NKR 50 Fald PICO 6 SSRI

Review information

Authors

Sundhedsstyrelsen[1]

[1][Empty affiliation]

Citation example: S. NKR 50 Fald PICO 6 SSRI. Cochrane Database of Systematic Reviews [Year], Issue [Issue].

Characteristics of studies

Characteristics of included studies

Kasper 2005

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Overall ● *Age (range)*: Mean age 75 (SD 7) ● *Depression score* : Mean MADRS total score 28.6 (SD 4.2) **Included criteria:** Inclusion: 65years of age or over and fulfilled DSM-IV criteria for MDD. They were required to have a MADRS total score of 22 or above and 40 or below at both the screening and baseline visit and a minimum score of 22 on the mini-mental state exam at the screening visit. **Excluded criteria:** If subjects met DSM-IV criteria for mania or any bipolar disorder, schizophrenia, or any psychotic disorder, OCD, eating disorder or mental retardation or pervasive developmental or cognitive disorder, had MADRS score of 5 or above on item 10 (suicidal); where receiving treatment with antipsychotic, antidepressant, hypnotics, anxiolytics, ongoing profylaktik treatment with lithium, sodium valprorat or carbamazepine, were receiving electroconvulsive therapy, treatment with behavioural therapy or psychotherapy; had received treatment with any investigational drug within 30days before entry; had a history of schizophrenia, psychotic disorder, or drug abuse; ad a history of severe drug allergy or hypersensitivity or had a lack of repsonse to more than one antidepressant treatment

	during the present depressive episode. **Pretreatment:** None detected
Interventions	**Intervention Characteristics** Intervention 1 ● *Description*: Escitalopram ● *Dose (mg)*: 10mg/day ● *Duration of treatment (weeks)*: 8 Intervention 2 ● *Description*: Fluoxetine ● *Dose (mg)*: 20 mg/day ● *Duration of treatment (weeks)*: 8 Control ● *Description*: Placebo ● *Dose (mg)*: ● *Duration of treatment (weeks)*: 8
Outcomes	*Død (death)* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Fully reported *Antal af personer som falder (med eller uden bevidsthedstab) (No. of persons with a fall (with/without loss of consciousness))* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Not reported *Fald (med eller uden bevidsthedstab) (Fall (with/without loss of consciousness)* ● **Outcome type**: ContinuousOutcome ● **Reporting**: Not reported ● **Notes**: Not really contiunous measurement but a rate. OBS! in RevMan *Fald (med eller uden bevidsthedstab) (Fall with/without loss of consciousness)* ● **Outcome type**: ContinuousOutcome ● **Reporting**: Not reported

	● **Notes**: Not really a continuous measurement. OBS! in RevMan *Fald med fraktur (major injuries) (Fall with fractures)* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Not reported *Livskvalitet (life quality)* ● **Outcome type**: ContinuousOutcome ● **Reporting**: Not reported *Svimmelhed (Dizziness) (%, N)* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Fully reported *Svimmelhed (Dizziness) (%, N).* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Not reported *Depression, SD. 6 months after start of treatment.* ● **Outcome type**: ContinuousOutcome ● **Reporting**: Partially reported ● **Scale**: MADRS - total score ● **Direction**: Lower is better ● **Data value**: Change from baseline ● **Notes**: Only reported means on a graf and a boundry P-value
Identification	**Sponsorship source:** Dr. Kasper hasreceived grant/research support from Eli Lilly, Lundbeck, Bristol-M yers Squibb, GlaxoSmithKline, Organon, and Servier; hasserved as a consultant or and the advisory board for AstraZeneca, Bristol-Myers Squibb, GlaxoSmithKline, Eli Lilly, Lundbeck, Pfizer, Organon, Janssen Pharmaceutica, and Novartis; and has served an the speakers' bureau for AstraZeneca , Eli Lilly, Lundbeck, and Janssen Pharmaceutica. Hans deSwart and Henning Friis Andersen are both full-time employees af H. Lundbeck A/S **Country:** Belgium, Czech Republic, Hungary, Italy, The Netherlands, Spain, Sweden and UK **Setting:** The study was conducted in 11 countries, in both general practice and specialist settings. **Comments:** **Authors name:** Siegfried Kasper **Institution:** Dept. of general Psychiatry, Medical University of Vienna

	Email: sci-genpsy@meduniwien.ac.at **Address:** Währinger Gürtel 18-20, A1090, Vienna, Austria
Notes	*Britta Tendal* on 14/11/2017 22:18 **Outcomes** Death is during 8 weeks of treatment and up to 1 week after treatment.

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement Comment: Not described
Allocation concealment (selection bias)	Unclear risk	Judgement Comment: Not described
Blinding of participants and personnel (performance bias)	Low risk	Judgement Comment: The study is described as: doubled blinded. It is unclear who this refers to.It is described as placebo controlled, hence low risk of bias
Blinding of outcome assessment (detection bias)	Low risk	Judgement Comment: Tolerability was measured by a cardiologist who was blinded to the randomized code. It is unclear if the assessor of the MADRS score was blinded. It is described as placebo controlled, hence low risk of bias
Incomplete outcome data (attrition bias)	Low risk	Judgement Comment: Overall completion rate 82.4. More loss to FU due to adverse events in the SSRI groups than in the placebo group. ITT including 517 out od 518 patients
Selective reporting (reporting bias)	Low risk	Judgement Comment: Some problems with partial reporting on outcomes that were not statistically significant
Other bias	Low risk	Judgement Comment: No other apparent sources of bias

Rapaport 2003

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Intervention 1 ● *Age (range)*: 60-88 ● *Depression score* : HAM-D 22.1 (SD 3.45) Intervention 2 ● *Age (range)*: 60-88 ● *Depression score* : HAM-D 22.3 (SD 3.15) Control ● *Age (range)*: 60-82 ● *Depression score* : HAM-D 22.1 (SD 3) **Included criteria:** Patients recruited for this trials were at least 60 years of age and fulfilled Diagnostic and Statistical Manual of Mental disorder , Fourth Edition (DSM—IV) criteria for major depressive disorder on the Structures Clinical Interview for DSM-IV. Eligible patients had a HAM-D (I7-item) total score of at least 18 at both the screen and baseline visits. **Excluded criteria:** Patients were ineligible if their HAM-D total score decreased by 25% or more between the screen and baseline visits. Additional exclusion criteria included concomitantt herapy with psychoactive medication other than chloral hydrate (for sleep disturbance); diagnosis of a primary or predominant Axis I disorder (other than major depressive disorder) within 6 months of the screen visit; history of brief depressive episodes lasting less than 8 weeks with spontanoues remission neurologic disorders contributing to secondary depression; dementia; Mini-Mental State Examination scores; serious medical conditions that would preclude paroxetine administration; history of seizure disorders; concomitant treatment with warfarin, phenytoin, cimetidine, sumatriptan, type IC antianhythmic agents, or quinidine; histoty of DSM IV substance abuse or dependence within 6 months; electroconvulsive therapy within 3 months; unresolved clinically abnormal laboratory or electrocardiogram (ECG) findings at baseline; and suicidal or homicidal tendencies. **Pretreatment:** The groups had similar demographic characteristics and historics of depression.

Interventions	**Intervention Characteristics** Intervention 1 ● *Description*: Paroxetine CR ● *Dose (mg)*: Flex dose 10-40 mg/day ● *Duration of treatment (weeks)*: 12 Intervention 2 ● *Description*: Paroxetine IR ● *Dose (mg)*: Flex dose 12.5-50 mg/day ● *Duration of treatment (weeks)*: 12 Control ● *Description*: Placebo ● *Dose (mg)*: ● *Duration of treatment (weeks)*: 12
Outcomes	*Død (death)* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Fully reported *Antal af personer som falder (med eller uden bevidsthedstab) (No. of persons with a fall (with/without loss of consciousness))* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Not reported *Fald (med eller uden bevidsthedstab) (Fall (with/without loss of consciousness)* ● **Outcome type**: ContinuousOutcome ● **Reporting**: Not reported *Fald (med eller uden bevidsthedstab) (Fall with/without loss of consciousness)* ● **Outcome type**: ContinuousOutcome ● **Reporting**: Not reported *Fald med fraktur (major injuries) (Fall with fractures)* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Not reported

	Livskvalitet (life quality) ● **Outcome type**: ContinuousOutcome ● **Reporting**: Not reported *Svimmelhed (Dizziness) (%, N)* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Not reported *Depression, SD. 6 months after start of treatment.* ● **Outcome type**: ContinuousOutcome ● **Reporting**: Partially reported ● **Scale**: HAMD-D total score (17 item) ● **Data value**: Change from baseline ● **Notes**: Only reported 3 months after start of treatment *Depression, CI* ● **Outcome type**: ContinuousOutcome ● **Reporting**: Not reported *Depression, SE* ● **Outcome type**: ContinuousOutcome ● **Reporting**: Not reported *Livskvalitet, SD* ● **Outcome type**: ContinuousOutcome ● **Reporting**: Not reported
Identification	**Sponsorship source:** Dr.Rapaport has been a consultant for and received grant/research support from GlaxoSmithKline, Pfizer, Forest, Janssen, and Lilly; has received honoraria from GlaxoSmithKline, Pfizer, Pharmacia, Forest, and Janssen; has participated in speakers/advisory boards for GlaxoSmithKline, Pfizer Pharmacia and Janssen; and has been an expert witness for Pfizer. Dr.Rapaport's wife was an employee of Forest until july 2003 and owns stock options in Forest. Dr.Sehneider has been a consultant for Lilly, Pfizer, Forest, Wyeth, GlaxoSmithKline, and Lundbeck. Dr.Dunner has been a consultant for Eli Lilly, GlaxSmithKline, Wyeth ,bristol Myers Squibb, Otsuka, Pharmacia, Janssen, Cypress, Cyberonics, and Novartis; has received grant/research support from Eli Lilly, GlaxoSmithKline, Pfizer, Pharmacia, Organon, Forest, Cyberonies, and UCB Pharma; and has participated in speakers bureaus for EliLilly, GlaxoSmithKline, Wyeth, Bristol-Myers Squibb, Organon and Forest. Mr.Davies is an employee of and major stock

	shareholder in GlaxoSmithKline. Dr.Pitts is an employee of GlaxoSmithKline. **Country:** US and Canada **Setting:** **Comments:** **Authors name:** Mark Hyman Rapaport **Institution:** Department of Psychiatry, Cedars-Sinai Medical Center at UCLA **Email:** mark.rapaport@cshs.org **Address:** David Geffen School of medicine at ULCA, 8730 Alden Dr. Suite C301, Los Angeles, CA 90048
Notes	*Britta Tendal* on 15/11/2017 00:27 **Outcomes** No mention of SAE or deaths.Data on HAM-D are at 12 weeks

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Patients were randomly assigned at the baseline visit to rcceive placebo, paroxetine Ck, or paroxetine 1k." Judgement Comment: Sequence generation not described
Allocation concealment (selection bias)	Unclear risk	Judgement Comment: Not described
Blinding of participants and personnel (performance bias)	Low risk	Quote: "Study mcdi cation was dispensed to patients at eaeh elinic visit and was overencapsulated in identically appearing capsules to main tam double-blind conditions." Judgement Comment: Probably blinded
Blinding of outcome assessment (detection bias)	Low risk	Judgement Comment: Placebo controlled
Incomplete outcome data (attrition bias)	High risk	Judgement Comment: Unclear how many were randomized, but 74,6% of the patients who were randomly assigned and received at least one dose of the study medication completed the study. More drop out due to adverse events in the SSRI groups than in placebo

Selective reporting (reporting bias)	Low risk	
Other bias	Low risk	Judgement Comment: No other apparent sources of bias

Rapaport 2009

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Intervention 1 ● *Age (range)*: mean (SD): 67 (6.11) ● *Depression score* : HAMD-total, mean (SD) 22.56 (3.59) Intervention 2 ● *Age (range)*: mean (SD): 67 (6.56) ● *Depression score* : HAMD-total, mean (SD) 23.1 (3.93) Control ● *Age (range)*: mean (SD): 68 (6.73) ● *Depression score* : HAMD-total, mean (SD) 22.73 (4) **Included criteria:** Study participants were men and women aged 60 years or older, who met criteria for a primary diagnosis of MDI) (without psychotic features), single or recurrent episode, according to the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM—IV). Eligibility criteria also included a curent episode of depression of at least 2 months in duration and a 17-item Hamilton Rating Scale for Depression (HAM-D) score >= 18 at both screening and baseline, with a score on item 1 (depressed mood) >=2 **Excluded criteria:** Patients who met any of the following criteria were not eligible for participation in the study: >=25% decrease in HAM-D) total score between screening and baseline; primary or predominant DSM-IV Axis 1 disorder (within 6 months prior to screening) other than MDD); lifetime schizophrenia, schizoaffective disorder, or bipolar disorder; alcohol or substance abuse or dependence within 6 months prior to screening; current diagnosis of dementia; Mini-Mental State Examination (MMSE) score =24; depression secondary to a medical condition; a history of brief depressive episodes (8 weeks with spontaneous remission); formal psychotherapy concurrently or in the 12 weeks prior to screening; attempted suicide within 6 months prior to screening or current suicidal or homicidal risk; electroconvulsive therapy or transcranial magnetic stimulation within 6 months prior to screening; lifetime history of seizure disorder; clinically significant eleetrocardiogram (ECG) abnormalities or abnomial laboratory findings; any current or recent use of

	other psychoactive drugs; history of intolerance to paroxetine; investigational drug use or other clinical trial participation within 3 months prior to screening; or likelihood of nonadherence with study procedures or study medication. **Pretreatment:** No apparent baseline differences
Interventions	**Intervention Characteristics** Intervention 1 ● *Description*: paroxetine CR, Active medieations were provided as over-encapsulated tablets, which were identical in appearance to placebo ● *Dose (mg)*: 12.5mg/day ● *Duration of treatment (weeks)*: 10 Intervention 2 ● *Description*: paroxetine CR ● *Dose (mg)*: 25 mg/day ● *Duration of treatment (weeks)*: 10 Control ● *Description*: Placebo ● *Dose (mg)*: ● *Duration of treatment (weeks)*: 10
Outcomes	*Død (death)* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Fully reported ● **Data value**: Endpoint *Antal af personer som falder (med eller uden bevidsthedstab) (No. of persons with a fall (with/without loss of consciousness))* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Not reported *Antal af personer som falder (med eller uden bevidsthedstab) (No. of persons with fall (with/without loss of consciousness))* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Not reported

Fald (med eller uden bevidsthedstab) (Fall (with/without loss of consciousness)
- **Outcome type**: ContinuousOutcome
- **Reporting**: Not reported

Fald (med eller uden bevidsthedstab) (Fall with/without loss of consciousness)
- **Outcome type**: ContinuousOutcome

Fald med fraktur (major injuries) (Fall with fractures)
- **Outcome type**: DichotomousOutcome
- **Reporting**: Not reported

Livskvalitet (life quality)
- **Outcome type**: ContinuousOutcome
- **Notes**: Britta oplyste, at dette studies måde at rapportere livskvalitet skal manuelt skrives ind i MAGIC, da programmerne ikke kan tale sammen vedr. denne scala.Nedenfor er listet det rapporterede fra studiet: Q—LES-Q item 16 (overall life satisfaction) Placebo N:150, Least Squares Mean (SE): 0.29 (0.094)Paroxeline CR 12.5 mg/d N: 138, Least Squares Mean: 0.60(0.095), Difference: 0.30, p Value: 0,015, 95% CI: 0.06 to 0.55 Paroxeline CR 25mg/d N: 146, Least Squares Mean: 0,82(0.095), Difference: 0,53, p Value: .001, 95% CI: 0.29 to 0,77

Svimmelhed (Dizziness) (%, N)
- **Outcome type**: DichotomousOutcome
- **Reporting**: Fully reported
- **Data value**: Endpoint
- **Notes**: Data value:Endpoint or change from baseline? Table 3 = Summary of frequent?Safety Assessment ...?

Svimmelhed (Dizziness) (%, N).
- **Outcome type**: DichotomousOutcome
- **Reporting**: Not reported

Depression, SD. 6 months after start of treatment.
- **Outcome type**: ContinuousOutcome

Depression, CI
- **Outcome type**: ContinuousOutcome

Depression, SE
- **Outcome type**: ContinuousOutcome

	● **Reporting**: Partially reported ● **Data value**: Change from baseline ● **Notes**: HAM-D total scoreChange from baseline to week 10 endpoint6 month: Not recorded
Identification	**Sponsorship source:** Dr. Rapaport has reccived grant/researchsupport from Astra Zeneca, Pflzer, Glaxo Smith Kline, Jansse, Forest, Eli Lilly, Abbott, Corcept Therapeutics, Cybcronics, Novartis, Phamiacia Upjohn, Sanofl. Syntlielaho, Sol'ay, The Stanley Foundation, Wyelh Ayerst. UCB Phama, National Institute of Mental Health (NIMH), and National Center for Complementary and Alternative Medicine; is a consultant for Cyberonies, Forest, Roche, Pfizer, Sanofi Synthelabo, Solsay. Wyeth, NIMH, National Institute on Drug Abuse, Glaxo Smith Klinc, Janssen, Neurocrine Bioseiences, Eli Lilly, Novartis, and Sumitomo; and is a stockholder of Forest, Dr. Lydiard has received grant/research support from AstraZeneca, Bristol-Myers Squibb. Forest. GlaxoSmithKline, MediciNova. Wyeth, Eli Lilly, Jazz, UCB Pharma, Cephalon. Pfizer, and Sanofi-Aventis; is a consultant for Eli Lilly, MediciNova. Novartis, Pfizer, and Roehe; and is a member of the speakers bureau for Eli Lilly. Neuroscience Education Institute, and Pfizer. Dr. Pitts and Iyengar are employees and stockholders af GlaxoSnithKline. Ms. Shaeffer and DRS. Carfagno and Lipschitz are employees of GlasoSmithKline. Dr. Bartolieb is an employee of i3 Research, a division af Ingenix Pharmaceutical Services, Inc. i3 Research sometimes provides services to GlaxoSmithKline and its affiliates ans well as to other pharmaceutical companies (some of which may be considered competitors of GlaxoSmithKline and its affiliates), including, but not limited to, services relating to this articla, and receives payments for these services. **Country:** US **Setting:** Elderly outpatients with MDD **Comments:** **Authors name:** Mark Hyman Rapaport **Institution:** Dep of Psychiatry and Behavioral Neurosciences **Email:** mark.rapaport@cshs.org **Address:** Cedar Sinai Medical Center, 8730 Alden Dr. Suite C301, LA, CA 90048
Notes	*Britta Tendal* on 03/11/2017 00:50 **Outcomes** All outcomes are at 10 weeks. No details on how the fractures occurred.QoL Q-LES-Q total score

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Randomization, Study Trea(ments, and Blinding At the baseline visit, patients were assigned in a I: 1:1 ratio to paroxetine CR 12.5 mg/day, paroxetine CR 25 mg1day, er placebo (Figure I) on the basis ofa pemiuted block randomization scheme (block size of 6 within study centers). Active medieations were provided as" Judgement Comment: Probably done via computer
Allocation concealment (selection bias)	Unclear risk	Judgement Comment: Not described
Blinding of participants and personnel (performance bias)	Low risk	Quote: "Active medieations were provided as over-encapsulated tablets. which were idencical iii appear ance to placebo."
Blinding of outcome assessment (detection bias)	Low risk	Judgement Comment: Placebo controlled
Incomplete outcome data (attrition bias)	High risk	Judgement Comment: Overall 76% of the patients completed the study. mITT (efficay) included 516 out of 525. Reasons for drop out similar. No imputation for safety
Selective reporting (reporting bias)	Low risk	
Other bias	Low risk	Judgement Comment: No other apparent bias

Roose 2004

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Intervention 1 ● *Age (range)*: ● *Depression score* : Intervention 2

	• *Age (range)*: • *Depression score* : Control • *Age (range)*: • *Depression score* : Overall • *Age (range)*: Mean age 79.6 (SD 4.4) • *Depression score* : HAM-D mean 24.3 (SD 4.1) **Included criteria:** Inclusion criteria were 1) 75 years old or older and not living ina residential setting; 2) with unipolar depression, single or recur-rent, nonpsychotic, by DSM-IV criteria with the modification thatthe current episode must be at least 4 weeks in duration; 3) with aHamilton depression scale score of ≥ 20 on the 24-item Hamiltondepression scale at the initial visit and at the end of 1 week of pla-cebo; and 4) willing and able to give informed consent. **Excluded criteria:** Exclusioncriteria were 1) having bipolar disorder, obsessive-compulsivedisorder, psychotic disorder, or current substance abuse or sub-stance dependence within the past year (other than nicotine) byDSM-IV criteria; 2) having current suicide intent or serious sui-cide attempt within the past year; 3) meeting National Institute ofNeurological and Communicative Disorders and Stroke and theAlzheimer's Disease and Related Disorders Association criteria forprobable Alzheimer's disease or probable vascular dementia; 4)having an MMSE score ≤ 18; 5) having Parkinson's disease; 6) hav-ing an acute, severe, or unstable medical illness, 7) in the currentepisode of major depression, failing to respond to either a trial ofa selective serotonin reuptake inhibitor (SSRI) (fluoxetine, parox-etine, or citalopram at 20 mg/day or sertraline 50 mg/day for atleast 4 weeks) or trials of two or more different classes of antidepressants other than SSRIs. **Pretreatment:**
Interventions	**Intervention Characteristics** Intervention 1 • *Description*: Citalopram • *Dose (mg)*: Flexdose 10-40 mg • *Duration of treatment (weeks)*: 8 Intervention 2 • *Description*: • *Dose (mg)*: • *Duration of treatment (weeks)*:

	Control ● *Description*: Placebo ● *Dose (mg)*: ● *Duration of treatment (weeks)*: 8
Outcomes	*Død (death)* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Not reported *Antal af personer som falder (med eller uden bevidsthedstab) (No. of persons with a fall (with/without loss of consciousness))* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Not reported *Antal af personer som falder (med eller uden bevidsthedstab) (No. of persons with fall (with/without loss of consciousness))* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Not reported *Fald (med eller uden bevidsthedstab) (Fall (with/without loss of consciousness)* ● **Outcome type**: ContinuousOutcome *Fald (med eller uden bevidsthedstab) (Fall with/without loss of consciousness)* ● **Outcome type**: ContinuousOutcome ● **Reporting**: Not reported *Fald med fraktur (major injuries) (Fall with fractures)* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Not reported *Livskvalitet (life quality)* ● **Outcome type**: ContinuousOutcome ● **Notes**: Symptomatic improvement and changes in quality of life can be dissociated, especially in the long-term treatment of patientswith late-life major depression. Changes in function comprisedanother set of primary outcomes. Raw scores on each of the eightMedical Outcomes Study 36-Item Short-Form Health Survey sub-scales were transformed into standardized scores, with a poten-tial range of 0 to 100 (28), and the change from baseline to

	post-treatment was computed for each subscale. A repeated-measuresANCOVA was conducted on these change scores, with treatmentgroup and site as between-subject factors, subscale as the re-peated-measures factor, and depression severity and age at onsetgroupings as covariates. *Svimmelhed (Dizziness) (%, N)* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Fully reported ● **Direction**: Lower is better ● **Data value**: Endpoint ● **Notes**: N as described in table 5 - not the total N:intervention N=84control N=90 *Svimmelhed (Dizziness) (%, N).* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Not reported *Depression, SD. 6 months after start of treatment.* ● **Outcome type**: ContinuousOutcome ● **Reporting**: Fully reported ● **Direction**: Lower is better ● **Data value**: Endpoint ● **Notes**: Percent change in Hamilton Depression Rating Scale scorOnly 8 weks chek (2 months after start of treatment) Lower is better?Endpoint? *Depression, CI* ● **Outcome type**: ContinuousOutcome ● **Reporting**: Not reported *Depression, SE* ● **Outcome type**: ContinuousOutcome ● **Reporting**: Not reported
Identification	**Sponsorship source:** Supported by a grant from Forest Laboratories. **Country:** US **Setting:** Community-dwelling patients **Comments:** **Authors name:** Dr. Roose, Steven P. Roose, M.D.

	Institution: New York State Psychiatric Institute, **Email:** spr2@columbia.edu. **Address:** 1051 Riverside Dr., New York, NY 10032;
Notes	*Britta Tendal* on 15/11/2017 01:15 **Outcomes** Data are from 8 weeks treatment

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Assignment to treatment group was performed by a computer-generated randomization schedule, and for each site, patient randomization numbers were assigned in ascending sequence."
Allocation concealment (selection bias)	Unclear risk	Judgement Comment: Not described
Blinding of participants and personnel (performance bias)	Low risk	Judgement Comment: Placebo controlled. Flex dose also applied for placebo. Probably blinded
Blinding of outcome assessment (detection bias)	Low risk	Judgement Comment: Placebo controlled. Probably blinded
Incomplete outcome data (attrition bias)	Low risk	Judgement Comment: Overall 83.3% completed the 8 weeks of treatment. More adverse events in SSRI group.
Selective reporting (reporting bias)	Low risk	
Other bias	Low risk	Judgement Comment: No other apparent sources of bias

Schatzberg 2006

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Intervention 1 ● *Age (range)*: ● *Depression score* : Intervention 2 ● *Age (range)*: ● *Depression score* : Control ● *Age (range)*: ● *Depression score* : Overall ● *Age (range)*: Mean age 71 years (SD 5) ● *Depression score* : HAM-D 22 (SD 3) **Included criteria:** Male or female subjects aged 65 years or older and not living in a residential setting were eligible for this study. In addition, eligible participants met diagnostic and statistical manual for mental disorders, Fourth edition criteria for unipolar depression (single or recurrent, nonpsychotic), with a current episode of at least four weeks in duration; had a 21-item HAM-D (HAM-D21) score of 20 or above at the initial visit; and were willing an able to provide informed consent. Subjects with no more than a 20% decrease in score after a single-blind, placebo lead-in week were randomized to treatment. **Excluded criteria:** Subjects with bipolar disorder, a psychotic disorder not related to depression, current substance abuse or substance dependence within the past year (other than nicotine), current suicidal intent, Mini Mental status Examination of 18 or below, and patients who had received treatment with Fluoxetine or venlafaxine in the past six months, electroconvulsivetherapy within the prior three months, or any investigational drug or antipsychotic medication within the prior 30 days were excluded from the study. Also excluded were subjects who used astemizole, cisapride, sumatriptan, terfenadine, paroxetine, sertraline or any monoamine oxidase inhibitor within 14 days, used any other antidepressant, anxiolytic or sedative-hypnotic drugs (except chloral hydrate) or any other psychotropic drug or substance within seven days of the start of the double-blind treatment period. Patients with a known hypersensitivity to venlafaxine or fluoxetine, those with clinically significant hepatic or renal disease, seizure disorder or myocardial

	infarction within the prior 6 months, and patients with a severe, acure or unstable medical illness were not allowed to participate in the study. **Pretreatment:** There was no statistically significant difference among the three treatment groups for any baseline or demographic characteristics.
Interventions	**Intervention Characteristics** Intervention 1 ● *Description*: Fluoxetine 20-60 mg/day ● *Dose (mg)*: Flexdose 20-60 mg/day ● *Duration of treatment (weeks)*: 8 Intervention 2 ● *Description*: ● *Dose (mg)*: ● *Duration of treatment (weeks)*: Control ● *Description*: Placebo ● *Dose (mg)*: ● *Duration of treatment (weeks)*: 8
Outcomes	*Død (death)* ● **Outcome type**: DichotomousOutcome *Antal af personer som falder (med eller uden bevidsthedstab) (No. of persons with a fall (with/without loss of consciousness))* ● **Outcome type**: DichotomousOutcome *Antal af personer som falder (med eller uden bevidsthedstab) (No. of persons with fall (with/without loss of consciousness))* ● **Outcome type**: DichotomousOutcome *Fald (med eller uden bevidsthedstab) (Fall (with/without loss of consciousness)* ● **Outcome type**: ContinuousOutcome *Fald (med eller uden bevidsthedstab) (Fall with/without loss of consciousness)* ● **Outcome type**: ContinuousOutcome

	Fald med fraktur (major injuries) (Fall with fractures) ● **Outcome type**: DichotomousOutcome *Livskvalitet (life quality)* ● **Outcome type**: ContinuousOutcome *Svimmelhed (Dizziness) (%, N)* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Fully reported ● **Direction**: Lower is better ● **Data value**: Change from baseline *Svimmelhed (Dizziness) (%, N).* ● **Outcome type**: DichotomousOutcome *Depression, SD. 6 months after start of treatment.* ● **Outcome type**: ContinuousOutcome *Depression, CI* ● **Outcome type**: ContinuousOutcome ● **Reporting**: Partially reported ● **Scale**: HAM-D21 total score ● **Direction**: Lower is better ● **Data value**: Endpoint ● **Notes**: Only data after 2months of treatmentThere are no precise estimates. Data extracted from a grapf. CI only provided for mean difference between groups: Venlafaxine versus placebo and Fluoxetine versus placebo. *Depression, SE* ● **Outcome type**: ContinuousOutcome
Identification	**Sponsorship source:** Funding for this study was provided by Wyeth Research **Country:** US **Setting:** **Comments:** **Authors name:** Alan Schatzberg **Institution:** Stanford University School of Medicine

	Email: afschatz@liland.stanford.edu **Address:** Stanford University School of medicine, 401 Quarry Rd. , Rm. 300, Stanford
Notes	*Britta Tendal* on 15/11/2017 01:46 **Outcomes** HAM-D total score final diff between SSRI and placebo 95%CI (-0.601 to 3.614) at 8 weeks.Data on dizziness is also at 8 weeks

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement Comment: Randomization was by number in six-patient units with equal numbers of each treatment.
Allocation concealment (selection bias)	Low risk	Judgement Comment: Medication for each patient was packaged individually and code-labeled with the study number and a unique patient randomization number. Units were distributed to study sites according to the lowest available randomization number.
Blinding of participants and personnel (performance bias)	Low risk	Judgement Comment: Described as double blind. Placebo controlled
Blinding of outcome assessment (detection bias)	Low risk	Judgement Comment: Placebo controlled
Incomplete outcome data (attrition bias)	High risk	Judgement Comment: Overall 78% completed the 8 weeks of treatment. Higher number of drop outs due to adverse events in the SSRI group than the placebo group
Selective reporting (reporting bias)	Low risk	
Other bias	Low risk	Judgement Comment: No other apparent sources of bias

Schneider 2003

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Intervention 1 ● *Age (range)*: 60-92 (mean 70.0) ● *Depression score* : endpoint mean(SD): 13.0(6.2) Intervention 2 ● *Age (range)*: ● *Depression score* : Control ● *Age (range)*: 59-97 (mean 69.6) ● *Depression score* : endpoint mean(SD): 14.5(6.2) Overall ● *Age (range)*: ● *Depression score* : **Included criteria:** The study participants were male or female community-dwell-ing outpatients age 60 years or overTo be eligi-ble, patients had to have a current diagnosis of major depressivedisorder, single episode or recurrent, without psychotic features(DSM-IV) of at least 4 weeks' duration, with a total score of 18 orhigher on the 17-item Hamilton depression scale at baseline (andwith a score of 2 or higher on item 1, "depressed mood"). **Excluded criteria:** The exclusion criteria included a current DSM-IV diagnosis ofdepressive disorder with psychotic features, dementia, organicmental disorder, or mental retardation; a score less than 24 on theMini-Mental State Examination (MMSE) (23); a current or pasthistory of any psychotic disorder or bipolar disorder; a diagnosisof drug or alcohol abuse or dependence within the previous 6months (except nicotine); a history of seizure disorder; previousnonresponse, known hypersensitivity, or contraindication to sertraline; participation in an investigational drug trial within 3months before this trial; significant suicide risk, a need for elec-troconvulsive therapy, additional psychotropic drugs, or hospital-ization; regular, daily use of benzodiazepines within 3 weeks, useof antidepressants within 2 weeks, use of monoamine oxidase in-hibitors or fluoxetine within 5 weeks of randomization; use of adepot antipsychotic drug within 6 months of entering the study;initiation of individual or group psychotherapy within 3 monthsof study entry; and any clinically significant unstable medical dis-order that might affect study participation (however, patientswith stable

	medical conditions such as insulin-dependent diabetes mellitus were allowed to participate). Concomitant treatmentwith any other centrally active medication was prohibited exceptfor as-needed use of zolpidem, up to 10 mg/day, or temazepam,up to 30 mg/day, for sleep during the first 4 weeks of the study, al-though such use was discouraged. Use of benzodiazepines asneeded for anxiety was not permitted. The subjects were asked torestrict alcohol intake during the study, and they were askedabout alcohol use at each visit. Subjects could be removed fromthe study at any time because of adverse experiences, insufficienttreatment response, or worsening of depression based on theclinical judgment of the investigator. **Pretreatment:** Overall, there were no significant differences between the treatment groups in any demographic or clinical characteristic at baseline.
Interventions	**Intervention Characteristics** Intervention 1 ● *Description*: Sertraline ● *Dose (mg)*: Flexdose 50 - 100 mg ● *Duration of treatment (weeks)*: 8 Intervention 2 ● *Description*: ● *Dose (mg)*: ● *Duration of treatment (weeks)*: Control ● *Description*: Placebo ● *Dose (mg)*: ● *Duration of treatment (weeks)*: 8
Outcomes	*Død (death)* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Not reported ● **Direction**: Lower is better ● **Notes**: All observed or volunteered adverse events, regardless of treatment group or suspected causal relationship tostudy drug, were recorded and rated as to severity. p. 1279 *Antal af personer som falder (med eller uden bevidsthedstab) (No. of persons with a fall (with/without loss of consciousness))*

- **Outcome type**: DichotomousOutcome
- **Reporting**: Not reported

Antal af personer som falder (med eller uden bevidsthedstab) (No. of persons with fall (with/without loss of consciousness))

- **Outcome type**: DichotomousOutcome
- **Reporting**: Not reported

Fald (med eller uden bevidsthedstab) (Fall (with/without loss of consciousness)

- **Outcome type**: ContinuousOutcome
- **Reporting**: Not reported

Fald (med eller uden bevidsthedstab) (Fall with/without loss of consciousness)

- **Outcome type**: ContinuousOutcome
- **Reporting**: Not reported

Fald med fraktur (major injuries) (Fall with fractures)

- **Outcome type**: DichotomousOutcome
- **Reporting**: Not reported

Livskvalitet (life quality)

- **Outcome type**: ContinuousOutcome
- **Reporting**: Fully reported
- **Direction**: Higher is better
- **Data value**: Endpoint
- **Notes**: Patients Who Completed 8-Week Study

Svimmelhed (Dizziness) (%, N)

- **Outcome type**: DichotomousOutcome
- **Reporting**: Fully reported
- **Direction**: Lower is better
- **Data value**: Endpoint

Svimmelhed (Dizziness) (%, N).

- **Outcome type**: DichotomousOutcome
- **Reporting**: Not reported

	Depression, SD. 6 months after start of treatment. ● **Outcome type**: ContinuousOutcome ● **Reporting**: Partially reported ● **Data value**: Endpoint ● **Notes**: Lower is better?Patients Who Completed 8-Week Study - recording 2 months after start of treatment, NOT 6 months *Depression, CI* ● **Outcome type**: ContinuousOutcome ● **Reporting**: Not reported *Depression, SE* ● **Outcome type**: ContinuousOutcome ● **Reporting**: Not reported
Identification	**Sponsorship source:** From the Department of Psychiatryand Behavioral Sciences, Keck School of Medicine, and the LeonardDavis School of Gerontology, University of Southern California, LosAngeles; the Department of Psychiatry, University of California, SanFrancisco; Pfizer, Inc., New York; the Clinical Neuroscience ResearchUnit, Department of Psychiatry, University of Vermont College ofMedicine, Burlington; the Department of Psychiatry, Duke University,Durham, N.C.; California Clinical Trials, Beverly Hills, Calif.; and the Department of Psychiatry and the Behavioral Sciences, George Wash-ington University, Washington, D.C. Supported by Pfizer, Inc. **Country:** US **Setting:** Outpatients **Comments:** **Authors name:** Dr. Schneider (Lon S. Schneider) M.D. **Institution:** Sertraline Elderly Depression Study Group **Email:** lschneid@usc.edu **Address:** KAM-400, 1975 Zonal Ave., Los Angeles, CA 90033
Notes	*Britta Tendal* on 15/11/2017 02:24 **Outcomes** All outcome are reported at 8 weeksOBS QoL final + change data

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "After a single-blind placebo washout period of 4 to 14 days, subjects meeting the en- try criteria were randomly assigned to 8 weeks of double-blind treatment with either sertraline or placebo." Judgement Comment: Not described
Allocation concealment (selection bias)	Unclear risk	Judgement Comment: Nor described
Blinding of participants and personnel (performance bias)	Low risk	Quote: "Each subject received either a 50-mg sertraline tablet or an identically appearing placebo tablet daily for the first 4 weeks, af- ter which the dose could be increased to 100 mg/day of sertraline (or matched placebo) for the final 4 weeks on the basis of the in- vestigator's assessment of clinical response and tolerability."
Blinding of outcome assessment (detection bias)	Low risk	Judgement Comment: Placebo controlled
Incomplete outcome data (attrition bias)	Low risk	Judgement Comment: Overall 79% of the 752 randomized patients completed the 8 weeks of treatment. ITT was based on 747 patients. More drop out due to adverse events in the SSRI group.
Selective reporting (reporting bias)	Low risk	
Other bias	Low risk	Judgement Comment: No other apparent sources of bias

Tollefson 1995

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Intervention 1 ● *Age (range)*: mean 67.4 SD 5.4 ● *Depression score* : HAM-D 22.2 SD 3.9 Intervention 2 ● *Age (range)*:

	● *Depression score* : Control ● *Age (range)*: Mean 68.1 SD 5.9 ● *Depression score* : HAM-D 22.1 SD 3.8 Overall ● *Age (range)*: ● *Depression score* : **Included criteria:** Subjects were male or female outpatients, aged 60 years and older, who met diagnostic and statistical manual of mental disorders (DSM- III-R) criteria for a current nonpsychotic unipolar major depression (except duration of illness must have been at least 1 month). Subjects were also required to have a score of at least 16 on the first 17 items of the 28-item hamilton depression rating scale (HAM-D17) at baseline. To eliminate placebo responders from the study population, subjects who exhibited 20% or greater improvement on the HAMD17 during the 1-week (4 - to 10 days) single-blind period were removed prior to random assignment. **Excluded criteria:** Subjects were excluded from the study if they had a mini-mental state examination score of less than 25; were at serious suicidal risk; or had a serious/nonstable comorbid medical disorder, a history of seizure disorder, any other other active DSM-III-R axis I disorder, a history of multiple adverse drug reactions or allergy to fluoxetine or mood-congruent or mood-incongruent psychotic features. Subjects with any clinical findings that suggested a contraindication for drug therapy or an organic affective diagnosis were excluded as were those with a history of nonreponse to at least two of the different classes of antidepressants at customary dosages and/or those having received electroconvulsive therapy within 12 months. Also excluded were subjects who had used a heterocyclic or monoamine oxidase inhibitor antidepressant within 14 days, Fluoxetine within 6 weeks of screening, or centrally active medications (except chloral hydrate), including investigational drugs, within 4 weeks of evaluation. **Pretreatment:** There were no statistically significant differences between treatment groups with respect to demographic characteristics.
Interventions	**Intervention Characteristics** Intervention 1 ● *Description*: Fluoxetine ● *Dose (mg)*: 20mg. Investigators could reduce the an every-other-day treatment regimen if patients experiences adverse events ● *Duration of treatment (weeks)*: 6 Intervention 2

	● *Description*: ● *Dose (mg)*: ● *Duration of treatment (weeks)*: Control ● *Description*: Placebo ● *Dose (mg)*: ● *Duration of treatment (weeks)*: 6
Outcomes	*Død (death)* ● **Outcome type**: DichotomousOutcome *Antal af personer som falder (med eller uden bevidsthedstab) (No. of persons with a fall (with/without loss of consciousness))* ● **Outcome type**: DichotomousOutcome *Antal af personer som falder (med eller uden bevidsthedstab) (No. of persons with fall (with/without loss of consciousness))* ● **Outcome type**: DichotomousOutcome *Fald (med eller uden bevidsthedstab) (Fall (with/without loss of consciousness)* ● **Outcome type**: ContinuousOutcome *Fald (med eller uden bevidsthedstab) (Fall with/without loss of consciousness)* ● **Outcome type**: ContinuousOutcome *Fald med fraktur (major injuries) (Fall with fractures)* ● **Outcome type**: DichotomousOutcome *Livskvalitet (life quality)* ● **Outcome type**: ContinuousOutcome *Svimmelhed (Dizziness) (%, N)* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Fully reported ● **Direction**: Lower is better ● **Notes**: Only results after 6 weeks

	Svimmelhed (Dizziness) (%, N). ● **Outcome type**: DichotomousOutcome *Depression, SD. 6 months after start of treatment.* ● **Outcome type**: ContinuousOutcome ● **Reporting**: Fully reported ● **Scale**: HAMD-D17 ● **Range**: 0-52 ● **Direction**: Lower is better ● **Data value**: Change from baseline ● **Notes**: Results only available after 6 weeks of treatment *Depression, CI* ● **Outcome type**: ContinuousOutcome *Depression, SE* ● **Outcome type**: ContinuousOutcome
Identification	**Sponsorship source:** Lilly Research Laboratories, Eli Lilly and Company **Country:** US **Setting:** Outpatients **Comments:** **Authors name:** Gary D. Tollefson **Institution:** Lilly Research Laboratories , Elli Lilly and Company **Email:** n/a **Address:** Lilly Corporate Center 2128, Indianapolis, IN 46285 US
Notes	*Britta Tendal* on 15/11/2017 02:51 **Outcomes** Data are from 6 weeks treatment

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement Comment: 'patients randomly assigned'No details
Allocation concealment (selection bias)	Unclear risk	Judgement Comment: Not described
Blinding of participants and personnel (performance bias)	Low risk	Judgement Comment: Described as 'double blind'.Placebo controlled
Blinding of outcome assessment (detection bias)	Low risk	Judgement Comment: Placebo controlled
Incomplete outcome data (attrition bias)	Low risk	Judgement Comment: Overall 79.6% completed the 6 weeks of treatment. They state that there were no differences in reasons for drop out.
Selective reporting (reporting bias)	Low risk	
Other bias	Low risk	Judgement Comment: No other apparent sources of bias

Footnotes

Characteristics of excluded studies

Campbell 1999

Reason for exclusion	Wrong intervention

Footnotes

Characteristics of studies awaiting classification

Footnotes

Characteristics of ongoing studies

Footnotes

Summary of findings tables

Additional tables

References to studies

Included studies

Kasper 2005

Kasper, S.; de Swart, H.; Friis Andersen, H.. Escitalopram in the treatment of depressed elderly patients. The American Journal of Geriatric Psychiatry : Official Journal of the American Association for Geriatric Psychiatry 2005;13(10):884-891. [DOI: 13/10/884 [pii]]

Rapaport 2003

Rapaport, M. H.; Schneider, L. S.; Dunner, D. L.; Davies, J. T.; Pitts, C. D.. Efficacy of controlled-release paroxetine in the treatment of late-life depression. The Journal of clinical psychiatry 2003;64(9):1065-1074. [DOI:]

Rapaport 2009

Rapaport, M. H.; Lydiard, R. B.; Pitts, C. D.; Schaefer, D.; Bartolic, E. I.; Iyengar, M.; Carfagno, M.; Lipschitz, A.. Low doses of controlled-release paroxetine in the treatment of late-life depression: a randomized, placebo-controlled trial. The Journal of clinical psychiatry 2009;70(1):46-57. [DOI: ej06m02996 [pii]]

Roose 2004

Roose, S. P.; Sackeim, H. A.; Krishnan, K. R.; Pollock, B. G.; Alexopoulos, G.; Lavretsky, H.; Katz, I. R.; Hakkarainen, H.; Old-Old Depression Study Group. Antidepressant pharmacotherapy in the treatment of depression in the very old: a randomized, placebo-controlled trial. The American Journal of Psychiatry

2004;161(11):2050-2059. [DOI: 161/11/2050 [pii]]

Schatzberg 2006

Schatzberg, A.; Roose, S.. A double-blind, placebo-controlled study of venlafaxine and fluoxetine in geriatric outpatients with major depression. The American Journal of Geriatric Psychiatry : Official Journal of the American Association for Geriatric Psychiatry 2006;14(4):361-370. [DOI: 14/4/361 [pii]]

Schneider 2003

Schneider, L. S.; Nelson, J. C.; Clary, C. M.; Newhouse, P.; Krishnan, K. R.; Shiovitz, T.; Weihs, K.; Sertraline Elderly Depression Study Group. An 8-week multicenter, parallel-group, double-blind, placebo-controlled study of sertraline in elderly outpatients with major depression. The American Journal of Psychiatry 2003;160(7):1277-1285. [DOI: 10.1176/appi.ajp.160.7.1277 [doi]]

Tollefson 1995

Tollefson, G. D.; Bosomworth, J. C.; Heiligenstein, J. H.; Potvin, J. H.; Holman, S.. A double-blind, placebo-controlled clinical trial of fluoxetine in geriatric patients with major depression. The Fluoxetine Collaborative Study Group. International psychogeriatrics 1995;7(1):89-104. [DOI:]

Excluded studies

Campbell 1999

Campbell, A. J.; Robertson, M. C.; Gardner, M. M.; Norton, R. N.; Buchner, D. M.. Psychotropic medication withdrawal and a home-based exercise program to prevent falls: a randomized, controlled trial. Journal of the American Geriatrics Society 1999;47(7):850-853. [DOI:]

Studies awaiting classification

Ongoing studies

Other references

Additional references

Other published versions of this review

Data and analyses

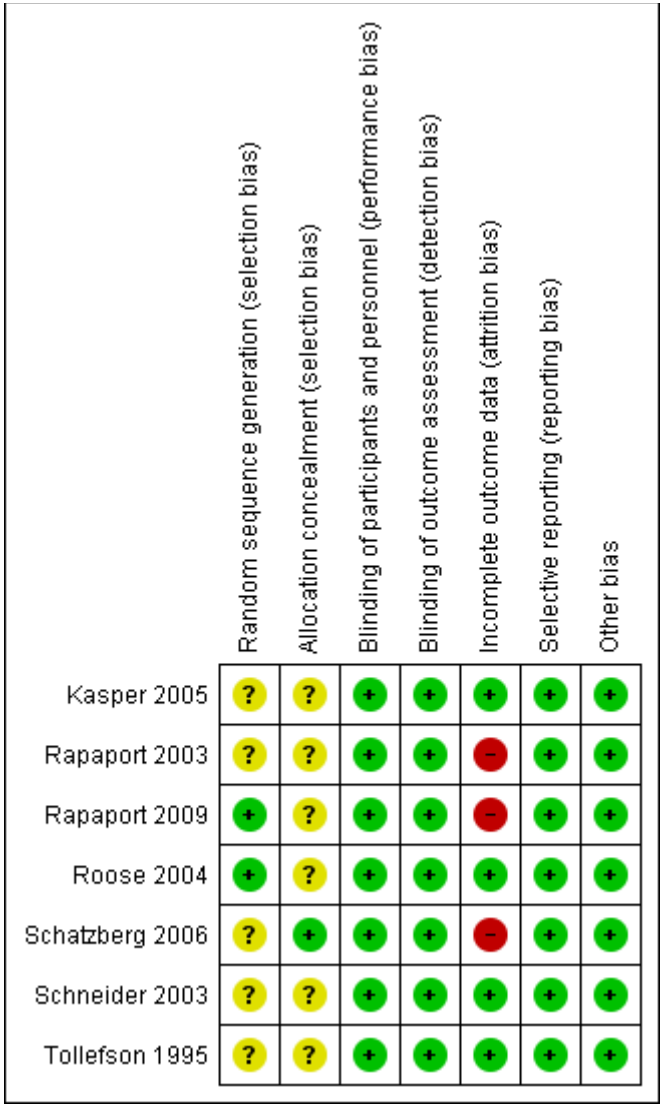
1 SSRI vs placebo

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
1.1 Fall 2 month after start of treatment	0	0	Odds Ratio (M-H, Fixed, 95% CI)	Not estimable
1.2 Fall 6 month after start of treatment	0	0	Odds Ratio (M-H, Fixed, 95% CI)	Not estimable
1.3 No. of persons with a fall 2 month after start of treatment	0		Risk Ratio (IV, Fixed, 95% CI)	No totals
1.4 No. of persons with a fall 6 month after start of treatment	0		Risk Ratio (IV, Fixed, 95% CI)	No totals
1.5 Mortality End of treatment	3	1780	Risk Ratio (IV, Random, 95% CI)	0.53 [0.03, 8.49]
1.5.1 Mortality EoT	3	1780	Risk Ratio (IV, Random, 95% CI)	0.53 [0.03, 8.49]
1.6 Mortality 1 year after start of treatment	0		Risk Ratio (IV, Fixed, 95% CI)	No totals
1.7 Dizziness 6 to 12 after start of treatment	6	2824	Risk Ratio (IV, Random, 95% CI)	1.43 [0.99, 2.07]
1.7.1 Dizziness 6 to 12 after start of treatment	6	2824	Risk Ratio (IV, Random, 95% CI)	1.43 [0.99, 2.07]
1.8 Dizziness 6 month after start of treatment	0		Risk Ratio (IV, Fixed, 95% CI)	No totals
1.10 Fractures End of treatment	2	1263	Risk Ratio (IV, Random, 95% CI)	2.84 [0.31, 25.58]
1.11 Fall with fracture 6 months after start of treatment	0		Risk Ratio (IV, Fixed, 95% CI)	No totals
1.12 Depression HAM-D End of treatment MELLEMREGNING	5	2214	Mean Difference (IV, Random, 95% CI)	-1.77 [-2.67, -0.87]
1.12.1 HAM-D EoT	5	2214	Mean Difference (IV, Random, 95% CI)	-1.77 [-2.67, -0.87]

1.13 Depression HAM-D End of treatment	5	2131	Mean Difference (IV, Random, 95% CI)	-1.71 [-2.47, -0.95]
1.13.1 HAM-D EoT	5	2131	Mean Difference (IV, Random, 95% CI)	-1.71 [-2.47, -0.95]
1.14 Depression 6 month after start of treatment	0	0	Mean Difference (IV, Fixed, 95% CI)	Not estimable
1.15 Quality of life End of treatment	2	1161	Std. Mean Difference (IV, Random, 95% CI)	0.21 [0.09, 0.33]
1.16 Quality of life 6 month after start of treatment	0	0	Mean Difference (IV, Fixed, 95% CI)	Not estimable

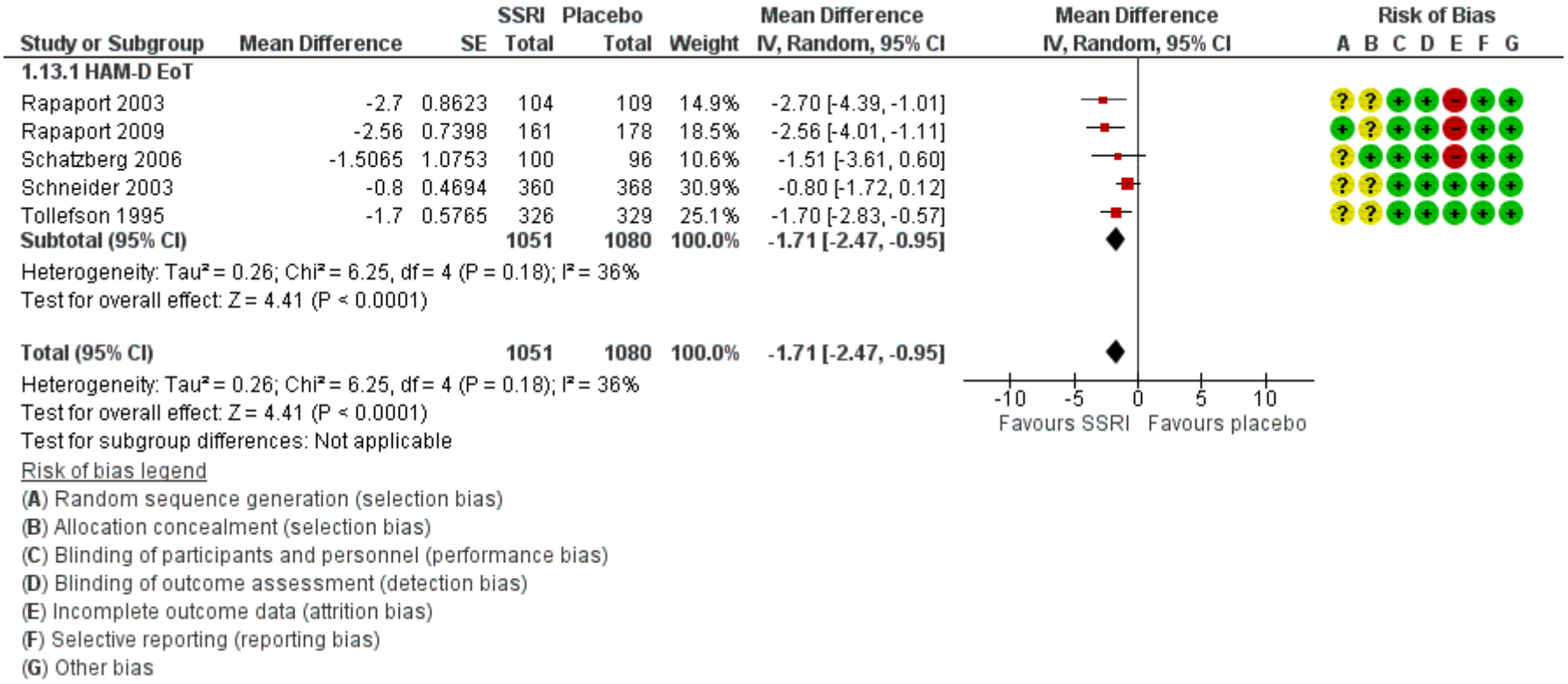
Figures

Figure 1



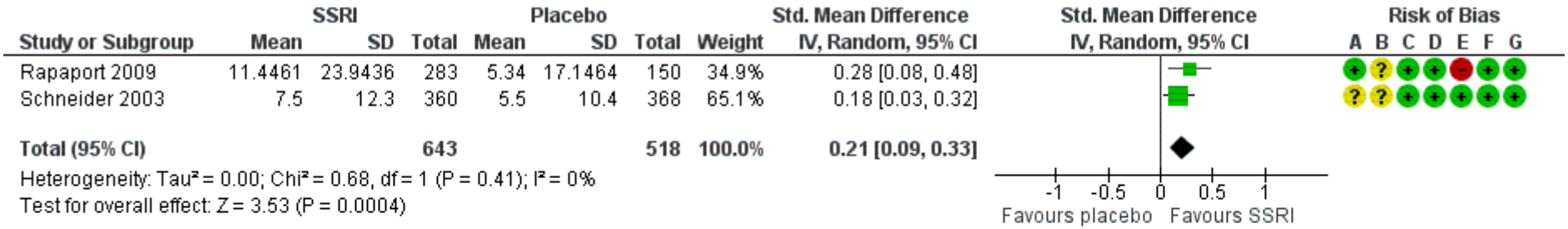
Risk of bias summary: review authors' judgements about each risk of bias item for each included study.

Figure 2 (Analysis 1.13)



Forest plot of comparison: 1 SSRI vs placebo, outcome: 1.13 Depression HAM-D End of treatment.

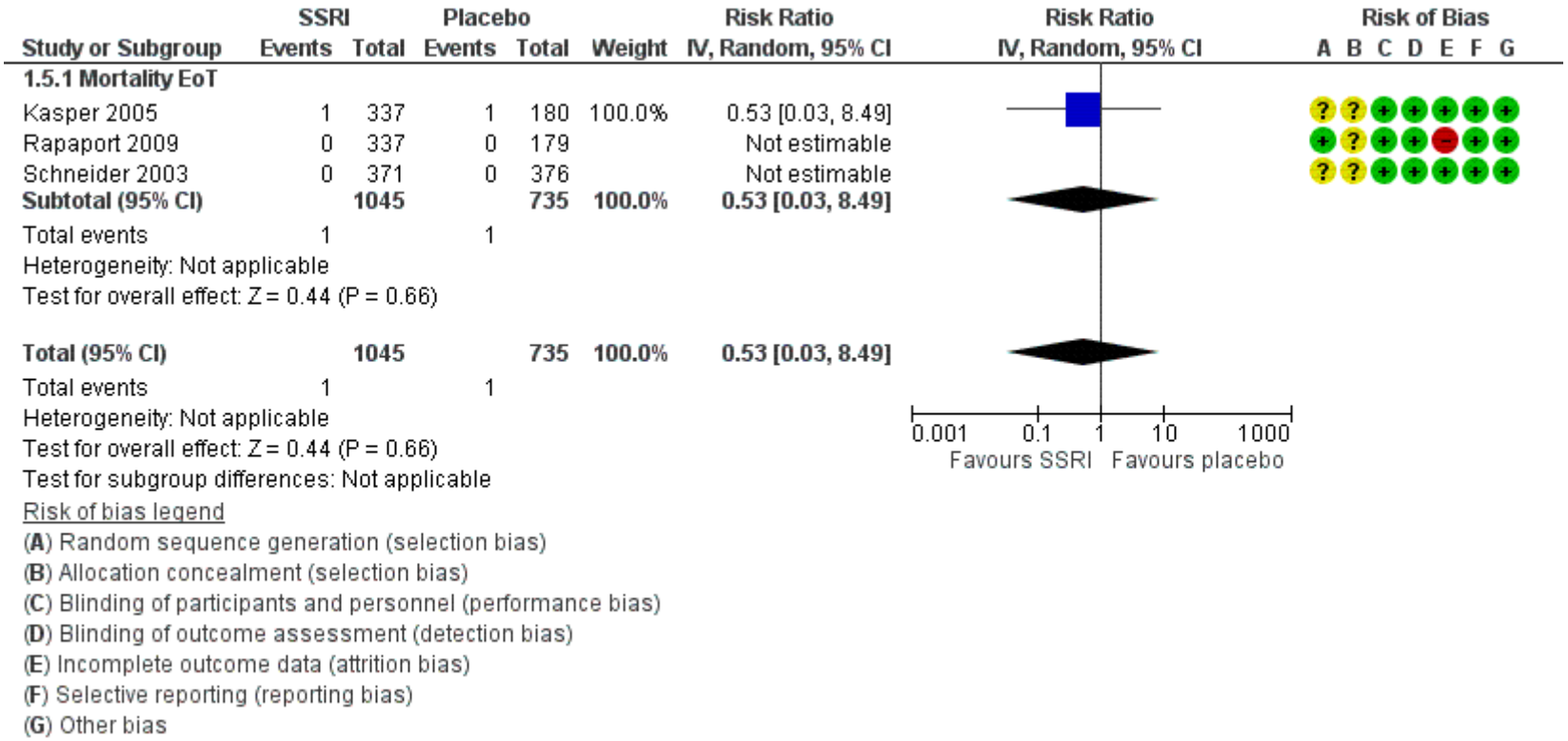
Figure 3 (Analysis 1.15)



Risk of bias legend
(**A**) Random sequence generation (selection bias)
(**B**) Allocation concealment (selection bias)
(**C**) Blinding of participants and personnel (performance bias)
(**D**) Blinding of outcome assessment (detection bias)
(**E**) Incomplete outcome data (attrition bias)
(**F**) Selective reporting (reporting bias)
(**G**) Other bias

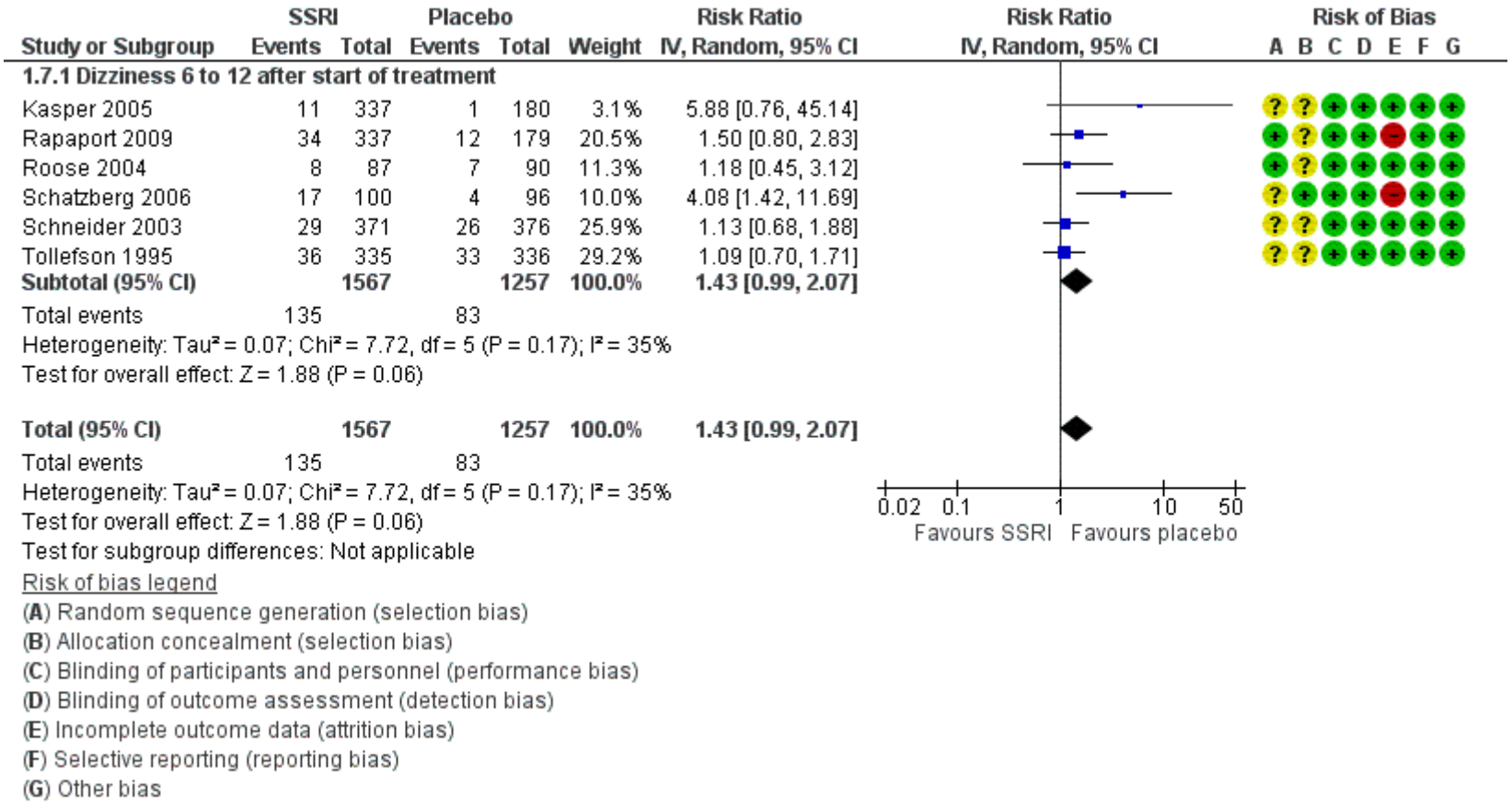
Forest plot of comparison: 1 SSRI vs placebo, outcome: 1.15 Quality of life End of treatment.

Figure 4 (Analysis 1.5)



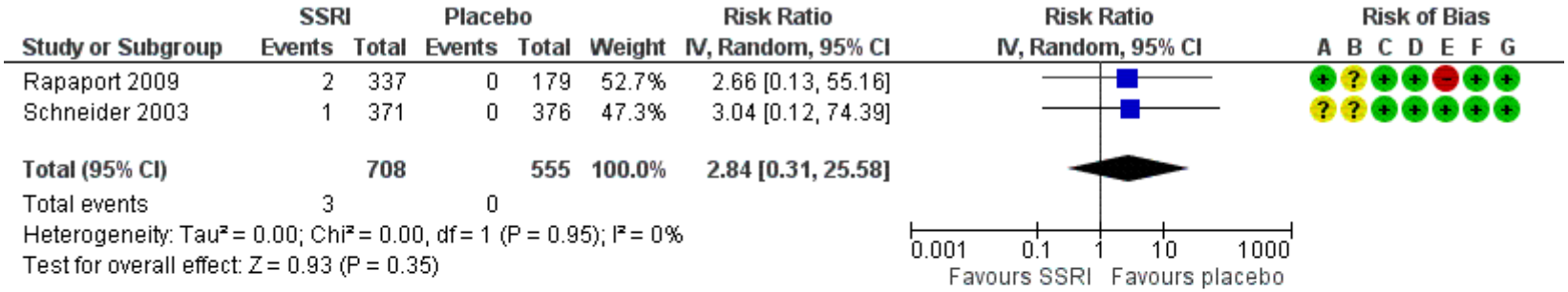
Forest plot of comparison: 1 SSRI vs placebo, outcome: 1.5 Mortality End of treatment.

Figure 5 (Analysis 1.7)



Forest plot of comparison: 1 SSRI vs placebo, outcome: 1.7 Dizziness 6 to 12 after start of treatment.

Figure 6 (Analysis 1.10)



Risk of bias legend
(**A**) Random sequence generation (selection bias)
(**B**) Allocation concealment (selection bias)
(**C**) Blinding of participants and personnel (performance bias)
(**D**) Blinding of outcome assessment (detection bias)
(**E**) Incomplete outcome data (attrition bias)
(**F**) Selective reporting (reporting bias)
(**G**) Other bias

Forest plot of comparison: 1 SSRI vs placebo, outcome: 1.10 Fractures End of treatment.