reviews when full texts were retrieved for detailed scrutiny;
- used Science Citation Index Cited Reference Search for forwards tracking of the included trials that were listed on Web of Science (February 2012);
- contacted researchers in the field.

Data collection and analysis

Selection of studies

Brenda Thomas, the Cochrane Stroke Group Trials Search Co-ordinator, ran the searches of CENTRAL, MEDLINE, EMBASE, CINAHL, AMED and PsycINFO and downloaded the resulting references into Reference Manager. At this point some duplicate references were removed automatically. Further scrutiny of each citation enabled Maureen Harding (who provided administrative support) to remove further duplicates.

One review author (GM) then scrutinised the resulting titles and abstracts and excluded obviously irrelevant reports. The same review author (GM) obtained the full text of the remaining studies and applied the inclusion and exclusion criteria. When there were uncertainties, she sought the views of a second review author. We had intended that two review authors would independently scrutinise all the citations but this was not possible owing to the large number of studies identified from the searches.

Two review authors (GM and RL) independently scrutinised the titles and abstracts (when available) from the electronic searches of Cochrane Depression Anxiety and Neurosis Group Trials Register. Two review authors (GM and MK) independently scrutinised

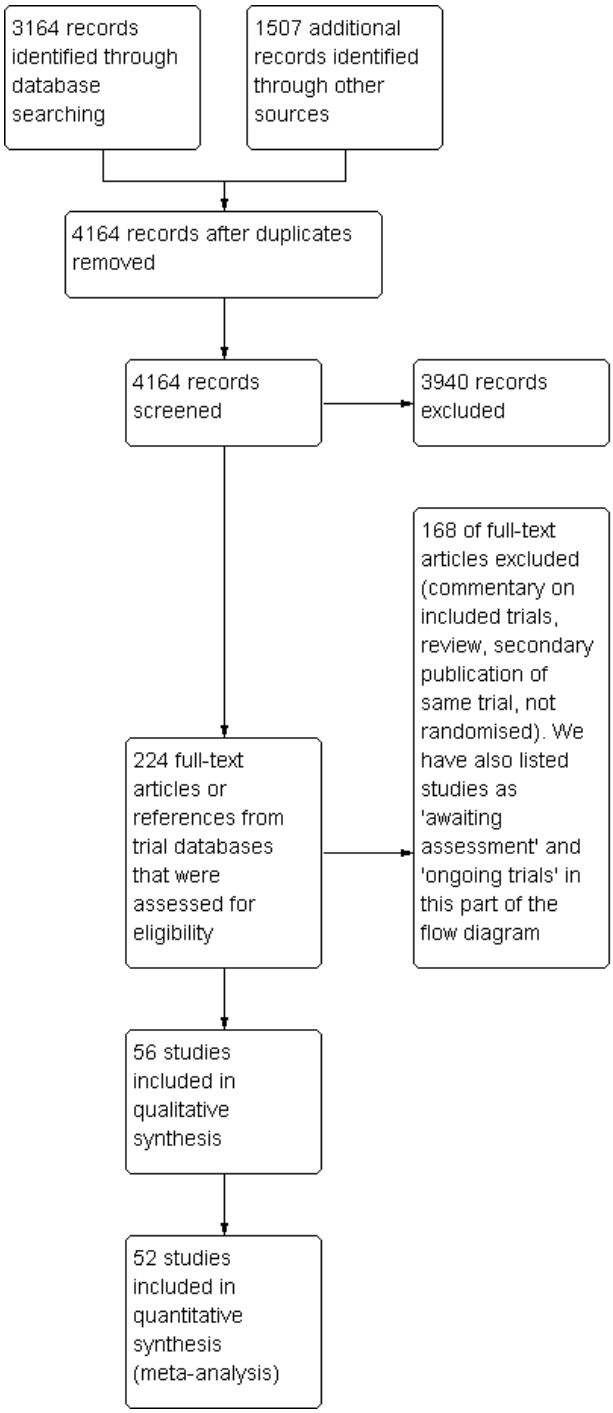
the titles and abstracts (when available) from searches of Cochrane Stroke Group Trials Register. The review authors excluded obviously irrelevant studies and obtained the full text of all remaining trials.

We had planned that one experienced review author (GM or MH or GH) and one less experienced review author (MK, RL or MB) would independently scrutinise each full-text article and decide whether they fulfilled inclusion criteria. Owing to the large number of studies that were obtained as full texts, this was not possible, and so one experienced review author (GM) applied the inclusion criteria to the full texts for all the papers written in English, and one Chinese speaking review author (C-F H) applied the inclusion criteria to the potentially eligible papers written in Chinese. We had planned to ask a third review author should any disagreements arose, but this was not necessary.

One review author (AC) searched the clinical trial databases, then sent a list of potentially eligible trials to GM for further scrutiny and agreement about whether the trials should be obtained in full text. AC and GM then decided whether these trials should be included.

We included a study flow diagram (Figure 1) that includes the number of unique references identified by the searches, the number of records excluded after preliminary screening of titles and abstracts, and the number of records retrieved in full text. We took appropriate notes during the search process and created an Excel spreadsheet listing the publications that were obtained as full text, thus ensuring that the flow diagram could be completed correctly.

Figure 1. Study flow diagram.



Data extraction and management

We developed a paper data extraction form based on the one used for previous Cochrane reviews in depression (Hackett 2008a; Hackett 2008b). It was piloted on three papers and we made minor modifications. We had planned that two review authors (an experienced one and a less experienced one) would independently extract data from each study, including risk of bias. We did this for all papers written in English, and for the single paper written in German, but for papers written in Chinese, only one review author (C-F H) extracted data.

We extracted the following data:

1. the report: author, year and source of publication;
2. the study: sample characteristics, social demography;
3. the participants: stroke sequence (first ever versus recurrent), social situation, time since stroke onset, prior history of psychiatric illness, current neurological status, stroke severity, whether people with aphasia were recruited, the proportion with depression at baseline (if recorded by trialists). We did not extract information on location or size of lesion as this was unlikely to have been recorded by the trialists, and brain imaging often does not show a visible lesion, particularly for patients with minor strokes;
4. the research design and features: adherence, non-response and length of follow-up;
5. the intervention: type, duration, dose, timing and mode of delivery;
6. the effect size: sample size, nature of outcome, estimate and standard deviation (SD) (or standard error (SE)).

We stored the data extraction sheets electronically as Word documents.

Assessment of risk of bias in included studies

We assessed risk of bias using The Cochrane Collaboration's risk of bias tool. For each study, we determined whether there was allocation concealment; how randomisation was performed (including how sequences were generated); whether there was blinding of patient, personnel and outcome assessors; whether there were incomplete outcome data and whether there was selective outcome data reporting. We were guided by the *Cochrane Handbook for Systematic Reviews of Interventions* when making these judgements (Higgins 2011).

We also recorded whether there was an imbalance in baseline characteristics. We also noted whether there was minimisation or stratification based on baseline variables, and early stopping of the intervention.

For randomisation, we categorised the trials as low risk of bias if there was computer-generated random numbers, or the use of a random number table. We categorised other methods of randomisation (e.g. 'flicking a coin', use of 'number tables') as 'unclear risk'. If a patient was allocated according to other criteria (e.g. sequence of admission) we categorised this as 'high risk'. If the randomisation method was not described, we categorised the random sequence generation as 'unclear risk'.

For allocation concealment, we categorised trials as 'low risk' if an opaque envelope was used, or if the allocation was performed by a computer. If the method was not described, we categorised this as 'unclear risk'. If other methods were used, we categorised them as 'high risk'.

For blinding of personnel and patients, we categorised studies as 'low risk' if a matching placebo was used. If a placebo was used but it was not described as matching, we categorised this as 'unclear risk'.

For blinding of outcome assessor, we categorised as 'low risk' if the outcome assessor was described as being blind. If the outcome assessor was not blind, we categorised as 'high risk'; for all other we categorised as 'unclear risk'. We did this at the level of a study rather than for individual outcomes, for example if there was blinding for the majority of outcomes (e.g. activities of daily living (ADL), neurological score and disability) but one outcome was by self-report (e.g. depression), we categorised the study as 'low risk'.

For incomplete outcome data, if the authors stated 'intention-to-treat' analysis (and they undertook it) and stated the method they used to impute missing values (e.g. last value carried forward, best and worst outcome/sensitivity, bootstrapping, etc) we categorised the study as 'low risk' of bias. If per-protocol analyses were presented only, we categorised as 'low risk' if the drop-outs were small (small was defined as less than 5%). If per-protocol analyses were presented only and drop-outs were greater than 5%, then risk of bias was 'high'.

For selective reporting, we categorised as 'low risk' those trials in which there was a published protocol (either as a full journal article or abstract), or a description of the trial design on a trial database prior to publication of the trial results, and when the outcome measures listed in the trial protocol were reported in the results. We defined as 'high risk' any trial that described an outcome measure in the methods but did not provide results. All other trials were categorised as 'unclear risk'.

Following editorial review, we extracted data on source of funding, and listed this under 'other sources of bias'. If the source of funding was not given, or if there were links with the pharmaceutical industry and no explicit statement that the funder had no input into the design or analysis of the study, we classified this as 'unclear risk'.

Following editorial review, we also extracted data on how adverse effects were recorded, and listed these in the descriptions of the studies.

Measures of treatment effect

We carried out statistical analyses using the Review Manager software, RevMan 5.1 (RevMan 2011). We calculated a summary statistic for each outcome measure used to describe the observed treatment effect. All summary statistics reported in this review referred to effects at either: (1) the end of intervention, or (2) the end of follow-up.

Unit of analysis issues

Prior to commencing the review, we anticipated that most of the trials would have a simple parallel group design where each individual was randomised to one of two treatment groups. We had planned to perform subgroup analyses should a trial have three (or more) arms, two of which were different doses of SSRIs. In fact, we did not find any such trials, but we did identify several trials with three arms: a control arm and two active arms (including the SSRI arm). For these trials, we included data only from the control arm and the SSRI arm.

Dealing with missing data

We had intended to approach primary investigators for missing data, but this was not possible owing to the larger than expected number of trials. We did, however, contact authors of studies published in abstract form to enquire whether they had been subsequently published as full-text articles.

Assessment of heterogeneity

Tests of heterogeneity seek to determine whether there are genuine differences underlying the results of the studies (heterogeneity), or whether the variation in findings is compatible with chance alone (homogeneity) (Higgins 2003). P values are obtained by comparing the statistic with a χ^2 distribution with k-1 degrees of freedom (where k is the number of studies). However, the test is known to be poor at detecting true heterogeneity among studies as significant. Thus, the I^2 statistic was developed to quantify the effect of heterogeneity, providing a measure of the degree of inconsistency in the studies' results (Higgins 2003). I^2 describes the percentage of total variation across studies that is because of heterogeneity rather than chance. In this review, we investigated statistical heterogeneity using the I^2 statistic available in RevMan (RevMan 2011).

We used I^2 as a measure of heterogeneity between trials and also between our pre-defined subgroups. We interpreted the amount of heterogeneity as low, moderate and high to I^2 values of 25%, 50% and 75%, respectively (Higgins 2003). We also stated whether the I^2 value was statistically significant, based on the P value.

Assessment of reporting biases

We assessed publication bias by a funnel plot, using disability as this was one of our primary outcomes.

We tried to avoid language bias by including all trials, irrespective of language: we sought translation where needed. Owing to the large number of papers written in Chinese, an additional review author (C-F H), who is fluent in Chinese, joined the team. He translated and extracted data from these papers.

We checked for selective reporting of results by scrutinising the aims and methods of the trials and comparing these with outcomes reported. We found several papers by the same authors, and contacted the authors to check whether the publications were duplicates.

Data synthesis

For dichotomous data, we reported risk ratios (RRs). For ordinal scales, where there was a well-recognised cut-point in the scale (e.g. mRS) we analysed the data as a dichotomous outcome (dependent or independent).

For ordinal scales with no recognised cut-point, we analysed the data as continuous data. The data required for meta-analyses of continuous data in RevMan are means and SDs. When extracting continuous data from the study reports, we checked whether trials reported SD or SE. We had planned to use SE or 95% CI to compute SD when SDs were missing, but this was not needed as all the trials reported SDs.

For ordinal scales and continuous data, we calculated standardised mean differences (SMD) because different scales were used for the same outcomes (e.g. Barthel Index and FIM for disability, the Beck Depression inventory (BDI) or the Hamilton Rating Scale for Depression (HAMD) for depression). It should be noted that the SMD does not correct for differences in the direction of the scale. As some scales increased with disease severity and others decreased, we multiplied the mean value from one set of trials by -1. An example of this is the National Institute of Health Stroke Scale (where a low score indicates a less severe stroke) and the Scandinavian Stroke Scale (SSS) (where a low score indicates a more severe stroke).

We used the random-effects model for all our analyses.

Subgroup analysis and investigation of heterogeneity

We performed the following subgroup analyses.

1. Type of SSRI.
2. Trials that stated that depression had to be present at recruitment and trials that did not have depression as an inclusion criterion.
3. Time since stroke at recruitment. We categorised these as less than three months, three to six months, six to nine months, nine to 12 months; where less than three months was equivalent to 0 to 90 days, three to six months was equivalent to 91 to 180

days, six to nine months was equivalent to 181 to 271 days and nine to 12 months was equivalent to 272 to 365 days.

We had intended to perform a subgroup analysis for motor or non-motor deficits at entry and for brand of drug, but there was insufficient information in the trial reports. Dose of drug was reported but most trials used the same dose for each individual SSRI, so we decided that there were insufficient data to explore the influence of dose of drug on outcome.

Sensitivity analysis

We performed sensitivity analyses to explore the influence of the key aspects of trial quality that we identified during our assessment of risk of bias (i.e. randomisation, allocation concealment, blinding, incomplete outcome data, selective reporting). We did this by excluding the trials that were categorised as 'high risk' and 'unclear' risk, and repeating the previous analyses on only those studies at low risk of bias.

We reported the effect sizes as being larger, similar or smaller than if all trials had been included, accepting that there was some degree of subjective assessment in making decisions about 'larger', 'similar' or 'smaller'. We also reported whether results were still statistically significant when only those at low risk of bias were included.

RESULTS

Description of studies

Results of the search

Figure 1 shows the flow diagram for the selection of studies. The searches by Brenda Thomas identified the 2673 citations (after electronic removal of 102 duplicates when importing into Reference Manager): 249 from MEDLINE, 1803 from EMBASE, 197 from CENTRAL, 170 from CINAHL, 20 from AMED and 234 from PsycINFO. We removed a further 405 duplicates by visual scrutiny of the searches. The remaining 2268 titles and abstracts (when available) were scrutinised by GM. We identified a further 27 citations relating to the same study, by the same author team. We retrieved 143 full texts for detailed scrutiny.

The search of the Cochrane Stroke Trials Register identified 32 citations, of which 11 were duplicates; we retrieved 24 full texts.

The search of the Cochrane Depression and Anxiety Group Trials register identified 47 citations, of which 13 were duplicates; we retrieved 21 full texts.

The search of www.pyscbite.com by GM identified 310 citations. We retrieved the full text for one of these, which had already been identified by other searches.

The searches of clinical trials registers identified 138 citations. Of these, we retrieved 27 citations for detailed scrutiny by two review authors (AC and GM).

The searches of the pharmaceutical websites identified 541 citations. We retrieved full texts for eight of these, of which one trial was eligible for inclusion.

One review author (RL) performed a cited reference search (5 February 2012) of 32 trials that were listed on Web of Science (Acler 2009; Almeida 2006; Andersen 1994; Brown 1998; Burns 1999; Chollet 2011; Dam 1996; Fruehwald 2003; He 2004; Ji 2000; Jia 2005; Kong 2007; Lai 2006; Li 2004a; Li 2004b; Li 2008; Liang 2003; Meara 1998; Miao 2004; Murray 2005; Rasmussen 2003; Robinson 2000a; Robinson 2000b; Robinson 2008; Sitzer 2002; Wiart 2000; Xie 2005; Xu 2001; Xu 2006; Yang 2002; Ye 2004; Zhou 2003) and identified 828 citations. These were all screened for relevance. No trials were identified that had not been identified previously.

We identified two trials that appeared to fulfil our inclusion criteria (Sitzer 2002; Whyte 2005). However, we could find no published results and when we sought further information from the authors, we received no responses. One of these trials is listed on www.clinicaltrials.gov as 'terminated because recruitment goals could not be met' (Whyte 2005). We have listed these two trials as 'awaiting assessment'.

We identified five ongoing trials that appeared to fulfil our inclusion criteria (2005-005266-37; AFFINITY 2011; Carda 2009; EMOTION 2011; FOCUS 2011).

Included studies

We identified four trials that fulfilled our inclusion criteria, but that did not provide data that we could use in a meta-analysis (Chen KN 2005; Meara 1998; Pariente 2001; Restifo 2001).

We identified a total of 51 completed trials that fulfilled our inclusion criteria and that provided data that we could use in the meta-analysis. Two of these studies (He 2005: Ye 2004) were each published twice in different journals.

Of the 51 trials that provided data that we included in our meta-analysis, one trial (Robinson 2000a/Robinson 2000b) reported data separately for depressed and non-depressed people, so we have split this study into two.

Thus, we have 52 trials. Together these 52 trials randomised a total of 4060 patients to SSRI or control.

Of the 52 trials that we could use in our meta-analysis:

- 28 trials used fluoxetine (Brown 1998; Chen 2001; Cheng 2003; Chollet 2011; Dam 1996; Feng 2004; Fruehwald 2003; He 2004; Hu 2002; Huang 2002; Ji 2000; Kong 2007; Li 2002; Li 2004a; Li 2004b; Li 2008; Liang 2003; Liu 2004; Robinson 2000a; Robinson 2000b; Song 2006; Wang 2003; Wen 2006; Wiart 2000; Xu 2001; Xu 2007; Zhou 2003; Zhou 2008);
- seven trials used sertraline (Almeida 2006; Burns 1999; Finkenzeller 2009; Guo 2009; Murray 2005; Rasmussen 2003;

Xie 2005);

- 10 used paroxetine (Chen 2002; Chen T 2005; GlaxoSmithKline 1998; He 2005; Lai 2006; Li 2005; Xu 2006; Yang 2002; Yang 2011; Ye 2004);
- five used citalopram (Acler 2009; Andersen 1994; Li 2006; Liu 2006; Miao 2004);
- one used escitalopram (Robinson 2008);
- one used either sertraline or fluoxetine (Jia 2005).

Patient characteristics

Of the 52 trials that provided data for meta-analysis, the mean age of patients ranged from 55 years (Liu 2004) to 77 years (Finkenzeller 2009), with most trials recruiting patients in their 60s. The included trials generally excluded patients who could not consent for themselves, patients with dementia, patients with communication difficulties and those with contraindications to SSRIs. Some trials recruited patients with either haemorrhagic or ischaemic stroke, and some restricted entry only to those with ischaemic stroke (see Characteristics of included studies). Some recruited people with depression and some recruited people without depression (see 'Depression as an inclusion criterion' below).

Mean time since stroke

Of the trials included in our meta-analysis, the mean time since stroke was zero to three months for 31 trials (Acler 2009; Andersen 1994; Almeida 2006; Chen 2001 Chen T 2005; Cheng 2003; Chollet 2011; Feng 2004; Fruehwald 2003; Finkenzeller 2009; He 2004; Hu 2002; Huang 2002; Kong 2007; Li 2004a; Li 2004b; Li 2008; Liang 2003; Liu 2004; Rasmussen 2003; Robinson 2008; Song 2006; Wiart 2000; Yang 2011; Ye 2004; Wen 2006; Xie 2005; Xu 2001; Xu 2006; Zhou 2003; Zhou 2008).
A further three trials (He 2005; Lai 2006; Li 2006) described participants as having an 'acute stroke' - we assumed this meant zero to three months, so included these in the zero- to three-month group. The mean time since stroke was between five and 16 weeks in two studies, so we included these in the zero- to three-month group (Robinson 2000a; Robinson 2000b).
We included four trials in the three- to six-months category: Dam 1996 (described as participants being one to six months); Miao 2004; Murray 2005 and Yang 2002 ('recovery phase of stroke' two to six months)
Two trials recruited between six and nine months (Guo 2009; Liu 2006).
No trials reported recruiting patients between nine and 12 months after stroke.
The time was not reported for 10 trials (Brown 1998; Burns 1999; Chen 2002; GlaxoSmithKline 1998 (less than 12 months); Ji 2000; Jia 2005; Li 2002 (at least two weeks after stroke onset); Li 2005; Xu 2007 and Wang 2003).

Depression as an inclusion criterion

In 17 of these 52 trials, a diagnosis of depression (however made) was not one of the inclusion criteria: Acler 2009; Almeida 2006; Brown 1998; Burns 1999; Chollet 2011; Dam 1996; He 2004; Kong 2007; Li 2004a; Liu 2004; Rasmussen 2003; Robinson 2000b; Robinson 2008; Wen 2006; Xu 2006; Zhou 2003 and Zhou 2008. In the remaining trials that had data that we could use in the meta-analysis, participants had to have depression (though criteria for diagnosing depression varied between trials).

Excluded studies

We listed as excluded studies non-randomised comparisons of SSRIs and control, studies that compared two active treatments (rather than SSRI versus control), and studies that recruited patients more than one year after stroke onset. Those that were obviously irrelevant (e.g. not an SSRI) or those that had been already been excluded from previous reviews (Hackett 2008a; Hackett 2008b) were excluded on the basis of an abstract only; we excluded the remaining studies only after we had scrutinised the full texts. In total, there were 48 excluded studies.

Risk of bias in included studies

Risk of bias is summarised in Figure 2 and Figure 3. The figures include all included studies, irrespective of whether they provided data that we could use in our meta-analysis.

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

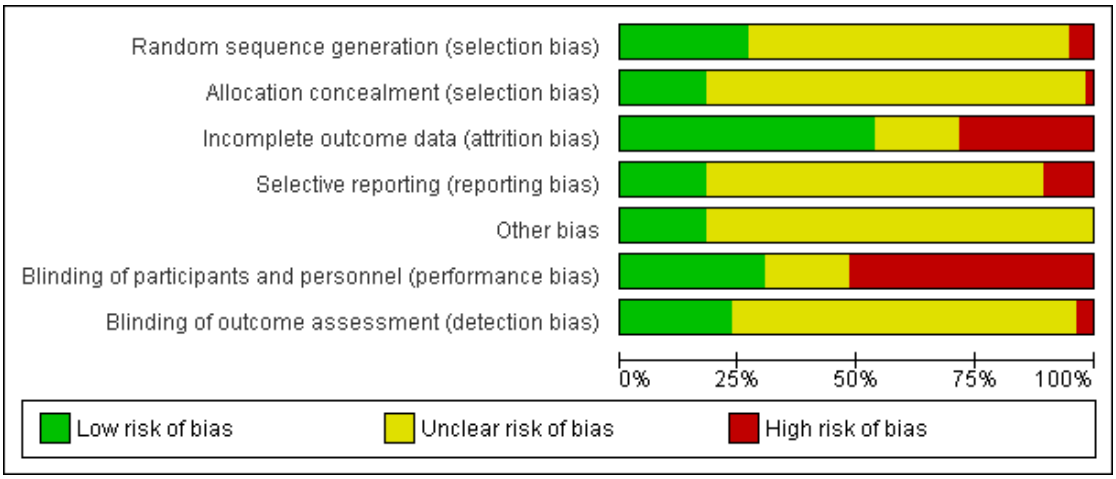
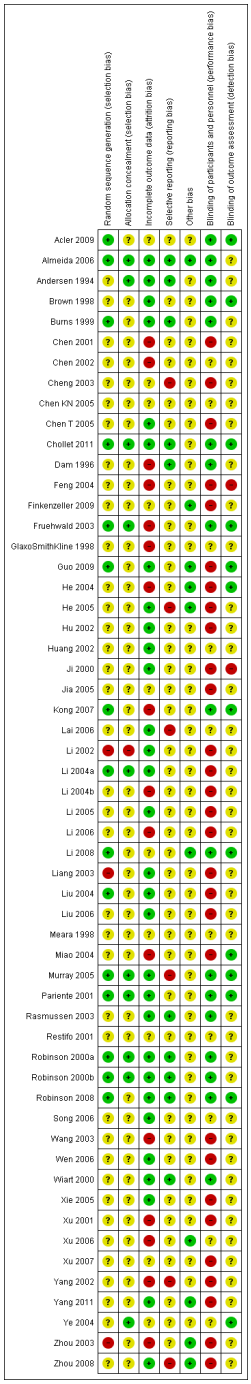


Figure 3. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.



In the text below, we have listed only the studies that did provide data for meta-analysis.

Allocation

Of the trials that provided data for meta-analysis, there was low risk of bias for random sequence generation for 14 trials (Acler 2009; Almeida 2006; Burns 1999; Chollet 2011; Fruehwald 2003; Guo 2009; Kong 2007; Li 2004a; Li 2008; Liu 2004; Murray 2005; Robinson 2000a; Robinson 2000b; Robinson 2008). The risk of bias in the other trials was either uncertain or high.

Of the trials that provided data for meta-analysis, there was low risk of bias for allocation concealment for nine trials (Almeida 2006; Andersen 1994; Chollet 2011; Fruehwald 2003; Li 2004a; Murray 2005; Robinson 2000a; Robinson 2000b; Ye 2004).

Blinding

For blinding of participants and personnel (performance bias), there was low risk of bias for 16 trials (Acler 2009; Almeida 2006; Andersen 1994; Brown 1998; Burns 1999; Chollet 2011; Dam 1996; Fruehwald 2003; Kong 2007; Li 2008; Murray 2005; Rasmussen 2003; Robinson 2000a; Robinson 2000b; Robinson 2008; Wiart 2000). The risk of bias in the other trials was either uncertain or high.

For blinding of outcome assessor (detection bias), there was low risk of bias for 11 trials (Acler 2009; Brown 1998; Chollet 2011; Fruehwald 2003; Guo 2009; He 2004; Kong 2007; Li 2008; Murray 2005; Robinson 2008; Ye 2004). The risk of bias in the other trials was either uncertain or high.

Incomplete outcome data

There was low risk of bias for incomplete outcome data (attrition bias) for 30 trials (Almeida 2006; Andersen 1994; Brown 1998; Burns 1999; Chen T 2005; Chollet 2011; Guo 2009; He 2005; Hu 2002; Huang 2002; Ji 2000; Lai 2006 Li 2002; Li 2004a; Li 2005; Liang 2003; Liu 2004; Liu 2006; Murray 2005; Pariente 2001; Rasmussen 2003; Robinson 2000a; Robinson 2000b; Robinson 2008; Song 2006; Wen 2006; Wiart 2000; Xie 2005; Yang 2011; Zhou 2008).

Selective reporting

There was sufficient information provided to assess that risk of bias was low in 10 trials (Almeida 2006; Andersen 1994; Burns 1999; Chollet 2011; Dam 1996; Rasmussen 2003; Robinson 2000a; Robinson 2000b; Robinson 2008; Wiart 2000). We classified the remaining trials as unclear because we could not determine from the information available whether all planned outcomes were reported. Several trials were reported as high risk as not all outcomes listed in the methods were reported in the results.

Other potential sources of bias

We checked for differences in baseline characteristics and other sources of bias. If there were differences in baseline characteristics, we made a judgement as to whether these differences would have introduced bias.

Following editorial review, the sources of funding and information on drug company involvement were extracted by GM from the papers written in English and from papers written in Chinese by CF-H. If the funding source was not stated, we categorised the study as 'unclear risk'.

Effects of interventions

Dependency at the end of treatment

Two trials reported data on dependency using the mRS (Almeida 2006; Chollet 2011) (Analysis 1.1). RR for reducing dependency at the end of treatment was 0.81 (95% CI 0.68 to 0.97); this analysis was based on one trial (Chollet 2011) because the RR was not estimable for the other trial (Almeida 2006).

GlaxoSmithKline 1998 provided data on the change in mRS but did not provide the SD of the change, so we could not use these data in the meta-analyses.

With the inclusion of only two trials, there were insufficient data to comment on effects in the different subgroups, that is type of SSRI (Analysis 1.1), time since stroke (Analysis 3.1) and depression at randomisation (Analysis 4.1).

Disability at the end of treatment

Several disability scales were used including the Barthel, modified Barthel, FIM, or 'ADL score'.

Several Chinese papers used an 'ADL score' but did not reference this (Cheng 2003; Feng 2004; Xie 2005; Yang 2002; Zhou 2008). Of these, one trial (Cheng 2003) did not provide a reference for the ADL score, but stated that a lower score was better (so we were able to use the data in our meta-analysis). One trial used an ADL score and did not reference it, but stated that a score of 100 meant independent, and a score of 0 to 20 very severe functional disability (Xie 2005); thus we used these data in our meta-analysis. We could not determine the direction of the ADL score in three trials (Feng 2004; Yang 2002; Zhou 2008), so we did not use these data in the meta-analysis.

For scales in which a higher score meant better function (e.g. Barthel), we entered the mean score as a positive number. For scales in which a higher score meant worse function, we multiplied the mean ADL score by -1 to correct for differences in direction of the score.

We were unable to use other disability data in the meta-analysis for the following reasons: GlaxoSmithKline 1998 provided data on change in Barthel score but no SD; Li 2004b reported a dichotomous Barthel (not continuous); Finkenzeller 2009 provided data on median and interquartile range (IQR) (not means and SD); Guo 2009 reported only FIM cognition and FIM mobility (so we could not include these data as a global measure of disability) and Robinson 2008 reported that FIM data improved over time, but did not provide raw data. Murray 2005 did not report the ADL data although the paper stated that they had collected these data. This left continuous data on disability from 22 trials (1310 participants) that could be used in the meta-analysis (Analysis 1.2). The SMD was 0.92 (95% CI 0.62 to 1.23) in favour of SSRI. There was high heterogeneity between trials (I^2 = 85%; P < 0.00001).

Subgroup: type of SSRI (Analysis 1.2)

Of these 22 trials, 13 used fluoxetine (Chen 2001; Cheng 2003; Dam 1996; Kong 2007; Li 2008; Liu 2004; Robinson 2000a; Robinson 2000b; Wang 2003; Wiart 2000; Xu 2001; Xu 2007; Zhou 2003), three used citalopram (Acler 2009; Li 2006; Liu 2006), one used sertraline (Xie 2005) and five used paroxetine (Chen 2002; Chen T 2005; He 2005; Xu 2006; Ye 2004). There was moderate heterogeneity between the subgroups (I^2 = 58%; P = 0.07) (Higgins 2002; Higgins 2003) (Analysis 1.2).

Subgroup: time since stroke (Analysis 3.2)

There was evidence of high heterogeneity between subgroups (I^2 = 89%; P < 0.00001). The largest effect size was observed in trials in which the time since stroke was not reported and the smallest effect size in trials that recruited patients between three and six months after stroke onset (Analysis 3.2).

Subgroup: depression had to be present at diagnosis (Analysis 4.2)

There was evidence of high heterogeneity between subgroups (I^2 = 79%; P = 0.03). The larger effect size was observed in those trials that stipulated that patients had to have depression at recruitment (Analysis 4.2).

Neurological deficit score at end of treatment

A number of different neurological deficit scores were reported including the Scandinavian neurological stroke scale (high score = better function, range 0 to 48), the Modified Scandinavian Edinburgh stroke scale (MESSS) (high score = worse function; total 45: 0 to 15: mild; 16 to 30: moderate; 31 to 45: severe), Chinese Stroke Scale (CSS), National Institutes of Health Stroke Score (NIHSS) (higher score = worse deficit), Canadian neurological scale, Neurological function defect scale (rated as recovery, obviously improved, improved no effect or deteriorated) and the Hemiplegic Stroke Scale (HSS) (0 to 100, higher score = greater deficit).

In the papers from China, different names were given to the neurological impairment scale used. We believe that this scale was originally proposed in 1995 at the Fourth National Science Meeting on Cerebral Vascular Disease in China (Chen 1996). Thus, the SSS, MESSS, CSS, Chinese neurological impairment scale (CNS) (Ye 2004), neurological function damage (Jia 2005), neurological function defect scale (Li 2002) and neurological function impairment (Wang 2003) were all the same scale.

Although some of the Chinese papers stated that they used the SSS, we believe that they are referring to the MESSS according to the references cited in their papers. The score range of the MESSS is from 0 to 45 points with severity degree (mild: 0 to 15; moderate: 16 to 30: severe: 31 to 45), lower is better. This applies to Cheng 2003; He 2004; He 2005 and Li 2005 (and fits with their description of effects, i.e. improvement in neurological function in the SSRI group).

Data from several trials could not be used in the meta-analysis: Hu 2002 (because the paper quoted values for MESS above certain decrement levels rather than the mean and SD at the end of treatment), Li 2004b (continuous data for CSS not given), Zhou 2008 (no raw data on MESS), Murray 2005 (did not provide raw data on SSS at follow-up) and Yang 2002 (stated that they would report the CSS but no data were reported).

In our meta-analysis, we included data from 29 trials (2011 participants) that reported a neurological deficit score at the end of treatment (Analysis 1.3). The SMD was -1.00 (95% CI -1.26 to -0.75) in favour of SSRI. There was high heterogeneity between trials (I^2 = 86%; P < 0.00001).

Subgroup: type of SSRI

There was moderate heterogeneity between subgroups (I^2 = 61%; P = 0.04) (Analysis 1.3). The largest effect size was for citalopram (though this was based on only three trials) and the smallest effect size for sertraline (though this was based only on two trials).

Subgroup: time since stroke (Analysis 3.3)

There was heterogeneity between subgroups (I^2 = 26%) but it was not statistically significant (P = 0.26) (Analysis 3.3).

Subgroup: patients had to have depression at the time of recruitment (Analysis 4.3)

There was evidence of high heterogeneity between subgroups (I^2 = 76.9%; P = 0.04), with the larger effect in patients who had to have depression at recruitment (Analysis 4.3).

Depression at end of treatment

If trials reported several outcomes (e.g. change in scores between baseline and follow-up, dichotomous data for depression scales, or continuous data at end of treatment or follow-up, or both), we decided, after having performed data extraction, to use the absolute depression score at the end of treatment (mean and SD). If those data were not available, we used dichotomous data (e.g. depressed/not depressed). If trials used both the HAMD and BDI, we used the HAMD.

We noted that for all the depression measures used (HAMD, BDI, Montgomery-Åsberg Depression Rating Scale (MADRS), Zung), a higher score means more severe depression. Song 2006 used a self-rated depression scale, we assumed that a higher score meant more severe depression, as this fits with the description of the benefit of fluoxetine.

For some trials, we could not use data in the meta-analysis. Brown 1998 quoted median (not mean) Hamilton Depression Rating Scale (HDRS), Hu 2002 reported HAMD as the 'proportion with a number of different decrement levels', Zhou 2008 and Yang 2002 provided no raw data, and Burns 1999 did not report depression scores at the end of treatment.

Continuous depression scores

For continuous depression scores (Analysis 1.4), there were 39 trials (2728 participants). The SMD was -1.91 (95% CI -2.34 to -1.48), a statistically significant effect in favour of SSRI. There was high heterogeneity between trials (I^2 = 95%; P < 0.00001).

Subgroup: type of SSRI (Analysis 1.4)

There was high heterogeneity between subgroups (I^2 = 78%; P = 0.001), with the largest effect seen for paroxetine and the smallest for sertraline (Analysis 1.4).

Subgroup: time since stroke (Analysis 3.4)

There was no heterogeneity between subgroups (I^2 = 0%; P = 0.66) (Analysis 3.4).

Subgroup: had to have depression at recruitment (Analysis 4.4)

There was heterogeneity between subgroups (I^2 = 35.5%) that was not statistically significant (P = 0.21) (Analysis 4.4).

Dichotomous depression scores

For dichotomous depression scores, we included eight trials (771 participants) in the meta-analysis (Analysis 1.5). The RR was 0.43 (95% CI 0.24 to 0.77), a statistically significant effect in favour of SSRI. There was high heterogeneity between trials (I^2 = 77%; P < 0.0001).

Subgroup: type of SSRI (Analysis 1.5)

There was no heterogeneity between subgroups of SSRIs (I^2 = 0%; P = 0.59) (Analysis 1.5).

Subgroup: time since stroke (Analysis 3.5)

There was high heterogeneity (I^2 = 93%; P = 0.00001), with the larger effect size seen in the trials that recruited patients within the first three months of stroke onset (Analysis 3.5).

Subgroup: depression at recruitment (Analysis 4.5)

There was low heterogeneity (I^2= 25%, P = 0.31) (Analysis 4.5). There was a smaller effect size for trials in which patients had to have depression at recruitment.

Anxiety at end of treatment

No trials reported dichotomous anxiety data.

Lai 2006 provided a 'self-rating anxiety scale', for which a lower score was better, so we included these data in the meta-analysis.

We included eight trials (413 participants) reporting continuous data for anxiety in the meta-analysis (Analysis 1.6). The SMD was -0.77 (95% CI -1.52 to -0.02). There was high heterogeneity between trials (I^2 = 92%; P < 0.00001).

Subgroup: type of SSRI (Analysis 1.6)

There was moderate heterogeneity between subgroups (I^2 = 70.6%; P = 0.03), with the largest effect seen for paroxetine (Analysis 1.6).

Subgroup: time since stroke (Analysis 3.7)

All trials included recruited patients between zero and three months, so there were no data available for this subgroup analysis (Analysis 3.7).

Subgroup: depression at recruitment (Analysis 4.6)

There was low heterogeneity (I^2 = 29.7%, P = 0.23) (Analysis 4.6).

Cognition at end of treatment

We could not use the cognition data from Almeida 2006 in the meta-analysis because the changes in scores between baseline and end of treatment were reported (there was no difference between placebo and sertraline group). Li 2004b reported that 20/31 in the fluoxetine group had a Mini-Mental State Examination (MMSE) score $\geq$ 24 compared with only 14/32 in the control group. It is not generally possible to combine dichotomous data with the continuous data in a meta-analysis. For resource reasons, we were unable to contact the authors to obtain raw data.

We included seven trials (425 participants) that reported continuous data in the meta-analysis (Analysis 1.8). The SMD was 0.32 (95% CI -0.23 to 0.86). There was high heterogeneity between trials (I^2 = 86%; P < 0.00001). This analysis included data from the Iowa subgroup of a larger trial (Robinson 2008). The scores at the end of treatment were similar in the two groups, but there had been a larger improvement in scores from baseline to end of treatment in those allocated an SSRI (Robinson 2008).

Subgroup: type of SSRI (Analysis 1.8)

There was high heterogeneity between subgroups (I^2 = 92.6%; P < 0.00001) with the largest effect size for citalopram, although this was based on a single trial (Analysis 1.8).

Subgroup: time since stroke (Analysis 3.8)

There was no heterogeneity (I^2 = 0%; P = 0.64) (Analysis 3.8).

Subgroup: depression at recruitment (Analysis 4.8)

There was moderate heterogeneity between subgroups (I^2 = 49.8%) but this was not statistically significant (P = 0.16) (Analysis 4.8).

Motor deficits

The FLAME trial reported the Fugl Myer total motor score (Chollet 2011) and Dam 1996 reported the HSS motor component. We combined these data using SMD (Analysis 1.16). The SMD was -0.33 (95% CI -1.22 to 0.56), a non-significant difference. There was high heterogeneity in relation to time since stroke (I^2 = 80%; P = 0.02) (Analysis 3.14). Both trials recruited people without depression, so we could not perform subgroup analyses for depression at onset.

Death at end of treatment

Five trials did not report deaths, and the number randomised did not equal the number at end of treatment, so we do not know how many patients had died (Chen 2002; GlaxoSmithKline 1998; Kong 2007; Rasmussen 2003; Wang 2003). One trial did not state the number randomised or the number who died (Finkenzeller 2009).

This left data from 46 trials (3344 participants) providing data for meta-analysis. RR for death was 0.76 (95% CI 0.34 to 1.70) (Analysis 1.9). There was no heterogeneity between trials (I^2 = 0%; P = 0.85).

Subgroup: type of SSRI (Analysis 1.9)

There was no heterogeneity between SSRIs (I^2 = 0%; P = 0.69) (Analysis 1.9).

Subgroup: time since stroke (Analysis 3.9)

There was no heterogeneity according to time since stroke (I^2 = 0%; P = 0.56) (Analysis 3.9).

Subgroup: depression at onset (Analysis 4.9)

There was no heterogeneity between subgroups (I^2 = 2.1%; P = 0.31) (Analysis 4.9).

Side effects at end of treatment

Side effects were reported in only some of the trials, and for the majority of these trials, it was unclear whether these had been collected systematically. Furthermore, when a particular side effect was not reported (e.g. seizures), we do not know whether this was because the side effect had not occurred or whether seizures had occurred but had not been reported.

Side effects: seizures at end of treatment

We decided that we would include data only if the trials specifically reported either seizures or no seizures. Thus, we did not include trials that listed adverse effects but did not mention either the presence or absence of seizures in the analyses. Therefore, we included data from the following seven trials (744 participants): Andersen 1994; Chollet 2011; Dam 1996; He 2004; Liang 2003; Wiart 2000 and Ye 2004. The RR was 2.67 (95% CI 0.61 to 11.63) (Analysis 1.10). There was no heterogeneity between trials.

Subgroups

There was no significant heterogeneity between subgroups of SSRI (Analysis 1.10), subgroups according to time since stroke at randomisation (Analysis 3.10) or according to depression at recruitment (Analysis 4.10).

Side effect: gastrointestinal side effects at end of treatment

Some trials split GI side effects into different symptoms and reported them in such a way that we do not know whether the side effects relate to 'events' or to 'patients'. If we were uncertain whether the trials reported 'events' or 'patients', we elected not to include them in our meta-analyses (Higgins 2011). This applied to Almeida 2006; GlaxoSmithKline 1998; Murray 2005; Rasmussen 2003; Robinson 2008. In two of these trials, GI side effects were more common (GlaxoSmithKline 1998; Murray 2005) and in the other three trials, there was no difference between groups (Almeida 2006; Rasmussen 2003; Robinson 2008).

One trial (Kong 2007) reported 'somatic side effects' as a reason for withdrawing from the trial, but did not stipulate what these side effects were. We did not include these data in the meta-analysis.

Two trials reported GI side effects for the treatment but not the control group (Wang 2003; Xie 2005) so could not be included in the meta-analysis.

We included 14 trials (902 participants) in the meta-analysis; the RR was 1.90 (95% CI 0.94 to 3.85) (Analysis 1.11).

There was no significant heterogeneity between trials (I^2 = 31%; P = 0.14) (Analysis 1.11).

Subgroup analyses

There was moderate heterogeneity between subgroups of SSRI (I^2 = 48.9%) that was not statistically significant (P = 0.14) (Analysis 1.11). There was no heterogeneity between the other subgroups (time since stroke: I^2 = 0%; P = 0.85 (Analysis 3.11); depression at onset: I^2 = 0%; P =0.57 (Analysis 4.11)).

Side effect: bleeding at end of treatment

Two trials reported bleeding as a side effect (GlaxoSmithKline 1998; Robinson 2008). The RR was 1.63 (95% CI 0.20 to 13.05) in favour of control (Analysis 1.12). There was no significant heterogeneity (I^2 = 0%; P = 0.59).

Change in cognition

Only one trial reported change in cognition and found no difference between groups (Analysis 1.14).

Leaving the study early (before the follow-up at the end of treatment)

Finkenzeller 2009 did not report drop-outs, Song 2006 did not report drop-outs from each group (though total drop outs were reported) and, in one trial, there were inconsistencies in reporting data (Xu 2007).

We included data from 49 trials (3851 participants) (Analysis 1.15). The RR was 1.02 (95% CI 0.86 to 1.21) in favour of control. There was no significant heterogeneity between trials.

There was no significant heterogeneity between SSRIs (Analysis 1.15) or the other subgroups (Analysis 3.12; Analysis 4.12).

Follow-up beyond treatment end

Only eight trials (Almeida 2006; Burns 1999; Cheng 2003; Fruehwald 2003; Guo 2009; Robinson 2000a; Robinson 2000b; Wang 2003) followed up participants beyond the treatment period, although Burns 1999 did not provide any long-term data. Note that in one trial, the duration of antidepressant treatment ranged from three to six months, so some patients followed up beyond three months were still taking the antidepressant (Wang 2003).

Of these, only one trial reported dependence (Almeida 2006), two disability (Almeida 2006; Wang 2003) (note that although Guo 2009 reported FIM cognition and mobility, these data could not be used because the total FIM score was not provided), five reported depression (Almeida 2006; Cheng 2003; Fruehwald 2003; Guo 2009; Wang 2003), two reported cognition (Almeida 2006; Guo 2009) and four reported neurological impairment (Cheng 2003; Fruehwald 2003; Guo 2009; Wang 2003). Three reported deaths (Cheng 2003; Guo 2009; Wang 2003). Two reported nine-year mortality (Robinson 2000a; Robinson 2000b); although these data could not be used in the meta-analysis, the trialists reported that those allocated an antidepressant (either nortriptyline or fluoxetine) were more likely to be alive at nine years.

For disability (two trials, 155 participants) (Analysis 2.2), there was a non-significant effect for SSRI. For neurological impairment scales (four trials, 275 participants (Analysis 2.3) there was a non-significant effect in favour of SSRI. For continuous depression scores, there was a significant benefit for SSRI (four trials, 275 participants) (Analysis 2.4) but for dichotomous depression scores (one trial, 99 participants) (Analysis 2.5) the benefit was not statistically significant. There were no statistically significant differences between SSRI and control for dependence (Analysis 2.1) and cognition (Analysis 2.6; Analysis 2.7). Note that the numbers of participants were small and CIs were wide.

Sensitivity analyses

We excluded trials with unclear or high risk of bias for each characteristic and repeated the same analyses for each outcome at the end of treatment, including only trials at low risk of bias (Analysis 1.1; Analysis 1.2; Analysis 1.3; Analysis 1.4; Analysis 1.5; Analysis 1.6; Analysis 1.7; Analysis 1.8; Analysis 1.9; Analysis 1.10; Analysis 1.11; Analysis 1.12; Analysis 1.13; Analysis 1.14; Analysis 1.15). We described the effect sizes (after exclusion of the trials at unclear or high risk of bias) as smaller, similar or bigger, in order to help the reader interpret the data. This was a subjective judgement by the review author (GM) performing the analyses.

Low risk of bias for randomisation

When only those trials with low risk of bias were included, the effect sizes for dependence was the same (although this was based only on two trials) (Analysis 5.1), the effect size for disability (Analysis 5.2), neurological deficit (Analysis 5.3), depression (Analysis 5.4; Analysis 5.5) and anxiety (Analysis 4.6; Analysis 3.8; Analysis 3.9) were all smaller, although still in favour of SSRI, but some of the effects were not statistically significant: depression (Analysis 5.4), anxiety (Analysis 5.6) and death (Analysis 5.9). The rate of seizures, GI side effects and leaving the trial early remained similar (Analysis 5.10; Analysis 5.11; Analysis 5.15, respectively) though the difference between SSRI and control for GI side effects did not reach statistical significance.

Low risk of allocation concealment

When only those trials with low risk of bias were included, the effect size for dependence was the same (although based only on two trials) (Analysis 6.1), the effect size for disability (Analysis 6.2), depression (continuous) (Analysis 6.4), neurological deficit (Analysis 6.3), anxiety (Analysis 6.6) and death (Analysis 6.9) were smaller and not significant for disability (Analysis 6.2), depression (Analysis 6.4; Analysis 6.5) and anxiety (Analysis 6.6). There was no significant difference in the rate of seizures between groups (Analysis 6.10).

Low risk of bias for patient/personnel blinding

When only those trials with low risk of bias were included, the effect size of dependence was the same (Analysis 7.1): the effect sizes for disability (Analysis 7.2), neurological deficit (Analysis 7.3), depression (Analysis 7.4; Analysis 7.5), anxiety (Analysis 7.6) and cognition (Analysis 7.8) were all smaller, and for cognition (Analysis 7.8) and anxiety (Analysis 7.6) were not statistically significant. The rate of seizures remained similar (Analysis 7.10) (but was not significantly different between SSRI and control) and the rate of GI side effect was lower and not significantly different between SSRI and control (Analysis 7.11).

Low risk of bias for blinding of outcome assessor

When only those trials with low risk of bias were included, the effect size of dependence was the same (Analysis 8.1): the effect sizes for disability were similar (Analysis 8.2), the effect sizes for neurological deficit (Analysis 8.3) and depression (Analysis 8.4; Analysis 8.5) were smaller. Cognition could not be estimated (Analysis 7.8). The effect on anxiety (Analysis 8.6) was larger and statistically significant. The rate of seizures and GI side effects were not statistically different between groups (Analysis 8.10; Analysis 8.11).

Low risk of bias for outcome data reporting

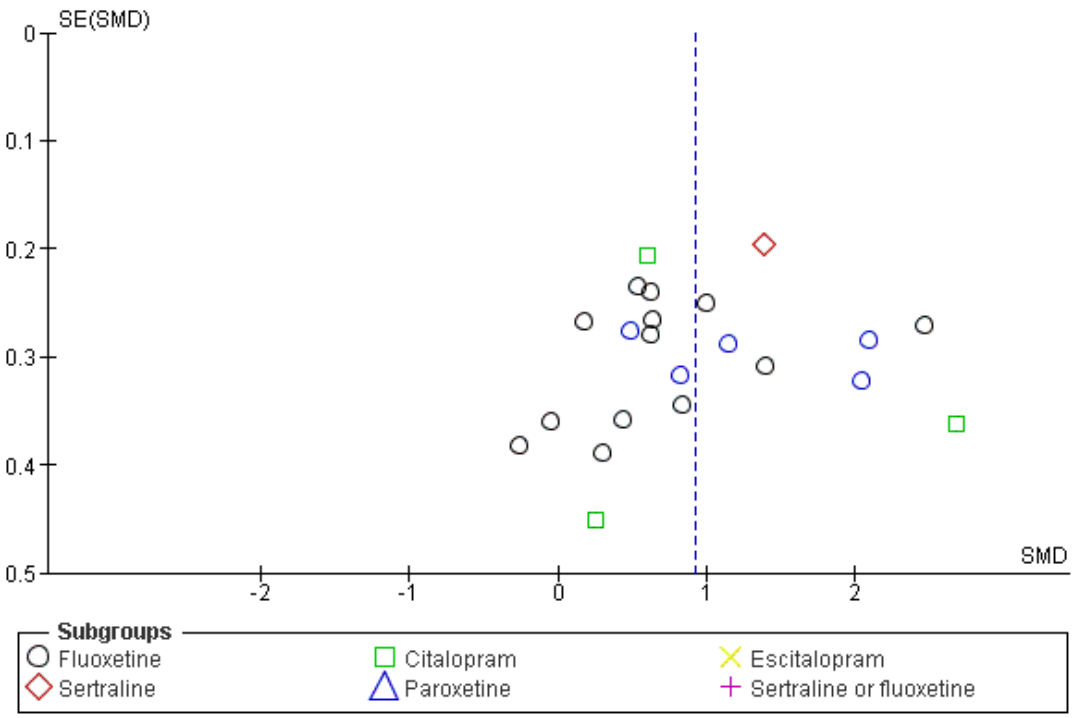
When only those trials with low risk of bias were included, the effect size for dependence was the same (Analysis 9.1), the effect sizes for disability (Analysis 9.2) and depression (dichotomous) (Analysis 9.5) were similar and statistically significant. The effect sizes for neurological deficit and continuous depression scores were larger and statistically significant (Analysis 9.3; Analysis 9.4). The effect sizes for death (Analysis 9.9), seizures (Analysis 9.10) and GI side effects (Analysis 9.11) were similar and not statistically different between SSRI and control.

Low risk of bias for selective reporting

When only those trials with low risk of bias were included, the effect size for dependence was the same (Analysis 10.1), the effect sizes for disability (Analysis 10.2), neurological deficit score (Analysis 10.3), depression (continuous) (Analysis 10.4), anxiety (Analysis 10.6) and cognition (Analysis 10.8) were all smaller and not significant. The rate of seizures remained similar though not significantly different between groups (Analysis 10.10) and the rate of GI side effects was lower and not significantly different between groups (Analysis 10.11).

The funnel plot for one of our primary outcomes (disability at the end of treatment) appeared to be asymmetric on visual inspection (Figure 4), although note that the interpretation is uncertain (Higgins 2011 Section 10.4.3.1.).

Figure 4. Funnel plot of comparison: 1 SSRI versus control at end of treatment, by SSRI, outcome: 1.2 Disability.



DISCUSSION

Summary of main results

We identified 56 completed trials comparing an SSRI with control, but four of these did not provide data that could be used in the meta-analysis (Chen KN 2005; Meara 1998; Pariente 2001; Restifo 2001). This left 52 trials with data that could be used in a meta-analysis. These trials were from all over the world, including China. They mostly recruited inpatients. Fluoxetine was the most commonly used SSRI. Most trials that reported time since stroke randomised patients who were within three months of stroke onset. Some trials stipulated that patients had to have depression, while some did not require that patients had to have depression at entry. Most of the trials excluded patients who could not consent for themselves (e.g. those with cognitive impairment and those with aphasia).

The duration of treatment varied from weeks to months. Only eight trials followed people up after treatment had been completed. There were insufficient data to determine whether withdrawal effects were experienced, because adverse events were not reported in the first few weeks after the SSRI had been discontinued.

There were beneficial effects of SSRIs on our two primary outcomes (dependence and disability) and some of our secondary outcomes (neurological deficit, mood, anxiety) at the end of treatment. There was substantial heterogeneity between trials. None of the trials reported fatigue, which is a common and distressing post-stroke problem, for which there is no treatment. None of the trials reported healthcare costs. The number of deaths was lower in the group allocated SSRI, but this difference was not statistically significant, and there was no heterogeneity between trials. There was a non-significant excess of seizures, GI side effects and bleeding in those allocated an SSRI. There was no difference between SSRI and control in the number leaving the trial early. The trials that followed up patients beyond the period of treatment reported beneficial effects of SSRI on disability, neurological deficit and depression, though CIs were wide.

A subgroup analysis did not identify any type of SSRI that had consistently better effects than the other SSRIs. Note that most of the data related to fluoxetine.

For the subgroup of time since stroke, there was no heterogeneity

between these subgroups less than three months after stroke and more than three months after stroke, though not all trials reported time since stroke.

There was statistically significant heterogeneity between trials that recruited those with depression at onset for disability (Analysis 4.2), and dichotomous depression scores (Analysis 4.5), with larger effect sizes seen in the trials that recruited patients with depression. These data suggest that SSRIs might be of more benefit in people with depression - although importantly, benefits were also observed in patients without depression.

Our sensitivity analyses, in which we excluded trials with high or unclear risk of bias, demonstrated that the effect sizes were generally smaller and, for some outcomes, were no longer significant. The number of adverse events remained similar after excluding trials at high or unclear risk of bias.

Overall completeness and applicability of evidence

We performed extensive searches and we identified many more trials than we had been anticipating based on our knowledge of previous systematic reviews, suggesting that other reviews may have missed relevant trials. Our review question was deliberately broad (including all SSRIs, given for any reason and at any time within the first year after stroke) to ensure that we identified all trials that were relevant to the question about whether SSRIs might be of benefit in stroke. We did not search Chinese databases and so we may have missed some papers that had titles and abstracts written only in Chinese. However, we did scrutinise relevant systematic reviews from Chinese authors who had searched the Chinese databases (Chen 2006; Chen 2007; Yi 2010). Our searches also identified papers written in Chinese that had English abstracts and we included these papers in our review.

The funnel plot appeared asymmetric on visual inspection, which would be consistent with publication bias - although note that there are many other causes of funnel plot asymmetry besides publication bias (Higgins 2011).

How do these data apply to 'real' patients? In these trials, the patients recruited were younger than patients with stroke (mean age generally in the 60s). Most trials excluded patients unable to consent for themselves (e.g. those with aphasia and those with cognitive impairment). This is an important limitation of the existing data. It is important to include these people in trials, because the risks and benefits may be different from other patients (e.g. an SSRI may be of more harm in patients who cannot report adverse effects, or may be of more benefit if undiagnosed depression is treated). Most trials recruited patients within three months of stroke, and so we cannot be certain about the effect of an SSRI initiated after this time.

Most trials included patients with both haemorrhagic and ischaemic stroke, and no trial reported data separately for these two pathological subtypes of stroke.

We cannot be sure whether the apparent benefits are because SSRIs might speed up the rate of recovery or influence the ultimate level of disability. This would need data from multiple time points and a repeated measures analysis. There were insufficient data to perform these analyses.

Quality of the evidence

The trials were generally small; the largest one recruited only 229 patients (GlaxoSmithKline 1998). There were multiple different sources of bias in most of the trials that we identified (Figure 2; Figure 3). Some trials did not report in detail important methodological aspects of the trials (including sequence generation, allocation concealment, blinding, incomplete outcome reporting, selective reporting), making it difficult to determine the risk of bias. When there was sufficient information to make judgements about sources of bias, we identified multiple sources of bias in many of the trials. The funding source was not reported for a substantial proportion of the trials. When funding was declared, there were frequently links with the pharmaceutical industry (e.g. provision of the drug and placebo, payment of honoraria and expenses).

Only some of the trials reported side effects, and of those that did, only some explained how side effects were collected.

When we performed sensitivity analyses including only those trials at low risk of bias, the effect sizes were smaller, suggesting that methodological limitations of the trials may have led to overestimation of effect sizes.

Potential biases in the review process

Only one author extracted data from studies written in Chinese. This author checked the data extraction carefully. The majority of Chinese papers had English abstracts, and so a second author was able to check data provided in the English abstract. We cannot be certain that there were no mistakes in data extraction, but if these did occur, it is unlikely that this would have led to a systematic overestimation or a systemic underestimation of effect sizes.

Only one author (GM) screened titles and abstracts for the MEDLINE and EMBASE searches. There is a small possibility that this single author might have missed trials, but there is no reason to suspect that any missed trials would have been systematically different (e.g. in relation to risk of bias, size of effects) than the trials that we identified.

We did not systematically search the Chinese databases. Of the Chinese papers that we did identify, there were frequently multiple sources of bias, so if we had identified additional Chinese publications, inclusion of such trials may have led to an overestimate of the true effects of treatment.

The database searches were performed in August 2011. It is possible that we have missed trials published since then, but our cited reference searches in February 2012 did not identify any new trials. When we update the review, we will search the databases from

September 2011 onwards.

Agreements and disagreements with other studies or reviews

One of the key limitation of previous reviews is that their research question was narrow (e.g. effect of SSRI on treating or preventing depression after stroke, effect of SSRI on motor recovery, or reviewing a single SSRI). By contrast, our review had broad inclusion criteria, providing a more complete picture of the evidence for SSRIs in stroke. Furthermore, we rigorously assessed risk of bias, performed sensitivity analyses and also performed subgroup analyses to determine the impact of depression at randomisation, the type of SSRI and the time since stroke at randomisation. We identified some studies that had not been included in previous systematic reviews.

A previous systematic review of fluoxetine (Yi 2010) found that it reduced disability and dependency and reduced the risk of post-stroke depression but the review (Yi 2010) did not explore the effect of all possible types of bias on the estimate of effect and did not include the FLAME Trial (Chollet 2011). Another review found only three RCTs of antidepressants and could not perform a meta-analysis (Bhogal 2005). One systematic review published in 2007 identified only 10 trials recruiting 703 non-depressed patients, and concluded that antidepressants given prophylactically reduced the rate of developing depression (Chen 2007), but other outcomes were not reported. One review of antidepressants for the treatment of post-stroke depression by the same authors (Chen 2006) found only 16 trials and concluded that antidepressants were of benefit for depression and other outcomes. In one review published in 2009 of six trials of any drug that might influence neurotransmitters, with motor function as the outcome of interest (Berends 2009b), the authors concluded that there was insufficient information to draw conclusions on the effect of SSRIs on motor recovery (Berends 2009b). One review of pharmacological interventions for post-stroke depression published in 2003 identified only 10 trials, and concluded that the SSRIs may be effective for treating post-stroke depression (Van de Meent 2003). One non-systematic review of antidepressants in the treatment of stroke suggested that antidepressants might be of benefit (Burns 2010).

In two reviews of interventions to treat and prevent depression after stroke (Hackett 2008a; Hackett 2008b) the authors pooled data from randomised placebo-controlled trials of all antidepressants. There were insufficient trials of adequate quality to perform subgroup analyses by antidepressant subtype. The authors concluded that there was evidence that antidepressants did not prevent depression after stroke and recommended that the evidence of benefit of antidepressants as a treatment strategy had to be weighed against the evidence of associated increased risk (adverse events). An explanation for these less supportive recommendations for antidepressant use lies in the differing inclusion criteria. Of the 32 trials contributing continuous depression data in this current review, only five trials (Andersen 1994; Fruehwald 2003; Murray 2005; Robinson 2000a; Wiart 2000) used matching placebo control arms and were included in the Hackett (Hackett 2008a; Hackett 2008b) reviews. The six trials that stated placebo was used (with uncertainty regarding matching Chen 2002; GlaxoSmithKline 1998; Huang 2002; Lai 2006; Li 2008; Song 2006) were not included. Seven (Acler 2009; Brown 1998; Burns 1999; Chollet 2011; Dam 1996; Kong 2007; Robinson 2000b) of the 10 trials contributing dichotomous data to the current review used matching placebo control arms; however, two (Acler 2009; Chollet 2011) of these were published after the Hackett reviews (Hackett 2008a; Hackett 2008b) and one (Kong 2007) was not identified in the searches performed for the Hackett reviews, presumably because it had not been indexed by the time of the searches.

Our searches also identified commentaries on our included trials, in particular on the more recently published, larger trials from high impact journals written in English. For example, there are multiple commentaries and letters (e.g. Anonymous 2011; Berends 2011; Friedman 2011; Robinson 2011) on the FLAME trial (Chollet 2011), and on the trial by Robinson 2008 and colleagues, in which cognitive outcomes for a subset of patients were published after the main trial results had been published (e.g. Anonymous 2010; Formulary Staff 2010). The message from these commentaries is that SSRIs are a promising intervention for stroke; and the general view is that further larger trials are needed.

AUTHORS' CONCLUSIONS

Implications for practice

Review data provide evidence of benefit of SSRI for reducing disability and neurological impairment scores in people with stroke. However, the extent of the benefit is uncertain, as our sensitivity analyses demonstrated that effect sizes were generally smaller when only methodologically robust trials were included. Furthermore, there was a statistically non-significant increase in risk of adverse effects in people given an SSRI, although data on adverse effects are limited. There is insufficient evidence from this review to make recommendations about which is the most effective SSRI, which has the fewest side effects, for how long it should be given and at what dose.

Current practice is often to give an antidepressant (often an SSRI) to stroke survivors with depression, in whom it is possible to assess for depressive symptoms. The results of this review demonstrate large effect sizes for mood scores at the end of treatment and appear to provide support for this practice, but these data predominantly come from comparison of an active drug with usual care, and data on adverse effects are limited, although generally in favour of the control arm. We suggest that the evidence tentatively supports the use of prescription antidepressants to treat depression in people

after stroke, but this must be considered in the light of evidence of an associated increase in harm and we recommend patients are well monitored for adverse effects. There are insufficient data to make recommendations about the risk of bleeding, which is of particular relevance to patients with haemorrhagic stroke who develop depression, and to patients with ischaemic stroke who are prescribed antiplatelet or anticoagulant drugs.

Patients with aphasia were generally excluded from the trials in this review, so we do not know whether SSRIs are effective in patients whose mood cannot be formally assessed. In clinical practice, if depression is suspected in patients with aphasia, a trial of antidepressants is often given. This review cannot confirm whether or not this practice should continue. This is an area where further research is needed.

Implications for research

Currently, SSRIs are not generally prescribed with the aim of improving neurological recovery or to prevent depression after stroke. Our review provided tantalising evidence of benefits of SSRIs in patients who did not have to have depression to enter the trial. These benefits included improvements in dependence, disability, neurological impairment scores and depressive symptoms. However, given the methodological limitations of a large proportion of the trials, and the wide CIs for effect sizes when only methodological sound trials are included, we cannot be sure whether these effects are real. If these effects are real, and if the risk of side effects is sufficiently low, then SSRIs would become an important (and low cost) treatment for patients with stroke. Thus, there is a need for a larger trial of SSRI in stroke (excluding those with depression) to determine the effect on both the rate of recovery and the ultimate level of disability and dependency. It is crucial that such a trial is methodologically sound with a low risk of bias. Furthermore, long-term follow-up, after treatment has been completed, is crucial to determine whether any benefits are sustained. Given that most of the evidence from this review relates to fluoxetine, this would seem the drug of choice to test in a big trial. Citalopram and escitalopram may lead to prolongation of the QT interval, and because a large proportion of stroke survivors have underlying coronary artery disease, these two drugs are not, in our view, the best choice of drugs to test in a future trial. It is important that patients with aphasia and cognitive impairment are included. There is a need to systematically report adverse events, including seizures and bleeding. It is important to ensure that follow-up data are as complete as possible, and that there is a method for dealing with any missing data. There should be subgroup analyses for patients with ischaemic and haemorrhagic stroke, to explore whether SSRIs might increase the risk of recurrent intracranial bleeding in patients with intracerebral haemorrhage, and whether there is a higher risk of haemorrhagic transformation of infarct when SSRIs are given to patients with ischaemic stroke who are also taking anticoagulants. Finally, protocols for trials should be published in advance to allow readers to determine whether or not there has been selective reporting of outcome assessments.

We identified five ongoing trials, including two large trials (AFFINITY 2011; FOCUS 2011) that aim to recruit 1580 patients and 3000 patients, respectively. Both of these large trials will start recruiting in 2012.

It will clearly be important to update this review with the results of ongoing trials. Furthermore, an individual patient meta-analysis would also be worthwhile; this would allow us to investigate the influence of covariates on heterogeneity of treatment effects fully, both within and between trials (Simmonds 2005).

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* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

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

Acler 2009

Methods	Parallel design Randomisation: computer generated, individual Allocation concealment: not described Blinding: patients, outcome assessors and physiotherapists all blinded Analysis: not stated whether ITT
Participants	Location: Italy Setting: inpatient Inclusion criteria: first-ever ischaemic stroke, CT or MRI documenting a single monohemispheric lesion, age below 80 years, within 3 months of onset Treatment: 10 people, mean age 68 ± 7 years, 6 men Control: 10 people, mean age 65 ± 7 years, 6 men
Interventions	Citalopram 10 mg daily Placebo: identical pill daily Duration of treatment: at least 4 months Duration of follow-up: not stated
Outcomes	Motor cortex excitability NIHSS Lindmark scale BI HDRS BDI No data on death, GI upset, bleeds or seizures
Notes	Exclusion criteria: major affective disorders, alcohol abuse and dementia leading to uncooperative behaviour, pacemakers, metal in the head, concomitant neuropathies, systemic vasculopathies, major affective disorders

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated random numbers
Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment not stated
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	It is not stated whether data from all recruited patients are reported

Acler 2009 (*Continued*)

Selective reporting (reporting bias)	Unclear risk	Side effects were not reported though they were assessed
Other bias	Unclear risk	Source of funding not stated; unclear whether or not a drug company was involved in the study
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Stated blinded, placebo was 'an identical pill'
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Stated blinded

Almeida 2006

Methods	Parallel design Randomisation: computer-generated random list of numbers Allocation concealment: centralised Blinding: double blind: participants: yes; investigators: yes; outcome assessors: unknown Analysis: ITT (last observation carried forward), withdrawn owing to becoming depressed, AE, treating practitioner started antidepressant, medical advice, no reason given, not contactable - numbers not included
Participants	Location: Australia Setting: inpatient Treatment: 55 people, mean ± SD age 68 ± 13 years, 67% men Control: 56 people, mean ± SD age 67 ± 13 years, 62% men Stroke criteria: acute ischaemic or haemorrhagic stroke, diagnosis by clinical signs (ICD-10) and CT (100% imaged, 10/111 CT scan did not show acute ischaemia); stroke on average < 2 weeks prior to randomisation Not depressed (HADS-D had to be over 7) Other entry criteria: not stated Comparability of treatment groups: more participants in treatment group with previous heart attack and stroke, also higher levels of hypertension
Interventions	Treatment: sertraline 50 mg daily (night) Control: matched placebo Duration: treatment continued for 24 weeks Duration of follow-up (post treatment to study end): 28 weeks
Outcomes	Depression: change in scores from baseline to end of treatment on HDRS, proportion depressed Change in MMSE scores mRS Death Leaving the trial early

Almeida 2006 (*Continued*)

	Check list of possible AEs read out to patient by a research nurse
Notes	Exclusion criteria: severe communication difficulties, unstable medical condition, severe cognitive impairment and depression (MMSE < 10), taking antidepressants within 4 weeks of stroke, contraindication to sertraline, previous reaction to sertraline, could not speak English

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Computer-generated random numbers
Allocation concealment (selection bias)	Low risk	Centralised
Incomplete outcome data (attrition bias) All outcomes	Low risk	Performed last observation carried forward
Selective reporting (reporting bias)	Low risk	Trial protocol published on www.strokecentre.org/trials
Other bias	Low risk	No other obvious biases Funded by an unrestricted grant from Rotary Health Research Fund
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Stated in paper, matched placebo
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated in paper

Andersen 1994

Methods	Parallel design Randomisation: blocks of 4 used Allocation concealment: centralised opaque envelopes Blinding: double blind reported, those blinded not stated Analysis (ITT) last observation carried forward and per protocol: death (1 treatment, 1 control) withdrawn owing to AE (6 treatment, 1 control), all excluded from analysis
Participants	Location: Denmark Setting: mixed Treatment: 33 people, mean ± SD age 68 ± 4 years, 36% men Control: 33 people, mean ± SD age 66 ± 9 years, 66% men Stroke criteria: ischaemic stroke and PICH; diagnosis via clinical signs and CT (100%)

	; stroke 2 to 52 weeks prior to randomisation (average time 12 weeks) Depression criteria: HDRS score > 12 (score transformed to appropriate DSM-III-R criteria) Other entry criteria: none stated Comparability of treatment groups: balanced
Interventions	Treatment: citalopram 10 mg in participants > 66 years, 20 mg in participants < 67 years daily; dose doubled if no response to treatment within 3 weeks Control: matched placebo Duration: treatment continued for 6 weeks Duration of follow-up (post treatment to study end): 0 Note that although the protocol on www.strokecentre.org/trialsstates that mood scores were measured up to 1 year post-stroke, this probably refers to the time since stroke at the time of randomisation
Outcomes	Depression: change in scores from baseline to end of treatment on HDRS Melancholia scale Proportion no longer meeting entry criteria (< 13 on HDRS) 50% reduction in HDRS score Additional: leaving the study early Death AEs (unwanted drug effects were registered and evaluated at the same intervals using a side effect scale) Unable to use: BI, Social Activities Index, MMSE (data not presented)
Notes	Exclusion criteria: depression within last year, receiving current treatment for depression, severe dementia or communication problems, degenerative or expansive neurological disease, decreased consciousness

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Blocks of 4 used
Allocation concealment (selection bias)	Low risk	Centralised opaque envelopes
Incomplete outcome data (attrition bias) All outcomes	Low risk	Although there were drop-outs, analysis performed both per protocol and using last observation carried forward
Selective reporting (reporting bias)	Low risk	Trial published on www.strokecentre.org/trials The primary outcome was reported
Other bias	Unclear risk	Funded by Lundbeck Foundation, Medical Research Foundation for North Jutland County, The Aalgorg Diocese Research

Andersen 1994 (*Continued*)

		Foundation, Consultant Otorhinolaryngologist Kopp's Foundation and Stine and Martinus Sorensen's Foundation. Lundbeck Pharma A/S provided the citalopram and placebo; thus we have classified this as 'unclear risk'
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Matched placebo
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Those who were blinded were not stated

Brown 1998

Methods	Parallel design Randomisation: unclear Allocation concealment: randomised by an independent statistician Blinding: double-blind participants: yes; nursing staff: yes; rating clinicians: yes Analysis: per protocol: 1 withdrawn (treatment), excluded from analysis
Participants	Diagnosis: stroke, time from stroke to randomisation not reported Randomised 10 to treatment and 10 to control. Treatment: 9 completed treatment, mean ± SD age 61.4 ± 8.6 years, 55% men Control: 10 people completed placebo, mean ± SD age 63.7 ± 5.4 years, 60% men Emotionalism criteria: emotionalism of at least 4 weeks' duration assessed during semi-structured interview using a modified Lawson and MacLeod rating scale, in addition to frequency of outbursts
Interventions	Treatment: fluoxetine 20 mg daily Control: matched placebo Duration: 10 days Duration of follow-up: (end of treatment to end of study) 0
Outcomes	Used leaving the study early Unable to use data from HDRS, Lawson and MacLeod Scale, self-rating scales (mean and SD not presented) Also reported emotional outbursts; we have not used these in our analyses AEs: not presented
Notes	Exclusion criteria: cognitive impairment, dysphasia, major depressive disorder
Risk of bias	

Brown 1998 (*Continued*)

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomisation method not stated
Allocation concealment (selection bias)	Unclear risk	Randomised by independent statistician
Incomplete outcome data (attrition bias) All outcomes	Low risk	Only 1 withdrawn (5% of participants) - we categorised this as low risk
Selective reporting (reporting bias)	Unclear risk	Insufficient information to make judgement
Other bias	Unclear risk	No other obvious biases, baseline balanced Funder not stated
Blinding of participants and personnel (performance bias) All outcomes	Low risk	States blinding, matched placebo
Blinding of outcome assessment (detection bias) All outcomes	Low risk	States blinding

Burns 1999

Methods	Parallel design Randomisation: blocks of 4 using list produced by medical statistics department Allocation concealment: unclear Blinding: run-in was single blind and run-out was single blind; treatment phase reported as double blind, those blinded not stated Analysis: ITT: 2 withdrawn and 1 death (treatment), 1 death (placebo), last value carried forward
Participants	Diagnosis: stroke. Months from stroke: median (range) 10.5 months (1 ± 156) in sertraline group and 5.5 months (1.5 ± 48) in the control group Treatment: 14 people Control: 14 people
Interventions	Treatment: sertraline 50 mg daily Control: matched placebo Duration: treatment continued for 8 weeks Duration of follow-up: 2 weeks off treatment. All scores became non-significant (though data not reported so could not be used in the analysis)
Outcomes	Able to use: 1. improved score on lability scale

	2. improved score on clinician's interview based impression of change 3. diminished tearfulness 4. leaving the study early 5. death 6. AEs Method of collecting AEs was not stated Unable to use: MADRS, BI, MMSE (data not presented)
Notes	Exclusion criteria: less than 1 month since stroke, depression or dementia using the DSM III-R criteria

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Blocks of 4 using list produced by medical statistics department
Allocation concealment (selection bias)	Unclear risk	Not stated
Incomplete outcome data (attrition bias) All outcomes	Low risk	Analysis: ITT, last observation carried forward
Selective reporting (reporting bias)	Low risk	Trial details published on www.strokecentre.org/trials, although unable to use data from MADRS Given that the main aim was to explore effect on emotionalism, this is unlikely to have biased results
Other bias	Unclear risk	Placebo group younger, uncertain influence on bias Funded by an unrestricted personal grant from Pfizer, the manufacturers of sertraline Statistical analysis was carried out independently by the Applied Statistics Research Unit in Canterbury
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Matched placebo
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Run out was single blind, treatment was double blind, but unclear whether outcome assessors were blind

Chen 2001

Methods	Randomised trial 3 groups: fluoxetine plus usual care versus YuLeShu plus usual care versus usual care. We used the fluoxetine plus usual care versus usual care alone in the comparison Aim: to observe effects of integrative Chinese herb YuLeShu and fluoxetine on the depressive symptoms and rehabilitation of neurological impairment in patients with post-stroke depression Randomisation: by computer Allocation concealment: unclear Blinding: not described Drop-outs: 2 people dropped out of the fluoxetine group, 1 dropped out of the YuLeShu group and 2 dropped out of the control group
Participants	Country: China Setting: not described Patients: internal carotid system cerebral infarction or haemorrhage within previous 2 months Fluoxetine: 19 people, mean age 61.71 ± 8.13 years, 8 men Control: 18 people, mean age 62.85 ± 7.32 years, 7 men Depression: diagnosis of depression according to DSM-IV Inclusion criteria: HDRS ≥ 20 but < 35 and/or Zung SDS ≥ 41 Exclusion criteria: HDRS > 35
Interventions	3 groups: fluoxetine plus usual care versus YuLeShu plus usual care versus usual care. We are using the fluoxetine plus usual care versus usual care alone in the comparison
Outcomes	HDRS Zung SDS BI Scandinavian Neurological Stroke Scale (also known as CSS) Stated no side effects, but not clear which side effects were sought, or how they were sought. They were reported at 4, 8 and 12 weeks after treatment
Notes	Excluded: previous depression, aphasia, severe cardiac, pulmonary, hepatic and renal diseases, previous stroke

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	States 'using a computer' but method not described
Allocation concealment (selection bias)	Unclear risk	Not described
Incomplete outcome data (attrition bias) All outcomes	High risk	4/37 drop-outs
Selective reporting (reporting bias)	Unclear risk	Protocol not published

Chen 2001 (*Continued*)

Other bias	Unclear risk	Reported that of the people who completed the tests, there were no differences in baseline No comment on whether there were differences in baseline for the entire group Funded by a local scientific academic fund, drug company not involved
Blinding of participants and personnel (performance bias) All outcomes	High risk	No placebo
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not described

Chen 2002

Methods	Parallel group (3 groups: doxepin, paroxetine, placebo; we used the paroxetine and placebo data in our review) Aim: treat depression and determine effect on neurological function Randomisation: not described Allocation concealment: not described Blinding: not described Drop-outs: 4 in placebo and 0 in paroxetine
Participants	Country: China Setting: unclear Stroke diagnosis: diagnostic criteria of the 4th National Meeting of the Cerebrovascular Diseases proved by CT or MRI Time since stroke: not known Depression diagnosis: Classification and Diagnosis of Psychosis in China (2nd edition) Treatment: 24 people, age and gender not given Control: 24 people, age and gender not given
Interventions	Treatment: paroxetine 20 mg daily Control: placebo guvitamine Duration of treatment: 8 weeks Duration of follow-up (post-treatment to study end): unclear: follow-up is performed 'after treatment' so we assume this is at 8 weeks (so post-treatment to study end = 0)
Outcomes	HAMD BI CSS Death/side effects/leaving the trial early Method of reporting side effects not stated

Chen 2002 (*Continued*)

Notes	Exclusion: pre-stroke mental disease, cognition disorder (MMSE < 24), marked deterioration in depression during treatment (HAMD > 24) or suicide mood, intolerance to drug Paroxetine given 3 times per day while placebo given once a day

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Method not described
Allocation concealment (selection bias)	Unclear risk	Not described
Incomplete outcome data (attrition bias) All outcomes	High risk	4/48 drop-outs
Selective reporting (reporting bias)	Unclear risk	No protocol available
Other bias	Unclear risk	Demographic data not provided, so we cannot determine whether the baseline was balanced Funder not stated, unclear if there was drug company involvement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Placebo was used, but unclear if this was matching
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not described

Chen KN 2005

Methods	Aim: to observe the changes of neurotransmitter in patients with post-stroke depression by using Encephalofluctuography Technology, and observe the effect of antidepression treatment on the activity of neurotransmitter
Participants	48 patients with post-stroke depression
Interventions	Treatment: 24 people received citalopram 20 mg plus usual care, or fluoxetine if side effects such as nausea, emesis Control: 24 people usual care alone
Outcomes	Encephalofluctuography Technology Level of sympathin and 5-hydroxytryptamine at 4 weeks and 3 months after treatment started

Chen KN 2005 (*Continued*)

Notes	No data from our endpoints of interest, so data not included in a meta-analysis	
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	'Randomly divided' but method not stated
Allocation concealment (selection bias)	Unclear risk	Method not stated
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not described
Selective reporting (reporting bias)	Unclear risk	Unclear
Other bias	Unclear risk	Unclear
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not described
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not described

Chen T 2005

Methods	Parallel group Randomisation: no description of method Allocation concealment: not described Blinding: not described Analysis: according to allocated treatment group Drop-outs: none
Participants	Country: China Setting: inpatient Stroke criteria: first ever stroke, onset time $\leq$ 7 days, haemorrhagic and ischaemic, clinical diagnosis plus confirmation by imaging (though not clear whether a stroke lesion had to be present), at least 1 limb with muscle power grade 3 or less, BI $\leq$ 50, no consciousness disturbance Mood criteria: HAMD > 16 Treatment: 40 people, mean age 63.5 years, 29 men Control: 38 people, mean age 65.8 years, 25 men No difference in baseline depression and BI between treatment and control group

Chen T 2005 (*Continued*)

Interventions	Treatment: paroxetine 20 mg daily plus routine stroke medication, nerve nutritional agents, acupuncture and rehabilitation Control: routine stroke medication, nerve nutritional agents, acupuncture and rehabilitation Duration of treatment: 12 weeks Duration of follow-up (post-treatment to study end): 0 weeks
Outcomes	HAMD BI Death Number completing the trial
Notes	Excluded: severe cardiac, hepatic and renal organic diseases, psychiatric disorders AEs not reported

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Method not described
Allocation concealment (selection bias)	Unclear risk	Not described
Incomplete outcome data (attrition bias) All outcomes	Low risk	No drop-outs
Selective reporting (reporting bias)	Unclear risk	No protocol
Other bias	Unclear risk	No obvious risks, baseline similar No description of funding
Blinding of participants and personnel (performance bias) All outcomes	High risk	No placebo
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated

Cheng 2003

Methods	Parallel design Aim: to treat depression and augment rehabilitation Randomisation: not stated Allocation concealment: not described Blinding: not described Analysis: according to allocated treatment group Drop-outs: none
Participants	Location: China Setting: inpatient Treatment: 25 people Control: 32 people Whole group (including non-depression group, depression control group and depression treatment group): 132 (mean age 62 ± 12 years, 79 men) Stroke: ischaemic stroke or PICH, clinical diagnosis plus confirmation on brain imaging (not clear that a stroke lesion had to be present), clear consciousness Depression diagnosis (at 2 weeks after stroke onset): psychiatric interview, DSM IV criteria
Interventions	Treatment: fluoxetine 20 mg daily Control: no fluoxetine Duration of treatment: 6 months Duration of follow-up (post-treatment to study end): 6 months
Outcomes	SSS ADL HAMD Zung SDS Zung SAS No deaths, none left trial early No data on AEs
Notes	Excluded: major psychological trauma history in previous 1 year, severe mental retardation, severe impairment of lingual expression or comprehension, major complicated medical event in previous 1 year

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Method not described
Allocation concealment (selection bias)	Unclear risk	Not described
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	59 patients were diagnosed to have depression by symptoms but only 57 were included in the results table

Cheng 2003 (*Continued*)

Selective reporting (reporting bias)	High risk	No protocol, no report of the results of the self rating anxiety scale
Other bias	Unclear risk	No clear description of differences between the treatment and control group. No description of funding
Blinding of participants and personnel (performance bias) All outcomes	High risk	No placebo
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not described

Chollet 2011

Methods	Randomised parallel group trial Randomisation: balanced by centre with an allocation based on a block size of 4 generated with a computer random-number generator Allocation concealment: sequentially numbered opaque envelopes Blinding: participants, those delivering the interventions and those assessing outcome Drop-outs: 2 patients died (1 in each group) and 3 dropped out - not stated how missing outcome data were dealt with
Participants	Location: France Setting: stroke units Inclusion criteria: aged 18 to 85 years with FMMS of 55 or less, acute ischaemic stroke with hemiparesis or hemiplegia, 5 to 10 days after stroke onset, unclear if there had to be a visible lesion on brain imaging Treatment: 59 people, mean ± SD age 66.4 ± 11.7 years; 63% men Control: 59 people, mean ± SD age 62.9 ± 13.4 years; 59% men Comparability of treatment groups: total FMMS score fluoxetine 17.1 compared with 13.4 in placebo Previous stroke more common in the fluoxetine group; fluoxetine group had more diabetes
Interventions	Treatment: fluoxetine 20 mg daily for 90 days Control: identical capsules to active drug Duration of treatment: 90 days Duration of follow-up (treatment end to study end): 0 days
Outcomes	Primary outcome: the mean change of FMMS score between inclusion (day 0) and day 90 after the start of the study drug Secondary endpoints were NIHSS, mRS and MADRS measured at days 0, 30 and 90
Notes	Exclusions: clinical depression or treatment with antidepressants, MADRS > 19, aphasia severe enough to mask detection/assessment of depression, pregnancy, patient on neu-

Chollet 2011 (*Continued*)

	roleptics/benzodiazepines, owing to undergo carotid endarterectomy, other major diseases that would prevent follow-up

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Balanced by centre with an allocation based on a block size of 4 generated with a computer random-number generator
Allocation concealment (selection bias)	Low risk	Sequentially numbered opaque envelopes
Incomplete outcome data (attrition bias) All outcomes	Low risk	5/188 drop-outs, which is less than 5%
Selective reporting (reporting bias)	Low risk	Trial protocol published on www.strokecentre.org/trials, all outcomes were reported
Other bias	Unclear risk	Note difference in baseline: it is not clear what effect this had on results, so we have classified this as 'unclear risk' Funded by French national programme for clinical research: the sponsor had no involvement in study design, data collection, data analysis, data interpretation or writing the report
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Identical capsules for control arm
Blinding of outcome assessment (detection bias) All outcomes	Low risk	All study site investigators and all investigators were masked to treatment allocation

Dam 1996

Methods	Parallel design Randomisation: unclear Allocation concealment: unclear Blinding: double blind reported - participants: unclear; examining neurologists: yes Analysis: per protocol: withdrawn because of AEs (2 treatment), all excluded from analysis
Participants	Location: Italy Setting: unclear Treatment: 18 people, mean ± SD age 68 ± 9 years, 44% men

Dam 1996 (*Continued*)

	Control: 17 people, mean ± SD age 68 ± 5.5 years, 44% men Stroke criteria: ischaemic, unilateral MCA territory stroke, diagnosis via clinical signs and CT (100%), stroke 1 to 6 months prior to randomisation (average time 3 months) Other entry criteria: unable to walk Comparability of treatment groups: balanced
Interventions	Treatment: fluoxetine 20 mg daily Control: matched placebo Duration: treatment continued on average 74 ± 6 days, duration not reported for control group Duration of follow-up (treatment end to study end): 0
Outcomes	Depression: change in scores from baseline to end of treatment on HDRS Additional: graded neurological scale (HSS), BI Leaving the study early Death AEs including seizures - unclear if these were reported systematically
Notes	Exclusion: history of major affective disorders; alcohol abuse; or a history or evidence or both of severe heart, lung, kidney or liver diseases or mental deterioration

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	No description
Allocation concealment (selection bias)	Unclear risk	No description
Incomplete outcome data (attrition bias) All outcomes	High risk	2/35 drop-outs, per-protocol analysis
Selective reporting (reporting bias)	Low risk	Trial available, including results on www.strokecentre.org/trials - all specified outcome measures were reported
Other bias	Unclear risk	Baseline characteristics similar in the 2 groups. Funding source not stated (so categorised as unclear risk)
Blinding of participants and personnel (performance bias) All outcomes	Low risk	"Examining neurologists blind to treatment". Unclear if this refers to outcome assessors or the neurologist caring for the patient. However, placebo was 'matched' so this is low risk

Dam 1996 (*Continued*)

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	See above

Feng 2004

Methods	4 groups: fluoxetine plus usual care, Jieyu Huoxue decoction plus usual care, usual care in people with depression, usual care in people with no depression We are using data from 'fluoxetine plus usual care' versus 'usual care in people with depression' Aim: to study the influence of Jieyu Huoxue decoction on rehabilitation of patients with depression after cerebral infarction Randomisation: method not stated Allocation concealment: no description Blinding: no description Drop-outs: 8 participants dropped out (2 in fluoxetine, 2 in depression control group, 1 in Jieyu Huoxue Decoction, 3 in no depression control)
Participants	Country: China Setting: mixed inpatient and outpatient Stroke criteria: ischaemic stroke within 1 month of stroke onset, clinical diagnosis plus confirmation by imaging. Did not state whether a visible lesion was needed to make a diagnosis Depression: psychiatric interview using DSM IV, Zung SDS $\geq$ 41 Included those with no previous psychiatric history 54 patients with post-stroke depression were randomised 18 received fluoxetine plus usual care, 18 received usual care only and 18 received Jieyu Huoxue decoction Of the 54 patients with depression randomised, mean age: 71.5 ± 6.7 years, 24 men
Interventions	Treatment: fluoxetine 20 mg daily plus usual stroke care Control: usual stroke care Duration of treatment: 60 days Duration of follow-up (post treatment to study end): 0 weeks
Outcomes	Zung SDS ADL - although score not referenced, so not used in analysis MESSS Reported side effects in fluoxetine group but not in the control group Unclear how side effects were collected
Notes	Excluded: previous stroke, previous depression, and severe cardiac, pulmonary, hepatic and renal diseases

Risk of bias

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

Feng 2004 (*Continued*)

Random sequence generation (selection bias)	Unclear risk	Method not stated
Allocation concealment (selection bias)	Unclear risk	No description
Incomplete outcome data (attrition bias) All outcomes	High risk	8 participants dropped out (2 in fluoxetine group, 2 in the depression control group, 1 in the Jieyu Huoxue decoction, 3 in no depression control)
Selective reporting (reporting bias)	Unclear risk	No protocol
Other bias	Unclear risk	Baseline balanced. Funding source not stated, so categorised as 'unclear risk'
Blinding of participants and personnel (performance bias) All outcomes	High risk	No placebo
Blinding of outcome assessment (detection bias) All outcomes	High risk	No blinding

Finkenzeller 2009

Methods	3-arm trial: sertraline plus psychotherapy versus psychotherapy alone versus sertraline alone. We are using the sertraline plus psychotherapy versus psychotherapy alone comparison Randomisation: by 'flicking a coin' Allocation concealment: not described Blinding: not described
Participants	Country: Germany Stroke diagnosis: ICD-9 or 10 (ischaemic cerebral infarction or haemorrhage) Mood: HAMD > 14 on 17-point version Treatment: 25 people, age 71.7 ± 7.1 years; 50% men Control: 27 people, age 65.8 ± 12.6 years; 41% men Time since stroke (days): 25.5 ± 12.2 in sertraline plus psychotherapy and 28.0 ± 16.6 in sertraline alone
Interventions	Treatment: sertraline 50 mg or 100 mg for 4 to 8 weeks (unclear how dose was decided) plus psychotherapy Control: psychotherapy alone Duration of treatment: 4 to 8 weeks Duration of follow-up (end of treatment to study end): 0

Finkenzeller 2009 (*Continued*)

Outcomes	Change in 17-item HDRS Change in HADS BI Extended BI	
Notes	Excluded: current or previous psychiatric history excluded including patients with substance abuse, personality disorders, higher levels of cognitive disorders including dementia, aphasia, acute suicidal ideation, delirium or renal failure excluded (creatinine > 2 mg/dL or urea > 40 mg/dL)	
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Randomised by flicking a coin
Allocation concealment (selection bias)	Unclear risk	Not described
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not described
Selective reporting (reporting bias)	Unclear risk	No protocol
Other bias	Low risk	Baseline balanced. Funded by an independent research grant from Pfizer Pharma GmbH, Karlsruhe (we have categorised this as low risk as the grant was 'independent')
Blinding of participants and personnel (performance bias) All outcomes	High risk	No placebo used
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not described

Fruehwald 2003

Methods	Parallel design Randomisation: permutated block design Allocation concealment: centralised Blinding: double blind; participants: yes; relatives: yes; clinical examiners: yes; nursing staff: yes Analysis: per protocol: Withdrawals: death (1 treatment), withdrawn owing to AEs (1 treatment, 2 control), all excluded from analysis
Participants	Location: Austria Setting: inpatients Treatment: 28 people, mean ± SD age 65 ± 14 years, 46% men Control: 26 people, mean ± SD age 64 ± 14 years, 71% men Stroke criteria: ischaemic stroke and PICH; diagnosis via clinical signs and CT (100%) ; stroke on average 11 days prior to randomisation Depression criteria: psychiatric interviews, HDRS score > 15 Other entry criteria: not stated Comparability of treatment groups: non-significant trend towards more females and right-sided strokes in treatment group
Interventions	Treatment: fluoxetine 20 mg daily, dose escalation at 4 weeks if HDRS score > 13 Control: matched placebo Duration of treatment: 12 weeks Duration of follow-up (end of treatment to study end): 15 months
Outcomes	Depression: change in scores from baseline to end of treatment of HDRS, BDI and CGI (item 1) Proportion of responders (< 13 HDRS) Additional: SSS Death AEs (selected data) Unable to use: RS, BI, MMSE (data not presented at follow-up) AEs data on dizziness, nausea and cephalalgia (data not presented by group)
Notes	Exclusion criteria: MMSE < 20, more than mild communication deficit, diseases of the central nervous system and previous neurodegenerative or expansive neurological disorders

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Computerised randomisation, using random permutated block design
Allocation concealment (selection bias)	Low risk	Centralised concealment

Fruehwald 2003 (*Continued*)

Incomplete outcome data (attrition bias) All outcomes	High risk	4/54, per protocol analysis
Selective reporting (reporting bias)	Unclear risk	No protocol
Other bias	Unclear risk	Baseline balanced The medication was supplied by Lannacher Heilmittel, Lannach, Austria All patients were randomly assigned to either fluoxetine or placebo treatment by the drug company independently of the research teams and the study centres
Blinding of participants and personnel (performance bias) All outcomes	Low risk	States blinded, used matching placebo
Blinding of outcome assessment (detection bias) All outcomes	Low risk	States blinded

GlaxoSmithKline 1998

Methods	Parallel group Randomisation: not stated Allocation concealment: not described Blinding: not described Analysis: according to treatment group
Participants	Location: not stated Setting: not stated Stroke criteria: "documented diagnosis of stroke within 12 months prior to screening" Mood: MADRS score > 17 Treatment: 112 people, age 64.3 ± 11.4 years, 61 men Control: 117 people, 65.6 ± 10.5 years, 64 men
Interventions	Treatment: paroxetine 20 to 50 mg daily Control: placebo (not stated whether matching) Duration of treatment: 8 weeks Duration of follow-up (treatment to study end): 0 weeks
Outcomes	Change from baseline to endpoint in MADRS Proportion of participants scoring < 8 on the MADRS total score at the endpoint (we used this in our analysis) Changes from baseline to endpoint on the BI Change from baseline to endpoint on RS score Change from baseline to endpoint on the Clinical Global Improvement Severity of Illness Score (CGI-S Proportion of responders based on CGI-Global Improvement (CGI-G)

GlaxoSmithKline 1998 (*Continued*)

	score (score of < 4) at endpoint GI side effects reported, but unclear whether these are 'events' or 'patients', so we cannot use these data. It is not clear how the side effects were collected Withdrawal from study
Notes	Excluded: concurrent psychiatric disorders, concurrent psychotropic pharmacotherapy, patients who posed a suicidal risk, patients with substance abuse/dependence, concurrent psychotropic pharmacotherapy, MMSE < 24, participating in another clinical trial, serious medical condition or clinically significant finding on screening or baseline evaluation that would preclude the administration of paroxetine and an intolerance to paroxetine

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Randomisation method not described
Allocation concealment (selection bias)	Unclear risk	Allocation concealment: not described
Incomplete outcome data (attrition bias) All outcomes	High risk	20 in each group dropped out
Selective reporting (reporting bias)	Unclear risk	No protocol
Other bias	Unclear risk	Insufficient information to make clear judgement. Source of funding not stated, but we assume it was funded by GlaxoSmithKline
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Blinding not described, used placebo but not stated whether identical
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Blinding not described

Guo 2009

Methods	Parallel group, 3-arm trial, comparing sertraline plus routine care versus routine care versus acupuncture plus routine care. We are using the sertraline plus routine care versus routine care in this review Aim: to treat depression Randomisation: random number table Allocation concealment: not described Blinding: blinding of outcome assessors Analysis: according to allocated treatment Drop-outs: none
Participants	Country: China Setting: unknown Stroke criteria: first ever stroke, clinical diagnosis plus relevant lesion on imaging, age ≥ 60 years old Depression criteria: HAMD score ≥ 8, no depression prior to stroke Treatment: 40 people, mean age 67.6 ± 12.43 years, 23 men Control: 40 people, mean age 64.5 ± 12.07 years, 22 men
Interventions	Treatment: sertraline 50 mg daily plus stroke care (acute, secondary prevention, rehabilitation and psychotherapy) Control: stroke care (acute, secondary prevention, rehabilitation and psychotherapy) Duration of treatment: 6 weeks Duration of follow-up: (treatment end to study end): 6 months
Outcomes	HAMD NIHSS FIM (reported cognition and mobility scores only) SF-36 AEs not reported
Notes	Exclusions: psychiatric disorders or family psychiatric disorders, severe cognitive impairment, global aphasia, sensory aphasia, apraxia, severe cardiac, hepatic, renal, lung or other severe somatic disorder, consciousness disturbance, severe deafness, family or patient unable to comply

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Random number table
Allocation concealment (selection bias)	Unclear risk	Not described
Incomplete outcome data (attrition bias) All outcomes	Low risk	No drop-outs, analysed by allocated treatment
Selective reporting (reporting bias)	Unclear risk	No protocol

Guo 2009 (*Continued*)

Other bias	Low risk	No obvious risk, balance baseline. Funded by a Local scientific academic fund
Blinding of participants and personnel (performance bias) All outcomes	High risk	No placebo
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome assessor blind

He 2004

Methods	Parallel group Randomisation: 'according to recruitment sequence' Allocation concealment: not described Blinding: of participants: not described; of those delivering intervention: no; of outcome assessors: yes Analysis: according to treatment allocation Drop-outs: 13 dropped out after randomisation
Participants	Location: China Setting: inpatient Inclusion criteria: all pathological types of stroke, clinical diagnosis plus confirmation by imaging (did not state that a visible lesion was needed to make the diagnosis), first ever stroke Depression diagnosis: 'HAMD scores'. Translation of paper: did not have to have depression at recruitment Treatment: 36 people, mean age 70.8 ± 6.7 years, 25 men Control: 35 people, mean age 70.4 ± 6.8 years, 23 men
Interventions	Treatment: fluoxetine 20 mg daily plus usual stroke care Control: usual stroke care Duration of treatment: 8 weeks Duration of follow-up (treatment end to study end): 0
Outcomes	HAMD SSS No description of how side effects were collected
Notes	Exclusion: psychiatric disorders, dysphasia, consciousness disturbance, agnosia, severe dementia Reported that there were no AEs, so we have assumed no seizures or GI side effects

Risk of bias

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

He 2004 (*Continued*)

Random sequence generation (selection bias)	Unclear risk	Not described
Allocation concealment (selection bias)	Unclear risk	Not described
Incomplete outcome data (attrition bias) All outcomes	High risk	13 dropped out after randomisation
Selective reporting (reporting bias)	Unclear risk	No protocol
Other bias	Low risk	Balanced baseline, no obvious risks. Funded by Local scientific academic fund
Blinding of participants and personnel (performance bias) All outcomes	High risk	No placebo
Blinding of outcome assessment (detection bias) All outcomes	Low risk	"Outcome assessors blind"

He 2005

Methods	Parallel design. 3 groups: paroxetine, paroxetine plus psychotherapy, control. We are using paroxetine and control data in this review Randomisation: "according to age, sex, stroke type, neurological function deficit", and level of depression/anxiety Allocation concealment: unknown Blinded: unclear Analysis: according to treatment group Drop-outs: none
Participants	Location: China Setting: inpatient Stroke criteria: first ever stroke; ischaemic and haemorrhagic, timing: "acute", clinical diagnosis plus confirmation by imaging (though not clear that a stroke lesion had to be present or not) Mood criteria: meets ICD-10 organic depression and organic anxiety diagnostic criteria on psychiatric interview, HAMD score $\geq$ 17 and HAMA score $\geq$ 14 Treatment: 27 people, mean age 62.4 ± 6.1 years, 14 men Control: 27 people, mean age 63.2 ± 5.7 years, 16 men
Interventions	Treatment: paroxetine 20 mg plus routine stroke treatment Control: routine stroke treatment Duration of treatment: 6 weeks Duration of follow-up: end of treatment to study end: 0

He 2005 (*Continued*)

Outcomes	SSS BI HAMD HAMA TESS Also reported GI upset and dizziness. They did not list any seizures in the list of AEs, so we are assuming no seizures in either groups Unclear how side effects were collected
Notes	Exclusion: previous psychiatric disorder, antidepressants and "nerve block agents" in recent 3 months, severe cognitive impairment, aphasia, severe cardiac, hepatic and renal function impairment, allergy to paroxetine, severe suicidal behaviour The authors mentioned using the SDS and the SAS for evaluation, but they did not report the results of SDS and SAS

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Method not described
Allocation concealment (selection bias)	Unclear risk	Not described
Incomplete outcome data (attrition bias) All outcomes	Low risk	No drop-outs, analysed according to treatment group
Selective reporting (reporting bias)	High risk	No protocol, the authors mentioned using the SDS and the SAS for evaluation but they did not report the results
Other bias	Low risk	Balanced baseline. Funded by a local scientific academic fund
Blinding of participants and personnel (performance bias) All outcomes	High risk	No placebo
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not described

Hu 2002

Methods	Parallel design Aim: to study effect of antidepressants on depressive symptoms and nervous function Randomisation: stated, but method not described Allocation concealment: not described Blinding: not described Drop-outs: none
Participants	Country: China Setting: inpatient Stroke criteria: all pathological stroke types, clinical diagnosis plus confirmation by imaging (though unclear whether a relevant lesion had to be visible), onset of stroke 0.5 to 2 months, no obvious aphasia Depression: according to CCMD-II-R Treatment: 42 people, mean age 61.4 ± 3.6 years, 32 men Control: 30 people, mean age 60 ± 4.8 years, 23 men
Interventions	Treatment: fluoxetine 20 mg daily Control: no other antidepressant Duration of treatment: 8 weeks Duration of follow-up (end of treatment to study end): 0
Outcomes	HAMD MESSS However, these data were not usable, as they were reported as proportions above or below "decrement levels" Reported side effects but unclear how this was done None left the trial early
Notes	-

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Randomisation method not described
Allocation concealment (selection bias)	Unclear risk	Not described
Incomplete outcome data (attrition bias) All outcomes	Low risk	No drop-outs
Selective reporting (reporting bias)	Unclear risk	No protocol
Other bias	Unclear risk	Balanced baseline, no other obvious risks. Source of funding not stated

Hu 2002 (*Continued*)

Blinding of participants and personnel (performance bias) All outcomes	High risk	No placebo
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not described

Huang 2002

Methods	Parallel design Aim: efficacy and tolerance of fluoxetine in early post-stroke depression Randomisation: method not stated Allocation concealment: not described Blinding: not described Analysis: according to treatment group Drop-outs: none
Participants	Country: China Setting: inpatient Stroke criteria: first ever stroke, with single unilateral lesion, clinical diagnosis with imaging consistent with stroke, both ischaemic and haemorrhagic, recruited 2 weeks after stroke onset Depression criteria: CCMD II-R depression diagnosis Treatment: 40 people, age and gender not stated Control: 40 people, age and gender not stated Patients in the treatment and control groups were selected from a group of 168 first ever acute stroke patients with average age of 62 ± 8.1 years, 76 men
Interventions	Treatment: fluoxetine 20 mg daily Control: placebo Duration of treatment: 4 weeks Duration of follow-up (treatment end to study end): 0
Outcomes	HAMD CSS Did not report death Unclear how AEs were reported
Notes	No obvious AEs were found, but they did not specifically report seizures

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Method not stated

Huang 2002 (*Continued*)

Allocation concealment (selection bias)	Unclear risk	Method not stated
Incomplete outcome data (attrition bias) All outcomes	Low risk	No drop-outs, analysed according to treatment group
Selective reporting (reporting bias)	Unclear risk	No protocol
Other bias	Unclear risk	No description of the differences between treatment and control group in baseline characteristics. Source of funding not stated
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Placebo used, but unclear if identical
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not described

Ji 2000

Methods	Parallel design Aim: to study effect of fluoxetine in treatment of depression after stroke Randomisation: method not described Allocation concealment: not described Blinding: not described Drop-outs: none
Participants	Country: China Setting: outpatient Stroke: clinical diagnosis plus confirmation of relevant lesion on imaging Depression: severe depression criteria of CCMD-II-R and HAMD score > 20 Other inclusion/exclusion criteria not stated Treatment: 20 people, age and gender not described Control: 20 people, age and gender not described
Interventions	Treatment: fluoxetine 20 mg daily, plus routine treatment and supportive psychotherapy Control: routine treatment and supportive psychotherapy Duration of treatment: 8 weeks Duration of follow-up (end of treatment to study end): 0
Outcomes	HAMD Did not report side effects No drop-outs, no deaths
Notes	-

Ji 2000 (*Continued*)

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Method not described
Allocation concealment (selection bias)	Unclear risk	Not described
Incomplete outcome data (attrition bias) All outcomes	Low risk	No drop outs
Selective reporting (reporting bias)	Unclear risk	No protocol
Other bias	Unclear risk	Balanced baseline Source of funding not stated
Blinding of participants and personnel (performance bias) All outcomes	High risk	No placebo
Blinding of outcome assessment (detection bias) All outcomes	High risk	Not described

Jia 2005

Methods	Parallel design Aim: to determine the effect of early intervention for post stroke depression on movement after 3 months of stroke Randomisation: method not stated Allocation concealment: not stated Blinding: none Drop-outs: 6 in treatment group (2 refused allocation), 4 in control group (2 refused allocation)
Participants	Country: China Setting: inpatient Inclusion: aged 40 to 75 years, all pathological types of stroke, clinical diagnosis plus confirmation by imaging (did not state whether a relevant lesion had to be present to make a diagnosis), able to give informed consent Depression diagnosis: Zung SDS > 41 for screening for depression, HDRS for evaluation of the depression severity level Treatment: 92 people randomised, 90 accepted allocation, mean age 55.6 ± 6.5 years, 60 men Control: 92 people randomised, 90 accepted allocation, mean age 55.1 ± 6.8, 55 men

Jia 2005 (*Continued*)

Interventions	Treatment: either fluoxetine or sertraline (given sertraline if also had anxiety) plus routine stroke care Control: routine stroke care Duration of treatment: 3 months Duration of follow-up: 3 years but the authors did not describe the extent of neurological function damage and HAMD scores in the third year
Outcomes	HAMD Extent of neurological damage Recurrent stroke Death Did not report AEs
Notes	Excluded: organic psychiatric disorders such as Alzheimer's disease or degenerative disease, functional disorders such as schizophrenia and affective disorders

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Not described
Allocation concealment (selection bias)	Unclear risk	Not described
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	10/184 (5.4%)
Selective reporting (reporting bias)	Unclear risk	No protocol
Other bias	Unclear risk	Balanced baseline Source of funding not stated
Blinding of participants and personnel (performance bias) All outcomes	High risk	No placebo
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No blinding

Kong 2007

Methods	Parallel Aim: to study whether fluoxetine could prevent post-stroke depression and improve neurological function Randomisation: computer-generated table of random digits Allocation concealment: not described Blinding: all blind Drop-outs: 17
Participants	Country: China Setting: inpatient Stroke: met diagnostic criteria of various cerebrovascular diseases formulated in the 4th National Cerebrovascular Disease conference and confirmed as stroke by CT or MRI, all hemiplegic, within 7 days of onset HAMD score of no depression Treatment: 48 people, mean age 64 ± 7 years, 60% men Control: 42 people, mean age 62 ± 7 years, 57% men
Interventions	Treatment: fluoxetine 20 mg daily Control: matching placebo capsules Duration of treatment: 8 weeks Duration of follow-up (end of treatment to end of study): 0
Outcomes	HAMD BI NIHSS Reported "somatic side effects and hyponatraemia" but not death or other side effects Authors state that "side effect rating was assessed at each visit" but unclear how this was done
Notes	Exclusion: major depression, current antidepressants, allergy to fluoxetine, substance abuse, bipolar disorder, schizophrenia, MMSE ≤ 23/30, substance abuse, obvious liver and renal deficit

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Computer-generated table of random digits
Allocation concealment (selection bias)	Unclear risk	Not described
Incomplete outcome data (attrition bias) All outcomes	High risk	17/90 drop-outs
Selective reporting (reporting bias)	Unclear risk	No protocol
Other bias	Unclear risk	Balanced baseline Source of funding not stated. Fluoxetine

Kong 2007 (*Continued*)

		and placebo were supplied by Lilly Pharmaceutical Company
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Identical capsules, participants blinded
Blinding of outcome assessment (detection bias) All outcomes	Low risk	States that researchers were blinded

Lai 2006

Methods	Parallel design Randomisation: randomised stated, method unclear Allocation concealment: unclear Blinding: unclear Analysis: analysed according to allocated treatment groups Drop-outs: none
Participants	Location China Setting: inpatients Treatment: 40 people Control: 40 people Total: mean age 60 ± 14 years, 43 men Stroke criteria: unclear stroke types, clinical diagnosis plus brain imaging (though not clear that stroke lesion had to be present), acute stroke Depression criteria: HAMD at least 7, or Zung SDS > 53, but no clear description about using which scale for inclusion criteria Other entry criteria: none stated Comparability of treatment groups: unclear
Interventions	Treatment: paroxetine 20 mg daily Control: placebo Duration: treatment continued for 2 months Duration of follow-up (end of treatment to end of study): 0
Outcomes	Depression: HAMD, Zung SDS (abnormal if the score is > 53) Additional: Zung SAS (abnormal is the score is > 50) Death The author described that they recorded AEs but they did not report any AEs
Notes	Exclusion criteria: unclear

Risk of bias

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

Lai 2006 (*Continued*)

Random sequence generation (selection bias)	Unclear risk	Method not stated
Allocation concealment (selection bias)	Unclear risk	Not stated
Incomplete outcome data (attrition bias) All outcomes	Low risk	No patient dropped out
Selective reporting (reporting bias)	High risk	No protocol, stated that they would evaluate side effects but these were not reported
Other bias	Unclear risk	Demographic details at baseline not described. Source of funding not stated
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Placebo used, not stated if matching
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated

Li 2002

Methods	Parallel trial Randomisation: according to the case sequence (odd number was paroxetine group, and even number was control group) Allocation concealment: unclear Blinding: unclear Analysis: according to allocated treatment group Drop-outs: none
Participants	Location: China Setting: not stated Treatment: 46 people, mean age 66 ± 5 years, 22 men Control: 46 people, mean age 64 ± 5 years, 20 men Stroke criteria: ischaemic stroke, clinical diagnosis plus brain imaging (though not clear that stroke lesion had to be present) Depression diagnosis: DSM III-R criteria diagnosed 2 weeks after stroke onset
Interventions	Treatment: fluoxetine 20 mg plus usual care Control: usual care (note, no placebo) Duration of treatment: 1 month Duration of follow-up (treatment end to study end): 0
Outcomes	Neurological function defect scale (this is the same as the CSS) HDRS Cerebral blood flow

Li 2002 (*Continued*)

	EEG No deaths or AEs reported	
Notes	Excluded previous stroke and previous TIA	
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	High risk	"According to case sequence"
Allocation concealment (selection bias)	High risk	"According to case sequence"; researchers would be able to predict treatment allocation
Incomplete outcome data (attrition bias) All outcomes	Low risk	No drop-outs
Selective reporting (reporting bias)	Unclear risk	No protocol
Other bias	Unclear risk	Baseline balanced Source of funding not stated
Blinding of participants and personnel (performance bias) All outcomes	High risk	No placebo
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unknown

Li 2004a

Methods	Parallel group Aim: to study effects of fluoxetine on neurological impairment and post-stroke depression Randomisation: computer random numbers Allocation concealment: opaque, sealed up, serial numbered envelopes Blinding: not described Drop-outs: none
Participants	Location: China Setting: inpatient Stroke: inclusion: all pathological types, clinical diagnosis plus confirmation by imaging that relevant lesion visible, CSS 16 to 30 Depression criteria: HAMD scores $\geq$ 17 and DSM IV diagnostic criteria Treatment: 33 people, mean age 60.33 years, 24 men Control: 34 people, mean age 60.44 years, 23 men

Li 2004a (*Continued*)

Interventions	Treatment: fluoxetine 20 mg daily plus routine acute stroke care Control: routine acute stroke care Duration of treatment: 4 weeks Duration of follow-up (end of treatment to end of study): 0
Outcomes	CSS Depression incidence Laboratory monitoring parameters AEs (method of reporting not stated)
Notes	Excluded severe psychiatric disorders, severe cardiac, pulmonary, hepatic and renal disease

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Computer random numbers
Allocation concealment (selection bias)	Low risk	Opaque sealed envelopes
Incomplete outcome data (attrition bias) All outcomes	Low risk	No drop-outs
Selective reporting (reporting bias)	Unclear risk	No protocol
Other bias	Unclear risk	Balanced baseline Source of funding not stated
Blinding of participants and personnel (performance bias) All outcomes	High risk	No placebo
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not described

Li 2004b

Methods	Parallel design Aim: to treat depression Randomisation: not stated Allocation concealment: not described Blinding: not stated Drop-outs: 6 in treatment and 4 in control group

Li 2004b (*Continued*)

Participants	Country: China Setting: inpatient Stroke criteria: ischaemic stroke, clinical diagnosis plus imaging confirmation (though not clear that a relevant lesion had to be seen), stroke onset time ≤ 7 days Depression criteria: HAMD score ≥ 8 Treatment: 37 people, age 48 to 87 years, 17 men Control: 36 people, age 53 to 82 years, 15 men
Interventions	Treatment: fluoxetine 20 mg daily plus usual stroke care Control: usual stroke care Duration: 8 weeks Duration of follow-up (treatment end to study end): 0
Outcomes	HAMD CSS (cannot use as reported as a categorical variable) MMSE (reported as a dichotomous variable) BI (reported as a dichotomous variable) Data for continuous variables not provided Death reported Side effects in only treatment group reported, not control group. Method of reporting side effects not stated
Notes	Exclusion: previous depression or psychiatric interview, dementia (according to MMSE scores), aphasia, severe cardiac, pulmonary, hepatic, renal function impairment, consciousness disturbance Note that the sum of numbers in each category of HAMD at 8 weeks in the control group adds up to 30, not 32

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Method not described
Allocation concealment (selection bias)	Unclear risk	Method not described
Incomplete outcome data (attrition bias) All outcomes	High risk	10/73 dropped out
Selective reporting (reporting bias)	Unclear risk	No protocol
Other bias	Unclear risk	Baseline balanced. Source of funding not stated
Blinding of participants and personnel (performance bias) All outcomes	High risk	No placebo

Li 2004b (*Continued*)

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated

Li 2005

Methods	Parallel design Improvement of post-stroke depression and augmentation of rehabilitation Randomisation: not described Allocation concealment: unknown Blinding: unclear
Participants	Country: China Setting: inpatient Stroke criteria: all stroke, clinical diagnosis plus confirmation on imaging (though not clear whether a relevant lesion had to be present) Depression according to CCMD-II-R Treatment: 74 patients Control: 74 patients Patients in the treatment and control groups were selected from a group of 368 stroke patients with an average age of 57 ± 11.8 years, age range 33 to 84 years, 240 men
Interventions	Treatment: paroxetine 20 mg daily plus routine stroke treatment Control: routine stroke treatment Duration of treatment: 4 weeks Duration of follow-up (end of treatment to study end): 0
Outcomes	HAMD SSS Deaths Side effects not recorded
Notes	Excluded: previous psychiatric disorders, severe dementia, aphasia, consciousness disturbance

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Randomisation method not described
Allocation concealment (selection bias)	Unclear risk	No description
Incomplete outcome data (attrition bias) All outcomes	Low risk	Analysed according to allocated treatment group, no participant dropped out
Selective reporting (reporting bias)	Unclear risk	No protocol

Li 2005 (*Continued*)

Other bias	Unclear risk	No description of differences between treatment and control group Source of funding not stated
Blinding of participants and personnel (performance bias) All outcomes	High risk	No placebo
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated whether blinded

Li 2006

Methods	Parallel group Randomisation: not described Blinding: unclear Drop-outs: 2 in treatment group, 4 in control group
Participants	All pathological types of stroke, CT or MRI needed for diagnosis Inclusion criteria: depression diagnosed by Chinese Classification of Mental Disorders 3 and HAMD $\geq$ 18, no previous organic brain disorder, and no previous psychiatric history, clear consciousness, no comprehension problems, normal language, first acute stroke, first episode of depression Treatment: 52 people, mean ± SD age 61.12 ± 10.25, 32 men Control: 53 people, mean ± SD age 60.89 ± 9.12, 35 men
Interventions	Treatment: citalopram 20 mg daily plus usual care Control: usual care Duration of treatment: 12 weeks Duration of follow-up (end of treatment to end of study): 0
Outcomes	HDRS (also known as HAMD) BI CSS MMSE Side effects reported according to the patient's complaints and observation, no description of who recorded AEs; and reported only for the treatment group
Notes	-

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	No description

Li 2006 (*Continued*)

Allocation concealment (selection bias)	Unclear risk	No description
Incomplete outcome data (attrition bias) All outcomes	High risk	2 drop-outs in treatment group, 4 in control group. 1 in treatment group died, and 2 in the control group died (i.e. > 5%)
Selective reporting (reporting bias)	Unclear risk	No protocol
Other bias	Unclear risk	Baseline balanced Source of funding not stated
Blinding of participants and personnel (performance bias) All outcomes	High risk	No placebo
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No description

Li 2008

Methods	Parallel trial, 3 (fluoxetine versus "free and easy wandering" versus placebo), we are using the fluoxetine versus placebo comparison in this review Randomisation: computer-generated randomisation Allocation concealment: not described Blinding: participants, those delivering the intervention and outcome assessors Drop-outs: 2 in fluoxetine group, 2 in placebo group
Participants	Country: China Setting: unclear Stroke criteria: by neuroimaging, ischaemic or PICH Depression diagnosis: "each patient was evaluated by a psychiatrist", HAMD > 20 included Fluoxetine group: 60 people, mean age 69.2 ± 3.5 years, men 41.6% Control: 30 people, mean age 67.8 ± 3.9 years, men 56.7%
Interventions	Treatment: fluoxetine 20 to 40 mg daily Control: placebo Duration of treatment: 8 weeks Duration of follow-up (treatment end to study end): 0
Outcomes	HAMD BI Description of why patients left the trial early AEs (reported by patient or observed/elicited by physician at each visit)

Li 2008 (*Continued*)

Notes	Excluded psychiatric illness other than depression, antidepressants within previous 2 weeks, MMSE < 23, severe aphasia Note twice as many in fluoxetine than control group

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated random numbers
Allocation concealment (selection bias)	Unclear risk	Unclear
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	4/90 dropped out (< 5%)
Selective reporting (reporting bias)	Unclear risk	No placebo
Other bias	Low risk	Balanced baseline. Funded by the Natural Science Foundation of Shandong Province, People's Republic of China. None of authors had financial ties with the companies producing the medications in this study
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Paper states blinded, used placebo (though unclear if matching)
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Blinded

Liang 2003

Methods	Parallel group Aim: treat depression and augment rehabilitation Randomisation: according to admission sequence Allocation concealment: not described Blinding: not described Dropouts: none
Participants	Country: China Setting: inpatient Stroke: clinical diagnosis plus confirmation by imaging (though not clear that a stroke lesion had to be present), MESSS ≥16, stroke onset in previous month, age ≤ 80 years old, absence of aphasia Depression: depression lasts for ≥ 2 weeks, DSM III-R depression, HAMD scale score ≥13

Liang 2003 (*Continued*)

	Treatment: 42 people, mean age 59.5 ± 7.9 years, 17 men Control: 21 people, mean age 61.8 ± 7.8 years, 10 men
Interventions	Treatment: fluoxetine 20 mg daily plus routine stroke care Control: routine stroke care Duration of treatment: 4 weeks Duration of follow-up (treatment end to study end): 0
Outcomes	HAMD MESSS Described AEs; no mention of seizures. Method of recording side effects not stated
Notes	Note twice as many in treatment compared with control group

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	High risk	Randomisation "according to admission sequence"
Allocation concealment (selection bias)	Unclear risk	Not described
Incomplete outcome data (attrition bias) All outcomes	Low risk	No drop-outs
Selective reporting (reporting bias)	Unclear risk	No protocol
Other bias	Unclear risk	Note twice as many in treatment compared with control group - unclear if this was intentional. Source of funding not stated
Blinding of participants and personnel (performance bias) All outcomes	High risk	No placebo
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not described

Liu 2004

Methods	Parallel design Randomisation: random number table, minimisation on age, gender and clinical condition Allocation concealment: not stated Blinding: states double-blind, but those who are blinded are not stated Analysis: according to allocated treatment group. Drop-outs: none
Participants	Location: China Setting: inpatient Treatment: 30 people, mean age 53 ± 10 years, 20 men Control: 30 people, mean age 58 ± 10 years, 18 men Stroke criteria: hemispheric stroke (infarct or haemorrhage). Clinical diagnosis of stroke plus confirmation by imaging. Did not state whether a visible lesion had to be present Around 2 weeks after stroke onset Anxiety criteria: HAMA $\geq$ 14 Other entry criteria: > 40 years, clear consciousness Comparability of treatment groups: no difference between treatment and control in age, sex, stroke type and level of clinical condition
Interventions	Treatment: fluoxetine 20 mg daily and alprazolam 0.2 mg 3 times a day for 60 days, plus usual stroke care Control: alprazolam 0.2 mg 3 times a day for 60 days, plus usual stroke care Duration of treatment: 60 days Duration of follow-up (treatment end to study end): 0
Outcomes	HAMA BI Modified SSS AEs reported, but not stated how data were collected
Notes	Exclusion criteria: personal or family history of psychiatric disorders, accompanied by psychiatric disorders other than depression and anxiety, severe cognitive impairment, obvious aphasia including partial motor aphasia without sensory aphasia, severe heart failure, respiratory failure, lung cancer or other severe physical diseases preventing the participants from coming to examinations

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Random number table
Allocation concealment (selection bias)	Unclear risk	Not stated
Incomplete outcome data (attrition bias) All outcomes	Low risk	No drop-outs

Liu 2004 (*Continued*)

Selective reporting (reporting bias)	Unclear risk	No protocol
Other bias	Unclear risk	Baseline balanced. Source of funding not stated
Blinding of participants and personnel (performance bias) All outcomes	High risk	Stated double blind, but those who were blinded were not stated, no placebo used
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Stated double blind, but those who were blinded were not stated

Liu 2006

Methods	Parallel design Aim: to study effect of citalopram on post-stroke depression and neurological functional rehabilitation Randomisation: method not described Allocation concealment: not described Blinding: not stated
Participants	Country: China Setting: inpatient Stroke criteria: stroke during "recovery phase" at 6 to 9 months, NIHSS score $\geq$ 13, HAMD score $\geq$ 17 60 people randomised, of whom 38 were men, mean age 60.7 ± 8.6 years. Demographics for treatment and control groups were not provided Treatment: 30 people, age and gender not stated Control: 30 people, age and gender not stated
Interventions	Treatment: citalopram 20 mg daily plus routine stroke care Control: routine stroke care Duration of treatment: 6 weeks Duration of follow-up (treatment end to study end): 0
Outcomes	HAMD NIHSS BI Death
Notes	Exclusion criteria: previous psychiatric disorder, dementia, aphasia, consciousness disturbance. AEs not reported

Risk of bias

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

Liu 2006 (*Continued*)

Random sequence generation (selection bias)	Unclear risk	Method not described
Allocation concealment (selection bias)	Unclear risk	Not described
Incomplete outcome data (attrition bias) All outcomes	Low risk	No drop-outs
Selective reporting (reporting bias)	Unclear risk	No protocol
Other bias	Unclear risk	Baseline balance reported by authors. Source of funding not stated
Blinding of participants and personnel (performance bias) All outcomes	High risk	No placebo
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated

Meara 1998

Methods	Parallel design Randomisation: unclear Allocation concealment: unclear Blinding: reported as double-blind but those not blinded were not stated Analysis: unclear
Participants	Location: Wales, UK Setting: inpatient Treatment: unclear Control: unclear Stroke criteria: ischaemic stroke > 11 weeks prior to randomisation Depression criteria: GDS (15-item) score > 4 Other entry criteria not stated
Interventions	Treatment: sertraline 50 mg daily, dose escalation to 100 mg for non-responders at 2 weeks Control: matched placebo Duration: treatment continued for 6 weeks
Outcomes	Depression: change in scores from baseline to end of treatment on GDS Unable to use GDS, BI, MMSE, FAI, FAST Leaving trial early Death AEs

Meara 1998 (*Continued*)

Notes	Exclusion criteria: moderate to severe dementia, severe aphasia, communication difficulties, poorly controlled epilepsy Contacted author for more details but no response We could not use the data in our meta-analysis

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Method not described
Allocation concealment (selection bias)	Unclear risk	Not described
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not described
Selective reporting (reporting bias)	Unclear risk	Insufficient data to make a judgement
Other bias	Unclear risk	Insufficient data to make a judgement. Source of funding not stated
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Double blind reported, those who were blind not described
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Double blind reported, those who were blind not described

Miao 2004

Methods	Parallel group Randomisation: "simple random sampling" Allocation concealment: not described Outcome assessors: stated that they are blinded 9 not allocated (5 in treatment group refused allocation, 4 in the control group refused allocation) Drop-outs: 6 in treatment group, 7 in control group
Participants	Country: China Setting: mixed inpatient and outpatient All stroke pathological types, clinical diagnosis plus confirmation by imaging that a relevant lesion was visible, 2 to 8 months after stroke, clear consciousness, no comprehension problem, 1 lesion in 1 hemisphere, normal language comprehension Mood: depression after stroke onset, HAMD score $\geq$ 20 Patients: 90 randomised, 34 in each group at treatment end Treatment: 34 people, age 58.16 ± 8.49 years, 19 men

Miao 2004 (*Continued*)

	Control: 34 people, age 62.45 ± 8.24 years, 18 men
Interventions	Treatment: citalopram 20 mg daily plus usual stroke care Control: usual stroke care Duration of treatment: 6 weeks Duration of follow-up (treatment end to study end): 0
Outcomes	HAMD SDS Efficacy Death AEs (only in the citalopram group) Method of recording AEs was not stated
Notes	Exclusion criteria: other organic brain disorders and other aetiologies-related depression

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	"Simple random sampling" - no further description given
Allocation concealment (selection bias)	Unclear risk	Allocation not described
Incomplete outcome data (attrition bias) All outcomes	High risk	9 not allocated after randomisation, 13 drop-outs
Selective reporting (reporting bias)	Unclear risk	No protocol
Other bias	Unclear risk	Baseline balanced. Source of funding not stated
Blinding of participants and personnel (performance bias) All outcomes	High risk	No placebo
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Blinding described

Murray 2005

Methods	Parallel design Randomisation: block Allocation concealment: centralised Blinding: double blind; participants: yes; relatives: yes; clinical examiners: yes; nursing staff: yes Analysis: ITT (last observation carried forward) and per-protocol: death (2 control), no efficacy (16 treatment, 22 control), withdrawn owing to AE (8 treatment, 5 control), withdrew consent (1 control), all excluded from analysis
Participants	Location: Sweden Setting: mixed Treatment: 62 people, mean ± SD age 71 ± 10 years, 52% men Control: 61 people, mean ± SD age 71 ± 10 years, 44% men Stroke criteria: all subtypes, diagnosis by WHO criteria and CT (100%); stroke 3 to 367 days prior to randomisation (average time 128 days) Depression criteria: psychiatric interview (DSM-IV, major and minor) and MADRS > 9 Other entry criteria: > 17 years of age, stroke within the previous 12 months Comparability of treatment groups: significant trend towards more left hemisphere lesion strokes in treatment group
Interventions	Treatment: sertraline 50 mg daily; possible dose escalation to 100 mg after 4 weeks Control: matching placebo Duration of treatment: 26 weeks Duration of follow-up: (treatment end to study end): 0
Outcomes	Depression: change in scores from baseline to end of treatment on MADRS Additional: leaving the study early Death Unable to use: Scandinavian Supervision Stroke Scale, BI, Stroke Unit Mental Status, Examination social performance, treatment costs, mortality, relative's situation, neuropsychological performance, neurological recovery (data not presented) AEs (selected data presented) using a modified version of the Udvalg for Kliniske Undersogelser side effect rating scale
Notes	Exclusion criteria: under 18 years of age, severely impaired communication, apparent difficulties adhering to study protocol, acute myocardial infarction, other psychiatric illnesses other than depression, significant risk of suicide, antidepressants during the month after randomisation, current use of psychotropic medication or opiate analgesic drugs Participants with less than 20% reduction in MADRS score at 6 weeks were excluded

Risk of bias

Bias	Authors' judgement	Support for judgement

Murray 2005 (*Continued*)

Random sequence generation (selection bias)	Low risk	Block randomisation
Allocation concealment (selection bias)	Low risk	Centralised randomisation
Incomplete outcome data (attrition bias) All outcomes	Low risk	ITT as well as per protocol
Selective reporting (reporting bias)	High risk	No protocol, paper stated that ADL data and SSS data were collected, but these were not reported
Other bias	Unclear risk	Balanced baseline except that more patients had left hemisphere brain lesion in sertraline group than in placebo group (statistically significant) Funded by an unrestricted grant, study drug and placebo from Pfizer AG Sweden and grants from the AFA Insurances and Marianne and Marcus Wallenberg Foundation
Blinding of participants and personnel (performance bias) All outcomes	Low risk	States blinding and used matching placebo
Blinding of outcome assessment (detection bias) All outcomes	Low risk	States blinding

Pariente 2001

Methods	Prospective double-blind cross-over placebo controlled study of 8 patients with pure motor hemiparesis
Participants	Lacunar ischaemic stroke, assessed by brain CT "Early phase of recovery"
Interventions	Single dose of fluoxetine
Outcomes	fMRI (raw data provided) Finger tapping (presented as a graph, no raw data) NIHSS, motricity index, BI, trunk control test, Ashworth scale, somatosensory scale (no data)
Notes	We could not use these data in our meta-analyses. The authors reported that fluoxetine led to hyperactivation in the ipsi-lesional (that is on the same side as the stroke lesion) primary motor cortex during a motor task; moreover, fluoxetine significantly improved

Pariente 2001 (*Continued*)

	motor skills of the affected side (Pariente 2001)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation code kept at the centre and broken at the end of the study
Allocation concealment (selection bias)	Low risk	Randomisation code kept at the centre and broken at the end of the study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Data on fMRI appears complete
Selective reporting (reporting bias)	Unclear risk	Data on clinical outcomes were not reported
Other bias	Unclear risk	Balanced baseline. Source of funding not stated
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double blind, placebo given
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double-blind

Rasmussen 2003

Methods	Parallel design Randomisation: unclear Allocation concealment: unclear Blinding: double blind reported, those blinded not stated Analysis: ITT (last observation carried forward) and per-protocol: details of those excluded from analyses (35 treatment, 35 control) unclear
Participants	Location: Denmark Setting: unclear Treatment: 70 people, mean ± SD age 72 ± 9, 50% men Control: 67 people, mean ± SD age 68 ± 11, (51% men Stroke criteria: ischaemic and PICH; diagnosis by clinical signs and symptoms; stroke 0 to 4 weeks prior to randomisation Other entry criteria: not stated Comparability of treatment groups: participants in treatment group older on average

Interventions	Treatment: sertraline 50 mg daily; at any time after 2 weeks dose could be increased in 50 mg increments up to 150 mg daily; average dose 62.9 mg daily Control: matched placebo Duration of treatment: 12 months Duration of follow-up (end of treatment to end of study): 0
Outcomes	Depression: change in scores from baseline to end of treatment on HDRS Proportion scoring > 2 on the CGI or > 16 on the GDS at end of treatment Additional: leaving the study early. Did not report death Unable to use: HDRS, GDS, aphasia severity rating scale, European Stroke Scale, MMSE, Cambridge Cognitive Examination, SF-36, BI (data not presented) AEs (detailed data not presented) evaluated by using the Udvalg for Kliniske Undersogelser Side Effect Rating Scale Did not report death
Notes	-

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Method not stated
Allocation concealment (selection bias)	Unclear risk	Method not stated
Incomplete outcome data (attrition bias) All outcomes	Low risk	Used ITT analysis and last observation carried forward
Selective reporting (reporting bias)	Low risk	Trial details published on www.strokecentre.org/trials
Other bias	Unclear risk	Those given sertraline were slightly older (by 4 years) but this is unlikely to introduce bias. There was no significant difference between groups Funding from Pfizer A/S, Gert Jorgensen legat and the Brain Cause. It is unclear whether the drug companies had input into the design and analysis of the study
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Matched placebo
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated

Restifo 2001

Methods	Double-blind study
Participants	10 participants with disabling hemiplegia owing to hemispheric ischaemic stroke in territory of left MCA
Interventions	Treatment: fluoxetine 20 mg daily for 3 months plus usual care (including Bobath rehabilitation) Control: usual care including Bobath rehabilitation
Outcomes	Transmagnetic stimulation to establish motor reorganisation The authors reported that fluoxetine might modulate the primary motor cortex reorganisation
Notes	Abstract only, full paper could not be found by our searches

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	"Random allocation" method not described
Allocation concealment (selection bias)	Unclear risk	"Random allocation", method not described
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Unclear from abstract
Selective reporting (reporting bias)	Unclear risk	Unclear from abstract
Other bias	Unclear risk	Unclear from abstract. Source of funding not stated
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	A placebo was used, not clear if it was matching
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear from abstract

Robinson 2000a

Methods	Parallel design Comparison on fluoxetine, nortriptyline and placebo. We are using the fluoxetine and placebo data Randomisation: random number table Allocation concealment: held by independent person Blinding: unclear Analysis: per protocol, number excluded from analyses varied Data provided for depressed and non-depressed separately. We are labelling the depressed group as Robinson 2000a (this trial), and the non-depressed group as Robinson 2000b
Participants	Location: USA and Argentina Setting: mixed Treatment: 23 people with depression, mean ± SD age 65 ± 14 years; 17 men Control: 17 people with depression, mean ± SD age 73 ± 10 years; 9 men Stroke criteria: all subtypes, diagnosis by clinical signs and CT (100%), stroke within 6 months of recruitment, 18 to 85 years of age Stroke on average 16 weeks (fluoxetine) and 6 weeks (placebo) prior to randomisation
Interventions	Treatment: fluoxetine 10 mg daily (3 weeks), 20 mg daily (3 weeks), 30 mg daily (3 weeks), 40 mg daily (3 weeks) Control: matched placebo Duration: treatment continued for 12 weeks Duration of follow-up (end of treatment to end of study): 0
Outcomes	Depression: change in scores from baseline to end of treatment on HDRS Additional: MMSE, JHFI Death AEs (method of reporting these was not stated)
Notes	Exclusion criteria: other significant medical illness, severe comprehension deficit, prior history of head injury, prior history of other brain disease (with the exception of stroke) , participants on antidepressants (other than fluoxetine) were allowed to stop their antidepressant for a 2-week washout period Note difference in time since stroke between treatment groups

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Random number table
Allocation concealment (selection bias)	Low risk	Concealment held by independent person
Incomplete outcome data (attrition bias) All outcomes	Low risk	Per-protocol and ITT analyses
Selective reporting (reporting bias)	Low risk	Protocol published www.strokecentre.org/trials

Robinson 2000a (*Continued*)

Other bias	Unclear risk	Imbalance in treatment groups for time since stroke and gender Funded by NIMH grants and grants from the Raul Carrea Institute of Neurological Research and Fundacion Perez Companc. Eli Lilly and company supplied the fluoxetine and placebo
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Matched placebo
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated

Robinson 2000b

Methods	Parallel design Comparison on fluoxetine, nortriptyline and placebo. We are using the fluoxetine and placebo data Randomisation: random number table Allocation concealment: held by independent person Blinding: unclear Analysis: per protocol, number excluded from analyses varies Data provided for depressed and non-depressed separately. We are labelling the depressed group as Robinson 2000a, and the non-depressed group as Robinson 2000b (this trial)
Participants	Location: USA and Argentina Setting: mixed Treatment: 17 non-depressed people, mean ± SD age 66 ± 13 years, 15 men Control: 16 non-depressed people, mean ± SD age 67 9 years, 12 men Stroke criteria: all subtypes, diagnosis by clinical signs and CT (100%), stroke within 6 months of recruitment, aged 18 to 85 years of age Stroke on average 8 weeks (treatment) and 5 weeks (control) prior to randomisation Comparability of treatment groups: unclear
Interventions	Treatment: fluoxetine 10 mg daily (3 weeks), 20 mg daily (3 weeks), 30 mg daily (3 weeks), 40 mg daily (3 weeks) Control: matched placebo Duration: treatment continued for 12 weeks Duration of follow-up (end of treatment to end of study): 0
Outcomes	Depression: change in scores from baseline to end of treatment on HDRS Additional: MMSE, JHFI Death AEs (method of reporting these was not stated)

Robinson 2000b (*Continued*)

Notes	Exclusion criteria: other significant medical illness, severe comprehension deficit, prior history of head injury, prior history of other brain disease (with the exception of stroke) , participants on antidepressants (other than fluoxetine) were allowed to stop their antidepressant for a 2-week washout period Note difference in time since stroke between groups

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Random number table
Allocation concealment (selection bias)	Low risk	Concealment held by independent person
Incomplete outcome data (attrition bias) All outcomes	Low risk	ITT and per-protocol
Selective reporting (reporting bias)	Low risk	Trial on www.strokecentre.org/trials
Other bias	Unclear risk	Note imbalance in time since stroke and in gender. Funded by NIMH grants and grants from the Raul Carrea Institute of Neurological Research and Fundacion Perez Companc. Eli Lilly and company supplied the fluoxetine and placebo
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Matched placebo
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated

Robinson 2008

Methods	Parallel group, 3-arm (escitalopram, placebo, problem-solving therapy group). We are using the escitalopram versus placebo arm in this review Randomisation: randomised, blocks of 3, 6 and 9 within each block assigned 1 of the 3 treatments Allocation concealment: unclear Blinding: placebo and escitalopram: identical pills, outcome assessors blind Analysis: ITT Drop-outs: 5 in placebo and 7 drop-outs in escitalopram - all patients included in analysis

Robinson 2008 (*Continued*)

Participants	Country: USA Setting: mixed: neurology department and newspaper advertisements Stroke criteria: ischaemic or haemorrhagic stroke not because of complications of intracranial aneurysm or intracranial vascular malformation; within 3 months of index stroke Mood: excluded if DSM IV for major or minor depression or HAMD > 17 Treatment (escitalopram): 59 people, mean ± SD age 61.2 ± 13.7, 38 men Control (matched placebo): 58 people, mean ± SD age 63.9 ± 11.1, 37 men
Interventions	Treatment: escitalopram 5 to 10 mg (depending on age - lower dose given to > 65 years old) Control: matched placebo Duration of treatment: 12 months Duration of follow-up (treatment end to study end): 0
Outcomes	Diagnosis of depression HAMD (dichotomised) FIM (though no raw data provided in the paper for meta-analysis) Social functioning examination Repeatable Battery for Neuropyschological Status The Iowa subset provided detailed information about cognition Patients, family members and primary care physicians were asked about AEs at 3 monthly intervals or sooner if an individual reported an AE using a standardised checklist
Notes	The escitalopram group had significantly more diabetes than the placebo group Exclusion: acute coronary syndrome, neurodegenerative disorders, DSM IV criteria for alcohol or substance abuse

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Randomised blocks of 3, 6 and 9
Allocation concealment (selection bias)	Unclear risk	Not described
Incomplete outcome data (attrition bias) All outcomes	Low risk	ITT analyses, all patients used in analysis
Selective reporting (reporting bias)	Low risk	All specified outcome data reported. Trial published on www.strokecentre.org/trials
Other bias	Unclear risk	There was more diabetes in the escitalopram group than placebo group The initial report states that "This work was supported solely by National Institute of Mental Health Grant RO1MH-65134.

Robinson 2008 (*Continued*)

		All the study medications were purchased using NIMH grant funds." In a subsequent letter to the Journal, the authors disclosed honoraria and expenses from pharmaceutical companies, and that 1 of the authors owned Pfizer stock. However, the authors stated that the design and analysis of any of the expenses of the study were supported by monies, materials or any intellectual input from Forest Laboratories
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Identical placebo
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome assessors were blind

Song 2006

Methods	Aim: to evaluate changes in depression and cognitive impairment in patients with post-stroke depression treated with fluoxetine Parallel trial Randomisation: not stated Allocation concealment: not described Blinding: not described Drop-outs: none
Participants	Country: China Setting: inpatient Stroke diagnosed by clinical criteria and "proved on CT" (though not clear if lesion had to be visible) Depression: diagnosed in accordance with the CCMD-II-R Treatment: 41 people, mean age 51 ± 7 years, 25 men), time since stroke: 3.5 days Control: 41 people, mean age 50 ± 8 years, 24 men), time since stroke: 3.7 days
Interventions	Treatment: fluoxetine 20 mg daily Control: placebo (although not stated whether this was identical to fluoxetine) Duration of treatment: 6 weeks Duration of follow-up (treatment end to study end): 0 Side effects not reported
Outcomes	SDS p300 (an event-related potential) Although the stated aim was to assess cognitive impairment, it is not clear how this was measured

Song 2006 (*Continued*)

Notes	Excluded: previous mental disorders, previous "neurological disorder", if other psychiatric drugs had been taken, these had to be stopped for 1 week before fluoxetine was administered

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Method not described
Allocation concealment (selection bias)	Unclear risk	Not described
Incomplete outcome data (attrition bias) All outcomes	Low risk	No drop-outs
Selective reporting (reporting bias)	Unclear risk	Unclear
Other bias	Unclear risk	Balanced baseline. Source of funding not stated
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Placebo - but not clear whether identical
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not described

Wang 2003

Methods	Parallel design 3-arm trial: routine care, fluoxetine plus routine care, amitriptyline plus routine care. We are using the routine care and fluoxetine plus routine care in this analysis Aim: to observe effects of antidepressant therapy on post-stroke and neurological rehabilitation in the elderly Randomisation: not described Allocation concealment: not described Blinding: not described
Participants	Country: China Setting: inpatient Stroke criteria: ischaemic stroke, clinical diagnosis plus confirmation by imaging (although not clear whether a stroke lesion had to be present) Depression diagnosed according to CCMD-II-R diagnostic criteria, HAMD $\geq$ 18 Treatment: 64 people, mean age 75.6 ± 19.7 years, 39 men Control: 56 people, mean age 74.9 ± 20.8 years, 29 men

Wang 2003 (*Continued*)

Interventions	Treatment: fluoxetine 20 to 80 mg daily (start at 20 mg/day, increase dosage at 3 weeks if poor therapeutic effect and no AE), plus usual stroke care Control: usual stroke care Duration of treatment: 12 to 24 weeks Duration of follow-up (treatment end to study end): 6 to 9 months
Outcomes	HAMD Neurological function impairment score BI AEs not recorded
Notes	Excluded: psychiatric disorder history, severe cardiac, pulmonary, hepatic and renal diseases

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Method not described
Allocation concealment (selection bias)	Unclear risk	Not described
Incomplete outcome data (attrition bias) All outcomes	High risk	13 dropped out of fluoxetine group, and 9 dropped out of control group
Selective reporting (reporting bias)	Unclear risk	No protocol
Other bias	Unclear risk	Baseline appeared balanced but no statistical comparison between groups. Source of funding not stated
Blinding of participants and personnel (performance bias) All outcomes	High risk	No placebo
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not described

Wen 2006

Methods	Parallel trial Aim: to explore effects of prophylactic antidepression therapy on nerve functional rehabilitation after stroke Randomisation: not described Allocation concealment: not described Blinding: not described Analysis: according to treatment group Drop-outs: none
Participants	Country: China Setting: inpatient Stroke criteria: acute stroke of all pathological subtypes, clinical diagnosis plus confirmation by imaging (although not clear whether a stroke lesion had to be present) Treatment: 42 people, mean age 56.8 years, men 19 Control: 42 people, mean age 57.2 years, men 16
Interventions	Treatment: fluoxetine 20 mg daily plus routine stroke care Control: routine stroke care Duration of treatment: 8 weeks Duration of follow-up (end of treatment to end of study): 0
Outcomes	HAMD MESSS AEs (method of obtaining data not stated) Death
Notes	Excluded those with primary psychiatric impairment and premorbid mood disorders, pre-existing neurological disease causing confusion, severe systematic diseases and pulmonary, hepatic and renal failure

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Method not described
Allocation concealment (selection bias)	Unclear risk	Not described
Incomplete outcome data (attrition bias) All outcomes	Low risk	Analysed according to treatment group, no drop-outs
Selective reporting (reporting bias)	Unclear risk	No protocol
Other bias	Unclear risk	Balanced baseline. Source of funding not stated

Wen 2006 (*Continued*)

Blinding of participants and personnel (performance bias) All outcomes	High risk	No placebo
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not described

Wiart 2000

Methods	Purpose: to treat early depression Parallel design Randomisation: stated, method unclear Allocation concealment: unclear Blinding: double-blind reported, those blind not stated. However, the treatment and placebo were "identical white tablets" - so reasonable to assume patients and those administering the treatment were blind Analysis: ITT (last observation carried forward), withdrawn owing to AE (1 treatment) , protocol violation (1 treatment)
Participants	Location: France Setting: unclear Treatment: 16 people, mean ± SD age 66 ± 7 years, 65% men) Control: 15 people, mean ± SD age 66 ± 12 years, 40% men Stroke criteria: ischaemic stroke and PICH, diagnosis by clinical signs and CT (100%); stroke on average 47 ± 22 days (treatment group) and 48 ± 20 days (control group) Depression criteria: psychiatric interview (ICD-10 criteria) and MADRS score > 19 Other entry criteria: all antidepressant or neuroleptic drugs stopped 10 days prior to enrolment Comparability of treatment groups: balanced
Interventions	Treatment: fluoxetine 20 mg daily Control: matched placebo Duration of treatment: 45 days Duration of follow-up (treatment end to study end): 0
Outcomes	Depression: change in scores from baseline to end of treatment of MADRS, 50% reduction in MADRS score Additional: FIMs MMSE Motricity Index Leaving the study early Death AEs ("evaluated qualitatively and quantitatively". Complete blood count, liver test and renal function test were carried out at each assessment visit)

Wiart 2000 (*Continued*)

Notes	Exclusion criteria: severe psychiatric problems which required hospitalisation, severe aphasia, previous stroke, severe cognitive impairment, chronic alcoholism, chronic associated handicapping pathology, contraindication to fluoxetine

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Method of randomisation not stated
Allocation concealment (selection bias)	Unclear risk	Method not stated
Incomplete outcome data (attrition bias) All outcomes	Low risk	Used last observation carried forward
Selective reporting (reporting bias)	Low risk	Trial published on www.strokecentre.org/trials. The primary outcome was reported
Other bias	Unclear risk	Baseline balanced. Lilly France Laboratory provided methodological and financial support
Blinding of participants and personnel (performance bias) All outcomes	Low risk	"Identical white capsules" given
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Method of blinding not stated

Xie 2005

Methods	Aim: to study the effect of treatment with sertraline in elderly patients with post-stroke depression Parallel study Randomisation: yes although method not stated Allocation concealment: not described Blinding: not described Drop-outs: none
Participants	Country: China Setting: unclear Recruited "clinically stable stroke patients with post-stroke depression" No other inclusion and exclusion criteria given Mood: Zung SDS score $\geq$ 40 or GDS score 5 to 10 Treatment: 65 people, mean age 69.8 years, 29 men Control: 65 people, mean age 70.7 years, 27 men

Xie 2005 (*Continued*)

	Time since stroke: mean 87.8 days, range 48 to 142 days
Interventions	Treatment: sertraline 50 mg/day plus usual stroke care Control: usual stroke care Duration of treatment: 12 weeks Duration of follow-up: 0
Outcomes	Zung SDS, GDS, ADL score AEs were not reported
Notes	-

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Method not described
Allocation concealment (selection bias)	Unclear risk	Not described
Incomplete outcome data (attrition bias) All outcomes	Low risk	No drop-outs
Selective reporting (reporting bias)	Unclear risk	No protocol
Other bias	Unclear risk	No clear description between treatment and control. Local scientific academic fund funded the study
Blinding of participants and personnel (performance bias) All outcomes	High risk	No placebo
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not described

Xu 2001

Methods	Parallel Aim: to study the effect of fluoxetine on depression in early recovery stage of cerebral infarction Randomisation: no description of method Allocation concealment: not described Blinding: not described Drop-outs: 6 in treatment group, 4 in control group
Participants	Country: China Setting: outpatient in rehabilitation clinic Stroke: first acute cerebral infarction, no description of the diagnostic criteria and the need for imaging confirmation, excluded large cerebral infarction or lacunar infarction (clinical condition too severe or too mild); onset to recruitment time mean 30 days Zung SDS $\geq$ 40 Treatment: 32 people Control: 31 people (no details of patient characteristics)
Interventions	Treatment: fluoxetine 20 mg daily plus usual stroke care Control: usual stroke care Duration of treatment: 8 weeks Duration of follow-up (treatment end to study end): 0
Outcomes	Zung SDS ADL (BI) Neural function deficient Death AEs not reported
Notes	Excluded if previous antidepressants

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Method not described
Allocation concealment (selection bias)	Unclear risk	Not described
Incomplete outcome data (attrition bias) All outcomes	High risk	10/62 drop outs
Selective reporting (reporting bias)	Unclear risk	No protocol
Other bias	Unclear risk	No clear description of stroke criteria and imaging. Source of funding not stated

Xu 2001 (*Continued*)

Blinding of participants and personnel (performance bias) All outcomes	High risk	No placebo
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not described

Xu 2006

Methods	Parallel group Aim: to test whether early prophylactic antidepressant treatment by paroxetine has any beneficial influence on the rate of post-stroke depression and rehabilitation Randomisation: "sequence numbers" Allocation concealment: not described Blinding: not described Drop-outs: 7
Participants	Country: China Setting: inpatient Stroke criteria: stroke onset time $\leq$ 3 days, age $\leq$ 75 years old, no previous psychiatric disorders, no obvious cognitive impairment or aphasia Depression diagnosis was not mentioned as an inclusion criteria, so we assumed that patients did not have to have depression to enter the trial Treatment: 32 people, mean age 65 ± 12 years, 17 men Control: 32 people, mean age 63 ± 11 years, 16 men
Interventions	Treatment: paroxetine 20 mg daily Control: placebo Duration of treatment: 12 weeks Duration of follow-up (treatment end to study end): 0
Outcomes	MESSS ADL Post-stroke diagnosis incidence of depression according to DSM IV AEs not recorded
Notes	Exclusion: no severe hepatic or renal impairment, DSM IV depression not stated as an inclusion, but none met criteria for depression initially The number of participants in Table 1 (p187) were wrong (paroxetine/placebo: N = 32/32 should be N = 28/29)

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	"Sequence numbers" - risk unclear

Xu 2006 (*Continued*)

Allocation concealment (selection bias)	Unclear risk	Not described
Incomplete outcome data (attrition bias) All outcomes	High risk	7 patients dropped out
Selective reporting (reporting bias)	Unclear risk	No protocol
Other bias	Low risk	Baseline balance. Study funded by local scientific academic fund
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Placebo used, but unclear if it was matched
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not described

Xu 2007

Methods	3-arm trial: "fluoxetine plus usual care" versus "Wuling capsule plus usual care" versus "fluoxetine plus usual care plus Wuling capsule" We are using the "fluoxetine plus Wuling capsule plus usual care" versus "Wuling capsule and usual care" comparison Aim: to evaluate the efficacy of Wuling capsule in treating patients with post-stroke depression Randomisation: "according to the number table" Allocation concealment: not described Blinding: not described Drop-outs: 2 in fluoxetine group, 2 in combined group
Participants	Country: China Setting: unclear Stroke criteria: stroke plus CT or MR for definitive diagnosis. Did not state that visible lesion was needed to make the diagnosis, no previous psychiatric disorder history, first acute stroke, available for follow-up and able to give informed consent Depression criteria: CCMD-3 depression diagnostic criteria, first ever depression, HAMD score > 17 Number randomised in each group was 36 Demographic data provided for fluoxetine plus Wuling capsule plus usual care: 36 people, mean age 61.1 ± 10.2 years, 19 men Wuling capsule plus usual care: 36 people, mean age 65.2 ± 14.2 years, 18 men This does not correspond to the 2 drop-outs in the combined group
Interventions	"Fluoxetine 20 mg daily plus usual care" versus "Wuling capsule plus usual care" versus "fluoxetine 20 mg daily plus usual care plus Wuling capsule" We are using the "fluoxetine plus Wuling capsule plus usual care" versus "Wuling capsule and usual care"

	Duration of treatment: 3 months Duration of follow-up (treatment end to study end): 0
Outcomes	HAMD MMSE MESSS BI Death Nausea Used Asberg Rating Scale for Side Effect. Recorded according to the patient's complaints and observation, no description of who recorded AEs
Notes	Excluded: no previous organic brain diseases. Note inconsistency in number of dropouts

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Unclear - states "number table" but not clear if this was a random number table
Allocation concealment (selection bias)	Unclear risk	Not described
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	2 patients in the combined "Wulung capsule plus fluoxetine plus usual care" dropped out. The authors did not report any drop-outs in the "Wulung capsule plus usual care" group
Selective reporting (reporting bias)	Unclear risk	Unclear
Other bias	Unclear risk	Note inconsistencies in relation to number of drop outs. Source of funding not stated
Blinding of participants and personnel (performance bias) All outcomes	High risk	No placebo
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not described

Yang 2002

Methods	Parallel group Aim: to study effects of antidepressant in treatment of patients with post-stroke depression Randomisation: not described Allocation concealment: not described Blinding: not described Drop-outs: 11; 4 in treatment group, 7 in control group
Participants	Country: China Setting: inpatients and outpatients Stroke criteria: recovery phase of stroke (2 to 6 months after ischaemic stroke, and 1.5 to 6 months after haemorrhagic stroke). We included this in the 3 to 6 month group. Clinical diagnosis of stroke (not stated whether confirmation by imaging was needed) Depression: HAMD > 7 Treatment: 64 people, mean age 64 ± 3 years, 40 men Control: 57 people, mean age 63 ± 5 years, 32 men
Interventions	Treatment: paroxetine 20 mg daily plus stroke treatment and rehabilitation Control: stroke treatment and rehabilitation Duration of treatment: 4 months Duration of follow-up: 0
Outcomes	Death They collected data on HAMD and CSS but did not report these data ADL score - did not state which one, so not used AEs not reported
Notes	-

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Method not described
Allocation concealment (selection bias)	Unclear risk	Not described
Incomplete outcome data (attrition bias) All outcomes	High risk	11/121 (9%) drop-outs
Selective reporting (reporting bias)	High risk	No protocol, the paper stated that ADL data and depression data were collected, but these data were not reported
Other bias	Unclear risk	No baseline differences between groups, no other obvious source of bias. Source of funding not reported

Yang 2002 (*Continued*)

Blinding of participants and personnel (performance bias) All outcomes	High risk	No placebo
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not described

Yang 2011

Methods	Aim: to treat early post-stroke depression Randomisation: according to "case sequence", but method not clearly described Allocation concealment: not described Blinding: not described Drop-outs: none
Participants	Country: China Setting: inpatient Stroke: all pathological types, clinical diagnosis plus confirmation of lesion on imaging, no previous psychiatric and psychological disorders, age < 75 years old, stroke onset time < 72 hours, NIHSS score: 4 to 19 Mood: HAMD $\geq$ 8 Treatment: 20 people, mean age 64 ± 8 years, 8 men Control: 22 people, mean age 64 ± 10 years, 13 men Note inconsistency between abstract (20 in treatment and 22 in control, but in tables of results, there are 22 in treatment and 20 in control). We have used the data from the abstract
Interventions	Treatment: paroxetine 20 mg daily plus usual stroke care Control: usual stroke care Duration of treatment: at least 3 months Duration of follow-up: 0
Outcomes	HAMD score, IL-1β and IL-6 level Death AEs not reported
Notes	Excluded: functional psychiatric disorder, functional depression, psychoactive substance and addictive substance induced psychiatric disorders, infectious disease, severe cognitive impairment to affect communication, severe aphasia to affect communication, severe cardiac, pulmonary, hepatic and renal function impairment, previous organic brain disease such as brain tumour, or symptomatic stroke, encephalitis

Risk of bias

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

Yang 2011 (*Continued*)

Random sequence generation (selection bias)	Unclear risk	"Case sequence" randomisation
Allocation concealment (selection bias)	Unclear risk	Not described
Incomplete outcome data (attrition bias) All outcomes	Low risk	No drop-outs
Selective reporting (reporting bias)	Unclear risk	No protocol
Other bias	Low risk	No difference in baseline. Source of funding: local scientific academic fund
Blinding of participants and personnel (performance bias) All outcomes	High risk	No placebo
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not described

Ye 2004

Methods	Aim: to investigate whether antidepressive therapy is needed for patients with post-stroke depression or not, and the effect of different antidepressive drugs on the rehabilitation of psychological and neurological function after stroke 3 groups: paroxetine, imipramine and control. We are using the paroxetine versus control arm in this review Randomisation: number table Allocation concealment and blinding: "the study designer did not involve in assessment and treatment, the assessors did not know the allocation" Blinding of those delivering the treatment: unclear Drop-outs: 1 in paroxetine group, none in control group
Participants	Country: China Setting: inpatient Stroke: all pathological subtypes, clinical diagnosis plus confirmation by imaging (did not state whether a visible lesion was needed to make the diagnosis), no positive psychiatric disorders or family history, clear consciousness, no comprehension problem Mood: inclusion criteria: HAMD score > 21, HAMA scale > 14 Treatment: 30 people, age 58.04 ± 8.28 years, 22 men Control: 30 people, age 59.21 ± 9.52 years, 17 men
Interventions	Treatment: paroxetine 20 mg/day plus acute stroke routine care and rehabilitation Control: acute stroke routine care plus rehabilitation Duration of treatment: 12 weeks Duration of follow-up (end of treatment to end of study): 0

Ye 2004 (*Continued*)

Outcomes	Chinese Neurological Impairment Scale, modified BI, HAMD, HAMA, Therapeutic Effect for Depression and Neurologic Function Death, GI upset Method of recording side effects not stated
Notes	Exclusion criteria: severe cardiac, hepatic and renal diseases, multiple infarcts or haemorrhage inconsistent description about the number of recruitment and randomisation between abstract (N = 90) and result part (N = 93) of the text. The number for final analysis is consistent in the text

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Used "number table" - but unclear if this was a random number table
Allocation concealment (selection bias)	Low risk	The study designer did not involve in assessment and treatment, the assessors did not know the allocation
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Only 1 dropped out in paroxetine group
Selective reporting (reporting bias)	Unclear risk	No protocol
Other bias	Unclear risk	Different numbers reported to have been recruited and randomised, baseline similar. Source of funding not stated
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	The participants were blinded. Not clear if those delivering the treatment were blind. But no placebo used
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Assessors were blinded

Zhou 2003

Methods	Parallel study Aim: effect of fluoxetine on functional recovery Randomisation: according to admission date Allocation concealment: not described Blinding: not described Drop-outs: 6
Participants	Country: China Setting: inpatient Stroke: all pathological types, clinical diagnosis plus confirmation on imaging (though not clear that stroke lesion had to be present) Onset to recruitment time was 13 to 34 days in the treatment group of stroke and 13 to 34 days in the control group Mood: HAMD ≤ 7 and HAMA ≤7 Exclusion criteria: HAMD ≥ 17 or HAMA ≥ 17 'during observation' Age ≤ 80 years Treatment: 30 people, mean age 65 ± 9 years, 16 men Control: 30 people, mean age 64 ± 9 years, 17 men
Interventions	Treatment: fluoxetine 20 mg plus usual stroke care Control: usual stroke care Duration of treatment: 60 days Duration of follow-up (end of treatment to end of study): 0
Outcomes	HAMD HAMA MESSS ADL AEs (in fluoxetine group only)
Notes	Exclusion criteria: severe psychiatric impairment, severe cognitive impairment, unable to complete the test, aphasia, severe cardiac, hepatic, pulmonary, and renal disorders, previous stroke Inclusion criteria: at least 1 limb with muscle power ≤ grade 3

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	High risk	"According to admission date"
Allocation concealment (selection bias)	Unclear risk	Unclear
Incomplete outcome data (attrition bias) All outcomes	High risk	6/60 (10%) drop-outs
Selective reporting (reporting bias)	Unclear risk	No protocol

Zhou 2003 (*Continued*)

Other bias	Low risk	Baseline characteristics balanced. Funded by local scientific academic fund
Blinding of participants and personnel (performance bias) All outcomes	High risk	No placebo
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not described

Zhou 2008

Methods	Aim: to study effect of early paroxetine on post-stroke depression and rehabilitation Parallel design Randomisation: not described Allocation concealment: not described Blinding: not stated Analysis: according to treatment groups Drop-outs
Participants	Country: China Setting: inpatient Stroke criteria: all stroke, clinical diagnosis plus confirmation by imaging (though not clear if a relevant stroke lesion had to be visible), stroke onset time $\leq$ 7 days, no obvious cognitive impairment, no obvious aphasia HAMD score < 8 Treatment: 36 people, mean age 63 ± 9.3 years, 16 men Control: 40 people, mean age 61 ± 9.6 years, 19 men
Interventions	Treatment: fluoxetine 20 mg daily plus acute stroke routine medication Control: acute stroke routine medication Duration of treatment: 8 weeks Duration of follow-up: 0
Outcomes	No raw data provided for any of the following outcomes: diagnosis of depression (CCMD-3, HAMD, ADL, MESSS) Reported no deaths in either group. Unclear how data on side effects were collected
Notes	Excluded: previous psychiatric disorders, severe hepatic and renal impairment, taking agents with obvious interaction with fluoxetine in recent 1 month

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Method not described

Zhou 2008 (*Continued*)

Allocation concealment (selection bias)	Unclear risk	Not described
Incomplete outcome data (attrition bias) All outcomes	Low risk	No drop-outs, analysed according to allocated treatment group
Selective reporting (reporting bias)	High risk	No protocol, no raw data provided for several of the outcomes
Other bias	Low risk	Baseline similar. Source of funding not stated
Blinding of participants and personnel (performance bias) All outcomes	High risk	No placebo
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not described

ADL: activities of daily livingAE: adverse events
BDI: Beck Depression Inventory
BI: Barthel Index
CCMD-II-R: Chinese Classification of Mental Disorders, second edition, revised
CCMD-3: Chinese Classification of Mental Disorders-3
CGI: Clinical Global Impressions Scale
CSS: Chinese Stroke Scale
CT: computerised tomography
EEG: electroencephalogram
FAI: Frenchay Activities Index
FAST: Frenchay Aphasia Screening Test
FIM: Functional Independence Measure
FMMS: Fugl-Meyer Motor Scale
fMRI: functional magnetic resonance imaging
GDS: Geriatric Depression Scale
GI: gastrointestinal
HADS: Hospital Anxiety and Depression Scale
HAMA: Hamilton Anxiety scales
HAMD/HDRS: Hamilton Depression Rating Scale
HSS: Hemispheric Stroke Scale
ICD: International Classification of Diseases
IL: interleukin
ITT: intention-to-treat
JHFI: Johns Hopkins Functioning Inventory
MADRS: Montgomery-Åsberg Depression Rating Scale
MCA: middle cerebral artery
MESSS: Modified Edinburgh-Scandinavian Stroke Scale
MMSE: Mini-Mental State Examination
MRI: magnetic resonance imaging

mRS: modified Rankin score
NIHSS: National Institutes of Health Stroke Scale
PICH: primary intracerebral haemorrhage
RS: Rankin score
SAS: Zung Self-rating Anxiety Scale
SD: standard deviation
SDS: Zung Self-rating Depression Scale
SF-36: Short Form-36
SSS: Scandinavian Stroke Scale
TESS: Treatment Emergent Symptom Scale
TIA: transient ischaemic attack
WHO: World Health Organization

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

Study	Reason for exclusion
Berends 2009a	Mean time from stroke onset to fluoxetine was 39.1 months. Also listed as flu2006 (EudraCT 2008-003349-97)
Bian 2006	Meclofenoxate plus fluoxetine versus fluoxetine alone
Chen SD 2005	Comparison of fluoxetine and clomipramine
Choi-Kwon 2008	Patients > 1 year post stroke
Cui 2001	Abstract, no data, unclear if randomised
Ding 2005	Combination of paroxetine and psychotherapy versus paroxetine alone
Erfurth 2001	Open trial
Fedin 2004	Coaxil is not an SSRI
Flu 2008	A clinical trial that ended prematurely because 3 patients had been recruited by 6 months (information from Professor MJ IJzerman)
Gao 2005	Not randomised - patients allocated according to their order of admission
Gekht 2002	Milnacipran is an SNRI, not a SSRI
Gonzalez-Torrecillas 1995	Not randomised
Havle 2010	All given citalopram, no control
He 2001	Some patients were > 1 year post stroke

(*Continued*)

He 2010	Patients with depression were given fluoxetine, measured 5HT and event-related potentials. not randomised, no clinical data
He Y 2004	Comparison of paroxetine and amitriptyline
Hong 2004	Comparison of the curative effects of yuxingchangzhi tang and fluoxetine
Horvath 2006	Open label phase IV study
Hu 2004	Comparison of fluoxetine and psychotherapy
Kimura 2002	Milnacipran, not a SSRI
Li W 1999	Comparison of 2 types of fluoxetine
Liang 2005	Used fluoxetine or clomipramine in the treatment group
Liu G 2006	Clinical control study of citalopram and amitriptyline in the treatment of post-stroke depression
Liu X 2004	Citalopram versus amitriptyline, no control group
Loubinoux 2002	A study of paroxetine in healthy individuals
Luo 2006	Comparison of amitriptyline and fluoxetine
Marko 1994	Comparison of mobeclamid and nortriptyline
Mei 2001	A controlled trial comparing paroxetine versus fluoxetine in the treatment of post stroke depression
Mitchell 2008	Combination of psychological intervention plus antidepressants
Miyai 1998	Comparison of 3 different antidepressants, no control
Mo 2004	Comparison of Saint John's Wort extract with fluoxetine in the treatment of post-stroke depression
Ooboshi 2008	Comparison of paroxetine and sulpiride
Rampello 2004	Comparison of citalopram and reboxetine
Ruddell 2007	1 patient randomised
Sato 2006	RCT of milnacipran, which is not an SSRI
Shan 2001	Onset to recruitment was more than 1 year in some patients
Simis 2006	Patients not randomised

(*Continued*)

Spalletta 2003	Open study of sertraline
Stamenkovic 1996	Sertraline given to 10 patients, no control group
Wu 2010	Comparison of acupuncture and medication for post-stroke depression
Yuan 2004	Comparison of paroxetine and amitriptyline
Zhang 2005	Comparison of acupuncture and fluoxetine
Zhao 1999	Compared fluoxetine and psychotherapy with fluoxetine, no placebo or standard care group
Zhao 2005	Comparison of citalopram and amitriptyline
Zhao F-T 2005	Citalopram versus venlafaxine
Zheng 2006	Paroxetine plus psychotherapy
Zifko 2002	Open trial
Zittel 2008	8 chronic stroke, mean duration of hemiparesis 36 months

RCT: randomised controlled trial
SNR: serotonin-norepinephrine reuptake inhibitor
SSRI: selective serotonin reuptake inhibitor

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

Sitzer 2002

Methods	Double blind, randomised placebo controlled trial
Participants	Patients will be within the first 6 days after hospital admission
Interventions	Randomised to 50 mg/day sertraline or placebo Aim to recruit 300 participants from 10 centres
Outcomes	Depressive symptoms will be assessed using the Hospital Anxiety and Depression Scale, the Montgomery-Asberg Depression Rating Scale, and the International Diagnosis Checklist for International Classification of Diseases-10 at baseline, 4 weeks, 12 weeks, and 24 weeks. Functional outcome will be determined by the European Stroke Scale, the modified Rankin score, and the Barthel Index. Cognitive performance will be assessed by the Mini-Mental State Examination and the Digit Span Test. Quality of life will be determined at 12 and 24 weeks using the SF-36. Treatment and follow-up are scheduled to continue for 6 months with follow-up visits after 4 weeks, 3 months and 6 months

Sitzer 2002 (*Continued*)

Notes	Listed as a major ongoing trial in Stroke (see citation). Randomisation and follow-ups August 2001 through to January 2003 Author did not respond to emails requesting more information Pre-dis is listed on the author's web page (www.zafes.com/institutes/neurology/index-sitzer.html) but there are no publications associated with this

Whyte 2005

Methods	Placebo-controlled trial of sertraline to prevent depression
Participants	Ischaemic stroke, within 3 months, > 40 years, speaks English Exclusion: major depression, current antidepressant treatment, severe language impairment, history of another central nervous system disorder, pregnant or breastfeeding, medical unstable, other medical contraindications
Interventions	Treatment: sertraline in doses increasing to 75 mg daily Control: placebo (matching) 10-month treatment period, 2-month naturalistic continuation phase
Outcomes	Primary outcome: major depression
Notes	Contacted author twice, no response. Website www.clinicaltrials.gov states that study was terminated as recruitment goals could not be met. No published data available through our searches

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

2005-005266-37

Trial name or title	Influence of escitalopram on the incidence of depression and dementia following acute middle cerebral artery territory infarction. A randomised, placebo-controlled, double-blind study
Methods	Randomised, placebo controlled
Participants	Acute MCA territory infarction Aiming to recruit 60 over 3 years Within 7 days of stroke onset Prepared to and considered able to follow the whole trial period Exclusions: dementia, recurrent major depression, major stroke, alcohol and drug dependency, pregnancy, breastfeeding, participating in other trials of medicinal products, impaired liver/kidney disease, life expectancy less than 6 months
Interventions	Escitalopram or placebo Duration of treatment: not stated
Outcomes	Depression (MADRS) after 180 days Incidence of dementia after 180 days (Clinical Dementia Rating scale) Severity of dementia

2005-005266-37 (*Continued*)

	Zarit Burden Interview Incidence of depression (Depression visual analogue scale) Severity of post-stroke depression Quality of life (SF-36) Bayer Activities of Daily Living score NPI
Starting date	MHRA approval 7 April 2006; start date not known
Contact information	Not available. National Competent authority is Germany-BFarm Sponsor Name: Central Institute for Mental Health, Mannheim, Division of Gerontopsychiatry
Notes	Details available on EudraCT website

AFFINITY 2011

Trial name or title	Assessment oF FluoxetINe In sTroke recoverY (AFFINITY) trial
Methods	Fluoxetine (20 mg once daily) for 6 months via oral capsule or enteral tube
Participants	Men or women aged 18 years or more with: • clinical diagnosis of stroke 2 to 15 days previously, and • brain imaging consistent with ischaemic or haemorrhagic stroke (including normal CT brain scan) • persisting measurable focal neurological deficits causing a functional deficit at the time of randomisation Aiming to recruit 1580 patients
Interventions	Fluoxetine 20 mg daily or matching placebo for 6 months
Outcomes	mRS, Stroke impact scale, depression (PHQ-9), vitality component of SF-36, Euroquol 5D, healthcare utilisation (data linkage to patient medical records and patient diary recording hospital admissions/visits and general practitioner/specialist visits), adverse events, social functioning (FAI), adherence to trial medication (patient self report of medication compliance and tablet counting), cognition (TICSm), Outcomes collected at 6 months and 12 months
Starting date	July 2012
Contact information	graeme.hankey@health.wa.gov.au
Notes	ACTRN12611000774921

Carda 2009

Trial name or title	Effects on clinical and functional outcome of escitalopram in adult stroke patients
Methods	Randomised, parallel assignment, double blind study.
Participants	> 18 years First ischaemic or haemorrhagic stroke Exclusions: unstable medical conditions, unable to understand study aims and procedures, severe aphasia, other progressive neurological disease, previous or concomitant psychiatric illness, patients not willing to participate
Interventions	Experimental: escitalopram and rehabilitation. Escitalopram given 5 mg od for the first week, 10 mg od from the second to fourth week, and 20 mg daily until the 6th month Comparator: placebo and rehabilitation
Outcomes	Not stated
Starting date	July 2009. Aiming to recruit 200
Contact information	stefano.carda@virgilio.it cisari@tin.it
Notes	Contacted author Prof Cisari; response received; data being analysed

EMOTION 2011

Trial name or title	The preventative effect of escitalopram on depression and related emotional disorders in acute stroke patients
Methods	Multicentre, randomised, parallel assignment, double-blind trial to prevent depression
Participants	Acute stroke, within 21 days of onset. Both haemorrhagic and ischaemic, mRS $\geq$ 2 on screening, without definite history of depression, without serious communication problem, those who agree to participate Long list of exclusion criteria
Interventions	Experimental: escitalopram: first week 5 mg, 2nd week ~ 12 week: 10 mg Placebo: "sugar pill". First week 5 mg, 2nd week ~ 12 week: 10 mg Stopped at 14 weeks At follow-up at 24 weeks, assessment for post-stroke depression and related symptoms
Outcomes	Not listed
Starting date	January 2011. Aiming to enrol 444 participants. Estimated primary completion date: December 2013
Contact information	jongskim@amc.seoul.kr
Notes	-

FOCUS 2011

Trial name or title	Fluoxetine or control under supervision
Methods	Randomised placebo-controlled, blinded trial
Participants	Men or women aged 18 years or more with: • clinical diagnosis of stroke 2 to 15 days previously, and • brain imaging consistent with ischaemic or haemorrhagic stroke (including normal CT brain scan) • persisting measurable focal neurological deficits causing a functional deficit at the time of randomisation Aiming to recruit 3000 patients
Interventions	Fluoxetine 20 mg daily or matching placebo for 6 months
Outcomes	mRS, Stroke Impact Scale, Mental Health Inventory 5, vitality component of SF-36, Euroquol 5D, resource use, adverse events. Outcomes collected at 6 and 12 months
Starting date	July 2012
Contact information	gmead@staffmail.ed.ac.uk
Notes	MHRA approval granted. Start up phase funded by The Stroke Association

CT: computerised tomography
FAI: Frenchay Activities Index
MADRS: Montgomery-Åsberg Depression Rating Scale
MCA: middle cerebral artery
MHRA: M edicines and Healthcare products Regulatory Agency
mRS: modified Rankin score
NPI: Neuropsychiatric Inventory Scale
od: once daily
PHQ-9: Patient Health Questionnaire
SF-36: Short Form-36
TICSm: telephone interview for cognitive status - modified

DATA AND ANALYSES

Comparison 1. SSRI versus control at end of treatment, by SSRI

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Dependent on modified Rankin score (mRS 3 to 5)	2	223	Risk Ratio (M-H, Random, 95% CI)	0.81 [0.68, 0.97]
1.1 Fluoxetine	1	112	Risk Ratio (M-H, Random, 95% CI)	0.81 [0.68, 0.97]
1.2 Sertraline	1	111	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
2 Disability	22	1310	Std. Mean Difference (IV, Random, 95% CI)	0.92 [0.62, 1.23]
2.1 Fluoxetine	13	708	Std. Mean Difference (IV, Random, 95% CI)	0.68 [0.31, 1.06]
2.2 Sertraline	1	130	Std. Mean Difference (IV, Random, 95% CI)	1.38 [0.99, 1.76]
2.3 Citalopram	3	179	Std. Mean Difference (IV, Random, 95% CI)	1.18 [-0.22, 2.58]
2.4 Paroxetine	5	293	Std. Mean Difference (IV, Random, 95% CI)	1.31 [0.67, 1.95]
2.5 Escitalopram	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2.6 Sertraline or fluoxetine	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3 Neurological deficit score	29	2011	Std. Mean Difference (IV, Random, 95% CI)	-1.00 [-1.26, -0.75]
3.1 Fluoxetine	17	1095	Std. Mean Difference (IV, Random, 95% CI)	-0.93 [-1.29, -0.57]
3.2 Sertraline	2	108	Std. Mean Difference (IV, Random, 95% CI)	-0.26 [-0.96, 0.45]
3.3 Citalopram	3	179	Std. Mean Difference (IV, Random, 95% CI)	-1.43 [-2.25, -0.60]
3.4 Paroxetine	6	455	Std. Mean Difference (IV, Random, 95% CI)	-1.21 [-1.68, -0.74]
3.5 Fluoxetine or sertraline	1	174	Std. Mean Difference (IV, Random, 95% CI)	-1.40 [-1.73, -1.06]
4 Depression (continuous data)	39	2728	Std. Mean Difference (IV, Random, 95% CI)	-1.91 [-2.34, -1.48]
4.1 Fluoxetine	21	1260	Std. Mean Difference (IV, Random, 95% CI)	-1.97 [-2.63, -1.32]
4.2 Sertraline	4	383	Std. Mean Difference (IV, Random, 95% CI)	-0.13 [-1.11, 0.85]
4.3 Citalopram	5	313	Std. Mean Difference (IV, Random, 95% CI)	-1.92 [-3.08, -0.75]
4.4 Paroxetine	8	598	Std. Mean Difference (IV, Random, 95% CI)	-2.81 [-3.66, -1.96]
4.5 Fluoxetine or sertraline	1	174	Std. Mean Difference (IV, Random, 95% CI)	-1.50 [-1.84, -1.16]
4.6 Escitalopram	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
5 Depression (dichotomous data)	8	771	Risk Ratio (M-H, Random, 95% CI)	0.43 [0.24, 0.77]
5.1 Fluoxetine	3	206	Risk Ratio (M-H, Random, 95% CI)	0.31 [0.17, 0.57]
5.2 Sertraline	2	166	Risk Ratio (M-H, Random, 95% CI)	0.59 [0.28, 1.25]
5.3 Citalopram	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
5.4 Paroxetine	2	282	Risk Ratio (M-H, Random, 95% CI)	0.53 [0.15, 1.92]
5.5 Escitalopram	1	117	Risk Ratio (M-H, Random, 95% CI)	0.38 [0.14, 0.99]
6 Anxiety (continuous data)	8	413	Std. Mean Difference (IV, Random, 95% CI)	-0.77 [-1.52, -0.02]
6.1 Fluoxetine	4	169	Std. Mean Difference (IV, Random, 95% CI)	-0.23 [-0.67, 0.21]
6.2 Sertraline	1	50	Std. Mean Difference (IV, Random, 95% CI)	0.36 [-0.20, 0.92]
6.3 Citalopram	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
6.4 Paroxetine	3	194	Std. Mean Difference (IV, Random, 95% CI)	-1.97 [-3.81, -0.12]
6.5 Escitalopram	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
7 Anxiety (dichotomous data)	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
8 Cognition (continuous scores end of treatment)	7	425	Std. Mean Difference (IV, Random, 95% CI)	0.32 [-0.23, 0.86]
8.1 Fluoxetine	4	158	Std. Mean Difference (IV, Random, 95% CI)	0.04 [-0.27, 0.35]
8.2 Sertraline	1	80	Std. Mean Difference (IV, Random, 95% CI)	0.53 [0.08, 0.98]
8.3 Citalopram	1	99	Std. Mean Difference (IV, Random, 95% CI)	1.69 [1.23, 2.16]
8.4 Escitalopram	1	88	Std. Mean Difference (IV, Random, 95% CI)	-0.07 [-0.49, 0.35]

9 Death	46	3344	Risk Ratio (M-H, Random, 95% CI)	0.76 [0.34, 1.70]
9.1 Fluoxetine	25	1502	Risk Ratio (M-H, Random, 95% CI)	0.78 [0.14, 4.39]
9.2 Sertraline	5	461	Risk Ratio (M-H, Random, 95% CI)	0.91 [0.20, 4.19]
9.3 Citalopram	5	341	Risk Ratio (M-H, Random, 95% CI)	0.77 [0.17, 3.38]
9.4 Paroxetine	9	739	Risk Ratio (M-H, Random, 95% CI)	0.2 [0.01, 4.01]
9.5 Escitalopram	1	117	Risk Ratio (M-H, Random, 95% CI)	4.92 [0.24, 100.25]
9.6 Sertraline or fluoxetine	1	184	Risk Ratio (M-H, Random, 95% CI)	0.2 [0.01, 4.11]
10 Seizures	7	444	Risk Ratio (M-H, Random, 95% CI)	2.67 [0.61, 11.63]
10.1 Fluoxetine	5	318	Risk Ratio (M-H, Random, 95% CI)	2.19 [0.41, 11.85]
10.2 Sertraline	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10.3 Citalopram	1	66	Risk Ratio (M-H, Random, 95% CI)	5.0 [0.25, 100.32]
10.4 Paroxetine	1	60	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10.5 Escitalopram	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10.6 Sertraline or fluoxetine	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
11 Gastrointestinal side effects	14	902	Risk Ratio (M-H, Random, 95% CI)	1.90 [0.94, 3.85]
11.1 Fluoxetine	11	760	Risk Ratio (M-H, Random, 95% CI)	1.68 [0.82, 3.42]
11.2 Sertraline	1	28	Risk Ratio (M-H, Random, 95% CI)	0.33 [0.01, 7.55]
11.3 Citalopram	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
11.4 Paroxetine	2	114	Risk Ratio (M-H, Random, 95% CI)	10.21 [1.32, 78.77]
11.5 Escitalopram	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
11.6 Sertraline and paroxetine	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
12 Bleeding	2	347	Risk Ratio (M-H, Random, 95% CI)	1.63 [0.20, 13.05]
12.1 Fluoxetine	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
12.2 Sertraline	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
12.3 Citalopram	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
12.4 Paroxetine	1	229	Risk Ratio (M-H, Random, 95% CI)	3.13 [0.13, 76.10]
12.5 Escitalopram	1	118	Risk Ratio (M-H, Random, 95% CI)	1.0 [0.06, 15.61]
12.6 Sertraline or fluoxetine	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
13 Change in depression scores between baseline and follow-up	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
13.1 Sertraline	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
14 Change in cognition between baseline and end of treatment	1	99	Std. Mean Difference (IV, Random, 95% CI)	0.0 [-0.39, 0.39]
14.1 Sertraline	1	99	Std. Mean Difference (IV, Random, 95% CI)	0.0 [-0.39, 0.39]
15 Leaving the trial before the end of scheduled follow-up	49	3851	Risk Ratio (M-H, Random, 95% CI)	1.02 [0.86, 1.21]
15.1 Fluoxetine	25	1585	Risk Ratio (M-H, Random, 95% CI)	1.21 [0.87, 1.67]
15.2 Sertraline	6	609	Risk Ratio (M-H, Random, 95% CI)	0.95 [0.69, 1.32]
15.3 Citalopram	5	339	Risk Ratio (M-H, Random, 95% CI)	1.20 [0.41, 3.47]
15.4 Paroxetine	11	1017	Risk Ratio (M-H, Random, 95% CI)	0.88 [0.51, 1.52]
15.5 Sertraline or fluoxetine	1	184	Risk Ratio (M-H, Random, 95% CI)	1.0 [0.26, 3.88]
15.6 Escitalopram	1	117	Risk Ratio (M-H, Random, 95% CI)	1.38 [0.46, 4.09]
16 Motor deficits	2	145	Std. Mean Difference (IV, Random, 95% CI)	-0.33 [-1.22, 0.56]
16.1 Fluoxetine	2	145	Std. Mean Difference (IV, Random, 95% CI)	-0.33 [-1.22, 0.56]

Comparison 2. SSRI versus control, at end of follow-up, by SSRI

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Dependent on modified Rankin score	1	94	Risk Ratio (M-H, Random, 95% CI)	0.38 [0.02, 9.04]
1.1 Sertraline	1	94	Risk Ratio (M-H, Random, 95% CI)	0.38 [0.02, 9.04]
1.2 Fluoxetine	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
2 Disability	2	155	Std. Mean Difference (IV, Random, 95% CI)	1.78 [-1.01, 4.57]
3 Neurological deficit score (higher score: worse outcome)	4	275	Std. Mean Difference (IV, Random, 95% CI)	-0.63 [-1.30, 0.04]
3.1 Fluoxetine	3	195	Std. Mean Difference (IV, Random, 95% CI)	-0.77 [-1.61, 0.08]
3.2 Sertraline	1	80	Std. Mean Difference (IV, Random, 95% CI)	-0.25 [-0.69, 0.19]
4 Depression (continuous data)	4	275	Std. Mean Difference (IV, Random, 95% CI)	-1.10 [-2.16, -0.04]
4.1 Fluoxetine	3	195	Std. Mean Difference (IV, Random, 95% CI)	-1.32 [-2.74, 0.11]
4.2 Sertraline	1	80	Std. Mean Difference (IV, Random, 95% CI)	-0.47 [-0.91, -0.03]
5 Depression (dichotomous data)	1	99	Risk Ratio (M-H, Random, 95% CI)	0.77 [0.34, 1.76]
5.1 Sertraline	1	99	Risk Ratio (M-H, Random, 95% CI)	0.77 [0.34, 1.76]
6 Cognition (higher score is better)	1	80	Std. Mean Difference (IV, Random, 95% CI)	0.26 [-0.18, 0.70]
6.1 Sertraline	1	80	Std. Mean Difference (IV, Random, 95% CI)	0.26 [-0.18, 0.70]
7 Change in cognition between baseline and follow-up	1	99	Std. Mean Difference (IV, Random, 95% CI)	0.02 [-0.37, 0.42]
7.1 Sertraline	1	99	Std. Mean Difference (IV, Random, 95% CI)	0.02 [-0.37, 0.42]
8 Death	3	257	Risk Ratio (M-H, Random, 95% CI)	0.08 [0.00, 1.41]

Comparison 3. SSRI versus control (according to time since stroke when recruited)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Dependent on modified Rankin score	2	223	Risk Ratio (M-H, Random, 95% CI)	0.81 [0.68, 0.97]
1.1 Mean time since stroke < 2 weeks	2	223	Risk Ratio (M-H, Random, 95% CI)	0.81 [0.68, 0.97]
1.2 Mean time since stroke 2 weeks to 3 months at randomisation	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
1.3 Mean time since stroke 3 to 6 months at randomisation	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
1.4 Mean time since stroke > 6 months and < 9 months	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
1.5 Mean time since stroke at randomisation 9 to 12 months	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
1.6 Mean time since stroke not known	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
2 Disability	22	1310	Std. Mean Difference (IV, Random, 95% CI)	0.92 [0.62, 1.23]

2.1 Mean time since stroke < 3 months	17	1004	Std. Mean Difference (IV, Random, 95% CI)	0.77 [0.47, 1.06]
2.2 Mean time since stroke 3 to 6 months at randomisation	1	32	Std. Mean Difference (IV, Random, 95% CI)	0.43 [-0.27, 1.14]
2.3 Mean time since stroke > 6 months and < 9 months	1	60	Std. Mean Difference (IV, Random, 95% CI)	2.67 [1.97, 3.38]
2.4 Mean time since stroke 9 to 12 months	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2.5 Mean time since stroke not known	3	214	Std. Mean Difference (IV, Random, 95% CI)	1.43 [0.40, 2.45]
3 Neurological deficit score	29	2011	Std. Mean Difference (IV, Random, 95% CI)	-1.00 [-1.26, -0.75]
3.1 Mean time since stroke < 3 months	19	1183	Std. Mean Difference (IV, Random, 95% CI)	-1.01 [-1.31, -0.72]
3.2 Mean time since stroke 3 to 6 months	1	32	Std. Mean Difference (IV, Random, 95% CI)	-0.27 [-0.97, 0.42]
3.3 Mean time since stroke 6 to 9 months	2	140	Std. Mean Difference (IV, Random, 95% CI)	-1.40 [-3.08, 0.28]
3.4 Mean time since stroke 9 to 12 months	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3.5 Mean time since stroke not known	7	656	Std. Mean Difference (IV, Random, 95% CI)	-0.96 [-1.56, -0.36]
4 Depression (continuous)	39	2728	Std. Mean Difference (IV, Random, 95% CI)	-1.91 [-2.34, -1.48]
4.1 Time since stroke < 3 months	27	1697	Std. Mean Difference (IV, Random, 95% CI)	-1.96 [-2.54, -1.37]
4.2 Time since stroke 3 to 6 months	3	223	Std. Mean Difference (IV, Random, 95% CI)	-1.16 [-2.97, 0.65]
4.3 Time since stroke 6 to 9 months	2	140	Std. Mean Difference (IV, Random, 95% CI)	-1.56 [-3.99, 0.86]
4.4 Time since stroke 9 to 12 months	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4.5 Time since stroke not known	7	668	Std. Mean Difference (IV, Random, 95% CI)	-2.19 [-2.62, -1.76]
5 Depression (dichotomous)	8	771	Risk Ratio (M-H, Random, 95% CI)	0.43 [0.24, 0.77]
5.1 Time since stroke < 3 months	7	546	Risk Ratio (M-H, Random, 95% CI)	0.39 [0.26, 0.57]
5.2 Time since stroke 3 to 6 months	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
5.3 Time since stroke 6 to 9 months	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
5.4 Time since stroke 9 to 12 months	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
5.5 Time since stroke unknown	1	225	Risk Ratio (M-H, Random, 95% CI)	0.87 [0.76, 0.99]
6 Anxiety (dichotomous)	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
6.1 Time since stroke < 3 months	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
6.2 Time since stroke 3 to 6 months	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
6.3 Time since stroke 6 to 9 months	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]

6.4 Time since stroke 9 to 12 months	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
6.5 Time from stroke onset unknown	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
7 Anxiety (continuous)	8	413	Std. Mean Difference (IV, Random, 95% CI)	-0.77 [-1.52, -0.02]
7.1 Time since stroke < 3 months	8	413	Std. Mean Difference (IV, Random, 95% CI)	-0.77 [-1.52, -0.02]
7.2 Time since stroke 3 to 6 months	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
7.3 Time since stroke 6 to 9 months	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
7.4 Time since stroke 9 to 12 months	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
7.5 Time since stroke unknown	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
8 Cognition	7	425	Std. Mean Difference (IV, Random, 95% CI)	0.32 [-0.23, 0.86]
8.1 Time since stroke < 3 months	5	273	Std. Mean Difference (IV, Random, 95% CI)	0.28 [-0.57, 1.13]
8.2 Time since stroke 3 to 6 months	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
8.3 Time since stroke 6 to 9 months	1	80	Std. Mean Difference (IV, Random, 95% CI)	0.53 [0.08, 0.98]
8.4 Time since stroke 9 to 12 months	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
8.5 Time since stroke unknown	1	72	Std. Mean Difference (IV, Random, 95% CI)	0.23 [-0.23, 0.69]
9 Death	46	3404	Risk Ratio (M-H, Random, 95% CI)	0.76 [0.34, 1.70]
9.1 Time since stroke < 3 months	34	2311	Risk Ratio (M-H, Random, 95% CI)	0.94 [0.38, 2.36]
9.2 Time since stroke 3 to 6 months	4	369	Risk Ratio (M-H, Random, 95% CI)	0.20 [0.01, 4.02]
9.3 Time since stroke 6 to 9 months	2	140	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
9.4 Time since stroke 9 to 12 months	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
9.5 Time since stroke unknown	7	584	Risk Ratio (M-H, Random, 95% CI)	0.49 [0.07, 3.65]
10 Seizure	7	444	Risk Ratio (M-H, Random, 95% CI)	2.67 [0.61, 11.63]
10.1 Time since stroke < 3 months	6	409	Risk Ratio (M-H, Random, 95% CI)	2.22 [0.41, 12.06]
10.2 Time since stroke 3 to 6 months	1	35	Risk Ratio (M-H, Random, 95% CI)	4.74 [0.24, 92.07]
10.3 Time since stroke 6 to 9 months	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10.4 Time since stroke 9 to 12 months	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10.5 Time since stroke unknown	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
11 Gastrointestinal side effects	14	902	Risk Ratio (M-H, Random, 95% CI)	1.90 [0.94, 3.85]
11.1 Time since stroke < 3 months	11	767	Risk Ratio (M-H, Random, 95% CI)	1.92 [0.83, 4.45]

11.2 Time since stroke 3 to 6 months	1	35	Risk Ratio (M-H, Random, 95% CI)	4.74 [0.24, 92.07]
11.3 Time since stroke 6 to 9 months	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
11.4 Time since stroke 9 to 12 months	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
11.5 Time since stroke unknown	2	100	Risk Ratio (M-H, Random, 95% CI)	1.51 [0.14, 16.29]
12 Leaving the trial early	49	3851	Risk Ratio (M-H, Random, 95% CI)	1.02 [0.86, 1.21]
12.1 Time since stroke < 3 months	34	2435	Risk Ratio (M-H, Random, 95% CI)	1.12 [0.90, 1.40]
12.2 Time since stroke 3 to 6 months	3	246	Risk Ratio (M-H, Random, 95% CI)	0.83 [0.59, 1.19]
12.3 Time since stroke 6 to 9 months	2	140	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
12.4 Time since stroke 9 to 12 months	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
12.5 Time since stroke not known	10	1030	Risk Ratio (M-H, Random, 95% CI)	0.97 [0.62, 1.51]
13 Bleeding	2	347	Risk Ratio (M-H, Random, 95% CI)	1.63 [0.20, 13.05]
13.1 Time since stroke < 3 months	1	118	Risk Ratio (M-H, Random, 95% CI)	1.0 [0.06, 15.61]
13.2 Time since stroke not known	1	229	Risk Ratio (M-H, Random, 95% CI)	3.13 [0.13, 76.10]
14 Motor deficits	2	145	Std. Mean Difference (IV, Random, 95% CI)	-0.33 [-1.22, 0.56]
14.1 < 3 months	1	113	Std. Mean Difference (IV, Random, 95% CI)	-0.74 [-1.12, -0.35]
14.2 3 to 6 months	1	32	Std. Mean Difference (IV, Random, 95% CI)	0.18 [-0.52, 0.87]

Comparison 4. SSRI versus control according to depression at time of recruitment

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Modified Rankin score	2	223	Risk Ratio (M-H, Random, 95% CI)	0.81 [0.68, 0.97]
1.1 Had to have depression at recruitment	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
1.2 Did not have to have depression at recruitment	2	223	Risk Ratio (M-H, Random, 95% CI)	0.81 [0.68, 0.97]
2 Disability	22	1310	Std. Mean Difference (IV, Random, 95% CI)	0.92 [0.62, 1.23]
2.1 Had to have depression at recruitment	15	986	Std. Mean Difference (IV, Random, 95% CI)	1.11 [0.71, 1.51]
2.2 Did not have to have depression at onset	7	324	Std. Mean Difference (IV, Random, 95% CI)	0.55 [0.27, 0.84]
3 Neurological deficit score	29	2011	Std. Mean Difference (IV, Random, 95% CI)	-1.00 [-1.26, -0.75]
3.1 Had to have depression at recruitment	19	1420	Std. Mean Difference (IV, Random, 95% CI)	-1.19 [-1.47, -0.91]
3.2 Did not have to have depression at recruitment	10	591	Std. Mean Difference (IV, Random, 95% CI)	-0.63 [-1.08, -0.17]
4 Depression (continuous)	39	2728	Std. Mean Difference (IV, Random, 95% CI)	-1.91 [-2.34, -1.48]

4.1 Had to have depression at recruitment	31	2256	Std. Mean Difference (IV, Random, 95% CI)	-2.06 [-2.54, -1.58]
4.2 Did not have to have depression at recruitment	8	472	Std. Mean Difference (IV, Random, 95% CI)	-1.35 [-2.35, -0.36]
5 Depression (dichotomous)	8	771	Risk Ratio (M-H, Random, 95% CI)	0.43 [0.24, 0.77]
5.1 Had to have depression at recruitment	2	288	Risk Ratio (M-H, Random, 95% CI)	0.66 [0.30, 1.46]
5.2 Did not have to have depression at recruitment	6	483	Risk Ratio (M-H, Random, 95% CI)	0.38 [0.25, 0.59]
6 Anxiety (continuous)	8	413	Std. Mean Difference (IV, Random, 95% CI)	-0.77 [-1.52, -0.02]
6.1 Had to have depression at recruitment	5	271	Std. Mean Difference (IV, Random, 95% CI)	-1.10 [-2.32, 0.12]
6.2 Did not have to have depression at recruitment	3	142	Std. Mean Difference (IV, Random, 95% CI)	-0.28 [-0.85, 0.29]
7 Anxiety (dichotomous)	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
7.1 Had to have depression at recruitment	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
7.2 Did not have to have depression at baseline	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
8 Cognition	7	425	Std. Mean Difference (IV, Random, 95% CI)	0.32 [-0.23, 0.86]
8.1 Had to have depression at recruitment	5	309	Std. Mean Difference (IV, Random, 95% CI)	0.48 [-0.21, 1.17]
8.2 Did not have to have depression at recruitment	2	116	Std. Mean Difference (IV, Random, 95% CI)	-0.08 [-0.45, 0.28]
9 Death	46	3344	Risk Ratio (M-H, Random, 95% CI)	0.76 [0.34, 1.70]
9.1 Had to have depression at recruitment	32	2468	Risk Ratio (M-H, Random, 95% CI)	0.53 [0.18, 1.54]
9.2 Did not have to have depression at recruitment	14	876	Risk Ratio (M-H, Random, 95% CI)	1.22 [0.36, 4.13]
10 Seizures	7	444	Risk Ratio (M-H, Random, 95% CI)	2.67 [0.61, 11.63]
10.1 Had to have depression at recruitment	4	220	Risk Ratio (M-H, Random, 95% CI)	1.97 [0.27, 14.55]
10.2 Did not have to have depression at recruitment	3	224	Risk Ratio (M-H, Random, 95% CI)	3.83 [0.44, 33.53]
11 Gastrointestinal side effects	14	902	Risk Ratio (M-H, Random, 95% CI)	1.90 [0.94, 3.85]
11.1 Had to have depression at recruitment	8	523	Risk Ratio (M-H, Random, 95% CI)	1.72 [0.58, 5.12]
11.2 Did not have to have depression at recruitment	6	379	Risk Ratio (M-H, Random, 95% CI)	2.53 [1.18, 5.42]
12 Leaving the trial early	49	3851	Risk Ratio (M-H, Random, 95% CI)	1.02 [0.86, 1.21]
12.1 Had to have depression at recruitment	35	2860	Risk Ratio (M-H, Random, 95% CI)	0.97 [0.77, 1.21]
12.2 Did not have to have depression at entry	14	991	Risk Ratio (M-H, Random, 95% CI)	1.10 [0.84, 1.44]
13 Bleeding	2	347	Risk Ratio (M-H, Random, 95% CI)	1.63 [0.20, 13.05]
13.1 Depression at onset	1	229	Risk Ratio (M-H, Random, 95% CI)	3.13 [0.13, 76.10]
13.2 No depression at onset	1	118	Risk Ratio (M-H, Random, 95% CI)	1.0 [0.06, 15.61]
14 Motor deficits	2	145	Std. Mean Difference (IV, Random, 95% CI)	-0.33 [-1.22, 0.56]
14.1 No depression at onset	2	145	Std. Mean Difference (IV, Random, 95% CI)	-0.33 [-1.22, 0.56]
14.2 Depression at onset	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]

Comparison 5. SSRI versus control, end of treatment, randomisation: low risk of bias

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Dependent on modified Rankin score (mRS 3 to 5)	2	223	Risk Ratio (M-H, Random, 95% CI)	0.81 [0.68, 0.97]
1.1 Fluoxetine	1	112	Risk Ratio (M-H, Random, 95% CI)	0.81 [0.68, 0.97]
1.2 Sertraline	1	111	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
2 Disability	7	325	Std. Mean Difference (IV, Random, 95% CI)	0.39 [0.15, 0.63]
2.1 Fluoxetine	6	305	Std. Mean Difference (IV, Random, 95% CI)	0.38 [0.11, 0.66]
2.2 Sertraline	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2.3 Citalopram	1	20	Std. Mean Difference (IV, Random, 95% CI)	0.25 [-0.63, 1.13]
2.4 Paroxetine	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2.5 Escitalopram	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2.6 Sertraline or fluoxetine	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3 Neurological deficit score	10	649	Std. Mean Difference (IV, Random, 95% CI)	-0.72 [-1.11, -0.33]
3.1 Fluoxetine	5	362	Std. Mean Difference (IV, Random, 95% CI)	-0.52 [-0.89, -0.15]
3.2 Sertraline	2	108	Std. Mean Difference (IV, Random, 95% CI)	-0.26 [-0.96, 0.45]
3.3 Citalopram	3	179	Std. Mean Difference (IV, Random, 95% CI)	-1.43 [-2.25, -0.60]
3.4 Paroxetine	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3.5 Fluoxetine or sertraline	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4 Depression (continuous data)	10	647	Std. Mean Difference (IV, Random, 95% CI)	-0.17 [-0.61, 0.28]
4.1 Fluoxetine	6	374	Std. Mean Difference (IV, Random, 95% CI)	-0.38 [-0.91, 0.16]
4.2 Sertraline	3	253	Std. Mean Difference (IV, Random, 95% CI)	0.28 [-0.63, 1.20]
4.3 Citalopram	1	20	Std. Mean Difference (IV, Random, 95% CI)	-0.40 [-1.29, 0.48]
4.4 Paroxetine	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4.5 Fluoxetine or sertraline	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
5 Depression (dichotomous data)	3	283	Risk Ratio (M-H, Random, 95% CI)	0.50 [0.27, 0.92]
5.1 Fluoxetine	1	67	Risk Ratio (M-H, Random, 95% CI)	0.26 [0.06, 1.12]
5.2 Sertraline	1	99	Risk Ratio (M-H, Random, 95% CI)	0.77 [0.34, 1.76]
5.3 Citalopram	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
5.4 Paroxetine	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
5.5 Escitalopram	1	117	Risk Ratio (M-H, Random, 95% CI)	0.38 [0.14, 0.99]
6 Anxiety (continuous data)	3	115	Std. Mean Difference (IV, Random, 95% CI)	-0.40 [-0.85, 0.05]
6.1 Fluoxetine	3	115	Std. Mean Difference (IV, Random, 95% CI)	-0.40 [-0.85, 0.05]
6.2 Sertraline	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
6.3 Citalopram	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
6.4 Paroxetine	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
6.5 Escitalopram	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
7 Anxiety (dichotomous data)	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
8 Cognition (continuous scores end of treatment)	4	223	Std. Mean Difference (IV, Random, 95% CI)	0.16 [-0.18, 0.49]
8.1 Fluoxetine	2	55	Std. Mean Difference (IV, Random, 95% CI)	0.03 [-0.50, 0.56]
8.2 Sertraline	1	80	Std. Mean Difference (IV, Random, 95% CI)	0.53 [0.08, 0.98]
8.3 Citalopram	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
8.4 Escitalopram	1	88	Std. Mean Difference (IV, Random, 95% CI)	-0.07 [-0.49, 0.35]
9 Death	13	920	Risk Ratio (M-H, Random, 95% CI)	1.06 [0.36, 3.09]
9.1 Fluoxetine	7	452	Risk Ratio (M-H, Random, 95% CI)	0.78 [0.14, 4.39]
9.2 Sertraline	4	331	Risk Ratio (M-H, Random, 95% CI)	0.91 [0.20, 4.19]
9.3 Citalopram	1	20	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
9.4 Paroxetine	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]

9.5 Escitalopram	1	117	Risk Ratio (M-H, Random, 95% CI)	4.92 [0.24, 100.25]
9.6 Sertraline or fluoxetine	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10 Seizures	1	118	Risk Ratio (M-H, Random, 95% CI)	3.0 [0.12, 72.18]
10.1 Fluoxetine	1	118	Risk Ratio (M-H, Random, 95% CI)	3.0 [0.12, 72.18]
10.2 Sertraline	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10.3 Citalopram	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10.4 Paroxetine	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10.5 Escitalopram	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10.6 Sertraline or fluoxetine	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
11 Gastrointestinal side effects	5	363	Risk Ratio (M-H, Random, 95% CI)	1.92 [0.98, 3.77]
11.1 Fluoxetine	4	335	Risk Ratio (M-H, Random, 95% CI)	2.09 [1.05, 4.18]
11.2 Sertraline	1	28	Risk Ratio (M-H, Random, 95% CI)	0.33 [0.01, 7.55]
11.3 Citalopram	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
11.4 Paroxetine	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
11.5 Escitalopram	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
11.6 Sertraline and paroxetine	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
12 Bleeding	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
12.1 Fluoxetine	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
12.2 Sertraline	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
12.3 Citalopram	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
12.4 Paroxetine	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
12.5 Escitalopram	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
12.6 Sertraline or fluoxetine	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
13 Change in depression scores between baseline and follow-up	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
13.1 Sertraline	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
14 Change in cognition between baseline and end of treatment	1	99	Std. Mean Difference (IV, Random, 95% CI)	0.0 [-0.39, 0.39]
14.1 Sertraline	1	99	Std. Mean Difference (IV, Random, 95% CI)	0.0 [-0.39, 0.39]
15 Leaving the trial before the end of scheduled follow-up	15	1168	Risk Ratio (M-H, Random, 95% CI)	0.99 [0.80, 1.23]
15.1 Fluoxetine	8	552	Risk Ratio (M-H, Random, 95% CI)	1.16 [0.72, 1.89]
15.2 Sertraline	5	479	Risk Ratio (M-H, Random, 95% CI)	0.95 [0.69, 1.32]
15.3 Citalopram	1	20	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
15.4 Paroxetine	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
15.5 Sertraline or fluoxetine	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
15.6 Escitalopram	1	117	Risk Ratio (M-H, Random, 95% CI)	1.38 [0.46, 4.09]
16 Bleeding	1	118	Risk Ratio (M-H, Random, 95% CI)	1.0 [0.06, 15.61]

Comparison 6. SSRI versus control at end of treatment, concealment of allocation: low risk

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Dependent on modified Rankin score (mRS 3 to 5)	2	223	Risk Ratio (M-H, Random, 95% CI)	0.81 [0.68, 0.97]
1.1 Fluoxetine	1	112	Risk Ratio (M-H, Random, 95% CI)	0.81 [0.68, 0.97]
1.2 Sertraline	1	111	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
2 Disability	3	115	Std. Mean Difference (IV, Random, 95% CI)	0.70 [-0.73, 2.13]
2.1 Fluoxetine	2	55	Std. Mean Difference (IV, Random, 95% CI)	0.01 [-0.54, 0.56]

2.2 Sertraline	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2.3 Citalopram	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2.4 Paroxetine	1	60	Std. Mean Difference (IV, Random, 95% CI)	2.04 [1.41, 2.67]
2.5 Escitalopram	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2.6 Sertraline or fluoxetine	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3 Neurological deficit score	4	289	Std. Mean Difference (IV, Random, 95% CI)	-0.94 [-1.63, -0.26]
3.1 Fluoxetine	3	229	Std. Mean Difference (IV, Random, 95% CI)	-0.68 [-1.30, -0.06]
3.2 Sertraline	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3.3 Citalopram	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3.4 Paroxetine	1	60	Std. Mean Difference (IV, Random, 95% CI)	-1.76 [-2.36, -1.15]
3.5 Fluoxetine or sertraline	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4 Depression (continuous data)	7	464	Std. Mean Difference (IV, Random, 95% CI)	-0.72 [-1.52, 0.07]
4.1 Fluoxetine	4	215	Std. Mean Difference (IV, Random, 95% CI)	-0.01 [-0.54, 0.53]
4.2 Sertraline	1	123	Std. Mean Difference (IV, Random, 95% CI)	-0.16 [-0.52, 0.19]
4.3 Citalopram	1	66	Std. Mean Difference (IV, Random, 95% CI)	-0.54 [-1.04, -0.05]
4.4 Paroxetine	1	60	Std. Mean Difference (IV, Random, 95% CI)	-5.32 [-6.43, -4.21]
4.5 Fluoxetine or sertraline	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
5 Depression (dichotomous data)	2	166	Risk Ratio (M-H, Random, 95% CI)	0.53 [0.19, 1.49]
5.1 Fluoxetine	1	67	Risk Ratio (M-H, Random, 95% CI)	0.26 [0.06, 1.12]
5.2 Sertraline	1	99	Risk Ratio (M-H, Random, 95% CI)	0.77 [0.34, 1.76]
5.3 Citalopram	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
5.4 Paroxetine	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
5.5 Escitalopram	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
6 Anxiety (continuous data)	3	115	Std. Mean Difference (IV, Random, 95% CI)	-0.66 [-1.74, 0.42]
6.1 Fluoxetine	2	55	Std. Mean Difference (IV, Random, 95% CI)	-0.13 [-0.66, 0.40]
6.2 Sertraline	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
6.3 Citalopram	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
6.4 Paroxetine	1	60	Std. Mean Difference (IV, Random, 95% CI)	-1.67 [-2.26, -1.08]
6.5 Escitalopram	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
7 Anxiety (dichotomous data)	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
8 Cognition (continuous scores end of treatment)	2	55	Std. Mean Difference (IV, Random, 95% CI)	0.03 [-0.50, 0.56]
8.1 Fluoxetine	2	55	Std. Mean Difference (IV, Random, 95% CI)	0.03 [-0.50, 0.56]
8.2 Sertraline	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
8.3 Citalopram	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
8.4 Escitalopram	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
9 Death	9	651	Risk Ratio (M-H, Random, 95% CI)	0.87 [0.30, 2.50]
9.1 Fluoxetine	5	302	Risk Ratio (M-H, Random, 95% CI)	0.78 [0.14, 4.39]
9.2 Sertraline	2	223	Risk Ratio (M-H, Random, 95% CI)	0.79 [0.08, 8.19]
9.3 Citalopram	1	66	Risk Ratio (M-H, Random, 95% CI)	1.0 [0.15, 6.68]
9.4 Paroxetine	1	60	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
9.5 Escitalopram	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
9.6 Sertraline or fluoxetine	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10 Seizures	3	244	Risk Ratio (M-H, Random, 95% CI)	3.93 [0.44, 34.85]
10.1 Fluoxetine	1	118	Risk Ratio (M-H, Random, 95% CI)	3.0 [0.12, 72.18]
10.2 Sertraline	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10.3 Citalopram	1	66	Risk Ratio (M-H, Random, 95% CI)	5.0 [0.25, 100.32]
10.4 Paroxetine	1	60	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10.5 Escitalopram	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10.6 Sertraline or fluoxetine	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
11 Gastrointestinal side effects	2	178	Risk Ratio (M-H, Random, 95% CI)	2.48 [1.06, 5.80]
11.1 Fluoxetine	1	118	Risk Ratio (M-H, Random, 95% CI)	2.33 [0.96, 5.66]

11.2 Sertraline	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
11.3 Citalopram	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
11.4 Paroxetine	1	60	Risk Ratio (M-H, Random, 95% CI)	5.0 [0.25, 99.95]
11.5 Escitalopram	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
11.6 Sertraline and paroxetine	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
12 Bleeding	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
12.1 Fluoxetine	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
12.2 Sertraline	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
12.3 Citalopram	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
12.4 Paroxetine	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
12.5 Escitalopram	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
12.6 Sertraline or fluoxetine	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
13 Change in depression scores between baseline and follow-up	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
13.1 Sertraline	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
14 Change in cognition between baseline and end of treatment	1	99	Std. Mean Difference (IV, Random, 95% CI)	0.0 [-0.39, 0.39]
14.1 Sertraline	1	99	Std. Mean Difference (IV, Random, 95% CI)	0.0 [-0.39, 0.39]
15 Leaving the trial before the end of scheduled follow-up	9	673	Risk Ratio (M-H, Random, 95% CI)	1.21 [0.75, 1.95]
15.1 Fluoxetine	5	312	Risk Ratio (M-H, Random, 95% CI)	1.11 [0.58, 2.11]
15.2 Sertraline	2	234	Risk Ratio (M-H, Random, 95% CI)	1.10 [0.47, 2.54]
15.3 Citalopram	1	66	Risk Ratio (M-H, Random, 95% CI)	6.00 [0.76, 47.14]
15.4 Paroxetine	1	61	Risk Ratio (M-H, Random, 95% CI)	3.10 [0.13, 73.16]
15.5 Sertraline or fluoxetine	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
15.6 Escitalopram	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
16 Bleeding	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]

Comparison 7. SSRI versus control at end of treatment, patient/personnel blind: low risk of bias

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Dependent on modified Rankin score (mRS 3 to 5)	2	223	Risk Ratio (M-H, Random, 95% CI)	0.81 [0.68, 0.97]
1.1 Fluoxetine	1	112	Risk Ratio (M-H, Random, 95% CI)	0.81 [0.68, 0.97]
1.2 Sertraline	1	111	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
2 Disability	7	297	Std. Mean Difference (IV, Random, 95% CI)	0.36 [0.12, 0.59]
2.1 Fluoxetine	6	277	Std. Mean Difference (IV, Random, 95% CI)	0.35 [0.08, 0.61]
2.2 Sertraline	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2.3 Citalopram	1	20	Std. Mean Difference (IV, Random, 95% CI)	0.25 [-0.63, 1.13]
2.4 Paroxetine	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2.5 Escitalopram	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2.6 Sertraline or fluoxetine	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3 Neurological deficit score	6	315	Std. Mean Difference (IV, Random, 95% CI)	-0.32 [-0.55, -0.10]
3.1 Fluoxetine	4	267	Std. Mean Difference (IV, Random, 95% CI)	-0.35 [-0.59, -0.11]
3.2 Sertraline	1	28	Std. Mean Difference (IV, Random, 95% CI)	0.17 [-0.57, 0.91]
3.3 Citalopram	1	20	Std. Mean Difference (IV, Random, 95% CI)	-0.68 [-1.59, 0.23]
3.4 Paroxetine	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3.5 Fluoxetine or sertraline	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]

4 Depression (continuous data)	11	646	Std. Mean Difference (IV, Random, 95% CI)	-0.40 [-0.71, -0.09]
4.1 Fluoxetine	8	437	Std. Mean Difference (IV, Random, 95% CI)	-0.40 [-0.83, 0.03]
4.2 Sertraline	1	123	Std. Mean Difference (IV, Random, 95% CI)	-0.16 [-0.52, 0.19]
4.3 Citalopram	2	86	Std. Mean Difference (IV, Random, 95% CI)	-0.51 [-0.94, -0.08]
4.4 Paroxetine	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4.5 Fluoxetine or sertraline	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
5 Depression (dichotomous data)	3	283	Risk Ratio (M-H, Random, 95% CI)	0.52 [0.30, 0.90]
5.1 Fluoxetine	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
5.2 Sertraline	2	166	Risk Ratio (M-H, Random, 95% CI)	0.59 [0.28, 1.25]
5.3 Citalopram	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
5.4 Paroxetine	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
5.5 Escitalopram	1	117	Risk Ratio (M-H, Random, 95% CI)	0.38 [0.14, 0.99]
6 Anxiety (continuous data)	2	55	Std. Mean Difference (IV, Random, 95% CI)	-0.13 [-0.66, 0.40]
6.1 Fluoxetine	2	55	Std. Mean Difference (IV, Random, 95% CI)	-0.13 [-0.66, 0.40]
6.2 Sertraline	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
6.3 Citalopram	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
6.4 Paroxetine	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
6.5 Escitalopram	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
7 Anxiety (dichotomous data)	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
8 Cognition (continuous scores end of treatment)	4	174	Std. Mean Difference (IV, Random, 95% CI)	-0.10 [-0.39, 0.20]
8.1 Fluoxetine	3	86	Std. Mean Difference (IV, Random, 95% CI)	-0.12 [-0.55, 0.30]
8.2 Sertraline	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
8.3 Citalopram	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
8.4 Escitalopram	1	88	Std. Mean Difference (IV, Random, 95% CI)	-0.07 [-0.49, 0.35]
9 Death	14	865	Risk Ratio (M-H, Random, 95% CI)	1.05 [0.41, 2.66]
9.1 Fluoxetine	8	411	Risk Ratio (M-H, Random, 95% CI)	0.78 [0.14, 4.39]
9.2 Sertraline	3	251	Risk Ratio (M-H, Random, 95% CI)	0.91 [0.20, 4.19]
9.3 Citalopram	2	86	Risk Ratio (M-H, Random, 95% CI)	1.0 [0.15, 6.68]
9.4 Paroxetine	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
9.5 Escitalopram	1	117	Risk Ratio (M-H, Random, 95% CI)	4.92 [0.24, 100.25]
9.6 Sertraline or fluoxetine	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10 Seizures	4	250	Risk Ratio (M-H, Random, 95% CI)	2.67 [0.61, 11.63]
10.1 Fluoxetine	3	184	Risk Ratio (M-H, Random, 95% CI)	2.19 [0.41, 11.85]
10.2 Sertraline	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10.3 Citalopram	1	66	Risk Ratio (M-H, Random, 95% CI)	5.0 [0.25, 100.32]
10.4 Paroxetine	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10.5 Escitalopram	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10.6 Sertraline or fluoxetine	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
11 Gastrointestinal side effects	5	303	Risk Ratio (M-H, Random, 95% CI)	1.37 [0.63, 2.98]
11.1 Fluoxetine	4	275	Risk Ratio (M-H, Random, 95% CI)	1.48 [0.65, 3.39]
11.2 Sertraline	1	28	Risk Ratio (M-H, Random, 95% CI)	0.33 [0.01, 7.55]
11.3 Citalopram	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
11.4 Paroxetine	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
11.5 Escitalopram	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
11.6 Sertraline and paroxetine	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
12 Bleeding	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
12.1 Fluoxetine	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
12.2 Sertraline	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
12.3 Citalopram	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
12.4 Paroxetine	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
12.5 Escitalopram	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]

12.6 Sertraline or fluoxetine	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
13 Change in depression scores between baseline and follow-up	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
13.1 Sertraline	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
14 Change in cognition between baseline and end of treatment	1	99	Std. Mean Difference (IV, Random, 95% CI)	0.0 [-0.39, 0.39]
14.1 Sertraline	1	99	Std. Mean Difference (IV, Random, 95% CI)	0.0 [-0.39, 0.39]
15 Leaving the trial before the end of scheduled follow-up	16	1111	Risk Ratio (M-H, Random, 95% CI)	1.05 [0.82, 1.36]
15.1 Fluoxetine	9	509	Risk Ratio (M-H, Random, 95% CI)	1.19 [0.74, 1.92]
15.2 Sertraline	4	399	Risk Ratio (M-H, Random, 95% CI)	0.95 [0.69, 1.32]
15.3 Citalopram	2	86	Risk Ratio (M-H, Random, 95% CI)	6.00 [0.76, 47.14]
15.4 Paroxetine	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
15.5 Sertraline or fluoxetine	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
15.6 Escitalopram	1	117	Risk Ratio (M-H, Random, 95% CI)	1.38 [0.46, 4.09]

Comparison 8. SSRI versus control at end of treatment, outcome assessor blind: low risk of bias

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Dependent on modified Rankin score (mRS 3 to 5)	2	223	Risk Ratio (M-H, Random, 95% CI)	0.81 [0.68, 0.97]
1.1 Fluoxetine	1	112	Risk Ratio (M-H, Random, 95% CI)	0.81 [0.68, 0.97]
1.2 Sertraline	1	111	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
2 Disability	4	239	Std. Mean Difference (IV, Random, 95% CI)	0.87 [0.16, 1.58]
2.1 Fluoxetine	2	159	Std. Mean Difference (IV, Random, 95% CI)	0.57 [0.24, 0.90]
2.2 Sertraline	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2.3 Citalopram	1	20	Std. Mean Difference (IV, Random, 95% CI)	0.25 [-0.63, 1.13]
2.4 Paroxetine	1	60	Std. Mean Difference (IV, Random, 95% CI)	2.04 [1.41, 2.67]
2.5 Escitalopram	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2.6 Sertraline or fluoxetine	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3 Neurological deficit score	8	640	Std. Mean Difference (IV, Random, 95% CI)	-0.76 [-1.15, -0.38]
3.1 Fluoxetine	4	306	Std. Mean Difference (IV, Random, 95% CI)	-0.41 [-0.63, -0.18]
3.2 Sertraline	1	80	Std. Mean Difference (IV, Random, 95% CI)	-0.56 [-1.01, -0.11]
3.3 Citalopram	1	20	Std. Mean Difference (IV, Random, 95% CI)	-0.68 [-1.59, 0.23]
3.4 Paroxetine	1	60	Std. Mean Difference (IV, Random, 95% CI)	-1.76 [-2.36, -1.15]
3.5 Fluoxetine or sertraline	1	174	Std. Mean Difference (IV, Random, 95% CI)	-1.40 [-1.73, -1.06]
4 Depression (continuous data)	10	741	Std. Mean Difference (IV, Random, 95% CI)	-1.39 [-2.10, -0.68]
4.1 Fluoxetine	5	390	Std. Mean Difference (IV, Random, 95% CI)	-1.01 [-1.69, -0.34]
4.2 Sertraline	2	203	Std. Mean Difference (IV, Random, 95% CI)	-0.23 [-0.51, 0.04]
4.3 Citalopram	2	88	Std. Mean Difference (IV, Random, 95% CI)	-1.85 [-4.65, 0.96]
4.4 Paroxetine	1	60	Std. Mean Difference (IV, Random, 95% CI)	-5.32 [-6.43, -4.21]
4.5 Fluoxetine or sertraline	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
5 Depression (dichotomous data)	1	117	Risk Ratio (M-H, Random, 95% CI)	0.38 [0.14, 0.99]
5.1 Fluoxetine	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
5.2 Sertraline	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
5.3 Citalopram	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
5.4 Paroxetine	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
5.5 Escitalopram	1	117	Risk Ratio (M-H, Random, 95% CI)	0.38 [0.14, 0.99]

6 Anxiety (continuous data)	1	60	Std. Mean Difference (IV, Random, 95% CI)	-1.67 [-2.26, -1.08]
6.1 Fluoxetine	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
6.2 Sertraline	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
6.3 Citalopram	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
6.4 Paroxetine	1	60	Std. Mean Difference (IV, Random, 95% CI)	-1.67 [-2.26, -1.08]
6.5 escitalopram	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
7 Anxiety (dichotomous data)	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
8 Cognition (continuous scores end of treatment)	2	168	Std. Mean Difference (IV, Random, 95% CI)	0.21 [-0.36, 0.78]
8.1 Fluoxetine	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
8.2 Sertraline	1	80	Std. Mean Difference (IV, Random, 95% CI)	0.51 [0.06, 0.95]
8.3 Citalopram	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
8.4 Escitalopram	1	88	Std. Mean Difference (IV, Random, 95% CI)	-0.07 [-0.49, 0.35]
9 Death	11	833	Risk Ratio (M-H, Random, 95% CI)	1.13 [0.25, 4.97]
9.1 Fluoxetine	5	343	Risk Ratio (M-H, Random, 95% CI)	1.28 [0.16, 10.11]
9.2 Sertraline	2	203	Risk Ratio (M-H, Random, 95% CI)	0.20 [0.01, 4.02]
9.3 Citalopram	2	110	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
9.4 Paroxetine	1	60	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
9.5 Escitalopram	1	117	Risk Ratio (M-H, Random, 95% CI)	4.92 [0.24, 100.25]
9.6 Sertraline or fluoxetine	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10 Seizures	3	249	Risk Ratio (M-H, Random, 95% CI)	3.0 [0.12, 72.18]
10.1 Fluoxetine	2	189	Risk Ratio (M-H, Random, 95% CI)	3.0 [0.12, 72.18]
10.2 Sertraline	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10.3 Citalopram	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10.4 Paroxetine	1	60	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10.5 Escitalopram	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10.6 Sertraline or fluoxetine	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
11 Gastrointestinal side effects	5	367	Risk Ratio (M-H, Random, 95% CI)	1.74 [0.87, 3.49]
11.1 Fluoxetine	3	279	Risk Ratio (M-H, Random, 95% CI)	1.77 [0.81, 3.85]
11.2 Sertraline	1	28	Risk Ratio (M-H, Random, 95% CI)	0.33 [0.01, 7.55]
11.3 Citalopram	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
11.4 Paroxetine	1	60	Risk Ratio (M-H, Random, 95% CI)	5.0 [0.25, 99.95]
11.5 Escitalopram	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
11.6 Sertraline and paroxetine	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
12 Bleeding	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
12.1 Fluoxetine	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
12.2 Sertraline	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
12.3 Citalopram	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
12.4 Paroxetine	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
12.5 Escitalopram	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
12.6 Sertraline or fluoxetine	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
13 Change in depression scores between baseline and follow-up	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
13.1 Sertraline	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
14 Change in cognition between baseline and end of treatment	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
14.1 Sertraline	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
15 Leaving the trial before the end of scheduled follow-up	12	947	Risk Ratio (M-H, Random, 95% CI)	0.94 [0.71, 1.24]
15.1 Fluoxetine	6	456	Risk Ratio (M-H, Random, 95% CI)	1.07 [0.65, 1.76]
15.2 Sertraline	2	203	Risk Ratio (M-H, Random, 95% CI)	0.79 [0.53, 1.18]
15.3 Citalopram	2	110	Risk Ratio (M-H, Random, 95% CI)	1.0 [0.48, 2.07]

15.4 Paroxetine	1	61	Risk Ratio (M-H, Random, 95% CI)	3.10 [0.13, 73.16]
15.5 Sertraline or fluoxetine	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
15.6 Escitalopram	1	117	Risk Ratio (M-H, Random, 95% CI)	1.38 [0.46, 4.09]

Comparison 9. SSRI versus control at end of treatment, incomplete outcome data: low risk of bias

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Dependent on modified Rankin score (mRS 3 to 5)	2	223	Risk Ratio (M-H, Random, 95% CI)	0.81 [0.68, 0.97]
1.1 Fluoxetine	1	112	Risk Ratio (M-H, Random, 95% CI)	0.81 [0.68, 0.97]
1.2 Sertraline	1	111	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
2 Disability	10	598	Std. Mean Difference (IV, Random, 95% CI)	0.77 [0.22, 1.33]
2.1 Fluoxetine	6	276	Std. Mean Difference (IV, Random, 95% CI)	0.22 [-0.12, 0.55]
2.2 Sertraline	1	130	Std. Mean Difference (IV, Random, 95% CI)	1.38 [0.99, 1.76]
2.3 Citalopram	1	60	Std. Mean Difference (IV, Random, 95% CI)	2.67 [1.97, 3.38]
2.4 Paroxetine	2	132	Std. Mean Difference (IV, Random, 95% CI)	1.28 [-0.29, 2.86]
2.5 Escitalopram	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2.6 Sertraline or fluoxetine	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3 Neurological deficit score	13	999	Std. Mean Difference (IV, Random, 95% CI)	-1.12 [-1.55, -0.68]
3.1 Fluoxetine	7	537	Std. Mean Difference (IV, Random, 95% CI)	-1.14 [-1.78, -0.49]
3.2 Sertraline	2	108	Std. Mean Difference (IV, Random, 95% CI)	-0.26 [-0.96, 0.45]
3.3 Citalopram	1	60	Std. Mean Difference (IV, Random, 95% CI)	-2.27 [-2.93, -1.61]
3.4 Paroxetine	3	294	Std. Mean Difference (IV, Random, 95% CI)	-1.29 [-2.09, -0.49]
3.5 Fluoxetine or sertraline	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4 Depression (continuous data)	20	1590	Std. Mean Difference (IV, Random, 95% CI)	-2.16 [-2.77, -1.55]
4.1 Fluoxetine	10	637	Std. Mean Difference (IV, Random, 95% CI)	-2.65 [-3.88, -1.41]
4.2 Sertraline	3	333	Std. Mean Difference (IV, Random, 95% CI)	-0.64 [-1.41, 0.14]
4.3 Citalopram	2	126	Std. Mean Difference (IV, Random, 95% CI)	-1.67 [-3.89, 0.56]
4.4 Paroxetine	6	494	Std. Mean Difference (IV, Random, 95% CI)	-2.50 [-3.37, -1.63]
4.5 Fluoxetine or sertraline	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
5 Depression (dichotomous data)	6	486	Risk Ratio (M-H, Random, 95% CI)	0.41 [0.26, 0.65]
5.1 Fluoxetine	3	203	Risk Ratio (M-H, Random, 95% CI)	0.25 [0.11, 0.57]
5.2 Sertraline	2	166	Risk Ratio (M-H, Random, 95% CI)	0.59 [0.28, 1.25]
5.3 Citalopram	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
5.4 Paroxetine	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
5.5 Escitalopram	1	117	Risk Ratio (M-H, Random, 95% CI)	0.38 [0.14, 0.99]
6 Anxiety (continuous data)	5	249	Std. Mean Difference (IV, Random, 95% CI)	-1.03 [-2.09, 0.04]
6.1 Fluoxetine	3	115	Std. Mean Difference (IV, Random, 95% CI)	-0.40 [-0.85, 0.05]
6.2 Sertraline	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
6.3 Citalopram	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
6.4 Paroxetine	2	134	Std. Mean Difference (IV, Random, 95% CI)	-2.16 [-5.83, 1.51]
6.5 Escitalopram	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
7 Anxiety (dichotomous data)	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
8 Cognition (continuous scores end of treatment)	5	254	Std. Mean Difference (IV, Random, 95% CI)	0.07 [-0.26, 0.40]
8.1 Fluoxetine	3	86	Std. Mean Difference (IV, Random, 95% CI)	-0.12 [-0.55, 0.30]
8.2 Sertraline	1	80	Std. Mean Difference (IV, Random, 95% CI)	0.53 [0.08, 0.98]
8.3 Citalopram	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]

8.4 Escitalopram	1	88	Std. Mean Difference (IV, Random, 95% CI)	-0.07 [-0.49, 0.35]
9 Death	28	2156	Risk Ratio (M-H, Random, 95% CI)	0.99 [0.37, 2.64]
9.1 Fluoxetine	15	958	Risk Ratio (M-H, Random, 95% CI)	0.55 [0.07, 4.34]
9.2 Sertraline	5	461	Risk Ratio (M-H, Random, 95% CI)	0.91 [0.20, 4.19]
9.3 Citalopram	2	126	Risk Ratio (M-H, Random, 95% CI)	1.0 [0.15, 6.68]
9.4 Paroxetine	6	494	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
9.5 Escitalopram	1	117	Risk Ratio (M-H, Random, 95% CI)	4.92 [0.24, 100.25]
9.6 Sertraline or fluoxetine	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10 Seizures	5	332	Risk Ratio (M-H, Random, 95% CI)	2.22 [0.41, 12.06]
10.1 Fluoxetine	3	212	Risk Ratio (M-H, Random, 95% CI)	1.52 [0.20, 11.80]
10.2 Sertraline	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10.3 Citalopram	1	66	Risk Ratio (M-H, Random, 95% CI)	5.0 [0.25, 100.32]
10.4 Paroxetine	1	54	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10.5 Escitalopram	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10.6 Sertraline or fluoxetine	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
11 Gastrointestinal side effects	8	507	Risk Ratio (M-H, Random, 95% CI)	1.67 [0.56, 4.97]
11.1 Fluoxetine	6	425	Risk Ratio (M-H, Random, 95% CI)	1.43 [0.47, 4.36]
11.2 Sertraline	1	28	Risk Ratio (M-H, Random, 95% CI)	0.33 [0.01, 7.55]
11.3 Citalopram	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
11.4 Paroxetine	1	54	Risk Ratio (M-H, Random, 95% CI)	19.00 [1.16, 310.94]
11.5 Escitalopram	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
11.6 Sertraline and paroxetine	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
12 Bleeding	1	54	Risk Ratio (M-H, Random, 95% CI)	19.00 [1.16, 310.94]
12.1 Fluoxetine	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
12.2 Sertraline	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
12.3 Citalopram	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
12.4 Paroxetine	1	54	Risk Ratio (M-H, Random, 95% CI)	19.00 [1.16, 310.94]
12.5 Escitalopram	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
12.6 Sertraline or fluoxetine	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
13 Change in depression scores between baseline and follow-up	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
13.1 Sertraline	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
14 Change in cognition between baseline and end of treatment	1	99	Std. Mean Difference (IV, Random, 95% CI)	0.0 [-0.39, 0.39]
14.1 Sertraline	1	99	Std. Mean Difference (IV, Random, 95% CI)	0.0 [-0.39, 0.39]
15 Leaving the trial before the end of scheduled follow-up	28	2130	Risk Ratio (M-H, Random, 95% CI)	1.51 [1.02, 2.23]
15.1 Fluoxetine	13	784	Risk Ratio (M-H, Random, 95% CI)	1.62 [0.75, 3.51]
15.2 Sertraline	6	609	Risk Ratio (M-H, Random, 95% CI)	1.46 [0.79, 2.72]
15.3 Citalopram	2	126	Risk Ratio (M-H, Random, 95% CI)	6.00 [0.76, 47.14]
15.4 Paroxetine	6	494	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
15.5 Sertraline or fluoxetine	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
15.6 Escitalopram	1	117	Risk Ratio (M-H, Random, 95% CI)	1.38 [0.46, 4.09]

Comparison 10. SSRI versus control at end of treatment, selective reporting: low risk

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Dependent on modified Rankin score (mRS 3 to 5)	2	223	Risk Ratio (M-H, Random, 95% CI)	0.81 [0.68, 0.97]
1.1 Fluoxetine	1	112	Risk Ratio (M-H, Random, 95% CI)	0.81 [0.68, 0.97]
1.2 Sertraline	1	111	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
2 Disability	4	118	Std. Mean Difference (IV, Random, 95% CI)	0.11 [-0.26, 0.47]
2.1 Fluoxetine	4	118	Std. Mean Difference (IV, Random, 95% CI)	0.11 [-0.26, 0.47]
2.2 Sertraline	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2.3 Citalopram	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2.4 Paroxetine	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2.5 Escitalopram	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2.6 Sertraline or fluoxetine	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3 Neurological deficit score	3	172	Std. Mean Difference (IV, Random, 95% CI)	-0.20 [-0.50, 0.10]
3.1 Fluoxetine	2	144	Std. Mean Difference (IV, Random, 95% CI)	-0.27 [-0.60, 0.06]
3.2 Sertraline	1	28	Std. Mean Difference (IV, Random, 95% CI)	0.17 [-0.57, 0.91]
3.3 Citalopram	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3.4 Paroxetine	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3.5 Fluoxetine or sertraline	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4 Depression (continuous data)	6	294	Std. Mean Difference (IV, Random, 95% CI)	-0.22 [-0.63, 0.18]
4.1 Fluoxetine	5	228	Std. Mean Difference (IV, Random, 95% CI)	-0.13 [-0.64, 0.37]
4.2 Sertraline	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4.3 Citalopram	1	66	Std. Mean Difference (IV, Random, 95% CI)	-0.54 [-1.04, -0.05]
4.4 Paroxetine	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4.5 Fluoxetine or sertraline	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
5 Depression (dichotomous data)	3	283	Risk Ratio (M-H, Random, 95% CI)	0.52 [0.30, 0.90]
5.1 Fluoxetine	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
5.2 Sertraline	2	166	Risk Ratio (M-H, Random, 95% CI)	0.59 [0.28, 1.25]
5.3 Citalopram	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
5.4 Paroxetine	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
5.5 Escitalopram	1	117	Risk Ratio (M-H, Random, 95% CI)	0.38 [0.14, 0.99]
6 Anxiety (continuous data)	2	55	Std. Mean Difference (IV, Random, 95% CI)	-0.13 [-0.66, 0.40]
6.1 Fluoxetine	2	55	Std. Mean Difference (IV, Random, 95% CI)	-0.13 [-0.66, 0.40]
6.2 Sertraline	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
6.3 Citalopram	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
6.4 Paroxetine	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
6.5 Escitalopram	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
7 Anxiety (dichotomous data)	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
8 Cognition (continuous scores end of treatment)	3	86	Std. Mean Difference (IV, Random, 95% CI)	-0.12 [-0.55, 0.30]
8.1 Fluoxetine	3	86	Std. Mean Difference (IV, Random, 95% CI)	-0.12 [-0.55, 0.30]
8.2 Sertraline	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
8.3 Citalopram	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
9 Death	9	568	Risk Ratio (M-H, Random, 95% CI)	1.20 [0.43, 3.37]
9.1 Fluoxetine	5	257	Risk Ratio (M-H, Random, 95% CI)	0.55 [0.07, 4.34]
9.2 Sertraline	2	128	Risk Ratio (M-H, Random, 95% CI)	1.54 [0.26, 9.07]
9.3 Citalopram	1	66	Risk Ratio (M-H, Random, 95% CI)	1.0 [0.15, 6.68]
9.4 Paroxetine	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
9.5 Escitalopram	1	117	Risk Ratio (M-H, Random, 95% CI)	4.92 [0.24, 100.25]

9.6 Sertraline or fluoxetine	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10 Seizures	4	250	Risk Ratio (M-H, Random, 95% CI)	2.67 [0.61, 11.63]
10.1 Fluoxetine	3	184	Risk Ratio (M-H, Random, 95% CI)	2.19 [0.41, 11.85]
10.2 Sertraline	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10.3 Citalopram	1	66	Risk Ratio (M-H, Random, 95% CI)	5.0 [0.25, 100.32]
10.4 Paroxetine	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10.5 Escitalopram	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10.6 Sertraline or fluoxetine	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
11 Gastrointestinal side effects	4	213	Risk Ratio (M-H, Random, 95% CI)	1.35 [0.42, 4.29]
11.1 Fluoxetine	3	185	Risk Ratio (M-H, Random, 95% CI)	1.60 [0.44, 5.77]
11.2 Sertraline	1	28	Risk Ratio (M-H, Random, 95% CI)	0.33 [0.01, 7.55]
11.3 Citalopram	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
11.4 Paroxetine	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
11.5 Escitalopram	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
11.6 Sertraline and paroxetine	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
12 Bleeding	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
12.1 Fluoxetine	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
12.2 Sertraline	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
12.3 Citalopram	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
12.4 Paroxetine	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
12.5 Escitalopram	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
12.6 Sertraline or fluoxetine	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
13 Change in depression scores between baseline and follow-up	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
13.1 Sertraline	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
14 Change in cognition between baseline and end of treatment	1	99	Std. Mean Difference (IV, Random, 95% CI)	0.0 [-0.39, 0.39]
14.1 Sertraline	1	99	Std. Mean Difference (IV, Random, 95% CI)	0.0 [-0.39, 0.39]
15 Leaving the trial before the end of scheduled follow-up	10	714	Risk Ratio (M-H, Random, 95% CI)	1.32 [0.87, 1.99]
15.1 Fluoxetine	5	255	Risk Ratio (M-H, Random, 95% CI)	1.55 [0.70, 3.45]
15.2 Sertraline	3	276	Risk Ratio (M-H, Random, 95% CI)	1.17 [0.63, 2.16]
15.3 Citalopram	1	66	Risk Ratio (M-H, Random, 95% CI)	6.00 [0.76, 47.14]
15.4 Paroxetine	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
15.5 Sertraline or fluoxetine	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
15.6 Escitalopram	1	117	Risk Ratio (M-H, Random, 95% CI)	1.38 [0.46, 4.09]

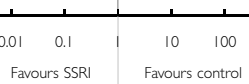
Analysis 1.1. Comparison 1 SSRI versus control at end of treatment, by SSRI, Outcome 1 Dependent on modified Rankin score (mRS 3 to 5).

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 1 SSRI versus control at end of treatment, by SSRI

Outcome: 1 Dependent on modified Rankin score (mRS 3 to 5)

Study or subgroup	SSRI n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
1 Fluoxetine				
Chollet 2011	42/57	50/55		0.81 [0.68, 0.97]
Subtotal (95% CI)	**57**	**55**		**0.81 [0.68, 0.97]**
Total events: 42 (SSRI), 50 (Control)				
Heterogeneity: not applicable				
Test for overall effect: Z = 2.34 (P = 0.019)				
2 Sertraline				
Almeida 2006	0/55	0/56		0.0 [0.0, 0.0]
Subtotal (95% CI)	**55**	**56**		**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)				
Heterogeneity: not applicable				
Test for overall effect: Z = 0.0 (P < 0.00001)				
Total (95% CI)	**112**	**111**		**0.81 [0.68, 0.97]**
Total events: 42 (SSRI), 50 (Control)				
Heterogeneity: Tau^2 = 0.0; Chi^2 = 0.0, df = 0 (P = 1.00); I^2 =0.0%				
Test for overall effect: Z = 2.34 (P = 0.019)				
Test for subgroup differences: Not applicable				



Analysis 1.2. Comparison 1 SSRI versus control at end of treatment, by SSRI, Outcome 2 Disability.

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 1 SSRI versus control at end of treatment, by SSRI

Outcome: 2 Disability

Study or subgroup	SSRI N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
1 Fluoxetine							
Chen 2001	19	79.31 (8.94)	18	71.56 (9.41)		4.3 %	0.83 [0.15, 1.50]
Cheng 2003	25	-26.38 (14.2)	32	-29.15 (17.38)		4.7 %	0.17 [-0.35, 0.69]
Dam 1996	16	61.9 (13)	16	54.1 (21.1)		4.3 %	0.43 [-0.27, 1.14]
Kong 2007	37	60.4 (12.5)	36	52.3 (13.5)		4.9 %	0.62 [0.15, 1.09]
Li 2008	58	40.8 (3.7)	28	38.4 (5.8)		4.9 %	0.53 [0.07, 0.99]
Liu 2004	30	70.33 (10.74)	30	64.33 (7.7)		4.7 %	0.63 [0.11, 1.15]
Robinson 2000a	14	59.2 (11.6)	13	56.2 (7.74)		4.1 %	0.29 [-0.47, 1.05]
Robinson 2000b	13	60.5 (10.8)	15	63.1 (8.2)		4.1 %	-0.27 [-1.01, 0.48]
Wang 2003	51	75 (4.2)	47	61 (6.9)		4.7 %	2.46 [1.93, 2.98]
Wiart 2000	16	87.4 (22.8)	15	88.7 (25.3)		4.3 %	-0.05 [-0.76, 0.65]
Xu 2001	26	73 (4.4)	27	67 (4.1)		4.5 %	1.39 [0.79, 2.00]
Xu 2007	36	64.4 (8.23)	36	56.9 (6.68)		4.8 %	0.99 [0.50, 1.48]
Zhou 2003	28	-27.8 (7.1)	26	-32.5 (7.8)		4.7 %	0.62 [0.07, 1.17]
Subtotal (95% CI)	**369**		**339**			**59.0 %**	**0.68 [0.31, 1.06]**
Heterogeneity: $Tau^2 = 0.38$; $Chi^2 = 65.71$, df = 12 (P<0.00001); I^2 =82%							
Test for overall effect: Z = 3.58 (P = 0.00034)							
2 Sertraline							
Xie 2005	65	88.7 (7.9)	65	79.8 (4.5)		5.1 %	1.38 [0.99, 1.76]
Subtotal (95% CI)	**65**		**65**			**5.1 %**	**1.38 [0.99, 1.76]**
Heterogeneity: not applicable							
Test for overall effect: Z = 7.03 (P < 0.00001)							
3 Citalopram							
Acler 2009	10	82 (28)	10	75 (25)		3.8 %	0.25 [-0.63, 1.13]
Li 2006	50	64.36 (8.23)	49	59.17 (9.02)		5.0 %	0.60 [0.19, 1.00]
Liu 2006	30	64.4 (12.1)	30	35.4 (9.1)		4.2 %	2.67 [1.97, 3.38]
Subtotal (95% CI)	**90**		**89**			**13.0 %**	**1.18 [-0.22, 2.58]**
Heterogeneity: $Tau^2 = 1.41$; $Chi^2 = 28.09$, df = 2 (P<0.00001); I^2 =93%							

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Study or subgroup	SSRI N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
Test for overall effect: Z = 1.65 (P = 0.099)							
4 Paroxetine							
Chen 2002	24	61 (12.2)	20	51.5 (10.3)		4.5 %	0.82 [0.20, 1.44]
Chen T 2005	40	65.76 (5.92)	38	51.76 (7.32)		4.6 %	2.09 [1.53, 2.64]
He 2005	27	84.26 (8.41)	27	78.33 (15.01)		4.7 %	0.48 [-0.06, 1.02]
Xu 2006	28	-27.63 (4.81)	29	-32.81 (4.13)		4.6 %	1.14 [0.58, 1.70]
Ye 2004	30	78.75 (14.19)	30	50.26 (13.4)		4.5 %	2.04 [1.41, 2.67]
Subtotal (95% CI)	**149**		**144**			**22.9 %**	**1.31 [0.67, 1.95]**
Heterogeneity: Tau^2 = 0.45; Chi^2 = 24.34, df = 4 (P = 0.00007); I^2 =84%							
Test for overall effect: Z = 4.01 (P = 0.000062)							
5 Escitalopram							
Subtotal (95% CI)	**0**		**0**			**0.0 %**	**0.0 [0.0, 0.0]**
Heterogeneity: not applicable							
Test for overall effect: not applicable							
6 Sertraline or fluoxetine							
Subtotal (95% CI)	**0**		**0**			**0.0 %**	**0.0 [0.0, 0.0]**
Heterogeneity: not applicable							
Test for overall effect: not applicable							
Total (95% CI)	**673**		**637**			**100.0 %**	**0.92 [0.62, 1.23]**
Heterogeneity: Tau^2 = 0.45; Chi^2 = 136.49, df = 21 (P<0.00001); I^2 =85%							
Test for overall effect: Z = 5.91 (P < 0.00001)							
Test for subgroup differences: Chi^2 = 7.11, df = 3 (P = 0.07), I^2 =58%							

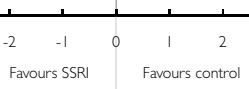
Analysis 1.3. Comparison 1 SSRI versus control at end of treatment, by SSRI, Outcome 3 Neurological deficit score.

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 1 SSRI versus control at end of treatment, by SSRI

Outcome: 3 Neurological deficit score

Study or subgroup	SSRI N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
1 Fluoxetine							
Chen 2001	19	-49.72 (4.07)	18	-43.13 (3.64)		3.0 %	-1.67 [-2.43, -0.91]
Cheng 2003	25	6.5 (3.19)	32	10.96 (8.13)		3.5 %	-0.68 [-1.22, -0.14]
Chollet 2011	57	5.8 (3.7)	55	6.9 (4.4)		3.8 %	-0.27 [-0.64, 0.10]
Dam 1996	16	44.1 (9.4)	16	46.8 (9.9)		3.2 %	-0.27 [-0.97, 0.42]
Feng 2004	16	9.1 (3.2)	16	14.4 (2.2)		2.8 %	-1.88 [-2.73, -1.03]
Fruehwald 2003	26	-55.5 (4.8)	24	-52.8 (5.4)		3.4 %	-0.52 [-1.09, 0.04]
He 2004	36	10.41 (6.36)	35	14.43 (7.94)		3.6 %	-0.55 [-1.03, -0.08]
Huang 2002	40	4.02 (1.86)	40	8.57 (3.64)		3.6 %	-1.56 [-2.06, -1.06]
Kong 2007	37	8.6 (6.4)	36	11.2 (6.4)		3.6 %	-0.40 [-0.87, 0.06]
Li 2004a	33	6.23 (3.11)	34	12.86 (6.36)		3.5 %	-1.30 [-1.83, -0.77]
Liang 2003	42	11.74 (3.23)	21	17.32 (5.19)		3.4 %	-1.38 [-1.96, -0.80]
Liu 2004	30	9.2 (2.06)	30	10.47 (9.2)		3.6 %	-0.19 [-0.70, 0.32]
Wang 2003	51	9.5 (3.5)	47	15.6 (4.6)		3.7 %	-1.49 [-1.94, -1.04]
Wen 2006	42	10.1 (1.9)	42	16.4 (2.5)		3.3 %	-2.81 [-3.42, -2.20]
Xu 2001	26	8.2 (5.2)	27	12.4 (4.3)		3.4 %	-0.87 [-1.43, -0.30]
Xu 2007	36	21.89 (1.57)	36	20.78 (4.06)		3.6 %	0.36 [-0.11, 0.82]
Zhou 2003	28	9 (3.8)	26	12.2 (6.1)		3.5 %	-0.63 [-1.17, -0.08]
Subtotal (95% CI)	**560**		**535**			**58.7 %**	**-0.93 [-1.29, -0.57]**
Heterogeneity: Tau^2 = 0.49; Chi^2 = 122.69, df = 16 (P<0.00001); I^2 =87%							
Test for overall effect: Z = 5.07 (P < 0.00001)							
2 Sertraline							
Burns 1999	14	-29.7 (14.7)	14	-32.2 (13.4)		3.1 %	0.17 [-0.57, 0.91]
Guo 2009	40	29.07 (8.02)	40	33.78 (8.63)		3.7 %	-0.56 [-1.01, -0.11]
Subtotal (95% CI)	**54**		**54**			**6.7 %**	**-0.26 [-0.96, 0.45]**
Heterogeneity: Tau^2 = 0.17; Chi^2 = 2.74, df = 1 (P = 0.10); I^2 =64%							



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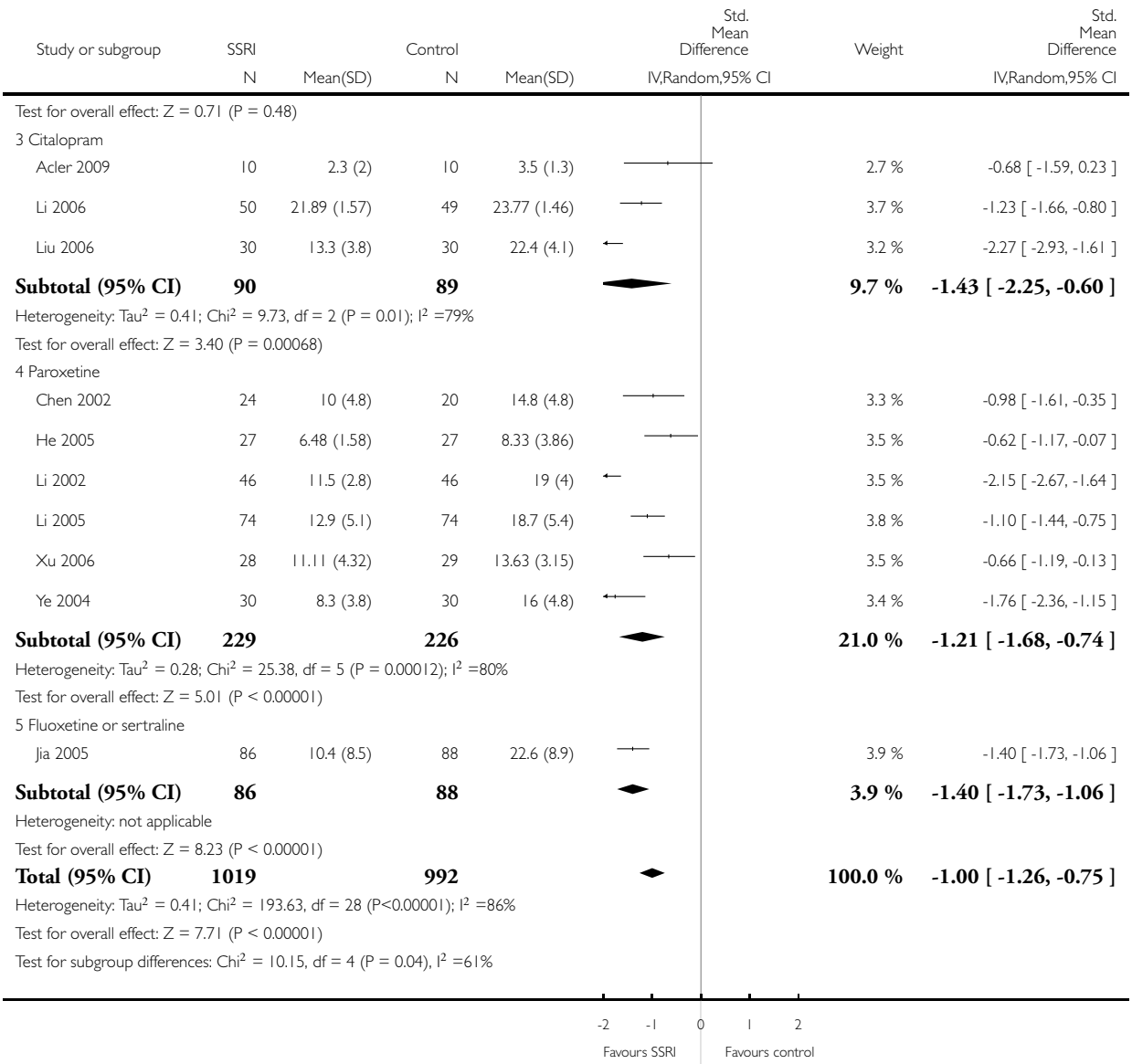


Analysis 1.4. Comparison 1 SSRI versus control at end of treatment, by SSRI, Outcome 4 Depression (continuous data).

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

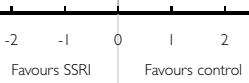
Comparison: 1 SSRI versus control at end of treatment, by SSRI

Outcome: 4 Depression (continuous data)

Study or subgroup	SSRI N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
1 Fluoxetine							
Chen 2001	19	10.82 (6.25)	18	18.48 (6.28)		2.6 %	-1.20 [-1.90, -0.49]
Cheng 2003	25	13.64 (11.02)	32	17.98 (12.53)		2.7 %	-0.36 [-0.89, 0.17]
Chollet 2011	56	5.4 (4.9)	54	8.4 (7.9)		2.7 %	-0.46 [-0.83, -0.08]
Dam 1996	16	8.8 (5.6)	16	9.4 (5.6)		2.6 %	-0.10 [-0.80, 0.59]
Feng 2004	16	34.9 (4.6)	16	41.1 (4.7)		2.5 %	-1.30 [-2.07, -0.53]
Fruehwald 2003	26	9.5 (7.9)	24	11.2 (12.4)		2.7 %	-0.16 [-0.72, 0.39]
He 2004	36	14.28 (2.31)	35	20.32 (2.82)		2.6 %	-2.32 [-2.93, -1.71]
Huang 2002	40	4.76 (0.6)	40	16.34 (1.3)		1.8 %	-11.33 [-13.18, -9.47]
Ji 2000	20	5.2 (1.5)	20	14.5 (2.7)		2.3 %	-4.17 [-5.32, -3.03]
Kong 2007	37	12.6 (5.3)	36	16.3 (3.7)		2.7 %	-0.80 [-1.28, -0.32]
Li 2008	58	14.5 (2.4)	28	18.7 (3.9)		2.7 %	-1.40 [-1.90, -0.90]
Liang 2003	42	9.67 (4.48)	21	19.19 (3.12)		2.6 %	-2.30 [-2.97, -1.63]
Robinson 2000a	14	18.5 (7.6)	13	12.2 (4.7)		2.5 %	0.96 [0.15, 1.76]
Robinson 2000b	13	5.9 (3.8)	15	6.2 (4.6)		2.6 %	-0.07 [-0.81, 0.67]
Song 2006	41	40.3 (7.25)	41	48.31 (8.02)		2.7 %	-1.04 [-1.50, -0.58]
Wang 2003	51	10.5 (2.9)	47	20 (6.1)		2.7 %	-2.00 [-2.49, -1.51]
Wen 2006	42	7 (1.1)	42	17.7 (1.8)		2.3 %	-7.11 [-8.29, -5.93]
Wiart 2000	16	11.8 (6.7)	15	18.7 (10)		2.6 %	-0.79 [-1.53, -0.06]
Xu 2001	26	23.6 (3.9)	27	44.7 (2.6)		2.2 %	-6.30 [-7.65, -4.94]
Xu 2007	36	5.61 (5.32)	36	17.73 (3.21)		2.6 %	-2.73 [-3.38, -2.08]
Zhou 2003	28	3.5 (1.3)	26	3.8 (1.6)		2.7 %	-0.20 [-0.74, 0.33]
Subtotal (95% CI)	**658**		**602**			**53.3 %**	**-1.97 [-2.63, -1.32]**

Heterogeneity: $Tau^2 = 2.16$; $Chi^2 = 448.43$, df = 20 (P<0.00001); $I^2 = 96\%$

Test for overall effect: Z = 5.92 (P < 0.00001)



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Study or subgroup	SSRI N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
2 Sertraline							
Finkenzeller 2009	23	12.1 (1.05)	27	10.6 (0.97)		2.6 %	1.47 [0.83, 2.10]
Guo 2009	40	14.82 (8.05)	40	17.61 (8)		2.7 %	-0.34 [-0.79, 0.10]
Murray 2005	62	10.5 (9.6)	61	12 (8.5)		2.7 %	-0.16 [-0.52, 0.19]
Xie 2005	65	30.9 (7.1)	65	39.7 (5.3)		2.7 %	-1.40 [-1.78, -1.01]
Subtotal (95% CI)	**190**		**193**			**10.8 %**	**-0.13 [-1.11, 0.85]**
Heterogeneity: $Tau^2 = 0.94$; $Chi^2 = 61.06$, df = 3 (P<0.00001); $I^2 = 95\%$							
Test for overall effect: Z = 0.27 (P = 0.79)							
3 Citalopram							
Acler 2009	10	6.6 (3.6)	10	8 (3)		2.5 %	-0.40 [-1.29, 0.48]
Andersen 1994	33	11.4 (5.1)	33	14.1 (4.7)		2.7 %	-0.54 [-1.04, -0.05]
Li 2006	50	5.61 (5.32)	49	20.26 (6.08)		2.7 %	-2.55 [-3.08, -2.01]
Liu 2006	30	17.2 (2.1)	30	25.1 (3.3)		2.6 %	-2.82 [-3.55, -2.09]
Miao 2004	34	6.45 (5.3)	34	23.74 (5.16)		2.6 %	-3.27 [-4.01, -2.53]
Subtotal (95% CI)	**157**		**156**			**13.0 %**	**-1.92 [-3.08, -0.75]**
Heterogeneity: $Tau^2 = 1.64$; $Chi^2 = 64.70$, df = 4 (P<0.00001); $I^2 = 94\%$							
Test for overall effect: Z = 3.23 (P = 0.0012)							
4 Paroxetine							
Chen 2002	24	10.3 (3)	20	16.5 (2.5)		2.6 %	-2.19 [-2.95, -1.42]
Chen T 2005	40	10.98 (3.74)	38	22.45 (3.56)		2.6 %	-3.11 [-3.78, -2.44]
He 2005	27	10.11 (1.08)	27	17.48 (1.05)		2.1 %	-6.82 [-8.26, -5.38]
Lai 2006	40	12.5 (8.4)	40	21.5 (4.3)		2.7 %	-1.34 [-1.82, -0.85]
Li 2002	46	10 (3)	46	22 (8)		2.7 %	-1.97 [-2.47, -1.47]
Li 2005	74	12.6 (2.1)	74	16.8 (2.3)		2.7 %	-1.90 [-2.29, -1.51]
Yang 2011	20	7 (4)	22	13 (6)		2.6 %	-1.14 [-1.80, -0.49]
Ye 2004	30	4.02 (3.07)	30	17.32 (1.66)		2.3 %	-5.32 [-6.43, -4.21]
Subtotal (95% CI)	**301**		**297**			**20.3 %**	**-2.81 [-3.66, -1.96]**
Heterogeneity: $Tau^2 = 1.35$; $Chi^2 = 101.50$, df = 7 (P<0.00001); $I^2 = 93\%$							
Test for overall effect: Z = 6.46 (P < 0.00001)							
5 Fluoxetine or sertraline							
Jia 2005	86	6.4 (6.2)	88	16.2 (6.8)		2.7 %	-1.50 [-1.84, -1.16]
Subtotal (95% CI)	**86**		**88**			**2.7 %**	**-1.50 [-1.84, -1.16]**
Heterogeneity: not applicable							
Test for overall effect: Z = 8.71 (P < 0.00001)							
6 Escitalopram							
Subtotal (95% CI)	**0**		**0**			**0.0 %**	**0.0 [0.0, 0.0]**

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Favours SSRI Favours control

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Study or subgroup	SSRI N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
Heterogeneity: not applicable							
Test for overall effect: not applicable							
Total (95% CI)	**1392**		**1336**			**100.0 %**	**-1.91 [-2.34, -1.48]**
Heterogeneity: Tau² = 1.74; Chi² = 817.95, df = 38 (P<0.00001); I² =95%							
Test for overall effect: Z = 8.70 (P < 0.00001)							
Test for subgroup differences: Chi² = 18.17, df = 4 (P = 0.00), I² =78%							

Analysis 1.5. Comparison 1 SSRI versus control at end of treatment, by SSRI, Outcome 5 Depression (dichotomous data).

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 1 SSRI versus control at end of treatment, by SSRI

Outcome: 5 Depression (dichotomous data)

Study or subgroup	SSRI n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
1 Fluoxetine					
Li 2004a	2/33	8/34		8.7 %	0.26 [0.06, 1.12]
Li 2004b	5/31	13/32		13.0 %	0.40 [0.16, 0.98]
Zhou 2008	4/36	18/40		12.3 %	0.25 [0.09, 0.66]
Subtotal (95% CI)	**100**	**106**		**34.0 %**	**0.31 [0.17, 0.57]**
Total events: 11 (SSRI), 39 (Control)					
Heterogeneity: Tau² = 0.0; Chi² = 0.56, df = 2 (P = 0.76); I² =0.0%					
Test for overall effect: Z = 3.80 (P = 0.00014)					
2 Sertraline					
Almeida 2006	8/48	11/51		13.8 %	0.77 [0.34, 1.76]
Rasmussen 2003	3/35	8/32		10.3 %	0.34 [0.10, 1.18]
Subtotal (95% CI)	**83**	**83**		**24.1 %**	**0.59 [0.28, 1.25]**

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Study or subgroup	SSRI n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Total events: 11 (SSRI), 19 (Control)					
Heterogeneity: Tau² = 0.05; Chi² = 1.16, df = 1 (P = 0.28); I² =14%					
Test for overall effect: Z = 1.37 (P = 0.17)					
3 Citalopram					
Subtotal (95% CI)	**0**	**0**		**0.0 %**	**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)					
Heterogeneity: not applicable					
Test for overall effect: not applicable					
4 Paroxetine					
GlaxoSmithKline 1998	82/111	97/114		18.5 %	0.87 [0.76, 0.99]
Xu 2006	3/28	12/29		10.9 %	0.26 [0.08, 0.82]
Subtotal (95% CI)	**139**	**143**		**29.5 %**	**0.53 [0.15, 1.92]**
Total events: 85 (SSRI), 109 (Control)					
Heterogeneity: Tau² = 0.71; Chi² = 5.04, df = 1 (P = 0.02); I² =80%					
Test for overall effect: Z = 0.96 (P = 0.33)					
5 Escitalopram					
Robinson 2008	5/59	13/58		12.5 %	0.38 [0.14, 0.99]
Subtotal (95% CI)	**59**	**58**		**12.5 %**	**0.38 [0.14, 0.99]**
Total events: 5 (SSRI), 13 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.97 (P = 0.048)					
Total (95% CI)	**381**	**390**		**100.0 %**	**0.43 [0.24, 0.77]**
Total events: 112 (SSRI), 180 (Control)					
Heterogeneity: Tau² = 0.49; Chi² = 30.48, df = 7 (P = 0.00008); I² =77%					
Test for overall effect: Z = 2.82 (P = 0.0049)					
Test for subgroup differences: Chi² = 1.93, df = 3 (P = 0.59), I² =0.0%					

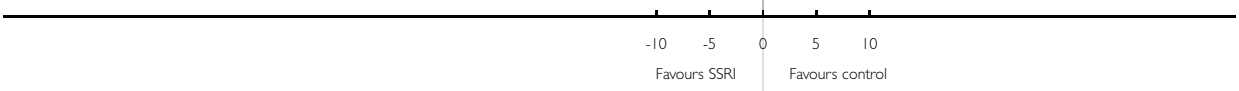
Analysis 1.6. Comparison 1 SSRI versus control at end of treatment, by SSRI, Outcome 6 Anxiety (continuous data).

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 1 SSRI versus control at end of treatment, by SSRI

Outcome: 6 Anxiety (continuous data)

Study or subgroup	SSRI N	SSRI Mean(SD)	Control N	Control Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
1 Fluoxetine							
Liu 2004	30	7.43 (3.63)	30	11 (5.63)		12.9 %	-0.74 [-1.27, -0.22]
Robinson 2000a	14	9.8 (4.8)	13	9.9 (5.1)		12.1 %	-0.02 [-0.77, 0.74]
Robinson 2000b	13	4.7 (3.8)	15	5.5 (2.9)		12.1 %	-0.23 [-0.98, 0.51]
Zhou 2003	28	3.5 (1.3)	26	3.3 (1.3)		12.9 %	0.15 [-0.38, 0.69]
Subtotal (95% CI)	**85**		**84**			**50.1 %**	**-0.23 [-0.67, 0.21]**
Heterogeneity: Tau² = 0.10; Chi² = 5.93, df = 3 (P = 0.11); I² =49%							
Test for overall effect: Z = 1.02 (P = 0.31)							
2 Sertraline							
Finkenzeller 2009	23	6.9 (0.57)	27	6.7 (0.53)		12.8 %	0.36 [-0.20, 0.92]
Subtotal (95% CI)	**23**		**27**			**12.8 %**	**0.36 [-0.20, 0.92]**
Heterogeneity: not applicable							
Test for overall effect: Z = 1.25 (P = 0.21)							
3 Citalopram							
Subtotal (95% CI)	**0**		**0**			**0.0 %**	**0.0 [0.0, 0.0]**
Heterogeneity: not applicable							
Test for overall effect: not applicable							
4 Paroxetine							
He 2005	27	5.37 (1.66)	27	12.78 (1.93)		11.3 %	-4.06 [-5.01, -3.10]
Lai 2006	40	50.2 (9.4)	40	54.2 (15.2)		13.2 %	-0.31 [-0.75, 0.13]
Ye 2004	30	9.82 (2.64)	30	14.02 (2.32)		12.7 %	-1.67 [-2.26, -1.08]
Subtotal (95% CI)	**97**		**97**			**37.1 %**	**-1.97 [-3.81, -0.12]**
Heterogeneity: Tau² = 2.54; Chi² = 52.14, df = 2 (P<0.00001); I² =96%							
Test for overall effect: Z = 2.09 (P = 0.037)							
5 Escitalopram							
Subtotal (95% CI)	**0**		**0**			**0.0 %**	**0.0 [0.0, 0.0]**
Heterogeneity: not applicable							
Test for overall effect: not applicable							
Total (95% CI)	**205**		**208**			**100.0 %**	**-0.77 [-1.52, -0.02]**
Heterogeneity: Tau² = 1.05; Chi² = 86.14, df = 7 (P<0.00001); I² =92%							
Test for overall effect: Z = 2.02 (P = 0.043)							
Test for subgroup differences: Chi² = 6.80, df = 2 (P = 0.03), I² =71%							



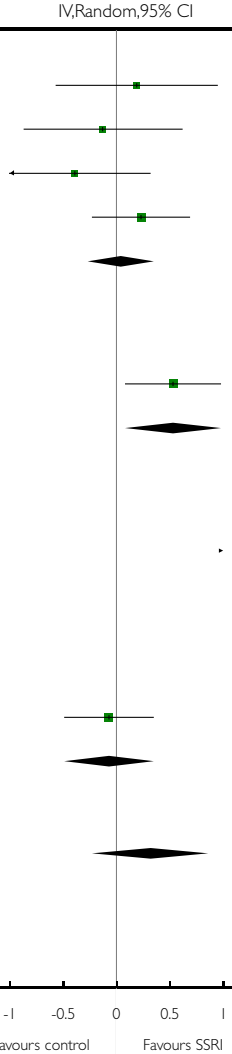
Analysis 1.8. Comparison 1 SSRI versus control at end of treatment, by SSRI, Outcome 8 Cognition (continuous scores end of treatment).

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 1 SSRI versus control at end of treatment, by SSRI

Outcome: 8 Cognition (continuous scores end of treatment)

Study or subgroup	SSRI N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
1 Fluoxetine							
Robinson 2000a	14	25.9 (7.5)	13	24.5 (6.8)		12.8 %	0.19 [-0.57, 0.95]
Robinson 2000b	13	26.1 (7.5)	15	26.8 (2.4)		12.9 %	-0.13 [-0.87, 0.62]
Wiart 2000	16	24.8 (3.9)	15	26.2 (3)		13.2 %	-0.39 [-1.10, 0.32]
Xu 2007	36	28.36 (2.57)	36	27.31 (5.88)		15.2 %	0.23 [-0.23, 0.69]
Subtotal (95% CI)	**79**		**79**			**54.1 %**	**0.04 [-0.27, 0.35]**
Heterogeneity: Tau^2 = 0.0; Chi^2 = 2.38, df = 3 (P = 0.50); I^2 =0.0%							
Test for overall effect: Z = 0.24 (P = 0.81)							
2 Sertraline							
Guo 2009	40	19.26 (6.87)	40	15.74 (6.28)		15.3 %	0.53 [0.08, 0.98]
Subtotal (95% CI)	**40**		**40**			**15.3 %**	**0.53 [0.08, 0.98]**
Heterogeneity: not applicable							
Test for overall effect: Z = 2.33 (P = 0.020)							
3 Citalopram							
Li 2006	50	28.36 (2.57)	49	24.32 (2.14)		15.2 %	1.69 [1.23, 2.16]
Subtotal (95% CI)	**50**		**49**			**15.2 %**	**1.69 [1.23, 2.16]**
Heterogeneity: not applicable							
Test for overall effect: Z = 7.19 (P < 0.00001)							
4 Escitalopram							
Robinson 2008	43	89.8 (15.1)	45	91 (17.8)		15.5 %	-0.07 [-0.49, 0.35]
Subtotal (95% CI)	**43**		**45**			**15.5 %**	**-0.07 [-0.49, 0.35]**
Heterogeneity: not applicable							
Test for overall effect: Z = 0.34 (P = 0.74)							
Total (95% CI)	**212**		**213**			**100.0 %**	**0.32 [-0.23, 0.86]**
Heterogeneity: Tau^2 = 0.45; Chi^2 = 42.83, df = 6 (P<0.00001); I^2 =86%							
Test for overall effect: Z = 1.15 (P = 0.25)							
Test for subgroup differences: Chi^2 = 40.45, df = 3 (P = 0.00), I^2 =93%							



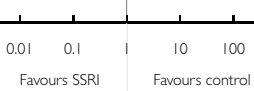
Analysis 1.9. Comparison 1 SSRI versus control at end of treatment, by SSRI, Outcome 9 Death.

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 1 SSRI versus control at end of treatment, by SSRI

Outcome: 9 Death

Study or subgroup	SSRI n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
1 Fluoxetine				
Brown 1998	0/10	0/10		0.0 [0.0, 0.0]
Chen 2001	0/21	0/20		0.0 [0.0, 0.0]
Cheng 2003	0/25	0/32		0.0 [0.0, 0.0]
Chollet 2011	1/59	1/59		1.00 [0.06, 15.61]
Dam 1996	0/18	0/17		0.0 [0.0, 0.0]
Feng 2004	0/18	0/18		0.0 [0.0, 0.0]
Fruehwald 2003	1/28	0/16		1.76 [0.08, 40.80]
He 2004	0/36	0/35		0.0 [0.0, 0.0]
Hu 2002	0/42	0/30		0.0 [0.0, 0.0]
Huang 2002	0/40	0/40		0.0 [0.0, 0.0]
Ji 2000	0/20	0/20		0.0 [0.0, 0.0]
Li 2004a	0/33	0/34		0.0 [0.0, 0.0]
Li 2004b	0/37	0/36		0.0 [0.0, 0.0]
Li 2008	0/60	0/30		0.0 [0.0, 0.0]
Liang 2003	0/42	0/21		0.0 [0.0, 0.0]
Liu 2004	0/30	0/30		0.0 [0.0, 0.0]
Robinson 2000a	0/23	1/17		0.25 [0.01, 5.79]
Robinson 2000b	0/17	0/16		0.0 [0.0, 0.0]
Song 2006	0/41	0/41		0.0 [0.0, 0.0]
Wen 2006	0/42	0/42		0.0 [0.0, 0.0]
Wiart 2000	0/16	0/15		0.0 [0.0, 0.0]



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Study or subgroup	SSRI n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
Xu 2001	0/32	0/31		0.0 [0.0, 0.0]
Xu 2007	0/36	0/36		0.0 [0.0, 0.0]
Zhou 2003	0/28	0/26		0.0 [0.0, 0.0]
Zhou 2008	0/36	0/40		0.0 [0.0, 0.0]
Subtotal (95% CI)	**790**	**712**		**0.78 [0.14, 4.39]**
Total events: 2 (SSRI), 2 (Control)				
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.79$, df = 2 (P = 0.67); $I^2 = 0.0\%$				
Test for overall effect: Z = 0.28 (P = 0.78)				
2 Sertraline				
Almeida 2006	2/48	1/52		2.17 [0.20, 23.14]
Burns 1999	1/14	1/14		1.00 [0.07, 14.45]
Guo 2009	0/40	0/40		0.0 [0.0, 0.0]
Murray 2005	0/62	2/61		0.20 [0.01, 4.02]
Xie 2005	0/65	0/65		0.0 [0.0, 0.0]
Subtotal (95% CI)	**229**	**232**		**0.91 [0.20, 4.19]**
Total events: 3 (SSRI), 4 (Control)				
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 1.54$, df = 2 (P = 0.46); $I^2 = 0.0\%$				
Test for overall effect: Z = 0.12 (P = 0.90)				
3 Citalopram				
Acler 2009	0/10	0/10		0.0 [0.0, 0.0]
Andersen 1994	2/33	2/33		1.00 [0.15, 6.68]
Li 2006	1/52	2/53		0.51 [0.05, 5.45]
Liu 2006	0/30	0/30		0.0 [0.0, 0.0]
Miao 2004	0/45	0/45		0.0 [0.0, 0.0]
Subtotal (95% CI)	**170**	**171**		**0.77 [0.17, 3.38]**
Total events: 3 (SSRI), 4 (Control)				
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.19$, df = 1 (P = 0.66); $I^2 = 0.0\%$				
Test for overall effect: Z = 0.35 (P = 0.73)				
4 Paroxetine				
Chen T 2005	0/40	0/38		0.0 [0.0, 0.0]
He 2005	0/27	0/27		0.0 [0.0, 0.0]
Lai 2006	0/40	0/40		0.0 [0.0, 0.0]
Li 2002	0/46	0/46		0.0 [0.0, 0.0]
Li 2005	0/74	0/74		0.0 [0.0, 0.0]
Xu 2006	0/32	2/32		0.20 [0.01, 4.01]

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Study or subgroup	SSRI n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
Yang 2002	0/64	0/57		0.0 [0.0, 0.0]
Yang 2011	0/20	0/22		0.0 [0.0, 0.0]
Ye 2004	0/30	0/30		0.0 [0.0, 0.0]
Subtotal (95% CI)	**373**	**366**		**0.20 [0.01, 4.01]**
Total events: 0 (SSRI), 2 (Control)				
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.0$, df = 0 (P = 1.00); $I^2 = 0.0\%$				
Test for overall effect: Z = 1.05 (P = 0.29)				
5 Escitalopram				
Robinson 2008	2/59	0/58		4.92 [0.24, 100.25]
Subtotal (95% CI)	**59**	**58**		**4.92 [0.24, 100.25]**
Total events: 2 (SSRI), 0 (Control)				
Heterogeneity: not applicable				
Test for overall effect: Z = 1.04 (P = 0.30)				
6 Sertraline or fluoxetine				
Jia 2005	0/92	2/92		0.20 [0.01, 4.11]
Subtotal (95% CI)	**92**	**92**		**0.20 [0.01, 4.11]**
Total events: 0 (SSRI), 2 (Control)				
Heterogeneity: not applicable				
Test for overall effect: Z = 1.04 (P = 0.30)				
Total (95% CI)	**1713**	**1631**		**0.76 [0.34, 1.70]**
Total events: 10 (SSRI), 14 (Control)				
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 5.54$, df = 10 (P = 0.85); $I^2 = 0.0\%$				
Test for overall effect: Z = 0.67 (P = 0.50)				
Test for subgroup differences: $Chi^2 = 3.04$, df = 5 (P = 0.69), $I^2 = 0.0\%$				

Analysis 1.10. Comparison 1 SSRI versus control at end of treatment, by SSRI, Outcome 10 Seizures.

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 1 SSRI versus control at end of treatment, by SSRI

Outcome: 10 Seizures

Study or subgroup	SSRI n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
1 Fluoxetine				
Chollet 2011	1/59	0/59		3.00 [0.12, 72.18]
Dam 1996	2/18	0/17		4.74 [0.24, 92.07]
He 2004	0/36	0/35		0.0 [0.0, 0.0]
Liang 2003	0/42	0/21		0.0 [0.0, 0.0]
Wiart 2000	1/16	1/15		0.94 [0.06, 13.68]
Subtotal (95% CI)	**171**	**147**		**2.19 [0.41, 11.85]**
Total events: 4 (SSRI), 1 (Control)				
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.69$, df = 2 (P = 0.71); $I^2 = 0.0\%$				
Test for overall effect: Z = 0.91 (P = 0.36)				
2 Sertraline				
Subtotal (95% CI)	**0**	**0**		**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)				
Heterogeneity: not applicable				
Test for overall effect: not applicable				
3 Citalopram				
Andersen 1994	2/33	0/33		5.00 [0.25, 100.32]
Subtotal (95% CI)	**33**	**33**		**5.00 [0.25, 100.32]**
Total events: 2 (SSRI), 0 (Control)				
Heterogeneity: not applicable				
Test for overall effect: Z = 1.05 (P = 0.29)				
4 Paroxetine				
Ye 2004	0/30	0/30		0.0 [0.0, 0.0]
Subtotal (95% CI)	**30**	**30**		**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)				
Heterogeneity: not applicable				
Test for overall effect: Z = 0.0 (P < 0.00001)				
5 Escitalopram				
Subtotal (95% CI)	**0**	**0**		**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)				
Heterogeneity: not applicable				
Test for overall effect: not applicable				

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Study or subgroup	SSRI n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
6 Sertraline or fluoxetine				
Subtotal (95% CI)	**0**	**0**		**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)				
Heterogeneity: not applicable				
Test for overall effect: not applicable				
Total (95% CI)	**234**	**210**		**2.67 [0.61, 11.63]**
Total events: 6 (SSRI), 1 (Control)				
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.91$, df = 3 (P = 0.82); $I^2 = 0.0\%$				
Test for overall effect: Z = 1.31 (P = 0.19)				
Test for subgroup differences: $Chi^2 = 0.22$, df = 1 (P = 0.64), $I^2 = 0.0\%$				

Analysis 1.11. Comparison 1 SSRI versus control at end of treatment, by SSRI, Outcome 11 Gastrointestinal side effects.

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 1 SSRI versus control at end of treatment, by SSRI

Outcome: 11 Gastrointestinal side effects

Study or subgroup	SSRI n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
1 Fluoxetine				
Chollet 2011	14/59	6/59		2.33 [0.96, 5.66]
Dam 1996	2/18	0/17		4.74 [0.24, 92.07]
He 2004	0/36	0/35		0.0 [0.0, 0.0]
Hu 2002	5/42	0/30		7.93 [0.46, 138.20]
Huang 2002	0/40	0/40		0.0 [0.0, 0.0]
Li 2004a	3/33	0/34		7.21 [0.39, 134.32]
Li 2008	6/60	3/30		1.00 [0.27, 3.72]

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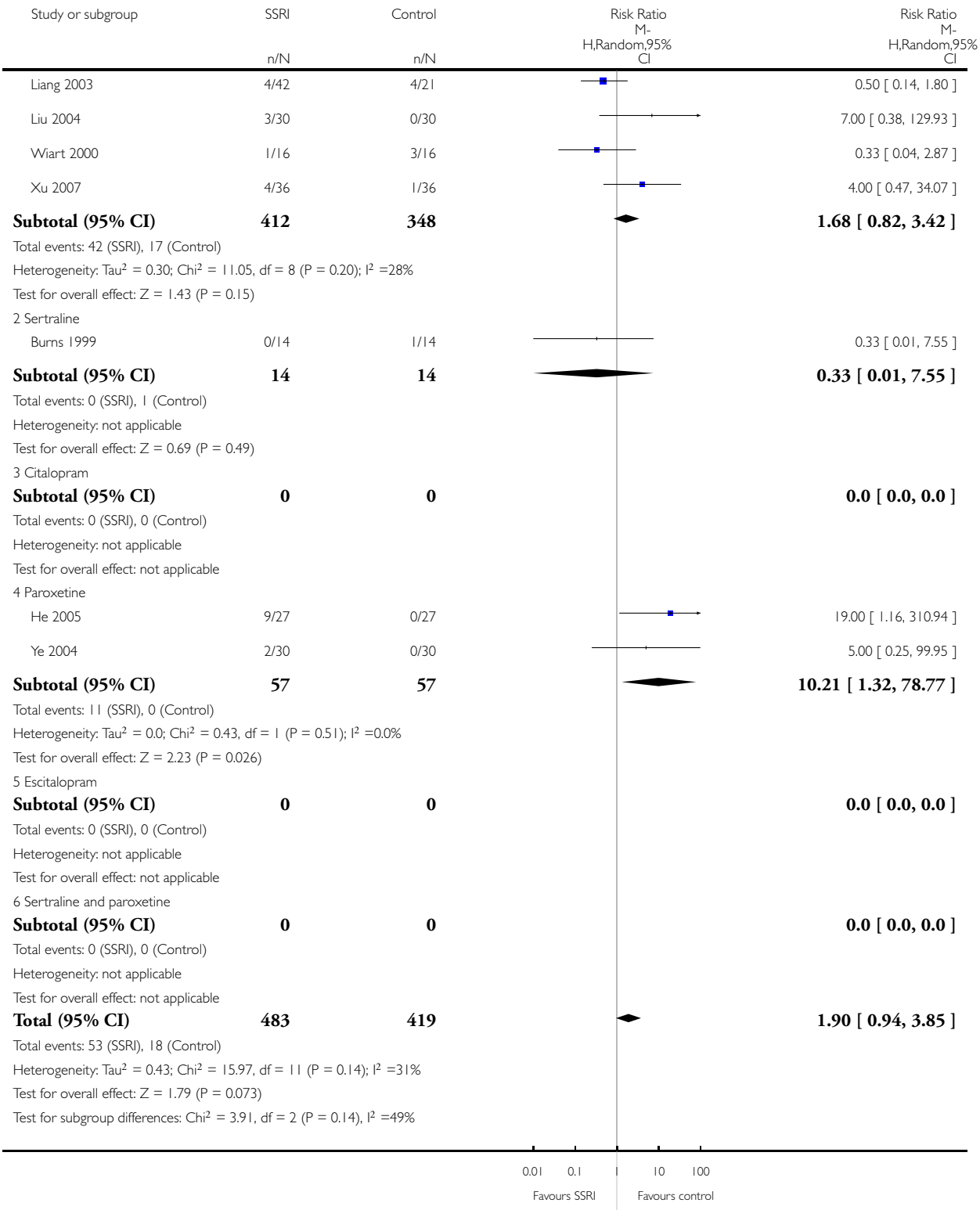

Analysis 1.12. Comparison 1 SSRI versus control at end of treatment, by SSRI, Outcome 12 Bleeding.

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 1 SSRI versus control at end of treatment, by SSRI

Outcome: 12 Bleeding

Study or subgroup	SSRI n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
1 Fluoxetine					
Subtotal (95% CI)	**0**	**0**		**0.0 %**	**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)					
Heterogeneity: not applicable					
Test for overall effect: not applicable					
2 Sertraline					
Subtotal (95% CI)	**0**	**0**		**0.0 %**	**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)					
Heterogeneity: not applicable					
Test for overall effect: not applicable					
3 Citalopram					
Subtotal (95% CI)	**0**	**0**		**0.0 %**	**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)					
Heterogeneity: not applicable					
Test for overall effect: not applicable					
4 Paroxetine					
GlaxoSmithKline 1998	1/112	0/117		42.6 %	3.13 [0.13, 76.10]
Subtotal (95% CI)	**112**	**117**		**42.6 %**	**3.13 [0.13, 76.10]**
Total events: 1 (SSRI), 0 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.70 (P = 0.48)					
5 Escitalopram					
Robinson 2008	1/59	1/59		57.4 %	1.00 [0.06, 15.61]
Subtotal (95% CI)	**59**	**59**		**57.4 %**	**1.00 [0.06, 15.61]**
Total events: 1 (SSRI), 1 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.0 (P = 1.0)					
6 Sertraline or fluoxetine					

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Study or subgroup	SSRI n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Subtotal (95% CI)	**0**	**0**		**0.0 %**	**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)					
Heterogeneity: not applicable					
Test for overall effect: not applicable					
Total (95% CI)	**171**	**176**		**100.0 %**	**1.63 [0.20, 13.05]**
Total events: 2 (SSRI), 1 (Control)					
Heterogeneity: Tau^2 = 0.0; Chi^2 = 0.28, df = 1 (P = 0.59); I^2 =0.0%					
Test for overall effect: Z = 0.46 (P = 0.65)					
Test for subgroup differences: Chi^2 = 0.28, df = 1 (P = 0.60), I^2 =0.0%					

Analysis 1.14. Comparison 1 SSRI versus control at end of treatment, by SSRI, Outcome 14 Change in cognition between baseline and end of treatment.

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 1 SSRI versus control at end of treatment, by SSRI

Outcome: 14 Change in cognition between baseline and end of treatment

Study or subgroup	SSRI N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
1 Sertraline							
Almeida 2006	48	2.6 (3.04)	51	2.6 (3.9)		100.0 %	0.0 [-0.39, 0.39]
Total (95% CI)	**48**		**51**			**100.0 %**	**0.0 [-0.39, 0.39]**
Heterogeneity: not applicable							
Test for overall effect: Z = 0.0 (P = 1.0)							
Test for subgroup differences: Not applicable							

Analysis 1.15. Comparison 1 SSRI versus control at end of treatment, by SSRI, Outcome 15 Leaving the trial before the end of scheduled follow-up.

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 1 SSRI versus control at end of treatment, by SSRI

Outcome: 15 Leaving the trial before the end of scheduled follow-up

Study or subgroup	SSRI n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
1 Fluoxetine				
Brown 1998	1/10	0/10		3.00 [0.14, 65.90]
Chen 2001	2/21	2/20		0.95 [0.15, 6.13]
Cheng 2003	0/25	0/32		0.0 [0.0, 0.0]
Chollet 2011	2/59	3/59		0.67 [0.12, 3.85]
Dam 1996	0/16	0/17		0.0 [0.0, 0.0]
Feng 2004	2/18	2/18		1.00 [0.16, 6.35]
Fruehwald 2003	6/28	8/26		0.70 [0.28, 1.74]
He 2004	8/44	5/40		1.45 [0.52, 4.08]
Hu 2002	0/42	0/30		0.0 [0.0, 0.0]
Huang 2002	0/40	0/40		0.0 [0.0, 0.0]
Ji 2000	0/20	0/20		0.0 [0.0, 0.0]
Kong 2007	11/48	6/42		1.60 [0.65, 3.96]
Li 2004a	0/33	0/34		0.0 [0.0, 0.0]
Li 2004b	6/37	4/36		1.46 [0.45, 4.74]
Li 2008	2/60	2/30		0.50 [0.07, 3.38]
Liang 2003	0/42	0/21		0.0 [0.0, 0.0]
Liu 2004	0/30	0/30		0.0 [0.0, 0.0]
Robinson 2000a	9/23	4/17		1.66 [0.61, 4.51]
Robinson 2000b	4/17	1/16		3.76 [0.47, 30.20]
Wang 2003	13/64	9/56		1.26 [0.58, 2.73]
Wen 2006	0/42	0/42		0.0 [0.0, 0.0]
Wiart 2000	0/16	0/15		0.0 [0.0, 0.0]
Xu 2001	6/32	4/31		1.45 [0.45, 4.66]

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Study or subgroup	SSRI n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
Zhou 2003	2/30	4/30		0.50 [0.10, 2.53]
Zhou 2008	0/36	0/40		0.0 [0.0, 0.0]
Subtotal (95% CI)	**833**	**752**		**1.21 [0.87, 1.67]**
Total events: 74 (SSRI), 54 (Control)				
Heterogeneity: Tau^2 = 0.0; Chi^2 = 6.48, df = 13 (P = 0.93); I^2 =0.0%				
Test for overall effect: Z = 1.13 (P = 0.26)				
2 Sertraline				
Almeida 2006	11/55	6/56		1.87 [0.74, 4.70]
Burns 1999	0/14	0/14		0.0 [0.0, 0.0]
Guo 2009	0/40	0/40		0.0 [0.0, 0.0]
Murray 2005	24/62	30/61		0.79 [0.53, 1.18]
Rasmussen 2003	35/70	35/67		0.96 [0.69, 1.33]
Xie 2005	0/65	0/65		0.0 [0.0, 0.0]
Subtotal (95% CI)	**306**	**303**		**0.95 [0.69, 1.32]**
Total events: 70 (SSRI), 71 (Control)				
Heterogeneity: Tau^2 = 0.03; Chi^2 = 2.93, df = 2 (P = 0.23); I^2 =32%				
Test for overall effect: Z = 0.29 (P = 0.77)				
3 Citalopram				
Acler 2009	0/10	0/10		0.0 [0.0, 0.0]
Andersen 1994	6/33	1/33		6.00 [0.76, 47.14]
Li 2006	2/50	4/53		0.53 [0.10, 2.77]
Liu 2006	0/30	0/30		0.0 [0.0, 0.0]
Miao 2004	11/45	11/45		1.00 [0.48, 2.07]
Subtotal (95% CI)	**168**	**171**		**1.20 [0.41, 3.47]**
Total events: 19 (SSRI), 16 (Control)				
Heterogeneity: Tau^2 = 0.40; Chi^2 = 3.52, df = 2 (P = 0.17); I^2 =43%				
Test for overall effect: Z = 0.33 (P = 0.74)				
4 Paroxetine				
Chen 2002	0/24	4/24		0.11 [0.01, 1.96]
Chen T 2005	0/40	0/38		0.0 [0.0, 0.0]
GlaxoSmithKline 1998	13/112	13/117		1.04 [0.51, 2.15]
He 2005	0/27	0/27		0.0 [0.0, 0.0]
Lai 2006	0/40	0/40		0.0 [0.0, 0.0]
Li 2002	0/46	0/46		0.0 [0.0, 0.0]
Li 2005	0/74	0/74		0.0 [0.0, 0.0]

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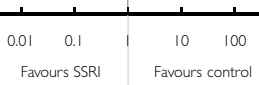
Study or subgroup	SSRI n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
Xu 2006	4/32	3/32		1.33 [0.32, 5.49]
Yang 2002	4/64	7/57		0.51 [0.16, 1.65]
Yang 2011	0/20	0/22		0.0 [0.0, 0.0]
Ye 2004	1/31	0/30		2.91 [0.12, 68.66]
Subtotal (95% CI)	**510**	**507**		**0.88 [0.51, 1.52]**
Total events: 22 (SSRI), 27 (Control)				
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 4.00$, df = 4 (P = 0.41); $I^2 = 0.0\%$				
Test for overall effect: Z = 0.45 (P = 0.65)				
5 Sertraline or fluoxetine				
Jia 2005	4/92	4/92		1.00 [0.26, 3.88]
Subtotal (95% CI)	**92**	**92**		**1.00 [0.26, 3.88]**
Total events: 4 (SSRI), 4 (Control)				
Heterogeneity: not applicable				
Test for overall effect: Z = 0.0 (P = 1.0)				
6 Escitalopram				
Robinson 2008	7/59	5/58		1.38 [0.46, 4.09]
Subtotal (95% CI)	**59**	**58**		**1.38 [0.46, 4.09]**
Total events: 7 (SSRI), 5 (Control)				
Heterogeneity: not applicable				
Test for overall effect: Z = 0.57 (P = 0.57)				
Total (95% CI)	**1968**	**1883**		**1.02 [0.86, 1.21]**
Total events: 196 (SSRI), 177 (Control)				
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 18.94$, df = 26 (P = 0.84); $I^2 = 0.0\%$				
Test for overall effect: Z = 0.23 (P = 0.82)				
Test for subgroup differences: $Chi^2 = 1.74$, df = 5 (P = 0.88), $I^2 = 0.0\%$				



Analysis 1.16. Comparison 1 SSRI versus control at end of treatment, by SSRI, Outcome 16 Motor deficits.

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 1 SSRI versus control at end of treatment, by SSRI

Outcome: 16 Motor deficits

Study or subgroup	SSRI N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
1 Fluoxetine							
Chollet 2011	57	-53.7 (27.8)	56	-35.1 (22)		55.3 %	-0.74 [-1.12, -0.35]
Dam 1996	16	32.4 (3.8)	16	31.6 (5)		44.7 %	0.18 [-0.52, 0.87]
Total (95% CI)	**73**		**72**			**100.0 %**	**-0.33 [-1.22, 0.56]**

Heterogeneity: $Tau^2 = 0.33$; $Chi^2 = 5.09$, df = 1 (P = 0.02); I^2 =80%

Test for overall effect: Z = 0.72 (P = 0.47)

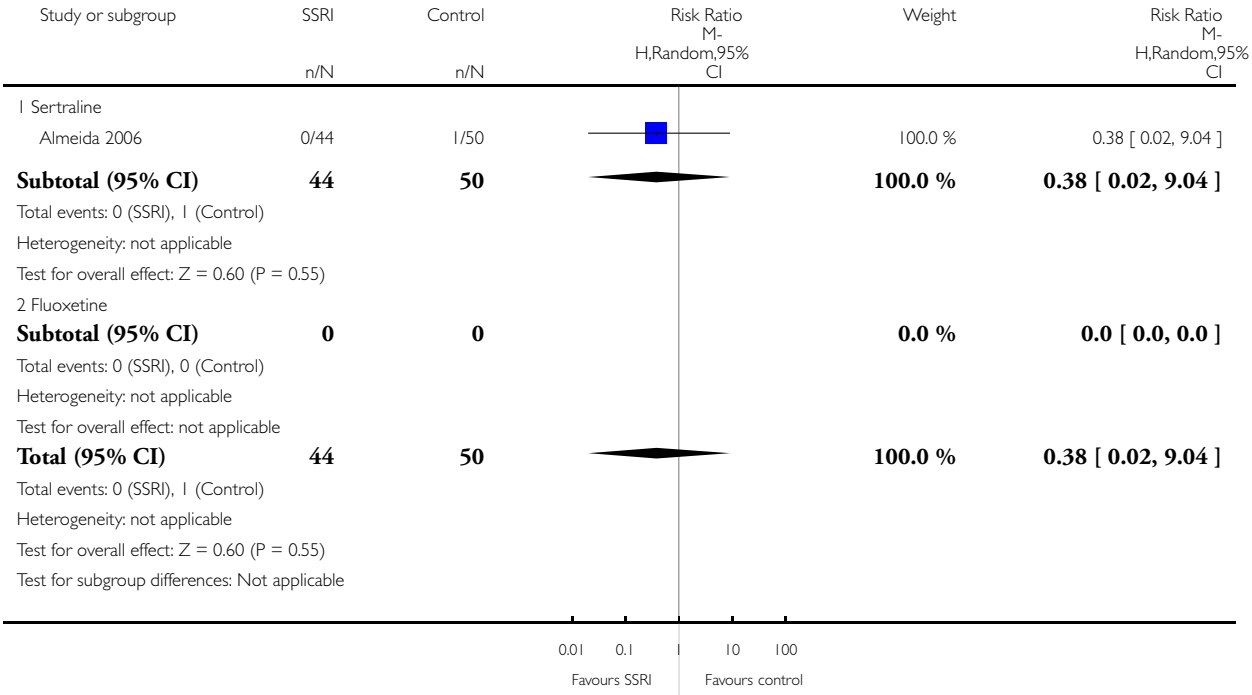
Test for subgroup differences: Not applicable

Analysis 2.1. Comparison 2 SSRI versus control, at end of follow-up, by SSRI, Outcome 1 Dependent on modified Rankin score.

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 2 SSRI versus control, at end of follow-up, by SSRI

Outcome: 1 Dependent on modified Rankin score



Analysis 2.2. Comparison 2 SSRI versus control, at end of follow-up, by SSRI, Outcome 2 Disability.

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 2 SSRI versus control, at end of follow-up, by SSRI

Outcome: 2 Disability

Study or subgroup	SSRI N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
Cheng 2003	25	-23.25 (10.12)	32	-28.67 (17.59)		50.1 %	0.36 [-0.17, 0.89]
Wang 2003	51	79 (4.7)	47	62 (5.8)		49.9 %	3.21 [2.60, 3.82]
Total (95% CI)	**76**		**79**			**100.0 %**	**1.78 [-1.01, 4.57]**

Heterogeneity: $Tau^2 = 3.97$; $Chi^2 = 48.25$, df = 1 ($P<0.00001$); $I^2 = 98\%$

Test for overall effect: Z = 1.25 (P = 0.21)

Test for subgroup differences: Not applicable

Analysis 2.3. Comparison 2 SSRI versus control, at end of follow-up, by SSRI, Outcome 3 Neurological deficit score (higher score: worse outcome).

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 2 SSRI versus control, at end of follow-up, by SSRI

Outcome: 3 Neurological deficit score (higher score: worse outcome)

Study or subgroup	SSRI N	SSRI Mean(SD)	Control N	Control Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
1 Fluoxetine							
Cheng 2003	25	4.63 (2.37)	32	10.85 (7.97)		24.4 %	-0.99 [-1.55, -0.44]
Fruehwald 2003	22	-52.9 (6.9)	18	-53.8 (6.5)		23.4 %	0.13 [-0.49, 0.75]
Wang 2003	51	7.2 (4.6)	47	13.9 (5.1)		26.1 %	-1.37 [-1.81, -0.93]
Subtotal (95% CI)	**98**		**97**			**73.9 %**	**-0.77 [-1.61, 0.08]**
Heterogeneity: $Tau^2 = 0.49$; $Chi^2 = 14.98$, df = 2 (P = 0.00056); $I^2 = 87\%$							
Test for overall effect: Z = 1.77 (P = 0.077)							
2 Sertraline							
Guo 2009	40	24.46 (8.27)	40	27.04 (12.2)		26.1 %	-0.25 [-0.69, 0.19]
Subtotal (95% CI)	**40**		**40**			**26.1 %**	**-0.25 [-0.69, 0.19]**
Heterogeneity: not applicable							
Test for overall effect: Z = 1.09 (P = 0.27)							
Total (95% CI)	**138**		**137**			**100.0 %**	**-0.63 [-1.30, 0.04]**
Heterogeneity: $Tau^2 = 0.40$; $Chi^2 = 20.85$, df = 3 (P = 0.00011); $I^2 = 86\%$							
Test for overall effect: Z = 1.86 (P = 0.064)							
Test for subgroup differences: $Chi^2 = 1.14$, df = 1 (P = 0.29), $I^2 = 12\%$							

Analysis 2.4. Comparison 2 SSRI versus control, at end of follow-up, by SSRI, Outcome 4 Depression (continuous data).

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 2 SSRI versus control, at end of follow-up, by SSRI

Outcome: 4 Depression (continuous data)

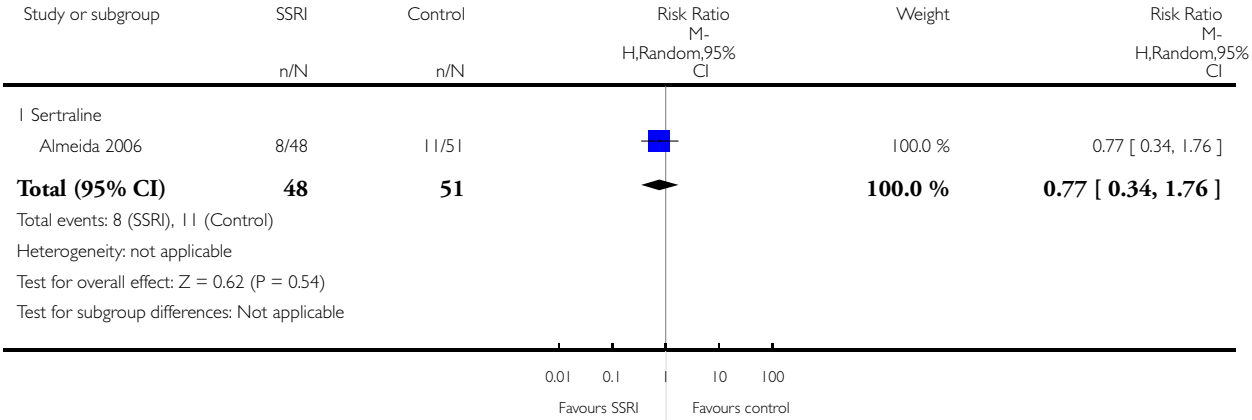
Study or subgroup	SSRI N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
1 Fluoxetine							
Cheng 2003	25	12.95 (11.54)	32	18.26 (13.72)		25.1 %	-0.41 [-0.94, 0.12]
Fruehwald 2003	22	10.8 (11.6)	18	22.2 (15)		24.3 %	-0.84 [-1.50, -0.19]
Wang 2003	51	10 (2.1)	47	21.1 (5.5)		25.0 %	-2.69 [-3.24, -2.14]
Subtotal (95% CI)	**98**		**97**			**74.4 %**	**-1.32 [-2.74, 0.11]**
Heterogeneity: Tau^2 = 1.51; Chi^2 = 37.03, df = 2 (P<0.00001); I^2 =95%							
Test for overall effect: Z = 1.80 (P = 0.071)							
2 Sertraline							
Guo 2009	40	12.71 (4.24)	40	15 (5.34)		25.6 %	-0.47 [-0.91, -0.03]
Subtotal (95% CI)	**40**		**40**			**25.6 %**	**-0.47 [-0.91, -0.03]**
Heterogeneity: not applicable							
Test for overall effect: Z = 2.07 (P = 0.038)							
Total (95% CI)	**138**		**137**			**100.0 %**	**-1.10 [-2.16, -0.04]**
Heterogeneity: Tau^2 = 1.08; Chi^2 = 46.35, df = 3 (P<0.00001); I^2 =94%							
Test for overall effect: Z = 2.04 (P = 0.041)							
Test for subgroup differences: Chi^2 = 1.22, df = 1 (P = 0.27), I^2 =18%							

Analysis 2.5. Comparison 2 SSRI versus control, at end of follow-up, by SSRI, Outcome 5 Depression (dichotomous data).

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 2 SSRI versus control, at end of follow-up, by SSRI

Outcome: 5 Depression (dichotomous data)

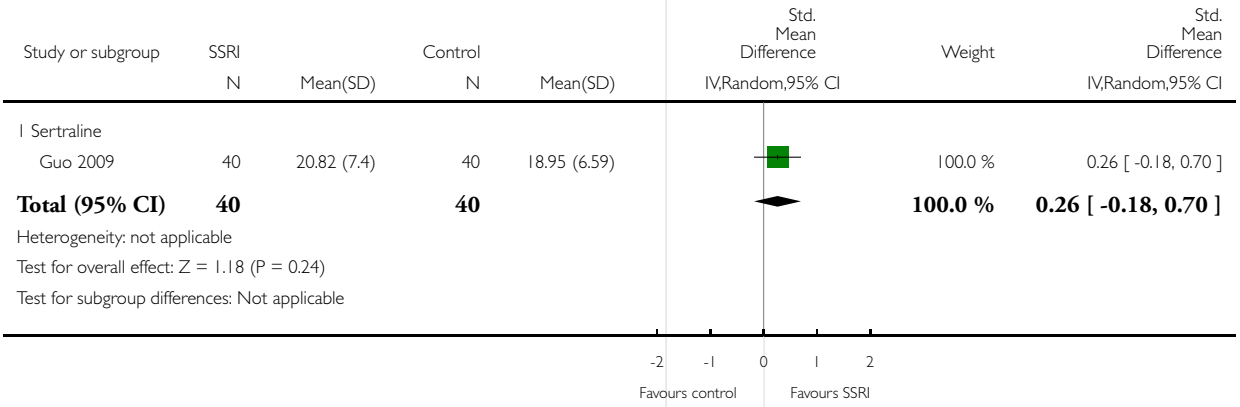


Analysis 2.6. Comparison 2 SSRI versus control, at end of follow-up, by SSRI, Outcome 6 Cognition (higher score is better).

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 2 SSRI versus control, at end of follow-up, by SSRI

Outcome: 6 Cognition (higher score is better)

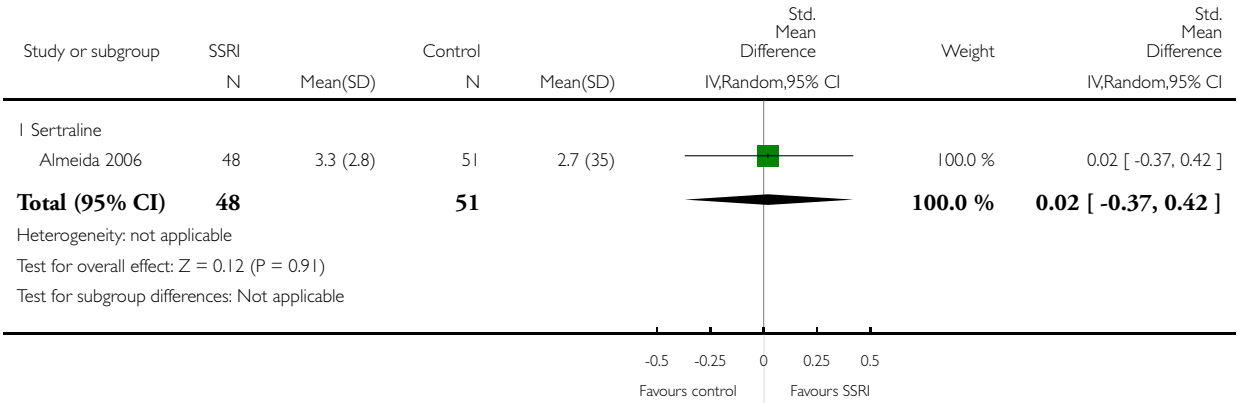


Analysis 2.7. Comparison 2 SSRI versus control, at end of follow-up, by SSRI, Outcome 7 Change in cognition between baseline and follow-up.

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 2 SSRI versus control, at end of follow-up, by SSRI

Outcome: 7 Change in cognition between baseline and follow-up



Analysis 2.8. Comparison 2 SSRI versus control, at end of follow-up, by SSRI, Outcome 8 Death.

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 2 SSRI versus control, at end of follow-up, by SSRI

Outcome: 8 Death

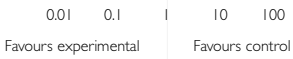
Study or subgroup	SSRI n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
Cheng 2003	0/25	0/32		0.0 [0.0, 0.0]
Guo 2009	0/40	0/40		0.0 [0.0, 0.0]
Wang 2003	0/64	5/56		0.08 [0.00, 1.41]
Total (95% CI)	**129**	**128**		**0.08 [0.00, 1.41]**

Total events: 0 (SSRI), 5 (Control)

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.0$, df = 0 (P = 1.00); $I^2 = 0.0\%$

Test for overall effect: Z = 1.73 (P = 0.084)

Test for subgroup differences: Not applicable



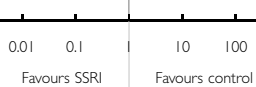
Analysis 3.1. Comparison 3 SSRI versus control (according to time since stroke when recruited), Outcome 1 Dependent on modified Rankin score.

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 3 SSRI versus control (according to time since stroke when recruited)

Outcome: 1 Dependent on modified Rankin score

Study or subgroup	SSRI n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
1 Mean time since stroke < 2 weeks				
Almeida 2006	0/55	0/56		0.0 [0.0, 0.0]
Chollet 2011	42/57	50/55		0.81 [0.68, 0.97]
Subtotal (95% CI)	**112**	**111**		**0.81 [0.68, 0.97]**
Total events: 42 (SSRI), 50 (Control)				
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.0$, df = 0 (P = 1.00); $I^2 = 0.0\%$				
Test for overall effect: Z = 2.34 (P = 0.019)				
2 Mean time since stroke 2 weeks to 3 months at randomisation				
Subtotal (95% CI)	**0**	**0**		**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)				
Heterogeneity: not applicable				
Test for overall effect: not applicable				
3 Mean time since stroke 3 to 6 months at randomisation				
Subtotal (95% CI)	**0**	**0**		**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)				
Heterogeneity: not applicable				
Test for overall effect: not applicable				
4 Mean time since stroke > 6 months and < 9 months				
Subtotal (95% CI)	**0**	**0**		**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)				
Heterogeneity: not applicable				
Test for overall effect: not applicable				
5 Mean time since stroke at randomisation 9 to 12 months				
Subtotal (95% CI)	**0**	**0**		**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)				
Heterogeneity: not applicable				
Test for overall effect: not applicable				
6 Mean time since stroke not known				
Subtotal (95% CI)	**0**	**0**		**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)				
Heterogeneity: not applicable				
Test for overall effect: not applicable				
Total (95% CI)	**112**	**111**		**0.81 [0.68, 0.97]**
Total events: 42 (SSRI), 50 (Control)				



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Study or subgroup	SSRI n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
Heterogeneity: Tau^2 = 0.0; Chi^2 = 0.0, df = 0 (P = 1.00); I^2 =0.0%				
Test for overall effect: Z = 2.34 (P = 0.019)				
Test for subgroup differences: Not applicable				

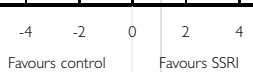
Analysis 3.2. Comparison 3 SSRI versus control (according to time since stroke when recruited), Outcome 2 Disability.

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 3 SSRI versus control (according to time since stroke when recruited)

Outcome: 2 Disability

Study or subgroup	SSRI N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
1 Mean time since stroke < 3 months							
Acler 2009	10	82 (28)	10	75 (25)		3.8 %	0.25 [-0.63, 1.13]
Chen 2001	19	79.31 (8.94)	18	71.56 (9.41)		4.3 %	0.83 [0.15, 1.50]
Chen T 2005	40	65.76 (5.92)	38	51.76 (7.32)		4.6 %	2.09 [1.53, 2.64]
Cheng 2003	25	-26.38 (14.2)	32	-29.15 (17.38)		4.7 %	0.17 [-0.35, 0.69]
He 2005	27	84.26 (8.41)	27	78.33 (15.01)		4.7 %	0.48 [-0.06, 1.02]
Kong 2007	37	60.4 (12.5)	36	52.3 (13.5)		4.9 %	0.62 [0.15, 1.09]
Li 2006	50	64.36 (8.23)	49	59.17 (9.02)		5.0 %	0.60 [0.19, 1.00]
Li 2008	58	40.8 (3.7)	28	38.4 (5.8)		4.9 %	0.53 [0.07, 0.99]
Liu 2004	30	70.33 (10.74)	30	64.33 (7.74)		4.7 %	0.63 [0.11, 1.15]
Robinson 2000a	14	59.2 (11.6)	13	56.2 (7.8)		4.1 %	0.29 [-0.47, 1.05]
Robinson 2000b	13	60.5 (10.8)	15	63.1 (8.2)		4.1 %	-0.27 [-1.01, 0.48]



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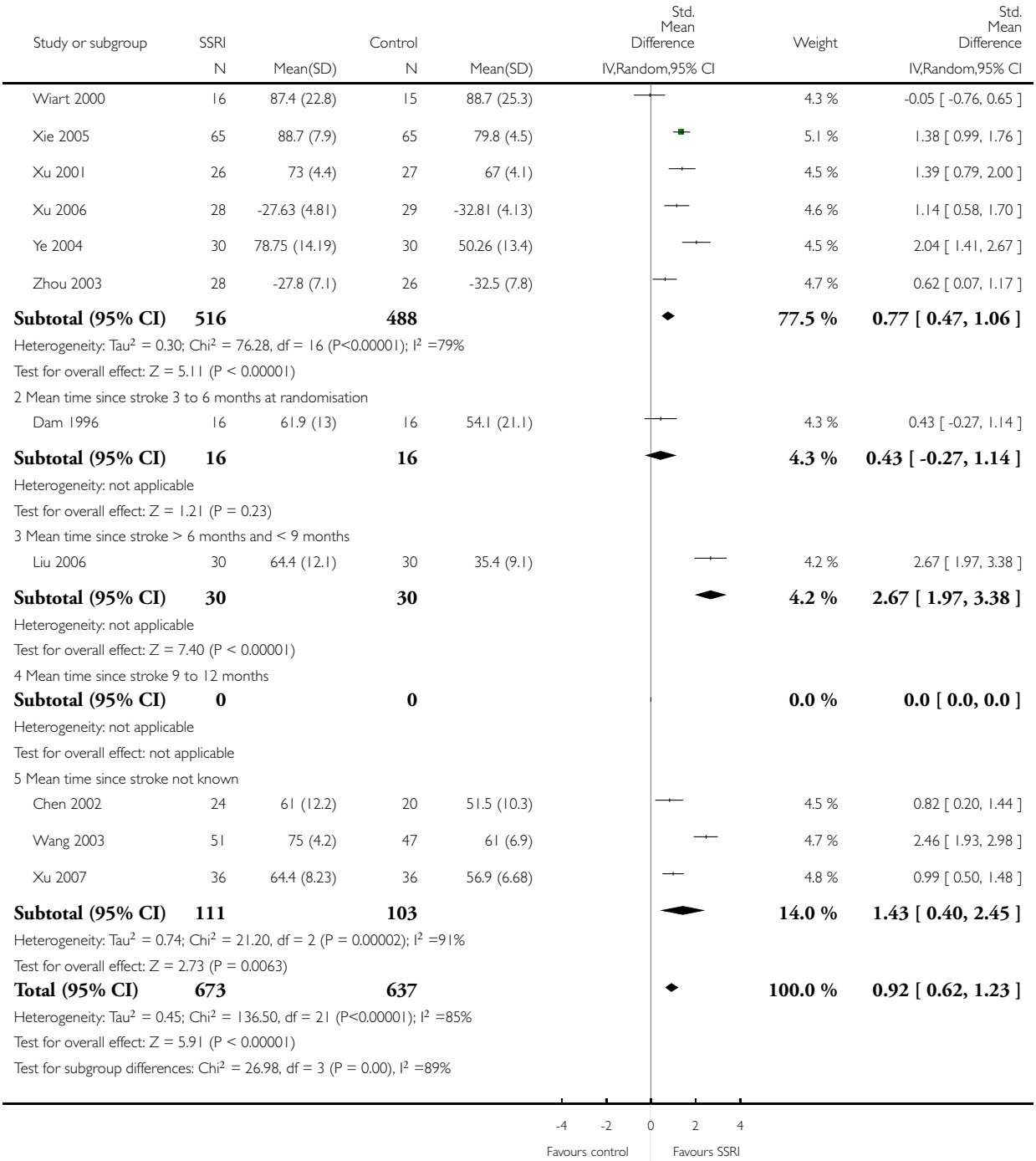
Study or subgroup	SSRI N	SSRI Mean(SD)	Control N	Control Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
Wiart 2000	16	87.4 (22.8)	15	88.7 (25.3)		4.3 %	-0.05 [-0.76, 0.65]
Xie 2005	65	88.7 (7.9)	65	79.8 (4.5)		5.1 %	1.38 [0.99, 1.76]
Xu 2001	26	73 (4.4)	27	67 (4.1)		4.5 %	1.39 [0.79, 2.00]
Xu 2006	28	-27.63 (4.81)	29	-32.81 (4.13)		4.6 %	1.14 [0.58, 1.70]
Ye 2004	30	78.75 (14.19)	30	50.26 (13.4)		4.5 %	2.04 [1.41, 2.67]
Zhou 2003	28	-27.8 (7.1)	26	-32.5 (7.8)		4.7 %	0.62 [0.07, 1.17]
Subtotal (95% CI)	**516**		**488**			**77.5 %**	**0.77 [0.47, 1.06]**
Heterogeneity: Tau² = 0.30; Chi² = 76.28, df = 16 (P<0.00001); I² =79%							
Test for overall effect: Z = 5.11 (P < 0.00001)							
2 Mean time since stroke 3 to 6 months at randomisation							
Dam 1996	16	61.9 (13)	16	54.1 (21.1)		4.3 %	0.43 [-0.27, 1.14]
Subtotal (95% CI)	**16**		**16**			**4.3 %**	**0.43 [-0.27, 1.14]**
Heterogeneity: not applicable							
Test for overall effect: Z = 1.21 (P = 0.23)							
3 Mean time since stroke > 6 months and < 9 months							
Liu 2006	30	64.4 (12.1)	30	35.4 (9.1)		4.2 %	2.67 [1.97, 3.38]
Subtotal (95% CI)	**30**		**30**			**4.2 %**	**2.67 [1.97, 3.38]**
Heterogeneity: not applicable							
Test for overall effect: Z = 7.40 (P < 0.00001)							
4 Mean time since stroke 9 to 12 months							
Subtotal (95% CI)	**0**		**0**			**0.0 %**	**0.0 [0.0, 0.0]**
Heterogeneity: not applicable							
Test for overall effect: not applicable							
5 Mean time since stroke not known							
Chen 2002	24	61 (12.2)	20	51.5 (10.3)		4.5 %	0.82 [0.20, 1.44]
Wang 2003	51	75 (4.2)	47	61 (6.9)		4.7 %	2.46 [1.93, 2.98]
Xu 2007	36	64.4 (8.23)	36	56.9 (6.68)		4.8 %	0.99 [0.50, 1.48]
Subtotal (95% CI)	**111**		**103**			**14.0 %**	**1.43 [0.40, 2.45]**
Heterogeneity: Tau² = 0.74; Chi² = 21.20, df = 2 (P = 0.00002); I² =91%							
Test for overall effect: Z = 2.73 (P = 0.0063)							
Total (95% CI)	**673**		**637**			**100.0 %**	**0.92 [0.62, 1.23]**
Heterogeneity: Tau² = 0.45; Chi² = 136.50, df = 21 (P<0.00001); I² =85%							
Test for overall effect: Z = 5.91 (P < 0.00001)							
Test for subgroup differences: Chi² = 26.98, df = 3 (P = 0.00), I² =89%							



Analysis 3.3. Comparison 3 SSRI versus control (according to time since stroke when recruited), Outcome 3 Neurological deficit score.

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 3 SSRI versus control (according to time since stroke when recruited)

Outcome: 3 Neurological deficit score

Study or subgroup	SSRI N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
1 Mean time since stroke < 3 months							
Acler 2009	10	2.3 (2)	10	3.5 (1.3)		2.7 %	-0.68 [-1.59, 0.23]
Chen 2001	19	-49.72 (4.07)	18	-43.13 (3.64)		3.0 %	-1.67 [-2.43, -0.91]
Cheng 2003	25	6.5 (3.19)	32	10.96 (8.13)		3.5 %	-0.68 [-1.22, -0.14]
Chollet 2011	57	5.8 (3.7)	55	6.9 (4.4)		3.8 %	-0.27 [-0.64, 0.10]
Feng 2004	16	9.1 (3.2)	16	14.4 (2.2)		2.8 %	-1.88 [-2.73, -1.03]
Fruehwald 2003	26	-55.5 (4.8)	24	-52.8 (5.4)		3.4 %	-0.52 [-1.09, 0.04]
He 2004	36	10.41 (6.36)	35	14.43 (7.94)		3.6 %	-0.55 [-1.03, -0.08]
He 2005	27	6.48 (1.58)	27	8.33 (3.86)		3.5 %	-0.62 [-1.17, -0.07]
Huang 2002	40	4.02 (1.86)	40	8.57 (3.64)		3.6 %	-1.56 [-2.06, -1.06]
Kong 2007	37	8.6 (6.4)	36	11.2 (6.4)		3.6 %	-0.40 [-0.87, 0.06]
Li 2004a	33	6.23 (3.11)	34	12.86 (6.36)		3.5 %	-1.30 [-1.83, -0.77]
Li 2006	50	21.89 (1.57)	49	23.77 (1.46)		3.7 %	-1.23 [-1.66, -0.80]
Liang 2003	42	11.74 (3.23)	21	17.32 (5.19)		3.4 %	-1.38 [-1.96, -0.80]
Liu 2004	30	9.2 (2.06)	30	10.47 (9.2)		3.6 %	-0.19 [-0.70, 0.32]
Wen 2006	42	10.1 (1.9)	42	16.4 (2.5)		3.3 %	-2.81 [-3.42, -2.20]
Xu 2001	26	8.2 (5.2)	27	12.4 (4.3)		3.4 %	-0.87 [-1.43, -0.30]
Xu 2006	28	11.11 (4.32)	29	13.63 (3.15)		3.5 %	-0.66 [-1.19, -0.13]
Ye 2004	30	8.3 (3.8)	30	16 (4.8)		3.4 %	-1.76 [-2.36, -1.15]
Zhou 2003	28	9 (3.8)	26	12.2 (6.1)		3.5 %	-0.63 [-1.17, -0.08]
Subtotal (95% CI)	**602**		**581**			**65.0 %**	**-1.01 [-1.31, -0.72]**
Heterogeneity: Tau^2 = 0.34; Chi^2 = 98.56, df = 18 (P<0.00001); I^2 =82%							
Test for overall effect: Z = 6.76 (P < 0.00001)							
2 Mean time since stroke 3 to 6 months							
Dam 1996	16	44.1 (9.4)	16	46.8 (9.9)		3.2 %	-0.27 [-0.97, 0.42]

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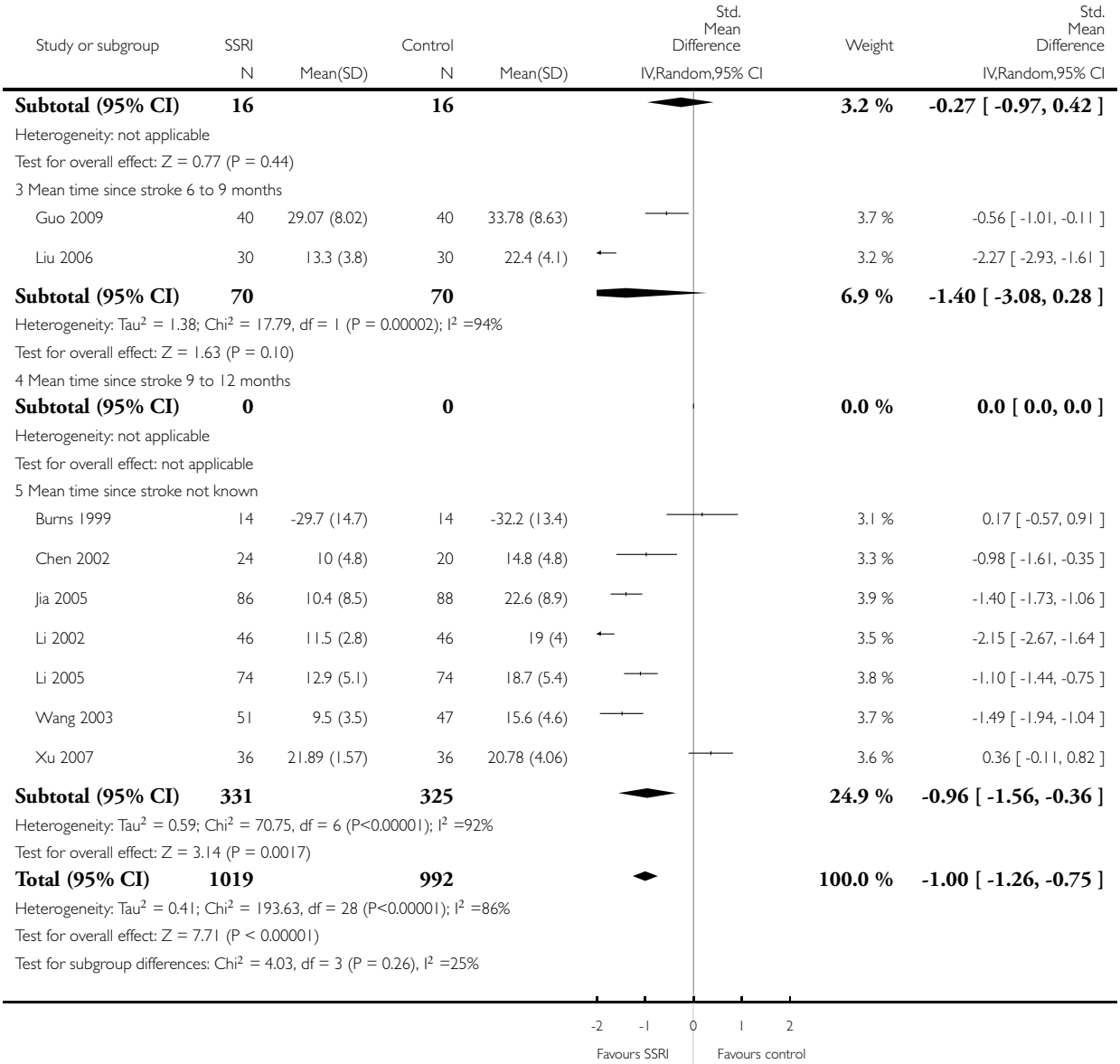


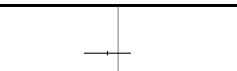
Analysis 3.4. Comparison 3 SSRI versus control (according to time since stroke when recruited), Outcome 4 Depression (continuous).

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 3 SSRI versus control (according to time since stroke when recruited)

Outcome: 4 Depression (continuous)

Study or subgroup	SSRI N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
1 Time since stroke < 3 months							
Acler 2009	10	6.6 (3.6)	10	8 (3)		2.5 %	-0.40 [-1.29, 0.48]
Andersen 1994	33	11.4 (5.1)	33	14.1 (4.7)		2.7 %	-0.54 [-1.04, -0.05]
Chen 2001	19	10.82 (6.25)	18	18.48 (6.28)		2.6 %	-1.20 [-1.90, -0.49]
Chen T 2005	40	10.98 (3.74)	38	22.45 (3.56)		2.6 %	-3.11 [-3.78, -2.44]
Cheng 2003	25	13.64 (11.02)	32	17.98 (12.53)		2.7 %	-0.36 [-0.89, 0.17]
Chollet 2011	56	5.4 (4.9)	54	8.4 (7.9)		2.7 %	-0.46 [-0.83, -0.08]
Feng 2004	16	34.9 (4.6)	16	41.1 (4.7)		2.5 %	-1.30 [-2.07, -0.53]
Finkenzeller 2009	23	12.1 (1.05)	27	10.6 (0.97)		2.6 %	1.47 [0.83, 2.10]
Fruehwald 2003	26	9.5 (7.9)	24	11.2 (12.4)		2.7 %	-0.16 [-0.72, 0.39]
He 2004	36	14.28 (2.31)	35	20.32 (2.82)		2.6 %	-2.32 [-2.93, -1.71]
He 2005	27	10.11 (1.08)	27	17.48 (1.05)		2.1 %	-6.82 [-8.26, -5.38]
Huang 2002	40	4.76 (0.6)	40	16.34 (1.3)		1.8 %	-11.33 [-13.18, -9.47]
Kong 2007	37	12.6 (5.3)	36	16.3 (3.7)		2.7 %	-0.80 [-1.28, -0.32]
Lai 2006	40	12.5 (8.4)	40	21.5 (4.3)		2.7 %	-1.34 [-1.82, -0.85]
Li 2006	50	5.61 (5.32)	49	20.26 (6.08)		2.7 %	-2.55 [-3.08, -2.01]
Li 2008	58	14.5 (2.4)	28	18.7 (3.9)		2.7 %	-1.40 [-1.90, -0.90]
Liang 2003	42	9.67 (4.48)	21	19.19 (3.12)		2.6 %	-2.30 [-2.97, -1.63]
Robinson 2000a	14	18.5 (7.6)	13	12.2 (4.7)		2.5 %	0.96 [0.15, 1.76]
Robinson 2000b	13	5.9 (3.8)	15	6.2 (4.6)		2.6 %	-0.07 [-0.81, 0.67]
Song 2006	41	40.3 (7.25)	41	48.31 (8.02)		2.7 %	-1.04 [-1.50, -0.58]
Wen 2006	42	7 (1.1)	42	17.7 (1.8)		2.3 %	-7.11 [-8.29, -5.93]
Wiart 2000	16	11.8 (6.7)	15	18.7 (10)		2.6 %	-0.79 [-1.53, -0.06]
Xie 2005	65	30.9 (7.1)	65	39.7 (5.3)		2.7 %	-1.40 [-1.78, -1.01]



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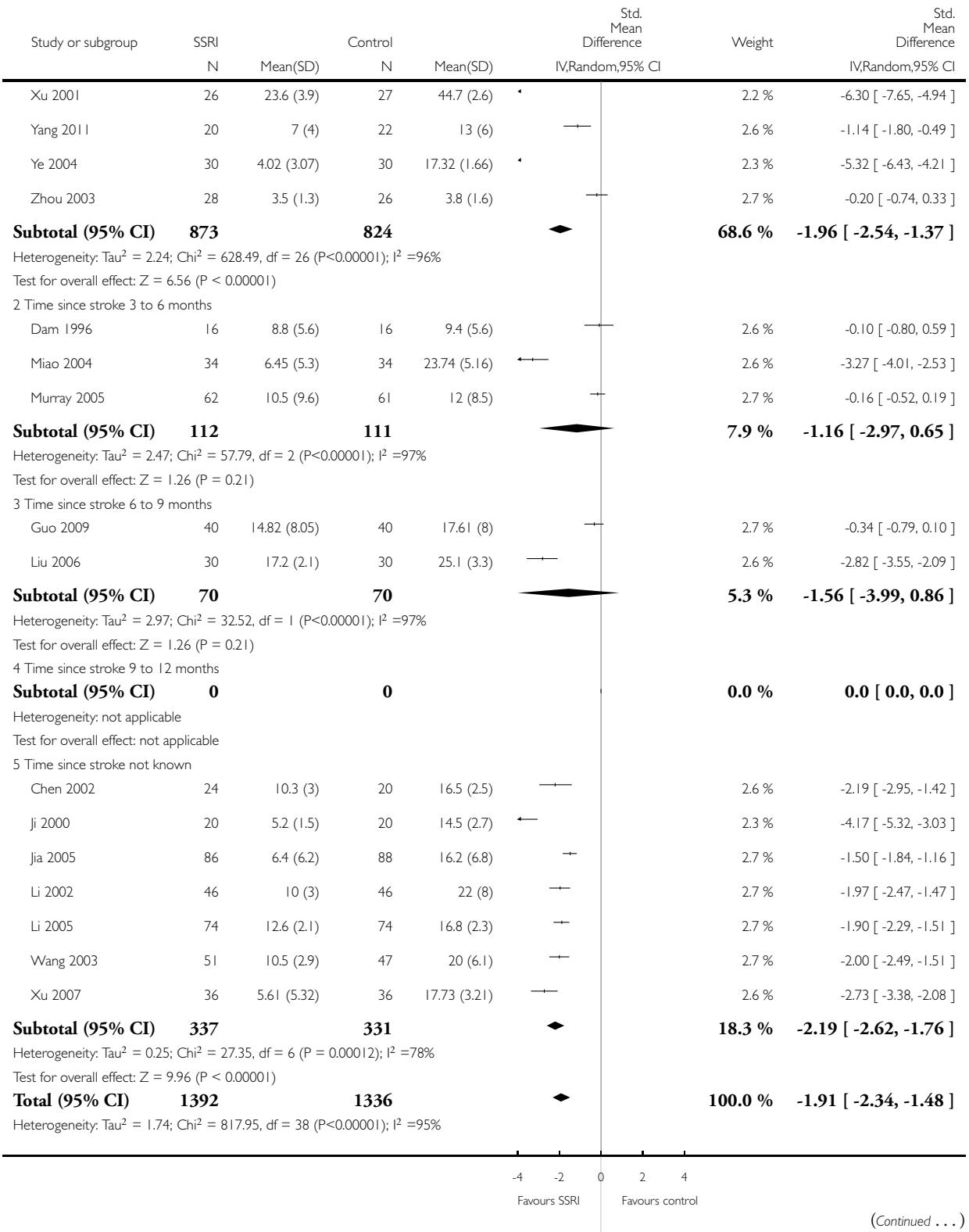

Study or subgroup	SSRI N	SSRI Mean(SD)	Control N	Control Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
Xu 2001	26	23.6 (3.9)	27	44.7 (2.6)		2.2 %	-6.30 [-7.65, -4.94]
Yang 2011	20	7 (4)	22	13 (6)		2.6 %	-1.14 [-1.80, -0.49]
Ye 2004	30	4.02 (3.07)	30	17.32 (1.66)		2.3 %	-5.32 [-6.43, -4.21]
Zhou 2003	28	3.5 (1.3)	26	3.8 (1.6)		2.7 %	-0.20 [-0.74, 0.33]
Subtotal (95% CI)	**873**		**824**			**68.6 %**	**-1.96 [-2.54, -1.37]**
Heterogeneity: Tau² = 2.24; Chi² = 628.49, df = 26 (P<0.00001); I² =96%							
Test for overall effect: Z = 6.56 (P < 0.00001)							
2 Time since stroke 3 to 6 months							
Dam 1996	16	8.8 (5.6)	16	9.4 (5.6)		2.6 %	-0.10 [-0.80, 0.59]
Miao 2004	34	6.45 (5.3)	34	23.74 (5.16)		2.6 %	-3.27 [-4.01, -2.53]
Murray 2005	62	10.5 (9.6)	61	12 (8.5)		2.7 %	-0.16 [-0.52, 0.19]
Subtotal (95% CI)	**112**		**111**			**7.9 %**	**-1.16 [-2.97, 0.65]**
Heterogeneity: Tau² = 2.47; Chi² = 57.79, df = 2 (P<0.00001); I² =97%							
Test for overall effect: Z = 1.26 (P = 0.21)							
3 Time since stroke 6 to 9 months							
Guo 2009	40	14.82 (8.05)	40	17.61 (8)		2.7 %	-0.34 [-0.79, 0.10]
Liu 2006	30	17.2 (2.1)	30	25.1 (3.3)		2.6 %	-2.82 [-3.55, -2.09]
Subtotal (95% CI)	**70**		**70**			**5.3 %**	**-1.56 [-3.99, 0.86]**
Heterogeneity: Tau² = 2.97; Chi² = 32.52, df = 1 (P<0.00001); I² =97%							
Test for overall effect: Z = 1.26 (P = 0.21)							
4 Time since stroke 9 to 12 months							
Subtotal (95% CI)	**0**		**0**			**0.0 %**	**0.0 [0.0, 0.0]**
Heterogeneity: not applicable							
Test for overall effect: not applicable							
5 Time since stroke not known							
Chen 2002	24	10.3 (3)	20	16.5 (2.5)		2.6 %	-2.19 [-2.95, -1.42]
Ji 2000	20	5.2 (1.5)	20	14.5 (2.7)		2.3 %	-4.17 [-5.32, -3.03]
Jia 2005	86	6.4 (6.2)	88	16.2 (6.8)		2.7 %	-1.50 [-1.84, -1.16]
Li 2002	46	10 (3)	46	22 (8)		2.7 %	-1.97 [-2.47, -1.47]
Li 2005	74	12.6 (2.1)	74	16.8 (2.3)		2.7 %	-1.90 [-2.29, -1.51]
Wang 2003	51	10.5 (2.9)	47	20 (6.1)		2.7 %	-2.00 [-2.49, -1.51]
Xu 2007	36	5.61 (5.32)	36	17.73 (3.21)		2.6 %	-2.73 [-3.38, -2.08]
Subtotal (95% CI)	**337**		**331**			**18.3 %**	**-2.19 [-2.62, -1.76]**
Heterogeneity: Tau² = 0.25; Chi² = 27.35, df = 6 (P = 0.00012); I² =78%							
Test for overall effect: Z = 9.96 (P < 0.00001)							
Total (95% CI)	**1392**		**1336**			**100.0 %**	**-1.91 [-2.34, -1.48]**
Heterogeneity: Tau² = 1.74; Chi² = 817.95, df = 38 (P<0.00001); I² =95%							

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Study or subgroup	SSRI N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
Test for overall effect: Z = 8.70 (P < 0.00001)							
Test for subgroup differences: Chi^2 = 1.58, df = 3 (P = 0.66), I^2 =0.0%							

Analysis 3.5. Comparison 3 SSRI versus control (according to time since stroke when recruited), Outcome 5 Depression (dichotomous).

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 3 SSRI versus control (according to time since stroke when recruited)

Outcome: 5 Depression (dichotomous)

Study or subgroup	SSRI n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
1 Time since stroke < 3 months					
Almeida 2006	8/48	11/51		13.8 %	0.77 [0.34, 1.76]
Li 2004a	2/33	8/34		8.7 %	0.26 [0.06, 1.12]
Li 2004b	5/31	13/32		13.0 %	0.40 [0.16, 0.98]
Rasmussen 2003	3/35	8/32		10.3 %	0.34 [0.10, 1.18]
Robinson 2008	5/59	13/58		12.5 %	0.38 [0.14, 0.99]
Xu 2006	3/28	12/29		10.9 %	0.26 [0.08, 0.82]
Zhou 2008	4/36	18/40		12.3 %	0.25 [0.09, 0.66]
Subtotal (95% CI)	**270**	**276**		**81.5 %**	**0.39 [0.26, 0.57]**
Total events: 30 (SSRI), 83 (Control)					
Heterogeneity: Tau^2 = 0.0; Chi^2 = 4.36, df = 6 (P = 0.63); I^2 =0.0%					
Test for overall effect: Z = 4.81 (P < 0.00001)					
2 Time since stroke 3 to 6 months					
Subtotal (95% CI)	**0**	**0**		**0.0 %**	**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)					

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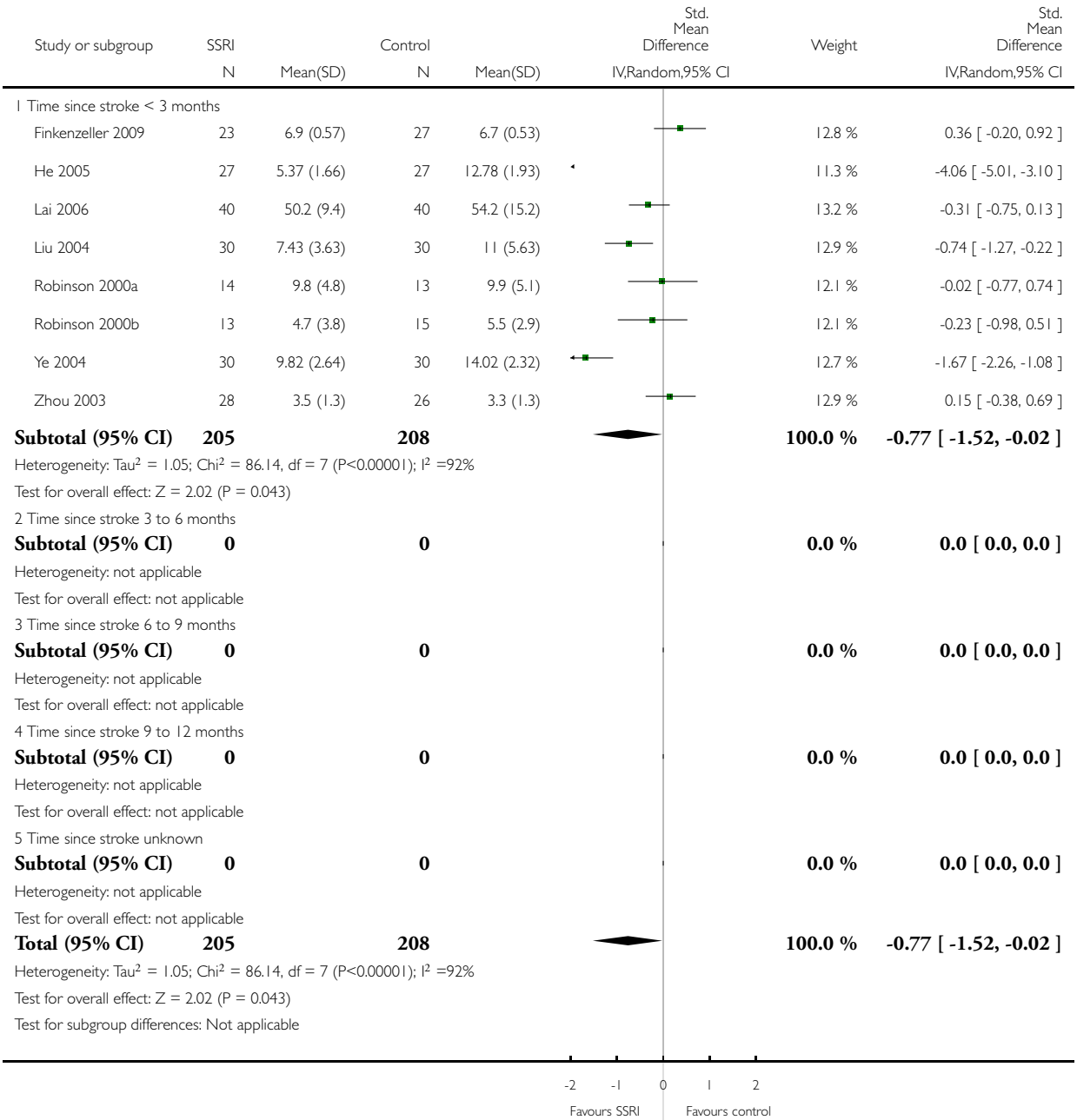
Study or subgroup	SSRI n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Heterogeneity: not applicable					
Test for overall effect: not applicable					
3 Time since stroke 6 to 9 months					
Subtotal (95% CI)	**0**	**0**		**0.0 %**	**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)					
Heterogeneity: not applicable					
Test for overall effect: not applicable					
4 Time since stroke 9 to 12 months					
Subtotal (95% CI)	**0**	**0**		**0.0 %**	**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)					
Heterogeneity: not applicable					
Test for overall effect: not applicable					
5 Time since stroke unknown					
GlaxoSmithKline 1998	82/111	97/114		18.5 %	0.87 [0.76, 0.99]
Subtotal (95% CI)	**111**	**114**		**18.5 %**	**0.87 [0.76, 0.99]**
Total events: 82 (SSRI), 97 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 2.06 (P = 0.040)					
Total (95% CI)	**381**	**390**		**100.0 %**	**0.43 [0.24, 0.77]**
Total events: 112 (SSRI), 180 (Control)					
Heterogeneity: Tau^2 = 0.49; Chi^2 = 30.48, df = 7 (P = 0.00008); I^2 =77%					
Test for overall effect: Z = 2.82 (P = 0.0049)					
Test for subgroup differences: Chi^2 = 14.92, df = 1 (P = 0.00), I^2 =93%					

Analysis 3.7. Comparison 3 SSRI versus control (according to time since stroke when recruited), Outcome 7 Anxiety (continuous).

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 3 SSRI versus control (according to time since stroke when recruited)

Outcome: 7 Anxiety (continuous)

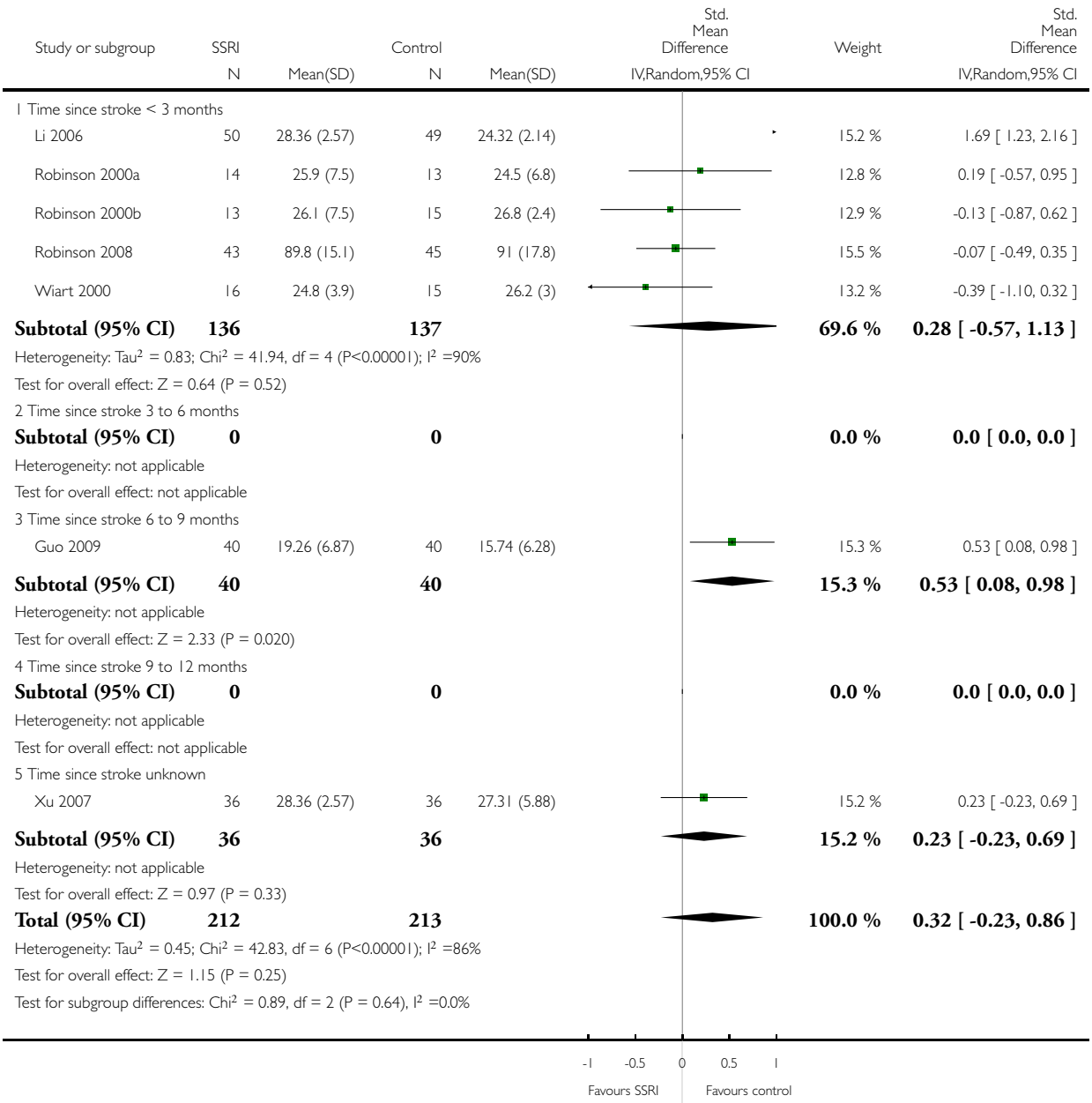


Analysis 3.8. Comparison 3 SSRI versus control (according to time since stroke when recruited), Outcome 8 Cognition.

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 3 SSRI versus control (according to time since stroke when recruited)

Outcome: 8 Cognition



Analysis 3.9. Comparison 3 SSRI versus control (according to time since stroke when recruited), Outcome 9 Death.

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 3 SSRI versus control (according to time since stroke when recruited)

Outcome: 9 Death

Study or subgroup	SSRI n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
1 Time since stroke < 3 months				
Acler 2009	0/10	0/10		0.0 [0.0, 0.0]
Almeida 2006	2/48	1/52		2.17 [0.20, 23.14]
Andersen 1994	2/33	2/33		1.00 [0.15, 6.68]
Chen 2001	0/21	0/20		0.0 [0.0, 0.0]
Chen T 2005	0/40	0/38		0.0 [0.0, 0.0]
Cheng 2003	0/25	0/32		0.0 [0.0, 0.0]
Chollet 2011	1/59	1/59		1.00 [0.06, 15.61]
Feng 2004	0/18	0/18		0.0 [0.0, 0.0]
Fruehwald 2003	1/28	0/16		1.76 [0.08, 40.80]
He 2004	0/36	0/35		0.0 [0.0, 0.0]
He 2005	0/27	0/27		0.0 [0.0, 0.0]
Hu 2002	0/42	0/30		0.0 [0.0, 0.0]
Huang 2002	0/40	0/40		0.0 [0.0, 0.0]
Lai 2006	0/40	0/40		0.0 [0.0, 0.0]
Li 2004a	0/33	0/34		0.0 [0.0, 0.0]
Li 2004b	0/37	0/36		0.0 [0.0, 0.0]
Li 2006	1/52	2/53		0.51 [0.05, 5.45]
Li 2008	0/60	0/30		0.0 [0.0, 0.0]
Liang 2003	0/42	0/21		0.0 [0.0, 0.0]

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Study or subgroup	SSRI n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
Liu 2004	0/30	0/30		0.0 [0.0, 0.0]
Liu 2006	0/30	0/30		0.0 [0.0, 0.0]
Robinson 2000a	0/23	1/17		0.25 [0.01, 5.79]
Robinson 2000b	0/17	0/16		0.0 [0.0, 0.0]
Robinson 2008	2/59	0/58		4.92 [0.24, 100.25]
Song 2006	0/41	0/41		0.0 [0.0, 0.0]
Wen 2006	0/42	0/42		0.0 [0.0, 0.0]
Wiart 2000	0/16	0/15		0.0 [0.0, 0.0]
Xie 2005	0/65	0/65		0.0 [0.0, 0.0]
Xu 2001	0/32	0/31		0.0 [0.0, 0.0]
Xu 2006	0/32	2/32		0.20 [0.01, 4.01]
Yang 2011	0/20	0/22		0.0 [0.0, 0.0]
Ye 2004	0/30	0/30		0.0 [0.0, 0.0]
Zhou 2003	0/28	0/26		0.0 [0.0, 0.0]
Zhou 2008	0/36	0/40		0.0 [0.0, 0.0]
Subtotal (95% CI)	**1192**	**1119**		**0.94 [0.38, 2.36]**
Total events: 9 (SSRI), 9 (Control)				
Heterogeneity: Tau^2 = 0.0; Chi^2 = 3.76, df = 7 (P = 0.81); I^2 =0.0%				
Test for overall effect: Z = 0.12 (P = 0.90)				
2 Time since stroke 3 to 6 months				
Dam 1996	0/18	0/17		0.0 [0.0, 0.0]
Miao 2004	0/45	0/45		0.0 [0.0, 0.0]
Murray 2005	0/62	2/61		0.20 [0.01, 4.02]
Yang 2002	0/64	0/57		0.0 [0.0, 0.0]
Subtotal (95% CI)	**189**	**180**		**0.20 [0.01, 4.02]**
Total events: 0 (SSRI), 2 (Control)				
Heterogeneity: Tau^2 = 0.0; Chi^2 = 0.0, df = 0 (P = 1.00); I^2 =0.0%				
Test for overall effect: Z = 1.06 (P = 0.29)				
3 Time since stroke 6 to 9 months				
Guo 2009	0/40	0/40		0.0 [0.0, 0.0]
Liu 2006	0/30	0/30		0.0 [0.0, 0.0]
Subtotal (95% CI)	**70**	**70**		**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)				
Heterogeneity: Tau^2 = 0.0; Chi^2 = 0.0, df = 0 (P<0.00001); I^2 =0.0%				
Test for overall effect: Z = 0.0 (P < 0.00001)				

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Study or subgroup	SSRI n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
4 Time since stroke 9 to 12 months				
Subtotal (95% CI)	**0**	**0**		**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)				
Heterogeneity: not applicable				
Test for overall effect: not applicable				
5 Time since stroke unknown				
Brown 1998	0/10	0/10		0.0 [0.0, 0.0]
Burns 1999	1/14	1/14		1.00 [0.07, 14.45]
Ji 2000	0/20	0/20		0.0 [0.0, 0.0]
Jia 2005	0/92	2/92		0.20 [0.01, 4.11]
Li 2002	0/46	0/46		0.0 [0.0, 0.0]
Li 2005	0/74	0/74		0.0 [0.0, 0.0]
Xu 2007	0/36	0/36		0.0 [0.0, 0.0]
Subtotal (95% CI)	**292**	**292**		**0.49 [0.07, 3.65]**
Total events: 1 (SSRI), 3 (Control)				
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.63$, df = 1 (P = 0.43); $I^2 = 0.0\%$				
Test for overall effect: Z = 0.69 (P = 0.49)				
Total (95% CI)	**1743**	**1661**		**0.76 [0.34, 1.70]**
Total events: 10 (SSRI), 14 (Control)				
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 5.54$, df = 10 (P = 0.85); $I^2 = 0.0\%$				
Test for overall effect: Z = 0.67 (P = 0.50)				
Test for subgroup differences: $Chi^2 = 1.16$, df = 2 (P = 0.56), $I^2 = 0.0\%$				

Analysis 3.10. Comparison 3 SSRI versus control (according to time since stroke when recruited), Outcome 10 Seizure.

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 3 SSRI versus control (according to time since stroke when recruited)

Outcome: 10 Seizure

Study or subgroup	SSRI n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
1 Time since stroke < 3 months				
Andersen 1994	2/33	0/33		5.00 [0.25, 100.32]
Chollet 2011	1/59	0/59		3.00 [0.12, 72.18]
He 2004	0/36	0/35		0.0 [0.0, 0.0]
Liang 2003	0/42	0/21		0.0 [0.0, 0.0]
Wiart 2000	1/16	1/15		0.94 [0.06, 13.68]
Ye 2004	0/30	0/30		0.0 [0.0, 0.0]
Subtotal (95% CI)	**216**	**193**		**2.22 [0.41, 12.06]**
Total events: 4 (SSRI), 1 (Control)				
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.73$, df = 2 (P = 0.70); $I^2 = 0.0\%$				
Test for overall effect: Z = 0.92 (P = 0.36)				
2 Time since stroke 3 to 6 months				
Dam 1996	2/18	0/17		4.74 [0.24, 92.07]
Subtotal (95% CI)	**18**	**17**		**4.74 [0.24, 92.07]**
Total events: 2 (SSRI), 0 (Control)				
Heterogeneity: not applicable				
Test for overall effect: Z = 1.03 (P = 0.30)				
3 Time since stroke 6 to 9 months				
Subtotal (95% CI)	**0**	**0**		**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)				
Heterogeneity: not applicable				
Test for overall effect: not applicable				
4 Time since stroke 9 to 12 months				
Subtotal (95% CI)	**0**	**0**		**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)				
Heterogeneity: not applicable				
Test for overall effect: not applicable				
5 Time since stroke unknown				
Subtotal (95% CI)	**0**	**0**		**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)				
Heterogeneity: not applicable				
Test for overall effect: not applicable				

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Study or subgroup	SSRI n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
Total (95% CI)	**234**	**210**		**2.67 [0.61, 11.63]**
Total events: 6 (SSRI), 1 (Control)				
Heterogeneity: Tau^2 = 0.0; Chi^2 = 0.91, df = 3 (P = 0.82); I^2 =0.0%				
Test for overall effect: Z = 1.31 (P = 0.19)				
Test for subgroup differences: Chi^2 = 0.19, df = 1 (P = 0.66), I^2 =0.0%				

Analysis 3.11. Comparison 3 SSRI versus control (according to time since stroke when recruited), Outcome 11 Gastrointestinal side effects.

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 3 SSRI versus control (according to time since stroke when recruited)

Outcome: 11 Gastrointestinal side effects

Study or subgroup	SSRI n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
1 Time since stroke < 3 months				
Chollet 2011	14/59	6/59		2.33 [0.96, 5.66]
He 2004	0/36	0/35		0.0 [0.0, 0.0]
He 2005	9/27	0/27		19.00 [1.16, 310.94]
Hu 2002	5/42	0/30		7.93 [0.46, 138.20]
Huang 2002	0/40	0/40		0.0 [0.0, 0.0]
Li 2004a	3/33	0/34		7.21 [0.39, 134.32]
Li 2008	6/60	3/30		1.00 [0.27, 3.72]
Liang 2003	4/42	4/21		0.50 [0.14, 1.80]
Liu 2004	3/30	0/30		7.00 [0.38, 129.93]
Wiart 2000	1/16	3/16		0.33 [0.04, 2.87]

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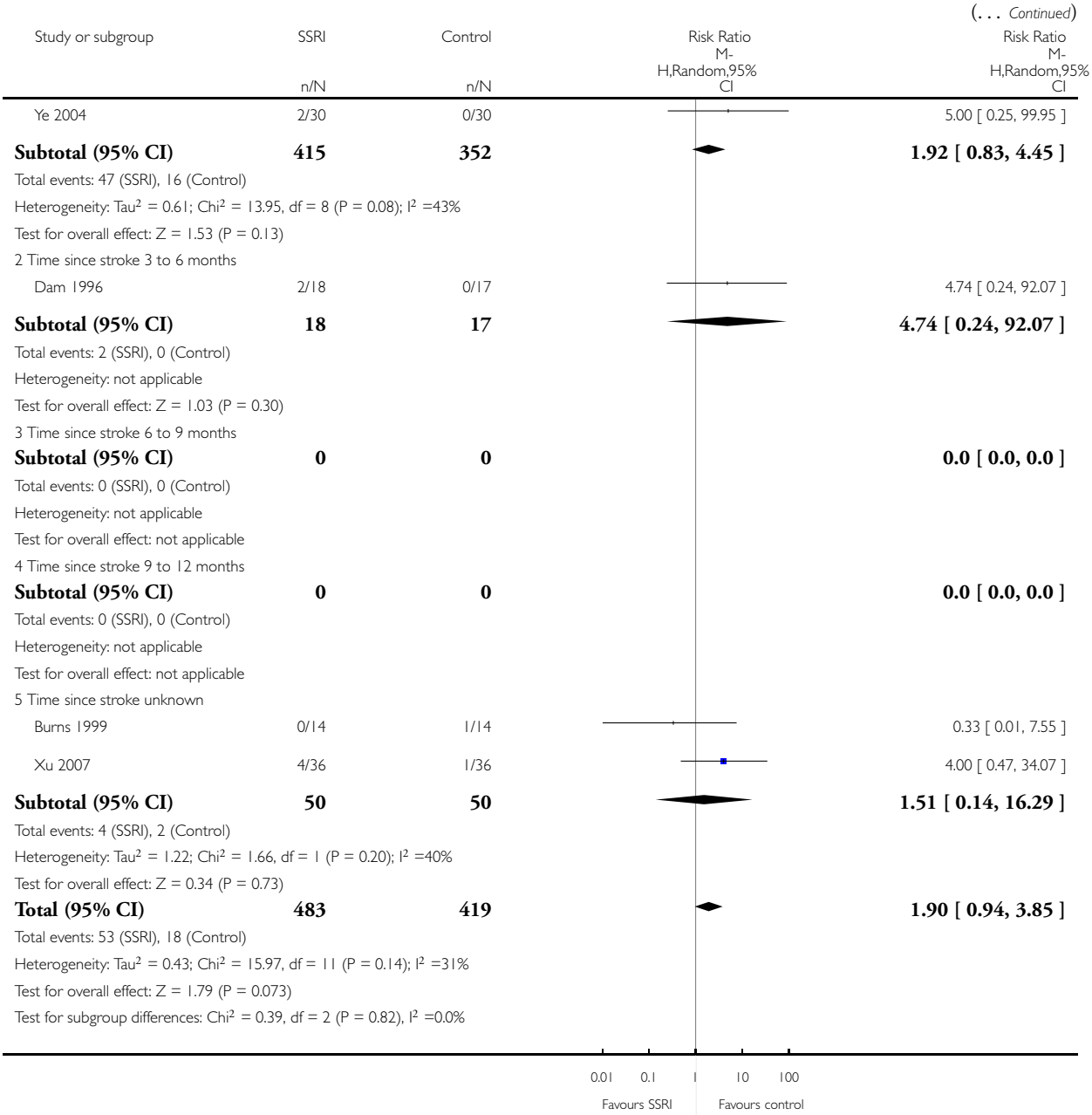

Analysis 3.12. Comparison 3 SSRI versus control (according to time since stroke when recruited), Outcome 12 Leaving the trial early.

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 3 SSRI versus control (according to time since stroke when recruited)

Outcome: 12 Leaving the trial early

Study or subgroup	SSRI n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
1 Time since stroke < 3 months				
Acler 2009	0/10	0/10		0.0 [0.0, 0.0]
Almeida 2006	11/55	6/56		1.87 [0.74, 4.70]
Andersen 1994	6/33	1/33		6.00 [0.76, 47.14]
Chen 2001	2/21	2/20		0.95 [0.15, 6.13]
Chen T 2005	0/40	0/38		0.0 [0.0, 0.0]
Cheng 2003	0/25	0/32		0.0 [0.0, 0.0]
Chollet 2011	2/59	3/59		0.67 [0.12, 3.85]
Feng 2004	2/18	2/18		1.00 [0.16, 6.35]
Fruehwald 2003	6/28	8/26		0.70 [0.28, 1.74]
He 2004	8/44	5/40		1.45 [0.52, 4.08]
He 2005	0/27	0/27		0.0 [0.0, 0.0]
Hu 2002	0/42	0/30		0.0 [0.0, 0.0]
Huang 2002	0/40	0/40		0.0 [0.0, 0.0]
Kong 2007	11/48	6/42		1.60 [0.65, 3.96]
Lai 2006	0/40	0/40		0.0 [0.0, 0.0]
Li 2004a	0/33	0/34		0.0 [0.0, 0.0]
Li 2004b	6/37	4/36		1.46 [0.45, 4.74]
Li 2006	2/50	4/53		0.53 [0.10, 2.77]
Li 2008	2/60	2/30		0.50 [0.07, 3.38]
Liang 2003	0/42	0/21		0.0 [0.0, 0.0]
Liu 2004	0/30	0/30		0.0 [0.0, 0.0]
Rasmussen 2003	35/70	35/67		0.96 [0.69, 1.33]
Robinson 2000a	9/23	4/17		1.66 [0.61, 4.51]

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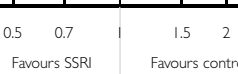
Study or subgroup	SSRI n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
Robinson 2000b	4/17	1/16		3.76 [0.47, 30.20]
Robinson 2008	7/59	5/58		1.38 [0.46, 4.09]
Wen 2006	0/42	0/42		0.0 [0.0, 0.0]
Wiart 2000	0/16	0/15		0.0 [0.0, 0.0]
Xie 2005	0/65	0/65		0.0 [0.0, 0.0]
Xu 2001	6/32	4/31		1.45 [0.45, 4.66]
Xu 2006	4/32	3/32		1.33 [0.32, 5.49]
Yang 2011	0/20	0/22		0.0 [0.0, 0.0]
Ye 2004	1/31	0/30		2.91 [0.12, 68.66]
Zhou 2003	2/30	4/30		0.50 [0.10, 2.53]
Zhou 2008	0/36	0/40		0.0 [0.0, 0.0]
Subtotal (95% CI)	**1255**	**1180**		**1.12 [0.90, 1.40]**
Total events: 126 (SSRI), 99 (Control)				
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 12.43$, df = 18 (P = 0.82); $I^2 = 0.0\%$				
Test for overall effect: Z = 1.00 (P = 0.32)				
2 Time since stroke 3 to 6 months				
Dam 1996	0/16	0/17		0.0 [0.0, 0.0]
Miao 2004	11/45	11/45		1.00 [0.48, 2.07]
Murray 2005	24/62	30/61		0.79 [0.53, 1.18]
Subtotal (95% CI)	**123**	**123**		**0.83 [0.59, 1.19]**
Total events: 35 (SSRI), 41 (Control)				
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.32$, df = 1 (P = 0.57); $I^2 = 0.0\%$				
Test for overall effect: Z = 1.02 (P = 0.31)				
3 Time since stroke 6 to 9 months				
Guo 2009	0/40	0/40		0.0 [0.0, 0.0]
Liu 2006	0/30	0/30		0.0 [0.0, 0.0]
Subtotal (95% CI)	**70**	**70**		**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)				
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.0$, df = 0 (P<0.00001); $I^2 = 0.0\%$				
Test for overall effect: Z = 0.0 (P < 0.00001)				
4 Time since stroke 9 to 12 months				
Subtotal (95% CI)	**0**	**0**		**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)				
Heterogeneity: not applicable				
Test for overall effect: not applicable				
5 Time since stroke not known				
Brown 1998	1/10	0/10		3.00 [0.14, 65.90]



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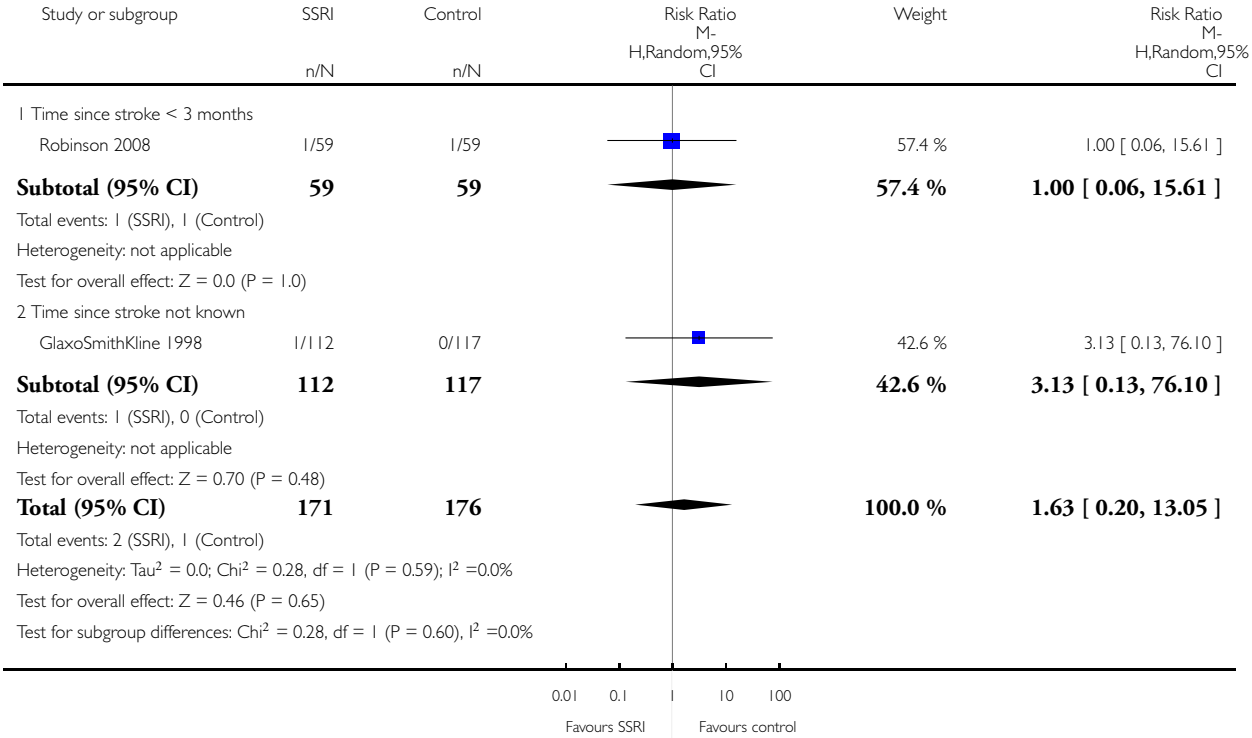
Study or subgroup	SSRI n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
Burns 1999	0/14	0/14		0.0 [0.0, 0.0]
Chen 2002	0/24	4/24		0.11 [0.01, 1.96]
GlaxoSmithKline 1998	13/112	13/117		1.04 [0.51, 2.15]
Ji 2000	0/20	0/20		0.0 [0.0, 0.0]
Jia 2005	4/92	4/92		1.00 [0.26, 3.88]
Li 2002	0/46	0/46		0.0 [0.0, 0.0]
Li 2005	0/74	0/74		0.0 [0.0, 0.0]
Wang 2003	13/64	9/56		1.26 [0.58, 2.73]
Yang 2002	4/64	7/57		0.51 [0.16, 1.65]
Subtotal (95% CI)	**520**	**510**		**0.97 [0.62, 1.51]**
Total events: 35 (SSRI), 37 (Control)				
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 4.44$, df = 5 (P = 0.49); $I^2 = 0.0\%$				
Test for overall effect: Z = 0.14 (P = 0.89)				
Total (95% CI)	**1968**	**1883**		**1.02 [0.86, 1.21]**
Total events: 196 (SSRI), 177 (Control)				
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 18.94$, df = 26 (P = 0.84); $I^2 = 0.0\%$				
Test for overall effect: Z = 0.23 (P = 0.82)				
Test for subgroup differences: $Chi^2 = 2.00$, df = 2 (P = 0.37), $I^2 = 0\%$				

Analysis 3.13. Comparison 3 SSRI versus control (according to time since stroke when recruited), Outcome 13 Bleeding.

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 3 SSRI versus control (according to time since stroke when recruited)

Outcome: 13 Bleeding



Analysis 3.14. Comparison 3 SSRI versus control (according to time since stroke when recruited), Outcome 14 Motor deficits.

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 3 SSRI versus control (according to time since stroke when recruited)

Outcome: 14 Motor deficits

Study or subgroup	SSRI N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
1 < 3 months							
Chollet 2011	57	-53.7 (27.8)	56	-35.1 (22)		55.3 %	-0.74 [-1.12, -0.35]
Subtotal (95% CI)	**57**		**56**			**55.3 %**	**-0.74 [-1.12, -0.35]**
Heterogeneity: not applicable							
Test for overall effect: Z = 3.78 (P = 0.00016)							
2 3 to 6 months							
Dam 1996	16	32.4 (3.8)	16	31.6 (5)		44.7 %	0.18 [-0.52, 0.87]
Subtotal (95% CI)	**16**		**16**			**44.7 %**	**0.18 [-0.52, 0.87]**
Heterogeneity: not applicable							
Test for overall effect: Z = 0.50 (P = 0.62)							
Total (95% CI)	**73**		**72**			**100.0 %**	**-0.33 [-1.22, 0.56]**
Heterogeneity: Tau² = 0.33; Chi² = 5.09, df = 1 (P = 0.02); I² =80%							
Test for overall effect: Z = 0.72 (P = 0.47)							
Test for subgroup differences: Chi² = 5.09, df = 1 (P = 0.02), I² =80%							

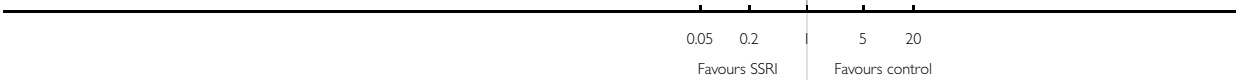
Analysis 4.1. Comparison 4 SSRI versus control according to depression at time of recruitment, Outcome 1 Modified Rankin score.

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 4 SSRI versus control according to depression at time of recruitment

Outcome: 1 Modified Rankin score

Study or subgroup	SSRI n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
1 Had to have depression at recruitment				
Subtotal (95% CI)	**0**	**0**		**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)				
Heterogeneity: not applicable				
Test for overall effect: not applicable				
2 Did not have to have depression at recruitment				
Almeida 2006	0/55	0/56		0.0 [0.0, 0.0]
Chollet 2011	42/57	50/55		0.81 [0.68, 0.97]
Subtotal (95% CI)	**112**	**111**		**0.81 [0.68, 0.97]**
Total events: 42 (SSRI), 50 (Control)				
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.0$, df = 0 (P = 1.00); $I^2 = 0.0\%$				
Test for overall effect: Z = 2.34 (P = 0.019)				
Total (95% CI)	**112**	**111**		**0.81 [0.68, 0.97]**
Total events: 42 (SSRI), 50 (Control)				
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.0$, df = 0 (P = 1.00); $I^2 = 0.0\%$				
Test for overall effect: Z = 2.34 (P = 0.019)				
Test for subgroup differences: Not applicable				



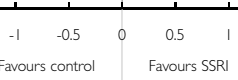
Analysis 4.2. Comparison 4 SSRI versus control according to depression at time of recruitment, Outcome 2 Disability.

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 4 SSRI versus control according to depression at time of recruitment

Outcome: 2 Disability

Study or subgroup	SSRI N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
1 Had to have depression at recruitment							
Chen 2001	19	79.31 (8.94)	18	71.56 (9.41)		4.3 %	0.83 [0.15, 1.50]
Chen 2002	24	61 (12.2)	20	51.5 (10.3)		4.5 %	0.82 [0.20, 1.44]
Chen T 2005	40	65.76 (5.92)	38	51.76 (7.32)		4.6 %	2.09 [1.53, 2.64]
Cheng 2003	25	-26.38 (14.2)	32	-29.15 (17.38)		4.7 %	0.17 [-0.35, 0.69]
He 2005	27	84.26 (8.41)	27	78.33 (15.01)		4.7 %	0.48 [-0.06, 1.02]
Li 2006	50	64.36 (8.23)	49	59.17 (9.02)		5.0 %	0.60 [0.19, 1.00]
Li 2008	58	40.8 (3.7)	28	38.4 (5.8)		4.9 %	0.53 [0.07, 0.99]
Liu 2006	30	64.4 (12.1)	30	35.4 (9.1)		4.2 %	2.67 [1.97, 3.38]
Robinson 2000a	14	59.2 (11.6)	13	56.2 (7.74)		4.1 %	0.29 [-0.47, 1.05]
Wang 2003	51	75 (4.2)	47	61 (6.9)		4.7 %	2.46 [1.93, 2.98]
Wiart 2000	16	87.4 (22.8)	15	88.7 (25.3)		4.3 %	-0.05 [-0.76, 0.65]
Xie 2005	65	88.7 (7.9)	65	79.8 (4.5)		5.1 %	1.38 [0.99, 1.76]
Xu 2001	26	73 (4.4)	27	67 (4.1)		4.5 %	1.39 [0.79, 2.00]
Xu 2007	36	64.4 (8.23)	36	56.9 (6.68)		4.8 %	0.99 [0.50, 1.48]
Ye 2004	30	78.75 (14.19)	30	50.26 (13.4)		4.5 %	2.04 [1.41, 2.67]
Subtotal (95% CI)	**511**		**475**			**68.9 %**	**1.11 [0.71, 1.51]**
Heterogeneity: $Tau^2 = 0.54$; $Chi^2 = 112.87$, df = 14 (P<0.00001); $I^2 = 88\%$							
Test for overall effect: Z = 5.43 (P < 0.00001)							
2 Did not have to have depression at onset							
Acler 2009	10	82 (28)	10	75 (25)		3.8 %	0.25 [-0.63, 1.13]
Dam 1996	16	61.9 (13)	16	54.1 (21.1)		4.3 %	0.43 [-0.27, 1.14]
Kong 2007	37	60.4 (12.5)	36	52.3 (13.5)		4.9 %	0.62 [0.15, 1.09]
Liu 2004	30	70.33 (10.74)	30	64.33 (7.7)		4.7 %	0.63 [0.11, 1.15]
Robinson 2000b	13	60.5 (10.8)	15	63.1 (8.2)		4.1 %	-0.27 [-1.01, 0.48]



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Study or subgroup	SSRI N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
Xu 2006	28	-27.63 (4.81)	29	-32.81 (4.13)		4.6 %	1.14 [0.58, 1.70]
Zhou 2003	28	-27.8 (7.1)	26	-32.5 (7.8)		4.7 %	0.62 [0.07, 1.17]
Subtotal (95% CI)	**162**		**162**			**31.1 %**	**0.55 [0.27, 0.84]**
Heterogeneity: $Tau^2 = 0.06$; $Chi^2 = 9.54$, df = 6 (P = 0.15); $I^2 = 37\%$							
Test for overall effect: Z = 3.76 (P = 0.00017)							
Total (95% CI)	**673**		**637**			**100.0 %**	**0.92 [0.62, 1.23]**
Heterogeneity: $Tau^2 = 0.45$; $Chi^2 = 136.49$, df = 21 (P<0.00001); $I^2 = 85\%$							
Test for overall effect: Z = 5.91 (P < 0.00001)							
Test for subgroup differences: $Chi^2 = 4.85$, df = 1 (P = 0.03), $I^2 = 79\%$							

Analysis 4.3. Comparison 4 SSRI versus control according to depression at time of recruitment, Outcome 3 Neurological deficit score.

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 4 SSRI versus control according to depression at time of recruitment

Outcome: 3 Neurological deficit score

Study or subgroup	SSRI N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
1 Had to have depression at recruitment							
Chen 2001	19	-49.72 (4.07)	18	-43.13 (3.64)		3.0 %	-1.67 [-2.43, -0.91]
Chen 2002	24	10 (4.8)	20	14.8 (4.8)		3.3 %	-0.98 [-1.61, -0.35]
Cheng 2003	25	6.5 (3.19)	32	10.96 (8.13)		3.5 %	-0.68 [-1.22, -0.14]
Feng 2004	16	9.1 (3.2)	16	14.4 (2.2)		2.8 %	-1.88 [-2.73, -1.03]
Fruehwald 2003	26	-55.5 (4.8)	24	-52.8 (5.4)		3.4 %	-0.52 [-1.09, 0.04]
Guo 2009	40	29.07 (8.02)	40	33.78 (8.63)		3.7 %	-0.56 [-1.01, -0.11]
He 2005	27	6.48 (1.58)	27	8.33 (3.86)		3.5 %	-0.62 [-1.17, -0.07]
Huang 2002	40	4.02 (1.86)	40	8.57 (3.64)		3.6 %	-1.56 [-2.06, -1.06]
Jia 2005	86	10.4 (8.5)	88	22.6 (8.9)		3.9 %	-1.40 [-1.73, -1.06]
Li 2002	46	11.5 (2.8)	46	19 (4)		3.5 %	-2.15 [-2.67, -1.64]
Li 2004a	33	6.23 (3.11)	34	12.86 (6.36)		3.5 %	-1.30 [-1.83, -0.77]
Li 2005	74	12.9 (5.1)	74	18.7 (5.4)		3.8 %	-1.10 [-1.44, -0.75]
Li 2006	50	21.89 (1.57)	49	23.77 (1.46)		3.7 %	-1.23 [-1.66, -0.80]
Liang 2003	42	11.74 (3.23)	21	17.32 (5.19)		3.4 %	-1.38 [-1.96, -0.80]
Liu 2006	30	13.3 (3.8)	30	22.4 (4.1)		3.2 %	-2.27 [-2.93, -1.61]
Wang 2003	51	9.5 (3.5)	47	15.6 (4.6)		3.7 %	-1.49 [-1.94, -1.04]
Xu 2001	26	8.2 (5.2)	27	12.4 (4.3)		3.4 %	-0.87 [-1.43, -0.30]
Xu 2007	36	21.89 (1.57)	36	20.78 (4.06)		3.6 %	0.36 [-0.11, 0.82]
Ye 2004	30	8.3 (3.8)	30	16 (4.8)		3.4 %	-1.76 [-2.36, -1.15]
Subtotal (95% CI)	**721**		**699**			**66.1 %**	**-1.19 [-1.47, -0.91]**
Heterogeneity: $Tau^2 = 0.31$; $Chi^2 = 101.51$, df = 18 (P<0.00001); $I^2 = 82\%$							
Test for overall effect: Z = 8.37 (P < 0.00001)							
2 Did not have to have depression at recruitment							
Acler 2009	10	2.3 (2)	10	3.5 (1.3)		2.7 %	-0.68 [-1.59, 0.23]

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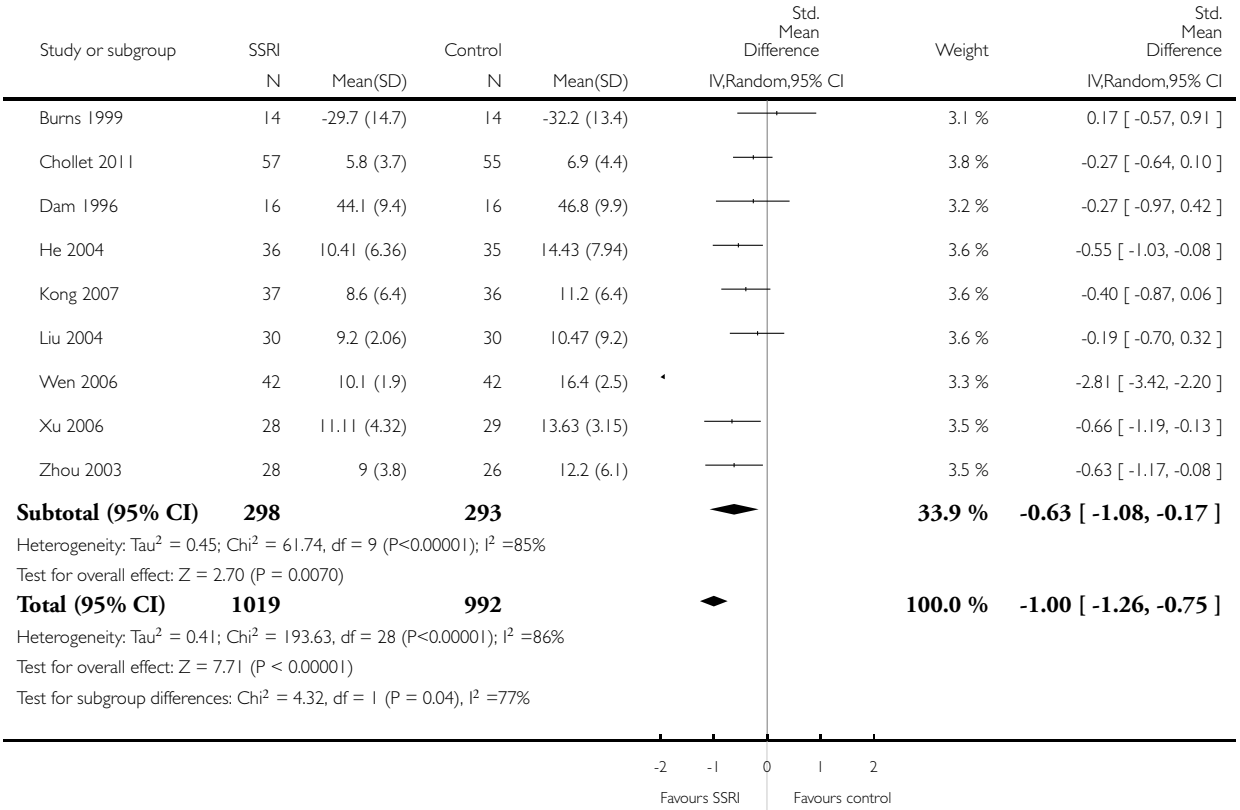

Analysis 4.4. Comparison 4 SSRI versus control according to depression at time of recruitment, Outcome 4 Depression (continuous).

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 4 SSRI versus control according to depression at time of recruitment

Outcome: 4 Depression (continuous)

Study or subgroup	SSRI N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
1 Had to have depression at recruitment							
Andersen 1994	33	11.4 (5.1)	33	14.1 (4.7)		2.7 %	-0.54 [-1.04, -0.05]
Chen 2001	19	10.82 (6.25)	18	18.48 (6.28)		2.6 %	-1.20 [-1.90, -0.49]
Chen 2002	24	10.3 (3)	20	16.5 (2.5)		2.6 %	-2.19 [-2.95, -1.42]
Chen T 2005	40	10.98 (3.74)	38	22.45 (3.56)		2.6 %	-3.11 [-3.78, -2.44]
Cheng 2003	25	13.64 (11.02)	32	17.98 (12.53)		2.7 %	-0.36 [-0.89, 0.17]
Feng 2004	16	34.9 (4.6)	16	41.1 (4.7)		2.5 %	-1.30 [-2.07, -0.53]
Finkenzeller 2009	23	12.1 (1.05)	27	10.6 (0.97)		2.6 %	1.47 [0.83, 2.10]
Fruehwald 2003	26	9.5 (7.9)	24	11.2 (12.4)		2.7 %	-0.16 [-0.72, 0.39]
Guo 2009	40	14.82 (8.05)	40	17.61 (8)		2.7 %	-0.34 [-0.79, 0.10]
He 2005	27	10.11 (1.08)	27	17.48 (1.05)		2.1 %	-6.82 [-8.26, -5.38]
Huang 2002	40	4.76 (0.6)	40	16.34 (1.3)		1.8 %	-11.33 [-13.18, -9.47]
Ji 2000	20	5.2 (1.5)	20	14.5 (2.7)		2.3 %	-4.17 [-5.32, -3.03]
Jia 2005	86	6.4 (6.2)	88	16.2 (6.8)		2.7 %	-1.50 [-1.84, -1.16]
Lai 2006	40	12.5 (8.4)	40	21.5 (4.3)		2.7 %	-1.34 [-1.82, -0.85]
Li 2002	46	10 (3)	46	22 (8)		2.7 %	-1.97 [-2.47, -1.47]
Li 2005	74	12.6 (2.1)	74	16.8 (2.3)		2.7 %	-1.90 [-2.29, -1.51]
Li 2006	50	5.61 (5.32)	49	20.26 (6.08)		2.7 %	-2.55 [-3.08, -2.01]
Li 2008	58	14.5 (2.4)	28	18.7 (3.9)		2.7 %	-1.40 [-1.90, -0.90]
Liang 2003	42	9.67 (4.48)	21	19.19 (3.12)		2.6 %	-2.30 [-2.97, -1.63]
Liu 2006	30	17.2 (2.1)	30	25.1 (3.3)		2.6 %	-2.82 [-3.55, -2.09]
Miao 2004	34	6.45 (5.3)	34	23.74 (5.16)		2.6 %	-3.27 [-4.01, -2.53]
Murray 2005	62	10.5 (9.6)	61	12 (8.5)		2.7 %	-0.16 [-0.52, 0.19]
Robinson 2000a	14	18.5 (7.6)	13	12.2 (4.7)		2.5 %	0.96 [0.15, 1.76]

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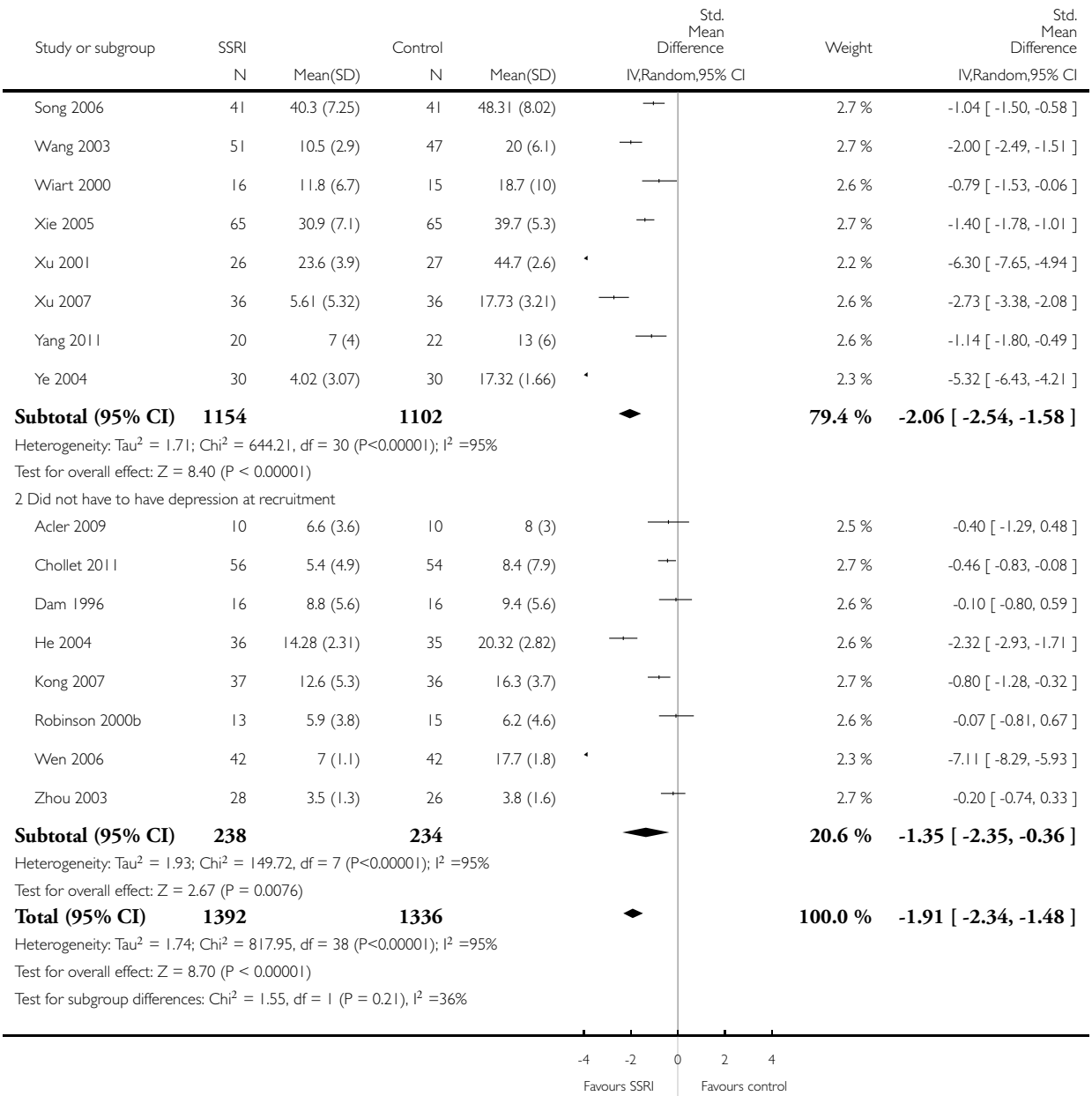
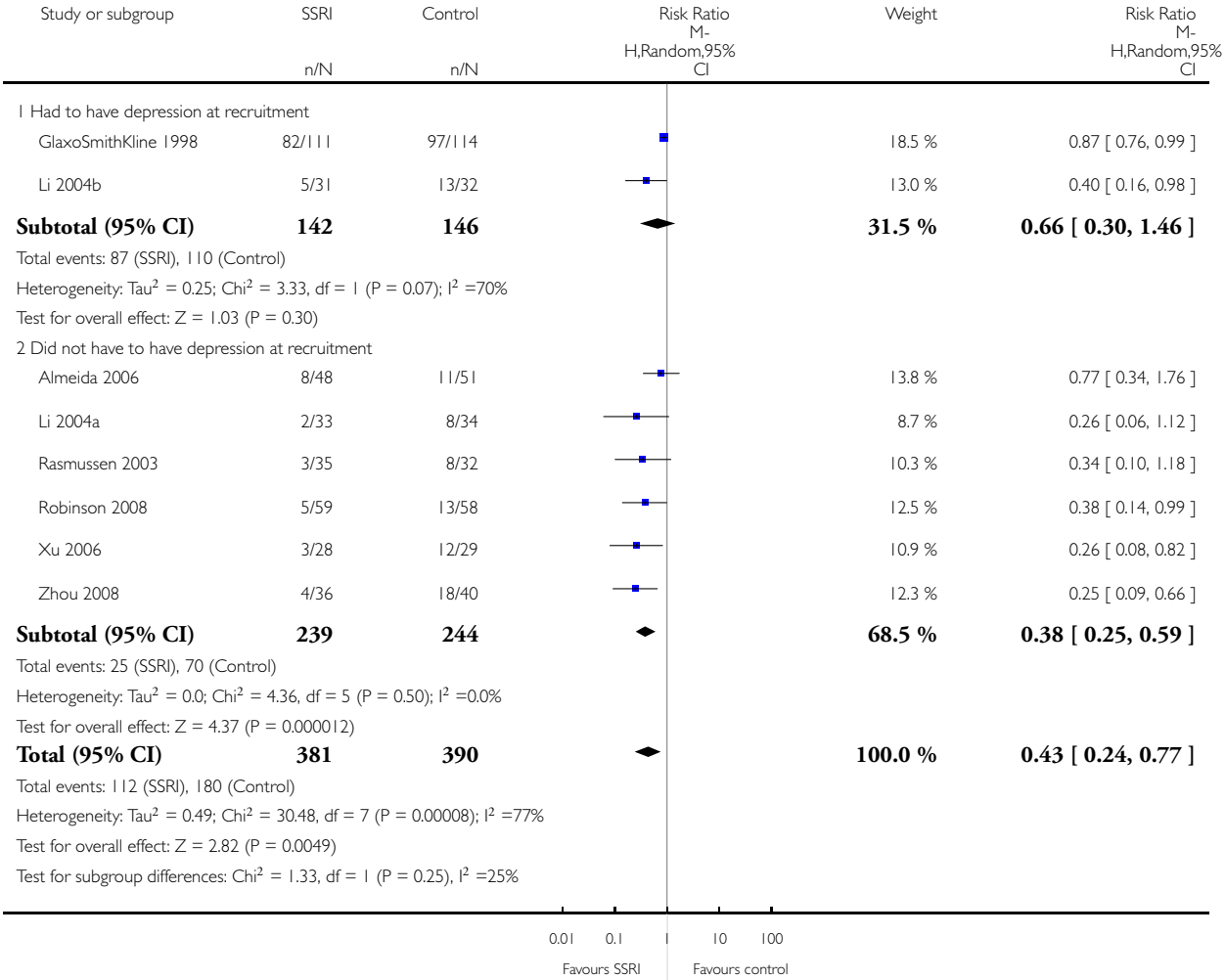


Analysis 4.5. Comparison 4 SSRI versus control according to depression at time of recruitment, Outcome 5 Depression (dichotomous).

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 4 SSRI versus control according to depression at time of recruitment

Outcome: 5 Depression (dichotomous)



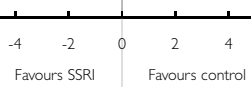
Analysis 4.6. Comparison 4 SSRI versus control according to depression at time of recruitment, Outcome 6 Anxiety (continuous).

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 4 SSRI versus control according to depression at time of recruitment

Outcome: 6 Anxiety (continuous)

Study or subgroup	SSRI N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
1 Had to have depression at recruitment							
Finkenzeller 2009	23	6.9 (0.57)	27	6.7 (0.53)		12.8 %	0.36 [-0.20, 0.92]
He 2005	27	5.37 (1.66)	27	12.78 (1.93)		11.3 %	-4.06 [-5.01, -3.10]
Lai 2006	40	50.2 (9.4)	40	54.2 (15.2)		13.2 %	-0.31 [-0.75, 0.13]
Robinson 2000a	14	9.8 (4.8)	13	9.9 (5.1)		12.1 %	-0.02 [-0.77, 0.74]
Ye 2004	30	9.82 (2.64)	30	14.02 (2.32)		12.7 %	-1.67 [-2.26, -1.08]
Subtotal (95% CI)	**134**		**137**			**62.0 %**	**-1.10 [-2.32, 0.12]**
Heterogeneity: Tau^2 = 1.81; Chi^2 = 77.25, df = 4 (P<0.00001); I^2 =95%							
Test for overall effect: Z = 1.77 (P = 0.077)							
2 Did not have to have depression at recruitment							
Liu 2004	30	7.43 (3.63)	30	11 (5.63)		12.9 %	-0.74 [-1.27, -0.22]
Robinson 2000b	13	4.7 (3.8)	15	5.5 (2.9)		12.1 %	-0.23 [-0.98, 0.51]
Zhou 2003	28	3.5 (1.3)	26	3.3 (1.3)		12.9 %	0.15 [-0.38, 0.69]
Subtotal (95% CI)	**71**		**71**			**38.0 %**	**-0.28 [-0.85, 0.29]**
Heterogeneity: Tau^2 = 0.16; Chi^2 = 5.52, df = 2 (P = 0.06); I^2 =64%							
Test for overall effect: Z = 0.97 (P = 0.33)							
Total (95% CI)	**205**		**208**			**100.0 %**	**-0.77 [-1.52, -0.02]**
Heterogeneity: Tau^2 = 1.05; Chi^2 = 86.14, df = 7 (P<0.00001); I^2 =92%							
Test for overall effect: Z = 2.02 (P = 0.043)							
Test for subgroup differences: Chi^2 = 1.42, df = 1 (P = 0.23), I^2 =30%							



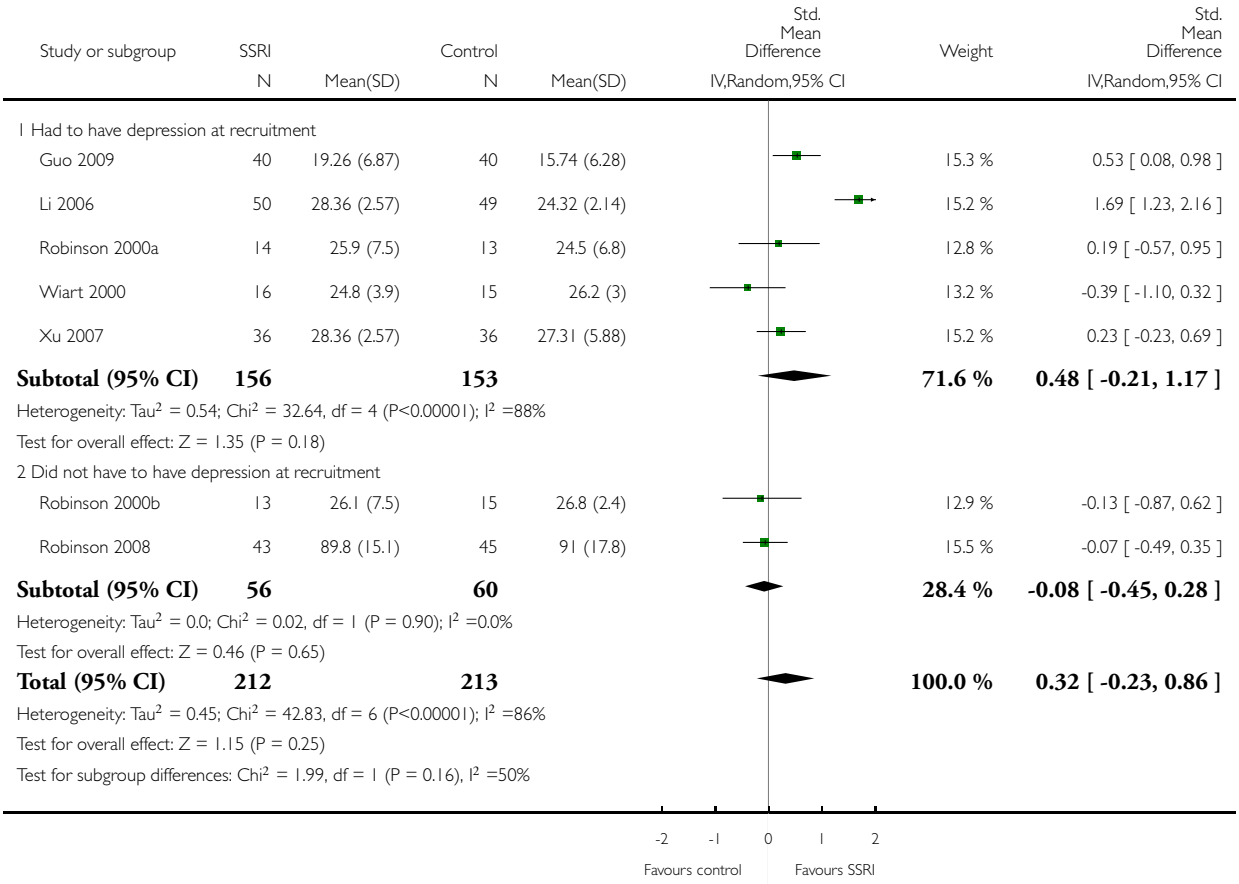
Analysis 4.8. Comparison 4 SSRI versus control according to depression at time of recruitment, Outcome 8 Cognition.

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 4 SSRI versus control according to depression at time of recruitment

Outcome: 8 Cognition

Study or subgroup	SSRI N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
1 Had to have depression at recruitment							
Guo 2009	40	19.26 (6.87)	40	15.74 (6.28)		15.3 %	0.53 [0.08, 0.98]
Li 2006	50	28.36 (2.57)	49	24.32 (2.14)		15.2 %	1.69 [1.23, 2.16]
Robinson 2000a	14	25.9 (7.5)	13	24.5 (6.8)		12.8 %	0.19 [-0.57, 0.95]
Wiart 2000	16	24.8 (3.9)	15	26.2 (3)		13.2 %	-0.39 [-1.10, 0.32]
Xu 2007	36	28.36 (2.57)	36	27.31 (5.88)		15.2 %	0.23 [-0.23, 0.69]
Subtotal (95% CI)	**156**		**153**			**71.6 %**	**0.48 [-0.21, 1.17]**
Heterogeneity: Tau^2 = 0.54; Chi^2 = 32.64, df = 4 (P<0.00001); I^2 =88%							
Test for overall effect: Z = 1.35 (P = 0.18)							
2 Did not have to have depression at recruitment							
Robinson 2000b	13	26.1 (7.5)	15	26.8 (2.4)		12.9 %	-0.13 [-0.87, 0.62]
Robinson 2008	43	89.8 (15.1)	45	91 (17.8)		15.5 %	-0.07 [-0.49, 0.35]
Subtotal (95% CI)	**56**		**60**			**28.4 %**	**-0.08 [-0.45, 0.28]**
Heterogeneity: Tau^2 = 0.0; Chi^2 = 0.02, df = 1 (P = 0.90); I^2 =0.0%							
Test for overall effect: Z = 0.46 (P = 0.65)							
Total (95% CI)	**212**		**213**			**100.0 %**	**0.32 [-0.23, 0.86]**
Heterogeneity: Tau^2 = 0.45; Chi^2 = 42.83, df = 6 (P<0.00001); I^2 =86%							
Test for overall effect: Z = 1.15 (P = 0.25)							
Test for subgroup differences: Chi^2 = 1.99, df = 1 (P = 0.16), I^2 =50%							



Analysis 4.9. Comparison 4 SSRI versus control according to depression at time of recruitment, Outcome 9 Death.

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 4 SSRI versus control according to depression at time of recruitment

Outcome: 9 Death

Study or subgroup	SSRI n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
1 Had to have depression at recruitment				
Andersen 1994	2/33	2/33		1.00 [0.15, 6.68]
Chen 2001	0/21	0/20		0.0 [0.0, 0.0]
Chen T 2005	0/40	0/38		0.0 [0.0, 0.0]
Cheng 2003	0/25	0/32		0.0 [0.0, 0.0]
Feng 2004	0/18	0/18		0.0 [0.0, 0.0]
Fruehwald 2003	1/28	0/16		1.76 [0.08, 40.80]
Guo 2009	0/40	0/40		0.0 [0.0, 0.0]
He 2004	0/36	0/35		0.0 [0.0, 0.0]
He 2005	0/27	0/27		0.0 [0.0, 0.0]
Hu 2002	0/42	0/30		0.0 [0.0, 0.0]
Huang 2002	0/40	0/40		0.0 [0.0, 0.0]
Ji 2000	0/20	0/20		0.0 [0.0, 0.0]
Jia 2005	0/92	2/92		0.20 [0.01, 4.11]
Lai 2006	0/40	0/40		0.0 [0.0, 0.0]
Li 2002	0/46	0/46		0.0 [0.0, 0.0]
Li 2004b	0/37	0/36		0.0 [0.0, 0.0]
Li 2005	0/74	0/74		0.0 [0.0, 0.0]
Li 2006	1/52	2/53		0.51 [0.05, 5.45]
Li 2008	0/60	0/30		0.0 [0.0, 0.0]
Liang 2003	0/42	0/21		0.0 [0.0, 0.0]
Liu 2006	0/30	0/30		0.0 [0.0, 0.0]
Miao 2004	0/45	0/45		0.0 [0.0, 0.0]
Murray 2005	0/62	2/61		0.20 [0.01, 4.02]
Robinson 2000a	0/23	1/17		0.25 [0.01, 5.79]

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Study or subgroup	SSRI n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
Song 2006	0/41	0/41		0.0 [0.0, 0.0]
Wiart 2000	0/16	0/15		0.0 [0.0, 0.0]
Xie 2005	0/65	0/65		0.0 [0.0, 0.0]
Xu 2001	0/32	0/31		0.0 [0.0, 0.0]
Xu 2007	0/36	0/36		0.0 [0.0, 0.0]
Yang 2002	0/64	0/57		0.0 [0.0, 0.0]
Yang 2011	0/20	0/22		0.0 [0.0, 0.0]
Ye 2004	0/30	0/30		0.0 [0.0, 0.0]
Subtotal (95% CI)	**1277**	**1191**		**0.53 [0.18, 1.54]**
Total events: 4 (SSRI), 9 (Control)				
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 2.04$, df = 5 (P = 0.84); $I^2 = 0.0\%$				
Test for overall effect: Z = 1.17 (P = 0.24)				
2 Did not have to have depression at recruitment				
Acler 2009	0/10	0/10		0.0 [0.0, 0.0]
Almeida 2006	2/48	1/52		2.17 [0.20, 23.14]
Brown 1998	0/10	0/10		0.0 [0.0, 0.0]
Burns 1999	1/14	1/14		1.00 [0.07, 14.45]
Chollet 2011	1/59	1/59		1.00 [0.06, 15.61]
Dam 1996	0/18	0/17		0.0 [0.0, 0.0]
Li 2004a	0/33	0/34		0.0 [0.0, 0.0]
Liu 2004	0/30	0/30		0.0 [0.0, 0.0]
Robinson 2000b	0/17	0/16		0.0 [0.0, 0.0]
Robinson 2008	2/59	0/58		4.92 [0.24, 100.25]
Wen 2006	0/42	0/42		0.0 [0.0, 0.0]
Xu 2006	0/32	2/32		0.20 [0.01, 4.01]
Zhou 2003	0/28	0/26		0.0 [0.0, 0.0]
Zhou 2008	0/36	0/40		0.0 [0.0, 0.0]
Subtotal (95% CI)	**436**	**440**		**1.22 [0.36, 4.13]**
Total events: 6 (SSRI), 5 (Control)				
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 2.49$, df = 4 (P = 0.65); $I^2 = 0.0\%$				
Test for overall effect: Z = 0.32 (P = 0.75)				
Total (95% CI)	**1713**	**1631**		**0.76 [0.34, 1.70]**
Total events: 10 (SSRI), 14 (Control)				
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 5.54$, df = 10 (P = 0.85); $I^2 = 0.0\%$				
Test for overall effect: Z = 0.67 (P = 0.50)				

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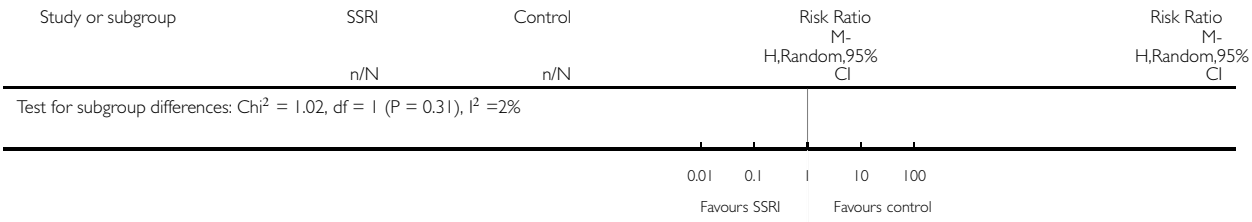
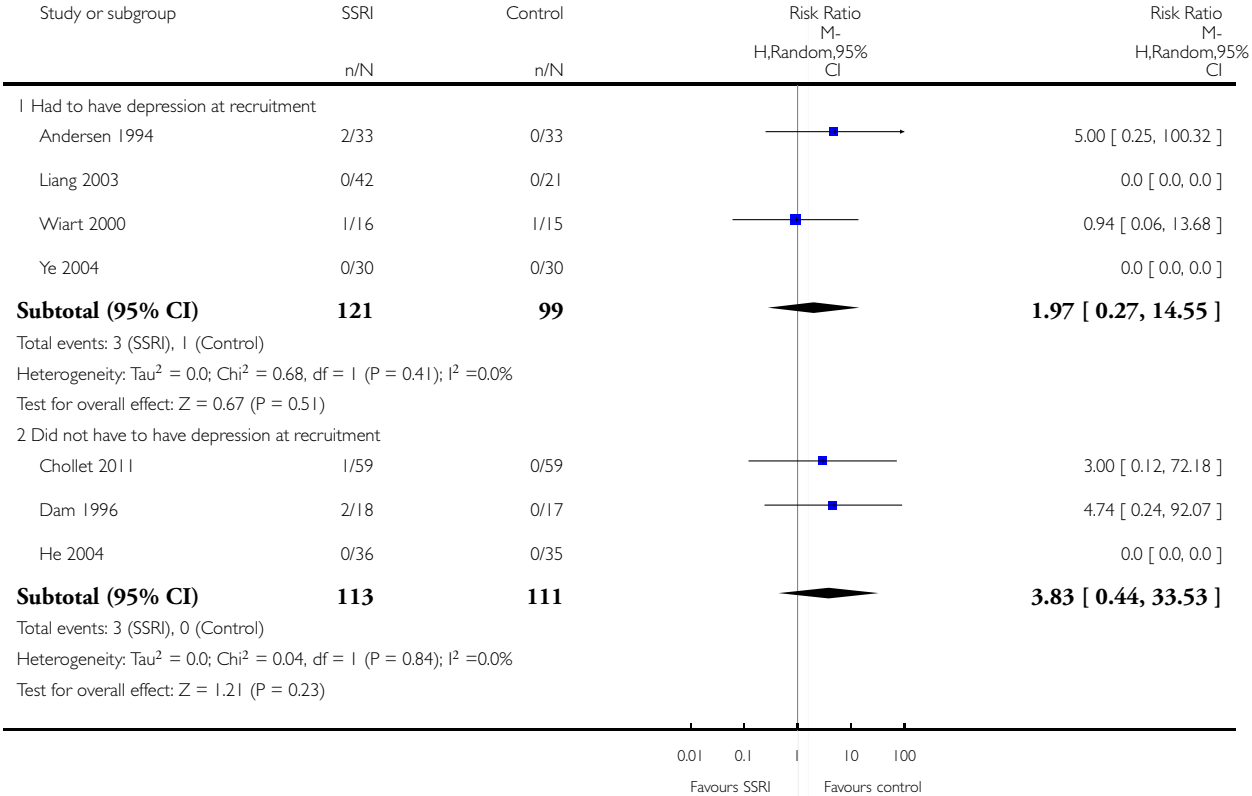


Analysis 4.10. Comparison 4 SSRI versus control according to depression at time of recruitment, Outcome 10 Seizures.

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 4 SSRI versus control according to depression at time of recruitment

Outcome: 10 Seizures



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Study or subgroup	SSRI n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
Total (95% CI)	**234**	**210**		**2.67 [0.61, 11.63]**
Total events: 6 (SSRI), 1 (Control)				
Heterogeneity: Tau^2 = 0.0; Chi^2 = 0.91, df = 3 (P = 0.82); I^2 =0.0%				
Test for overall effect: Z = 1.31 (P = 0.19)				
Test for subgroup differences: Chi^2 = 0.19, df = 1 (P = 0.66), I^2 =0.0%				

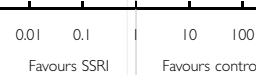
Analysis 4.11. Comparison 4 SSRI versus control according to depression at time of recruitment, Outcome 11 Gastrointestinal side effects.

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 4 SSRI versus control according to depression at time of recruitment

Outcome: 11 Gastrointestinal side effects

Study or subgroup	SSRI n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
1 Had to have depression at recruitment				
He 2005	9/27	0/27		19.00 [1.16, 310.94]
Hu 2002	5/42	0/30		7.93 [0.46, 138.20]
Huang 2002	0/40	0/40		0.0 [0.0, 0.0]
Li 2008	6/60	3/30		1.00 [0.27, 3.72]
Liang 2003	4/42	4/21		0.50 [0.14, 1.80]
Wiart 2000	1/16	3/16		0.33 [0.04, 2.87]
Xu 2007	4/36	1/36		4.00 [0.47, 34.07]
Ye 2004	2/30	0/30		5.00 [0.25, 99.95]
Subtotal (95% CI)	**293**	**230**		**1.72 [0.58, 5.12]**
Total events: 31 (SSRI), 11 (Control)				
Heterogeneity: Tau^2 = 1.00; Chi^2 = 12.00, df = 6 (P = 0.06); I^2 =50%				



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Study or subgroup	SSRI n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
Test for overall effect: Z = 0.98 (P = 0.33)				
2 Did not have to have depression at recruitment				
Burns 1999	0/14	1/14		0.33 [0.01, 7.55]
Chollet 2011	14/59	6/59		2.33 [0.96, 5.66]
Dam 1996	2/18	0/17		4.74 [0.24, 92.07]
He 2004	0/36	0/35		0.0 [0.0, 0.0]
Li 2004a	3/33	0/34		7.21 [0.39, 134.32]
Liu 2004	3/30	0/30		7.00 [0.38, 129.93]
Subtotal (95% CI)	**190**	**189**		**2.53 [1.18, 5.42]**
Total events: 22 (SSRI), 7 (Control)				
Heterogeneity: Tau^2 = 0.0; Chi^2 = 2.80, df = 4 (P = 0.59); I^2 =0.0%				
Test for overall effect: Z = 2.39 (P = 0.017)				
Total (95% CI)	**483**	**419**		**1.90 [0.94, 3.85]**
Total events: 53 (SSRI), 18 (Control)				
Heterogeneity: Tau^2 = 0.43; Chi^2 = 15.97, df = 11 (P = 0.14); I^2 =31%				
Test for overall effect: Z = 1.79 (P = 0.073)				
Test for subgroup differences: Chi^2 = 0.32, df = 1 (P = 0.57), I^2 =0.0%				

Analysis 4.12. Comparison 4 SSRI versus control according to depression at time of recruitment, Outcome 12 Leaving the trial early.

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 4 SSRI versus control according to depression at time of recruitment

Outcome: 12 Leaving the trial early

Study or subgroup	SSRI n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
1 Had to have depression at recruitment				
Andersen 1994	6/33	1/33		6.00 [0.76, 47.14]
Chen 2001	2/21	2/20		0.95 [0.15, 6.13]
Chen 2002	0/24	4/24		0.11 [0.01, 1.96]
Chen T 2005	0/40	0/38		0.0 [0.0, 0.0]
Cheng 2003	0/25	0/32		0.0 [0.0, 0.0]
Feng 2004	2/18	2/18		1.00 [0.16, 6.35]
Fruehwald 2003	6/28	8/26		0.70 [0.28, 1.74]
GlaxoSmithKline 1998	13/112	13/117		1.04 [0.51, 2.15]
Guo 2009	0/40	0/40		0.0 [0.0, 0.0]
He 2004	8/44	5/40		1.45 [0.52, 4.08]
He 2005	0/27	0/27		0.0 [0.0, 0.0]
Hu 2002	0/42	0/30		0.0 [0.0, 0.0]
Huang 2002	0/40	0/40		0.0 [0.0, 0.0]
Ji 2000	0/20	0/20		0.0 [0.0, 0.0]
Jia 2005	4/92	4/92		1.00 [0.26, 3.88]
Lai 2006	0/40	0/40		0.0 [0.0, 0.0]
Li 2002	0/46	0/46		0.0 [0.0, 0.0]
Li 2004a	0/33	0/34		0.0 [0.0, 0.0]
Li 2004b	6/37	4/36		1.46 [0.45, 4.74]
Li 2005	0/74	0/74		0.0 [0.0, 0.0]
Li 2006	2/50	4/53		0.53 [0.10, 2.77]
Li 2008	2/60	2/30		0.50 [0.07, 3.38]
Liang 2003	0/42	0/21		0.0 [0.0, 0.0]

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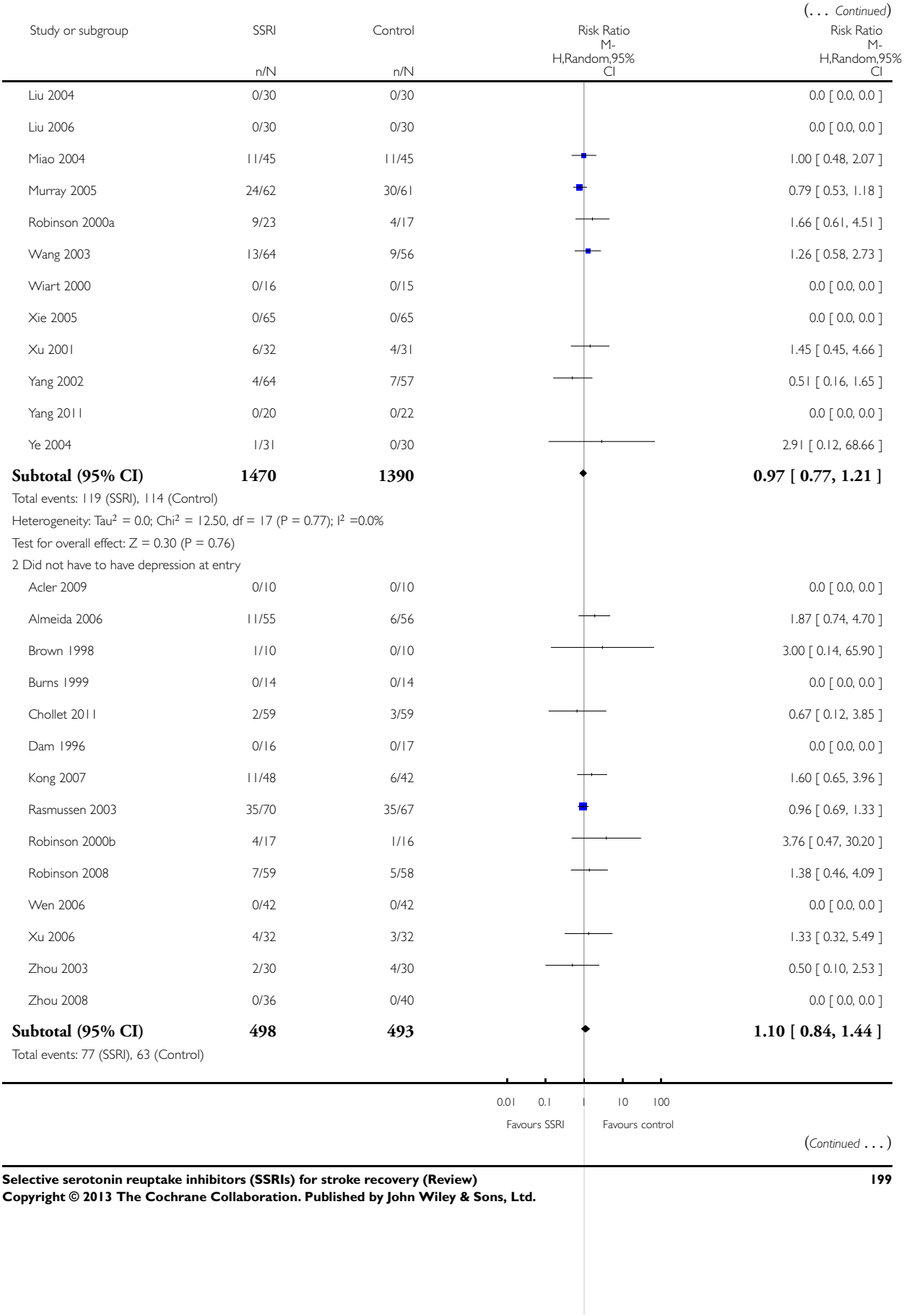

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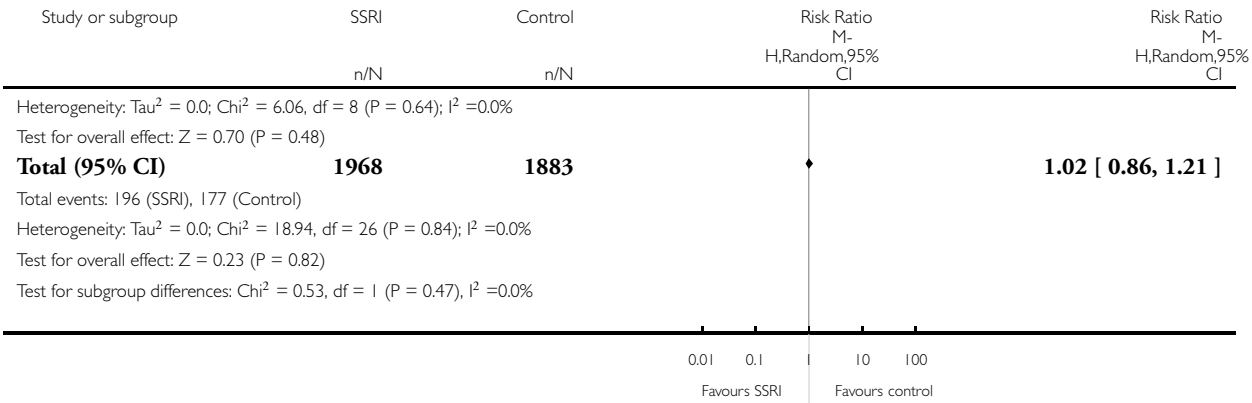
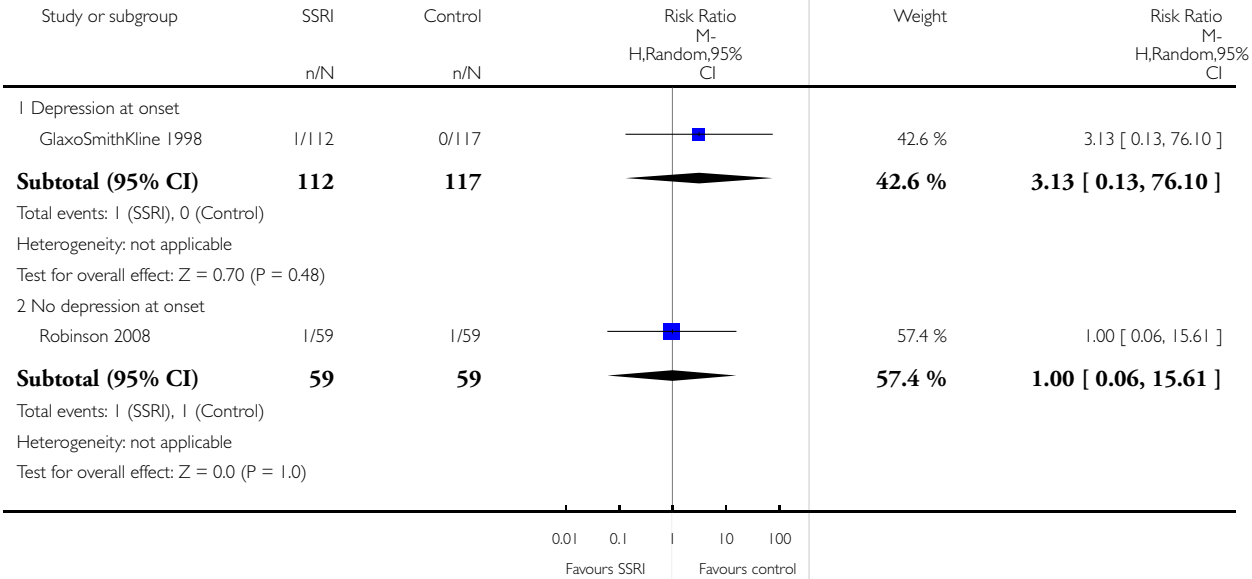


Analysis 4.13. Comparison 4 SSRI versus control according to depression at time of recruitment, Outcome 13 Bleeding.

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 4 SSRI versus control according to depression at time of recruitment

Outcome: 13 Bleeding



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Study or subgroup	SSRI n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Total (95% CI)	**171**	**176**		**100.0 %**	**1.63 [0.20, 13.05]**
Total events: 2 (SSRI), 1 (Control)					
Heterogeneity: Tau^2 = 0.0; Chi^2 = 0.28, df = 1 (P = 0.59); I^2 =0.0%					
Test for overall effect: Z = 0.46 (P = 0.65)					
Test for subgroup differences: Chi^2 = 0.28, df = 1 (P = 0.60), I^2 =0.0%					

Analysis 4.14. Comparison 4 SSRI versus control according to depression at time of recruitment, Outcome 14 Motor deficits.

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 4 SSRI versus control according to depression at time of recruitment

Outcome: 14 Motor deficits

Study or subgroup	SSRI N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
1 No depression at onset							
Chollet 2011	57	-53.7 (27.8)	56	-35.1 (22)		55.3 %	-0.74 [-1.12, -0.35]
Dam 1996	16	32.4 (3.8)	16	31.6 (5)		44.7 %	0.18 [-0.52, 0.87]
Subtotal (95% CI)	**73**		**72**			**100.0 %**	**-0.33 [-1.22, 0.56]**
Heterogeneity: Tau^2 = 0.33; Chi^2 = 5.09, df = 1 (P = 0.02); I^2 =80%							
Test for overall effect: Z = 0.72 (P = 0.47)							
2 Depression at onset							
Subtotal (95% CI)	**0**		**0**			**0.0 %**	**0.0 [0.0, 0.0]**
Heterogeneity: not applicable							
Test for overall effect: not applicable							
Total (95% CI)	**73**		**72**			**100.0 %**	**-0.33 [-1.22, 0.56]**
Heterogeneity: Tau^2 = 0.33; Chi^2 = 5.09, df = 1 (P = 0.02); I^2 =80%							
Test for overall effect: Z = 0.72 (P = 0.47)							
Test for subgroup differences: Not applicable							

Analysis 5.1. Comparison 5 SSRI versus control, end of treatment, randomisation: low risk of bias, Outcome 1 Dependent on modified Rankin score (mRS 3 to 5).

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 5 SSRI versus control, end of treatment, randomisation: low risk of bias

Outcome: 1 Dependent on modified Rankin score (mRS 3 to 5)

Study or subgroup	SSRI n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
1 Fluoxetine				
Chollet 2011	42/57	50/55		0.81 [0.68, 0.97]
Subtotal (95% CI)	**57**	**55**		**0.81 [0.68, 0.97]**
Total events: 42 (SSRI), 50 (Control)				
Heterogeneity: not applicable				
Test for overall effect: Z = 2.34 (P = 0.019)				
2 Sertraline				
Almeida 2006	0/55	0/56		0.0 [0.0, 0.0]
Subtotal (95% CI)	**55**	**56**		**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)				
Heterogeneity: not applicable				
Test for overall effect: Z = 0.0 (P < 0.00001)				
Total (95% CI)	**112**	**111**		**0.81 [0.68, 0.97]**
Total events: 42 (SSRI), 50 (Control)				
Heterogeneity: Tau^2 = 0.0; Chi^2 = 0.0, df = 0 (P = 1.00); I^2 =0.0%				
Test for overall effect: Z = 2.34 (P = 0.019)				
Test for subgroup differences: Not applicable				

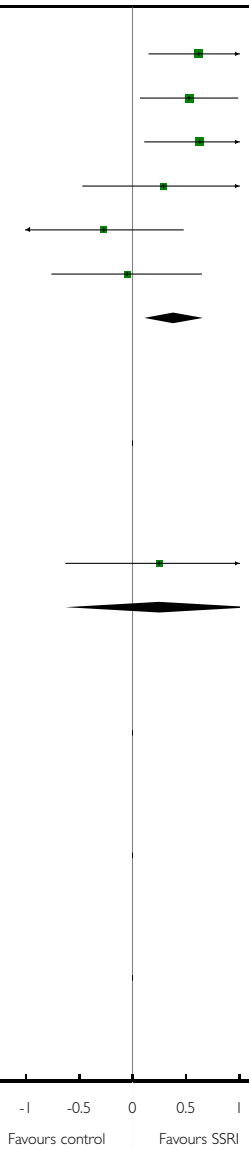
Analysis 5.2. Comparison 5 SSRI versus control, end of treatment, randomisation: low risk of bias, Outcome 2 Disability.

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 5 SSRI versus control, end of treatment, randomisation: low risk of bias

Outcome: 2 Disability

Study or subgroup	SSRI N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
1 Fluoxetine							
Kong 2007	37	60.4 (12.5)	36	52.3 (13.5)		21.9 %	0.62 [0.15, 1.09]
Li 2008	58	40.8 (3.7)	28	38.4 (5.8)		22.8 %	0.53 [0.07, 0.99]
Liu 2004	30	70.33 (10.74)	30	64.33 (7.74)		18.5 %	0.63 [0.11, 1.15]
Robinson 2000a	14	59.2 (11.6)	13	56.2 (7.8)		9.3 %	0.29 [-0.47, 1.05]
Robinson 2000b	13	60.5 (10.8)	15	63.1 (8.2)		9.7 %	-0.27 [-1.01, 0.48]
Wiart 2000	16	87.4 (22.8)	15	88.7 (25.3)		10.7 %	-0.05 [-0.76, 0.65]
Subtotal (95% CI)	**168**		**137**			**92.9 %**	**0.38 [0.11, 0.66]**
Heterogeneity: Tau² = 0.03; Chi² = 6.61, df = 5 (P = 0.25); I² =24%							
Test for overall effect: Z = 2.76 (P = 0.0059)							
2 Sertraline							
Subtotal (95% CI)	**0**		**0**			**0.0 %**	**0.0 [0.0, 0.0]**
Heterogeneity: not applicable							
Test for overall effect: not applicable							
3 Citalopram							
Acler 2009	10	82 (28)	10	75 (25)		7.1 %	0.25 [-0.63, 1.13]
Subtotal (95% CI)	**10**		**10**			**7.1 %**	**0.25 [-0.63, 1.13]**
Heterogeneity: not applicable							
Test for overall effect: Z = 0.56 (P = 0.57)							
4 Paroxetine							
Subtotal (95% CI)	**0**		**0**			**0.0 %**	**0.0 [0.0, 0.0]**
Heterogeneity: not applicable							
Test for overall effect: not applicable							
5 Escitalopram							
Subtotal (95% CI)	**0**		**0**			**0.0 %**	**0.0 [0.0, 0.0]**
Heterogeneity: not applicable							
Test for overall effect: not applicable							
6 Sertraline or fluoxetine							
Subtotal (95% CI)	**0**		**0**			**0.0 %**	**0.0 [0.0, 0.0]**
Heterogeneity: not applicable							
Test for overall effect: not applicable							



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Study or subgroup	SSRI N	SSRI Mean(SD)	Control N	Control Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
Total (95% CI)	**178**		**147**			**100.0 %**	**0.39 [0.15, 0.63]**
Heterogeneity: Tau^2 = 0.01; Chi^2 = 6.72, df = 6 (P = 0.35); I^2 =11%							
Test for overall effect: Z = 3.15 (P = 0.0017)							
Test for subgroup differences: Chi^2 = 0.08, df = 1 (P = 0.78), I^2 =0.0%							

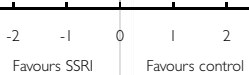
Analysis 5.3. Comparison 5 SSRI versus control, end of treatment, randomisation: low risk of bias, Outcome 3 Neurological deficit score.

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 5 SSRI versus control, end of treatment, randomisation: low risk of bias

Outcome: 3 Neurological deficit score

Study or subgroup	SSRI N	SSRI Mean(SD)	Control N	Control Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
1 Fluoxetine							
Chollet 2011	57	5.8 (3.7)	55	6.9 (4.4)		11.3 %	-0.27 [-0.64, 0.10]
Fruehwald 2003	26	-55.5 (4.8)	24	-52.8 (5.4)		10.0 %	-0.52 [-1.09, 0.04]
Kong 2007	37	8.6 (6.4)	36	11.2 (6.4)		10.7 %	-0.40 [-0.87, 0.06]
Li 2004a	33	6.23 (3.11)	34	12.86 (6.36)		10.3 %	-1.30 [-1.83, -0.77]
Liu 2004	30	9.2 (2.06)	30	10.47 (9.2)		10.4 %	-0.19 [-0.70, 0.32]
Subtotal (95% CI)	**183**		**179**			**52.7 %**	**-0.52 [-0.89, -0.15]**
Heterogeneity: Tau^2 = 0.12; Chi^2 = 11.89, df = 4 (P = 0.02); I^2 =66%							
Test for overall effect: Z = 2.75 (P = 0.0060)							
2 Sertraline							
Burns 1999	14	-29.7 (14.7)	14	-32.2 (13.4)		8.7 %	0.17 [-0.57, 0.91]
Guo 2009	40	29.07 (8.02)	40	33.78 (8.63)		10.8 %	-0.56 [-1.01, -0.11]



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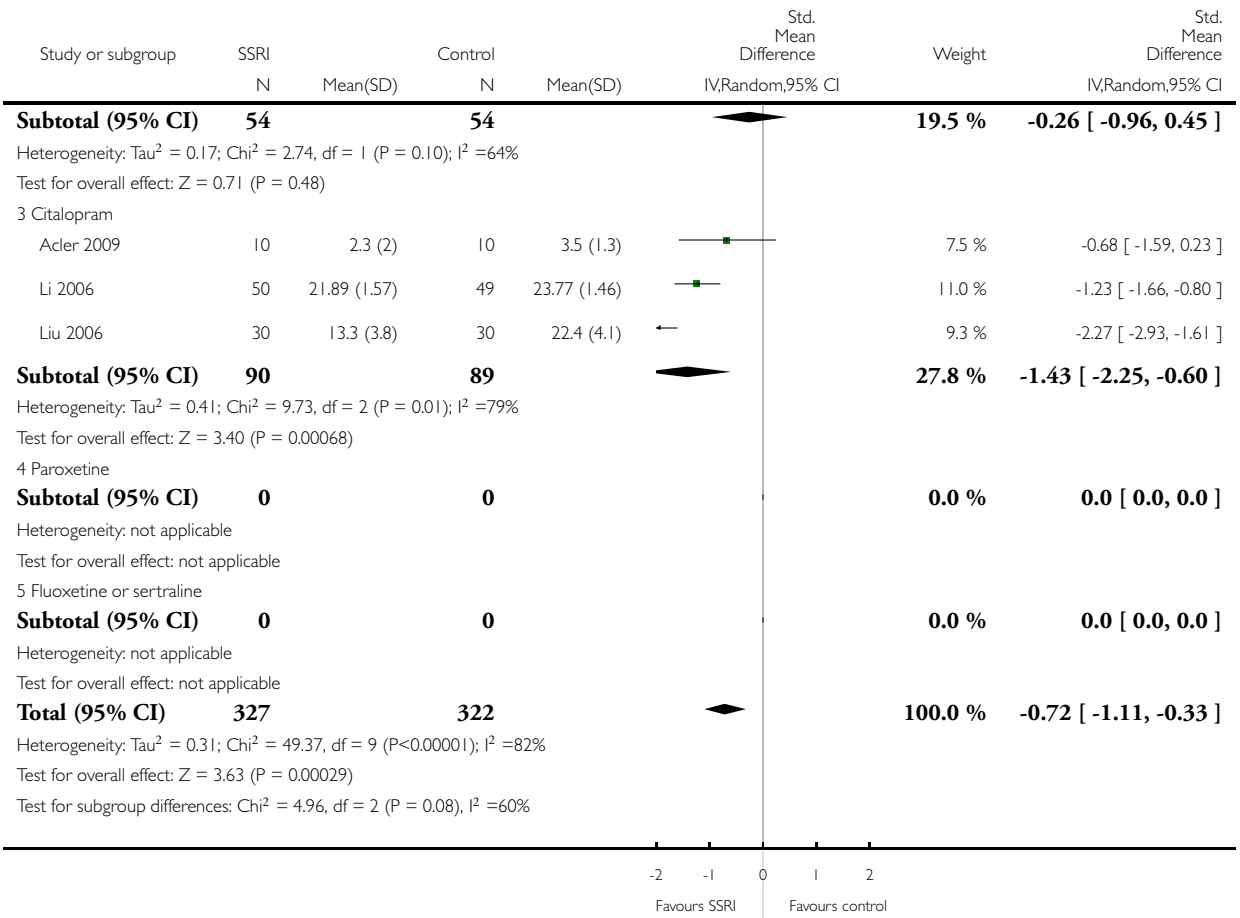
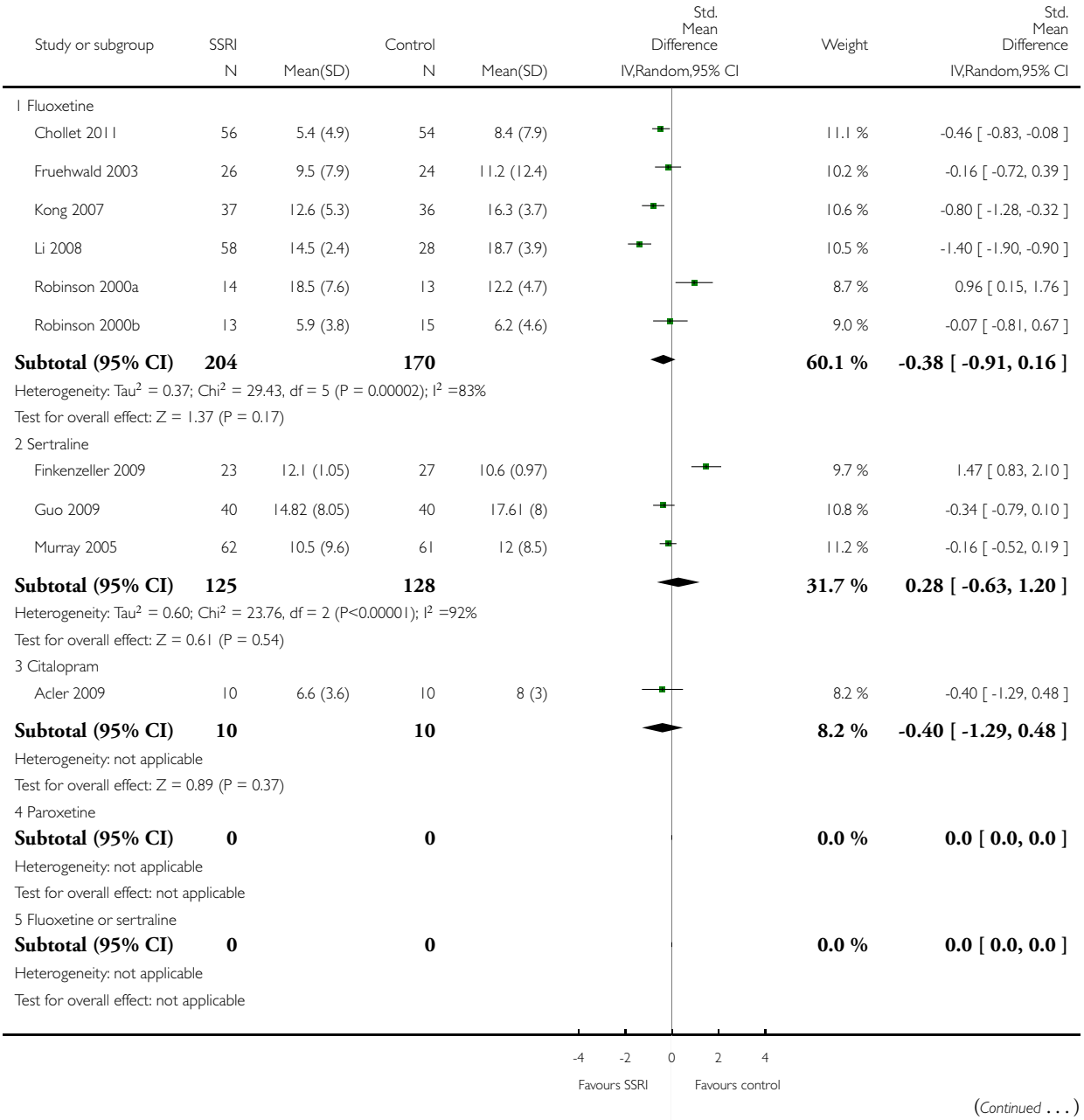


Analysis 5.4. Comparison 5 SSRI versus control, end of treatment, randomisation: low risk of bias, Outcome 4 Depression (continuous data).

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 5 SSRI versus control, end of treatment, randomisation: low risk of bias

Outcome: 4 Depression (continuous data)



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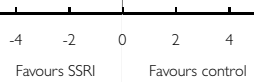
Study or subgroup	SSRI N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
Total (95% CI)	**339**		**308**			**100.0 %**	**-0.17 [-0.61, 0.28]**
Heterogeneity: Tau^2 = 0.43; Chi^2 = 64.26, df = 9 (P<0.00001); I^2 =86%							
Test for overall effect: Z = 0.74 (P = 0.46)							
Test for subgroup differences: Chi^2 = 1.63, df = 2 (P = 0.44), I^2 =0.0%							



Analysis 5.5. Comparison 5 SSRI versus control, end of treatment, randomisation: low risk of bias, Outcome 5 Depression (dichotomous data).

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 5 SSRI versus control, end of treatment, randomisation: low risk of bias

Outcome: 5 Depression (dichotomous data)

Study or subgroup	SSRI n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
1 Fluoxetine					
Li 2004a	2/33	8/34		16.4 %	0.26 [0.06, 1.12]
Subtotal (95% CI)	**33**	**34**		**16.4 %**	**0.26 [0.06, 1.12]**
Total events: 2 (SSRI), 8 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.80 (P = 0.071)					
2 Sertraline					
Almeida 2006	8/48	11/51		47.7 %	0.77 [0.34, 1.76]
Subtotal (95% CI)	**48**	**51**		**47.7 %**	**0.77 [0.34, 1.76]**
Total events: 8 (SSRI), 11 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.62 (P = 0.54)					
3 Citalopram					
Subtotal (95% CI)	**0**	**0**		**0.0 %**	**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)					

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Study or subgroup	SSRI n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Heterogeneity: not applicable					
Test for overall effect: not applicable					
4 Paroxetine					
Subtotal (95% CI)	**0**	**0**		**0.0 %**	**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)					
Heterogeneity: not applicable					
Test for overall effect: not applicable					
5 Escitalopram					
Robinson 2008	5/59	13/58		35.9 %	0.38 [0.14, 0.99]
Subtotal (95% CI)	**59**	**58**		**35.9 %**	**0.38 [0.14, 0.99]**
Total events: 5 (SSRI), 13 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.97 (P = 0.048)					
Total (95% CI)	**140**	**143**		**100.0 %**	**0.50 [0.27, 0.92]**
Total events: 15 (SSRI), 32 (Control)					
Heterogeneity: Tau^2 = 0.03; Chi^2 = 2.21, df = 2 (P = 0.33); I^2 =9%					
Test for overall effect: Z = 2.22 (P = 0.026)					
Test for subgroup differences: Chi^2 = 2.18, df = 2 (P = 0.34), I^2 =8%					

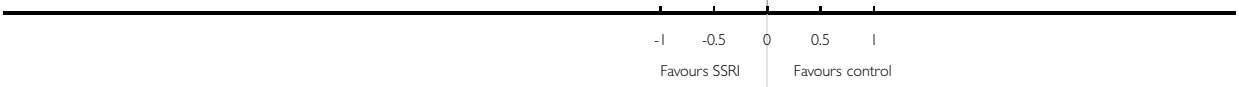
Analysis 5.6. Comparison 5 SSRI versus control, end of treatment, randomisation: low risk of bias, Outcome 6 Anxiety (continuous data).

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 5 SSRI versus control, end of treatment, randomisation: low risk of bias

Outcome: 6 Anxiety (continuous data)

Study or subgroup	SSRI N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
1 Fluoxetine							
Liu 2004	30	7.43 (3.63)	30	11 (5.63)		45.1 %	-0.74 [-1.27, -0.22]
Robinson 2000a	14	9.8 (4.8)	13	9.9 (5.1)		27.2 %	-0.02 [-0.77, 0.74]
Robinson 2000b	13	4.7 (3.8)	15	5.5 (2.9)		27.7 %	-0.23 [-0.98, 0.51]
Subtotal (95% CI)	**57**		**58**			**100.0 %**	**-0.40 [-0.85, 0.05]**
Heterogeneity: $Tau^2 = 0.05$; $Chi^2 = 2.78$, df = 2 (P = 0.25); $I^2 = 28\%$							
Test for overall effect: Z = 1.76 (P = 0.078)							
2 Sertraline							
Subtotal (95% CI)	**0**		**0**			**0.0 %**	**0.0 [0.0, 0.0]**
Heterogeneity: not applicable							
Test for overall effect: not applicable							
3 Citalopram							
Subtotal (95% CI)	**0**		**0**			**0.0 %**	**0.0 [0.0, 0.0]**
Heterogeneity: not applicable							
Test for overall effect: not applicable							
4 Paroxetine							
Subtotal (95% CI)	**0**		**0**			**0.0 %**	**0.0 [0.0, 0.0]**
Heterogeneity: not applicable							
Test for overall effect: not applicable							
5 Escitalopram							
Subtotal (95% CI)	**0**		**0**			**0.0 %**	**0.0 [0.0, 0.0]**
Heterogeneity: not applicable							
Test for overall effect: not applicable							
Total (95% CI)	**57**		**58**			**100.0 %**	**-0.40 [-0.85, 0.05]**
Heterogeneity: $Tau^2 = 0.05$; $Chi^2 = 2.78$, df = 2 (P = 0.25); $I^2 = 28\%$							
Test for overall effect: Z = 1.76 (P = 0.078)							
Test for subgroup differences: Not applicable							



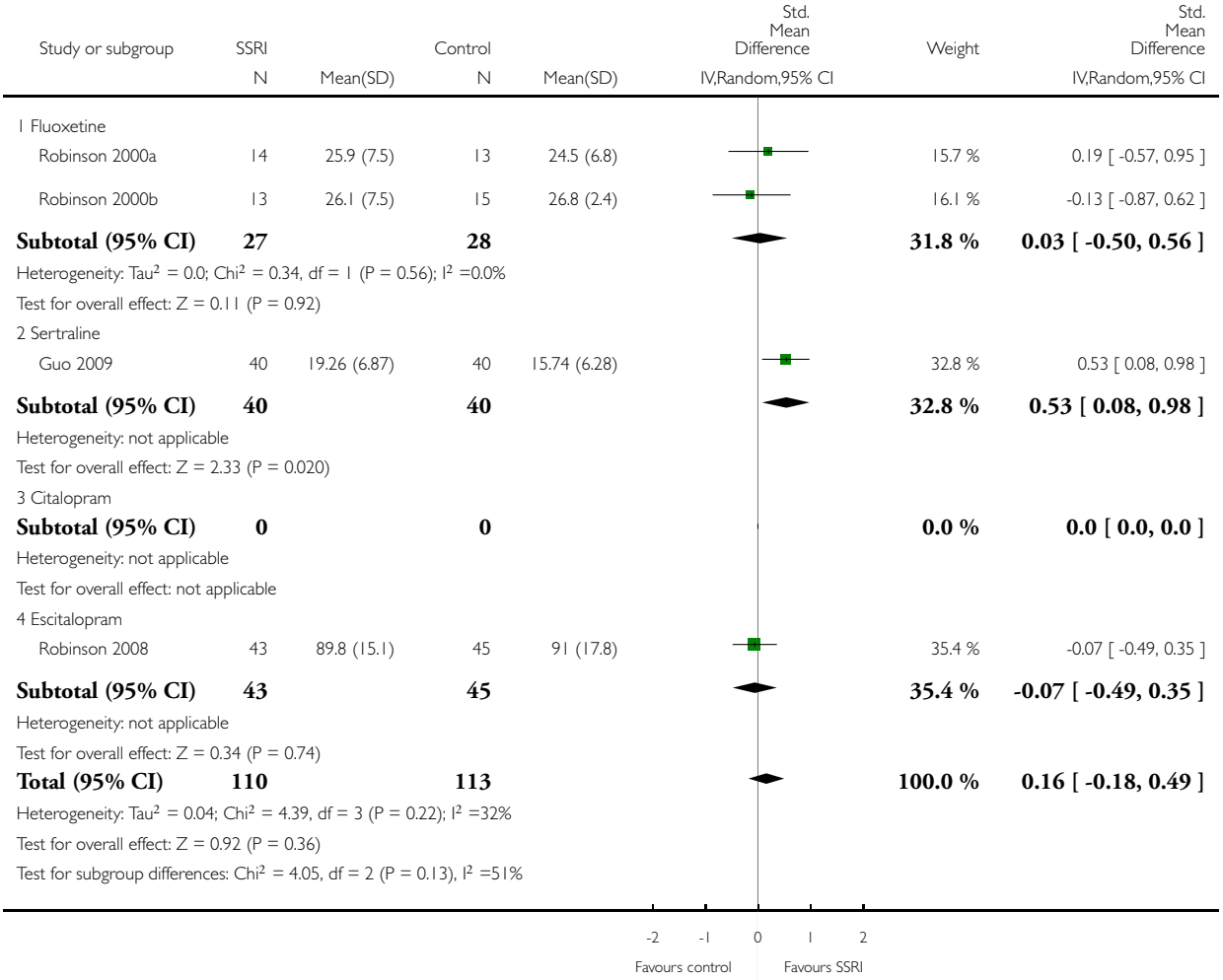
Analysis 5.8. Comparison 5 SSRI versus control, end of treatment, randomisation: low risk of bias, Outcome 8 Cognition (continuous scores end of treatment).

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 5 SSRI versus control, end of treatment, randomisation: low risk of bias

Outcome: 8 Cognition (continuous scores end of treatment)

Study or subgroup	SSRI N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
1 Fluoxetine							
Robinson 2000a	14	25.9 (7.5)	13	24.5 (6.8)		15.7 %	0.19 [-0.57, 0.95]
Robinson 2000b	13	26.1 (7.5)	15	26.8 (2.4)		16.1 %	-0.13 [-0.87, 0.62]
Subtotal (95% CI)	**27**		**28**			**31.8 %**	**0.03 [-0.50, 0.56]**
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.34$, df = 1 (P = 0.56); $I^2 = 0.0\%$							
Test for overall effect: Z = 0.11 (P = 0.92)							
2 Sertraline							
Guo 2009	40	19.26 (6.87)	40	15.74 (6.28)		32.8 %	0.53 [0.08, 0.98]
Subtotal (95% CI)	**40**		**40**			**32.8 %**	**0.53 [0.08, 0.98]**
Heterogeneity: not applicable							
Test for overall effect: Z = 2.33 (P = 0.020)							
3 Citalopram							
Subtotal (95% CI)	**0**		**0**			**0.0 %**	**0.0 [0.0, 0.0]**
Heterogeneity: not applicable							
Test for overall effect: not applicable							
4 Escitalopram							
Robinson 2008	43	89.8 (15.1)	45	91 (17.8)		35.4 %	-0.07 [-0.49, 0.35]
Subtotal (95% CI)	**43**		**45**			**35.4 %**	**-0.07 [-0.49, 0.35]**
Heterogeneity: not applicable							
Test for overall effect: Z = 0.34 (P = 0.74)							
Total (95% CI)	**110**		**113**			**100.0 %**	**0.16 [-0.18, 0.49]**
Heterogeneity: $Tau^2 = 0.04$; $Chi^2 = 4.39$, df = 3 (P = 0.22); $I^2 = 32\%$							
Test for overall effect: Z = 0.92 (P = 0.36)							
Test for subgroup differences: $Chi^2 = 4.05$, df = 2 (P = 0.13), $I^2 = 51\%$							

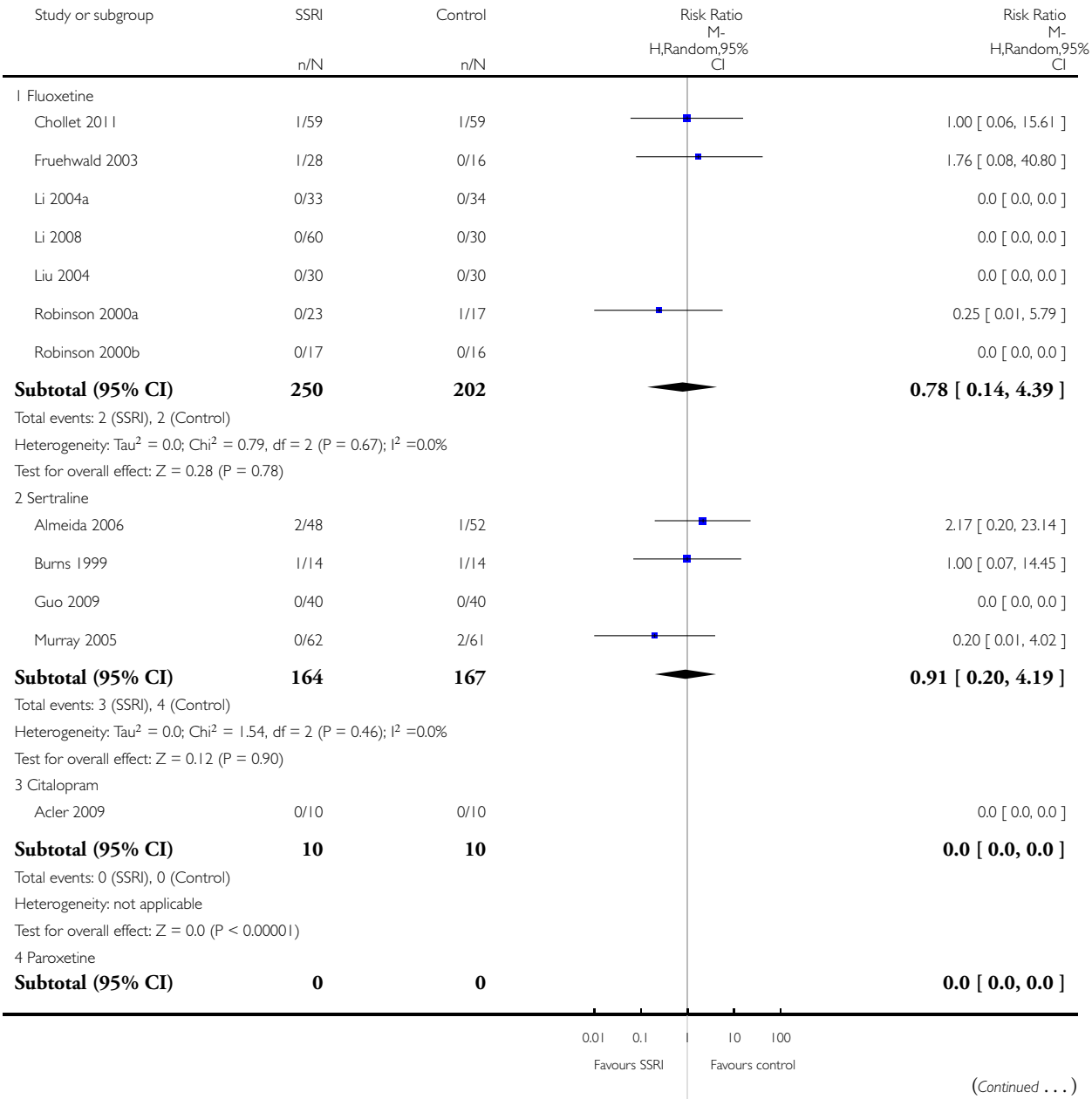


Analysis 5.9. Comparison 5 SSRI versus control, end of treatment, randomisation: low risk of bias, Outcome 9 Death.

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 5 SSRI versus control, end of treatment, randomisation: low risk of bias

Outcome: 9 Death



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Study or subgroup	SSRI n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
Total events: 0 (SSRI), 0 (Control)				
Heterogeneity: not applicable				
Test for overall effect: not applicable				
5 Escitalopram				
Robinson 2008	2/59	0/58		4.92 [0.24, 100.25]
Subtotal (95% CI)	**59**	**58**		**4.92 [0.24, 100.25]**
Total events: 2 (SSRI), 0 (Control)				
Heterogeneity: not applicable				
Test for overall effect: Z = 1.04 (P = 0.30)				
6 Sertraline or fluoxetine				
Subtotal (95% CI)	**0**	**0**		**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)				
Heterogeneity: not applicable				
Test for overall effect: not applicable				
Total (95% CI)	**483**	**437**		**1.06 [0.36, 3.09]**
Total events: 7 (SSRI), 6 (Control)				
Heterogeneity: Tau^2 = 0.0; Chi^2 = 3.46, df = 6 (P = 0.75); I^2 =0.0%				
Test for overall effect: Z = 0.11 (P = 0.91)				
Test for subgroup differences: Chi^2 = 1.16, df = 2 (P = 0.56), I^2 =0.0%				

Analysis 5.10. Comparison 5 SSRI versus control, end of treatment, randomisation: low risk of bias, Outcome 10 Seizures.

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 5 SSRI versus control, end of treatment, randomisation: low risk of bias

Outcome: 10 Seizures

Study or subgroup	SSRI n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
1 Fluoxetine					
Chollet 2011	1/59	0/59		100.0 %	3.00 [0.12, 72.18]
Subtotal (95% CI)	**59**	**59**		**100.0 %**	**3.00 [0.12, 72.18]**
Total events: 1 (SSRI), 0 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.68 (P = 0.50)					
2 Sertraline					
Subtotal (95% CI)	**0**	**0**		**0.0 %**	**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)					
Heterogeneity: not applicable					
Test for overall effect: not applicable					
3 Citalopram					
Subtotal (95% CI)	**0**	**0**		**0.0 %**	**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)					
Heterogeneity: not applicable					
Test for overall effect: not applicable					
4 Paroxetine					
Subtotal (95% CI)	**0**	**0**		**0.0 %**	**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)					
Heterogeneity: not applicable					
Test for overall effect: not applicable					
5 Escitalopram					
Subtotal (95% CI)	**0**	**0**		**0.0 %**	**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)					
Heterogeneity: not applicable					
Test for overall effect: not applicable					
6 Sertraline or fluoxetine					
Subtotal (95% CI)	**0**	**0**		**0.0 %**	**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)					
Heterogeneity: not applicable					
Test for overall effect: not applicable					
Total (95% CI)	**59**	**59**		**100.0 %**	**3.00 [0.12, 72.18]**
Total events: 1 (SSRI), 0 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.68 (P = 0.50)					
Test for subgroup differences: Not applicable					

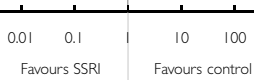
Analysis 5.11. Comparison 5 SSRI versus control, end of treatment, randomisation: low risk of bias, Outcome 11 Gastrointestinal side effects.

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 5 SSRI versus control, end of treatment, randomisation: low risk of bias

Outcome: 11 Gastrointestinal side effects

Study or subgroup	SSRI n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
1 Fluoxetine					
Chollet 2011	14/59	6/59		58.2 %	2.33 [0.96, 5.66]
Li 2004a	3/33	0/34		5.3 %	7.21 [0.39, 134.32]
Li 2008	6/60	3/30		26.4 %	1.00 [0.27, 3.72]
Liu 2004	3/30	0/30		5.4 %	7.00 [0.38, 129.93]
Subtotal (95% CI)	**182**	**153**		**95.3 %**	**2.09 [1.05, 4.18]**
Total events: 26 (SSRI), 9 (Control)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 2.67$, df = 3 (P = 0.44); $I^2 = 0.0\%$					
Test for overall effect: Z = 2.09 (P = 0.037)					
2 Sertraline					
Burns 1999	0/14	1/14		4.7 %	0.33 [0.01, 7.55]
Subtotal (95% CI)	**14**	**14**		**4.7 %**	**0.33 [0.01, 7.55]**
Total events: 0 (SSRI), 1 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.69 (P = 0.49)					
3 Citalopram					
Subtotal (95% CI)	**0**	**0**		**0.0 %**	**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)					
Heterogeneity: not applicable					
Test for overall effect: not applicable					
4 Paroxetine					
Subtotal (95% CI)	**0**	**0**		**0.0 %**	**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)					
Heterogeneity: not applicable					
Test for overall effect: not applicable					
5 Escitalopram					
Subtotal (95% CI)	**0**	**0**		**0.0 %**	**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)					
Heterogeneity: not applicable					
Test for overall effect: not applicable					



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Study or subgroup	SSRI n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
6 Sertraline and paroxetine					
Subtotal (95% CI)	**0**	**0**		**0.0 %**	**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)					
Heterogeneity: not applicable					
Test for overall effect: not applicable					
Total (95% CI)	**196**	**167**		**100.0 %**	**1.92 [0.98, 3.77]**
Total events: 26 (SSRI), 10 (Control)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 3.92$, df = 4 (P = 0.42); $I^2 = 0.0\%$					
Test for overall effect: Z = 1.89 (P = 0.059)					
Test for subgroup differences: $Chi^2 = 1.27$, df = 1 (P = 0.26), $I^2 = 21\%$					

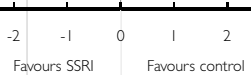
Analysis 5.14. Comparison 5 SSRI versus control, end of treatment, randomisation: low risk of bias, Outcome 14 Change in cognition between baseline and end of treatment.

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 5 SSRI versus control, end of treatment, randomisation: low risk of bias

Outcome: 14 Change in cognition between baseline and end of treatment

Study or subgroup	SSRI N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
1 Sertraline							
Almeida 2006	48	2.6 (3.04)	51	2.6 (3.9)		100.0 %	0.0 [-0.39, 0.39]
Total (95% CI)	**48**		**51**			**100.0 %**	**0.0 [-0.39, 0.39]**
Heterogeneity: not applicable							
Test for overall effect: Z = 0.0 (P = 1.0)							
Test for subgroup differences: Not applicable							

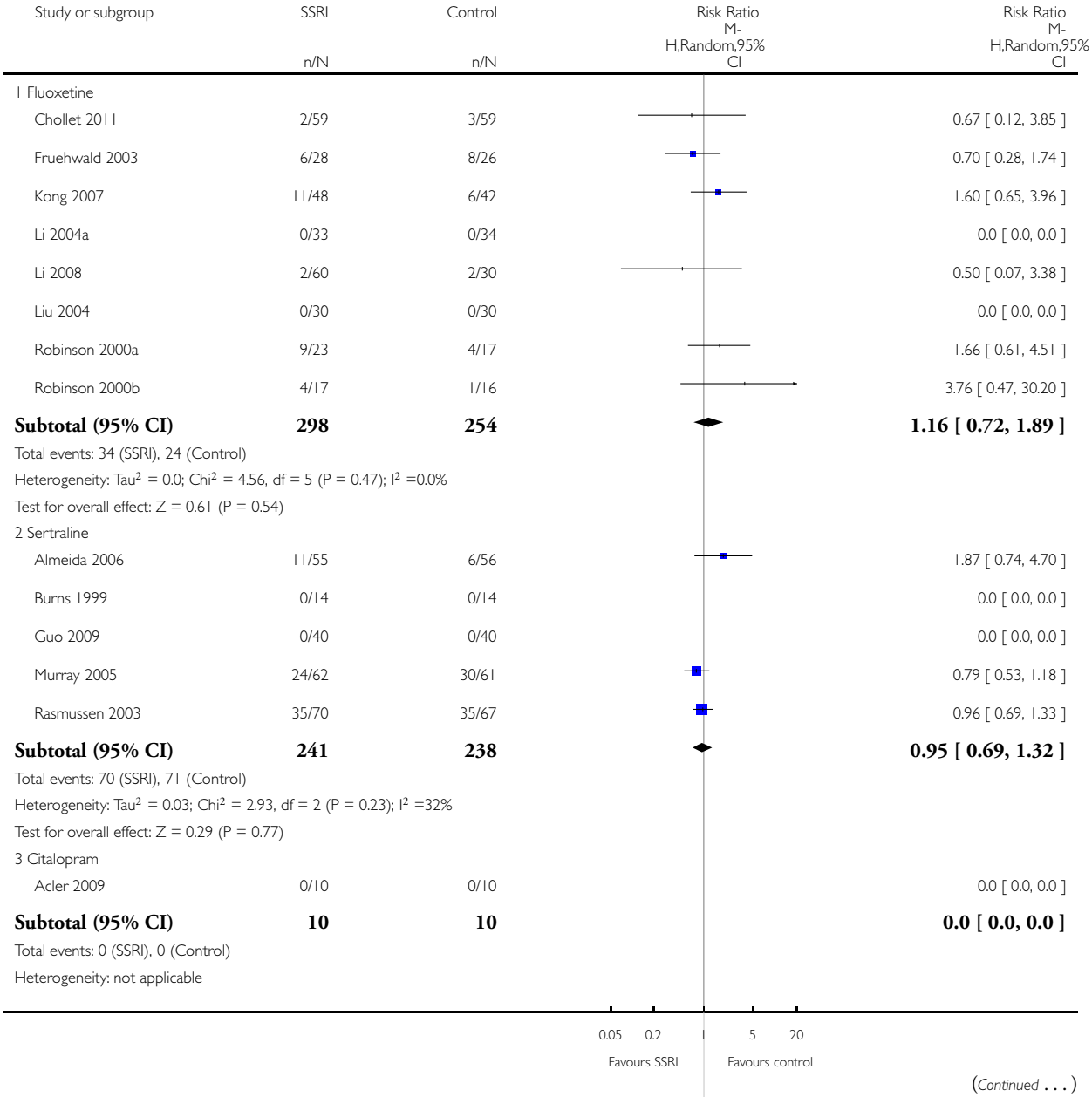


Analysis 5.15. Comparison 5 SSRI versus control, end of treatment, randomisation: low risk of bias, Outcome 15 Leaving the trial before the end of scheduled follow-up.

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 5 SSRI versus control, end of treatment, randomisation: low risk of bias

Outcome: 15 Leaving the trial before the end of scheduled follow-up



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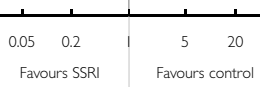
Study or subgroup	SSRI n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
Test for overall effect: Z = 0.0 (P < 0.00001)				
4 Paroxetine				
Subtotal (95% CI)	**0**	**0**		**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)				
Heterogeneity: not applicable				
Test for overall effect: not applicable				
5 Sertraline or fluoxetine				
Subtotal (95% CI)	**0**	**0**		**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)				
Heterogeneity: not applicable				
Test for overall effect: not applicable				
6 Escitalopram				
Robinson 2008	7/59	5/58		1.38 [0.46, 4.09]
Subtotal (95% CI)	**59**	**58**		**1.38 [0.46, 4.09]**
Total events: 7 (SSRI), 5 (Control)				
Heterogeneity: not applicable				
Test for overall effect: Z = 0.57 (P = 0.57)				
Total (95% CI)	**608**	**560**		**0.99 [0.80, 1.23]**
Total events: 111 (SSRI), 100 (Control)				
Heterogeneity: Tau^2 = 0.0; Chi^2 = 8.61, df = 9 (P = 0.47); I^2 =0.0%				
Test for overall effect: Z = 0.10 (P = 0.92)				
Test for subgroup differences: Chi^2 = 0.73, df = 2 (P = 0.69), I^2 =0.0%				



Analysis 5.16. Comparison 5 SSRI versus control, end of treatment, randomisation: low risk of bias, Outcome 16 Bleeding.

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 5 SSRI versus control, end of treatment, randomisation: low risk of bias

Outcome: 16 Bleeding

Study or subgroup	SSRI n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Robinson 2008	1/59	1/59		100.0 %	1.00 [0.06, 15.61]
Total (95% CI)	**59**	**59**		**100.0 %**	**1.00 [0.06, 15.61]**
Total events: 1 (SSRI), 1 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.0 (P = 1.0)					
Test for subgroup differences: Not applicable					

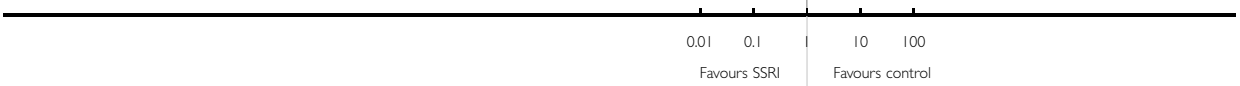
Analysis 6.1. Comparison 6 SSRI versus control at end of treatment, concealment of allocation: low risk, Outcome 1 Dependent on modified Rankin score (mRS 3 to 5).

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 6 SSRI versus control at end of treatment, concealment of allocation: low risk

Outcome: 1 Dependent on modified Rankin score (mRS 3 to 5)

Study or subgroup	SSRI n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
1 Fluoxetine				
Chollet 2011	42/57	50/55		0.81 [0.68, 0.97]
Subtotal (95% CI)	**57**	**55**		**0.81 [0.68, 0.97]**
Total events: 42 (SSRI), 50 (Control)				
Heterogeneity: not applicable				
Test for overall effect: Z = 2.34 (P = 0.019)				
2 Sertraline				
Almeida 2006	0/55	0/56		0.0 [0.0, 0.0]
Subtotal (95% CI)	**55**	**56**		**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)				
Heterogeneity: not applicable				
Test for overall effect: Z = 0.0 (P < 0.00001)				
Total (95% CI)	**112**	**111**		**0.81 [0.68, 0.97]**
Total events: 42 (SSRI), 50 (Control)				
Heterogeneity: Tau^2 = 0.0; Chi^2 = 0.0, df = 0 (P = 1.00); I^2 =0.0%				
Test for overall effect: Z = 2.34 (P = 0.019)				
Test for subgroup differences: Not applicable				



Analysis 6.2. Comparison 6 SSRI versus control at end of treatment, concealment of allocation: low risk, Outcome 2 Disability.

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 6 SSRI versus control at end of treatment, concealment of allocation: low risk

Outcome: 2 Disability

Study or subgroup	SSRI N	SSRI Mean(SD)	Control N	Control Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
1 Fluoxetine							
Robinson 2000a	14	59.2 (11.6)	13	56.2 (7.8)		33.0 %	0.29 [-0.47, 1.05]
Robinson 2000b	13	60.5 (10.8)	15	63.1 (8.2)		33.1 %	-0.27 [-1.01, 0.48]
Subtotal (95% CI)	**27**		**28**			**66.0 %**	**0.01 [-0.54, 0.56]**
Heterogeneity: $Tau^2 = 0.01$; $Chi^2 = 1.06$, df = 1 (P = 0.30); $I^2 = 5\%$							
Test for overall effect: Z = 0.03 (P = 0.98)							
2 Sertraline							
Subtotal (95% CI)	**0**		**0**			**0.0 %**	**0.0 [0.0, 0.0]**
Heterogeneity: not applicable							
Test for overall effect: not applicable							
3 Citalopram							
Subtotal (95% CI)	**0**		**0**			**0.0 %**	**0.0 [0.0, 0.0]**
Heterogeneity: not applicable							
Test for overall effect: not applicable							
4 Paroxetine							
Ye 2004	30	78.75 (14.19)	30	50.26 (13.4)		34.0 %	2.04 [1.41, 2.67]
Subtotal (95% CI)	**30**		**30**			**34.0 %**	**2.04 [1.41, 2.67]**
Heterogeneity: not applicable							
Test for overall effect: Z = 6.33 (P < 0.00001)							
5 Escitalopram							
Subtotal (95% CI)	**0**		**0**			**0.0 %**	**0.0 [0.0, 0.0]**
Heterogeneity: not applicable							
Test for overall effect: not applicable							
6 Sertraline or fluoxetine							
Subtotal (95% CI)	**0**		**0**			**0.0 %**	**0.0 [0.0, 0.0]**
Heterogeneity: not applicable							
Test for overall effect: not applicable							
Total (95% CI)	**57**		**58**			**100.0 %**	**0.70 [-0.73, 2.13]**
Heterogeneity: $Tau^2 = 1.46$; $Chi^2 = 24.26$, df = 2 (P<0.00001); $I^2 = 92\%$							
Test for overall effect: Z = 0.96 (P = 0.34)							
Test for subgroup differences: $Chi^2 = 22.68$, df = 1 (P = 0.00), $I^2 = 96\%$							

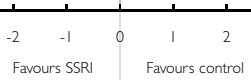
Analysis 6.3. Comparison 6 SSRI versus control at end of treatment, concealment of allocation: low risk, Outcome 3 Neurological deficit score.

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 6 SSRI versus control at end of treatment, concealment of allocation: low risk

Outcome: 3 Neurological deficit score

Study or subgroup	SSRI N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
1 Fluoxetine							
Chollet 2011	57	5.8 (3.7)	55	6.9 (4.4)		26.9 %	-0.27 [-0.64, 0.10]
Fruehwald 2003	26	-55.5 (4.8)	24	-52.8 (5.4)		24.4 %	-0.52 [-1.09, 0.04]
Li 2004a	33	6.23 (3.11)	34	12.86 (6.36)		24.9 %	-1.30 [-1.83, -0.77]
Subtotal (95% CI)	**116**		**113**			**76.1 %**	**-0.68 [-1.30, -0.06]**
Heterogeneity: $Tau^2 = 0.24$; $Chi^2 = 9.86$, df = 2 (P = 0.01); $I^2 = 80\%$							
Test for overall effect: Z = 2.15 (P = 0.032)							
2 Sertraline							
Subtotal (95% CI)	**0**		**0**			**0.0 %**	**0.0 [0.0, 0.0]**
Heterogeneity: not applicable							
Test for overall effect: not applicable							
3 Citalopram							
Subtotal (95% CI)	**0**		**0**			**0.0 %**	**0.0 [0.0, 0.0]**
Heterogeneity: not applicable							
Test for overall effect: not applicable							
4 Paroxetine							
Ye 2004	30	8.3 (3.8)	30	16 (4.8)		23.9 %	-1.76 [-2.36, -1.15]
Subtotal (95% CI)	**30**		**30**			**23.9 %**	**-1.76 [-2.36, -1.15]**
Heterogeneity: not applicable							
Test for overall effect: Z = 5.72 (P < 0.00001)							
5 Fluoxetine or sertraline							
Subtotal (95% CI)	**0**		**0**			**0.0 %**	**0.0 [0.0, 0.0]**
Heterogeneity: not applicable							
Test for overall effect: not applicable							
Total (95% CI)	**146**		**143**			**100.0 %**	**-0.94 [-1.63, -0.26]**
Heterogeneity: $Tau^2 = 0.42$; $Chi^2 = 21.89$, df = 3 (P = 0.00007); $I^2 = 86\%$							
Test for overall effect: Z = 2.69 (P = 0.0071)							
Test for subgroup differences: $Chi^2 = 5.93$, df = 1 (P = 0.01), $I^2 = 83\%$							



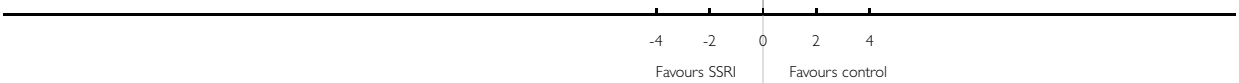
Analysis 6.4. Comparison 6 SSRI versus control at end of treatment, concealment of allocation: low risk, Outcome 4 Depression (continuous data).

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 6 SSRI versus control at end of treatment, concealment of allocation: low risk

Outcome: 4 Depression (continuous data)

Study or subgroup	SSRI N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
1 Fluoxetine							
Chollet 2011	56	5.4 (4.9)	54	8.4 (7.9)		15.3 %	-0.46 [-0.83, -0.08]
Fruehwald 2003	26	9.5 (7.9)	24	11.2 (12.4)		14.7 %	-0.16 [-0.72, 0.39]
Robinson 2000a	14	18.5 (7.6)	13	12.2 (4.7)		13.6 %	0.96 [0.15, 1.76]
Robinson 2000b	13	5.9 (3.8)	15	6.2 (4.6)		13.9 %	-0.07 [-0.81, 0.67]
Subtotal (95% CI)	**109**		**106**			**57.6 %**	**-0.01 [-0.54, 0.53]**
Heterogeneity: $Tau^2 = 0.20$; $Chi^2 = 9.81$, df = 3 (P = 0.02); $I^2 = 69\%$							
Test for overall effect: Z = 0.02 (P = 0.98)							
2 Sertraline							
Murray 2005	62	10.5 (9.6)	61	12 (8.5)		15.4 %	-0.16 [-0.52, 0.19]
Subtotal (95% CI)	**62**		**61**			**15.4 %**	**-0.16 [-0.52, 0.19]**
Heterogeneity: not applicable							
Test for overall effect: Z = 0.91 (P = 0.36)							
3 Citalopram							
Andersen 1994	33	11.4 (5.1)	33	14.1 (4.7)		14.9 %	-0.54 [-1.04, -0.05]
Subtotal (95% CI)	**33**		**33**			**14.9 %**	**-0.54 [-1.04, -0.05]**
Heterogeneity: not applicable							
Test for overall effect: Z = 2.17 (P = 0.030)							
4 Paroxetine							
Ye 2004	30	4.02 (3.07)	30	17.32 (1.66)		12.1 %	-5.32 [-6.43, -4.21]
Subtotal (95% CI)	**30**		**30**			**12.1 %**	**-5.32 [-6.43, -4.21]**
Heterogeneity: not applicable							
Test for overall effect: Z = 9.42 (P < 0.00001)							
5 Fluoxetine or sertraline							
Subtotal (95% CI)	**0**		**0**			**0.0 %**	**0.0 [0.0, 0.0]**
Heterogeneity: not applicable							
Test for overall effect: not applicable							
Total (95% CI)	**234**		**230**			**100.0 %**	**-0.72 [-1.52, 0.07]**
Heterogeneity: $Tau^2 = 1.05$; $Chi^2 = 90.38$, df = 6 (P<0.00001); $I^2 = 93\%$							
Test for overall effect: Z = 1.78 (P = 0.075)							
Test for subgroup differences: $Chi^2 = 79.51$, df = 3 (P = 0.00), $I^2 = 96\%$							

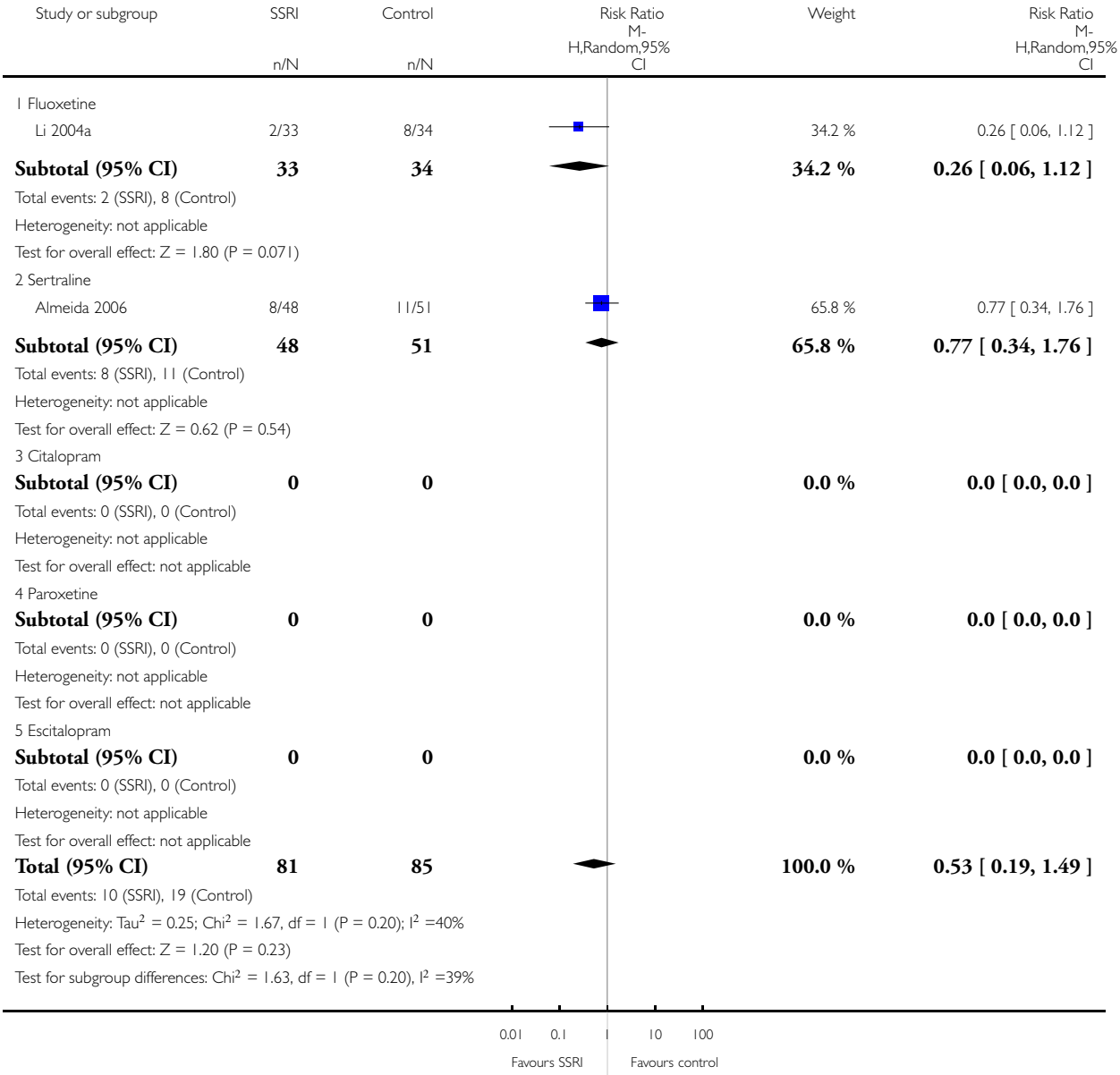


Analysis 6.5. Comparison 6 SSRI versus control at end of treatment, concealment of allocation: low risk, Outcome 5 Depression (dichotomous data).

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 6 SSRI versus control at end of treatment, concealment of allocation: low risk

Outcome: 5 Depression (dichotomous data)



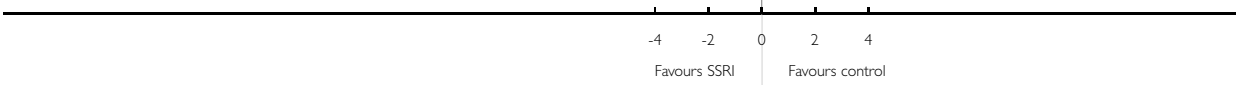
Analysis 6.6. Comparison 6 SSRI versus control at end of treatment, concealment of allocation: low risk, Outcome 6 Anxiety (continuous data).

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 6 SSRI versus control at end of treatment, concealment of allocation: low risk

Outcome: 6 Anxiety (continuous data)

Study or subgroup	SSRI N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
1 Fluoxetine							
Robinson 2000a	14	9.8 (4.8)	13	9.9 (5.1)		32.6 %	-0.02 [-0.77, 0.74]
Robinson 2000b	13	4.7 (3.8)	15	5.5 (2.9)		32.7 %	-0.23 [-0.98, 0.51]
Subtotal (95% CI)	**27**		**28**			**65.3 %**	**-0.13 [-0.66, 0.40]**
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.15$, df = 1 (P = 0.69); $I^2 = 0.0\%$							
Test for overall effect: Z = 0.47 (P = 0.64)							
2 Sertraline							
Subtotal (95% CI)	**0**		**0**			**0.0 %**	**0.0 [0.0, 0.0]**
Heterogeneity: not applicable							
Test for overall effect: not applicable							
3 Citalopram							
Subtotal (95% CI)	**0**		**0**			**0.0 %**	**0.0 [0.0, 0.0]**
Heterogeneity: not applicable							
Test for overall effect: not applicable							
4 Paroxetine							
Ye 2004	30	9.82 (2.64)	30	14.02 (2.32)		34.7 %	-1.67 [-2.26, -1.08]
Subtotal (95% CI)	**30**		**30**			**34.7 %**	**-1.67 [-2.26, -1.08]**
Heterogeneity: not applicable							
Test for overall effect: Z = 5.52 (P < 0.00001)							
5 Escitalopram							
Subtotal (95% CI)	**0**		**0**			**0.0 %**	**0.0 [0.0, 0.0]**
Heterogeneity: not applicable							
Test for overall effect: not applicable							
Total (95% CI)	**57**		**58**			**100.0 %**	**-0.66 [-1.74, 0.42]**
Heterogeneity: $Tau^2 = 0.79$; $Chi^2 = 14.57$, df = 2 (P = 0.00069); $I^2 = 86\%$							
Test for overall effect: Z = 1.20 (P = 0.23)							
Test for subgroup differences: $Chi^2 = 14.41$, df = 1 (P = 0.00), $I^2 = 93\%$							



Analysis 6.8. Comparison 6 SSRI versus control at end of treatment, concealment of allocation: low risk, Outcome 8 Cognition (continuous scores end of treatment).

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 6 SSRI versus control at end of treatment, concealment of allocation: low risk

Outcome: 8 Cognition (continuous scores end of treatment)

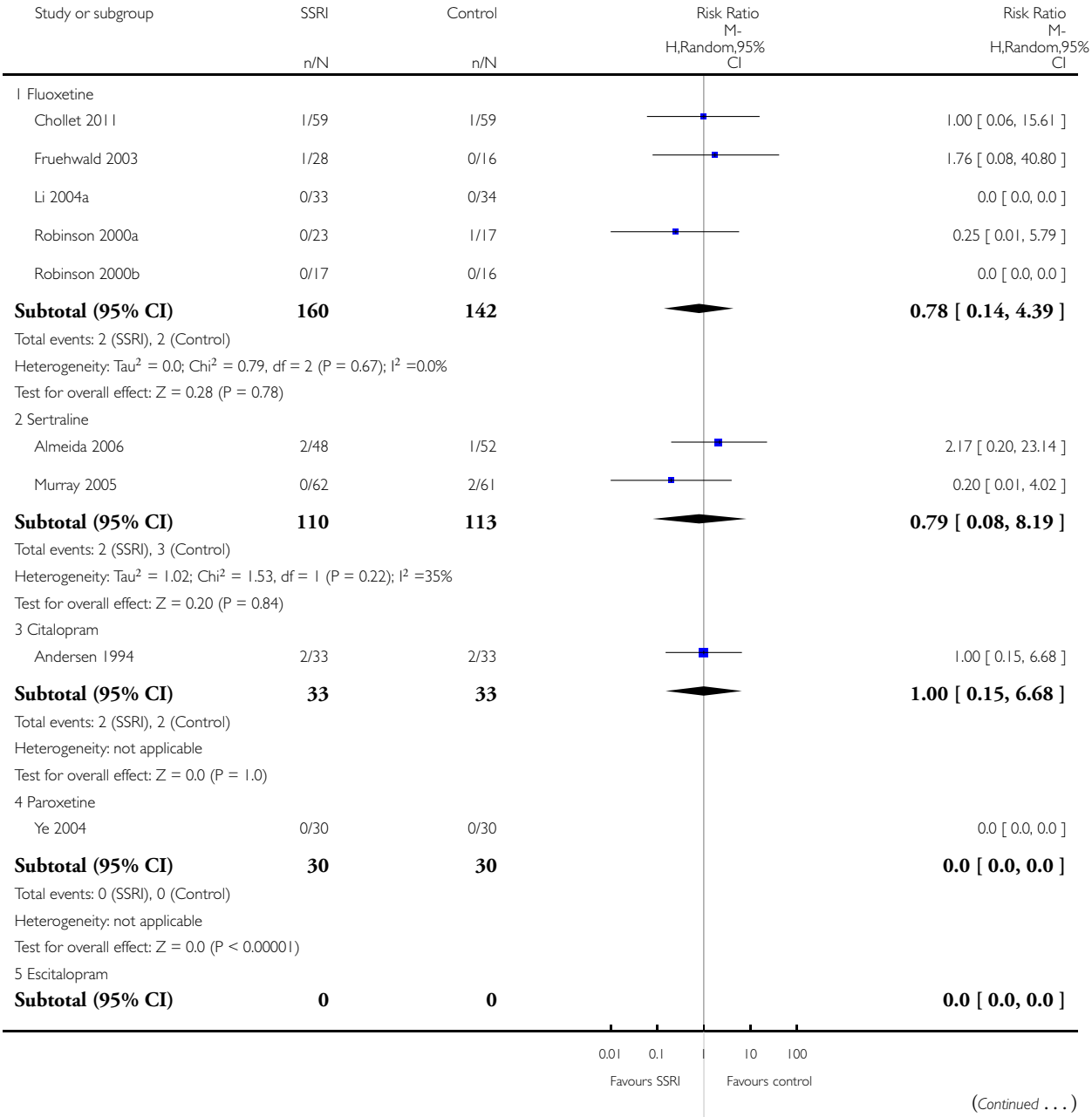
Study or subgroup	SSRI N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
1 Fluoxetine							
Robinson 2000a	14	25.9 (7.5)	13	24.5 (6.8)		49.1 %	0.19 [-0.57, 0.95]
Robinson 2000b	13	26.1 (7.5)	15	26.8 (2.4)		50.9 %	-0.13 [-0.87, 0.62]
Subtotal (95% CI)	**27**		**28**			**100.0 %**	**0.03 [-0.50, 0.56]**
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.34$, df = 1 (P = 0.56); $I^2 = 0.0\%$							
Test for overall effect: Z = 0.11 (P = 0.92)							
2 Sertraline							
Subtotal (95% CI)	**0**		**0**			**0.0 %**	**0.0 [0.0, 0.0]**
Heterogeneity: not applicable							
Test for overall effect: not applicable							
3 Citalopram							
Subtotal (95% CI)	**0**		**0**			**0.0 %**	**0.0 [0.0, 0.0]**
Heterogeneity: not applicable							
Test for overall effect: not applicable							
4 Escitalopram							
Subtotal (95% CI)	**0**		**0**			**0.0 %**	**0.0 [0.0, 0.0]**
Heterogeneity: not applicable							
Test for overall effect: not applicable							
Total (95% CI)	**27**		**28**			**100.0 %**	**0.03 [-0.50, 0.56]**
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.34$, df = 1 (P = 0.56); $I^2 = 0.0\%$							
Test for overall effect: Z = 0.11 (P = 0.92)							
Test for subgroup differences: Not applicable							

Analysis 6.9. Comparison 6 SSRI versus control at end of treatment, concealment of allocation: low risk, Outcome 9 Death.

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 6 SSRI versus control at end of treatment, concealment of allocation: low risk

Outcome: 9 Death



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Study or subgroup	SSRI n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
Total events: 0 (SSRI), 0 (Control)				
Heterogeneity: not applicable				
Test for overall effect: not applicable				
6 Sertraline or fluoxetine				
Subtotal (95% CI)	**0**	**0**		**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)				
Heterogeneity: not applicable				
Test for overall effect: not applicable				
Total (95% CI)	**333**	**318**		**0.87 [0.30, 2.50]**
Total events: 6 (SSRI), 7 (Control)				
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 2.35$, df = 5 (P = 0.80); $I^2 = 0.0\%$				
Test for overall effect: Z = 0.26 (P = 0.80)				
Test for subgroup differences: $Chi^2 = 0.04$, df = 2 (P = 0.98), $I^2 = 0.0\%$				

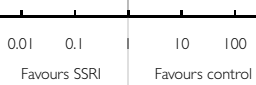
Analysis 6.10. Comparison 6 SSRI versus control at end of treatment, concealment of allocation: low risk, Outcome 10 Seizures.

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 6 SSRI versus control at end of treatment, concealment of allocation: low risk

Outcome: 10 Seizures

Study or subgroup	SSRI n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
1 Fluoxetine				
Chollet 2011	1/59	0/59		3.00 [0.12, 72.18]
Subtotal (95% CI)	**59**	**59**		**3.00 [0.12, 72.18]**
Total events: 1 (SSRI), 0 (Control)				
Heterogeneity: not applicable				
Test for overall effect: Z = 0.68 (P = 0.50)				
2 Sertraline				
Subtotal (95% CI)	**0**	**0**		**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)				
Heterogeneity: not applicable				
Test for overall effect: not applicable				
3 Citalopram				
Andersen 1994	2/33	0/33		5.00 [0.25, 100.32]
Subtotal (95% CI)	**33**	**33**		**5.00 [0.25, 100.32]**
Total events: 2 (SSRI), 0 (Control)				
Heterogeneity: not applicable				
Test for overall effect: Z = 1.05 (P = 0.29)				
4 Paroxetine				
Ye 2004	0/30	0/30		0.0 [0.0, 0.0]
Subtotal (95% CI)	**30**	**30**		**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)				
Heterogeneity: not applicable				
Test for overall effect: Z = 0.0 (P < 0.00001)				
5 Escitalopram				
Subtotal (95% CI)	**0**	**0**		**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)				
Heterogeneity: not applicable				
Test for overall effect: not applicable				
6 Sertraline or fluoxetine				
Subtotal (95% CI)	**0**	**0**		**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)				
Heterogeneity: not applicable				
Test for overall effect: not applicable				



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Study or subgroup	SSRI n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
Total (95% CI)	**122**	**122**		**3.93 [0.44, 34.85]**
Total events: 3 (SSRI), 0 (Control)				
Heterogeneity: Tau^2 = 0.0; Chi^2 = 0.05, df = 1 (P = 0.82); I^2 =0.0%				
Test for overall effect: Z = 1.23 (P = 0.22)				
Test for subgroup differences: Chi^2 = 0.05, df = 1 (P = 0.82), I^2 =0.0%				

Analysis 6.11. Comparison 6 SSRI versus control at end of treatment, concealment of allocation: low risk, Outcome 11 Gastrointestinal side effects.

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 6 SSRI versus control at end of treatment, concealment of allocation: low risk

Outcome: 11 Gastrointestinal side effects

Study or subgroup	SSRI n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
1 Fluoxetine					
Chollet 2011	14/59	6/59		92.0 %	2.33 [0.96, 5.66]
Subtotal (95% CI)	**59**	**59**		**92.0 %**	**2.33 [0.96, 5.66]**
Total events: 14 (SSRI), 6 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.88 (P = 0.061)					
2 Sertraline					
Subtotal (95% CI)	**0**	**0**		**0.0 %**	**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)					
Heterogeneity: not applicable					
Test for overall effect: not applicable					
3 Citalopram					
Subtotal (95% CI)	**0**	**0**		**0.0 %**	**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)					
Heterogeneity: not applicable					

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Study or subgroup	SSRI n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Test for overall effect: not applicable					
4 Paroxetine					
Ye 2004	2/30	0/30		8.0 %	5.00 [0.25, 99.95]
Subtotal (95% CI)	**30**	**30**		**8.0 %**	**5.00 [0.25, 99.95]**
Total events: 2 (SSRI), 0 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.05 (P = 0.29)					
5 Escitalopram					
Subtotal (95% CI)	**0**	**0**		**0.0 %**	**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)					
Heterogeneity: not applicable					
Test for overall effect: not applicable					
6 Sertraline and paroxetine					
Subtotal (95% CI)	**0**	**0**		**0.0 %**	**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)					
Heterogeneity: not applicable					
Test for overall effect: not applicable					
Total (95% CI)	**89**	**89**		**100.0 %**	**2.48 [1.06, 5.80]**
Total events: 16 (SSRI), 6 (Control)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.23$, df = 1 (P = 0.63); $I^2 = 0.0\%$					
Test for overall effect: Z = 2.10 (P = 0.036)					
Test for subgroup differences: $Chi^2 = 0.23$, df = 1 (P = 0.63), $I^2 = 0.0\%$					

Analysis 6.14. Comparison 6 SSRI versus control at end of treatment, concealment of allocation: low risk, Outcome 14 Change in cognition between baseline and end of treatment.

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 6 SSRI versus control at end of treatment, concealment of allocation: low risk

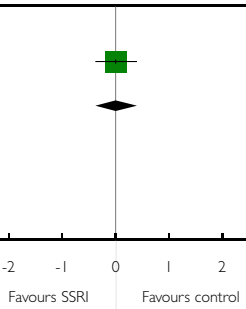
Outcome: 14 Change in cognition between baseline and end of treatment

Study or subgroup	SSRI N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
1 Sertraline							
Almeida 2006	48	2.6 (3.04)	51	2.6 (3.9)		100.0 %	0.0 [-0.39, 0.39]
Total (95% CI)	**48**		**51**			**100.0 %**	**0.0 [-0.39, 0.39]**

Heterogeneity: not applicable

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

Test for subgroup differences: Not applicable

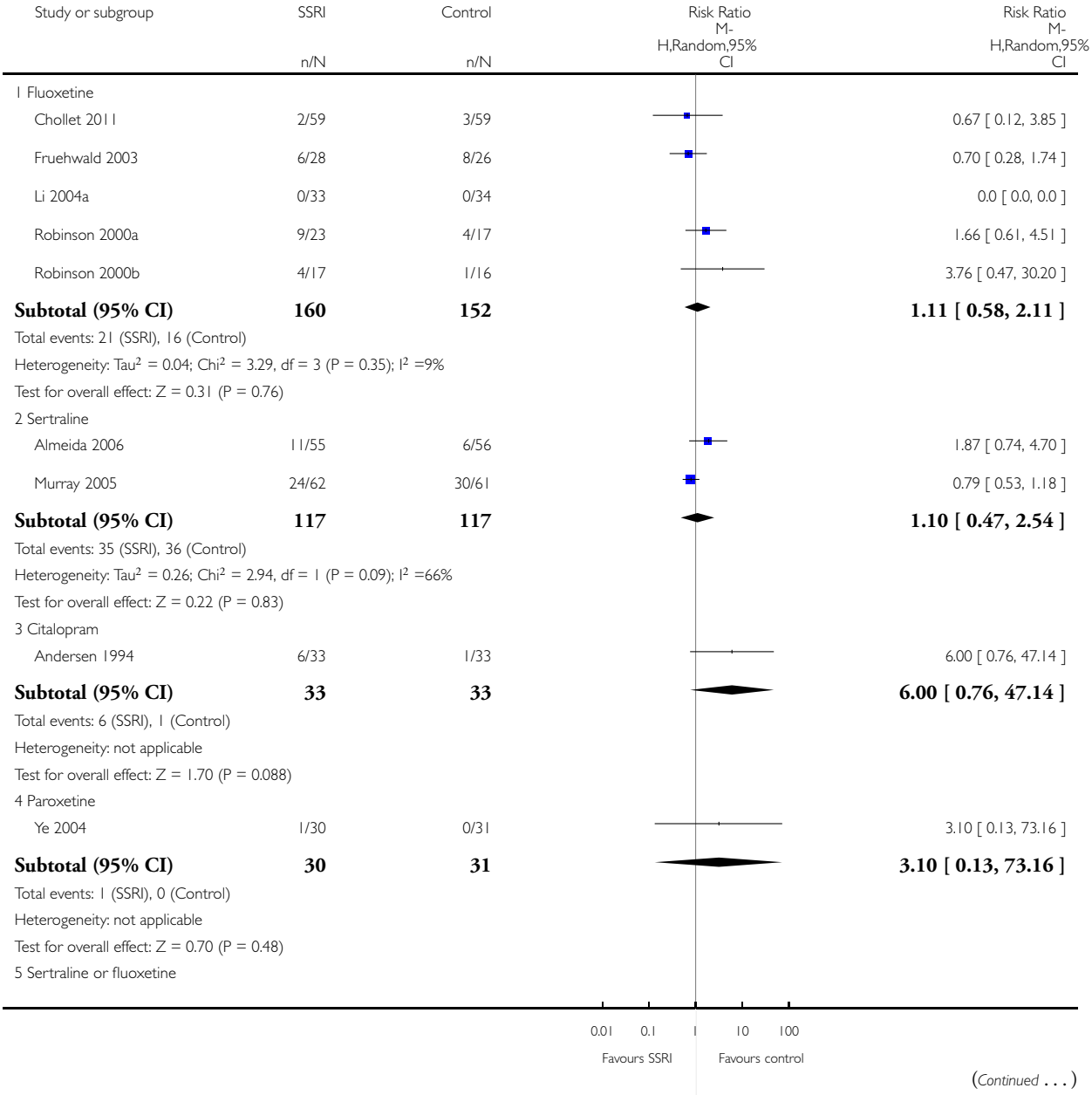


Analysis 6.15. Comparison 6 SSRI versus control at end of treatment, concealment of allocation: low risk, Outcome 15 Leaving the trial before the end of scheduled follow-up.

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 6 SSRI versus control at end of treatment, concealment of allocation: low risk

Outcome: 15 Leaving the trial before the end of scheduled follow-up



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Study or subgroup	SSRI n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
Subtotal (95% CI)	**0**	**0**		**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)				
Heterogeneity: not applicable				
Test for overall effect: not applicable				
6 Escitalopram				
Subtotal (95% CI)	**0**	**0**		**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)				
Heterogeneity: not applicable				
Test for overall effect: not applicable				
Total (95% CI)	**340**	**333**		**1.21 [0.75, 1.95]**
Total events: 63 (SSRI), 53 (Control)				
Heterogeneity: $Tau^2 = 0.14$; $Chi^2 = 10.42$, df = 7 (P = 0.17); $I^2 = 33\%$				
Test for overall effect: Z = 0.77 (P = 0.44)				
Test for subgroup differences: $Chi^2 = 2.77$, df = 3 (P = 0.43), $I^2 = 0.0\%$				

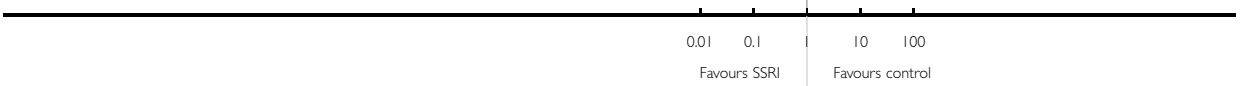
Analysis 7.1. Comparison 7 SSRI versus control at end of treatment, patient/personnel blind: low risk of bias, Outcome 1 Dependent on modified Rankin score (mRS 3 to 5).

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 7 SSRI versus control at end of treatment, patient/personnel blind: low risk of bias

Outcome: 1 Dependent on modified Rankin score (mRS 3 to 5)

Study or subgroup	SSRI n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
1 Fluoxetine				
Chollet 2011	42/57	50/55		0.81 [0.68, 0.97]
Subtotal (95% CI)	**57**	**55**		**0.81 [0.68, 0.97]**
Total events: 42 (SSRI), 50 (Control)				
Heterogeneity: not applicable				
Test for overall effect: Z = 2.34 (P = 0.019)				
2 Sertraline				
Almeida 2006	0/55	0/56		0.0 [0.0, 0.0]
Subtotal (95% CI)	**55**	**56**		**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)				
Heterogeneity: not applicable				
Test for overall effect: Z = 0.0 (P < 0.00001)				
Total (95% CI)	**112**	**111**		**0.81 [0.68, 0.97]**
Total events: 42 (SSRI), 50 (Control)				
Heterogeneity: Tau^2 = 0.0; Chi^2 = 0.0, df = 0 (P = 1.00); I^2 =0.0%				
Test for overall effect: Z = 2.34 (P = 0.019)				
Test for subgroup differences: Not applicable				

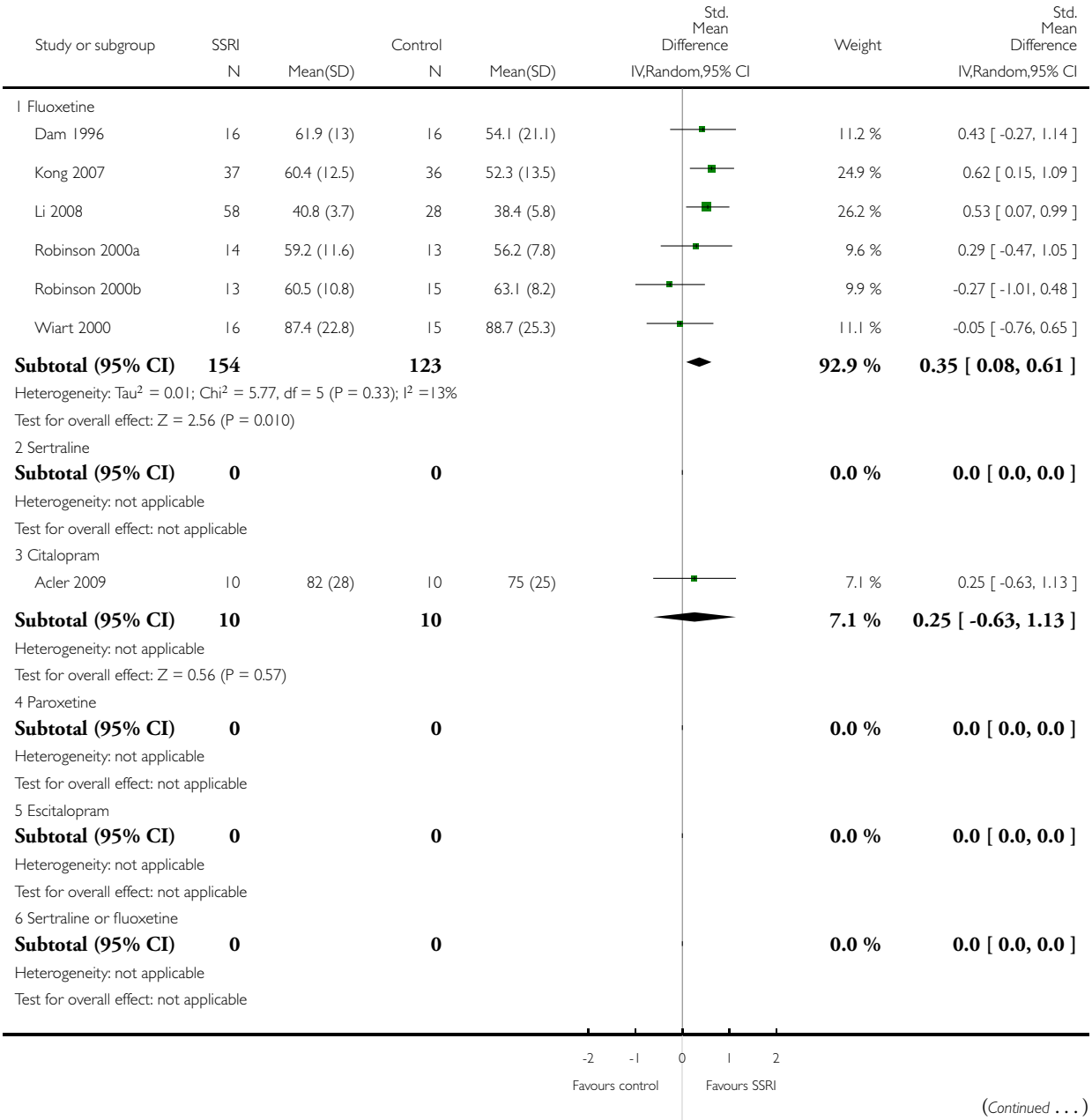


Analysis 7.2. Comparison 7 SSRI versus control at end of treatment, patient/personnel blind: low risk of bias, Outcome 2 Disability.

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 7 SSRI versus control at end of treatment, patient/personnel blind: low risk of bias

Outcome: 2 Disability



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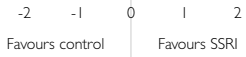
Study or subgroup	SSRI N	SSRI Mean(SD)	Control N	Control Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
Total (95% CI)	**164**		**133**			**100.0 %**	**0.36 [0.12, 0.59]**

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 5.82$, df = 6 (P = 0.44); $I^2 = 0.0\%$

Test for overall effect: Z = 2.96 (P = 0.0030)

Test for subgroup differences: $Chi^2 = 0.04$, df = 1 (P = 0.84), $I^2 = 0.0\%$



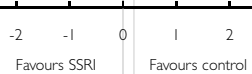
Analysis 7.3. Comparison 7 SSRI versus control at end of treatment, patient/personnel blind: low risk of bias, Outcome 3 Neurological deficit score.

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 7 SSRI versus control at end of treatment, patient/personnel blind: low risk of bias

Outcome: 3 Neurological deficit score

Study or subgroup	SSRI N	SSRI Mean(SD)	Control N	Control Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
1 Fluoxetine							
Chollet 2011	57	5.8 (3.7)	55	6.9 (4.4)		35.9 %	-0.27 [-0.64, 0.10]
Dam 1996	16	44.1 (9.4)	16	46.8 (9.9)		10.3 %	-0.27 [-0.97, 0.42]
Fruehwald 2003	26	-55.5 (4.8)	24	-52.8 (5.4)		15.6 %	-0.52 [-1.09, 0.04]
Kong 2007	37	8.6 (6.4)	36	11.2 (6.4)		23.1 %	-0.40 [-0.87, 0.06]
Subtotal (95% CI)	**136**		**131**			**84.9 %**	**-0.35 [-0.59, -0.11]**
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.63$, df = 3 (P = 0.89); $I^2 = 0.0\%$							
Test for overall effect: Z = 2.85 (P = 0.0044)							
2 Sertraline							
Burns 1999	14	-29.7 (14.7)	14	-32.2 (13.4)		9.0 %	0.17 [-0.57, 0.91]
Subtotal (95% CI)	**14**		**14**			**9.0 %**	**0.17 [-0.57, 0.91]**
Heterogeneity: not applicable							
Test for overall effect: Z = 0.46 (P = 0.65)							



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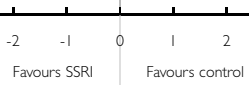
Study or subgroup	SSRI N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
3 Citalopram							
Acler 2009	10	2.3 (2)	10	3.5 (1.3)		6.0 %	-0.68 [-1.59, 0.23]
Subtotal (95% CI)	**10**		**10**			**6.0 %**	**-0.68 [-1.59, 0.23]**
Heterogeneity: not applicable							
Test for overall effect: Z = 1.47 (P = 0.14)							
4 Paroxetine							
Subtotal (95% CI)	**0**		**0**			**0.0 %**	**0.0 [0.0, 0.0]**
Heterogeneity: not applicable							
Test for overall effect: not applicable							
5 Fluoxetine or sertraline							
Subtotal (95% CI)	**0**		**0**			**0.0 %**	**0.0 [0.0, 0.0]**
Heterogeneity: not applicable							
Test for overall effect: not applicable							
Total (95% CI)	**160**		**155**			**100.0 %**	**-0.32 [-0.55, -0.10]**
Heterogeneity: Tau^2 = 0.0; Chi^2 = 3.00, df = 5 (P = 0.70); I^2 =0.0%							
Test for overall effect: Z = 2.85 (P = 0.0043)							
Test for subgroup differences: Chi^2 = 2.37, df = 2 (P = 0.31), I^2 =15%							

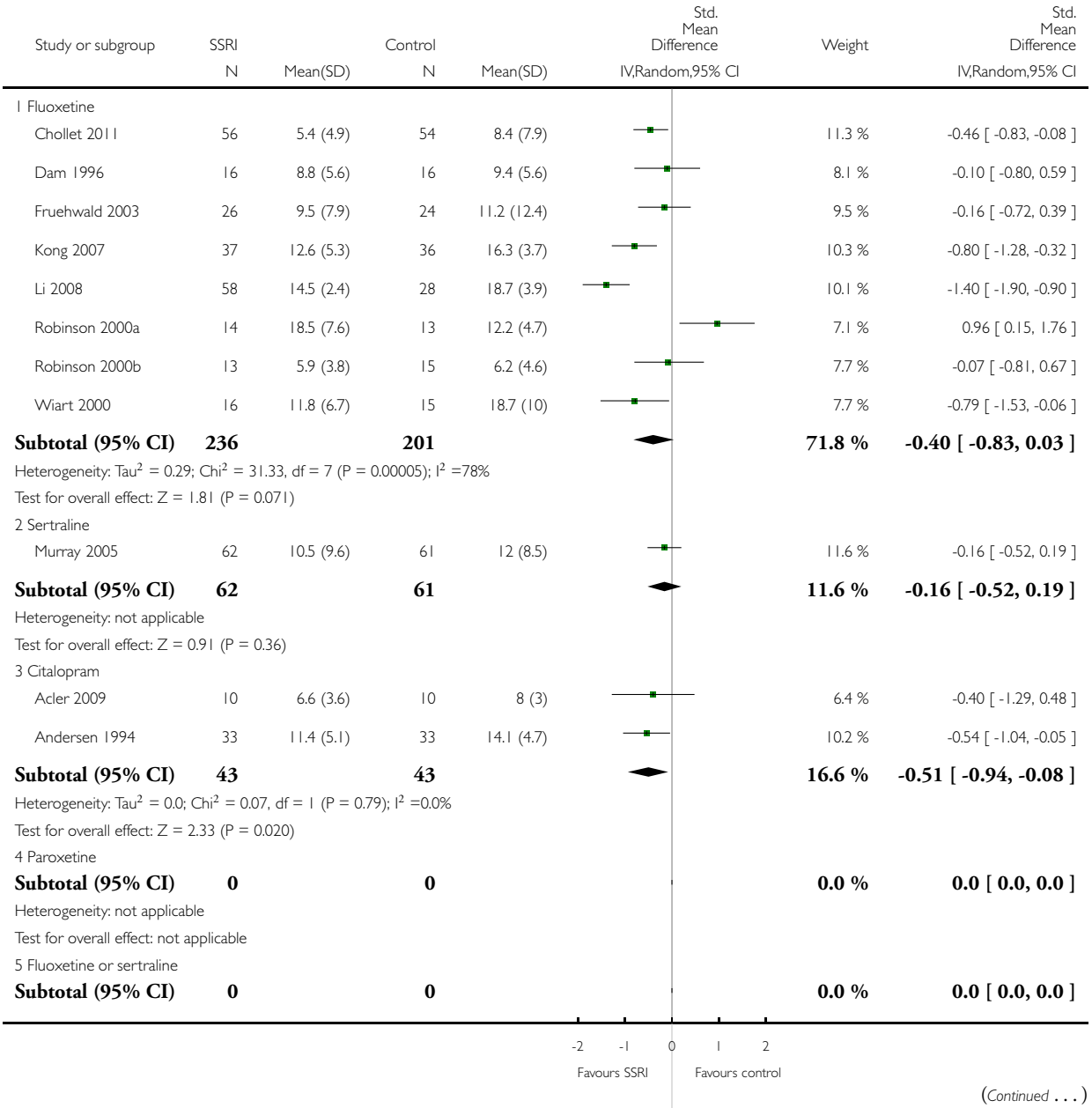


Analysis 7.4. Comparison 7 SSRI versus control at end of treatment, patient/personnel blind: low risk of bias, Outcome 4 Depression (continuous data).

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 7 SSRI versus control at end of treatment, patient/personnel blind: low risk of bias

Outcome: 4 Depression (continuous data)



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Study or subgroup	SSRI N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
Heterogeneity: not applicable							
Test for overall effect: not applicable							
Total (95% CI)	**341**		**305**			**100.0 %**	**-0.40 [-0.71, -0.09]**
Heterogeneity: Tau² = 0.18; Chi² = 34.30, df = 10 (P = 0.00016); I² =71%							
Test for overall effect: Z = 2.51 (P = 0.012)							
Test for subgroup differences: Chi² = 1.62, df = 2 (P = 0.44), I² =0.0%							

Analysis 7.5. Comparison 7 SSRI versus control at end of treatment, patient/personnel blind: low risk of bias, Outcome 5 Depression (dichotomous data).

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 7 SSRI versus control at end of treatment, patient/personnel blind: low risk of bias

Outcome: 5 Depression (dichotomous data)

Study or subgroup	SSRI n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
1 Fluoxetine					
Subtotal (95% CI)	**0**	**0**		**0.0 %**	**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)					
Heterogeneity: not applicable					
Test for overall effect: not applicable					
2 Sertraline					
Almeida 2006	8/48	11/51		46.2 %	0.77 [0.34, 1.76]
Rasmussen 2003	3/35	8/32		20.4 %	0.34 [0.10, 1.18]
Subtotal (95% CI)	**83**	**83**		**66.6 %**	**0.59 [0.28, 1.25]**
Total events: 11 (SSRI), 19 (Control)					
Heterogeneity: Tau² = 0.05; Chi² = 1.16, df = 1 (P = 0.28); I² =14%					
Test for overall effect: Z = 1.37 (P = 0.17)					
3 Citalopram					

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Study or subgroup	SSRI n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Subtotal (95% CI)	**0**	**0**		**0.0 %**	**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)					
Heterogeneity: not applicable					
Test for overall effect: not applicable					
4 Paroxetine					
Subtotal (95% CI)	**0**	**0**		**0.0 %**	**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)					
Heterogeneity: not applicable					
Test for overall effect: not applicable					
5 Escitalopram					
Robinson 2008	5/59	13/58		33.4 %	0.38 [0.14, 0.99]
Subtotal (95% CI)	**59**	**58**		**33.4 %**	**0.38 [0.14, 0.99]**
Total events: 5 (SSRI), 13 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.97 (P = 0.048)					
Total (95% CI)	**142**	**141**		**100.0 %**	**0.52 [0.30, 0.90]**
Total events: 16 (SSRI), 32 (Control)					
Heterogeneity: Tau^2 = 0.0; Chi^2 = 1.76, df = 2 (P = 0.41); I^2 =0.0%					
Test for overall effect: Z = 2.32 (P = 0.020)					
Test for subgroup differences: Chi^2 = 0.51, df = 1 (P = 0.48), I^2 =0.0%					

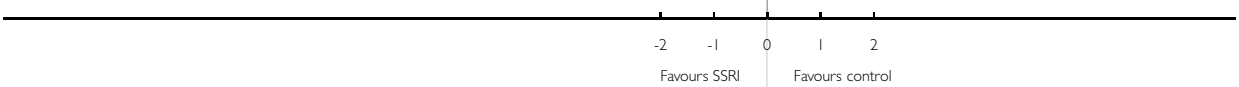
Analysis 7.6. Comparison 7 SSRI versus control at end of treatment, patient/personnel blind: low risk of bias, Outcome 6 Anxiety (continuous data).

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 7 SSRI versus control at end of treatment, patient/personnel blind: low risk of bias

Outcome: 6 Anxiety (continuous data)

Study or subgroup	SSRI N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
1 Fluoxetine							
Robinson 2000a	14	9.8 (4.8)	13	9.9 (5.1)		49.4 %	-0.02 [-0.77, 0.74]
Robinson 2000b	13	4.7 (3.8)	15	5.5 (2.9)		50.6 %	-0.23 [-0.98, 0.51]
Subtotal (95% CI)	**27**		**28**			**100.0 %**	**-0.13 [-0.66, 0.40]**
Heterogeneity: Tau² = 0.0; Chi² = 0.15, df = 1 (P = 0.69); I² =0.0%							
Test for overall effect: Z = 0.47 (P = 0.64)							
2 Sertraline							
Subtotal (95% CI)	**0**		**0**			**0.0 %**	**0.0 [0.0, 0.0]**
Heterogeneity: not applicable							
Test for overall effect: not applicable							
3 Citalopram							
Subtotal (95% CI)	**0**		**0**			**0.0 %**	**0.0 [0.0, 0.0]**
Heterogeneity: not applicable							
Test for overall effect: not applicable							
4 Paroxetine							
Subtotal (95% CI)	**0**		**0**			**0.0 %**	**0.0 [0.0, 0.0]**
Heterogeneity: not applicable							
Test for overall effect: not applicable							
5 Escitalopram							
Subtotal (95% CI)	**0**		**0**			**0.0 %**	**0.0 [0.0, 0.0]**
Heterogeneity: not applicable							
Test for overall effect: not applicable							
Total (95% CI)	**27**		**28**			**100.0 %**	**-0.13 [-0.66, 0.40]**
Heterogeneity: Tau² = 0.0; Chi² = 0.15, df = 1 (P = 0.69); I² =0.0%							
Test for overall effect: Z = 0.47 (P = 0.64)							
Test for subgroup differences: Not applicable							

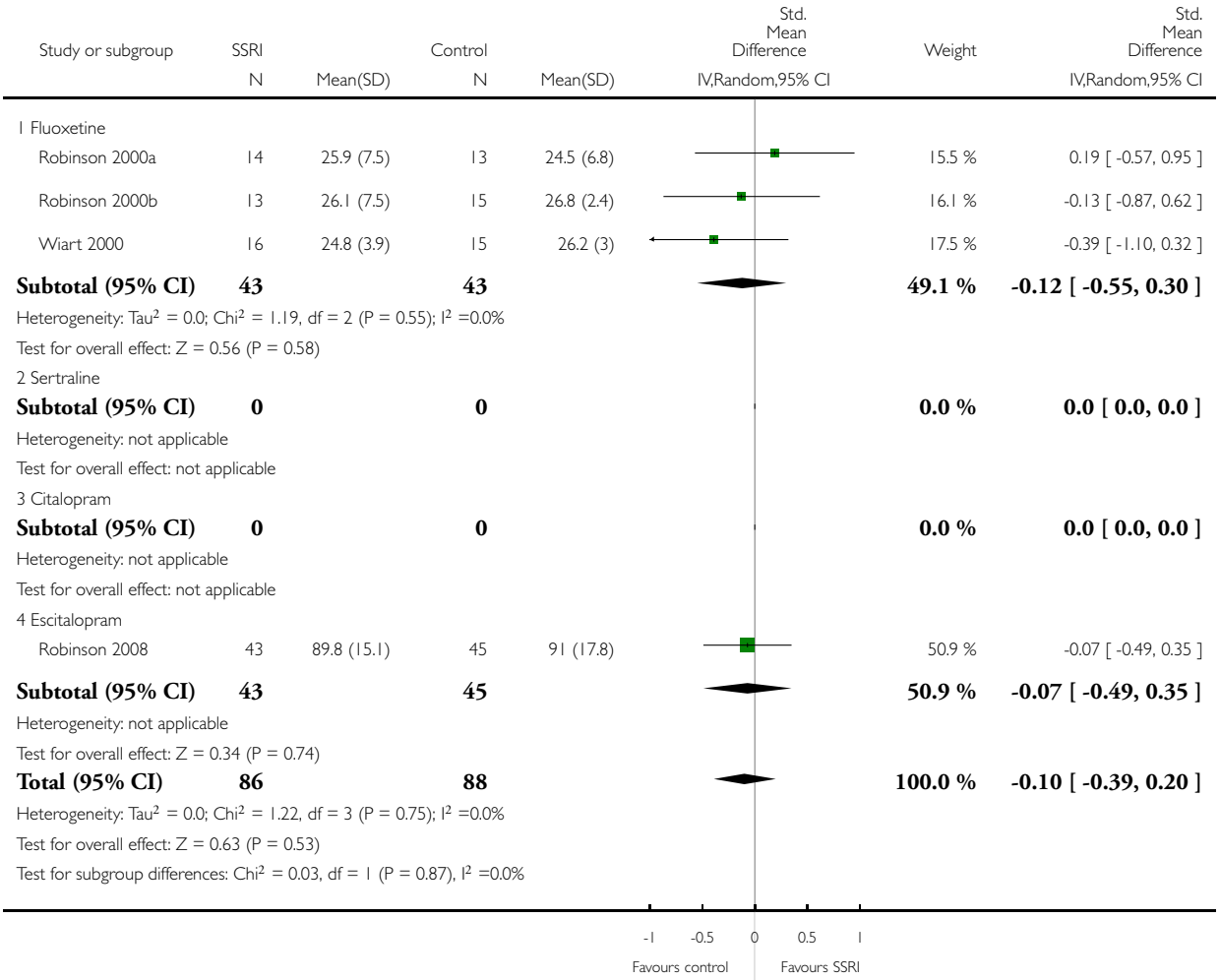


Analysis 7.8. Comparison 7 SSRI versus control at end of treatment, patient/personnel blind: low risk of bias, Outcome 8 Cognition (continuous scores end of treatment).

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 7 SSRI versus control at end of treatment, patient/personnel blind: low risk of bias

Outcome: 8 Cognition (continuous scores end of treatment)

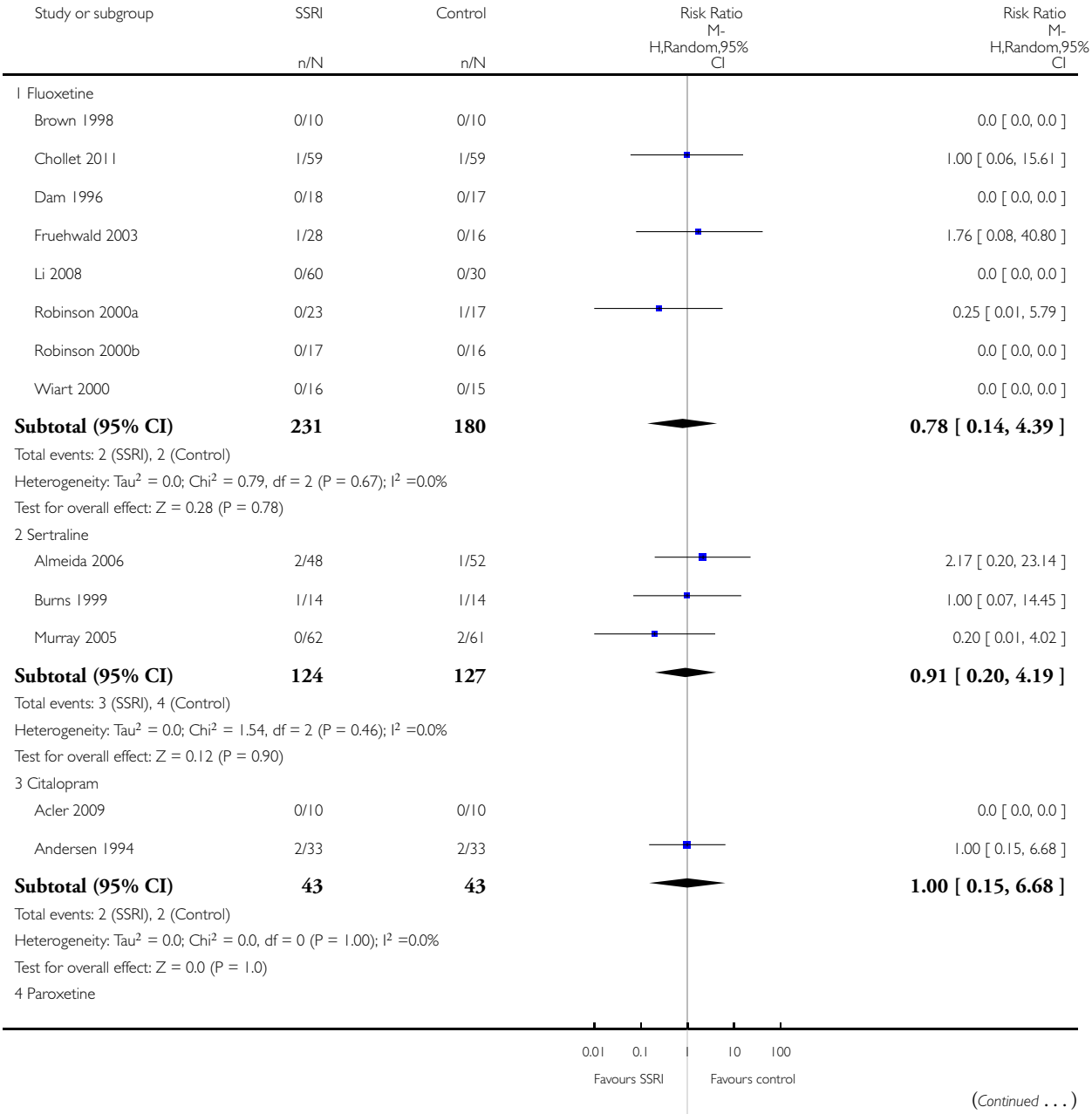


Analysis 7.9. Comparison 7 SSRI versus control at end of treatment, patient/personnel blind: low risk of bias, Outcome 9 Death.

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 7 SSRI versus control at end of treatment, patient/personnel blind: low risk of bias

Outcome: 9 Death



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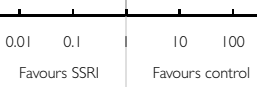
Study or subgroup	SSRI n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
Subtotal (95% CI)	**0**	**0**		**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)				
Heterogeneity: not applicable				
Test for overall effect: not applicable				
5 Escitalopram				
Robinson 2008	2/59	0/58		4.92 [0.24, 100.25]
Subtotal (95% CI)	**59**	**58**		**4.92 [0.24, 100.25]**
Total events: 2 (SSRI), 0 (Control)				
Heterogeneity: not applicable				
Test for overall effect: Z = 1.04 (P = 0.30)				
6 Sertraline or fluoxetine				
Subtotal (95% CI)	**0**	**0**		**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)				
Heterogeneity: not applicable				
Test for overall effect: not applicable				
Total (95% CI)	**457**	**408**		**1.05 [0.41, 2.66]**
Total events: 9 (SSRI), 8 (Control)				
Heterogeneity: Tau^2 = 0.0; Chi^2 = 3.46, df = 7 (P = 0.84); I^2 =0.0%				
Test for overall effect: Z = 0.09 (P = 0.93)				
Test for subgroup differences: Chi^2 = 1.16, df = 3 (P = 0.76), I^2 =0.0%				



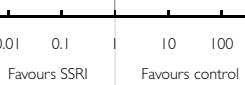
Analysis 7.10. Comparison 7 SSRI versus control at end of treatment, patient/personnel blind: low risk of bias, Outcome 10 Seizures.

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 7 SSRI versus control at end of treatment, patient/personnel blind: low risk of bias

Outcome: 10 Seizures

Study or subgroup	SSRI n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
1 Fluoxetine					
Chollet 2011	1/59	0/59		21.4 %	3.00 [0.12, 72.18]
Dam 1996	2/18	0/17		24.5 %	4.74 [0.24, 92.07]
Wiart 2000	1/16	1/15		30.1 %	0.94 [0.06, 13.68]
Subtotal (95% CI)	**93**	**91**		**76.0 %**	**2.19 [0.41, 11.85]**
Total events: 4 (SSRI), 1 (Control)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.69$, df = 2 (P = 0.71); $I^2 = 0.0\%$					
Test for overall effect: Z = 0.91 (P = 0.36)					
2 Sertraline					
Subtotal (95% CI)	**0**	**0**		**0.0 %**	**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)					
Heterogeneity: not applicable					
Test for overall effect: not applicable					
3 Citalopram					
Andersen 1994	2/33	0/33		24.0 %	5.00 [0.25, 100.32]
Subtotal (95% CI)	**33**	**33**		**24.0 %**	**5.00 [0.25, 100.32]**
Total events: 2 (SSRI), 0 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.05 (P = 0.29)					
4 Paroxetine					
Subtotal (95% CI)	**0**	**0**		**0.0 %**	**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)					
Heterogeneity: not applicable					
Test for overall effect: not applicable					
5 Escitalopram					
Subtotal (95% CI)	**0**	**0**		**0.0 %**	**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)					
Heterogeneity: not applicable					
Test for overall effect: not applicable					
6 Sertraline or fluoxetine					
Subtotal (95% CI)	**0**	**0**		**0.0 %**	**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)					
Heterogeneity: not applicable					



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Study or subgroup	SSRI n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Test for overall effect: not applicable					
Total (95% CI)	**126**	**124**		**100.0 %**	**2.67 [0.61, 11.63]**
Total events: 6 (SSRI), 1 (Control)					
Heterogeneity: Tau^2 = 0.0; Chi^2 = 0.91, df = 3 (P = 0.82); I^2 =0.0%					
Test for overall effect: Z = 1.31 (P = 0.19)					
Test for subgroup differences: Chi^2 = 0.22, df = 1 (P = 0.64), I^2 =0.0%					

Analysis 7.11. Comparison 7 SSRI versus control at end of treatment, patient/personnel blind: low risk of bias, Outcome 11 Gastrointestinal side effects.

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 7 SSRI versus control at end of treatment, patient/personnel blind: low risk of bias

Outcome: 11 Gastrointestinal side effects

Study or subgroup	SSRI n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
1 Fluoxetine					
Chollet 2011	14/59	6/59		48.1 %	2.33 [0.96, 5.66]
Dam 1996	2/18	0/17		6.5 %	4.74 [0.24, 92.07]
Li 2008	6/60	3/30		27.5 %	1.00 [0.27, 3.72]
Wiart 2000	1/16	3/16		11.9 %	0.33 [0.04, 2.87]
Subtotal (95% CI)	**153**	**122**		**94.1 %**	**1.48 [0.65, 3.39]**
Total events: 23 (SSRI), 12 (Control)					
Heterogeneity: Tau^2 = 0.15; Chi^2 = 3.74, df = 3 (P = 0.29); I^2 =20%					
Test for overall effect: Z = 0.93 (P = 0.35)					
2 Sertraline					
Burns 1999	0/14	1/14		5.9 %	0.33 [0.01, 7.55]
Subtotal (95% CI)	**14**	**14**		**5.9 %**	**0.33 [0.01, 7.55]**

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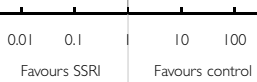
Study or subgroup	SSRI n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Total events: 0 (SSRI), 1 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.69 (P = 0.49)					
3 Citalopram					
Subtotal (95% CI)	**0**	**0**		**0.0 %**	**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)					
Heterogeneity: not applicable					
Test for overall effect: not applicable					
4 Paroxetine					
Subtotal (95% CI)	**0**	**0**		**0.0 %**	**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)					
Heterogeneity: not applicable					
Test for overall effect: not applicable					
5 Escitalopram					
Subtotal (95% CI)	**0**	**0**		**0.0 %**	**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)					
Heterogeneity: not applicable					
Test for overall effect: not applicable					
6 Sertraline and paroxetine					
Subtotal (95% CI)	**0**	**0**		**0.0 %**	**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)					
Heterogeneity: not applicable					
Test for overall effect: not applicable					
Total (95% CI)	**167**	**136**		**100.0 %**	**1.37 [0.63, 2.98]**
Total events: 23 (SSRI), 13 (Control)					
Heterogeneity: $Tau^2 = 0.12$; $Chi^2 = 4.67$, df = 4 (P = 0.32); $I^2 = 14\%$					
Test for overall effect: Z = 0.79 (P = 0.43)					
Test for subgroup differences: $Chi^2 = 0.82$, df = 1 (P = 0.37), $I^2 = 0.0\%$					



Analysis 7.14. Comparison 7 SSRI versus control at end of treatment, patient/personnel blind: low risk of bias, Outcome 14 Change in cognition between baseline and end of treatment.

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 7 SSRI versus control at end of treatment, patient/personnel blind: low risk of bias

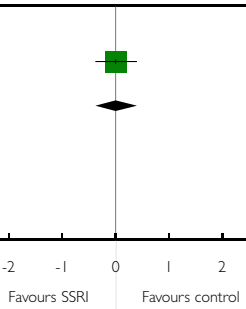
Outcome: 14 Change in cognition between baseline and end of treatment

Study or subgroup	SSRI N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
1 Sertraline							
Almeida 2006	48	2.6 (3.04)	51	2.6 (3.9)		100.0 %	0.0 [-0.39, 0.39]
Total (95% CI)	**48**		**51**			**100.0 %**	**0.0 [-0.39, 0.39]**

Heterogeneity: not applicable

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

Test for subgroup differences: Not applicable

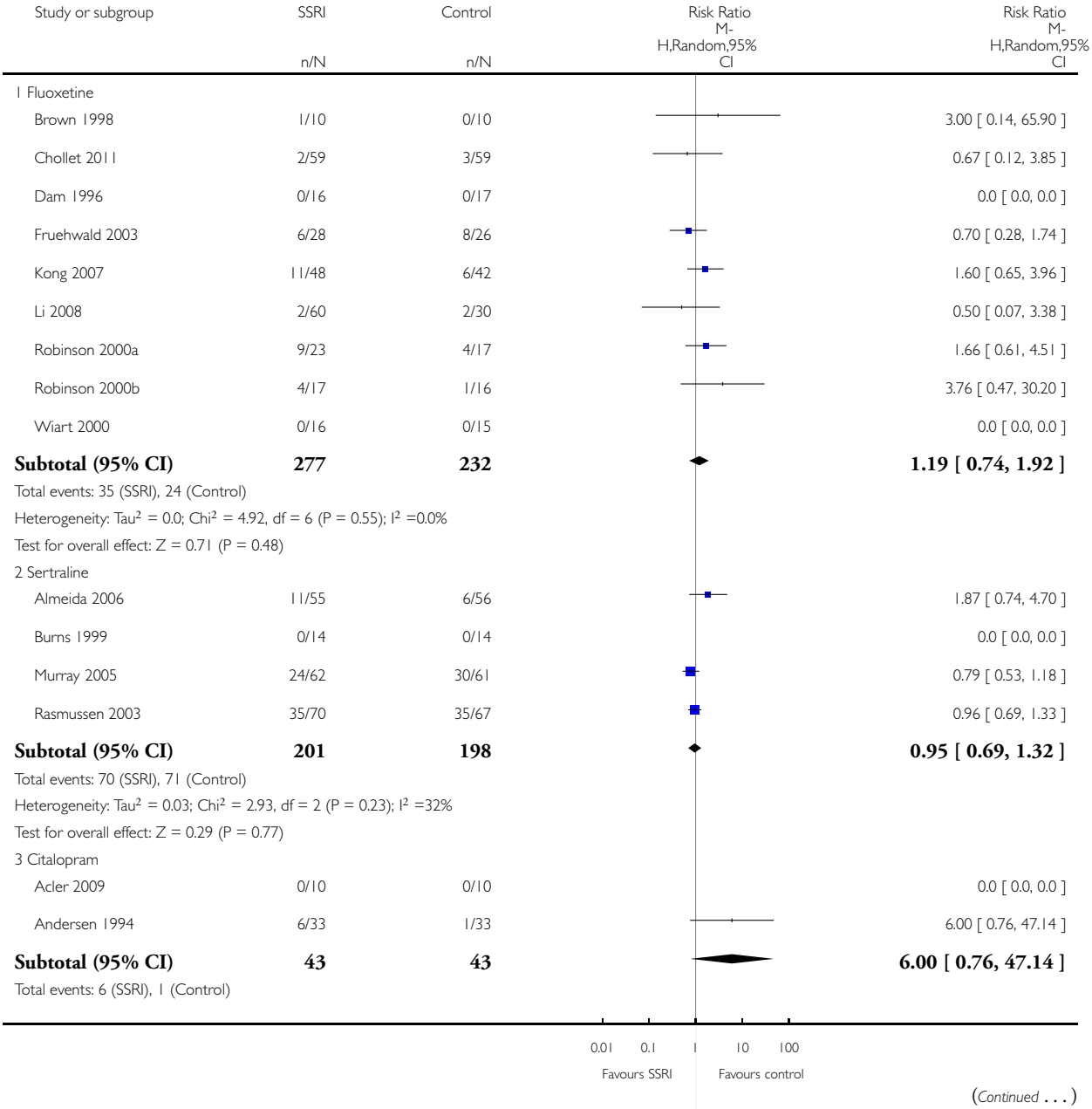


Analysis 7.15. Comparison 7 SSRI versus control at end of treatment, patient/personnel blind: low risk of bias, Outcome 15 Leaving the trial before the end of scheduled follow-up.

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 7 SSRI versus control at end of treatment, patient/personnel blind: low risk of bias

Outcome: 15 Leaving the trial before the end of scheduled follow-up



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Study or subgroup	SSRI	Control	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
	n/N	n/N		
Heterogeneity: Tau^2 = 0.0; Chi^2 = 0.0, df = 0 (P = 1.00); I^2 =0.0%				
Test for overall effect: Z = 1.70 (P = 0.088)				
4 Paroxetine				
Subtotal (95% CI)	**0**	**0**		**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)				
Heterogeneity: not applicable				
Test for overall effect: not applicable				
5 Sertraline or fluoxetine				
Subtotal (95% CI)	**0**	**0**		**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)				
Heterogeneity: not applicable				
Test for overall effect: not applicable				
6 Escitalopram				
Robinson 2008	7/59	5/58		1.38 [0.46, 4.09]
Subtotal (95% CI)	**59**	**58**		**1.38 [0.46, 4.09]**
Total events: 7 (SSRI), 5 (Control)				
Heterogeneity: not applicable				
Test for overall effect: Z = 0.57 (P = 0.57)				
Total (95% CI)	**580**	**531**		**1.05 [0.82, 1.36]**
Total events: 118 (SSRI), 101 (Control)				
Heterogeneity: Tau^2 = 0.02; Chi^2 = 12.31, df = 11 (P = 0.34); I^2 =11%				
Test for overall effect: Z = 0.41 (P = 0.68)				
Test for subgroup differences: Chi^2 = 3.57, df = 3 (P = 0.31), I^2 =16%				

Analysis 8.1. Comparison 8 SSRI versus control at end of treatment, outcome assessor blind: low risk of bias, Outcome 1 Dependent on modified Rankin score (mRS 3 to 5).

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 8 SSRI versus control at end of treatment, outcome assessor blind: low risk of bias

Outcome: 1 Dependent on modified Rankin score (mRS 3 to 5)

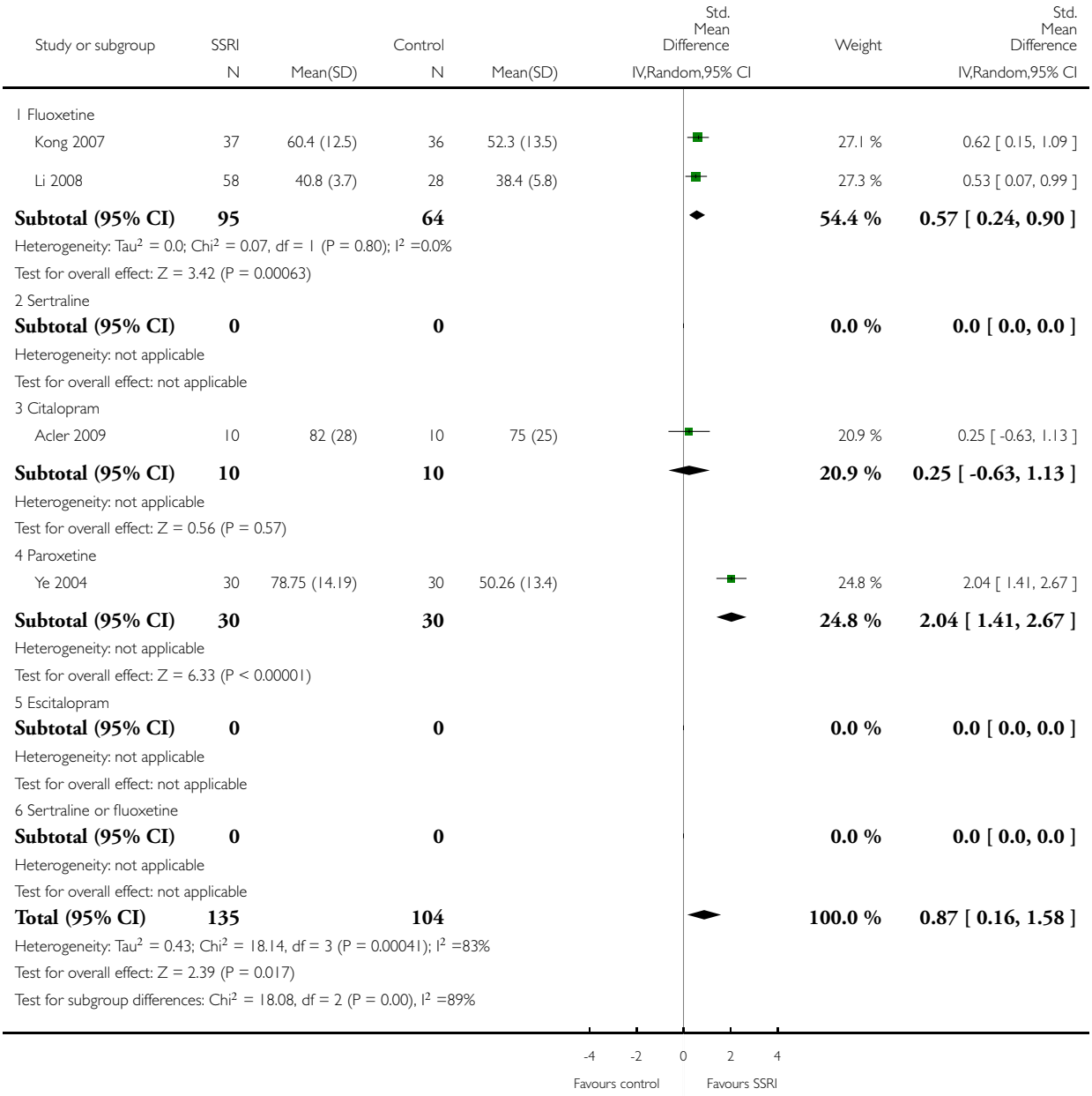
Study or subgroup	SSRI n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
1 Fluoxetine				
Chollet 2011	42/57	50/55		0.81 [0.68, 0.97]
Subtotal (95% CI)	**57**	**55**		**0.81 [0.68, 0.97]**
Total events: 42 (SSRI), 50 (Control)				
Heterogeneity: not applicable				
Test for overall effect: Z = 2.34 (P = 0.019)				
2 Sertraline				
Almeida 2006	0/55	0/56		0.0 [0.0, 0.0]
Subtotal (95% CI)	**55**	**56**		**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)				
Heterogeneity: not applicable				
Test for overall effect: Z = 0.0 (P < 0.00001)				
Total (95% CI)	**112**	**111**		**0.81 [0.68, 0.97]**
Total events: 42 (SSRI), 50 (Control)				
Heterogeneity: Tau^2 = 0.0; Chi^2 = 0.0, df = 0 (P = 1.00); I^2 =0.0%				
Test for overall effect: Z = 2.34 (P = 0.019)				
Test for subgroup differences: Not applicable				

Analysis 8.2. Comparison 8 SSRI versus control at end of treatment, outcome assessor blind: low risk of bias, Outcome 2 Disability.

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 8 SSRI versus control at end of treatment, outcome assessor blind: low risk of bias

Outcome: 2 Disability

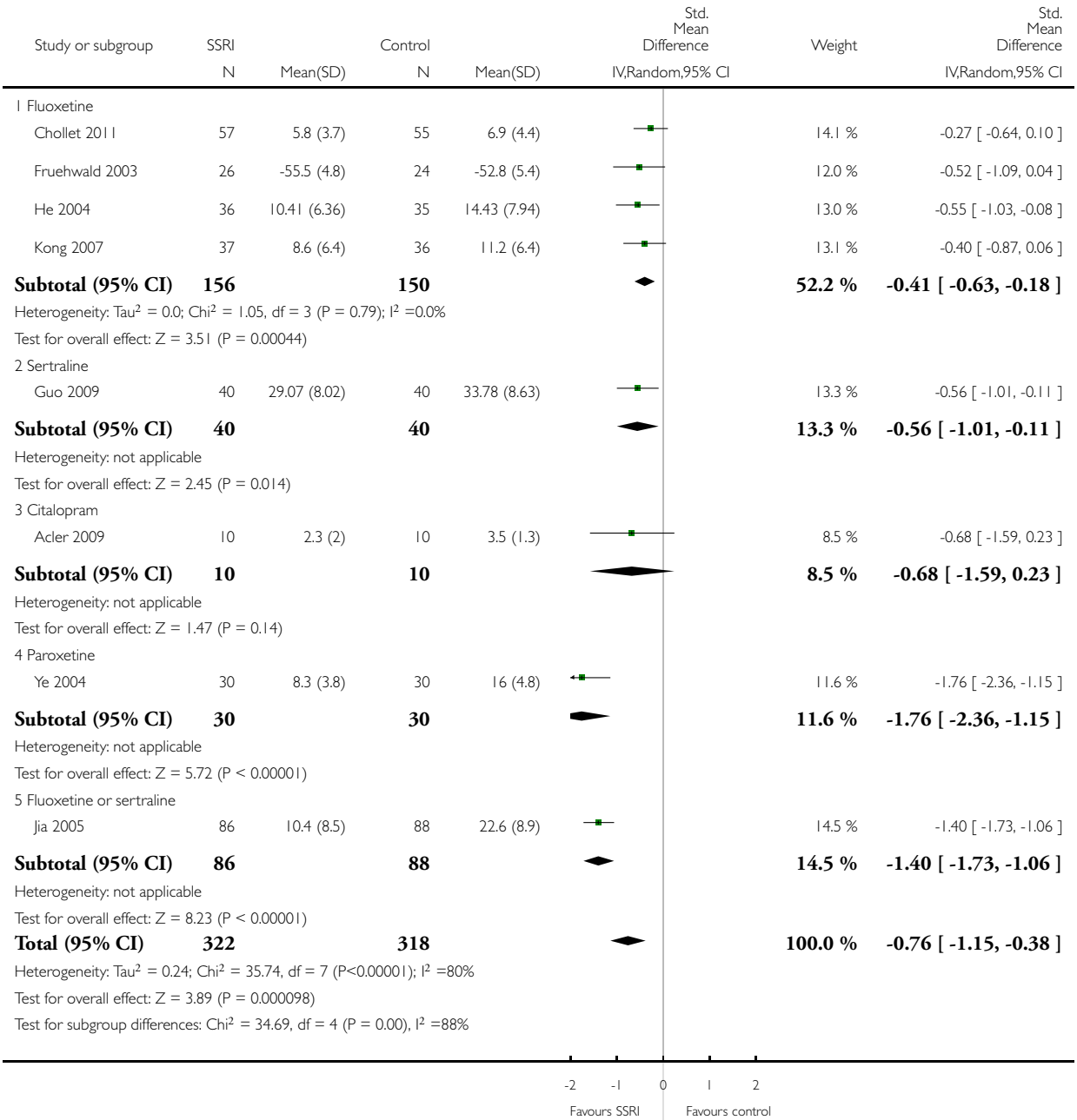


Analysis 8.3. Comparison 8 SSRI versus control at end of treatment, outcome assessor blind: low risk of bias, Outcome 3 Neurological deficit score.

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 8 SSRI versus control at end of treatment, outcome assessor blind: low risk of bias

Outcome: 3 Neurological deficit score



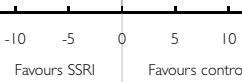
Analysis 8.4. Comparison 8 SSRI versus control at end of treatment, outcome assessor blind: low risk of bias, Outcome 4 Depression (continuous data).

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 8 SSRI versus control at end of treatment, outcome assessor blind: low risk of bias

Outcome: 4 Depression (continuous data)

Study or subgroup	SSRI N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
1 Fluoxetine							
Chollet 2011	56	5.4 (4.9)	54	8.4 (7.9)		10.5 %	-0.46 [-0.83, -0.08]
Fruehwald 2003	26	9.5 (7.9)	24	11.2 (12.4)		10.2 %	-0.16 [-0.72, 0.39]
He 2004	36	14.28 (2.31)	35	20.32 (2.82)		10.1 %	-2.32 [-2.93, -1.71]
Kong 2007	37	12.6 (5.3)	36	16.3 (3.7)		10.4 %	-0.80 [-1.28, -0.32]
Li 2008	58	14.5 (2.4)	28	18.7 (3.9)		10.3 %	-1.40 [-1.90, -0.90]
Subtotal (95% CI)	**213**		**177**			**51.4 %**	**-1.01 [-1.69, -0.34]**
Heterogeneity: $Tau^2 = 0.52$; $Chi^2 = 37.06$, df = 4 (P<0.00001); I^2 =89%							
Test for overall effect: Z = 2.95 (P = 0.0031)							
2 Sertraline							
Guo 2009	40	14.82 (8.05)	40	17.61 (8)		10.4 %	-0.34 [-0.79, 0.10]
Murray 2005	62	10.5 (9.6)	61	12 (8.5)		10.6 %	-0.16 [-0.52, 0.19]
Subtotal (95% CI)	**102**		**101**			**21.0 %**	**-0.23 [-0.51, 0.04]**
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.39$, df = 1 (P = 0.53); I^2 =0.0%							
Test for overall effect: Z = 1.67 (P = 0.096)							
3 Citalopram							
Acler 2009	10	6.6 (3.6)	10	8 (3)		9.3 %	-0.40 [-1.29, 0.48]
Miao 2004	34	6.45 (5.3)	34	23.74 (5.16)		9.7 %	-3.27 [-4.01, -2.53]
Subtotal (95% CI)	**44**		**44**			**19.0 %**	**-1.85 [-4.65, 0.96]**
Heterogeneity: $Tau^2 = 3.93$; $Chi^2 = 23.61$, df = 1 (P<0.00001); I^2 =96%							
Test for overall effect: Z = 1.29 (P = 0.20)							
4 Paroxetine							
Ye 2004	30	4.02 (3.07)	30	17.32 (1.66)		8.6 %	-5.32 [-6.43, -4.21]
Subtotal (95% CI)	**30**		**30**			**8.6 %**	**-5.32 [-6.43, -4.21]**
Heterogeneity: not applicable							
Test for overall effect: Z = 9.42 (P < 0.00001)							
5 Fluoxetine or sertraline							



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Study or subgroup	SSRI N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
Subtotal (95% CI)	**0**		**0**			**0.0 %**	**0.0 [0.0, 0.0]**
Heterogeneity: not applicable							
Test for overall effect: not applicable							
Total (95% CI)	**389**		**352**		◆	**100.0 %**	**-1.39 [-2.10, -0.68]**
Heterogeneity: Tau^2 = 1.20; Chi^2 = 161.35, df = 9 (P<0.00001); I^2 =94%							
Test for overall effect: Z = 3.86 (P = 0.00012)							
Test for subgroup differences: Chi^2 = 78.73, df = 3 (P = 0.00), I^2 =96%							

-10 -5 0 5 10

Favours SSRI Favours control

Analysis 8.5. Comparison 8 SSRI versus control at end of treatment, outcome assessor blind: low risk of bias, Outcome 5 Depression (dichotomous data).

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 8 SSRI versus control at end of treatment, outcome assessor blind: low risk of bias

Outcome: 5 Depression (dichotomous data)

Study or subgroup	SSRI n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
1 Fluoxetine					
Subtotal (95% CI)	**0**	**0**		**0.0 %**	**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)					
Heterogeneity: not applicable					
Test for overall effect: not applicable					
2 Sertraline					
Subtotal (95% CI)	**0**	**0**		**0.0 %**	**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)					
Heterogeneity: not applicable					
Test for overall effect: not applicable					
3 Citalopram					
Subtotal (95% CI)	**0**	**0**		**0.0 %**	**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)					

0.01 0.1 1 10 100

Favours SSRI Favours control

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Study or subgroup	SSRI n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Heterogeneity: not applicable					
Test for overall effect: not applicable					
4 Paroxetine					
Subtotal (95% CI)	**0**	**0**		**0.0 %**	**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)					
Heterogeneity: not applicable					
Test for overall effect: not applicable					
5 Escitalopram					
Robinson 2008	5/59	13/58		100.0 %	0.38 [0.14, 0.99]
Subtotal (95% CI)	**59**	**58**		**100.0 %**	**0.38 [0.14, 0.99]**
Total events: 5 (SSRI), 13 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.97 (P = 0.048)					
Total (95% CI)	**59**	**58**		**100.0 %**	**0.38 [0.14, 0.99]**
Total events: 5 (SSRI), 13 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.97 (P = 0.048)					
Test for subgroup differences: Not applicable					

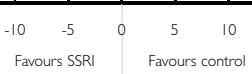
Analysis 8.6. Comparison 8 SSRI versus control at end of treatment, outcome assessor blind: low risk of bias, Outcome 6 Anxiety (continuous data).

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 8 SSRI versus control at end of treatment, outcome assessor blind: low risk of bias

Outcome: 6 Anxiety (continuous data)

Study or subgroup	SSRI N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
1 Fluoxetine							
Subtotal (95% CI)	**0**		**0**			**0.0 %**	**0.0 [0.0, 0.0]**
Heterogeneity: not applicable							
Test for overall effect: not applicable							
2 Sertraline							
Subtotal (95% CI)	**0**		**0**			**0.0 %**	**0.0 [0.0, 0.0]**
Heterogeneity: not applicable							
Test for overall effect: not applicable							
3 Citalopram							
Subtotal (95% CI)	**0**		**0**			**0.0 %**	**0.0 [0.0, 0.0]**
Heterogeneity: not applicable							
Test for overall effect: not applicable							
4 Paroxetine							
Ye 2004	30	9.82 (2.64)	30	14.02 (2.32)		100.0 %	-1.67 [-2.26, -1.08]
Subtotal (95% CI)	**30**		**30**			**100.0 %**	**-1.67 [-2.26, -1.08]**
Heterogeneity: not applicable							
Test for overall effect: Z = 5.52 (P < 0.00001)							
5 escitalopram							
Subtotal (95% CI)	**0**		**0**			**0.0 %**	**0.0 [0.0, 0.0]**
Heterogeneity: not applicable							
Test for overall effect: not applicable							
Total (95% CI)	**30**		**30**			**100.0 %**	**-1.67 [-2.26, -1.08]**
Heterogeneity: not applicable							
Test for overall effect: Z = 5.52 (P < 0.00001)							
Test for subgroup differences: Not applicable							



Analysis 8.8. Comparison 8 SSRI versus control at end of treatment, outcome assessor blind: low risk of bias, Outcome 8 Cognition (continuous scores end of treatment).

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 8 SSRI versus control at end of treatment, outcome assessor blind: low risk of bias

Outcome: 8 Cognition (continuous scores end of treatment)

Study or subgroup	SSRI N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
1 Fluoxetine							
Subtotal (95% CI)	**0**		**0**			**0.0 %**	**0.0 [0.0, 0.0]**
Heterogeneity: not applicable							
Test for overall effect: not applicable							
2 Sertraline							
Guo 2009	40	19.26 (6.87)	40	15.74 (6.82)		49.1 %	0.51 [0.06, 0.95]
Subtotal (95% CI)	**40**		**40**			**49.1 %**	**0.51 [0.06, 0.95]**
Heterogeneity: not applicable							
Test for overall effect: Z = 2.24 (P = 0.025)							
3 Citalopram							
Subtotal (95% CI)	**0**		**0**			**0.0 %**	**0.0 [0.0, 0.0]**
Heterogeneity: not applicable							
Test for overall effect: not applicable							
4 Escitalopram							
Robinson 2008	43	89.8 (15.1)	45	91 (17.8)		50.9 %	-0.07 [-0.49, 0.35]
Subtotal (95% CI)	**43**		**45**			**50.9 %**	**-0.07 [-0.49, 0.35]**
Heterogeneity: not applicable							
Test for overall effect: Z = 0.34 (P = 0.74)							
Total (95% CI)	**83**		**85**			**100.0 %**	**0.21 [-0.36, 0.78]**
Heterogeneity: Tau^2 = 0.12; Chi^2 = 3.47, df = 1 (P = 0.06); I^2 =71%							
Test for overall effect: Z = 0.73 (P = 0.46)							
Test for subgroup differences: Chi^2 = 3.47, df = 1 (P = 0.06), I^2 =71%							

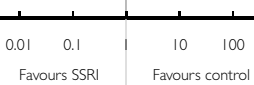
Analysis 8.9. Comparison 8 SSRI versus control at end of treatment, outcome assessor blind: low risk of bias, Outcome 9 Death.

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 8 SSRI versus control at end of treatment, outcome assessor blind: low risk of bias

Outcome: 9 Death

Study or subgroup	SSRI n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
1 Fluoxetine				
Brown 1998	0/10	0/10		0.0 [0.0, 0.0]
Chollet 2011	1/59	1/59		1.00 [0.06, 15.61]
Fruehwald 2003	1/28	0/16		1.76 [0.08, 40.80]
He 2004	0/36	0/35		0.0 [0.0, 0.0]
Li 2008	0/60	0/30		0.0 [0.0, 0.0]
Subtotal (95% CI)	**193**	**150**		**1.28 [0.16, 10.11]**
Total events: 2 (SSRI), 1 (Control)				
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.07$, df = 1 (P = 0.79); $I^2 = 0.0\%$				
Test for overall effect: Z = 0.23 (P = 0.82)				
2 Sertraline				
Guo 2009	0/40	0/40		0.0 [0.0, 0.0]
Murray 2005	0/62	2/61		0.20 [0.01, 4.02]
Subtotal (95% CI)	**102**	**101**		**0.20 [0.01, 4.02]**
Total events: 0 (SSRI), 2 (Control)				
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.0$, df = 0 (P = 1.00); $I^2 = 0.0\%$				
Test for overall effect: Z = 1.06 (P = 0.29)				
3 Citalopram				
Acler 2009	0/10	0/10		0.0 [0.0, 0.0]
Miao 2004	0/45	0/45		0.0 [0.0, 0.0]
Subtotal (95% CI)	**55**	**55**		**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)				
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.0$, df = 0 (P<0.00001); $I^2 = 0.0\%$				
Test for overall effect: Z = 0.0 (P < 0.00001)				
4 Paroxetine				
Ye 2004	0/30	0/30		0.0 [0.0, 0.0]
Subtotal (95% CI)	**30**	**30**		**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)				
Heterogeneity: not applicable				
Test for overall effect: Z = 0.0 (P < 0.00001)				



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Study or subgroup	SSRI n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
5 Escitalopram				
Robinson 2008	2/59	0/58		4.92 [0.24, 100.25]
Subtotal (95% CI)	**59**	**58**		**4.92 [0.24, 100.25]**
Total events: 2 (SSRI), 0 (Control)				
Heterogeneity: not applicable				
Test for overall effect: Z = 1.04 (P = 0.30)				
6 Sertraline or fluoxetine				
Subtotal (95% CI)	**0**	**0**		**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)				
Heterogeneity: not applicable				
Test for overall effect: not applicable				
Total (95% CI)	**439**	**394**		**1.13 [0.25, 4.97]**
Total events: 4 (SSRI), 3 (Control)				
Heterogeneity: Tau^2 = 0.0; Chi^2 = 2.29, df = 3 (P = 0.51); I^2 =0.0%				
Test for overall effect: Z = 0.16 (P = 0.88)				
Test for subgroup differences: Chi^2 = 2.22, df = 2 (P = 0.33), I^2 =10%				

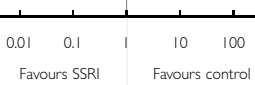
Analysis 8.10. Comparison 8 SSRI versus control at end of treatment, outcome assessor blind: low risk of bias, Outcome 10 Seizures.

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 8 SSRI versus control at end of treatment, outcome assessor blind: low risk of bias

Outcome: 10 Seizures

Study or subgroup	SSRI n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
1 Fluoxetine				
Chollet 2011	1/59	0/59		3.00 [0.12, 72.18]
He 2004	0/36	0/35		0.0 [0.0, 0.0]
Subtotal (95% CI)	**95**	**94**		**3.00 [0.12, 72.18]**
Total events: 1 (SSRI), 0 (Control)				
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.0$, df = 0 (P = 1.00); $I^2 = 0.0\%$				
Test for overall effect: Z = 0.68 (P = 0.50)				
2 Sertraline				
Subtotal (95% CI)	**0**	**0**		**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)				
Heterogeneity: not applicable				
Test for overall effect: not applicable				
3 Citalopram				
Subtotal (95% CI)	**0**	**0**		**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)				
Heterogeneity: not applicable				
Test for overall effect: not applicable				
4 Paroxetine				
Ye 2004	0/30	0/30		0.0 [0.0, 0.0]
Subtotal (95% CI)	**30**	**30**		**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)				
Heterogeneity: not applicable				
Test for overall effect: Z = 0.0 (P < 0.00001)				
5 Escitalopram				
Subtotal (95% CI)	**0**	**0**		**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)				
Heterogeneity: not applicable				
Test for overall effect: not applicable				
6 Sertraline or fluoxetine				
Subtotal (95% CI)	**0**	**0**		**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)				
Heterogeneity: not applicable				
Test for overall effect: not applicable				



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Study or subgroup	SSRI n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
Total (95% CI)	**125**	**124**		**3.00 [0.12, 72.18]**
Total events: 1 (SSRI), 0 (Control)				
Heterogeneity: Tau^2 = 0.0; Chi^2 = 0.0, df = 0 (P = 1.00); I^2 =0.0%				
Test for overall effect: Z = 0.68 (P = 0.50)				
Test for subgroup differences: Not applicable				

Analysis 8.11. Comparison 8 SSRI versus control at end of treatment, outcome assessor blind: low risk of bias, Outcome 11 Gastrointestinal side effects.

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 8 SSRI versus control at end of treatment, outcome assessor blind: low risk of bias

Outcome: 11 Gastrointestinal side effects

Study or subgroup	SSRI n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
1 Fluoxetine				
Chollet 2011	14/59	6/59		2.33 [0.96, 5.66]
He 2004	0/36	0/35		0.0 [0.0, 0.0]
Li 2008	6/60	3/30		1.00 [0.27, 3.72]
Subtotal (95% CI)	**155**	**124**		**1.77 [0.81, 3.85]**
Total events: 20 (SSRI), 9 (Control)				
Heterogeneity: Tau^2 = 0.03; Chi^2 = 1.10, df = 1 (P = 0.29); I^2 =9%				
Test for overall effect: Z = 1.43 (P = 0.15)				
2 Sertraline				
Burns 1999	0/14	1/14		0.33 [0.01, 7.55]
Subtotal (95% CI)	**14**	**14**		**0.33 [0.01, 7.55]**
Total events: 0 (SSRI), 1 (Control)				
Heterogeneity: not applicable				
Test for overall effect: Z = 0.69 (P = 0.49)				

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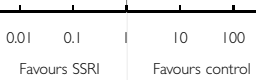
Study or subgroup	SSRI n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
3 Citalopram				
Subtotal (95% CI)	**0**	**0**		**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)				
Heterogeneity: not applicable				
Test for overall effect: not applicable				
4 Paroxetine				
Ye 2004	2/30	0/30		5.00 [0.25, 99.95]
Subtotal (95% CI)	**30**	**30**		**5.00 [0.25, 99.95]**
Total events: 2 (SSRI), 0 (Control)				
Heterogeneity: not applicable				
Test for overall effect: Z = 1.05 (P = 0.29)				
5 Escitalopram				
Subtotal (95% CI)	**0**	**0**		**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)				
Heterogeneity: not applicable				
Test for overall effect: not applicable				
6 Sertraline and paroxetine				
Subtotal (95% CI)	**0**	**0**		**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)				
Heterogeneity: not applicable				
Test for overall effect: not applicable				
Total (95% CI)	**199**	**168**		**1.74 [0.87, 3.49]**
Total events: 22 (SSRI), 10 (Control)				
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 2.66$, df = 3 (P = 0.45); $I^2 = 0.0\%$				
Test for overall effect: Z = 1.56 (P = 0.12)				
Test for subgroup differences: $Chi^2 = 1.55$, df = 2 (P = 0.46), $I^2 = 0.0\%$				



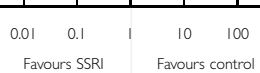
Analysis 8.15. Comparison 8 SSRI versus control at end of treatment, outcome assessor blind: low risk of bias, Outcome 15 Leaving the trial before the end of scheduled follow-up.

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 8 SSRI versus control at end of treatment, outcome assessor blind: low risk of bias

Outcome: 15 Leaving the trial before the end of scheduled follow-up

Study or subgroup	SSRI n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
1 Fluoxetine				
Brown 1998	1/10	0/10		3.00 [0.14, 65.90]
Chollet 2011	2/59	3/59		0.67 [0.12, 3.85]
Fruehwald 2003	6/28	8/26		0.70 [0.28, 1.74]
He 2004	8/44	5/40		1.45 [0.52, 4.08]
Kong 2007	11/48	6/42		1.60 [0.65, 3.96]
Li 2008	2/60	2/30		0.50 [0.07, 3.38]
Subtotal (95% CI)	**249**	**207**		**1.07 [0.65, 1.76]**
Total events: 30 (SSRI), 24 (Control)				
Heterogeneity: Tau^2 = 0.0; Chi^2 = 3.28, df = 5 (P = 0.66); I^2 =0.0%				
Test for overall effect: Z = 0.28 (P = 0.78)				
2 Sertraline				
Guo 2009	0/40	0/40		0.0 [0.0, 0.0]
Murray 2005	24/62	30/61		0.79 [0.53, 1.18]
Subtotal (95% CI)	**102**	**101**		**0.79 [0.53, 1.18]**
Total events: 24 (SSRI), 30 (Control)				
Heterogeneity: Tau^2 = 0.0; Chi^2 = 0.0, df = 0 (P = 1.00); I^2 =0.0%				
Test for overall effect: Z = 1.16 (P = 0.25)				
3 Citalopram				
Acler 2009	0/10	0/10		0.0 [0.0, 0.0]
Miao 2004	11/45	11/45		1.00 [0.48, 2.07]
Subtotal (95% CI)	**55**	**55**		**1.00 [0.48, 2.07]**
Total events: 11 (SSRI), 11 (Control)				
Heterogeneity: Tau^2 = 0.0; Chi^2 = 0.0, df = 0 (P = 1.00); I^2 =0.0%				
Test for overall effect: Z = 0.0 (P = 1.0)				
4 Paroxetine				
Ye 2004	1/30	0/31		3.10 [0.13, 73.16]
Subtotal (95% CI)	**30**	**31**		**3.10 [0.13, 73.16]**
Total events: 1 (SSRI), 0 (Control)				
Heterogeneity: not applicable				



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Study or subgroup	SSRI n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
Test for overall effect: Z = 0.70 (P = 0.48)				
5 Sertraline or fluoxetine				
Subtotal (95% CI)	**0**	**0**		**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)				
Heterogeneity: not applicable				
Test for overall effect: not applicable				
6 Escitalopram				
Robinson 2008	7/59	5/58		1.38 [0.46, 4.09]
Subtotal (95% CI)	**59**	**58**		**1.38 [0.46, 4.09]**
Total events: 7 (SSRI), 5 (Control)				
Heterogeneity: not applicable				
Test for overall effect: Z = 0.57 (P = 0.57)				
Total (95% CI)	**495**	**452**		**0.94 [0.71, 1.24]**
Total events: 73 (SSRI), 70 (Control)				
Heterogeneity: Tau^2 = 0.0; Chi^2 = 5.44, df = 9 (P = 0.79); I^2 =0.0%				
Test for overall effect: Z = 0.43 (P = 0.67)				
Test for subgroup differences: Chi^2 = 2.06, df = 4 (P = 0.72), I^2 =0.0%				

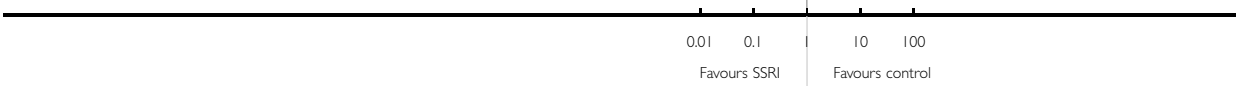
Analysis 9.1. Comparison 9 SSRI versus control at end of treatment, incomplete outcome data: low risk of bias, Outcome 1 Dependent on modified Rankin score (mRS 3 to 5).

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 9 SSRI versus control at end of treatment, incomplete outcome data: low risk of bias

Outcome: 1 Dependent on modified Rankin score (mRS 3 to 5)

Study or subgroup	SSRI n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
1 Fluoxetine				
Chollet 2011	42/57	50/55		0.81 [0.68, 0.97]
Subtotal (95% CI)	**57**	**55**		**0.81 [0.68, 0.97]**
Total events: 42 (SSRI), 50 (Control)				
Heterogeneity: not applicable				
Test for overall effect: Z = 2.34 (P = 0.019)				
2 Sertraline				
Almeida 2006	0/55	0/56		0.0 [0.0, 0.0]
Subtotal (95% CI)	**55**	**56**		**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)				
Heterogeneity: not applicable				
Test for overall effect: Z = 0.0 (P < 0.00001)				
Total (95% CI)	**112**	**111**		**0.81 [0.68, 0.97]**
Total events: 42 (SSRI), 50 (Control)				
Heterogeneity: Tau^2 = 0.0; Chi^2 = 0.0, df = 0 (P = 1.00); I^2 =0.0%				
Test for overall effect: Z = 2.34 (P = 0.019)				
Test for subgroup differences: Not applicable				



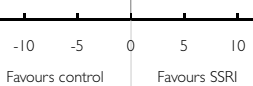
Analysis 9.2. Comparison 9 SSRI versus control at end of treatment, incomplete outcome data: low risk of bias, Outcome 2 Disability.

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 9 SSRI versus control at end of treatment, incomplete outcome data: low risk of bias

Outcome: 2 Disability

Study or subgroup	SSRI N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
1 Fluoxetine							
Cheng 2003	25	26.38 (14.2)	32	29.15 (17.38)		10.3 %	-0.17 [-0.69, 0.35]
Kong 2007	37	60.4 (12.5)	36	52.3 (13.5)		10.5 %	0.62 [0.15, 1.09]
Liu 2004	30	70.33 (10.74)	30	64.33 (7.74)		10.3 %	0.63 [0.11, 1.15]
Robinson 2000a	14	59.2 (11.6)	13	56.2 (7.8)		9.3 %	0.29 [-0.47, 1.05]
Robinson 2000b	13	60.5 (10.8)	15	63.1 (8.2)		9.4 %	-0.27 [-1.01, 0.48]
Wiart 2000	16	87.4 (22.8)	15	88.7 (25.3)		9.6 %	-0.05 [-0.76, 0.65]
Subtotal (95% CI)	**135**		**141**			**59.3 %**	**0.22 [-0.12, 0.55]**
Heterogeneity: $Tau^2 = 0.08$; $Chi^2 = 9.44$, df = 5 (P = 0.09); $I^2 = 47\%$							
Test for overall effect: Z = 1.26 (P = 0.21)							
2 Sertraline							
Xie 2005	65	88.7 (7.9)	65	79.8 (4.5)		10.7 %	1.38 [0.99, 1.76]
Subtotal (95% CI)	**65**		**65**			**10.7 %**	**1.38 [0.99, 1.76]**
Heterogeneity: not applicable							
Test for overall effect: Z = 7.03 (P < 0.00001)							
3 Citalopram							
Liu 2006	30	64.4 (12.1)	30	35.4 (9.1)		9.6 %	2.67 [1.97, 3.38]
Subtotal (95% CI)	**30**		**30**			**9.6 %**	**2.67 [1.97, 3.38]**
Heterogeneity: not applicable							
Test for overall effect: Z = 7.40 (P < 0.00001)							
4 Paroxetine							
Chen T 2005	40	65.76 (5.92)	38	51.76 (7.32)		10.2 %	2.09 [1.53, 2.64]
He 2005	27	84.26 (8.41)	27	78.33 (15.01)		10.2 %	0.48 [-0.06, 1.02]
Subtotal (95% CI)	**67**		**65**			**20.4 %**	**1.28 [-0.29, 2.86]**
Heterogeneity: $Tau^2 = 1.21$; $Chi^2 = 16.45$, df = 1 (P = 0.00005); $I^2 = 94\%$							
Test for overall effect: Z = 1.60 (P = 0.11)							
5 Escitalopram							
Subtotal (95% CI)	**0**		**0**			**0.0 %**	**0.0 [0.0, 0.0]**
Heterogeneity: not applicable							
Test for overall effect: not applicable							



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Study or subgroup	SSRI N	SSRI Mean(SD)	Control N	Control Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
6 Sertraline or fluoxetine							
Subtotal (95% CI)	**0**		**0**			**0.0 %**	**0.0 [0.0, 0.0]**
Heterogeneity: not applicable							
Test for overall effect: not applicable							
Total (95% CI)	**297**		**301**			**100.0 %**	**0.77 [0.22, 1.33]**
Heterogeneity: $Tau^2 = 0.70$; $Chi^2 = 86.62$, df = 9 (P<0.00001); I^2 =90%							
Test for overall effect: Z = 2.75 (P = 0.0060)							
Test for subgroup differences: $Chi^2 = 45.82$, df = 3 (P = 0.00), I^2 =93%							

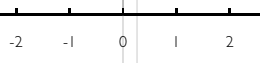
Analysis 9.3. Comparison 9 SSRI versus control at end of treatment, incomplete outcome data: low risk of bias, Outcome 3 Neurological deficit score.

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 9 SSRI versus control at end of treatment, incomplete outcome data: low risk of bias

Outcome: 3 Neurological deficit score

Study or subgroup	SSRI N	SSRI Mean(SD)	Control N	Control Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
1 Fluoxetine							
Chollet 2011	57	5.8 (3.7)	55	6.9 (4.4)		8.2 %	-0.27 [-0.64, 0.10]
He 2004	36	10.41 (6.36)	35	14.43 (7.94)		7.9 %	-0.55 [-1.03, -0.08]
Huang 2002	40	4.02 (1.86)	40	8.57 (3.64)		7.8 %	-1.56 [-2.06, -1.06]
Li 2004a	33	6.23 (3.11)	34	12.86 (6.36)		7.7 %	-1.30 [-1.83, -0.77]
Liang 2003	42	11.74 (3.23)	21	17.32 (5.19)		7.5 %	-1.38 [-1.96, -0.80]
Liu 2004	30	9.2 (2.06)	30	10.47 (9.2)		7.8 %	-0.19 [-0.70, 0.32]
Wen 2006	42	10.1 (1.9)	42	16.4 (2.5)		7.4 %	-2.81 [-3.42, -2.20]



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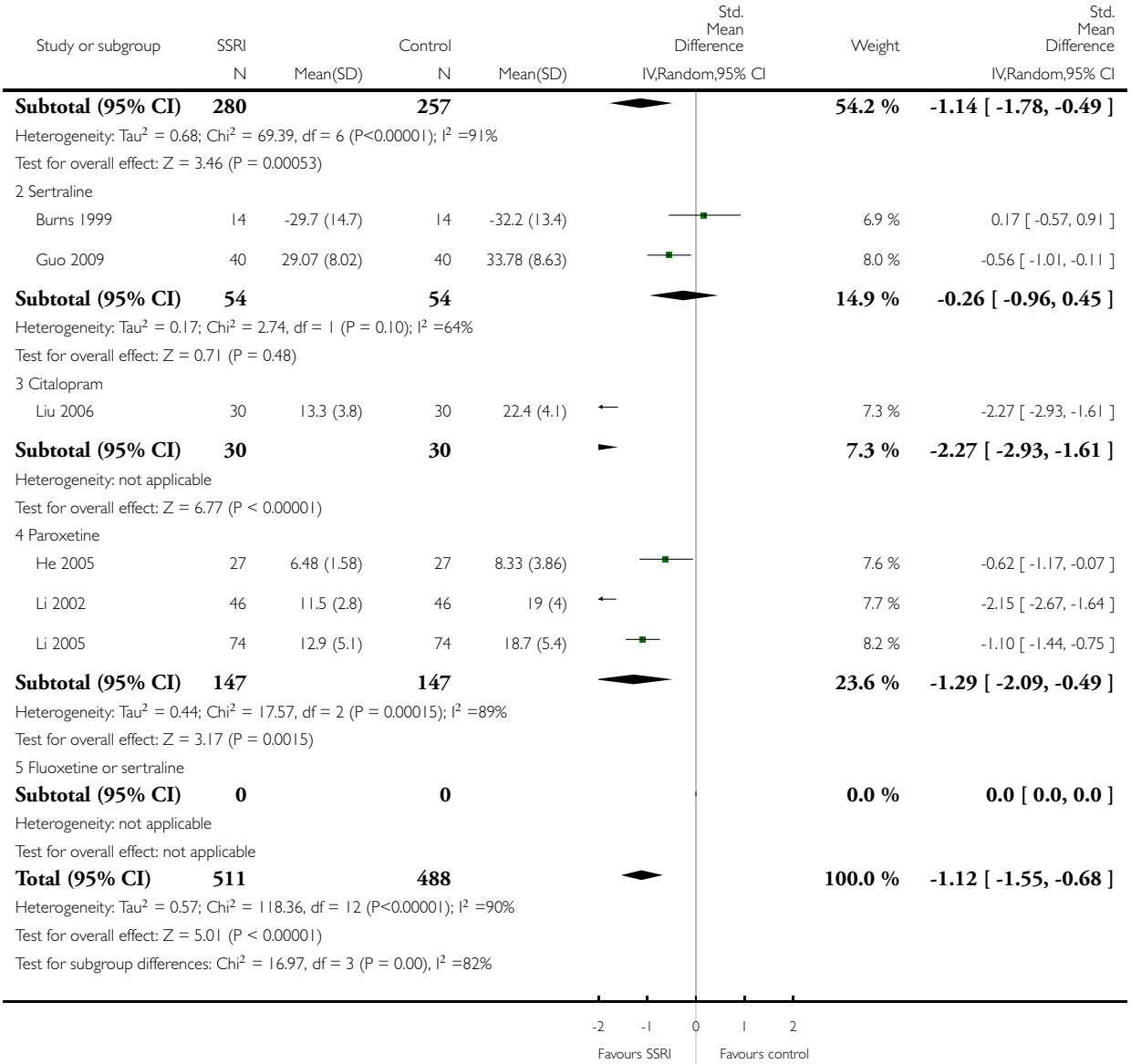
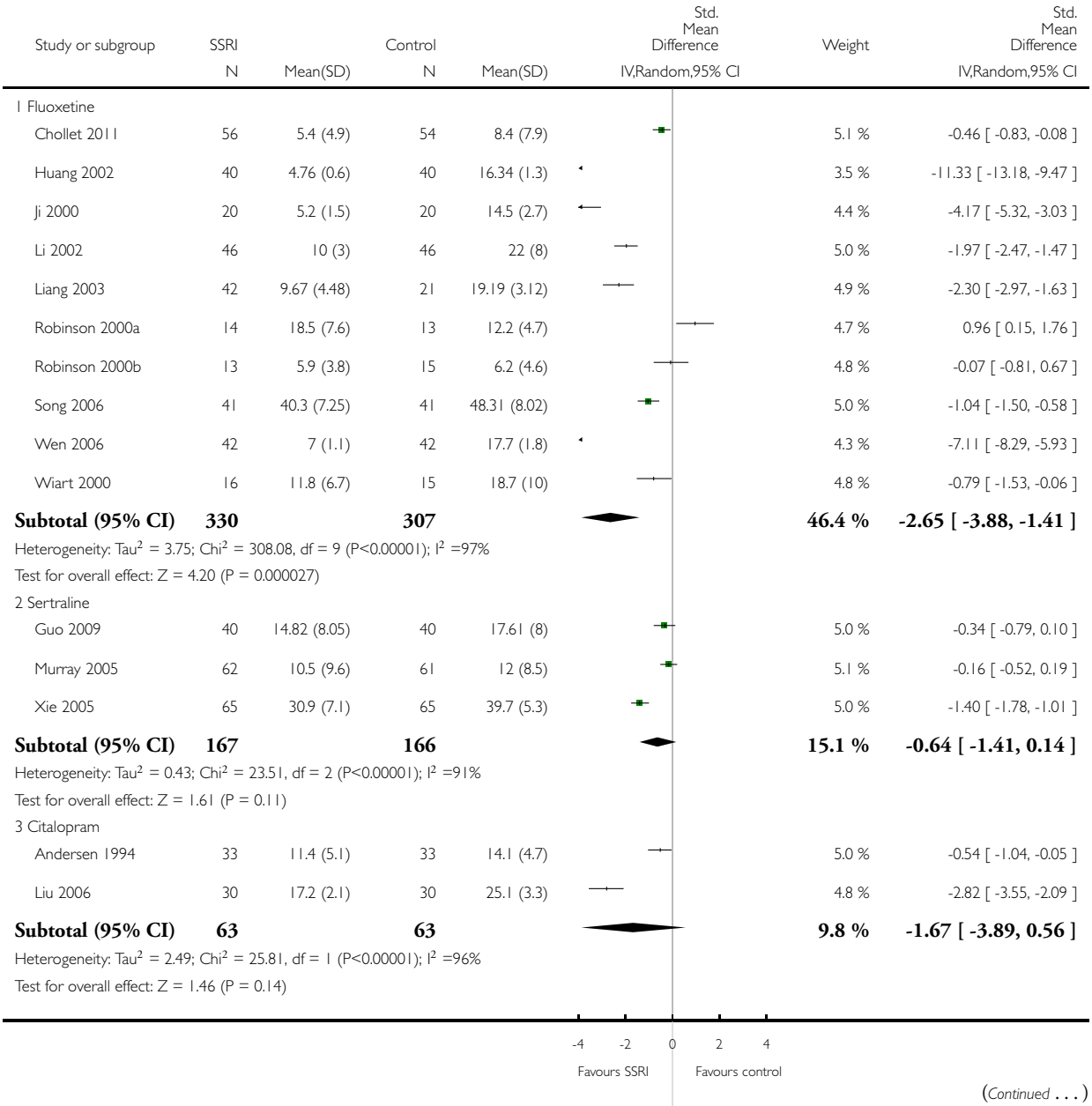


Analysis 9.4. Comparison 9 SSRI versus control at end of treatment, incomplete outcome data: low risk of bias, Outcome 4 Depression (continuous data).

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 9 SSRI versus control at end of treatment, incomplete outcome data: low risk of bias

Outcome: 4 Depression (continuous data)



Study or subgroup	SSRI N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
1 Fluoxetine							
Chollet 2011	56	5.4 (4.9)	54	8.4 (7.9)		5.1 %	-0.46 [-0.83, -0.08]
Huang 2002	40	4.76 (0.6)	40	16.34 (1.3)		3.5 %	-11.33 [-13.18, -9.47]
Ji 2000	20	5.2 (1.5)	20	14.5 (2.7)		4.4 %	-4.17 [-5.32, -3.03]
Li 2002	46	10 (3)	46	22 (8)		5.0 %	-1.97 [-2.47, -1.47]
Liang 2003	42	9.67 (4.48)	21	19.19 (3.12)		4.9 %	-2.30 [-2.97, -1.63]
Robinson 2000a	14	18.5 (7.6)	13	12.2 (4.7)		4.7 %	0.96 [0.15, 1.76]
Robinson 2000b	13	5.9 (3.8)	15	6.2 (4.6)		4.8 %	-0.07 [-0.81, 0.67]
Song 2006	41	40.3 (7.25)	41	48.31 (8.02)		5.0 %	-1.04 [-1.50, -0.58]
Wen 2006	42	7 (1.1)	42	17.7 (1.8)		4.3 %	-7.11 [-8.29, -5.93]
Wiart 2000	16	11.8 (6.7)	15	18.7 (10)		4.8 %	-0.79 [-1.53, -0.06]
Subtotal (95% CI)	**330**		**307**			**46.4 %**	**-2.65 [-3.88, -1.41]**
Heterogeneity: Tau^2 = 3.75; Chi^2 = 308.08, df = 9 (P<0.00001); I^2 =97%							
Test for overall effect: Z = 4.20 (P = 0.000027)							
2 Sertraline							
Guo 2009	40	14.82 (8.05)	40	17.61 (8)		5.0 %	-0.34 [-0.79, 0.10]
Murray 2005	62	10.5 (9.6)	61	12 (8.5)		5.1 %	-0.16 [-0.52, 0.19]
Xie 2005	65	30.9 (7.1)	65	39.7 (5.3)		5.0 %	-1.40 [-1.78, -1.01]
Subtotal (95% CI)	**167**		**166**			**15.1 %**	**-0.64 [-1.41, 0.14]**
Heterogeneity: Tau^2 = 0.43; Chi^2 = 23.51, df = 2 (P<0.00001); I^2 =91%							
Test for overall effect: Z = 1.61 (P = 0.11)							
3 Citalopram							
Andersen 1994	33	11.4 (5.1)	33	14.1 (4.7)		5.0 %	-0.54 [-1.04, -0.05]
Liu 2006	30	17.2 (2.1)	30	25.1 (3.3)		4.8 %	-2.82 [-3.55, -2.09]
Subtotal (95% CI)	**63**		**63**			**9.8 %**	**-1.67 [-3.89, 0.56]**
Heterogeneity: Tau^2 = 2.49; Chi^2 = 25.81, df = 1 (P<0.00001); I^2 =96%							
Test for overall effect: Z = 1.46 (P = 0.14)							

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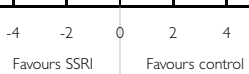
Study or subgroup	SSRI N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
4 Paroxetine							
Chen T 2005	40	10.98 (3.74)	38	22.45 (3.56)		4.9 %	-3.11 [-3.78, -2.44]
He 2005	27	10.11 (1.08)	27	17.48 (1.05)		4.0 %	-6.82 [-8.26, -5.38]
Lai 2006	40	12.5 (8.4)	40	21.5 (4.3)		5.0 %	-1.34 [-1.82, -0.85]
Li 2002	46	10 (3)	46	22 (8)		5.0 %	-1.97 [-2.47, -1.47]
Li 2005	74	12.6 (2.1)	74	16.8 (2.3)		5.0 %	-1.90 [-2.29, -1.51]
Yang 2011	20	7 (4)	22	13 (6)		4.9 %	-1.14 [-1.80, -0.49]
Subtotal (95% CI)	**247**		**247**			**28.7 %**	**-2.50 [-3.37, -1.63]**
Heterogeneity: Tau^2 = 1.06; Chi^2 = 67.49, df = 5 (P<0.00001); I^2 =93%							
Test for overall effect: Z = 5.61 (P < 0.00001)							
5 Fluoxetine or sertraline							
Subtotal (95% CI)	**0**		**0**			**0.0 %**	**0.0 [0.0, 0.0]**
Heterogeneity: not applicable							
Test for overall effect: not applicable							
Total (95% CI)	**807**		**783**			**100.0 %**	**-2.16 [-2.77, -1.55]**
Heterogeneity: Tau^2 = 1.87; Chi^2 = 492.43, df = 20 (P<0.00001); I^2 =96%							
Test for overall effect: Z = 6.96 (P < 0.00001)							
Test for subgroup differences: Chi^2 = 12.71, df = 3 (P = 0.01), I^2 =76%							



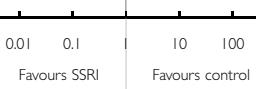
Analysis 9.5. Comparison 9 SSRI versus control at end of treatment, incomplete outcome data: low risk of bias, Outcome 5 Depression (dichotomous data).

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 9 SSRI versus control at end of treatment, incomplete outcome data: low risk of bias

Outcome: 5 Depression (dichotomous data)

Study or subgroup	SSRI n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
1 Fluoxetine				
Li 2004a	2/33	8/34		0.26 [0.06, 1.12]
Liu 2004	0/30	0/30		0.0 [0.0, 0.0]
Zhou 2008	4/36	18/40		0.25 [0.09, 0.66]
Subtotal (95% CI)	**99**	**104**		**0.25 [0.11, 0.57]**
Total events: 6 (SSRI), 26 (Control)				
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.00$, df = 1 (P = 0.96); $I^2 = 0.0\%$				
Test for overall effect: Z = 3.32 (P = 0.00091)				
2 Sertraline				
Almeida 2006	8/48	11/51		0.77 [0.34, 1.76]
Rasmussen 2003	3/35	8/32		0.34 [0.10, 1.18]
Subtotal (95% CI)	**83**	**83**		**0.59 [0.28, 1.25]**
Total events: 11 (SSRI), 19 (Control)				
Heterogeneity: $Tau^2 = 0.05$; $Chi^2 = 1.16$, df = 1 (P = 0.28); $I^2 = 14\%$				
Test for overall effect: Z = 1.37 (P = 0.17)				
3 Citalopram				
Subtotal (95% CI)	**0**	**0**		**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)				
Heterogeneity: not applicable				
Test for overall effect: not applicable				
4 Paroxetine				
Subtotal (95% CI)	**0**	**0**		**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)				
Heterogeneity: not applicable				
Test for overall effect: not applicable				
5 Escitalopram				
Robinson 2008	5/59	13/58		0.38 [0.14, 0.99]
Subtotal (95% CI)	**59**	**58**		**0.38 [0.14, 0.99]**
Total events: 5 (SSRI), 13 (Control)				
Heterogeneity: not applicable				
Test for overall effect: Z = 1.97 (P = 0.048)				
Total (95% CI)	**241**	**245**		**0.41 [0.26, 0.65]**



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Study or subgroup	SSRI n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
Total events: 22 (SSRI), 58 (Control)				
Heterogeneity: Tau² = 0.0; Chi² = 3.84, df = 4 (P = 0.43); I² =0.0%				
Test for overall effect: Z = 3.79 (P = 0.00015)				
Test for subgroup differences: Chi² = 2.29, df = 2 (P = 0.32), I² =13%				

Analysis 9.6. Comparison 9 SSRI versus control at end of treatment, incomplete outcome data: low risk of bias, Outcome 6 Anxiety (continuous data).

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 9 SSRI versus control at end of treatment, incomplete outcome data: low risk of bias

Outcome: 6 Anxiety (continuous data)

Study or subgroup	SSRI N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
1 Fluoxetine							
Liu 2004	30	7.43 (3.63)	30	11 (5.63)		20.8 %	-0.74 [-1.27, -0.22]
Robinson 2000a	14	9.8 (4.8)	13	9.9 (5.1)		19.7 %	-0.02 [-0.77, 0.74]
Robinson 2000b	13	4.7 (3.8)	15	5.5 (2.9)		19.8 %	-0.23 [-0.98, 0.51]
Subtotal (95% CI)	**57**		**58**			**60.3 %**	**-0.40 [-0.85, 0.05]**
Heterogeneity: Tau² = 0.05; Chi² = 2.78, df = 2 (P = 0.25); I² =28%							
Test for overall effect: Z = 1.76 (P = 0.078)							
2 Sertraline							
Subtotal (95% CI)	**0**		**0**			**0.0 %**	**0.0 [0.0, 0.0]**
Heterogeneity: not applicable							
Test for overall effect: not applicable							
3 Citalopram							
Subtotal (95% CI)	**0**		**0**			**0.0 %**	**0.0 [0.0, 0.0]**
Heterogeneity: not applicable							

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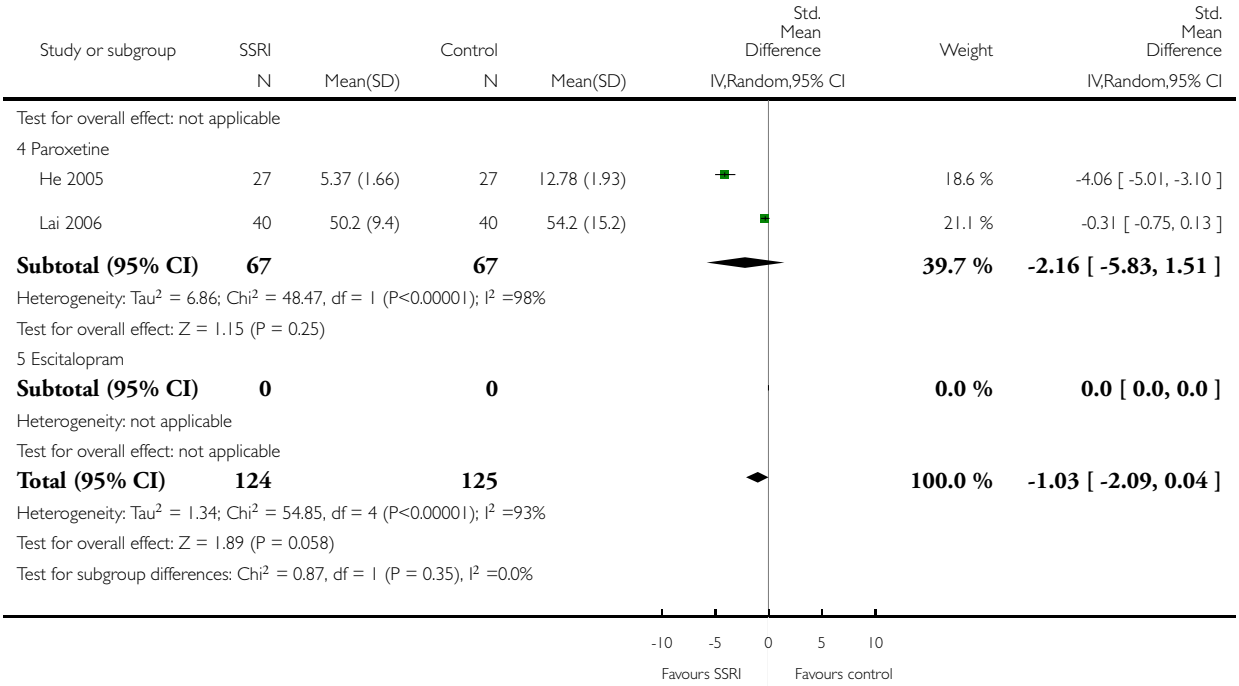
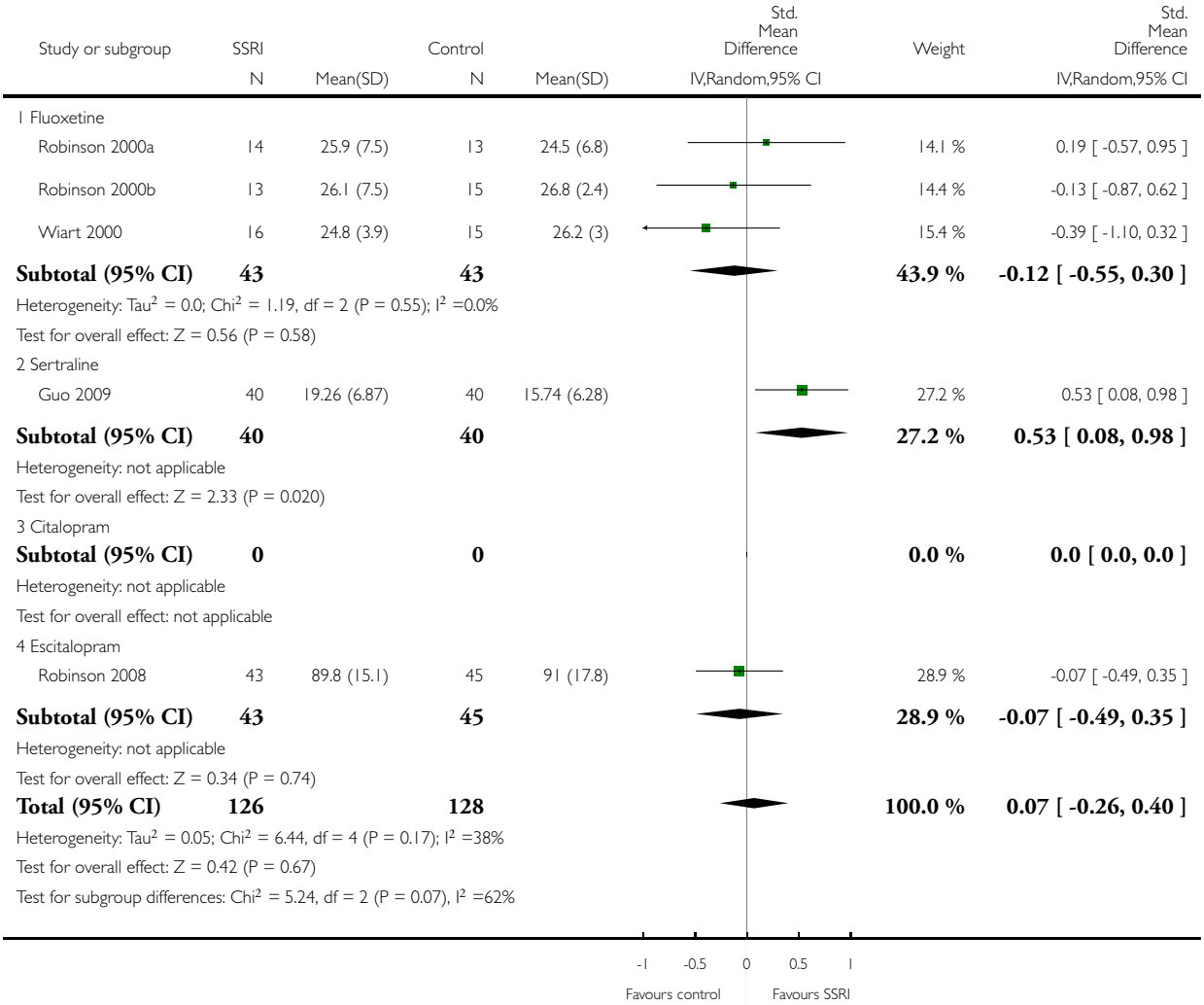


Analysis 9.8. Comparison 9 SSRI versus control at end of treatment, incomplete outcome data: low risk of bias, Outcome 8 Cognition (continuous scores end of treatment).

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 9 SSRI versus control at end of treatment, incomplete outcome data: low risk of bias

Outcome: 8 Cognition (continuous scores end of treatment)

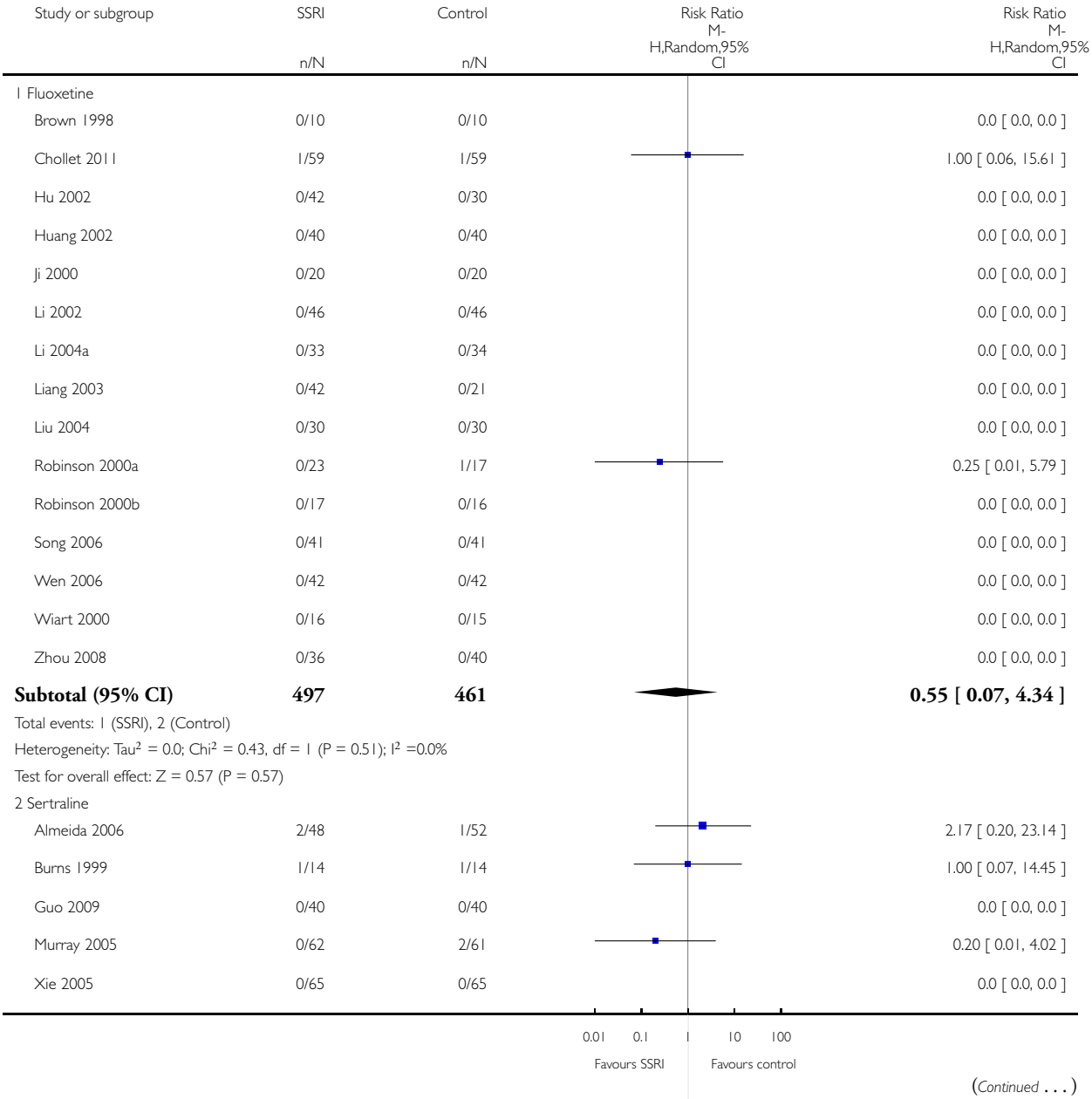


Analysis 9.9. Comparison 9 SSRI versus control at end of treatment, incomplete outcome data: low risk of bias, Outcome 9 Death.

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 9 SSRI versus control at end of treatment, incomplete outcome data: low risk of bias

Outcome: 9 Death



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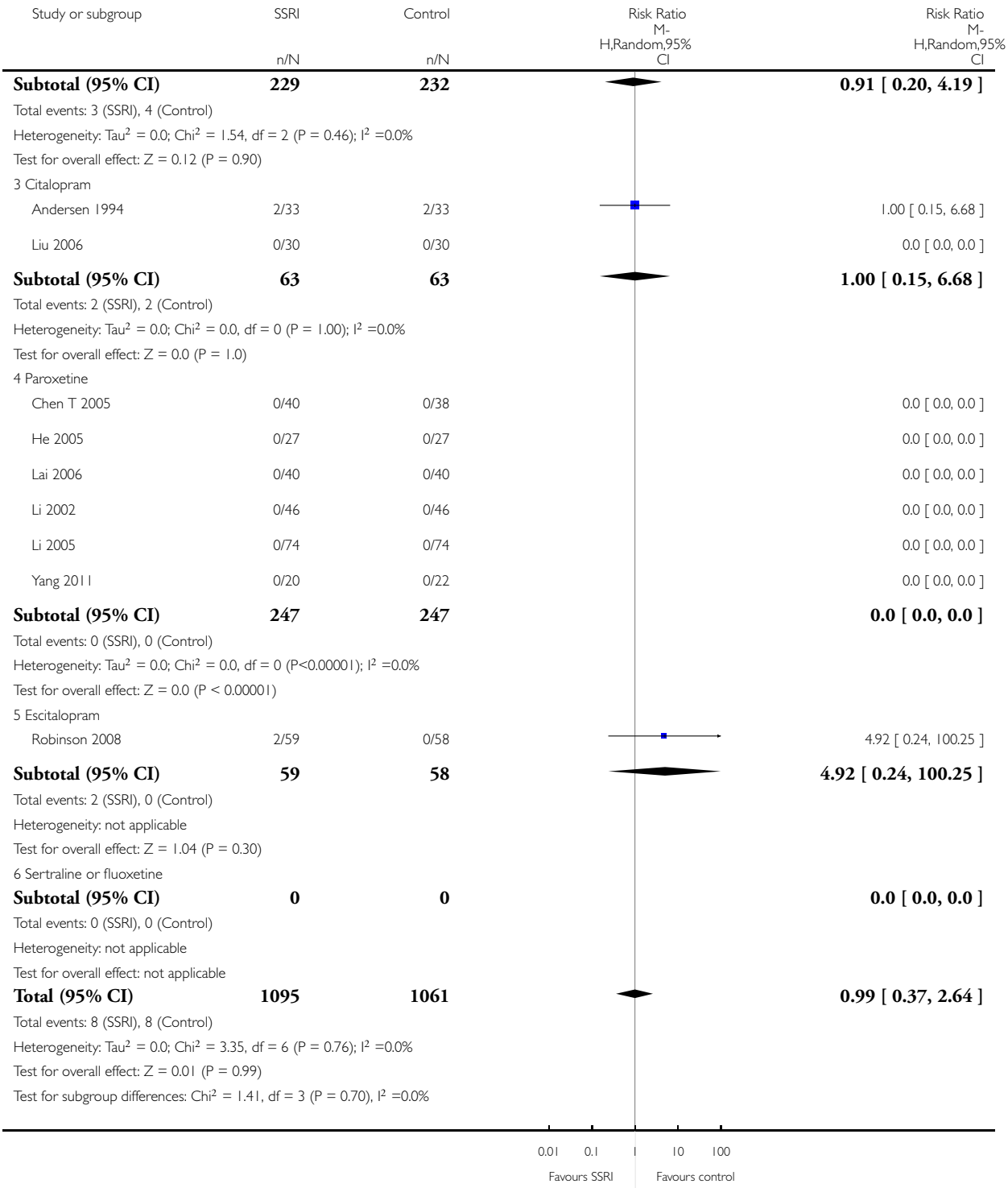


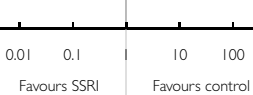
Analysis 9.10. Comparison 9 SSRI versus control at end of treatment, incomplete outcome data: low risk of bias, Outcome 10 Seizures.

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 9 SSRI versus control at end of treatment, incomplete outcome data: low risk of bias

Outcome: 10 Seizures

Study or subgroup	SSRI n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
1 Fluoxetine				
Chollet 2011	1/59	0/59		3.00 [0.12, 72.18]
Liang 2003	0/42	0/21		0.0 [0.0, 0.0]
Wiart 2000	1/16	1/15		0.94 [0.06, 13.68]
Subtotal (95% CI)	**117**	**95**		**1.52 [0.20, 11.80]**
Total events: 2 (SSRI), 1 (Control)				
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.30$, df = 1 (P = 0.58); $I^2 = 0.0\%$				
Test for overall effect: Z = 0.40 (P = 0.69)				
2 Sertraline				
Subtotal (95% CI)	**0**	**0**		**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)				
Heterogeneity: not applicable				
Test for overall effect: not applicable				
3 Citalopram				
Andersen 1994	2/33	0/33		5.00 [0.25, 100.32]
Subtotal (95% CI)	**33**	**33**		**5.00 [0.25, 100.32]**
Total events: 2 (SSRI), 0 (Control)				
Heterogeneity: not applicable				
Test for overall effect: Z = 1.05 (P = 0.29)				
4 Paroxetine				
He 2005	0/27	0/27		0.0 [0.0, 0.0]
Subtotal (95% CI)	**27**	**27**		**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)				
Heterogeneity: not applicable				
Test for overall effect: Z = 0.0 (P < 0.00001)				
5 Escitalopram				
Subtotal (95% CI)	**0**	**0**		**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)				
Heterogeneity: not applicable				
Test for overall effect: not applicable				



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Study or subgroup	SSRI n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
6 Sertraline or fluoxetine				
Subtotal (95% CI)	**0**	**0**		**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)				
Heterogeneity: not applicable				
Test for overall effect: not applicable				
Total (95% CI)	**177**	**155**		**2.22 [0.41, 12.06]**
Total events: 4 (SSRI), 1 (Control)				
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.73$, df = 2 (P = 0.70); $I^2 = 0.0\%$				
Test for overall effect: Z = 0.92 (P = 0.36)				
Test for subgroup differences: $Chi^2 = 0.41$, df = 1 (P = 0.52), $I^2 = 0.0\%$				

Analysis 9.11. Comparison 9 SSRI versus control at end of treatment, incomplete outcome data: low risk of bias, Outcome 11 Gastrointestinal side effects.

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 9 SSRI versus control at end of treatment, incomplete outcome data: low risk of bias

Outcome: 11 Gastrointestinal side effects

Study or subgroup	SSRI n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
1 Fluoxetine				
Chollet 2011	14/59	6/59		2.33 [0.96, 5.66]
Hu 2002	5/42	0/30		7.93 [0.46, 138.20]
Huang 2002	0/40	0/40		0.0 [0.0, 0.0]
Liang 2003	4/42	4/21		0.50 [0.14, 1.80]
Liu 2004	3/30	0/30		7.00 [0.38, 129.93]
Wiart 2000	1/16	3/16		0.33 [0.04, 2.87]
Subtotal (95% CI)	**229**	**196**		**1.43 [0.47, 4.36]**

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Study or subgroup	SSRI n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
Total events: 27 (SSRI), 13 (Control)				
Heterogeneity: Tau^2 = 0.75; Chi^2 = 8.16, df = 4 (P = 0.09); I^2 =51%				
Test for overall effect: Z = 0.63 (P = 0.53)				
2 Sertraline				
Burns 1999	0/14	1/14		0.33 [0.01, 7.55]
Subtotal (95% CI)	**14**	**14**		**0.33 [0.01, 7.55]**
Total events: 0 (SSRI), 1 (Control)				
Heterogeneity: not applicable				
Test for overall effect: Z = 0.69 (P = 0.49)				
3 Citalopram				
Subtotal (95% CI)	**0**	**0**		**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)				
Heterogeneity: not applicable				
Test for overall effect: not applicable				
4 Paroxetine				
He 2005	9/27	0/27		19.00 [1.16, 310.94]
Subtotal (95% CI)	**27**	**27**		**19.00 [1.16, 310.94]**
Total events: 9 (SSRI), 0 (Control)				
Heterogeneity: not applicable				
Test for overall effect: Z = 2.06 (P = 0.039)				
5 Escitalopram				
Subtotal (95% CI)	**0**	**0**		**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)				
Heterogeneity: not applicable				
Test for overall effect: not applicable				
6 Sertraline and paroxetine				
Subtotal (95% CI)	**0**	**0**		**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)				
Heterogeneity: not applicable				
Test for overall effect: not applicable				
Total (95% CI)	**270**	**237**		**1.67 [0.56, 4.97]**
Total events: 36 (SSRI), 14 (Control)				
Heterogeneity: Tau^2 = 1.00; Chi^2 = 12.75, df = 6 (P = 0.05); I^2 =53%				
Test for overall effect: Z = 0.92 (P = 0.36)				
Test for subgroup differences: Chi^2 = 4.00, df = 2 (P = 0.14), I^2 =50%				

Analysis 9.12. Comparison 9 SSRI versus control at end of treatment, incomplete outcome data: low risk of bias, Outcome 12 Bleeding.

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 9 SSRI versus control at end of treatment, incomplete outcome data: low risk of bias

Outcome: 12 Bleeding

Study or subgroup	SSRI n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
1 Fluoxetine					
Subtotal (95% CI)	**0**	**0**		**0.0 %**	**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)					
Heterogeneity: not applicable					
Test for overall effect: not applicable					
2 Sertraline					
Subtotal (95% CI)	**0**	**0**		**0.0 %**	**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)					
Heterogeneity: not applicable					
Test for overall effect: not applicable					
3 Citalopram					
Subtotal (95% CI)	**0**	**0**		**0.0 %**	**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)					
Heterogeneity: not applicable					
Test for overall effect: not applicable					
4 Paroxetine					
He 2005	9/27	0/27		100.0 %	19.00 [1.16, 310.94]
Subtotal (95% CI)	**27**	**27**		**100.0 %**	**19.00 [1.16, 310.94]**
Total events: 9 (SSRI), 0 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 2.06 (P = 0.039)					
5 Escitalopram					
Subtotal (95% CI)	**0**	**0**		**0.0 %**	**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)					
Heterogeneity: not applicable					
Test for overall effect: not applicable					
6 Sertraline or fluoxetine					
Subtotal (95% CI)	**0**	**0**		**0.0 %**	**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)					
Heterogeneity: not applicable					
Test for overall effect: not applicable					
Total (95% CI)	**27**	**27**		**100.0 %**	**19.00 [1.16, 310.94]**
Total events: 9 (SSRI), 0 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 2.06 (P = 0.039)					
Test for subgroup differences: Not applicable					

Analysis 9.14. Comparison 9 SSRI versus control at end of treatment, incomplete outcome data: low risk of bias, Outcome 14 Change in cognition between baseline and end of treatment.

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 9 SSRI versus control at end of treatment, incomplete outcome data: low risk of bias

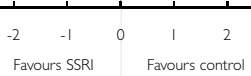
Outcome: 14 Change in cognition between baseline and end of treatment

Study or subgroup	SSRI N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
1 Sertraline							
Almeida 2006	48	2.6 (3.04)	51	2.6 (3.9)		100.0 %	0.0 [-0.39, 0.39]
Total (95% CI)	**48**		**51**			**100.0 %**	**0.0 [-0.39, 0.39]**

Heterogeneity: not applicable

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

Test for subgroup differences: Not applicable

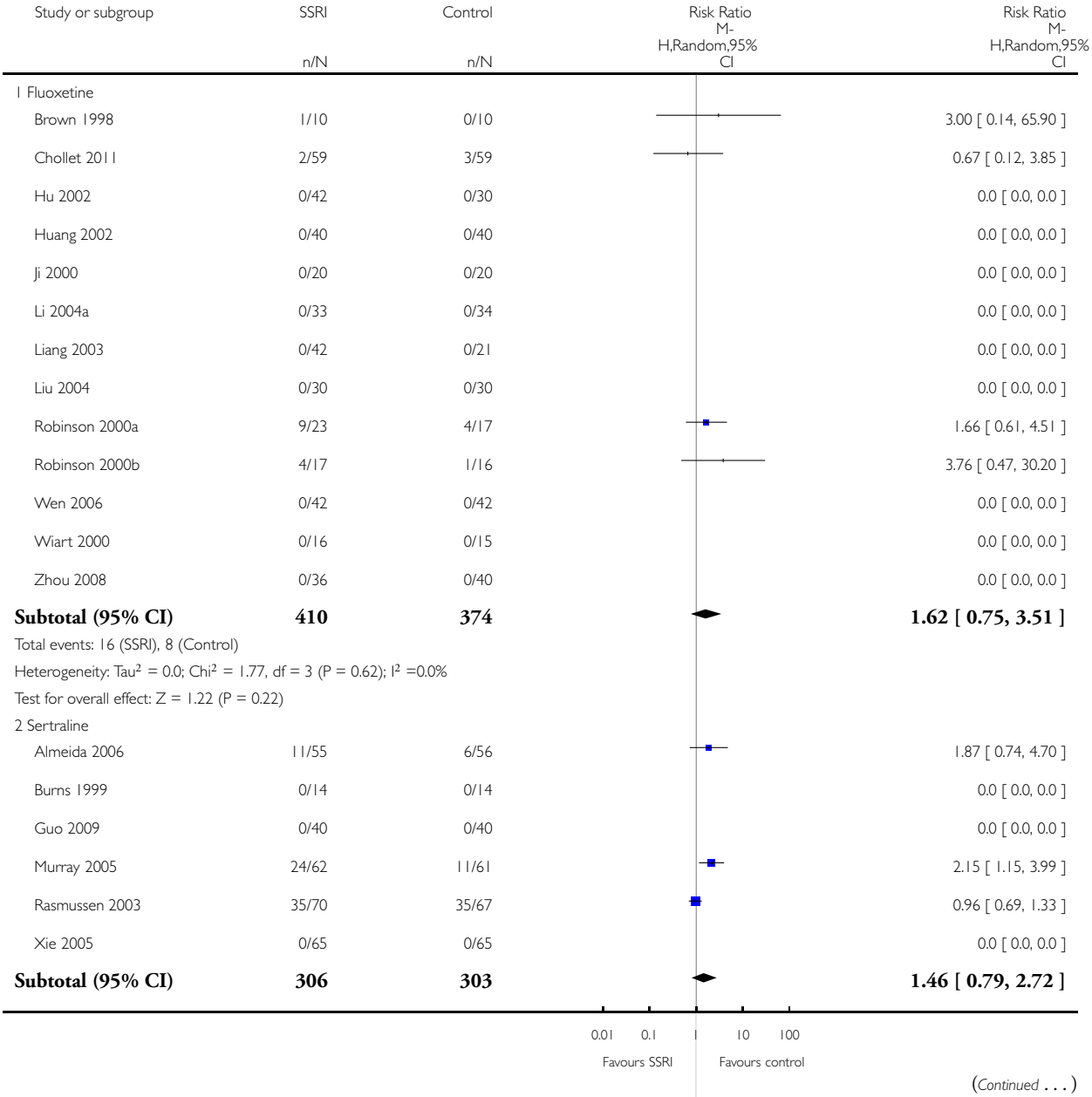


Analysis 9.15. Comparison 9 SSRI versus control at end of treatment, incomplete outcome data: low risk of bias, Outcome 15 Leaving the trial before the end of scheduled follow-up.

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 9 SSRI versus control at end of treatment, incomplete outcome data: low risk of bias

Outcome: 15 Leaving the trial before the end of scheduled follow-up



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Study or subgroup	SSRI n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
Total events: 70 (SSRI), 52 (Control)				
Heterogeneity: $Tau^2 = 0.20$; $Chi^2 = 6.53$, df = 2 (P = 0.04); $I^2 = 69\%$				
Test for overall effect: Z = 1.20 (P = 0.23)				
3 Citalopram				
Andersen 1994	6/33	1/33		6.00 [0.76, 47.14]
Liu 2006	0/30	0/30		0.0 [0.0, 0.0]
Subtotal (95% CI)	**63**	**63**		**6.00 [0.76, 47.14]**
Total events: 6 (SSRI), 1 (Control)				
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.0$, df = 0 (P = 1.00); $I^2 = 0.0\%$				
Test for overall effect: Z = 1.70 (P = 0.088)				
4 Paroxetine				
Chen T 2005	0/40	0/38		0.0 [0.0, 0.0]
He 2005	0/27	0/27		0.0 [0.0, 0.0]
Lai 2006	0/40	0/40		0.0 [0.0, 0.0]
Li 2002	0/46	0/46		0.0 [0.0, 0.0]
Li 2005	0/74	0/74		0.0 [0.0, 0.0]
Yang 2011	0/20	0/22		0.0 [0.0, 0.0]
Subtotal (95% CI)	**247**	**247**		**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)				
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.0$, df = 0 (P<0.00001); $I^2 = 0.0\%$				
Test for overall effect: Z = 0.0 (P < 0.00001)				
5 Sertraline or fluoxetine				
Subtotal (95% CI)	**0**	**0**		**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)				
Heterogeneity: not applicable				
Test for overall effect: not applicable				
6 Escitalopram				
Robinson 2008	7/59	5/58		1.38 [0.46, 4.09]
Subtotal (95% CI)	**59**	**58**		**1.38 [0.46, 4.09]**
Total events: 7 (SSRI), 5 (Control)				
Heterogeneity: not applicable				
Test for overall effect: Z = 0.57 (P = 0.57)				
Total (95% CI)	**1085**	**1045**		**1.51 [1.02, 2.23]**
Total events: 99 (SSRI), 66 (Control)				
Heterogeneity: $Tau^2 = 0.09$; $Chi^2 = 11.46$, df = 8 (P = 0.18); $I^2 = 30\%$				
Test for overall effect: Z = 2.07 (P = 0.038)				
Test for subgroup differences: $Chi^2 = 1.73$, df = 3 (P = 0.63), $I^2 = 0.0\%$				

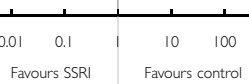
Analysis 10.1. Comparison 10 SSRI versus control at end of treatment, selective reporting: low risk, Outcome 1 Dependent on modified Rankin score (mRS 3 to 5).

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 10 SSRI versus control at end of treatment, selective reporting: low risk

Outcome: 1 Dependent on modified Rankin score (mRS 3 to 5)

Study or subgroup	SSRI n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
1 Fluoxetine				
Chollet 2011	42/57	50/55		0.81 [0.68, 0.97]
Subtotal (95% CI)	**57**	**55**		**0.81 [0.68, 0.97]**
Total events: 42 (SSRI), 50 (Control)				
Heterogeneity: not applicable				
Test for overall effect: Z = 2.34 (P = 0.019)				
2 Sertraline				
Almeida 2006	0/55	0/56		0.0 [0.0, 0.0]
Subtotal (95% CI)	**55**	**56**		**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)				
Heterogeneity: not applicable				
Test for overall effect: Z = 0.0 (P < 0.00001)				
Total (95% CI)	**112**	**111**		**0.81 [0.68, 0.97]**
Total events: 42 (SSRI), 50 (Control)				
Heterogeneity: Tau^2 = 0.0; Chi^2 = 0.0, df = 0 (P = 1.00); I^2 =0.0%				
Test for overall effect: Z = 2.34 (P = 0.019)				
Test for subgroup differences: Not applicable				



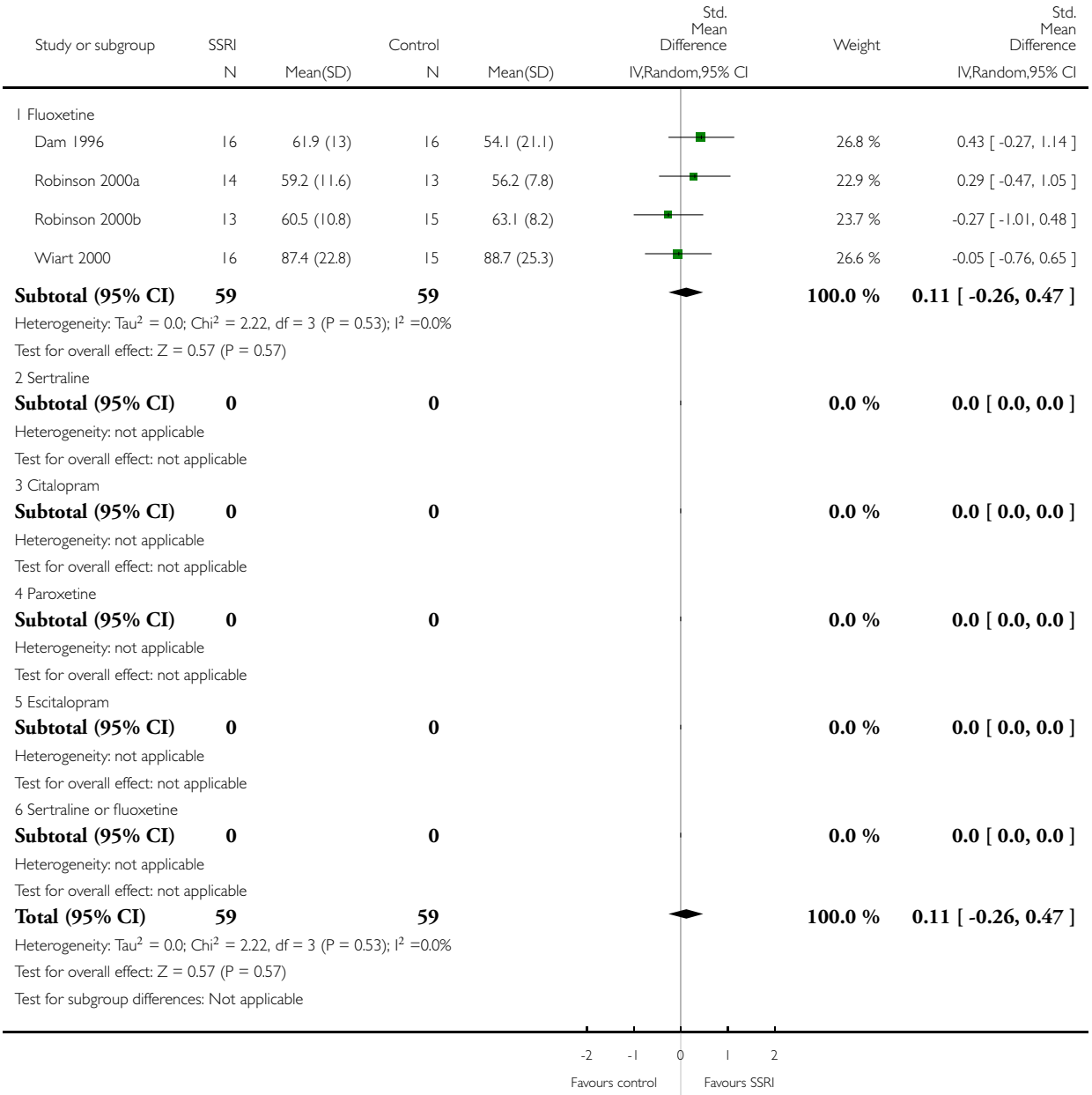
Analysis 10.2. Comparison 10 SSRI versus control at end of treatment, selective reporting: low risk, Outcome 2 Disability.

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 10 SSRI versus control at end of treatment, selective reporting: low risk

Outcome: 2 Disability

Study or subgroup	SSRI N	SSRI Mean(SD)	Control N	Control Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
1 Fluoxetine							
Dam 1996	16	61.9 (13)	16	54.1 (21.1)		26.8 %	0.43 [-0.27, 1.14]
Robinson 2000a	14	59.2 (11.6)	13	56.2 (7.8)		22.9 %	0.29 [-0.47, 1.05]
Robinson 2000b	13	60.5 (10.8)	15	63.1 (8.2)		23.7 %	-0.27 [-1.01, 0.48]
Wiart 2000	16	87.4 (22.8)	15	88.7 (25.3)		26.6 %	-0.05 [-0.76, 0.65]
Subtotal (95% CI)	**59**		**59**			**100.0 %**	**0.11 [-0.26, 0.47]**
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 2.22$, df = 3 (P = 0.53); $I^2 = 0.0\%$							
Test for overall effect: Z = 0.57 (P = 0.57)							
2 Sertraline							
Subtotal (95% CI)	**0**		**0**			**0.0 %**	**0.0 [0.0, 0.0]**
Heterogeneity: not applicable							
Test for overall effect: not applicable							
3 Citalopram							
Subtotal (95% CI)	**0**		**0**			**0.0 %**	**0.0 [0.0, 0.0]**
Heterogeneity: not applicable							
Test for overall effect: not applicable							
4 Paroxetine							
Subtotal (95% CI)	**0**		**0**			**0.0 %**	**0.0 [0.0, 0.0]**
Heterogeneity: not applicable							
Test for overall effect: not applicable							
5 Escitalopram							
Subtotal (95% CI)	**0**		**0**			**0.0 %**	**0.0 [0.0, 0.0]**
Heterogeneity: not applicable							
Test for overall effect: not applicable							
6 Sertraline or fluoxetine							
Subtotal (95% CI)	**0**		**0**			**0.0 %**	**0.0 [0.0, 0.0]**
Heterogeneity: not applicable							
Test for overall effect: not applicable							
Total (95% CI)	**59**		**59**			**100.0 %**	**0.11 [-0.26, 0.47]**
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 2.22$, df = 3 (P = 0.53); $I^2 = 0.0\%$							
Test for overall effect: Z = 0.57 (P = 0.57)							
Test for subgroup differences: Not applicable							



Analysis 10.3. Comparison 10 SSRI versus control at end of treatment, selective reporting: low risk, Outcome 3 Neurological deficit score.

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 10 SSRI versus control at end of treatment, selective reporting: low risk

Outcome: 3 Neurological deficit score

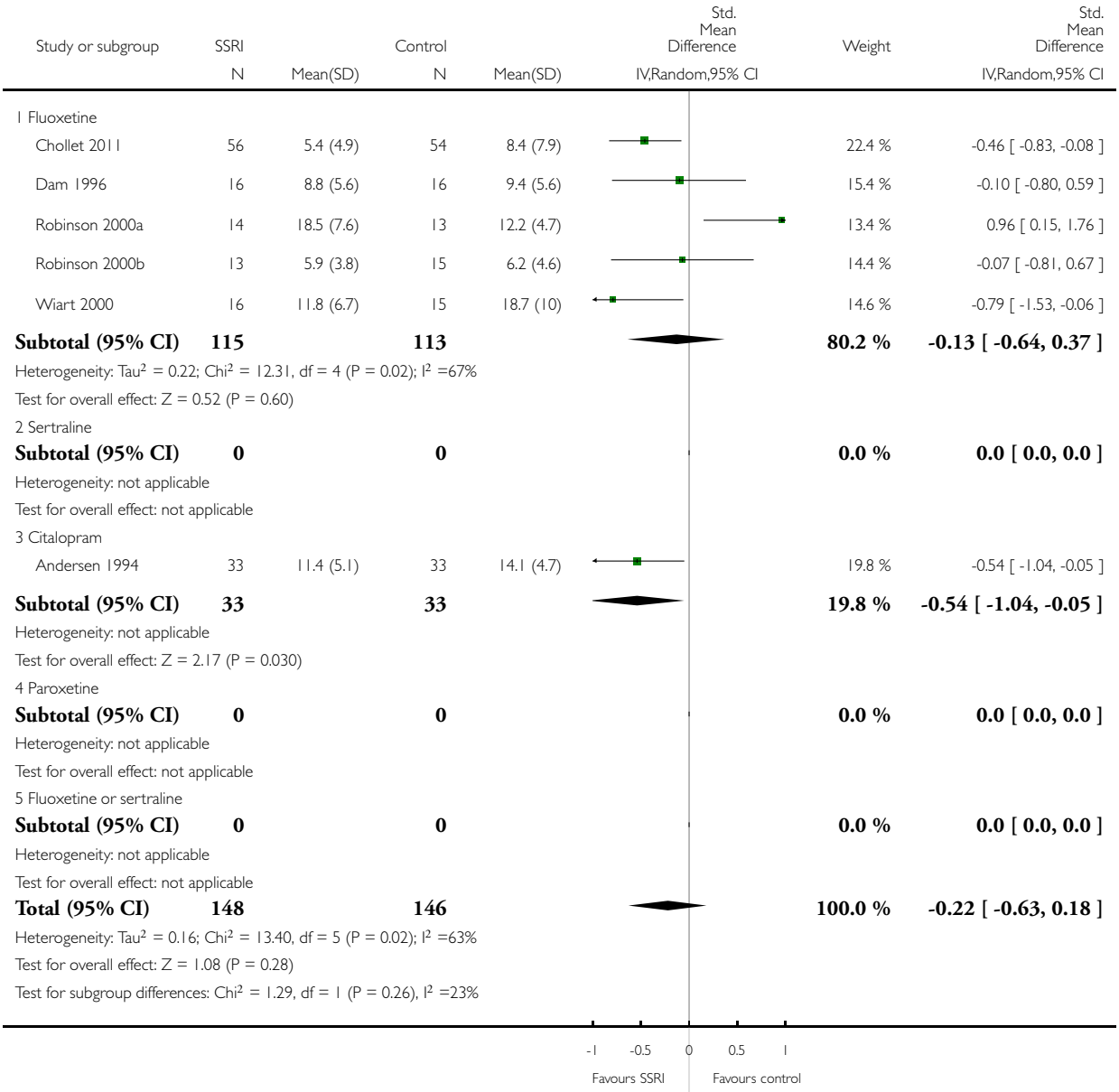
Study or subgroup	SSRI N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
1 Fluoxetine							
Chollet 2011	57	5.8 (3.7)	55	6.9 (4.4)		65.1 %	-0.27 [-0.64, 0.10]
Dam 1996	16	44.1 (9.4)	16	46.8 (9.9)		18.6 %	-0.27 [-0.97, 0.42]
Subtotal (95% CI)	**73**		**71**			**83.6 %**	**-0.27 [-0.60, 0.06]**
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.00$, df = 1 (P = 0.99); $I^2 = 0.0\%$							
Test for overall effect: Z = 1.61 (P = 0.11)							
2 Sertraline							
Burns 1999	14	-29.7 (14.7)	14	-32.2 (13.4)		16.4 %	0.17 [-0.57, 0.91]
Subtotal (95% CI)	**14**		**14**			**16.4 %**	**0.17 [-0.57, 0.91]**
Heterogeneity: not applicable							
Test for overall effect: Z = 0.46 (P = 0.65)							
3 Citalopram							
Subtotal (95% CI)	**0**		**0**			**0.0 %**	**0.0 [0.0, 0.0]**
Heterogeneity: not applicable							
Test for overall effect: not applicable							
4 Paroxetine							
Subtotal (95% CI)	**0**		**0**			**0.0 %**	**0.0 [0.0, 0.0]**
Heterogeneity: not applicable							
Test for overall effect: not applicable							
5 Fluoxetine or sertraline							
Subtotal (95% CI)	**0**		**0**			**0.0 %**	**0.0 [0.0, 0.0]**
Heterogeneity: not applicable							
Test for overall effect: not applicable							
Total (95% CI)	**87**		**85**			**100.0 %**	**-0.20 [-0.50, 0.10]**
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 1.14$, df = 2 (P = 0.57); $I^2 = 0.0\%$							
Test for overall effect: Z = 1.29 (P = 0.20)							
Test for subgroup differences: $Chi^2 = 1.14$, df = 1 (P = 0.29), $I^2 = 12\%$							

Analysis 10.4. Comparison 10 SSRI versus control at end of treatment, selective reporting: low risk, Outcome 4 Depression (continuous data).

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 10 SSRI versus control at end of treatment, selective reporting: low risk

Outcome: 4 Depression (continuous data)



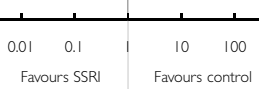
Analysis 10.5. Comparison 10 SSRI versus control at end of treatment, selective reporting: low risk, Outcome 5 Depression (dichotomous data).

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 10 SSRI versus control at end of treatment, selective reporting: low risk

Outcome: 5 Depression (dichotomous data)

Study or subgroup	SSRI n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
1 Fluoxetine					
Subtotal (95% CI)	**0**	**0**		**0.0 %**	**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)					
Heterogeneity: not applicable					
Test for overall effect: not applicable					
2 Sertraline					
Almeida 2006	8/48	11/51		46.2 %	0.77 [0.34, 1.76]
Rasmussen 2003	3/35	8/32		20.4 %	0.34 [0.10, 1.18]
Subtotal (95% CI)	**83**	**83**		**66.6 %**	**0.59 [0.28, 1.25]**
Total events: 11 (SSRI), 19 (Control)					
Heterogeneity: $Tau^2 = 0.05$; $Chi^2 = 1.16$, df = 1 (P = 0.28); $I^2 = 14\%$					
Test for overall effect: Z = 1.37 (P = 0.17)					
3 Citalopram					
Subtotal (95% CI)	**0**	**0**		**0.0 %**	**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)					
Heterogeneity: not applicable					
Test for overall effect: not applicable					
4 Paroxetine					
Subtotal (95% CI)	**0**	**0**		**0.0 %**	**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)					
Heterogeneity: not applicable					
Test for overall effect: not applicable					
5 Escitalopram					
Robinson 2008	5/59	13/58		33.4 %	0.38 [0.14, 0.99]
Subtotal (95% CI)	**59**	**58**		**33.4 %**	**0.38 [0.14, 0.99]**
Total events: 5 (SSRI), 13 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.97 (P = 0.048)					
Total (95% CI)	**142**	**141**		**100.0 %**	**0.52 [0.30, 0.90]**
Total events: 16 (SSRI), 32 (Control)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 1.76$, df = 2 (P = 0.41); $I^2 = 0.0\%$					
Test for overall effect: Z = 2.32 (P = 0.020)					
Test for subgroup differences: $Chi^2 = 0.51$, df = 1 (P = 0.48), $I^2 = 0.0\%$					



Analysis 10.6. Comparison 10 SSRI versus control at end of treatment, selective reporting: low risk, Outcome 6 Anxiety (continuous data).

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 10 SSRI versus control at end of treatment, selective reporting: low risk

Outcome: 6 Anxiety (continuous data)

Study or subgroup	SSRI N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
1 Fluoxetine							
Robinson 2000a	14	9.8 (4.8)	13	9.9 (5.1)		49.4 %	-0.02 [-0.77, 0.74]
Robinson 2000b	13	4.7 (3.8)	15	5.5 (2.9)		50.6 %	-0.23 [-0.98, 0.51]
Subtotal (95% CI)	**27**		**28**			**100.0 %**	**-0.13 [-0.66, 0.40]**
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.15$, df = 1 (P = 0.69); $I^2 = 0.0\%$							
Test for overall effect: Z = 0.47 (P = 0.64)							
2 Sertraline							
Subtotal (95% CI)	**0**		**0**			**0.0 %**	**0.0 [0.0, 0.0]**
Heterogeneity: not applicable							
Test for overall effect: not applicable							
3 Citalopram							
Subtotal (95% CI)	**0**		**0**			**0.0 %**	**0.0 [0.0, 0.0]**
Heterogeneity: not applicable							
Test for overall effect: not applicable							
4 Paroxetine							
Subtotal (95% CI)	**0**		**0**			**0.0 %**	**0.0 [0.0, 0.0]**
Heterogeneity: not applicable							
Test for overall effect: not applicable							
5 Escitalopram							
Subtotal (95% CI)	**0**		**0**			**0.0 %**	**0.0 [0.0, 0.0]**
Heterogeneity: not applicable							
Test for overall effect: not applicable							
Total (95% CI)	**27**		**28**			**100.0 %**	**-0.13 [-0.66, 0.40]**
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.15$, df = 1 (P = 0.69); $I^2 = 0.0\%$							
Test for overall effect: Z = 0.47 (P = 0.64)							
Test for subgroup differences: Not applicable							

Analysis 10.8. Comparison 10 SSRI versus control at end of treatment, selective reporting: low risk, Outcome 8 Cognition (continuous scores end of treatment).

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 10 SSRI versus control at end of treatment, selective reporting: low risk

Outcome: 8 Cognition (continuous scores end of treatment)

Study or subgroup	SSRI N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
1 Fluoxetine							
Robinson 2000a	14	25.9 (7.5)	13	24.5 (6.8)		31.6 %	0.19 [-0.57, 0.95]
Robinson 2000b	13	26.1 (7.5)	15	26.8 (2.4)		32.7 %	-0.13 [-0.87, 0.62]
Wiart 2000	16	24.8 (3.9)	15	26.2 (3)		35.7 %	-0.39 [-1.10, 0.32]
Subtotal (95% CI)	**43**		**43**			**100.0 %**	**-0.12 [-0.55, 0.30]**
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 1.19$, df = 2 (P = 0.55); $I^2 = 0.0\%$							
Test for overall effect: Z = 0.56 (P = 0.58)							
2 Sertraline							
Subtotal (95% CI)	**0**		**0**			**0.0 %**	**0.0 [0.0, 0.0]**
Heterogeneity: not applicable							
Test for overall effect: not applicable							
3 Citalopram							
Subtotal (95% CI)	**0**		**0**			**0.0 %**	**0.0 [0.0, 0.0]**
Heterogeneity: not applicable							
Test for overall effect: not applicable							
Total (95% CI)	**43**		**43**			**100.0 %**	**-0.12 [-0.55, 0.30]**
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 1.19$, df = 2 (P = 0.55); $I^2 = 0.0\%$							
Test for overall effect: Z = 0.56 (P = 0.58)							
Test for subgroup differences: Not applicable							

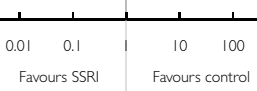
Analysis 10.9. Comparison 10 SSRI versus control at end of treatment, selective reporting: low risk, Outcome 9 Death.

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 10 SSRI versus control at end of treatment, selective reporting: low risk

Outcome: 9 Death

Study or subgroup	SSRI n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
1 Fluoxetine				
Chollet 2011	1/59	1/59		1.00 [0.06, 15.61]
Dam 1996	0/18	0/17		0.0 [0.0, 0.0]
Robinson 2000a	0/23	1/17		0.25 [0.01, 5.79]
Robinson 2000b	0/17	0/16		0.0 [0.0, 0.0]
Wiart 2000	0/16	0/15		0.0 [0.0, 0.0]
Subtotal (95% CI)	**133**	**124**		**0.55 [0.07, 4.34]**
Total events: 1 (SSRI), 2 (Control)				
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.43$, df = 1 (P = 0.51); $I^2 = 0.0\%$				
Test for overall effect: Z = 0.57 (P = 0.57)				
2 Sertraline				
Almeida 2006	2/48	1/52		2.17 [0.20, 23.14]
Burns 1999	1/14	1/14		1.00 [0.07, 14.45]
Subtotal (95% CI)	**62**	**66**		**1.54 [0.26, 9.07]**
Total events: 3 (SSRI), 2 (Control)				
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.18$, df = 1 (P = 0.67); $I^2 = 0.0\%$				
Test for overall effect: Z = 0.48 (P = 0.63)				
3 Citalopram				
Andersen 1994	2/33	2/33		1.00 [0.15, 6.68]
Subtotal (95% CI)	**33**	**33**		**1.00 [0.15, 6.68]**
Total events: 2 (SSRI), 2 (Control)				
Heterogeneity: not applicable				
Test for overall effect: Z = 0.0 (P = 1.0)				
4 Paroxetine				
Subtotal (95% CI)	**0**	**0**		**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)				
Heterogeneity: not applicable				
Test for overall effect: not applicable				
5 Escitalopram				
Robinson 2008	2/59	0/58		4.92 [0.24, 100.25]
Subtotal (95% CI)	**59**	**58**		**4.92 [0.24, 100.25]**



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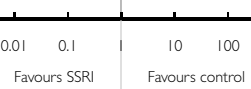
Study or subgroup	SSRI n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
Total events: 2 (SSRI), 0 (Control)				
Heterogeneity: not applicable				
Test for overall effect: Z = 1.04 (P = 0.30)				
6 Sertraline or fluoxetine				
Subtotal (95% CI)	**0**	**0**		**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)				
Heterogeneity: not applicable				
Test for overall effect: not applicable				
Total (95% CI)	**287**	**281**		**1.20 [0.43, 3.37]**
Total events: 8 (SSRI), 6 (Control)				
Heterogeneity: Tau^2 = 0.0; Chi^2 = 2.11, df = 5 (P = 0.83); I^2 =0.0%				
Test for overall effect: Z = 0.35 (P = 0.73)				
Test for subgroup differences: Chi^2 = 1.50, df = 3 (P = 0.68), I^2 =0.0%				



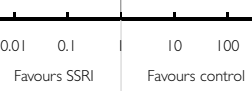
Analysis 10.10. Comparison 10 SSRI versus control at end of treatment, selective reporting: low risk, Outcome 10 Seizures.

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 10 SSRI versus control at end of treatment, selective reporting: low risk

Outcome: 10 Seizures

Study or subgroup	SSRI n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
1 Fluoxetine					
Chollet 2011	1/59	0/59		21.4 %	3.00 [0.12, 72.18]
Dam 1996	2/18	0/17		24.5 %	4.74 [0.24, 92.07]
Wiart 2000	1/16	1/15		30.1 %	0.94 [0.06, 13.68]
Subtotal (95% CI)	**93**	**91**		**76.0 %**	**2.19 [0.41, 11.85]**
Total events: 4 (SSRI), 1 (Control)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.69$, df = 2 (P = 0.71); $I^2 = 0.0\%$					
Test for overall effect: Z = 0.91 (P = 0.36)					
2 Sertraline					
Subtotal (95% CI)	**0**	**0**		**0.0 %**	**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)					
Heterogeneity: not applicable					
Test for overall effect: not applicable					
3 Citalopram					
Andersen 1994	2/33	0/33		24.0 %	5.00 [0.25, 100.32]
Subtotal (95% CI)	**33**	**33**		**24.0 %**	**5.00 [0.25, 100.32]**
Total events: 2 (SSRI), 0 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.05 (P = 0.29)					
4 Paroxetine					
Subtotal (95% CI)	**0**	**0**		**0.0 %**	**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)					
Heterogeneity: not applicable					
Test for overall effect: not applicable					
5 Escitalopram					
Subtotal (95% CI)	**0**	**0**		**0.0 %**	**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)					
Heterogeneity: not applicable					
Test for overall effect: not applicable					
6 Sertraline or fluoxetine					
Subtotal (95% CI)	**0**	**0**		**0.0 %**	**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)					
Heterogeneity: not applicable					



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Study or subgroup	SSRI n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Test for overall effect: not applicable					
Total (95% CI)	**126**	**124**		**100.0 %**	**2.67 [0.61, 11.63]**
Total events: 6 (SSRI), 1 (Control)					
Heterogeneity: Tau^2 = 0.0; Chi^2 = 0.91, df = 3 (P = 0.82); I^2 =0.0%					
Test for overall effect: Z = 1.31 (P = 0.19)					
Test for subgroup differences: Chi^2 = 0.22, df = 1 (P = 0.64), I^2 =0.0%					

Analysis 10.11. Comparison 10 SSRI versus control at end of treatment, selective reporting: low risk, Outcome 11 Gastrointestinal side effects.

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 10 SSRI versus control at end of treatment, selective reporting: low risk

Outcome: 11 Gastrointestinal side effects

Study or subgroup	SSRI n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
1 Fluoxetine					
Chollet 2011	14/59	6/59		54.2 %	2.33 [0.96, 5.66]
Dam 1996	2/18	0/17		12.8 %	4.74 [0.24, 92.07]
Wiart 2000	1/16	3/16		21.2 %	0.33 [0.04, 2.87]
Subtotal (95% CI)	**93**	**92**		**88.2 %**	**1.60 [0.44, 5.77]**
Total events: 17 (SSRI), 9 (Control)					
Heterogeneity: Tau^2 = 0.51; Chi^2 = 3.08, df = 2 (P = 0.21); I^2 =35%					
Test for overall effect: Z = 0.72 (P = 0.47)					
2 Sertraline					
Burns 1999	0/14	1/14		11.8 %	0.33 [0.01, 7.55]
Subtotal (95% CI)	**14**	**14**		**11.8 %**	**0.33 [0.01, 7.55]**
Total events: 0 (SSRI), 1 (Control)					
Heterogeneity: not applicable					

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Study or subgroup	SSRI n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Test for overall effect: Z = 0.69 (P = 0.49)					
3 Citalopram					
Subtotal (95% CI)	**0**	**0**		**0.0 %**	**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)					
Heterogeneity: not applicable					
Test for overall effect: not applicable					
4 Paroxetine					
Subtotal (95% CI)	**0**	**0**		**0.0 %**	**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)					
Heterogeneity: not applicable					
Test for overall effect: not applicable					
5 Escitalopram					
Subtotal (95% CI)	**0**	**0**		**0.0 %**	**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)					
Heterogeneity: not applicable					
Test for overall effect: not applicable					
6 Sertraline and paroxetine					
Subtotal (95% CI)	**0**	**0**		**0.0 %**	**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)					
Heterogeneity: not applicable					
Test for overall effect: not applicable					
Total (95% CI)	**107**	**106**		**100.0 %**	**1.35 [0.42, 4.29]**
Total events: 17 (SSRI), 10 (Control)					
Heterogeneity: Tau² = 0.44; Chi² = 4.21, df = 3 (P = 0.24); I² =29%					
Test for overall effect: Z = 0.50 (P = 0.62)					
Test for subgroup differences: Chi² = 0.83, df = 1 (P = 0.36), I² =0.0%					

Analysis 10.14. Comparison 10 SSRI versus control at end of treatment, selective reporting: low risk, Outcome 14 Change in cognition between baseline and end of treatment.

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 10 SSRI versus control at end of treatment, selective reporting: low risk

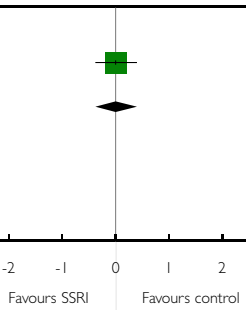
Outcome: 14 Change in cognition between baseline and end of treatment

Study or subgroup	SSRI N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
1 Sertraline							
Almeida 2006	48	2.6 (3.04)	51	2.6 (3.9)		100.0 %	0.0 [-0.39, 0.39]
Total (95% CI)	**48**		**51**			**100.0 %**	**0.0 [-0.39, 0.39]**

Heterogeneity: not applicable

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

Test for subgroup differences: Not applicable

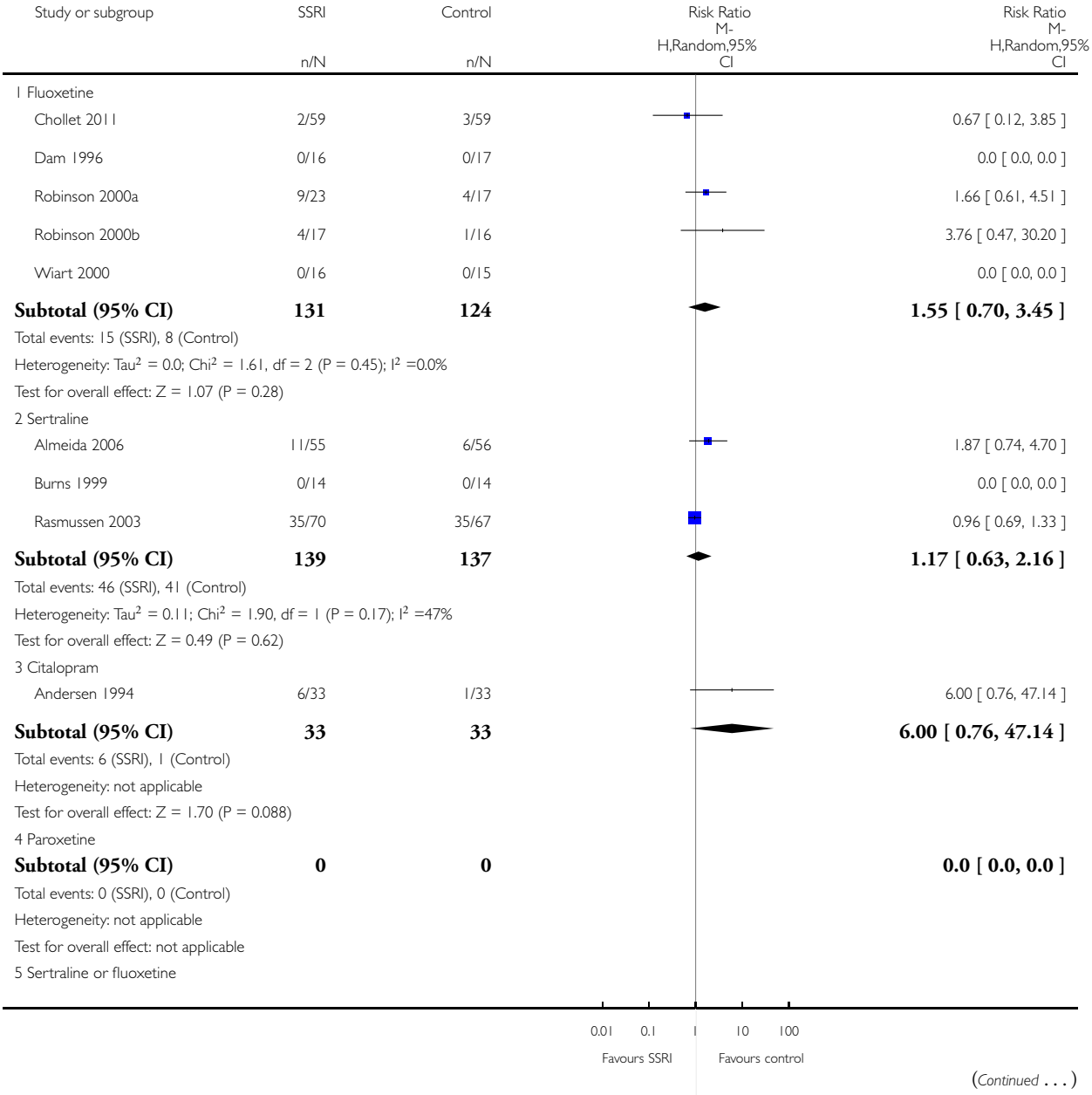


Analysis 10.15. Comparison 10 SSRI versus control at end of treatment, selective reporting: low risk, Outcome 15 Leaving the trial before the end of scheduled follow-up.

Review: Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery

Comparison: 10 SSRI versus control at end of treatment, selective reporting: low risk

Outcome: 15 Leaving the trial before the end of scheduled follow-up



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Study or subgroup	SSRI n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
Subtotal (95% CI)	**0**	**0**		**0.0 [0.0, 0.0]**
Total events: 0 (SSRI), 0 (Control)				
Heterogeneity: not applicable				
Test for overall effect: not applicable				
6 Escitalopram				
Robinson 2008	7/59	5/58		1.38 [0.46, 4.09]
Subtotal (95% CI)	**59**	**58**		**1.38 [0.46, 4.09]**
Total events: 7 (SSRI), 5 (Control)				
Heterogeneity: not applicable				
Test for overall effect: Z = 0.57 (P = 0.57)				
Total (95% CI)	**362**	**352**		**1.32 [0.87, 1.99]**
Total events: 74 (SSRI), 55 (Control)				
Heterogeneity: Tau^2 = 0.07; Chi^2 = 7.61, df = 6 (P = 0.27); I^2 =21%				
Test for overall effect: Z = 1.32 (P = 0.19)				
Test for subgroup differences: Chi^2 = 2.32, df = 3 (P = 0.51), I^2 =0.0%				

APPENDICES

Appendix 1. Cochrane Central Register of Controlled Trials (CENTRAL) search strategy

#1. MeSH descriptor Cerebrovascular Disorders explode all trees
#2. (stroke in Title, Abstract or Keywords or poststroke in Title, Abstract or Keywords or post-stroke in Title, Abstract or Keywords or cerebrovasc* in Title, Abstract or Keywords or (brain in Title, Abstract or Keywords and vasc* in Title, Abstract or Keywords) or (cerebral in Title, Abstract or Keywords and vasc* in Title, Abstract or Keywords) or cva* in Title, Abstract or Keywords or apoplex* in Title, Abstract or Keywords or SAH in Title, Abstract or Keywords)
#3. ((brain* in Title, Abstract or Keywords or cerebr* in Title, Abstract or Keywords or cerebell* in Title, Abstract or Keywords or intracran* in Title, Abstract or Keywords or intracerebral in Title, Abstract or Keywords) and (ischemi* in Title, Abstract or Keywords or ischaemi* in Title, Abstract or Keywords or infarct* in Title, Abstract or Keywords or thrombo* in Title, Abstract or Keywords or emboli* in Title, Abstract or Keywords or occlus* in Title, Abstract or Keywords))
#4. ((brain* in Title, Abstract or Keywords or cerebr* in Title, Abstract or Keywords or cerebell* in Title, Abstract or Keywords or intracerebral in Title, Abstract or Keywords or intracranial in Title, Abstract or Keywords or subarachnoid in Title, Abstract or Keywords) and (haemorrhage* in Title, Abstract or Keywords or hemorrhage* in Title, Abstract or Keywords or haematoma* in Title, Abstract or Keywords or hematoma* in Title, Abstract or Keywords or bleed* in Title, Abstract or Keywords))
#5. MeSH descriptor hemiplegia this term only
#6. MeSH descriptor paresis explode all trees
#7. MeSH descriptor Gait Disorders, Neurologic explode all trees

#8. (hemipleg* in Title, Abstract or Keywords or hemipar* in Title, Abstract or Keywords or paresis in Title, Abstract or Keywords or paretic in Title, Abstract or Keywords)
#9. (#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8)
#10. MeSH descriptor Serotonin Uptake Inhibitors explode all trees
#11. (serotonin in Title, Abstract or Keywords or 5-HT in Title, Abstract or Keywords or "5 HT" in Title, Abstract or Keywords or 5-hydroxytryptamine in Title, Abstract or Keywords or "5 hydroxytryptamine" in Title, Abstract or Keywords)
#12. (uptake in Title, Abstract or Keywords or reuptake in Title, Abstract or Keywords or re-uptake in Title, Abstract or Keywords)
#13. inhib* in Title, Abstract or Keywords
#14. (#11 and #12 and #13)
#15. SSRI* in Title, Abstract or Keywords
#16. (alaproclat* in Title, Abstract or Keywords or cericlamin* in Title, Abstract or Keywords or citalopram in Title, Abstract or Keywords or dapoxetin* in Title, Abstract or Keywords or escitalopram in Title, Abstract or Keywords or femoxetin* in Title, Abstract or Keywords or fluoxetin* in Title, Abstract or Keywords or fluvoxamin* in Title, Abstract or Keywords or paroxetin* in Title, Abstract or Keywords or sertralin* in Title, Abstract or Keywords or trazodone in Title, Abstract or Keywords or vilazodone in Title, Abstract or Keywords or zimelidine in Title, Abstract or Keywords)
#17. (Celexa in Title, Abstract or Keywords or Cipramil in Title, Abstract or Keywords or Cipram in Title, Abstract or Keywords or Recital in Title, Abstract or Keywords or Emocal in Title, Abstract or Keywords or Dalsan in Title, Abstract or Keywords or Sepram in Title, Abstract or Keywords or Seropram in Title, Abstract or Keywords or Citox in Title, Abstract or Keywords or Priligy in Title, Abstract or Keywords or Lexapro in Title, Abstract or Keywords or Cipralex in Title, Abstract or Keywords or Seroplex in Title, Abstract or Keywords or Esertia in Title, Abstract or Keywords or Prozac in Title, Abstract or Keywords or Fontex in Title, Abstract or Keywords or Seromex in Title, Abstract or Keywords or Seronil in Title, Abstract or Keywords or Sarafem in Title, Abstract or Keywords or Ladose in Title, Abstract or Keywords or Motivest in Title, Abstract or Keywords or Fluctin in Title, Abstract or Keywords or fluox in Title, Abstract or Keywords or Lovan in Title, Abstract or Keywords or Luvox in Title, Abstract or Keywords or Fevarin in Title, Abstract or Keywords or Faverin in Title, Abstract or Keywords or Favoxil in Title, Abstract or Keywords or Movox in Title, Abstract or Keywords or Paxil in Title, Abstract or Keywords or Seroxat in Title, Abstract or Keywords or Sereupin in Title, Abstract or Keywords or Aropax in Title, Abstract or Keywords or Deroxat in Title, Abstract or Keywords or Divarius in Title, Abstract or Keywords or Rexetin in Title, Abstract or Keywords or Xetanor in Title, Abstract or Keywords or Paroxat in Title, Abstract or Keywords or Loxamine in Title, Abstract or Keywords or Zoloft in Title, Abstract or Keywords or Lustral in Title, Abstract or Keywords or Serlain in Title, Abstract or Keywords or Asentra in Title, Abstract or Keywords)
#18. (#10 or #14 or #15 or #16 or #17)
#19. (#9 and #18)

Appendix 2. MEDLINE (Ovid) search strategy

1. cerebrovascular disorders/ or exp basal ganglia cerebrovascular disease/ or exp brain ischemia/ or exp carotid artery diseases/ or exp intracranial arterial diseases/ or exp "intracranial embolism and thrombosis"/ or exp intracranial hemorrhages/ or stroke/ or exp brain infarction/ or vertebral artery dissection/
2. (stroke or poststroke or post-stroke or cerebrovasc$ or brain vasc$ or cerebral vasc$ or cva$ or apoplex$ or SAH).tw.
3. ((brain$ or cerebr$ or cerebell$ or intracran$ or intracerebral) adj5 (isch?emi$ or infarct$ or thrombo$ or emboli$ or occlus$)).tw.
4. ((brain$ or cerebr$ or cerebell$ or intracerebral or intracranial or subarachnoid) adj5 (haemorrhage$ or hemorrhage$ or haematoma$ or hematoma$ or bleed$)).tw.
5. hemiplegia/ or exp paresis/
6. (hemipleg$ or hemipar$ or paresis or paretic).tw.
7. exp Gait Disorders, Neurologic/
8. or/1-7
9. exp Serotonin Uptake Inhibitors/
10. ((serotonin or 5-HT or 5 HT or 5-hydroxytryptamine or 5 hydroxytryptamine) adj5 (uptake or reuptake or re-uptake) adj5 inhib$).tw.
11. SSRI$1.tw.
12. (alaproclat$ or cericlamin$ or citalopram or dapoxetin$ or escitalopram or femoxetin$ or fluoxetin$ or fluvoxamin$ or paroxetin$ or sertralin$ or trazodone or vilazodone or zimelidine).tw,nm.

13. (Celexa or Cipramil or Cipram or Recital or Emocal or Dalsan or Sepram or Seropram or Citox or Priligy or Lexapro or Cipralex or Seroplex or Esertia or Prozac or Fontex or Seromex or Seronil or Sarafem or Ladose or Motivest or Fluctin or fluox or Lovan or Luvox or Fevarin or Faverin or Favoxil or Movox or Paxil or Seroxat or Sereupin or Aropax or Deroxat or Divarius or Rexetin or Xetanor or Paroxat or Loxamine or Zoloft or Lustral or Serlain or Asentra).tw,nm.
14. 9 or 10 or 11 or 12 or 13
15. 8 and 14
16. exp animals/ not humans.sh.
17. 15 not 16
18. Randomized Controlled Trials as Topic/
19. random allocation/
20. Controlled Clinical Trials as Topic/
21. control groups/
22. clinical trials as topic/ or clinical trials, phase i as topic/ or clinical trials, phase ii as topic/ or clinical trials, phase iii as topic/ or clinical trials, phase iv as topic/
23. Clinical Trials Data Monitoring Committees/
24. double-blind method/
25. single-blind method/
26. Placebos/
27. placebo effect/
28. cross-over studies/
29. Multicenter Studies as Topic/
30. Therapies, Investigational/
31. Drug Evaluation/
32. Research Design/
33. Program Evaluation/
34. evaluation studies as topic/
35. randomized controlled trial.pt.
36. controlled clinical trial.pt.
37. (clinical trial or clinical trial phase i or clinical trial phase ii or clinical trial phase iii or clinical trial phase iv).pt.
38. multicenter study.pt.
39. (evaluation studies or comparative study).pt.
40. meta analysis.pt.
41. meta-analysis as topic/
42. random$.tw.
43. (controlled adj5 (trial$ or stud$)).tw.
44. (clinical$ adj5 trial$).tw.
45. ((control or treatment or experiment$ or intervention) adj5 (group$ or subject$ or patient$)).tw.
46. (quasi-random$ or quasi random$ or pseudo-random$ or pseudo random$).tw.
47. ((multicenter or multicentre or therapeutic) adj5 (trial$ or stud$)).tw.
48. ((control or experiment$ or conservative) adj5 (treatment or therapy or procedure or manage$)).tw.
49. ((singl$ or doubl$ or tripl$ or trebl$) adj5 (blind$ or mask$)).tw.
50. (coin adj5 (flip or flipped or toss$)).tw.
51. latin square.tw.
52. versus.tw.
53. (cross-over or cross over or crossover).tw.
54. placebo$.tw.
55. sham.tw.
56. (assign$ or alternate or allocat$ or counterbalance$ or multiple baseline).tw.
57. controls.tw.
58. (treatment$ adj6 order).tw.
59. (meta-analy$ or metaanaly$ or meta analy$ or systematic review or systematic overview).tw.
60. or/18-59
61. 17 and 60

Appendix 3. EMBASE (Ovid) search strategy

1. cerebrovascular disease/ or basal ganglion hemorrhage/ or exp brain hematoma/ or exp brain hemorrhage/ or exp brain infarction/ or exp brain ischemia/ or exp carotid artery disease/ or cerebral artery disease/ or cerebrovascular accident/ or exp intracranial aneurysm/ or exp occlusive cerebrovascular disease/ or stroke/
2. stroke unit/ or stroke patient/
3. (stroke or poststroke or post-stroke or cerebrovasc$ or brain vasc$ or cerebral vasc$ or cva$ or apoplex$ or SAH).tw.
4. ((brain$ or cerebr$ or cerebell$ or intracran$ or intracerebral) adj5 (isch?emi$ or infarct$ or thrombo$ or emboli$ or occlus$)).tw.
5. ((brain$ or cerebr$ or cerebell$ or intracerebral or intracranial or subarachnoid) adj5 (haemorrhage$ or hemorrhage$ or haematoma$ or hematoma$ or bleed$)).tw.
6. hemiparesis/ or hemiplegia/ or paresis/
7. (hemipleg$ or hemipar$ or paresis or paretic).tw.
8. or/1-7
9. exp serotonin uptake inhibitor/
10. ((serotonin or 5-HT or 5 HT or 5-hydroxytryptamine or 5 hydroxytryptamine) adj5 (uptake or reuptake or re-uptake) adj5 inhib$).tw.
11. SSRI$1.tw.
12. (alaproclat$ or cericlamin$ or citalopram or dapoxetin$ or escitalopram or femoxetin$ or fluoxetin$ or fluvoxamin$ or paroxetin$ or sertralin$ or trazodone or vilazodone or zimelidine).tw.
13. (Celexa or Cipramil or Cipram or Recital or Emocal or Dalsan or Sepram or Seropram or Citox or Priligy or Lexapro or Cipralex or Seroplex or Esertia or Prozac or Fontex or Seromex or Seronil or Sarafem or Ladose or Motivest or Fluctin or fluox or Lovan or Luvox or Fevarin or Faverin or Favoxil or Movox or Paxil or Seroxat or Sereupin or Aropax or Deroxat or Divarius or Rexetin or Xetanor or Paroxat or Loxamine or Zoloft or Lustral or Serlain or Asentra).tw,tn.
14. 9 or 10 or 11 or 12 or 13
15. 8 and 14
16. limit 15 to human
17. Randomized Controlled Trial/
18. Randomization/
19. Controlled Study/
20. control group/
21. clinical trial/ or phase 1 clinical trial/ or phase 2 clinical trial/ or phase 3 clinical trial/ or phase 4 clinical trial/ or controlled clinical trial/
22. Double Blind Procedure/
23. Single Blind Procedure/ or triple blind procedure/
24. placebo/
25. "types of study"/
26. research subject/
27. random$.tw.
28. (controlled adj5 (trial$ or stud$)).tw.
29. (clinical$ adj5 trial$).tw.
30. ((control or treatment or experiment$ or intervention) adj5 (group$ or subject$ or patient$)).tw.
31. (quasi-random$ or quasi random$ or pseudo-random$ or pseudo random$).tw.
32. ((singl$ or doubl$ or tripl$ or trebl$) adj5 (blind$ or mask$)).tw.
33. (coin adj5 (flip or flipped or toss$)).tw.
34. versus.tw.
35. placebo$.tw.
36. controls.tw.
37. or/17-36
38. 16 and 37

Appendix 4. CINAHL (Ebsco) search strategy

S23. S12 and S22
S22. S13 or S17 or S18 or S19 or S20 or S21
S21. AB Celexa or Cipramil or Cipram or Recital or Emocal or Dalsan or Sepram or Seropram or Citox or Priligy or Lexapro or Cipralex or Seroplex or Esertia or Prozac or Fontex or Seromex or Seronil or Sarafem or Ladose or Motivest or Fluctin or fluox or Lovan or Luvox or Fevarin or Faverin or Favoxil or Movox or Paxil or Seroxat or Sereupin or Aropax or Deroxat or Divarius or Rexetin or Xetanor or Paroxat or Loxamine or Zoloft or Lustral or Serlain or Asentra
S20. TI Celexa or Cipramil or Cipram or Recital or Emocal or Dalsan or Sepram or Seropram or Citox or Priligy or Lexapro or Cipralex or Seroplex or Esertia or Prozac or Fontex or Seromex or Seronil or Sarafem or Ladose or Motivest or Fluctin or fluox or Lovan or Luvox or Fevarin or Faverin or Favoxil or Movox or Paxil or Seroxat or Sereupin or Aropax or Deroxat or Divarius or Rexetin or Xetanor or Paroxat or Loxamine or Zoloft or Lustral or Serlain or Asentra
S19. TI (alaproclat* or cericlamin* or citalopram or dapoxetin* or escitalopram or femoxetin* or fluoxetin* or fluvoxamin* or paroxetin* or sertralin* or trazodone or vilazodone or zimelidine) OR AB (alaproclat* or cericlamin* or citalopram or dapoxetin* or escitalopram or femoxetin* or fluoxetin* or fluvoxamin* or paroxetin* or sertralin* or trazodone or vilazodone or zimelidine)
S18. TI SSRI* OR AB SSRI*
S17. S14 and S15 and S16
S16. TI inhib* OR AB inhib*
S15. TI (uptake or reuptake or re-uptake) OR AB (uptake or reuptake or re-uptake)
S14. TI (serotonin or 5-HT or 5 HT or 5-hydroxytryptamine or 5 hydroxytryptamine) OR AB (serotonin or 5-HT or 5 HT or 5-hydroxytryptamine or 5 hydroxytryptamine)
S13. (MH "Serotonin Uptake Inhibitors+")
S12. S1 or S2 or S3 or S6 or S9 or S10 or S11
S11. TI (hemipleg* or hemipar* or paresis or paretic) or AB (hemipleg* or hemipar* or paresis or paretic)
S10. (MH "Hemiplegia")
S9. S7 and S8
S8. TI (haemorrhage* or hemorrhage* or haematoma* or hematoma* or bleed*) or AB (haemorrhage* or hemorrhage* or haematoma* or hematoma* or bleed*)
S7. TI (brain* or cerebr* or cerebell* or intracerebral or intracranial or subarachnoid) or AB (brain* or cerebr* or cerebell* or intracerebral or intracranial or subarachnoid)
S6. S4 and S5
S5. TI (ischemi* or ischaemi* or infarct* or thrombo* or emboli* or occlus*) or AB (ischemi* or ischaemi* or infarct* or thrombo* or emboli* or occlus*)
S4. TI (brain* or cerebr* or cerebell* or intracran* or intracerebral) or AB (brain* or cerebr* or cerebell* or intracran* or intracerebral)
S3. TI (stroke or poststroke or post-stroke or cerebrovasc* or brain vasc* or cerebral vasc or cva or apoplex or SAH) or AB (stroke or poststroke or post-stroke or cerebrovasc* or brain vasc* or cerebral vasc or cva or apoplex or SAH)
S2. (MH "Stroke Patients") OR (MH "Stroke Units")
S1. (MH "Cerebrovascular Disorders") OR (MH "Basal Ganglia Cerebrovascular Disease+") OR (MH "Carotid Artery Diseases+") OR (MH "Cerebral Ischemia+") OR (MH "Cerebral Vasospasm") OR (MH "Intracranial Arterial Diseases+") OR (MH "Intracranial Embolism and Thrombosis") OR (MH "Intracranial Hemorrhage+") OR (MH "Stroke") OR (MH "Vertebral Artery Dissections")

Appendix 5. AMED (Ovid) search strategy

1. cerebrovascular disorders/ or cerebral hemorrhage/ or cerebral infarction/ or cerebral ischemia/ or cerebrovascular accident/ or stroke/
2. (stroke or poststroke or post-stroke or cerebrovasc$ or brain vasc$ or cerebral vasc$ or cva$ or apoplex$ or SAH).tw.
3. ((brain$ or cerebr$ or cerebell$ or intracran$ or intracerebral) adj5 (isch?emi$ or infarct$ or thrombo$ or emboli$ or occlus$)).tw.
4. ((brain$ or cerebr$ or cerebell$ or intracerebral or intracranial or subarachnoid) adj5 (haemorrhage$ or hemorrhage$ or haematoma$ or hematoma$ or bleed$)).tw.
5. hemiplegia/
6. (hemipleg$ or hemipar$ or paresis or paretic).tw.
7. or/1-6
8. antidepressive agents/

9. ((serotonin or 5-HT or 5 HT or 5-hydroxytryptamine or 5 hydroxytryptamine) adj5 (uptake or reuptake or re-uptake) adj5 inhib$).tw.
10. SSRI$1.tw.
11. (alaproclat$ or cericlamin$ or citalopram or dapoxetin$ or escitalopram or femoxetin$ or fluoxetin$ or fluvoxamin$ or paroxetin$ or sertralin$ or trazodone or vilazodone or zimelidine).tw.
12. (Celexa or Cipramil or Cipram or Recital or Emocal or Dalsan or Sepram or Seropram or Citox or Priligy or Lexapro or Cipralex or Seroplex or Esertia or Prozac or Fontex or Seromex or Seronil or Sarafem or Ladose or Motivest or Fluctin or fluox or Lovan or Luvox or Fevarin or Faverin or Favoxil or Movox or Paxil or Seroxat or Sereupin or Aropax or Deroxat or Divarius or Rexetin or Xetanor or Paroxat or Loxamine or Zoloft or Lustral or Serlain or Asentra).tw.
13. 8 or 9 or 10 or 11 or 12
14. 7 and 13

Appendix 6. PsycINFO (Ovid) search strategy

1. cerebrovascular disorders/ or cerebral hemorrhage/ or exp cerebral ischemia/ or cerebral small vessel disease/ or cerebrovascular accidents/ or subarachnoid hemorrhage/
2. (stroke or poststroke or post-stroke or cerebrovasc$ or brain vasc$ or cerebral vasc$ or cva$ or apoplex$ or SAH).tw.
3. ((brain$ or cerebr$ or cerebell$ or intracran$ or intracerebral) adj5 (isch?emi$ or infarct$ or thrombo$ or emboli$ or occlus$)).tw.
4. ((brain$ or cerebr$ or cerebell$ or intracerebral or intracranial or subarachnoid) adj5 (haemorrhage$ or hemorrhage$ or haematoma$ or hematoma$ or bleed$)).tw.
5. (hemipleg$ or hemipar$ or paresis or paretic).tw.
6. hemiparesis/ or hemiplegia/
7. or/1-6
8. exp serotonin reuptake inhibitors/
9. ((serotonin or 5-HT or 5 HT or 5-hydroxytryptamine or 5 hydroxytryptamine) adj5 (uptake or reuptake or re-uptake) adj5 inhib$).tw.
10. SSRI$1.tw.
11. (alaproclat$ or cericlamin$ or citalopram or dapoxetin$ or escitalopram or femoxetin$ or fluoxetin$ or fluvoxamin$ or paroxetin$ or sertralin$ or trazodone or vilazodone or zimelidine).tw.
12. (Celexa or Cipramil or Cipram or Recital or Emocal or Dalsan or Sepram or Seropram or Citox or Priligy or Lexapro or Cipralex or Seroplex or Esertia or Prozac or Fontex or Seromex or Seronil or Sarafem or Ladose or Motivest or Fluctin or fluox or Lovan or Luvox or Fevarin or Faverin or Favoxil or Movox or Paxil or Seroxat or Sereupin or Aropax or Deroxat or Divarius or Rexetin or Xetanor or Paroxat or Loxamine or Zoloft or Lustral or Serlain or Asentra).tw.
13. 8 or 9 or 10 or 11 or 12
14. 7 and 13

WHAT'S NEW

Last assessed as up-to-date: 10 July 2012.

Date	Event	Description
26 August 2013	Amended	The review authors identified minor errors following publication of the previous version. These errors have now been corrected and have resulted in very minor changes in SMD for disability and some I^2 values. The changes have not materially changed the results or conclusions of the review Changes made: (1) the total number of participants has been changed from 4059 to 4060; (2) Almeida 2006 recruited people without depression; this has been corrected in the 'Characteristics of included studies' table, and data have been moved to 'did not have to have depression' in the relevant subgroup analyses; (3) disability data for Acler 2009 had been entered incorrectly; this has now been corrected

CONTRIBUTIONS OF AUTHORS

Dr Mead, Dr Hackett and Professor Hankey wrote the protocol. Dr Kutlubaev and Dr Lee read the protocol and approved it. All authors contributed to the searches, or selection of trials or data extraction, as indicated in the text. Dr Mead performed the analyses.

DECLARATIONS OF INTEREST

Gillian Mead, Maree Hackett and Graeme Hankey are co-principal investigators on the planned FOCUS trial (Fluoxetine or control under supervision) in the UK and the AFFINITY (Assessment of fluoxetine in stroke recovery) trial in Australia designed to assess the impact of fluoxetine on disability and dependency after stroke. These trials fulfil our inclusion criteria.

SOURCES OF SUPPORT

Internal sources

- None, Not specified.

External sources

- Stroke Research Network, UK.

Stroke Research Network in England provided some financial support to the Cochrane Stroke Group for assistance with the searches

- Scotland, Not specified.

Scottish Stroke Research Network provided some funding to the Cochrane Stroke group for assistance with the searches

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

We had planned to search the Organon and Wyeth pharmaceutical websites, but when the searches were done, these websites no longer existed. We decided to search the Lundbeck website as this company makes citalopram.

We had planned to search www.ClinicalStudyResults.org, but this was removed from the Internet in 2011.

We stated that we would include trials in which patients were recruited within three months of stroke onset. However, when we started our searches, we identified several trials in which patients had been recruited after three months. In order to ensure that our review provides a complete as possible picture about the role of SSRIs for stroke recovery, we decided to include trials in which the mean time since stroke onset was less than one year, and to perform subgroup analyses to explore the effect of time since onset on effect sizes. This decision was made before any data extraction and analysis had been performed.

We stated that two review authors would independently scrutinise the full-text articles retrieved from the searches, but this was not possible for the main MEDLINE and EMBASE searches because of the large number of full texts retrieved; for these searches, one experienced review author (GM) scrutinised the full texts.

We also stated that two review authors would extract data. Several of our included trials had already been included in other Cochrane reviews led by Dr Hackett, one of our review authors. For these trials, only one additional review author extracted data and checked this against the data extraction that had previously been performed for the previous reviews.

We had not anticipated such as large number of Chinese studies. An additional review author joined the team to perform data extraction for these Chinese papers, but we could not find a second independent reviewer who was sufficiently fluent in Chinese to perform data extraction.

We had intended to use random-effects models only if there was evidence of statistical heterogeneity. Following editorial review, we use random-effects models for all our analyses.

We extracted data on sources of funding, and included this as part of risk of bias assessment.

INDEX TERMS

Medical Subject Headings (MeSH)

Anxiety [*drug therapy]; Citalopram [therapeutic use]; Cognition [drug effects]; Depression [*drug therapy]; Fluoxetine [therapeutic use]; Nervous System Diseases [drug therapy]; Paroxetine [therapeutic use]; Randomized Controlled Trials as Topic; Serotonin Uptake Inhibitors [adverse effects; *therapeutic use]; Sertraline [therapeutic use]; Stroke [*drug therapy; psychology; rehabilitation]

MeSH check words

Adult; Humans