NKR 53 demens og adfærds PICO 10

Review information

Authors

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Citation example: S. NKR 53 demens og adfærds PICO 10. Cochrane Database of Systematic Reviews [Year], Issue [Issue].

Characteristics of studies

Characteristics of included studies

DeDeyn 2004

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Overall ● *Age. Mean, SD*: 76.6, 10.4 ● *MMSE*: 13.7, 5.1 **Included criteria:** Patients were male or female, aged 40 years andabove, resided in long-term nursing homes or continu-ing-care hospitals in Europe, Australia, Israel, Lebanon, and South Africa, and were expected tocontinue patient status for 6 months following enroll-ment. All patients met the NINCDS-ADRDA (McKhannet al., 1984) and DSM-IV-TR (AmericanPsychiatric Association, 2000) criteria for possible or probable Alzheimer's disease (AD), and all exhib-ited clinically significant psychotic symptoms (delu-sions or hallucinations) due to AD. The delusions or hallucinations had to: (1) be at least moderate in severity (i.e. impair patients' functional capacity or cause them to pose a threat to themselves) at study entry (Visit 1) and at randomization (Visit 2); (2) be present at least once per week for the month preced-ing study entry; and (3) require pharmacological intervention, in the opinion of the investigator. Aminimum score of 5 on the Mini-Mental State Exam-ination (MMSE; Folsteinet al., 1975) was required at Visit 1 and Visit 2. **Excluded criteria:** Exclusionary criteria included a diagnosis of current primary mood disorder or other Axis I disorder

	with onset prior to diagnosis of AD, including but not limited to schizophrenia, bipolar disorder, or delusional disorder. **Pretreatment:** Patient demographics and illness characteristics at baselinewere not statistically different among treatment groups
Interventions	**Intervention Characteristics** Intervention 1 ● *Description*: Olanzapine 7.5mg ● *Length of treatment*: 10 weeks ● *Longest follow-up after end of treatment*: None Intervention 2 ● *Description*: Olanzapine 5.0mg ● *Length of treatment*: 10 weeks ● *Longest follow-up after end of treatment*: None Control ● *Description*: Placebo ● *Length of treatment*: 10 weeks ● *Longest follow-up after end of treatment*: None
Outcomes	*Serious adverse events, n* ● **Outcome type**: DichotomousOutcome *Mortality, n* ● **Outcome type**: DichotomousOutcome ● **Notes**: OBS! Includes both patients that died during the intervention and 30 days after. *BPSD (NPI), SD* ● **Outcome type**: ContinuousOutcome
Identification	
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement Comment: Described as randomized, no details
Allocation concealment (selection bias)	Unclear risk	Judgement Comment: Described as randomized, no details
Blinding of participants and personnel (performance bias)	Low risk	Judgement Comment: Placebo-controlled fixed dose
Blinding of outcome assessment (detection bias)	Unclear risk	Judgement Comment: Not described
Incomplete outcome data (attrition bias)	High risk	Judgement Comment: Percent completing ranged from 70.5 in the placebo group to 75.2 in the olanzapine groups. Reasons differed between group
Selective reporting (reporting bias)	Low risk	Judgement Comment: None detected
Other bias	Low risk	Judgement Comment: No other apparent sources of bias

DeDeyn 2005

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Overall ● *Age. Mean, SD*: 81.5 **Included criteria:** Noninstutitionalized men and women, aged 55-95 years of age, diagnosed with AD, with symptoms of delusions or hallucinations present for 1 month or longer. MMSE score of 6-24, and NPI delusion/halluciation at baseline of >= 6. **Excluded criteria:** Diagnosis of delirium, amnesic disorder, bipolar disorder, schizophrenia or schizoaffective disorder or mood disorder with psychotic feature, psychotic symptom better accounted for by general medical condition or direct psychologic effects of substances. Refractory to neuroleptics used to treat psychotic symptoms in the past. **Pretreatment:** Patient characteristics were similar between groups at baseline.

Interventions	**Intervention Characteristics** Intervention ● *Description*: Aripiprazole. Dose starting at 2mg, that could be titrated to higher dosage (5mg, 10mg, 15mg) at 2 weeks intervals. ● *Length of treatment*: 10 weeks ● *Longest follow-up after end of treatment*: None Control ● *Description*: Placebo ● *Length of treatment*: 10 weeks ● *Longest follow-up after end of treatment*: None
Outcomes	*Serious adverse events, n* ● **Outcome type**: DichotomousOutcome *BPSD (NPI), SD* ● **Outcome type**: ContinuousOutcome *Kognition (MMSE), SD* ● **Outcome type**: ContinuousOutcome
Identification	
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement Comment: Described as randomized, no details given
Allocation concealment (selection bias)	Unclear risk	Judgement Comment: Described as randomized, no details given

Blinding of participants and personnel (performance bias)	Unclear risk	Judgement Comment: Described as double-blind, probable that the patients were blinded. Apripiprazole could be tritrated to higher dose if there was insufficient clinical response. The same is not described for placebo. Therefore it is unclear if the personnel was blinded.
Blinding of outcome assessment (detection bias)	Unclear risk	Judgement Comment: Not described
Incomplete outcome data (attrition bias)	Low risk	Judgement Comment: 83% completed the treatment, reasons for withdrawal were similar
Selective reporting (reporting bias)	Low risk	Judgement Comment: None detected
Other bias	Low risk	Judgement Comment: No other apparent sources of bias

Mintzer 2007

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Intervention 1 ● *Age. Mean, SD*: 82.3 (56.0-94.0 range) Intervention 2 ● *Age. Mean, SD*: 82.4 (60.0-97.0 range) Control ● *Age. Mean, SD*: 82.2 (56.0-96.0 range) ● *MMSE*: **Included criteria:** Men and women, age 55-95 years, diagnosed with AD and psychotic symptoms of delusions or hallucinations, living in nursing homes or residential assisted-living facilities for a minimum of 4 weeks before study entry. Patients required to be capable of selflocomotion and have an identified proxy caregiver. **Excluded criteria:** Axis 1 diagnosis of delirium, amnestic disorder, bipolar disorder, schizophrenia or schizoaffective disorder, or mood disorder with psychotic features; non-AD: a current MD episode with psychotic symptoms of hallucinations or delusions. **Pretreatment:** There were no apparent differences at baseline between the groups.

Interventions	**Intervention Characteristics** Intervention 1 ● *Description*: Aripiprazole 10mg ● *Length of treatment*: 10 weeks ● *Longest follow-up after end of treatment*: None Intervention 2 ● *Description*: Aripiprazole 5mg ● *Length of treatment*: 10 weeks ● *Longest follow-up after end of treatment*: None Control ● *Description*: Placebo ● *Length of treatment*: 10 weeks ● *Longest follow-up after end of treatment*: None
Outcomes	*Serious adverse events, n* ● **Outcome type**: DichotomousOutcome *Mortality, %* ● **Outcome type**: DichotomousOutcome *BPSD (NPI), SD* ● **Outcome type**: ContinuousOutcome *Kognition (MMSE), SD* ● **Outcome type**: ContinuousOutcome *Agitation (CMAI), SD* ● **Outcome type**: ContinuousOutcome
Identification	
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement Comment: Described as randomized, no details
Allocation concealment (selection bias)	Unclear risk	Judgement Comment: Described as randomized, no details
Blinding of participants and personnel (performance bias)	Low risk	Judgement Comment: Described as double-blind, placebo controlled fixed dose
Blinding of outcome assessment (detection bias)	Unclear risk	Judgement Comment: No details
Incomplete outcome data (attrition bias)	Low risk	Judgement Comment: 487 randomized (4 groups), safety population 480, efficacy population 475
Selective reporting (reporting bias)	Low risk	Judgement Comment: None detected
Other bias	Low risk	Judgement Comment: No other apparent sources of bias

Street 2000

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Intervention 1 ● *Age. Mean, SD*: 82.9 (6.5) ● *MMSE*: 7.3 (6.5) Intervention 2 ● *Age. Mean, SD*: 83.6 (6.5) ● *MMSE*: 6.6 (6.7) Intervention 3 ● *Age. Mean, SD*: 83.0 (6.7) ● *MMSE*: 6.4 (6.7)

	Control ● *Age. Mean, SD*: 81.4 (6.7) ● *MMSE*: 7.3 (6.3) **Included criteria:** Patients must have scored 3 or higher on any of this items in the NPI **Excluded criteria:** History of axis I disorder, any neurological condition other than AD that could be contribute to psychosis or dementia, a MMSE score of greater than 24 and beridden status. **Pretreatment:** Patient characteristics were similar at baseline across groups
Interventions	**Intervention Characteristics** Intervention 1 ● *Description*: Olanzapine 5mg ● *Length of treatment*: 6 weeks ● *Longest follow-up after end of treatment*: None Intervention 2 ● *Description*: Olanzapine 10mg ● *Length of treatment*: 6 weeks ● *Longest follow-up after end of treatment*: None Intervention 3 ● *Description*: Olanzapine 15mg ● *Length of treatment*: 6 weeks ● *Longest follow-up after end of treatment*: None Control ● *Description*: Placebo ● *Length of treatment*: 6 weeks ● *Longest follow-up after end of treatment*: None
Outcomes	*Serious adverse events, n* ● **Outcome type**: DichotomousOutcome *BPSD (NPI), SD* ● **Outcome type**: ContinuousOutcome *Kognition (MMSE), SD*

	● **Outcome type**: ContinuousOutcome
Identification	
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Judgement Comment: Randomization by the assignment of a unique kit number using a permuted block design at investigational site
Allocation concealment (selection bias)	Low risk	Judgement Comment: Study medication was in identical tablets and dosed once daily.
Blinding of participants and personnel (performance bias)	Low risk	Judgement Comment: Described as double-blind placebo controlled fixed dose
Blinding of outcome assessment (detection bias)	Unclear risk	Judgement Comment: No details
Incomplete outcome data (attrition bias)	High risk	Judgement Comment: Proportion completed ranged from 66% to 80.4%, different reasons for drop out
Selective reporting (reporting bias)	Unclear risk	Judgement Comment: No reporting on SAE or death
Other bias	Low risk	Judgement Comment: No other apparent sources of bias

Streim 2008

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Intervention ● *Age. Mean, SD*: 83,0 (61.0-96.0 range) Control

	● *Age. Mean, SD*: 83.0 (59.0-96.0 range) **Included criteria:** Men and women aged 55-95 years, diagnosed with AD, had psychotic symptoms of delusions or hallucinations for =>1 month. Subjects had to be institutionalized for =>4 weeks before study entry, capable of self-locomotion or locomotion with aid and have caregiver or famility member who could serve as a collateral informant for study information. Patients were required to have a MMSE score between 6-22 at screening with a score of => 6 on either the delusions or hallucinations items of the NPI at baseline. **Excluded criteria:** Axis 1 diagnosis of delerium or schizophrenia, a schizoaffective mood, bipolar or amnestic disorder, any reversible cause of dementia, continous symptoms of psychosis before onset of dementia, psychotic symptoms better accounted for by another medical condition or direct effects of a substance. Current episodes of MD with symptoms of psychosis; dementia resulting from vascular causes and specific non- AD type dementia caused by trauma, disease, infection or substance abuse, a seizure disorder and/or unstable thyroid pathology within the past 3 months. Previously refractory to antipsychotic medicin for psychosis, had participated in any clinical study with an investigational agent =1 month before randomization: had received recent treatment with a long-acting antipsychotic agent in which the last dose was administered 1 full cycle plus 1 week prior to randomization, met DSM-IC criteriafor any significant substance use disorder, were deemed to be a significant risk of suicide; were likely to require prohibited concomitant thereapy, were known to be allergic or hypersensitive to aripiprazole or quinolionens, had any laboratory test, vital sign or EEG abnormalities that could indicate elevated risk for significant adverse events or any medical condition that would make study partiticpation unsafe. **Pretreatment:** Groups were similar at baseline
Interventions	**Intervention Characteristics** Intervention ● *Description*: Aripiprazole. Starting at 2mg/day, with titration to higher dosage (5, 10, 15mg/day) depending on clinical judgement. ● *Length of treatment*: 10 weeks ● *Longest follow-up after end of treatment*: None Control ● *Description*: Placebo ● *Length of treatment*: 10 weeks ● *Longest follow-up after end of treatment*: None

Outcomes	*Serious adverse events, n* ● **Outcome type**: DichotomousOutcome *BPSD (NPI), SD* ● **Outcome type**: ContinuousOutcome *Kognition (MMSE), SD* ● **Outcome type**: ContinuousOutcome *ADL (ADCS-ADL), SD* ● **Outcome type**: ContinuousOutcome *Agitation (CMAI), SE* ● **Outcome type**: ContinuousOutcome
Identification	
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement Comment: Described as randomized, no details
Allocation concealment (selection bias)	Unclear risk	Judgement Comment: Described as randomized, no details
Blinding of participants and personnel (performance bias)	Low risk	Judgement Comment: Described as double-blind. Aripiprazole dose was flexible, no details on placebo titrating
Blinding of outcome assessment (detection bias)	Unclear risk	Judgement Comment: Described as double-blind. Aripiprazole dose was flexible, no details on placebo titrating. No details on assessors
Incomplete outcome data (attrition bias)	High risk	Judgement Comment: In the placebo group 51% completed and in the aripiprazole group the number was 66%. The reasons differed.

Selective reporting (reporting bias)	Low risk	Judgement Comment: None detected
Other bias	Low risk	Judgement Comment: No other apparent sources of bias

Sultzer 2008

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Overall ● *Age. Mean, SD*: Mean 77.9 SD7.5 ● *MMSE*: Mean 15 SD 5.8 **Included criteria:** To participate in the trial, patients met DSM-IV criteria for dementia of the Alzheimer's type(19) or met NINCDS-ADRDA criteria for probable AD (20), after a thorough history, physicaland cognitive examination, and laboratory assessment were completed. Enrolled patients wereoutpatients living at home or in an assisted-living facility, had a knowledgeable informant, andwere ambulatory. Patients in skilled nursing homes were not included. Mini-Mental State Exam(MMSE) (21) score was 5 to 26. Entry criteria required that delusions, hallucinations, agitation,or aggression had occurred nearly every day over the previous week or intermittently over 4 weeks. Symptoms had to have been rated at least moderate in severity on the Brief PsychiatricRating Scale (BPRS) conceptual disorganization, suspiciousness, or hallucinatory behavioritem, or had occurred at least weekly with moderate severity or greater on the delusion,hallucination, agitation, or aberrant motor behavior item of the Neuropsychiatric Inventory(NPI).Patients could be taking stable cholinesterase inhibitor medication; memantine had not been approved in the U.S. during the enrollment period. **Excluded criteria:** Patients were excluded if they were takingantidepressants or anticonvulsants for mood stabilization **Pretreatment:** There was no difference on any baseline symptom score across the treatment groups, except for NPI totalscore (p=0.02; ANOVA)
Interventions	**Intervention Characteristics** Intervention 1 ● *Description*: Olanzapine (2.5mg or 5mg), flexdose ● *Length of treatment*: 12 weeks ● *Longest follow-up after end of treatment*: None as we are only interested in the first 12 weeks of this study. In the following part of the study there is no placebo group

	Intervention 2 ● *Description*: Quetiapine (25mg or 50mg) flexdose ● *Length of treatment*: 12 weeks Intervention 3 ● *Description*: Risperidone (0.5mg or 1mg) flexdose ● *Length of treatment*: 12 weeks Control ● *Description*: Placebo ● *Length of treatment*: 12 weeks
Outcomes	*Serious adverse events, n* ● **Outcome type**: DichotomousOutcome *Mortality, n* ● **Outcome type**: DichotomousOutcome *BPSD (NPI), SD* ● **Outcome type**: ContinuousOutcome *Kognition (MMSE), SD* ● **Outcome type**: ContinuousOutcome *ADL (ADCS-ADL), SD* ● **Outcome type**: ContinuousOutcome *Quality of life* ● **Outcome type**: ContinuousOutcome ● **Reporting**: Fully reported ● **Scale**: ADRQL ● **Unit of measure**: Points ● **Direction**: Higher is better ● **Data value**: Change from baseline
Identification	

Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement Comment: Described as randomized, no details
Allocation concealment (selection bias)	Low risk	Quote: "according to IRB guidelines. Treatments Medications were prepared in low-dose and high-dose identically-appearing capsules that contained either olanzapine (2.5mg or 5mg), quetiapine (25mg or 50mg), risperidone (0.5mg or 1mg), or placebo. The clinician selected the number"
Blinding of participants and personnel (performance bias)	Low risk	Judgement Comment: Described as 'double-blind'. Identical capsules so participants and personnel were probably blinded
Blinding of outcome assessment (detection bias)	Unclear risk	Judgement Comment: Not described
Incomplete outcome data (attrition bias)	High risk	Judgement Comment: High for ADL, MMSE and QoL. Low for SAE and death
Selective reporting (reporting bias)	Low risk	Judgement Comment: Match to protocol, except Beck Depression Inventory
Other bias	Low risk	Judgement Comment: No other apparant sources of bias

Zhong 2007

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Intervention 1 ● *Age. Mean, SD*: 83.5 (8.0) ● *MMSE*: 5.6 (3.6)

	Intervention 2 ● *Age. Mean, SD*: 83.0 (7.2) ● *MMSE*: 4.8 (4.0) Control ● *Age. Mean, SD*: 83.2 (7.2) ● *MMSE*: 5.5 (4.0) **Included criteria:** Participants were residents of nursing homes and assistedliving facilities, enrolled between September 2002 andNovember 2003 from 53 centers in the United States. Theyhad diagnoses of probable or possible AD or vascular de-mentia according to Diagnostic and Statistical Manual ofMental Disorders – fourth edition [DSM-IV] or the NationalInstitute of Neurological and Communicative Disorders andStroke/the Alzheimer's Disease and Related Disorders Asso-ciation [NINCDS/ADRDA]) criteria. Other inclusion criteriawere as follows: minimum age of 55 years, ambulatory orambulatory with assistance, documented clinical symptomsof agitation that did not result directly from the participant'smedical condition and required treatment with antipsychoticmedication in the opinion of the investigator, a total score of>14 on the PANSS-EC and a score of >4 on one of the 5PANSS-EC items (hostility, tension, uncooperativeness, ex-citement, poor impulse control) both at screening and at ran-domization. **Excluded criteria:** Key exclusion criteria included a history ofschizophrenia, schizoaffective disorder or bipolar disorder,agitation that was judged not to be related to dementia, fail-ure to respond to a prior adequate trial of atypical antipsy-chotics for the treatment of agitation, and unstable medicalillness (this included but was not limited to: cardiovascular,renal, hepatic, hematological, endocrine, and cerebrovasculardisorders). Any participants with abnormal ECG results thatwere considered clinically significant were also excludedfrom the study **Pretreatment:** The demographic and baseline characteristics were simi-lar among the three treatment groups
Interventions	**Intervention Characteristics** Intervention 1 ● *Description*: Quetiapine 200mg ● *Length of treatment*: 10 weeks ● *Longest follow-up after end of treatment*: None Intervention 2 ● *Description*: Quetiapine 100mg ● *Length of treatment*: 10 weeks ● *Longest follow-up after end of treatment*: None Control

	● *Description*: Placebo ● *Length of treatment*: 10 weeks ● *Longest follow-up after end of treatment*: None
Outcomes	*Serious adverse events, n* ● **Outcome type**: DichotomousOutcome *Mortality, %* ● **Outcome type**: DichotomousOutcome *BPSD (NPI), SD* ● **Outcome type**: ContinuousOutcome *Agitation (CMAI), SD* ● **Outcome type**: ContinuousOutcome
Identification	
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "The centralized randomization schedule was generated using a random block size of 8 and was created using random seed and treatment allocation ratios of 3:3:2 and maintained blinded by the sponsor's randomization group."
Allocation concealment (selection bias)	Low risk	Quote: "Medication was dis- tributed to centers in randomization blocks of 8. Each kit contained 10 blister wallets with the same number of tablets and the same configuration of color, size, and shape. Study medication was administered twice daily from blister wallets."
Blinding of participants and personnel (performance bias)	Low risk	Judgement Comment: Placebo controlled fixed dose

Blinding of outcome assessment (detection bias)	Low risk	
Incomplete outcome data (attrition bias)	High risk	Quote: "Two hundred and fifteen participants (65%) completed the study; the completion rates were comparable among the three groups"
Selective reporting (reporting bias)	Low risk	Judgement Comment: None detected
Other bias	Low risk	Judgement Comment: No other apparent sources of bias

Footnotes

Characteristics of excluded studies

Steinberg 2003

Reason for exclusion	Wrong study design

Veselinovic 2013

Reason for exclusion	Wrong patient population

Footnotes

Characteristics of studies awaiting classification

Footnotes

Characteristics of ongoing studies

Footnotes

Summary of findings tables

Additional tables

References to studies

Included studies

DeDeyn 2004

De Deyn, P. P.; Carrasco, M. M.; Deberdt, W.; Jeandel, C.; Hay, D. P.; Feldman, P. D.; Young, C. A.; Lehman, D. L.; Breier, A.. Olanzapine versus placebo in the treatment of psychosis with or without associated behavioral disturbances in patients with Alzheimer's disease. International journal of geriatric psychiatry 2004;19(2):115-126. [DOI: 10.1002/gps.1032 [doi]]

DeDeyn 2005

De Deyn, P.; Jeste, D. V.; Swanink, R.; Kostic, D.; Breder, C.; Carson, W. H.; Iwamoto, T.. Aripiprazole for the treatment of psychosis in patients with Alzheimer's disease: a randomized, placebo-controlled study. Journal of clinical psychopharmacology 2005;25(5):463-467. [DOI: 00004714-200510000-00010 [pii]]

Mintzer 2007

Mintzer, J. E.; Tune, L. E.; Breder, C. D.; Swanink, R.; Marcus, R. N.; McQuade, R. D.; Forbes, A.. Aripiprazole for the treatment of psychoses in institutionalized patients with Alzheimer dementia: a multicenter, randomized, double-blind, placebo-controlled assessment of three fixed doses. The American Journal of Geriatric Psychiatry : Official Journal of the American Association for Geriatric Psychiatry 2007;15(11):918-931. [DOI: 15/11/918 [pii]]

Street 2000

Street, J. S.; Clark, W. S.; Gannon, K. S.; Cummings, J. L.; Bymaster, F. P.; Tamura, R. N.; Mitan, S. J.; Kadam, D. L.; Sanger, T. M.; Feldman, P. D.; Tollefson, G. D.; Breier, A.. Olanzapine treatment of psychotic and behavioral symptoms in patients with Alzheimer disease in nursing care facilities: a double-blind, randomized, placebo-controlled trial. The HGEU Study Group. Archives of General Psychiatry 2000;57(10):968-976. [DOI: yoa20048 [pii]]

Streim 2008

Streim, J. E.; Porsteinsson, A. P.; Breder, C. D.; Swanink, R.; Marcus, R.; McQuade, R.; Carson, W. H.. A randomized, double-blind, placebo-controlled study of aripiprazole for the treatment of psychosis in nursing home patients with Alzheimer disease. The American Journal of Geriatric Psychiatry : Official Journal of the American Association for Geriatric Psychiatry 2008;16(7):537-550. [DOI: 10.1097/JGP.0b013e318165db77 [doi]]

Sultzer 2008

Sultzer, D. L.; Davis, S. M.; Tariot, P. N.; Dagerman, K. S.; Lebowitz, B. D.; Lyketsos, C. G.; Rosenheck, R. A.; Hsiao, J. K.; Lieberman, J. A.; Schneider, L. S.; CATIE-AD Study Group. Clinical symptom responses to atypical antipsychotic medications in Alzheimer's disease: phase 1 outcomes from the CATIE-AD effectiveness trial. The American Journal of Psychiatry 2008;165(7):844-854. [DOI: 10.1176/appi.ajp.2008.07111779 [doi]]

Zhong 2007

Zhong, K. X.; Tariot, P. N.; Mintzer, J.; Minkwitz, M. C.; Devine, N. A.. Quetiapine to treat agitation in dementia: a randomized, double-blind, placebo-controlled study. Current Alzheimer research 2007;4(1):81-93. [DOI:]

Excluded studies

Steinberg 2003

Steinberg, M.; Sheppard, J. M.; Tschanz, J. T.; Norton, M. C.; Steffens, D. C.; Breitner, J. C.; Lyketsos, C. G.. The incidence of mental and behavioral disturbances in dementia: the cache county study. The Journal of neuropsychiatry and clinical neurosciences 2003;15(3):340-345. [DOI: 10.1176/jnp.15.3.340 [doi]]

Veselinovic 2013

Veselinovic, T.; Schorn, H.; Vernaleken, I. B.; Hiemke, C.; Zernig, G.; Gur, R.; Grunder, G.. Effects of antipsychotic treatment on cognition in healthy subjects. Journal of psychopharmacology (Oxford, England) 2013;27(4):374-385. [DOI: 10.1177/0269881112466183 [doi]]

Studies awaiting classification

Ongoing studies

Other references

Additional references

Other published versions of this review

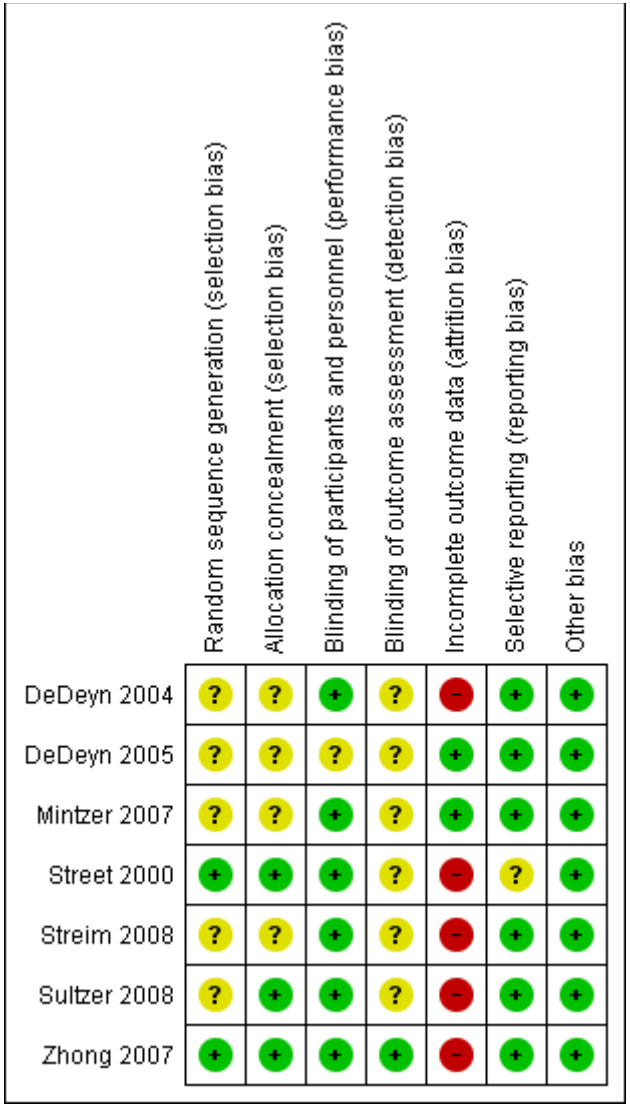
Data and analyses

1 Atypical antipsychotics vs placebo

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
1.1 BPSD (NPI) End of treatment	6	1716	Mean Difference (IV, Random, 95% CI)	-3.23 [-4.93, -1.53]
1.2 BPSD Follow up	0	0	Mean Difference (IV, Fixed, 95% CI)	Not estimable
1.3 Cognition (MMSE) End of treatment	6	1354	Mean Difference (IV, Random, 95% CI)	-0.25 [-0.67, 0.16]
1.4 Cognition Follow up	0	0	Mean Difference (IV, Fixed, 95% CI)	Not estimable
1.5 ADL (ADCS-ADL) End of treatment	2	334	Mean Difference (IV, Random, 95% CI)	-1.75 [-4.52, 1.01]
1.6 Agitation (CMAI), Follow up	0	0	Mean Difference (IV, Fixed, 95% CI)	Not estimable
1.7 Quality of life End of treatment	1	151	Mean Difference (IV, Fixed, 95% CI)	1.03 [-4.07, 6.12]
1.8 Serious adverse events, End of treatment	5	1577	Risk Ratio (IV, Random, 95% CI)	1.15 [0.86, 1.53]
1.10 Mortality,End of treatment	6	1963	Risk Ratio (IV, Random, 95% CI)	1.47 [0.80, 2.69]

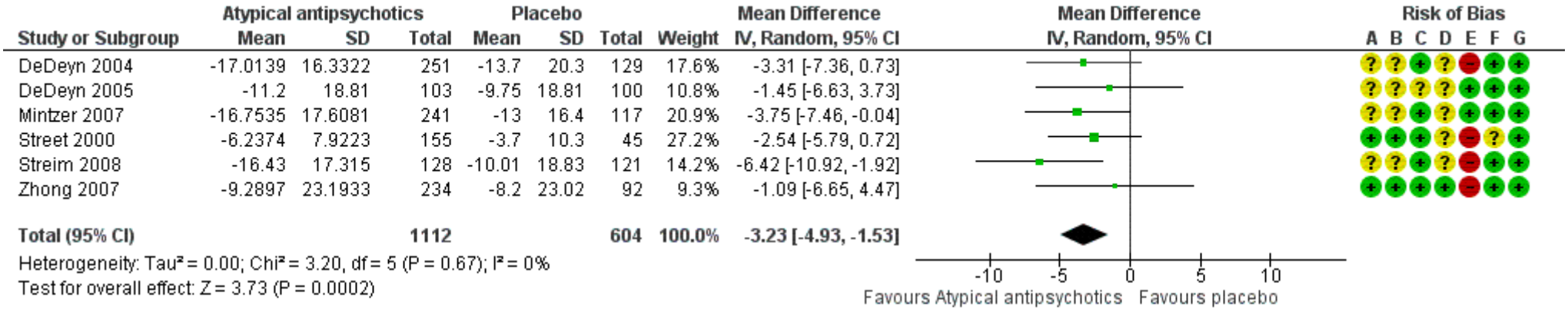
Figures

Figure 1



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

Figure 2 (Analysis 1.1)



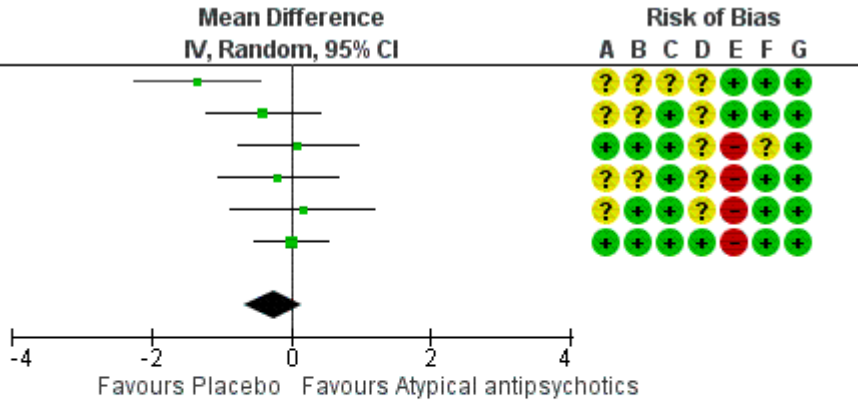
Risk of bias legend
(**A**) Random sequence generation (selection bias)
(**B**) Allocation concealment (selection bias)
(**C**) Blinding of participants and personnel (performance bias)
(**D**) Blinding of outcome assessment (detection bias)
(**E**) Incomplete outcome data (attrition bias)
(**F**) Selective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

Forest plot of comparison: 1 Atypical antipsychotics vs placebo, outcome: 1.1 BPSD (NPI) End of treatment.

Figure 3 (Analysis 1.3)

Study or Subgroup	Atypical antipsychotics Mean	SD	Total	Placebo Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
DeDeyn 2005	-0.81	2.985	94	0.53	3.17	86	14.4%	-1.34 [-2.24, -0.44]
Mintzer 2007	-1.3015	3.6043	199	-0.9	3.1	92	16.6%	-0.40 [-1.21, 0.41]
Street 2000	-0.2032	3.5278	155	-0.3	2.2	45	15.6%	0.10 [-0.75, 0.95]
Streim 2008	-0.77	2.985	106	-0.57	3.17	93	15.3%	-0.20 [-1.06, 0.66]
Sultzer 2008	-0.5308	3.562	104	-0.7	2.7	47	11.8%	0.17 [-0.86, 1.20]
Zhong 2007	0	2.6531	241	0	2	92	26.3%	0.00 [-0.53, 0.53]
Total (95% CI)			**899**			**455**	**100.0%**	**-0.25 [-0.67, 0.16]**

Heterogeneity: Tau² = 0.09; Chi² = 7.87, df = 5 (P = 0.16); I² = 36%
Test for overall effect: Z = 1.21 (P = 0.22)



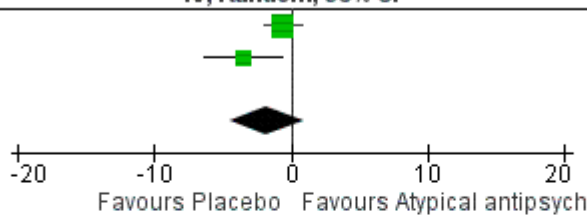
Risk of bias legend
(**A**) Random sequence generation (selection bias)
(**B**) Allocation concealment (selection bias)
(**C**) Blinding of participants and personnel (performance bias)
(**D**) Blinding of outcome assessment (detection bias)
(**E**) Incomplete outcome data (attrition bias)
(**F**) Selective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

Forest plot of comparison: 1 Atypical antipsychotics vs placebo, outcome: 1.3 Cognition (MMSE) End of treatment.

Figure 4 (Analysis 1.5)

Study or Subgroup	Atypical antipsychotics Mean	SD	Total	Placebo Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI	Risk of Bias A B C D E F G
Streim 2008	-0.83	4.94	93	-0.22	4.515	90	60.3%	-0.61 [-1.98, 0.76]	? ? + ? - + +
Sultzer 2008	-2.9933	8.537	104	0.5	8.4	47	39.7%	-3.49 [-6.40, -0.58]	? + + ? - + +
Total (95% CI)			**197**			**137**	**100.0%**	**-1.75 [-4.52, 1.01]**	

Heterogeneity: Tau² = 2.81; Chi² = 3.09, df = 1 (P = 0.08); I² = 68%
Test for overall effect: Z = 1.24 (P = 0.21)



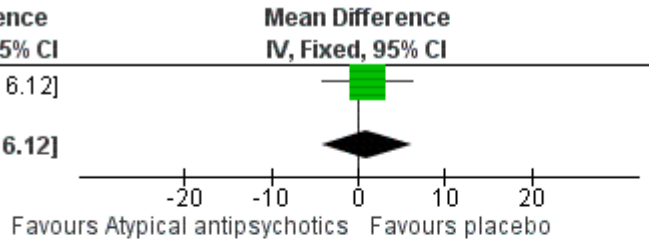
Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting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

Forest plot of comparison: 1 Atypical antipsychotics vs placebo, outcome: 1.5 ADL (ADCS-ADL) End of treatment.

Figure 5 (Analysis 1.7)

Study or Subgroup	Atypical antipsychotics Mean	SD	Total	Placebo Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI	Risk of Bias A B C D E F G
Sultzer 2008	5.125	12.2385	104	4.1	15.8	47	100.0%	1.03 [-4.07, 6.12]	? + + ? - + +
Total (95% CI)			**104**			**47**	**100.0%**	**1.03 [-4.07, 6.12]**	

Heterogeneity: Not applicable
Test for overall effect: Z = 0.39 (P = 0.69)



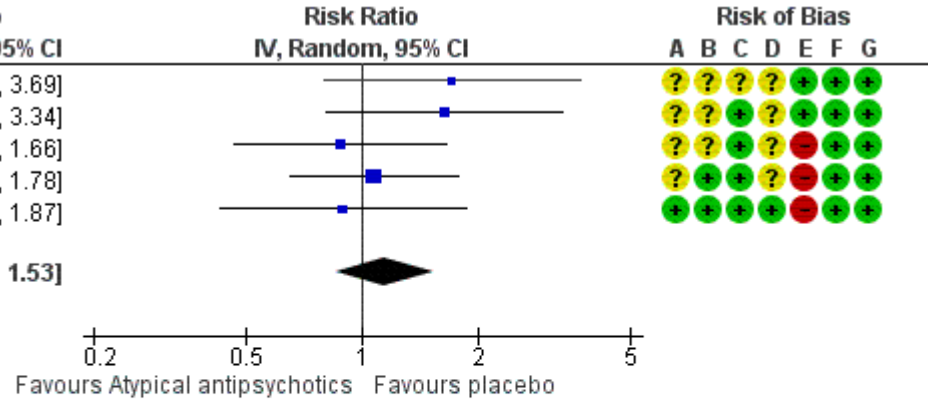
Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting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

Forest plot of comparison: 1 Atypical antipsychotics vs placebo, outcome: 1.7 Quality of life End of treatment.

Figure 6 (Analysis 1.8)

Study or Subgroup	Atypical antipsychotics Events	Total	Placebo Events	Total	Weight	Risk Ratio IV, Random, 95% CI
DeDeyn 2005	16	106	9	102	14.3%	1.71 [0.79, 3.69]
Mintzer 2007	30	244	9	120	16.7%	1.64 [0.80, 3.34]
Streim 2008	16	130	17	121	20.9%	0.88 [0.46, 1.66]
Sultzer 2008	40	279	19	142	32.9%	1.07 [0.65, 1.78]
Zhong 2007	21	241	9	92	15.3%	0.89 [0.42, 1.87]
Total (95% CI)		**1000**		**577**	**100.0%**	**1.15 [0.86, 1.53]**
Total events	123		63			

Heterogeneity: Tau² = 0.00; Chi² = 3.20, df = 4 (P = 0.52); I² = 0%
Test for overall effect: Z = 0.92 (P = 0.36)



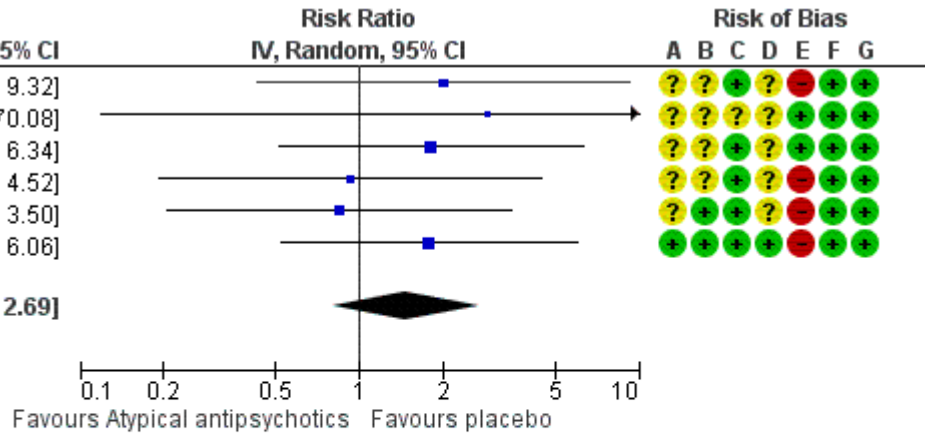
Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting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

Forest plot of comparison: 1 Atypical antipsychotics vs placebo, outcome: 1.8 Serious adverse events, End of treatment.

Figure 7 (Analysis 1.10)

Study or Subgroup	Atypical antipsychotics Events	Total	Placebo Events	Total	Weight	Risk Ratio IV, Random, 95% CI
DeDeyn 2004	8	257	2	129	15.6%	2.01 [0.43, 9.32]
DeDeyn 2005	1	106	0	102	3.6%	2.89 [0.12, 70.08]
Mintzer 2007	11	244	3	120	23.2%	1.80 [0.51, 6.34]
Streim 2008	3	130	3	121	14.7%	0.93 [0.19, 4.52]
Sultzer 2008	5	279	3	142	18.3%	0.85 [0.21, 3.50]
Zhong 2007	14	241	3	92	24.5%	1.78 [0.52, 6.06]
Total (95% CI)		**1257**		**706**	**100.0%**	**1.47 [0.80, 2.69]**
Total events	42		14			

Heterogeneity: Tau² = 0.00; Chi² = 1.43, df = 5 (P = 0.92); I² = 0%
Test for overall effect: Z = 1.25 (P = 0.21)



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 Atypical antipsychotics vs placebo, outcome: 1.10 Mortality,End of treatment.