Characteristics of studies

Characteristics of included studies

Allain 2000

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group **Other:**
Participants	**Baseline Characteristics** Intervention 1 ● *Age in years, mean (SD)*: 79.9 (7.9) ● *Females (%)*: 63 (62%) ● *Numbers (%) with BPSD*: 100% ● *Alzheimer´s disease, number (%)*: ● *Vascular demnetia, number (%)*: ● *Levy Body dementia, number (%)*: ● *Frontotemporal dementia, number (%)*: ● *Nursing home recidents, number (%)*: ● *Inpatients, number (%)*: ● *Living in their own homes, number (%)*: 0% Intervention 2 ● *Age in years, mean (SD)*: ● *Females (%)*: ● *Numbers (%) with BPSD*: ● *Alzheimer´s disease, number (%)*: ● *Vascular demnetia, number (%)*: ● *Levy Body dementia, number (%)*: ● *Frontotemporal dementia, number (%)*: ● *Nursing home recidents, number (%)*: ● *Inpatients, number (%)*: ● *Living in their own homes, number (%)*: Intervention 3 ● *Age in years, mean (SD)*: ● *Females (%)*: ● *Numbers (%) with BPSD*: ● *Alzheimer´s disease, number (%)*: ● *Vascular demnetia, number (%)*: ● *Levy Body dementia, number (%)*: ● *Frontotemporal dementia, number (%)*:

- *Nursing home recidents, number (%)*:
- *Inpatients, number (%)*:
- *Living in their own homes, number (%)*:

Intervention 4
- *Age in years, mean (SD)*:
- *Females (%)*:
- *Numbers (%) with BPSD*:
- *Alzheimer´s disease, number (%)*:
- *Vascular demnetia, number (%)*:
- *Levy Body dementia, number (%)*:
- *Frontotemporal dementia, number (%)*:
- *Nursing home recidents, number (%)*:
- *Inpatients, number (%)*:
- *Living in their own homes, number (%)*:

Control
- *Age in years, mean (SD)*: 78.6 (7.3)
- *Females (%)*: 71/103 (69%)
- *Numbers (%) with BPSD*: 100%
- *Alzheimer´s disease, number (%)*:
- *Vascular demnetia, number (%)*:
- *Levy Body dementia, number (%)*:
- *Frontotemporal dementia, number (%)*:
- *Nursing home recidents, number (%)*:
- *Inpatients, number (%)*:
- *Living in their own homes, number (%)*: 0%

Overall
- *Age in years, mean (SD)*: 79.6 (7.6)
- *Females (%)*: 64%
- *Numbers (%) with BPSD*: 100%
- *Alzheimer´s disease, number (%)*:
- *Vascular demnetia, number (%)*:
- *Levy Body dementia, number (%)*:
- *Frontotemporal dementia, number (%)*:
- *Nursing home recidents, number (%)*:
- *Inpatients, number (%)*:
- *Living in their own homes, number (%)*: 0%

Included criteria: Patients aged 55–90 years, fulfilling the DSM III R criteria(American Psychiatric Association 1987) for mild or moderate de-mentia and presenting behavioural troubles were included. Irrita-bility/aggressiveness was assessed through the MultidimensionalObservation Scale for Elderly Subjects (MOSES) (Helmes 1988)with a score on the subscale between 16 and 30. Patients had to behospitalized or in a nursing home for at least 21 days. The maincategories of dementia (Alzheimer’s disease, vascular dementiaand mixed dementia) were accepted for inclusion, under the

	condi-tion that behavioural symptoms were present. **Excluded criteria:** Non-inclusion criterion was at least one item rated 5 or no re-sponse for at least one item on the MOSES irritability/aggressive-ness subscale. Other psychiatric disorders such as depression (as-sessed with the Montgomery and Asberg Depression Rating Scale)and psychosis precluded the patient's inclusion in the study, as didrecent stroke and more generally any condition or treatment (i.e.antipsychotics or benzodiazepines) which could interfere with thestudy treatment or assessment. All psychotropics drug were ex-cluded except benzodiazepines prescribed as hypnotics, zopicloneand zolpidem and antidepressants prescribed at low doses (lessthan a third of the usual dose for major depression). Such drugscould be continued during the study under the condition that dosesremained unchanged for a month and during the period of thestudy. **Pretreatment:** **Total sample size:** 306 **Other:**
Interventions	**Intervention Characteristics** Intervention 1 ● *Number of participants allocated*: 101 ● *Dose*: Haloperidol 2-6mg/day (1-3mg twice a day). Recommended dose was 4mg/day (2mg twice a day) ● *Length of treatment*: 21 days ● *Other*: Intervention 2 ● *Number of participants allocated*: ● *Dose*: ● *Length of treatment*: ● *Other*: Intervention 3 ● *Number of participants allocated*: ● *Dose*: ● *Length of treatment*: ● *Other*: Intervention 4 ● *Number of participants allocated*: ● *Dose*: ● *Length of treatment*: ● *Other*: Control ● *Number of participants allocated*: 103 ● *Dose*: ● *Length of treatment*: 21 days ● *Other*:

Outcomes	*Serious adverse events* ● **Outcome type**: DichotomousOutcome ● **Direction**: Lower is better ● **Data value**: Endpoint *Mortality* ● **Outcome type**: DichotomousOutcome ● **Direction**: Lower is better ● **Data value**: Endpoint *BPSD* ● **Outcome type**: ContinuousOutcome ● **Direction**: Lower is better ● **Data value**: Endpoint *Agitation* ● **Outcome type**: ContinuousOutcome ● **Direction**: Lower is better ● **Data value**: Endpoint *Cognition* ● **Outcome type**: ContinuousOutcome ● **Direction**: Higher is better ● **Data value**: Endpoint *Activity of Daily Living (ADL)* ● **Outcome type**: ContinuousOutcome ● **Direction**: Higher is better ● **Data value**: Endpoint *Quality of life* ● **Outcome type**: ContinuousOutcome ● **Direction**: Higher is better ● **Data value**: Endpoint *BPSD_dikotom* ● **Outcome type**: DichotomousOutcome ● **Direction**: Lower is better ● **Data value**: Endpoint
Identification	**Sponsorship source:** **Country:** France, The Netherlands, Germany, Latvia and Portugal **Setting:** Multicenter, international, hospital or nursing home **Comments:** **Authors name:** Herve Allain

	Institution: Laboratoire de Pharmacologie Clinique **Email:** Herve.Allain@univ-rennes1.fr **Address:** Avenue du Pr Léon Bernard, 35043 Rennes, France **Start date:** April 25 1995 **End date:** December 17 1996 **Other:**
Notes	*NKA Demens 2023* on 25/04/2024 23:12 **Select** P: personer med demensdiagnose som ikke modtager AP i forvejenI+C: tiapride vs. haloperidol vs. placebo

Risk of bias table

Bias	Authors' judgement	Support for judgement
Selective outcome reporting	Low risk	Judgement Comment: All outcomes described in methods section are reported in the results section
Blinding of participants and personnel	Unclear risk	Judgement Comment: From Cochrane: Double blind but no further information
Allocation concealment	Unclear risk	Judgement Comment: Not mentioned in study
Incomplete outcome data	High risk	Judgement Comment: Forty-seven patients (15%) dropped out from the study, ten in the tiapridegroup (adverse event five; lack of efficacy one; uncooperativeness three; recovery one), 21 in the haloperidol group (adverse event 17; lack of efficacyone; uncooperativeness two; concomitant medication one) and 16 in theplacebo group (adverse event six; lack of efficacy eight; uncooperativenesstwo).
Sequence Generation	Unclear risk	Judgement Comment: Patients were randomly allocated to tiapride 100 mg/day (50 mg twice a day),haloperidol 2 mg/day (1 mg twice a day) or placebo
Other sources of bias	Low risk	Judgement Comment: No run-in period.
Blinding of outcome assessors	Unclear risk	Judgement Comment: Double blind but no further information

Alva 2024

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group **Other:**
Participants	**Baseline Characteristics** Intervention 1 ● *Age in years, mean (SD)*: 72.7 (0.35) ● *Females (%)*: 240 (61.2) ● *Numbers (%) with BPSD*: ● *Alzheimer´s disease, number (%)*: 276 (70.4)

- *Vascular demnetia, number (%)*: 71 (18.1)
- *Levy Body dementia, number (%)*: 5 (1.3)
- *Frontotemporal dementia, number (%)*: 8 (2)
- *Nursing home recidents, number (%)*:
- *Inpatients, number (%)*:
- *Living in their own homes, number (%)*:

Control

- *Age in years, mean (SD)*: 72.1 (0.36)
- *Females (%)*: 213 (54.3)
- *Numbers (%) with BPSD*:
- *Alzheimer´s disease, number (%)*: 260 (66.3)
- *Vascular demnetia, number (%)*: 80 (20.4)
- *Levy Body dementia, number (%)*: 6 (1.5)
- *Frontotemporal dementia, number (%)*: 9 (2.3)
- *Nursing home recidents, number (%)*:
- *Inpatients, number (%)*:
- *Living in their own homes, number (%)*:

Overall

- *Age in years, mean (SD)*: 72.4 (0.25)
- *Females (%)*: 453 (57.8)
- *Numbers (%) with BPSD*: 784 (100)
- *Alzheimer´s disease, number (%)*: 536 (68.4)
- *Vascular demnetia, number (%)*: 151 (19.3)
- *Levy Body dementia, number (%)*: 11 (1.4)
- *Frontotemporal dementia, number (%)*: 17 (2.2)
- *Nursing home recidents, number (%)*:
- *Inpatients, number (%)*:
- *Living in their own homes, number (%)*:

Included criteria: 1) male or female ≥ 60 years of age and able to provide written informed consent themselves or through a legal representative or caregiver;2) patient requires some or complete assistance with instrumental or basic activities of daily living; 3) patient meets clinical criteria for an NDD (including PD [with or without dementia], dementia with Lewy bodies, Alzheimer's disease, and all-cause dementia) and has a Mini-Mental State Examination (MMSE) score ≥6 and a Clinical Global Impression-Severity (CGI-S)score (a measure of neuropsychiatric symptoms) ≥4 at baseline; and 4) patient has a neuropsychiatric symptom severe enough to warrant antipsychotic treatment, as evidenced by a Neuropsychiatric Inventory (NPI) score (frequency × severity) ≥4 on at least one domain: (a) delusions, (b) hallucinations, (c) depression or dysphoria, (d) apathy/indifference, (e) disinhibition, (f) irritability or lability, and (g) sleep disorders.
Excluded criteria: The main exclusion criteria for the study included the following:1) patient with neuropsychiatric symptoms attributable to substance abuse;2) patient in hospice or receiving end-of-life palliative care or bedridden;3) patient with an unstable medical disorder.
Pretreatment:
Total sample size: 784
Other:

Interventions	**Intervention Characteristics** Intervention 1 ● *Number of participants allocated*: ● *Dose*: ● *Length of treatment*: ● *Other*: Control ● *Number of participants allocated*: ● *Dose*: ● *Length of treatment*: ● *Other*:
Outcomes	*Quality of life* ● **Outcome type**: ContinuousOutcome *Activity of Daily Living (ADL)* ● **Outcome type**: ContinuousOutcome *Cognition* ● **Outcome type**: ContinuousOutcome *Agitation* ● **Outcome type**: ContinuousOutcome *BPSD* ● **Outcome type**: ContinuousOutcome *Serious adverse events* ● **Outcome type**: DichotomousOutcome *Mortality* ● **Outcome type**: DichotomousOutcome
Identification	**Sponsorship source:** This study was funded by Acadia Pharmaceuticals Inc. **Country:** North America, Europe and rest of the world **Setting:** Multicenter, international **Comments:** **Authors name:** Gustavo Alva **Institution:** Department of Psychiatry and Neuroscience, ATP Clinical Research, University of California at Riverside, Riverside, CA, USA **Email:** galva@atpcr.com **Address:** **Start date:** 2018-05-21 (from protocol) **End date:** 2022-05-06 (from protocol) **Other:**

Notes	*NKA Demens 2023* on 06/05/2024 19:17 **Select** P: personer med demens og agitationI: pimavanserinC: placebo

Risk of bias table

Bias	Authors' judgement	Support for judgement
Selective outcome reporting	Low risk	Judgement Comment: Low risk for the ouotcome death and SAE: The study's primary and secondary outcomes is in accordance with the prespecified trial protocol (NCT03575052). The exploratory outcomes CGI-S, CGI-I and EQ-5D-5L were not mentioned in the protocol.For the outcome BPSD and quality of life: High risk
Blinding of participants and personnel	Low risk	Judgement Comment: Double-blinded. All patients and investigators were blinded to treatment allocation throughout the study period.
Allocation concealment	Unclear risk	Judgement Comment: There is no information regarding the method of allocation concealment.
Incomplete outcome data	Low risk	Judgement Comment: Overall, 93% of patients completed the study. There is information about reasons for discontinuation in the study, and discontinuations are almost equal in both groups, making it unlikely to be related to the true outcome.TEAEs lead to discontinuation or study termination in 19 patients (overall: 2.4%; pimavanserin [2.6%] vs placebo [2.3%]).Four patients (0.5% in each group) had a TEAE resulting in death.92.6% of patients treated with pimavanserin completed the study. 93.6% of patients treated with placebo completed the study.
Sequence Generation	Unclear risk	Judgement Comment: Patients were randomized, but there is no information about the sequence generation process.
Other sources of bias	Low risk	
Blinding of outcome assessors	Low risk	Judgement Comment: The investigators assessed the outcome. Both investigators and patients were blinded and it is unlikely that this blinding could have been broken.

Auchus 1997

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group **Other:**
Participants	**Baseline Characteristics** Intervention 1 ● *Age in years, mean (SD)*: ● *Females (%)*: ● *Numbers (%) with BPSD*: ● *Alzheimer´s disease, number (%)*: ● *Vascular demnetia, number (%)*: ● *Levy Body dementia, number (%)*:

	● *Frontotemporal dementia, number (%)*: ● *Nursing home recidents, number (%)*: ● *Inpatients, number (%)*: ● *Living in their own homes, number (%)*: Control ● *Age in years, mean (SD)*: ● *Females (%)*: ● *Numbers (%) with BPSD*: ● *Alzheimer´s disease, number (%)*: ● *Vascular demnetia, number (%)*: ● *Levy Body dementia, number (%)*: ● *Frontotemporal dementia, number (%)*: ● *Nursing home recidents, number (%)*: ● *Inpatients, number (%)*: ● *Living in their own homes, number (%)*: Overall ● *Age in years, mean (SD)*: 75.6 (7.5) ● *Females (%)*: 10 (67) ● *Numbers (%) with BPSD*: 15 (100) ● *Alzheimer´s disease, number (%)*: ● *Vascular demnetia, number (%)*: ● *Levy Body dementia, number (%)*: ● *Frontotemporal dementia, number (%)*: ● *Nursing home recidents, number (%)*: ● *Inpatients, number (%)*: ● *Living in their own homes, number (%)*: 15 (100) **Included criteria:** Community-dwelling outpatients meeting NINCDS-ADRDA criteria for probable or possible AD who showed disruptive agitated behaviors and who scored ≥25 on the short form Cohen-Mansfield Agitation Inventory (CMAI) were enrolled in this study. **Excluded criteria:** Patients with a history of schizophrenia, schizoaffective disorder, or Parkinson's disease were excluded, as were patients who currently met DSM-III-R criteria for major depressive episode or for manic episode. **Pretreatment:** **Total sample size:** 15 (3 terminated due to treatment-associated toxicity) **Other:**
Interventions	**Intervention Characteristics** Intervention 1 ● *Number of participants allocated*: 6 ● *Dose*: ● *Length of treatment*: ● *Other*:

	Control ● *Number of participants allocated*: 6 ● *Dose*: ● *Length of treatment*: ● *Other*:
Outcomes	*Serious adverse events* ● **Outcome type**: DichotomousOutcome *Mortality* ● **Outcome type**: DichotomousOutcome *BPSD* ● **Outcome type**: ContinuousOutcome *Agitation* ● **Outcome type**: ContinuousOutcome *Cognition* ● **Outcome type**: ContinuousOutcome *Activity of Daily Living (ADL)* ● **Outcome type**: ContinuousOutcome *Quality of life* ● **Outcome type**: ContinuousOutcome *BPSD_dikotom* ● **Outcome type**: DichotomousOutcome
Identification	**Sponsorship source:** This work was supported by Grant 226-93 from the Emory University Research Council and by Grant P30AG10130 (Alzheimer's Disease Core Center) from the National Institute on Aging. **Country:** USA **Setting:** Single-center, community-dwelling outpatients **Comments:** **Authors name:** Alexander P. Auchus **Institution:** Department of Neurology and Center for Geriatrics, Emory University School of Medicine **Email:** **Address:** Wesley Woods Center, 1841 Clifton Road, NE, Atlanta, GA 30329 **Start date:** **End date:** **Other:**

Notes	*NKA Demens 2023* on 03/05/2024 20:49 **Select** P: personer med mulig alzheimers og agitationI: haloperidol (eller fluoxetin)C: placebo

Risk of bias table

Bias	Authors' judgement	Support for judgement
Selective outcome reporting	Low risk	Judgement Comment: All outcomes reported in methods section are reported in the results section
Blinding of participants and personnel	Unclear risk	Judgement Comment: "double blind", but it is not described if haloperidol and placebo tablets didlook the same and no other actions to secure blinding of personnel and participants are described. Patients probably blinded but unclear if blinding of personnel was performed.
Allocation concealment	Unclear risk	Judgement Comment: Insufficient information
Incomplete outcome data	High risk	Judgement Comment: High rate of drop-out: 2/6 haloperidol (33%) and 1/6 (17%) placebo treated patients drop-out.
Sequence Generation	Unclear risk	Judgement Comment: Not reported
Other sources of bias	High risk	Judgement Comment: Subjects in each group completed a 2-week washout period during which anycurrent psychotropic medications were carefully withdrawn.
Blinding of outcome assessors	Unclear risk	Judgement Comment: Insufficient information

Ballard 2005

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group **Other:**
Participants	**Baseline Characteristics** Intervention 1 ● *Age in years, mean (SD)*: 84.2 (8.6) ● *Females (%)*: 27 (87.1) ● *Numbers (%) with BPSD*: 31 (100) ● *Alzheimer´s disease, number (%)*: ● *Vascular demnetia, number (%)*: ● *Levy Body dementia, number (%)*: ● *Frontotemporal dementia, number (%)*: ● *Nursing home recidents, number (%)*: 31 (100) ● *Inpatients, number (%)*: ● *Living in their own homes, number (%)*: Control

	● *Age in years, mean (SD)*: 83 (6.8) ● *Females (%)*: 24 (77.4) ● *Numbers (%) with BPSD*: 31 (100) ● *Alzheimer´s disease, number (%)*: ● *Vascular demnetia, number (%)*: ● *Levy Body dementia, number (%)*: ● *Frontotemporal dementia, number (%)*: ● *Nursing home recidents, number (%)*: 31 (100) ● *Inpatients, number (%)*: ● *Living in their own homes, number (%)*: Overall ● *Age in years, mean (SD)*: 83.8 (7.7) ● *Females (%)*: 74 (79.6) ● *Numbers (%) with BPSD*: 93 (100) ● *Alzheimer´s disease, number (%)*: ● *Vascular demnetia, number (%)*: ● *Levy Body dementia, number (%)*: ● *Frontotemporal dementia, number (%)*: ● *Nursing home recidents, number (%)*: 93 (100) ● *Inpatients, number (%)*: ● *Living in their own homes, number (%)*: **Included criteria:** Our inclusion criteria were a diagnosis of probable or possible Alzheimer's disease; age > 60; clinically significant agitation for at least six weeks and scores ≥ 4 on the irritability or aberrant motor behaviour scales of the neuropsychiatric inventory; and no use of antipsychotics or cholinesterase inhibitors for four weeks before entry into the study. **Excluded criteria:** We excluded patients known to be sensitive to cholinesterase inhibitors or antipsychotics and those with advanced, severe, progressive, or unstable disease that might interfere with efficacy or put the patient at special risk; disability that might prevent them fromcompleting study procedures; those with severe, unstable, or poorly controlled medical conditions; bradycardia (< 50), sick sinus syndrome, or conduction defects; current diagnosis of active uncontrolled peptic ulceration within the past three months; and clinically significant urinary obstruction. **Pretreatment:** **Total sample size:** 93 were randomized **Other:**
Interventions	**Intervention Characteristics** Intervention 1 ● *Number of participants allocated*: 31 ● *Dose*: 25-50 mg Quetiapin (twice a day) ● *Length of treatment*: 26 weeks ● *Other*: Control ● *Number of participants allocated*: 31 ● *Dose*:

	● *Length of treatment*: 26 weeks ● *Other*:
Outcomes	*Serious adverse events* ● **Outcome type**: DichotomousOutcome *Mortality* ● **Outcome type**: DichotomousOutcome *BPSD* ● **Outcome type**: ContinuousOutcome *Agitation* ● **Outcome type**: ContinuousOutcome *Cognition* ● **Outcome type**: ContinuousOutcome *Activity of Daily Living (ADL)* ● **Outcome type**: ContinuousOutcome *Quality of life* ● **Outcome type**: ContinuousOutcome *BPSD_dikotom* ● **Outcome type**: DichotomousOutcome
Identification	**Sponsorship source:** The study was funded largely from general donations to CB's research programme and profits from previously completed commercially funded clinical trials, with additional support from the Alzheimer's Research Trust. **Country:** England **Setting:** Multicenter, care facilities in the north east of England **Comments:** **Authors name:** Clive Ballard **Institution:** Institute of Psychiatry, King's College, London **Email:** Correspondence to: R Jacoby Robin.Jacoby@psych.ox.ac.uk **Address:** Institute of Psychiatry, King's College, London SE5 8AF **Start date:** September 2001 **End date:** April 2003 **Other:**
Notes	*NKA Demens 2023* on 25/04/2024 23:21 **Select** P: personer med diagnosticeret eller plausibel alzheimers og agitation i min. 4-6 uger, tager ikke API: quetiapin eller rivastigmin eller "placebo-quetiapin"C: "placebo-rivastigmin" eller "placebo-quetiapin"

Risk of bias table

Bias	Authors' judgement	Support for judgement
Selective outcome reporting	High risk	Judgement Comment: Few outcomes compared to what is common in these trials. ECG and full bloodcount not reported. Adverse events/ side effects missing in general.
Blinding of participants and personnel	Low risk	Judgement Comment: Design: Randomised double blind (clinician, patient, outcomes assessor)placebo controlled trial.
Allocation concealment	Unclear risk	Judgement Comment: It is reported that: "The study statistician randomly assigned patients." "Therandomising clinician faxed a form to the statistician, who communicated allocation to the pharmacy, ensuring concealment."The procedure is not clearly described because it first suggests that the statistician performs the randomisation, and later that the clinician randomises (which would be wrong).
Incomplete outcome data	High risk	Judgement Comment: Drop-out was: 8/31 in quetiapine group and 1/31 in placebo group. ModifiedITT analysis (those who dropped out not included, and LOCF)
Sequence Generation	Low risk	Judgement Comment: "The allocations were computer generated with block randomisation (blocksizes of three and six)."
Other sources of bias	Low risk	Judgement Comment: No run-in period
Blinding of outcome assessors	Low risk	Judgement Comment: Quote: "Assessors were blind to treatment allocation."

Ballard 2018

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group **Other:**
Participants	**Baseline Characteristics** Intervention 1 ● *Age in years, mean (SD)*: 85.6 (7) ● *Females (%)*: 71 (82) ● *Numbers (%) with BPSD*: ● *Alzheimer´s disease, number (%)*: ● *Vascular demnetia, number (%)*: ● *Levy Body dementia, number (%)*: ● *Frontotemporal dementia, number (%)*: ● *Nursing home recidents, number (%)*: ● *Inpatients, number (%)*: ● *Living in their own homes, number (%)*: Control ● *Age in years, mean (SD)*: 86.1 (6)

- *Females (%)*: 73 (80)
- *Numbers (%) with BPSD*:
- *Alzheimer´s disease, number (%)*:
- *Vascular demnetia, number (%)*:
- *Levy Body dementia, number (%)*:
- *Frontotemporal dementia, number (%)*:
- *Nursing home recidents, number (%)*:
- *Inpatients, number (%)*:
- *Living in their own homes, number (%)*:

Overall

- *Age in years, mean (SD)*:
- *Females (%)*:
- *Numbers (%) with BPSD*: 191 (100)
- *Alzheimer´s disease, number (%)*: 191 (100)
- *Vascular demnetia, number (%)*:
- *Levy Body dementia, number (%)*:
- *Frontotemporal dementia, number (%)*:
- *Nursing home recidents, number (%)*: 191 (100)
- *Inpatients, number (%)*:
- *Living in their own homes, number (%)*:

Included criteria: We included participants of either sex who were aged 50 years or older with possible or probable Alzheimer's disease as defined by the National Institute of Neurological and Communicative Disorders and Stroke–Alzheimer's Disease and Related Disorders Association and who met the Jeste and Finkel criteria for psychosis of Alzheimer's disease. We considered participants eligible if they had psychotic symptoms including visual or auditory hallucinations, delusions, or both, that developed after the diagnosis was established. Participants must also have been a nursing home resident for 4 weeks or more before randomisation, not bedridden, and expected to remain in the facility throughout the study. Additionally, they must have actively experienced and verbally communicated psychotic symptoms during the month before screening, at least once per week during the previous 2 weeks before baseline, and required treatment for symptoms of psychosis in Alzheimer's disease. We required participants to have symptoms at screening and baseline severe enough to warrant treatment with an antipsychotic agent, and to have a score of 4 or more on either the hallucinations (frequency×severity) or delusions (frequency×severity) domains of the Neuropsychiatric Inventory–Nursing Home version (NPI–NH)23 psychosis scale, or a total combined score of 6 or more (hallucinations+delusions).
Excluded criteria: We excluded participants receiving treatment with antipsychotics, medications that prolong the QT interval, centrally acting anticholinergic medications, mianserin, nefazodone, cyproheptadine, and fluvoxamine. We also excluded those whose dose of antidepressant and anxiolytic drugs, if used, changed during the study. Those receiving an acetylcholinesterase inhibitor or memantine, or both, must have been on stable doses for 3 months before baseline and during the study. Additionally, participants were excluded if they were unable to communicate verbally and had a history of significant psychotic disorders before or concomitantly with the diagnosis of Alzheimer's disease, including but not limited to schizophrenia or bipolar disorder, as well as any medical condition or surgical procedure that could interfere with the conduct of the study.
Pretreatment:
Total sample size: 181 were randomized
Other:

Interventions	**Intervention Characteristics** Intervention 1 ● *Number of participants allocated*: 90 ● *Dose*: Pimavanserin 17 mg x 2 (34 mg) ● *Length of treatment*: 12 weeks ● *Other*: Control ● *Number of participants allocated*: 91 ● *Dose*: 2 tablets ● *Length of treatment*: 12 weeks ● *Other*:
Outcomes	*Serious adverse events* ● **Outcome type**: DichotomousOutcome *Mortality* ● **Outcome type**: DichotomousOutcome *BPSD* ● **Outcome type**: ContinuousOutcome *Agitation* ● **Outcome type**: ContinuousOutcome *Cognition* ● **Outcome type**: ContinuousOutcome *Activity of Daily Living (ADL)* ● **Outcome type**: ContinuousOutcome *Quality of life* ● **Outcome type**: ContinuousOutcome *BPSD_dikotom* ● **Outcome type**: DichotomousOutcome
Identification	**Sponsorship source:** ACADIA Pharmaceuticals **Country:** United Kingdom **Setting:** Single-center, with multiple affiliated nursing home sites, across the United Kingdom. **Comments:** **Authors name:** Clive Ballard **Institution:** Institute of Health Research, University of Exeter Medical School, Exeter EX1 2LU, UK **Email:** c.ballard@exeter.ac.uk **Address:** Institute of Health Research, University of Exeter Medical School, Exeter EX1 2LU, UK

	Start date: January 16, 2014 **End date:** October 27, 2016 **Other:**
Notes	*NKA Demens 2023* on 03/05/2024 20:52 **Select** P: personer med mulig alzheimers og psykotiske symptomerI: pimavansesinC: placebo

Risk of bias table

Bias	Authors' judgement	Support for judgement
Selective outcome reporting	High risk	Judgement Comment: A lot of analyses with subscores and various weeks of follow-up. Primary outcome was reduction of psychotic symptoms at 12 weeks according to protocolin clinicaltrials.gov. In article, the primary outcome was reduction of psychoticsymptoms at 6 weeks. There was not difference in symptoms at 12 weeks
Blinding of participants and personnel	Low risk	Judgement Comment: "We masked participants, caregivers, the study sponsor, and study personnel at the clinic site to treatment assignment. We achieved masking of activetreatment and placebo by using identical-appearing tablets."
Allocation concealment	Unclear risk	Judgement Comment: No information reported.
Incomplete outcome data	Unclear risk	Judgement Comment: No information
Sequence Generation	Low risk	Judgement Comment: "An independent statistician without any other involvement in the study generated the randomisation sequence with use of permuted block sizes of four,which was implemented using Trident software (version 1.2)."
Other sources of bias	High risk	Judgement Comment: This period also allowed for washout in participants taking antipsychotic medication.During screening, participants entered a 3-week period in which BPST wasused to ensure that only individuals who required a pharmacological treatment progressed to randomisation in the study, to minimise subsequentplacebo response.
Blinding of outcome assessors	Low risk	Judgement Comment: According to clinicaltrials.gov: Masking: Quadruple (Participant, Care Provider,Investigator, Outcomes Assessor)

Brodaty 2003

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group **Other:**
Participants	**Baseline Characteristics** Intervention 1 ● *Age in years, mean (SD)*: 83.2 (0.51) ● *Females (%)*: 109 (71.2) ● *Numbers (%) with BPSD*: 153 (100)

- *Alzheimer´s disease, number (%)*: 87 (56.9)
- *Vascular demnetia, number (%)*: 44 (28.8)
- *Levy Body dementia, number (%)*:
- *Frontotemporal dementia, number (%)*:
- *Nursing home recidents, number (%)*: 153 (100)
- *Inpatients, number (%)*:
- *Living in their own homes, number (%)*:

Control

- *Age in years, mean (SD)*: 82.7 (0.64)
- *Females (%)*: 113 (72.4)
- *Numbers (%) with BPSD*: 156 (100)
- *Alzheimer´s disease, number (%)*: 93 (59.6)
- *Vascular demnetia, number (%)*: 44 (28.2)
- *Levy Body dementia, number (%)*:
- *Frontotemporal dementia, number (%)*:
- *Nursing home recidents, number (%)*: 156 (100)
- *Inpatients, number (%)*:
- *Living in their own homes, number (%)*:

Overall

- *Age in years, mean (SD)*:
- *Females (%)*:
- *Numbers (%) with BPSD*: 309 (100)
- *Alzheimer´s disease, number (%)*:
- *Vascular demnetia, number (%)*:
- *Levy Body dementia, number (%)*:
- *Frontotemporal dementia, number (%)*:
- *Nursing home recidents, number (%)*: 309 (100)
- *Inpatients, number (%)*:
- *Living in their own homes, number (%)*:

Included criteria: Inclusion criteria were a diagnosis of dementia with aggressive behaviors; dementia was of the Alzheimer's type, vascular dementia, or a combination of the 2 (i.e., mixed dementia), according to the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV). Patients were required to be 55 years of age and to have a score of 4 on the Functional Assessment Staging Test(FAST) and ≤23 on the Mini-Mental State Examination (MMSE). Eligible patients were required to have at least a minimum aggression score on the Cohen-Mansfield Agitation Inventory (CMAI): a score of 4 on at least 1 aggressive item, or a score of 3 on at least 2 aggressive items, or a score of 2 on at least 3 aggressive items, or 2 aggressive items occurring at a frequency of 2 and 1 at a frequency of 3. Patients had to reside in a nursing horne for atleast 1 month prior to enroilment. Caregivers of these patients were professionally trained nurses who could assist with medication and who could assess patient functioning.
Excluded criteria: Exclusion criteria included medical or neurologic conditions other than dementia that diminish cognitive function, other types of dementia, major depression within the last 6 months, other psychiatric disorders that could have accounted for observed psychotic disturbances, a history of tardive dyskinesia, clinically uncontrolled organic disease, clinically relevant laboratory abnormalities, administration of a depot neuroleptic within 2 treatment cycles, a history of neuroleptic malignant syndrome or an allergic reaction to neuroleptic drugs, history of failure to respond to

	risperidone treatment of at least 4 weeks' duration, and participation in clinical trial(s) with any investigational drugs during the 4 weeks preceding selection. **Pretreatment:** **Total sample size:** 345 were randomized **Other:**
Interventions	**Intervention Characteristics** Intervention 1 ● *Number of participants allocated*: 173 ● *Dose*: Risperidone 1 mg/day (max 2 mg/day) ● *Length of treatment*: 12 weeks ● *Other*: Control ● *Number of participants allocated*: 172 ● *Dose*: 1 mL/day (max 2 mL/day) ● *Length of treatment*: 12 weeks ● *Other*:
Outcomes	*Serious adverse events* ● **Outcome type**: DichotomousOutcome *Mortality* ● **Outcome type**: DichotomousOutcome *BPSD* ● **Outcome type**: ContinuousOutcome *Agitation* ● **Outcome type**: ContinuousOutcome *Cognition* ● **Outcome type**: ContinuousOutcome *Activity of Daily Living (ADL)* ● **Outcome type**: ContinuousOutcome *Quality of life* ● **Outcome type**: ContinuousOutcome *BPSD_dikotom* ● **Outcome type**: DichotomousOutcome

Identification	**Sponsorship source:** Dr. Brodaty is a consultant for Janssen and AstraZeneca and has received grant/research support and honoraria from Janssen. **Country:** Australia and New Zealand **Setting:** Multicenter, nursing homes in Australia and New Zealand **Comments:** **Authors name:** Henry Brodaty **Institution:** Academic Department for Old Age Psychiatry, School of Psychiatry, University of New South Wales, Sydney, Australia **Email:** h.brodaty@unsw.edu.au **Address:** Academic Department for Old Age Psychiatry, Euroa Centre, Prince of Wales Hospital, Randwick, Sydney, NSW, 2031, Australia **Start date:** February 19, 1998 **End date:** February 7, 2001 **Other:**
Notes	*NKA Demens 2023* on 25/04/2024 23:37 **Select** P: personer med diagnostiseret demens med en min. score på CMAII: risperidonC: placeboObs: studie #66: "Risperidone for psychosis of Alzheimer's disease and mixed dementia: results of a double-blind, placebo-controlled trial" af Brodaty et al. 2005 er et sub-studie med samme population

Risk of bias table

Bias	Authors' judgement	Support for judgement
Selective outcome reporting	High risk	Judgement Comment: Results on all reported measures are reported. However, effect on MMSE andFAST not reported in numbers. Post-hoc subgroup analysis with respect to effect on psychosis.One site excluded. Only adjusted least square means are reported. Crude means are only mentioned in a figure without providing exactnumbers. No CI or SD or SE are reported for the change from baseline. Only difference of LS between placebo and risperidone.
Blinding of participants and personnel	Unclear risk	Judgement Comment: No information
Allocation concealment	Unclear risk	Judgement Comment: No information
Incomplete outcome data	High risk	Judgement Comment: Agitation: In the article, 152 for placebo and 149 for risperidone were reportedinstead of 170 and 167 who received at least once the study medication.
Sequence Generation	Unclear risk	Judgement Comment: No information
Other sources of bias	High risk	Judgement Comment: The double-blind treatment period was preceded by a maximum 7-day, single-blind washout period, during which patients took 0.5 mL of placebo oralsolution each evening while existing psychotropic medication was discontinued
Blinding of outcome assessors	Unclear risk	Judgement Comment: No information

Deberdt 2005

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group **Other:**
Participants	**Baseline Characteristics** Intervention 1 ● *Age in years, mean (SD)*: 77.9 (7.7) ● *Females (%)*: 141 (69.1) ● *Numbers (%) with BPSD*: 204 (100) ● *Alzheimer´s disease, number (%)*: 158 (77.5) ● *Vascular demnetia, number (%)*: 11 (5.4) ● *Levy Body dementia, number (%)*: ● *Frontotemporal dementia, number (%)*: ● *Nursing home recidents, number (%)*: ● *Inpatients, number (%)*: ● *Living in their own homes, number (%)*: Intervention 1 ● *Age in years, mean (SD)*: ● *Females (%)*: ● *Numbers (%) with BPSD*: ● *Alzheimer´s disease, number (%)*: ● *Vascular demnetia, number (%)*: ● *Levy Body dementia, number (%)*: ● *Frontotemporal dementia, number (%)*: ● *Nursing home recidents, number (%)*: ● *Inpatients, number (%)*: ● *Living in their own homes, number (%)*: Intervention 2 ● *Age in years, mean (SD)*: 78.0 (6.9) ● *Females (%)*: 123 (62.8) ● *Numbers (%) with BPSD*: 196 (100) ● *Alzheimer´s disease, number (%)*: 166 (84.7) ● *Vascular demnetia, number (%)*: 11 (5.6) ● *Levy Body dementia, number (%)*: ● *Frontotemporal dementia, number (%)*: ● *Nursing home recidents, number (%)*: ● *Inpatients, number (%)*: ● *Living in their own homes, number (%)*:

	Control ● *Age in years, mean (SD)*: 79.8 (7.2) ● *Females (%)*: 60 (63.8) ● *Numbers (%) with BPSD*: 94 (100) ● *Alzheimer´s disease, number (%)*: 78 (83.0) ● *Vascular demnetia, number (%)*: 6 (6.4) ● *Levy Body dementia, number (%)*: ● *Frontotemporal dementia, number (%)*: ● *Nursing home recidents, number (%)*: ● *Inpatients, number (%)*: ● *Living in their own homes, number (%)*: Overall ● *Age in years, mean (SD)*: ● *Females (%)*: ● *Numbers (%) with BPSD*: 494 (100) ● *Alzheimer´s disease, number (%)*: 402 (81.4) ● *Vascular demnetia, number (%)*: 28 (5.7) ● *Levy Body dementia, number (%)*: ● *Frontotemporal dementia, number (%)*: ● *Nursing home recidents, number (%)*: ● *Inpatients, number (%)*: ● *Living in their own homes, number (%)*: **Included criteria:** Patients ≥40 years old were recruited from outpatient or residential settings (nursing homes or assisted living centers). AU patients exhibited clinically significant psychotic symptorns associated with Alzheimer disease (AD), vascular, or mixed dementia. Dementia diagnoses were defined by the NINCDS ADRDA or DSM-IV criteria. To be eligible, patients must have scored ≥6 (severity X frequency) on the sum of the Hallucinations and Delusions items on the Neuropsychiatric Inventory (NPI) or its nursing-home version (NPI/NH) at study entry (Visit 1) andrandomization (Visit 2). **Excluded criteria:** Exclusion criteria included Parkinson disease, Lewy-body dementia, Pick disease, frontotemporal dementia; or a Mini-Mental State Exam (MMSE) score <5 or >24. **Pretreatment:** **Total sample size:** 494 patients were randomized. **Other:**
Interventions	**Intervention Characteristics** Intervention 1 ● *Number of participants allocated*: 204 ● *Dose*: Olanzapine 2.5-10 mg/day ● *Length of treatment*: 10 weeks ● *Other*: Intervention 1 ● *Number of participants allocated*:

	● *Dose*: ● *Length of treatment*: ● *Other*: Intervention 2 ● *Number of participants allocated*: 196 ● *Dose*: Risperidone 0.5-2 mg/day ● *Length of treatment*: 10 weeks ● *Other*: Control ● *Number of participants allocated*: 94 ● *Dose*: ● *Length of treatment*: 10 weeks ● *Other*:
Outcomes	*Serious adverse events* ● **Outcome type**: DichotomousOutcome *BPSD* ● **Outcome type**: ContinuousOutcome *Mortality* ● **Outcome type**: DichotomousOutcome *Agitation* ● **Outcome type**: ContinuousOutcome *Cognition* ● **Outcome type**: ContinuousOutcome *Activity of Daily Living (ADL)* ● **Outcome type**: ContinuousOutcome *Quality of life* ● **Outcome type**: ContinuousOutcome *BPSD_dikotom* ● **Outcome type**: DichotomousOutcome
Identification	**Sponsorship source:** Eli Lilly and Company. **Country:** USA **Setting:** Multicenter, outpatients and residential settings (nursing homes or assisted-living centres) **Comments:** **Authors name:** Walter G. Deberdt **Institution:** Lilly Research Laboratories, Indianapolis, IN (WGD, PDF, CAY, DPH, DLL, EKO, AB)

	Email: deberdt_walter@lilly.com **Address:** Stoofstraat 52, 1000 Brussels, Belgium **Start date:** **End date:** **Other:**
Notes	*NKA Demens 2023* on 26/04/2024 20:21 **Select** P: personer med demens + psykotiske symptomer scoret ved 2 domæner på NPII: olanzapin eller risperidonC: placebo

Risk of bias table

Bias	Authors' judgement	Support for judgement
Selective outcome reporting	Low risk	Judgement Comment: Any adverse events" and "serious adverse events" not reported, but reportedmeasurement were all reported. Negative trial.
Blinding of participants and personnel	Unclear risk	Judgement Comment: No information
Allocation concealment	Unclear risk	Judgement Comment: No information
Incomplete outcome data	High risk	Judgement Comment: Dropout was high (42%). Analyses not with all randomized. LOCF for missingdata.
Sequence Generation	Unclear risk	Judgement Comment: No information
Other sources of bias	High risk	Judgement Comment: "After a 3- to 14-day placebo/washout period (...)"
Blinding of outcome assessors	Unclear risk	Judgement Comment: No information

DeDeyn 1999

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group **Other:**
Participants	**Baseline Characteristics** Intervention 1 ● *Age in years, mean (SD)*: 81 (median) ● *Females (%)*: 65 (56) ● *Numbers (%) with BPSD*: 115 (100) ● *Alzheimer´s disease, number (%)*: 92 (80) ● *Vascular demnetia, number (%)*: 30 (26) ● *Levy Body dementia, number (%)*: ● *Frontotemporal dementia, number (%)*: ● *Nursing home recidents, number (%)*: 115 (100)

- *Inpatients, number (%)*:
- *Living in their own homes, number (%)*:

Intervention 1
- *Age in years, mean (SD)*:
- *Females (%)*:
- *Numbers (%) with BPSD*:
- *Alzheimer´s disease, number (%)*:
- *Vascular demnetia, number (%)*:
- *Levy Body dementia, number (%)*:
- *Frontotemporal dementia, number (%)*:
- *Nursing home recidents, number (%)*:
- *Inpatients, number (%)*:
- *Living in their own homes, number (%)*:

Intervention 2
- *Age in years, mean (SD)*: 82 (median)
- *Females (%)*: 62 (54)
- *Numbers (%) with BPSD*: 115 (100)
- *Alzheimer´s disease, number (%)*: 82 (71)
- *Vascular demnetia, number (%)*: 44 (38)
- *Levy Body dementia, number (%)*:
- *Frontotemporal dementia, number (%)*:
- *Nursing home recidents, number (%)*: 115 (100)
- *Inpatients, number (%)*:
- *Living in their own homes, number (%)*:

Control
- *Age in years, mean (SD)*: 81 (median)
- *Females (%)*: 67 (59)
- *Numbers (%) with BPSD*: 114 (100)
- *Alzheimer´s disease, number (%)*: 80 (70)
- *Vascular demnetia, number (%)*: 41 (36)
- *Levy Body dementia, number (%)*:
- *Frontotemporal dementia, number (%)*:
- *Nursing home recidents, number (%)*: 114 (100)
- *Inpatients, number (%)*:
- *Living in their own homes, number (%)*:

Overall
- *Age in years, mean (SD)*: 81 (median)
- *Females (%)*: 194 (56)
- *Numbers (%) with BPSD*: 344 (100)
- *Alzheimer´s disease, number (%)*: 254 (74)

	● *Vascular demnetia, number (%)*: 115 (33) ● *Levy Body dementia, number (%)*: ● *Frontotemporal dementia, number (%)*: ● *Nursing home recidents, number (%)*: 344 (100) ● *Inpatients, number (%)*: ● *Living in their own homes, number (%)*: **Included criteria:** Patients were eligible for inclusion in the trial if they were at least 55 years of age, were institutionalized, and had a diagnosis of primary degenerative dementia of the Alzheimer type, vascular dementia, or mixed dementia according to the Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV). Eligible patients had scores of ≥4 on the Functional Assessment Staging (FAST); ≤23 on the Mini-Mental State Examination (MMSE); >1 on the Behavior Pathology in Alzheimer's Disease Rating Scale (BEHAVE-AD) global rating; and ≥8 on the BEHAVE-AD total score. **Excluded criteria:** Exclusion criteria included other conditions that diminish cognitive function; other psychiatric disorders; clinically relevant organic or neurologic disease; ECG or laboratory abnormalities; administration of a depot neuroleptic within one treatment cycle of Visit 1; history of allergic reaction to neuroleptics or history of neuroleptic malignant syndrome; or participation in clinical trial(s) with investigational drugs during the 4 weeks preceding this trial. **Pretreatment:** **Total sample size:** 344 were randomized **Other:**
Interventions	**Intervention Characteristics** Intervention 1 ● *Number of participants allocated*: 115 ● *Dose*: Risperidone max 2 mg twice a day ● *Length of treatment*: 12 weeks ● *Other*: Intervention 1 ● *Number of participants allocated*: ● *Dose*: ● *Length of treatment*: ● *Other*: Intervention 2 ● *Number of participants allocated*: 115 ● *Dose*: Haloperidol max 2 mg twice a day ● *Length of treatment*: 12 weeks ● *Other*: Control ● *Number of participants allocated*: 114 ● *Dose*: ● *Length of treatment*: 12 weeks ● *Other*:

Outcomes	*Serious adverse events* ● **Outcome type**: DichotomousOutcome *Mortality* ● **Outcome type**: DichotomousOutcome *BPSD* ● **Outcome type**: ContinuousOutcome *Agitation* ● **Outcome type**: ContinuousOutcome *Cognition* ● **Outcome type**: ContinuousOutcome *Activity of Daily Living (ADL)* ● **Outcome type**: ContinuousOutcome *Quality of life* ● **Outcome type**: ContinuousOutcome *BPSD_dikotom* ● **Outcome type**: DichotomousOutcome
Identification	**Sponsorship source:** Supported in part by a grant from the Janssen Research Foundation, Beerse, Belgium. **Country:** 8 countries (not defined which countries) **Setting:** International, institutionalized patients in 8 countries **Comments:** **Authors name:** Peter Paul De Deyn **Institution:** Department of Neurology, General Hospital Middelheim and Laboratory of Neurochemistry and Behavior, Born-Bunge Foundation, University of Antwerp **Email:** ppdedeyn@uia.ua.ac.be **Address:** Universiteitsplein 1, 2610 Wilrijk-Antwerp, Belgium **Start date:** March 1995 **End date:** December 1996 **Other:**
Notes	*NKA Demens 2023* on 26/04/2024 20:08 **Select** P: personer med diagnostiseret demens (alzheimers, vaskulær og blandet)I: riseperidon, haloperidolC: placebo

Risk of bias table

Bias	Authors' judgement	Support for judgement
Selective outcome reporting	Unclear risk	Judgement Comment: There is supposedly published a study protocol on beforehand but this cannot be found. It is not known if all of the predefined outcomes are reported. It can be expected that mortality would be an important outcome in this type of study, however, this is not reported.
Blinding of participants and personnel	Unclear risk	Judgement Comment: The trial is described as double blinded. No information of who was blinded
Allocation concealment	Unclear risk	Judgement Comment: Not described whether allocation was adequately concealed.
Incomplete outcome data	Low risk	Judgement Comment: All randomized participants were included in all analyses. There is data on the 'completers' (those who completed the 12 weeks follow up) and on endpoint (last evaluation for each patient who was randomized and received at least one treatment).
Sequence Generation	Low risk	Judgement Comment: Trial medication was blinded and randomized using a computer-generated code.
Other sources of bias	Low risk	
Blinding of outcome assessors	Unclear risk	Judgement Comment: It is not known whether the outcome assessors were blinded.

DeDeyn 2004

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group **Other:**
Participants	**Baseline Characteristics** Intervention 1 ● *Age in years, mean (SD)*: ● *Females (%)*: ● *Numbers (%) with BPSD*: 129 (100) ● *Alzheimer´s disease, number (%)*: 129 (100) ● *Vascular demnetia, number (%)*: ● *Levy Body dementia, number (%)*: ● *Frontotemporal dementia, number (%)*: ● *Nursing home recidents, number (%)*: ● *Inpatients, number (%)*: ● *Living in their own homes, number (%)*: Intervention 1 ● *Age in years, mean (SD)*: ● *Females (%)*: ● *Numbers (%) with BPSD*: ● *Alzheimer´s disease, number (%)*:

- *Vascular demnetia, number (%)*:
- *Levy Body dementia, number (%)*:
- *Frontotemporal dementia, number (%)*:
- *Nursing home recidents, number (%)*:
- *Inpatients, number (%)*:
- *Living in their own homes, number (%)*:

Intervention 1

- *Age in years, mean (SD)*:
- *Females (%)*:
- *Numbers (%) with BPSD*:
- *Alzheimer´s disease, number (%)*:
- *Vascular demnetia, number (%)*:
- *Levy Body dementia, number (%)*:
- *Frontotemporal dementia, number (%)*:
- *Nursing home recidents, number (%)*:
- *Inpatients, number (%)*:
- *Living in their own homes, number (%)*:

Intervention 1

- *Age in years, mean (SD)*:
- *Females (%)*:
- *Numbers (%) with BPSD*:
- *Alzheimer´s disease, number (%)*:
- *Vascular demnetia, number (%)*:
- *Levy Body dementia, number (%)*:
- *Frontotemporal dementia, number (%)*:
- *Nursing home recidents, number (%)*:
- *Inpatients, number (%)*:
- *Living in their own homes, number (%)*:

Intervention 2

- *Age in years, mean (SD)*:
- *Females (%)*:
- *Numbers (%) with BPSD*: 134 (100)
- *Alzheimer´s disease, number (%)*: 134 (100)
- *Vascular demnetia, number (%)*:
- *Levy Body dementia, number (%)*:
- *Frontotemporal dementia, number (%)*:
- *Nursing home recidents, number (%)*:
- *Inpatients, number (%)*:
- *Living in their own homes, number (%)*:

Intervention 3

- *Age in years, mean (SD)*:
- *Females (%)*:
- *Numbers (%) with BPSD*: 125 (100)
- *Alzheimer´s disease, number (%)*: 125 (100)
- *Vascular demnetia, number (%)*:
- *Levy Body dementia, number (%)*:
- *Frontotemporal dementia, number (%)*:
- *Nursing home recidents, number (%)*:
- *Inpatients, number (%)*:
- *Living in their own homes, number (%)*:

Intervention 4

- *Age in years, mean (SD)*:
- *Females (%)*:
- *Numbers (%) with BPSD*: 132 (100)
- *Alzheimer´s disease, number (%)*: 132 (100)
- *Vascular demnetia, number (%)*:
- *Levy Body dementia, number (%)*:
- *Frontotemporal dementia, number (%)*:
- *Nursing home recidents, number (%)*:
- *Inpatients, number (%)*:
- *Living in their own homes, number (%)*:

Control

- *Age in years, mean (SD)*:
- *Females (%)*:
- *Numbers (%) with BPSD*: 129 (100)
- *Alzheimer´s disease, number (%)*: 129 (100)
- *Vascular demnetia, number (%)*:
- *Levy Body dementia, number (%)*:
- *Frontotemporal dementia, number (%)*:
- *Nursing home recidents, number (%)*:
- *Inpatients, number (%)*:
- *Living in their own homes, number (%)*:

Overall

- *Age in years, mean (SD)*: 76.6 (10.4)
- *Females (%)*: 489 (75)
- *Numbers (%) with BPSD*: 652 (100)
- *Alzheimer´s disease, number (%)*: 652 (100)
- *Vascular demnetia, number (%)*:
- *Levy Body dementia, number (%)*:
- *Frontotemporal dementia, number (%)*:

	● *Nursing home recidents, number (%)*: ● *Inpatients, number (%)*: ● *Living in their own homes, number (%)*: **Included criteria:** Patients were male or female, aged 40 years and above, resided in long-term nursing homes or continuing-care hospitals in Europe, Australia, Israel, Lebanon, and South Africa, and were expected to continue patient status for 6 months following enrollment. All patients met the NINCDS-ADRDA and DSM-IV-TR criteria for possible or probable Alzheimer's disease (AD), and all exhibited clinically significant psychotic symptoms (delusions 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 preceding study entry; and (3) require pharmacological intervention, in the opinion of the investigator. Aminimum score of 5 on the Mini-Mental State Examination 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:** **Total sample size:** 652 patients were randomized. **Other:**
Interventions	**Intervention Characteristics** Intervention 1 ● *Number of participants allocated*: 129 ● *Dose*: Olanzapine 1.0 mg/day ● *Length of treatment*: 10 weeks ● *Other*: Intervention 1 ● *Number of participants allocated*: 134 ● *Dose*: olanzapine 2.5 mg/day ● *Length of treatment*: 10 weeks ● *Other*: Intervention 1 ● *Number of participants allocated*: 125 ● *Dose*: olanzapine 5.0 mg/day ● *Length of treatment*: 10 weeks ● *Other*: Intervention 1 ● *Number of participants allocated*: 132 ● *Dose*: olanzapine 7.5 mg/day ● *Length of treatment*: 10 weeks ● *Other*: Intervention 2 ● *Number of participants allocated*: 134

	● *Dose*: olanzapine 2.5 mg/day ● *Length of treatment*: 10 weeks ● *Other*: Intervention 3 ● *Number of participants allocated*: 125 ● *Dose*: olanzapine 5.0 mg/day ● *Length of treatment*: 10 weeks ● *Other*: Intervention 4 ● *Number of participants allocated*: 132 ● *Dose*: olanzapine 7.5 mg/day ● *Length of treatment*: 10 weeks ● *Other*: Control ● *Number of participants allocated*: 129 ● *Dose*: placebo ● *Length of treatment*: 10 weeks ● *Other*:
Outcomes	*Serious adverse events* ● **Outcome type**: DichotomousOutcome *Mortality* ● **Outcome type**: DichotomousOutcome *BPSD* ● **Outcome type**: ContinuousOutcome *Agitation* ● **Outcome type**: ContinuousOutcome *Cognition* ● **Outcome type**: ContinuousOutcome *Activity of Daily Living (ADL)* ● **Outcome type**: ContinuousOutcome *Quality of life* ● **Outcome type**: ContinuousOutcome *BPSD_dikotom* ● **Outcome type**: DichotomousOutcome

Identification	**Sponsorship source:** Eli Lilly and Company **Country:** Europe, Australia, Israel, Lebanon, and South Africa. **Setting:** Multicenter, international, long-term nursing homes and continuing-care hospitals **Comments:** **Authors name:** Peter Paul De Deyn **Institution:** Department of Neurology, Middelheim Hospital, University of Antwerp; Antwerp, Belgium **Email:** deberdt_walter@lilly.com **Address:** Lilly Research Laboratories, Lilly Corporate Center D.C. 4133, Indianapolis, IN 46285, USA **Start date:** 23 January 2001 **End date:** 22 October 2002 **Other:**
Notes	*NKA Demens 2023* on 26/04/2024 20:13 **Select** P: personer med alzheimers demens inkl. moderat til svære psykotiske symptomer, til fare for sig selv og med behov for medicinsk behandlingI: olanzapinC: placebo *Anja Ussing* on 07/05/2024 19:06 **Select** be at least moderate inseverity (i.e. impair patients' functional capacity orcause them to pose a threat to themselves) *Anja Ussing* on 07/05/2024 19:10 **Select** er inkluderet i oprindelig NKR fra 2018 *Anja Ussing* on 23/05/2024 20:23 **Select** vi inkluderer men er opmærksom på om studiet skaber heterogenitet, evt. sensitivitetsanalyse

Risk of bias table

Bias	Authors' judgement	Support for judgement
Selective outcome reporting	High risk	Judgement Comment: Many subanalyses, for instance with the individual NPI items. Post-hoc analyses. Each time for all four drug groups. No adjustment for multiple testing.Much missing data on adverse events (no information f.i. on somnolence, orjust summary information, f.i. on cognitive function).
Blinding of participants and personnel	Unclear risk	Judgement Comment: No information
Allocation concealment	Unclear risk	Judgement Comment: No information
Incomplete outcome data	High risk	Judgement Comment: Total number randomized 652 does not agree with numbers randomized pergroup (520 and 129).

Sequence Generation	Unclear risk	Judgement Comment: No information
Other sources of bias	High risk	Judgement Comment: "Following a placebo lead-in phase of up to a maximum of 14 days (...)"
Blinding of outcome assessors	Unclear risk	Judgement Comment: No information

DeDeyn 2005

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group **Other:**
Participants	**Baseline Characteristics** Intervention 1 ● *Age in years, mean (SD)*: ● *Females (%)*: ● *Numbers (%) with BPSD*: 106 (100) ● *Alzheimer´s disease, number (%)*: 106 (100) ● *Vascular demnetia, number (%)*: ● *Levy Body dementia, number (%)*: ● *Frontotemporal dementia, number (%)*: ● *Nursing home recidents, number (%)*: ● *Inpatients, number (%)*: ● *Living in their own homes, number (%)*: 106 (100) Control ● *Age in years, mean (SD)*: ● *Females (%)*: ● *Numbers (%) with BPSD*: 102 (100) ● *Alzheimer´s disease, number (%)*: 102 (100) ● *Vascular demnetia, number (%)*: ● *Levy Body dementia, number (%)*: ● *Frontotemporal dementia, number (%)*: ● *Nursing home recidents, number (%)*: ● *Inpatients, number (%)*: ● *Living in their own homes, number (%)*: 102 (100) Overall ● *Age in years, mean (SD)*: 81.5 ● *Females (%)*: (72) ● *Numbers (%) with BPSD*: 208 (100) ● *Alzheimer´s disease, number (%)*: 208 (100) ● *Vascular demnetia, number (%)*: ● *Levy Body dementia, number (%)*:

	● *Frontotemporal dementia, number (%)*: ● *Nursing home recidents, number (%)*: ● *Inpatients, number (%)*: ● *Living in their own homes, number (%)*: 208 (100) **Included criteria:** Noninstitutionalized men and women (ie, those living in assisted living facilities or adult communities, or with a caregiver), aged 55–95 years, diagnosed with AD (Diagnostic and Statistical Manual of Mental Disorder, Fourth Edition criteria), and with symptoms of delusions or hallucinations present (at least intermittently) for 1 month or longer were eligible for enrollment in the study. In addition, for inclusion, patients had to have a Mini-Mental State Examination (MMSE) score of 6–24, and a score of ≥6 on the delusions or hallucinations items of the Neuropsychiatric Inventory (NPI) assessment at baseline. **Excluded criteria:** Main study exclusion criteria included: an Axis I (Diagnostic and Statistical Manual of Mental Disorder, Fourth Edition) diagnosis of delirium, amnesic disorders, bipolar disorder, schizophrenia or schizoaffective disorder, or mood disorder with psychotic features; psychotic symptoms better accounted for by another general medical condition or direct physiologic effects of a substance (eg, medication); refractory to neuroleptics used to treat psychotic symptoms in the past. **Pretreatment:** **Total sample size:** 208 patients were randomized **Other:**
Interventions	**Intervention Characteristics** Intervention 1 ● *Number of participants allocated*: 106 ● *Dose*: Aripiprazole 10 mg/day (titrated from 2-15 mg/day) ● *Length of treatment*: 10 weeks (excluding minimum 1 week washout period to remove AP) ● *Other*: Control ● *Number of participants allocated*: 102 ● *Dose*: ● *Length of treatment*: 10 weeks (excluding minimum 1 week washout period to remove AP) ● *Other*:
Outcomes	*Serious adverse events* ● **Outcome type**: DichotomousOutcome *Mortality* ● **Outcome type**: DichotomousOutcome *BPSD* ● **Outcome type**: ContinuousOutcome *Agitation* ● **Outcome type**: ContinuousOutcome *Cognition* ● **Outcome type**: ContinuousOutcome

	Activity of Daily Living (ADL) ● **Outcome type**: ContinuousOutcome *Quality of life* ● **Outcome type**: ContinuousOutcome *BPSD_dikotom* ● **Outcome type**: DichotomousOutcome
Identification	**Sponsorship source:** This study was supported by Bristol-Myers Squibb and Otsuka Pharmaceutical Co., Ltd. **Country:** USA **Setting:** Multicenter, outpatients (noninstitutionalized men and women) **Comments:** **Authors name:** Peter De Deyn **Institution:** University of Antwerp **Email:** dedeyn@skynet.be **Address:** Lindendreef 1, 2020, Antwerp, Belgium. **Start date:** **End date:** **Other:**
Notes	*NKA Demens 2023* on 26/04/2024 20:10 **Select** P: hjemmeboende personer med alzheimer demens + hallucinationer/vrangforestillinger på NPI-skalaI: aripiprazolC: placebo *Anja Ussing* on 07/05/2024 19:17 **Included** inkludueret i NKR fra 2018

Risk of bias table

Bias	Authors' judgement	Support for judgement
Selective outcome reporting	High risk	Judgement Comment: Insufficient information about outcomes in the protocol. Lots of secondaryoutcomes
Blinding of participants and personnel	Unclear risk	Judgement Comment: No comments
Allocation concealment	Unclear risk	Judgement Comment: No comments
Incomplete outcome data	Unclear risk	Judgement Comment: Judgement Comment: Drop-out was just below 20% and did not differ >5% between groups.It seems that not all patients were included in the analyses (seetable with results on outcomes). Missing data were imputed with LOCF.
Sequence Generation	Unclear risk	Judgement Comment: No comments

Other sources of bias	High risk	Judgement Comment: "Following screening and a minimum 7-day washout period for previous psychotropic medication (...)"
Blinding of outcome assessors	Unclear risk	Judgement Comment: No comments

Devanand 1998

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group **Other:**
Participants	**Baseline Characteristics** Intervention 1 ● *Age in years, mean (SD)*: ● *Females (%)*: ● *Numbers (%) with BPSD*: ● *Alzheimer´s disease, number (%)*: ● *Vascular demnetia, number (%)*: ● *Levy Body dementia, number (%)*: ● *Frontotemporal dementia, number (%)*: ● *Nursing home recidents, number (%)*: ● *Inpatients, number (%)*: ● *Living in their own homes, number (%)*: Intervention 1 ● *Age in years, mean (SD)*: ● *Females (%)*: ● *Numbers (%) with BPSD*: ● *Alzheimer´s disease, number (%)*: ● *Vascular demnetia, number (%)*: ● *Levy Body dementia, number (%)*: ● *Frontotemporal dementia, number (%)*: ● *Nursing home recidents, number (%)*: ● *Inpatients, number (%)*: ● *Living in their own homes, number (%)*: Intervention 2 ● *Age in years, mean (SD)*: ● *Females (%)*: ● *Numbers (%) with BPSD*: ● *Alzheimer´s disease, number (%)*: ● *Vascular demnetia, number (%)*: ● *Levy Body dementia, number (%)*:

- *Frontotemporal dementia, number (%)*:
- *Nursing home recidents, number (%)*:
- *Inpatients, number (%)*:
- *Living in their own homes, number (%)*:

Control
- *Age in years, mean (SD)*:
- *Females (%)*:
- *Numbers (%) with BPSD*:
- *Alzheimer´s disease, number (%)*:
- *Vascular demnetia, number (%)*:
- *Levy Body dementia, number (%)*:
- *Frontotemporal dementia, number (%)*:
- *Nursing home recidents, number (%)*:
- *Inpatients, number (%)*:
- *Living in their own homes, number (%)*:

Overall
- *Age in years, mean (SD)*: 72.1 (9.6)
- *Females (%)*: (64.8)
- *Numbers (%) with BPSD*: 71 (100)
- *Alzheimer´s disease, number (%)*: 71 (100)
- *Vascular demnetia, number (%)*:
- *Levy Body dementia, number (%)*:
- *Frontotemporal dementia, number (%)*:
- *Nursing home recidents, number (%)*:
- *Inpatients, number (%)*:
- *Living in their own homes, number (%)*: 71 (100)

Included criteria: Subjects were required to meet the DSM-III-R criteria for dementia and the criteria for probable Alzheimer's disease of the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association.Patients who met the criteria for either psychosis or disruptive behaviors were eligible for the study. The criteria for psychosis required the presence of a delusion or hallucination as defined by the Schedule for Affective Disorders and Schizophrenia (SADS), as well as a Brief Psychiatric Rating Scale (BPRS) score of at least4 (moderate severity) on the hallucinatory behavior or unusual thought content item, or a total score of 6 or more on these two items. The criterion for disruptive behaviors was a score of 4 or more (moderate severity) on the item for physical aggression or psychomotor agitation on the Behavioral Syndromes Scale for Dementia.
Excluded criteria: Exclusion criteria were drug or alcohol dependence, stroke (clinical evidence or a lesion of 2 cm or more in diameter on any CT or MRI slice), and a history or clinical evidence of other causes of dementia, including head trauma, Parkinson's disease, Huntington's disease, and multiple sclerosis. Patients who had had extrapyramidal signs before the onset of cognitive impairment were considered to have Parkinson's disease and were excluded.
Pretreatment:
Total sample size: 71
Other:

Interventions	**Intervention Characteristics** Intervention 1 ● *Number of participants allocated*: ● *Dose*: Haloperidol 0.50-0.75 mg/day ● *Length of treatment*: 6 weeks ● *Other*: Intervention 1 ● *Number of participants allocated*: ● *Dose*: ● *Length of treatment*: ● *Other*: Intervention 2 ● *Number of participants allocated*: ● *Dose*: Haloperidol 2-3 mg/day ● *Length of treatment*: 6 weeks ● *Other*: Control ● *Number of participants allocated*: ● *Dose*: ● *Length of treatment*: 6 weeks ● *Other*:
Outcomes	*Serious adverse events* ● **Outcome type**: DichotomousOutcome *Mortality* ● **Outcome type**: DichotomousOutcome *Agitation* ● **Outcome type**: ContinuousOutcome *BPSD* ● **Outcome type**: ContinuousOutcome *Cognition* ● **Outcome type**: ContinuousOutcome *Activity of Daily Living (ADL)* ● **Outcome type**: ContinuousOutcome *Quality of life* ● **Outcome type**: ContinuousOutcome

	BPSD_dikotom ● **Outcome type**: DichotomousOutcome
Identification	**Sponsorship source:** Supported in part by grants MH-44176, MH-50038, and MH-55735 from NIMH; grants AG-07370, AG-07232, and AG-08702from the National Institute on Aging; NIH grant RR-00645; and the Charles S. Robertson Memorial Gift for Alzheimer's DiseaseResearch from the Banbury Fund. **Country:** USA **Setting:** Single-center, outpatients **Comments:** **Authors name:** Davangere P. Devanand **Institution:** Department of Biological Psychiatry, New York State Psychiatric Institute, NY 10032, USA **Email:** **Address:** New York State Psychiatric Institute, 722 West 168th St., New York, NY 10032. **Start date:** **End date:** **Other:**
Notes	*NKA Demens 2023* on 06/05/2024 17:15 **Select** P: personer med alzheimers og psykotiske symptomer/aggresiv adfærdI: haloperidol (2 forskellige doser)C: placebo

Risk of bias table

Bias	Authors' judgement	Support for judgement
Selective outcome reporting	Unclear risk	Judgement Comment: No protocol available
Blinding of participants and personnel	Low risk	Judgement Comment: Raters and patients were blind to the study design throughout phase A andphase B
Allocation concealment	Unclear risk	Judgement Comment: No information
Incomplete outcome data	Unclear risk	Judgement Comment: Drop-out was 9% overall. Results of completers analyses were shown in detail."Intent-to-treat analyses were also conducted for the phase A sample, carryingforward the last observation", but results were not shown in detail. Apparently, they were not very different.
Sequence Generation	Unclear risk	Judgement Comment: No information
Other sources of bias	High risk	Judgement Comment: In the initial 1-week single-blind phase, all patients received placebo. At theend of this week, the patients who still met the entry criteria were eligible forphase A
Blinding of outcome assessors	Low risk	Judgement Comment: The blinded research psychiatrist (D.P.D.) who evaluated the patients was also in charge of treatment, including dose adjustment, at all time points in thestudy.

Grossberg 2020a

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group **Other:**
Participants	**Baseline Characteristics** Intervention 1 ● *Age in years, mean (SD)*: 73.9 (9.1) ● *Females (%)*: 12 (60.0) ● *Numbers (%) with BPSD*: 20 (100) ● *Alzheimer´s disease, number (%)*: 20 (100) ● *Vascular demnetia, number (%)*: ● *Levy Body dementia, number (%)*: ● *Frontotemporal dementia, number (%)*: ● *Nursing home recidents, number (%)*: 20 (100) ● *Inpatients, number (%)*: ● *Living in their own homes, number (%)*: Intervention 1 ● *Age in years, mean (SD)*: ● *Females (%)*: ● *Numbers (%) with BPSD*: ● *Alzheimer´s disease, number (%)*: ● *Vascular demnetia, number (%)*: ● *Levy Body dementia, number (%)*: ● *Frontotemporal dementia, number (%)*: ● *Nursing home recidents, number (%)*: ● *Inpatients, number (%)*: ● *Living in their own homes, number (%)*: Intervention 1 ● *Age in years, mean (SD)*: ● *Females (%)*: ● *Numbers (%) with BPSD*: ● *Alzheimer´s disease, number (%)*: ● *Vascular demnetia, number (%)*: ● *Levy Body dementia, number (%)*: ● *Frontotemporal dementia, number (%)*: ● *Nursing home recidents, number (%)*: ● *Inpatients, number (%)*: ● *Living in their own homes, number (%)*: Intervention 2

- *Age in years, mean (SD)*: 73.8 (8.8)
- *Females (%)*: 78 (56.9)
- *Numbers (%) with BPSD*: 137 (100)
- *Alzheimer´s disease, number (%)*: 137 (100)
- *Vascular demnetia, number (%)*:
- *Levy Body dementia, number (%)*:
- *Frontotemporal dementia, number (%)*:
- *Nursing home recidents, number (%)*: 137 (100)
- *Inpatients, number (%)*:
- *Living in their own homes, number (%)*:

Intervention 3

- *Age in years, mean (SD)*: 73.7 (8.1)
- *Females (%)*: 79 (56.4)
- *Numbers (%) with BPSD*: 140 (100)
- *Alzheimer´s disease, number (%)*: 140 (100)
- *Vascular demnetia, number (%)*:
- *Levy Body dementia, number (%)*:
- *Frontotemporal dementia, number (%)*:
- *Nursing home recidents, number (%)*: 140 (100)
- *Inpatients, number (%)*:
- *Living in their own homes, number (%)*:

Control

- *Age in years, mean (SD)*: 74.1 (8.0)
- *Females (%)*: 70 (51.5)
- *Numbers (%) with BPSD*: 136 (100)
- *Alzheimer´s disease, number (%)*: 136 (100)
- *Vascular demnetia, number (%)*:
- *Levy Body dementia, number (%)*:
- *Frontotemporal dementia, number (%)*:
- *Nursing home recidents, number (%)*: 136 (100)
- *Inpatients, number (%)*:
- *Living in their own homes, number (%)*:

Overall

- *Age in years, mean (SD)*:
- *Females (%)*:
- *Numbers (%) with BPSD*: 433 (100)
- *Alzheimer´s disease, number (%)*: 433 (100)
- *Vascular demnetia, number (%)*:
- *Levy Body dementia, number (%)*:
- *Frontotemporal dementia, number (%)*:

	● *Nursing home recidents, number (%)*: 433 (100) ● *Inpatients, number (%)*: ● *Living in their own homes, number (%)*: **Included criteria:** Eligible patients were male or female, aged 55−90 years, with a diagnosis of probable AD according to National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association (NINCDS-ADRDA) criteria, and a Mini-Mental State Examination (MMSE) score of 5−22 at screening and baseline. Patients must have had a previous magnetic resonance imaging (MRI) or computed tomography (CT) scan of the brain, with findings consistent with a diagnosis of AD; if a previous scan was not available, MRI or CT was performed during screening. Patients were also required to have symptoms of agitation or aggression (confirmed by a score of ≥4 on the Neuropsychiatric Inventory − Nursing Home version [NPI-NH] Agitation/Aggression domain), to require pharmacotherapy for the treatment of agitation in the investigator's judgment after an evaluation for reversible factors (e.g., delirium, pain, infection, and polypharmacy) and trial of nonpharmacologic interventions, and to be able to benefit from pharmacotherapy per the investigator's judgment. The NPI-NH Agitation/Aggression domain was chosen as an entry criterion to identify patients with baseline agitation or aggression while avoiding use of the primary endpoint (CMAI) for this purpose. The NPI-NH was completed by a clinician based on an interview with the patient's caregiver. The Agitation/Aggression domain score was obtained by multiplying the frequency rating, from 1 (rarely) to 4 (very often), by the severity rating, from 1 (mild) to 3 (severe). A score of ≥4 is considered to be clinically relevant and is often used as an entry criterion for clinical trials in dementia with neuropsychiatric symptoms. The IPA definition of AAD was not available at the time of study initiation but recruitment criteria are aligned with the target symptoms of the definition. Patients could be living in a care facility (e.g., nursing home, dementia unit, assisted living facility, or any other residential care facility providing long-term care) or in a community-based setting provided the patient was not living alone. Patients must have been residing at their current location for at least 14 days prior to screening and were expected to remain at the same location for the duration of the trial. In either setting, the patient was required to have a caregiver who could spend a minimum of 2 hours/day for 4 days/week with the patient in order to assess changes in the patient's condition. **Excluded criteria:** Key exclusion criteria were dementia or memory impairment due to a reason other than AD (including mixed pathologies; the Hachinski Ischemic Scale [Rosen modification] was used to exclude patients with probable vascular dementia), diagnosisof a specified Diagnostic and Statistical Manual of Mental Disorders, 4th edition, text revision (DSM-IV-TR) Axis I disorder (including current major depressive disorder [unless on a stable dose of antidepressant medication for 30 days prior to randomization], a history of bipolar disorder, or a history of a psychotic disorder not related to dementia), any other specifiedcomorbidity including a history of stroke, and being likely to require prohibited concomitant therapy during the trial (listed below). **Pretreatment:** **Total sample size:** 433 were randomized **Other:**
Interventions	**Intervention Characteristics** Intervention 1 ● *Number of participants allocated*: 20 ● *Dose*: Brexpiprazole 0.5 mg/day ● *Length of treatment*: 12 weeks ● *Other*: Intervention 1 ● *Number of participants allocated*: 137 ● *Dose*: Brexpiprazole 1 mg/day ● *Length of treatment*: 12 weeks ● *Other*:

	Intervention 1 ● *Number of participants allocated*: 140 ● *Dose*: Brexpiprazole 2 mg/day ● *Length of treatment*: 12 weeks ● *Other*: Intervention 2 ● *Number of participants allocated*: 137 ● *Dose*: Brexpiprazole 1 mg/day ● *Length of treatment*: 12 weeks ● *Other*: Intervention 3 ● *Number of participants allocated*: 140 ● *Dose*: Brexpiprazole 2 mg/day ● *Length of treatment*: 12 weeks ● *Other*: Control ● *Number of participants allocated*: 136 ● *Dose*: ● *Length of treatment*: 12 weeks ● *Other*:
Outcomes	*Serious adverse events* ● **Outcome type**: DichotomousOutcome *Mortality* ● **Outcome type**: DichotomousOutcome *BPSD* ● **Outcome type**: ContinuousOutcome *Agitation* ● **Outcome type**: ContinuousOutcome *Cognition* ● **Outcome type**: ContinuousOutcome *Activity of Daily Living (ADL)* ● **Outcome type**: ContinuousOutcome *Quality of life* ● **Outcome type**: ContinuousOutcome *BPSD_dikotom*

	● **Outcome type**: DichotomousOutcome
Identification	**Sponsorship source:** These studies were supported by Otsuka Pharmaceutical Development & Commercialization Inc. (Princeton, NJ, USA) and H. Lundbeck A/S (Valby, Denmark). **Country:** Russia, USA, Ukraine, Serbia, Croatia, Spain and Germany. **Setting:** Multicenter, care facility or community-based setting **Comments:** **Authors name:** George T. Grossberg **Institution:** Department of Psychiatry & Behavioral Neuroscience, St. Louis University **Email:** george.grossberg@health.slu.edu **Address:** Department of Psychiatry & Behavioral Neuroscience, St. Louis University, 1438 South Grand Blvd., St. Louis, MO 63104 **Start date:** July 11, 2013 **End date:** March 15, 2017 **Other:**
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Selective outcome reporting	High risk	Judgement Comment: Many outcomes reported on clinical trials.gov were not reported
Blinding of participants and personnel	Low risk	Judgement Comment: "Treatment assignments were blinded to patients, investigators, and sponsorpersonnel..."”Brexpiprazole and matching placebo tablets were provided by the sponsor,packaged in numbered, weekly blister cards."
Allocation concealment	Unclear risk	Judgement Comment: No information provided
Incomplete outcome data	High risk	Judgement Comment: No efficacy data for one study group (0.5mg/day). Overall and differentialdrop-out low. No ITT analysis of efficacy.
Sequence Generation	Low risk	Judgement Comment: "Treatments were assigned by an interactive voice/web response systembased on a fixed-block, computer-generated randomization code provided bythe study sponsor and stratified by study center."
Other sources of bias	High risk	Judgement Comment: Run-in of 6 weeks to wash out of antipsychotics, and other types of medication
Blinding of outcome assessors	Low risk	Judgement Comment: "Treatment assignments were blinded to patients, investigators, and sponsorpersonnel..."

Grossberg 2020b

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group **Other:**
Participants	**Baseline Characteristics** Overall 270 participants (133 brexpiprazole, 137 placebo) ● *Age in years, mean (SD)*: 73.8 ● *Females (%)*: 170 (63.0) ● *Numbers (%) with BPSD*: 270 (100) ● *Alzheimer´s disease, number (%)*: 270 (100) ● *Vascular demnetia, number (%)*: ● *Levy Body dementia, number (%)*: ● *Frontotemporal dementia, number (%)*: ● *Nursing home recidents, number (%)*: 270 (100) ● *Inpatients, number (%)*: ● *Living in their own homes, number (%)*: **Included criteria:** Eligible patients were male or female, aged 55−90 years, with a diagnosis of probable AD according to National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association (NINCDS-ADRDA) criteria, and a Mini-Mental State Examination (MMSE) score of 5−22 at screening and baseline. Patients must have had a previous magnetic resonance imaging (MRI) or computed tomography (CT) scan of the brain, with findings consistent with a diagnosis of AD; if a previous scan was not available, MRI or CT was performed during screening. Patients were also required to have symptoms of agitation or aggression (confirmed by a score of ≥4 on the Neuropsychiatric Inventory − Nursing Home version [NPI-NH] Agitation/Aggression domain), to require pharmacotherapy for the treatment of agitation in the investigator's judgment after an evaluation for reversible factors (e.g., delirium, pain, infection, and polypharmacy) and trial of nonpharmacologic interventions, and to be able to benefit from pharmacotherapy per the investigator's judgment. The NPI-NH Agitation/Aggression domain was chosen as an entry criterion to identify patients with baseline agitation or aggression while avoiding use of the primary endpoint (CMAI) for this purpose. The NPI-NH was completed by a clinician based on an interview with the patient's caregiver. The Agitation/Aggression domain score was obtained by multiplying the frequency rating, from 1 (rarely) to 4 (very often), by the severity rating, from 1 (mild) to 3 (severe). A score of ≥4 is considered to be clinically relevant and is often used as an entry criterion for clinical trials in dementia with neuropsychiatric symptoms. The IPA definition of AAD was not available at the time of study initiation but recruitment criteria are aligned with the target symptoms of the definition. Patients could be living in a care facility (e.g., nursing home, dementia unit, assisted living facility, or any other residential care facility providing long-term care) or in a community-based setting provided the patient was not living alone. Patients must have been residing at their current location for at least 14 days prior to screening and were expected to remain at the same location for the duration of the trial. In either setting, the patient was required to have a caregiver who could spend a minimum of 2 hours/day for 4 days/week with the patient in order to assess changes in the patient's condition. **Excluded criteria:** Key exclusion criteria were dementia or memory impairment due to a reason other than AD (including mixed pathologies; the Hachinski Ischemic Scale [Rosen modification] was used to exclude patients with probable vascular dementia), diagnosisof a specified Diagnostic and Statistical Manual of Mental Disorders, 4th edition, text revision (DSM-IV-TR) Axis I disorder (including current major depressive disorder [unless on a stable dose of antidepressant medication for 30 days prior to randomization], a history of bipolar disorder, or a history of a psychotic disorder not related to dementia), any other specifiedcomorbidity including a history of stroke, and being likely to require prohibited concomitant therapy during the trial (listed below). **Pretreatment:**

	Total sample size: 433 were randomized **Other:**
Interventions	**Intervention Characteristics** Flexible dose of brexpiprazole 0.5 mg to 2 mg/day. mean dose: 1.54 mg/day. placebo
Outcomes	*Serious adverse events* ● **Outcome type**: DichotomousOutcome *Mortality* ● **Outcome type**: DichotomousOutcome *BPSD* ● **Outcome type**: ContinuousOutcome *Agitation* ● **Outcome type**: ContinuousOutcome *Cognition* ● **Outcome type**: ContinuousOutcome *Activity of Daily Living (ADL)* ● **Outcome type**: ContinuousOutcome *Quality of life* ● **Outcome type**: ContinuousOutcome *BPSD_dikotom* ● **Outcome type**: DichotomousOutcome
Identification	**Sponsorship source:** These studies were supported by Otsuka Pharmaceutical Development & Commercialization Inc. (Princeton, NJ, USA) and H. Lundbeck A/S (Valby, Denmark). **Country:** Russia, USA, Ukraine, Serbia, Croatia, Spain and Germany. **Setting:** Multicenter, care facility or community-based setting **Comments:** **Authors name:** George T. Grossberg **Institution:** Department of Psychiatry & Behavioral Neuroscience, St. Louis University **Email:** george.grossberg@health.slu.edu **Address:** Department of Psychiatry & Behavioral Neuroscience, St. Louis University, 1438 South Grand Blvd., St. Louis, MO 63104 **Start date:** July 11, 2013 **End date:** March 15, 2017 **Other:**
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Selective outcome reporting	High risk	Judgement Comment: Many outcomes reported on clinical trials.gov were not reported
Blinding of participants and personnel	Low risk	Judgement Comment: "Treatment assignments were blinded to patients, investigators, and sponsorpersonnel...""Brexpiprazole and matching placebo tablets were provided by the sponsor,packaged in numbered, weekly blister cards."
Allocation concealment	Unclear risk	Judgement Comment: No information provided
Incomplete outcome data	Low risk	Judgement Comment: No efficacy data for one study group (0.5mg/day). Overall and differentialdrop-out low. No ITT analysis of efficacy.
Sequence Generation	Low risk	Judgement Comment: "Treatments were assigned by an interactive voice/web response systembased on a fixed-block, computer-generated randomization code provided bythe study sponsor and stratified by study center."
Other sources of bias	High risk	Judgement Comment: Run-in of 6 weeks to wash out of antipsychotics, and other types of medication
Blinding of outcome assessors	Low risk	Judgement Comment: "Treatment assignments were blinded to patients, investigators, and sponsorpersonnel..."

Katz 1999

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group **Other:**
Participants	**Baseline Characteristics** Intervention 1 ● *Age in years, mean (SD)*: 83.2 (7.9) ● *Females (%)*: 108 (72.5) ● *Numbers (%) with BPSD*: 149 (100) ● *Alzheimer´s disease, number (%)*: 120 (80.5) ● *Vascular demnetia, number (%)*: 17 (11.4) ● *Levy Body dementia, number (%)*: ● *Frontotemporal dementia, number (%)*: ● *Nursing home recidents, number (%)*: ● *Inpatients, number (%)*: ● *Living in their own homes, number (%)*: Intervention 1 ● *Age in years, mean (SD)*: ● *Females (%)*: ● *Numbers (%) with BPSD*: ● *Alzheimer´s disease, number (%)*:

- *Vascular demnetia, number (%)*:
- *Levy Body dementia, number (%)*:
- *Frontotemporal dementia, number (%)*:
- *Nursing home recidents, number (%)*:
- *Inpatients, number (%)*:
- *Living in their own homes, number (%)*:

Intervention 1

- *Age in years, mean (SD)*:
- *Females (%)*:
- *Numbers (%) with BPSD*:
- *Alzheimer´s disease, number (%)*:
- *Vascular demnetia, number (%)*:
- *Levy Body dementia, number (%)*:
- *Frontotemporal dementia, number (%)*:
- *Nursing home recidents, number (%)*:
- *Inpatients, number (%)*:
- *Living in their own homes, number (%)*:

Intervention 2

- *Age in years, mean (SD)*: 83.1 (7.2)
- *Females (%)*: 98 (66.2)
- *Numbers (%) with BPSD*: 148 (100)
- *Alzheimer´s disease, number (%)*: 110 (74.3)
- *Vascular demnetia, number (%)*: 26 (17.6)
- *Levy Body dementia, number (%)*:
- *Frontotemporal dementia, number (%)*:
- *Nursing home recidents, number (%)*:
- *Inpatients, number (%)*:
- *Living in their own homes, number (%)*:

Intervention 3

- *Age in years, mean (SD)*: 82.0 (7.8)
- *Females (%)*: 108 (65.5)
- *Numbers (%) with BPSD*: 165 (100)
- *Alzheimer´s disease, number (%)*: 111 (67.3)
- *Vascular demnetia, number (%)*: 27 (16.4)
- *Levy Body dementia, number (%)*:
- *Frontotemporal dementia, number (%)*:
- *Nursing home recidents, number (%)*:
- *Inpatients, number (%)*:
- *Living in their own homes, number (%)*:

Control

	● *Age in years, mean (SD)*: 82.6 (7.7) ● *Females (%)*: 110 (67.5) ● *Numbers (%) with BPSD*: 163 (100) ● *Alzheimer´s disease, number (%)*: 115 (70.6) ● *Vascular demnetia, number (%)*: 27 (16.6) ● *Levy Body dementia, number (%)*: ● *Frontotemporal dementia, number (%)*: ● *Nursing home recidents, number (%)*: ● *Inpatients, number (%)*: ● *Living in their own homes, number (%)*: Overall ● *Age in years, mean (SD)*: 82.7 (7.7) ● *Females (%)*: 424 (67.8) ● *Numbers (%) with BPSD*: 625 (100) ● *Alzheimer´s disease, number (%)*: 456 (73.0) ● *Vascular demnetia, number (%)*: 97 (15.5) ● *Levy Body dementia, number (%)*: ● *Frontotemporal dementia, number (%)*: ● *Nursing home recidents, number (%)*: ● *Inpatients, number (%)*: ● *Living in their own homes, number (%)*: **Included criteria:** Patients were required to be 55 years or older, to reside in a nursing home or chronic disease hospital, and to have Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) diagnoses of Alzheimer's disease, vascular dementia, or a combination of the two, with scores of 4 or greater on the Functional Assessment Staging rating scale and 23 or lower on the Mini-Mental State Examination. They were required to have a total score ≥8 and a gloval rating ≥1 on the Behavioral Pathology in Alzheimer's Disease (BEHAVE-AD) rating scale, indicating significant psychotic and behavioral symptoms. **Excluded criteria:** Excluded were patients with untreated reversible causes of dementia, patients with medical or neurologic conditions that diminish cognition, patients with a diagnosis of dementia related to infection with the human immunodeficiency virus or substance-induced persistent dementia, patients with a diagnosis of delirium or amnestic disorder, and patients with a psychiatric diagnosis that could have accounted for the observed psychotic disturbances. **Pretreatment:** **Total sample size:** 625 were randomized **Other:**
Interventions	**Intervention Characteristics** Intervention 1 ● *Number of participants allocated*: 149 ● *Dose*: Risperidone 0.5 mg/day ● *Length of treatment*: 12 weeks ● *Other*: Intervention 1

	● *Number of participants allocated*: 148 ● *Dose*: Risperidone 1 mg ● *Length of treatment*: 12 weeks ● *Other*: Intervention 1 ● *Number of participants allocated*: 165 ● *Dose*: Risperidone 2 mg ● *Length of treatment*: 12 weeks ● *Other*: Intervention 2 ● *Number of participants allocated*: 148 ● *Dose*: Risperidone 1 mg/day ● *Length of treatment*: 12 weeks ● *Other*: Intervention 3 ● *Number of participants allocated*: 165 ● *Dose*: Risperidone 2 mg/day ● *Length of treatment*: 12 weeks ● *Other*: Control ● *Number of participants allocated*: 163 ● *Dose*: ● *Length of treatment*: 12 weeks ● *Other*:
Outcomes	*Serious adverse events* ● **Outcome type**: DichotomousOutcome *Mortality* ● **Outcome type**: DichotomousOutcome *BPSD* ● **Outcome type**: ContinuousOutcome *Agitation* ● **Outcome type**: ContinuousOutcome *Cognition* ● **Outcome type**: ContinuousOutcome *Activity of Daily Living (ADL)* ● **Outcome type**: ContinuousOutcome

	Quality of life ● **Outcome type**: ContinuousOutcome *BPSD_dikotom* ● **Outcome type**: DichotomousOutcome
Identification	**Sponsorship source:** Janssen Research Foundation, Titusville, N.J. **Country:** USA **Setting:** Multicenter, institutionalized (nursing home or chronic disease hospital) in the USA **Comments:** **Authors name:** Ira R. Katz **Institution:** Department of Psychiatry, University of Pennsylvania Medical School, Philadelphia **Email:** katzi@mail.med.upenn.edu **Address:** Section of Geriatric Psychiatry, University of Pennsylvania, 3600 Market St., Room 758, Philadelphia, PA 19104 **Start date:** July 31, 1995 **End date:** March 7, 1997 **Other:**
Notes	*NKA Demens 2023* on 26/04/2024 20:46 **Select** P: personer med diagnostisteret demens og symptomer ved BEHAVE-skemaI: riperidon (3 forskellige doser)C: placebo *Kasper Jørgensen* on 08/05/2024 17:57 **Select** 12 ugers behandling

Risk of bias table

Bias	Authors' judgement	Support for judgement
Selective outcome reporting	Unclear risk	Judgement Comment: This is a secondary report of the trial based on the patients with psychosis only. Primary results are presented for the 1.0 and 2.0 group combined. Unclearwhy. Many outcomes that were reported in the main results paper based on allparticipants were not reported here. The authors don't describe a study protocol that was published before conducting the study and the protocol can't be found anywhere. It is therefore not clear whether the study is free of selective outcome reporting. The authors don't describe a study protocol that was published before conducting the study and the protocol can't be found anywhere. It is therefore not clear whether the study is free of selective outcome reporting.
Blinding of participants and personnel	Unclear risk	Judgement Comment: Identically appearing risperidone (0.25, 0.5, and 1.0 mg) and placebo tabletswere supplied by the sponsor. Each patient received 2 tablets twice daily. Alltrial drugs were appropriately labelled with a 2-part la- bel containing the visit, protocol, patient numbers, and directions for administration. The first partof the label remained attached to the medication carton and the second part(double-blind portion) was detached and placed in the case report

		form.Onlysays double blind but doesn't mention the persons who were blinded.
Allocation concealment	Unclear risk	Judgement Comment: It is not described which method was used to conceal the allocation sequence. It is therefore not known if intervention allocations could have been foreseen in advance of, or during enrolment.
Incomplete outcome data	High risk	Judgement Comment: The proportion of participants that discontinued prematurely as well as the reason for discontinuation is outlined in table 1 for each study group. There seems to be more discontinuations in the group with the highest dose of risperidone (2 mg/day) compared to the other groups, mostly due to adverse events. This may be related to the true outcome as there is an imbalance in the number of discontinuations in the group with 2 mg/day of risperidone.Modified (all patients who received at least one dose and one post baseline assessment) ITT analysis performed. Imputation LOCF. Discontinuation rates imbalanced across groups (range from 27% in the placebo group to 42% in thegroup receiving 2mg risperidone).
Sequence Generation	Low risk	Judgement Comment: Patients were randomly assigned according to a randomization code provided by the sponsor (Janssen Research Foundation).
Other sources of bias	Low risk	Judgement Comment: After a single-blind placebo washout period of 3 to 7 days, eligible patientswere randomly assigned to placebo or to 0.5, 1.0, or 2.0 mg/day of risperidone
Blinding of outcome assessors	Unclear risk	Judgement Comment: Insufficient information if trained raters were blinded.are blinded, however, it is not known for sure.

Kennedy 2005

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group **Other:**
Participants	**Baseline Characteristics** Intervention 1 ● *Age in years, mean (SD)*: 78 (8.0) ● *Females (%)*: 98 (55.1) ● *Numbers (%) with BPSD*: ● *Alzheimer´s disease, number (%)*: 178 (100) ● *Vascular demnetia, number (%)*: ● *Levy Body dementia, number (%)*: ● *Frontotemporal dementia, number (%)*: ● *Nursing home recidents, number (%)*: ● *Inpatients, number (%)*: ● *Living in their own homes, number (%)*: 178 (100) Control ● *Age in years, mean (SD)*: 78 (7.8) ● *Females (%)*: 52 (57.8) ● *Numbers (%) with BPSD*:

	● *Alzheimer´s disease, number (%)*: 90 (100) ● *Vascular demnetia, number (%)*: ● *Levy Body dementia, number (%)*: ● *Frontotemporal dementia, number (%)*: ● *Nursing home recidents, number (%)*: ● *Inpatients, number (%)*: ● *Living in their own homes, number (%)*: 90 (100) Overall ● *Age in years, mean (SD)*: 78 ● *Females (%)*: ● *Numbers (%) with BPSD*: ● *Alzheimer´s disease, number (%)*: 268 (100) ● *Vascular demnetia, number (%)*: ● *Levy Body dementia, number (%)*: ● *Frontotemporal dementia, number (%)*: ● *Nursing home recidents, number (%)*: ● *Inpatients, number (%)*: ● *Living in their own homes, number (%)*: 268 (100) **Included criteria:** Patients were aged ≥40 years, outpatients or in assisted living, and met the National Institute of Neurological and Communicative Disorders and Stroke-Alzheimer's Disease and Related DisordersAssociation criteria for possible or probable Alzheimer's disease. For study inclusion, patients must have scored between 14 and 26 onthe Mini-Mental State Examination at screening and baseline. **Excluded criteria:** Exclusion criteria included having a score >1 on any one of the following Neuropsychiatric Inventory items: delusions, hallucinations, agitation/aggression, dysphoria; having a score of 1 on any three of these four items; current use of any cholinesterase inhibitor, antioxidant or herbal supplements considered to have possible beneficial effects in improving cognitive features of Alzheimer's within4 weeks prior to enrollment into the study; a history of any other DSM-IV Axis I disorder, or any neurological condition other than Alzheimer's dementia. **Pretreatment:** **Total sample size:** 268 were randomized **Other:**
Interventions	**Intervention Characteristics** Intervention 1 ● *Number of participants allocated*: 178 ● *Dose*: Olanzapine 2.5-7.5 mg/day ● *Length of treatment*: 12 weeks ● *Other*: Control ● *Number of participants allocated*: 90 ● *Dose*: ● *Length of treatment*: 12 weeks ● *Other*:

Outcomes	*Serious adverse events* ● **Outcome type**: DichotomousOutcome *Mortality* ● **Outcome type**: DichotomousOutcome *BPSD* ● **Outcome type**: ContinuousOutcome *Agitation* ● **Outcome type**: ContinuousOutcome *Cognition* ● **Outcome type**: ContinuousOutcome *Activity of Daily Living (ADL)* ● **Outcome type**: ContinuousOutcome *Quality of life* ● **Outcome type**: ContinuousOutcome *BPSD_dikotom* ● **Outcome type**: DichotomousOutcome
Identification	**Sponsorship source:** Eli Lilly and Company, Indianapolis, IN, USA. **Country:** USA **Setting:** Multicenter, outpatients and assisted living in the USA **Comments:** **Authors name:** John Kennedy **Institution:** University of Alberta and Chinook Regional Health System, Alberta, Canada **Email:** Deberdt_Walter@lilly.com **Address:** Lilly Research Laboratories, Eli Lilly and Company, Indianapolis, IN, USA. **Start date:** **End date:** **Other:**
Notes	*NKA Demens 2023* on 26/04/2024 20:50 **Select** P: personer med alzheimers demens og med minimal agitation/psykosel: olanzapinC: placebo

Risk of bias table

Bias	Authors' judgement	Support for judgement
Selective outcome reporting	Unclear risk	Judgement Comment: The authors don't describe a study protocol that was published before conducting the study and the protocol can't be found anywhere. It is therefore not clear whether the study is free of selective outcome reporting.
Blinding of participants and personnel	Unclear risk	Judgement Comment: The authors describe that it is a double-blind study, however, it is not specified who is blinded. It is unclear whether the participants, personnel or outcome assessors were blinded. In this case, it is supposed that the participants and the personnel were blinded, however, this is not clear.
Allocation concealment	Unclear risk	Judgement Comment: The method used to conceal the allocation sequence is not described. It's only described that the patients were randomized but it's not specified how this was done. It can therefore not be ruled out that intervention allocation could have been foreseen in advance of, or during, enrolment.
Incomplete outcome data	High risk	Judgement Comment: The reasons for discontinuation in the study are outlined in figure 1 for each study group. It can be seen that more participants discontinued in the olanzapine group compared to the placebo group. Adverse events are among the main reasons for discontinuation, and it is much more prevalent in the olanzapine group. There is an imbalance in the amount of participants discontinuing because of adverse events between the groups and the missing outcome data is likely to be related to the true outcome.
Sequence Generation	Unclear risk	Judgement Comment: The method used to generate the allocation sequence is not described. It's only described that the patients were randomized but it's not specified how this was done.
Other sources of bias	Low risk	
Blinding of outcome assessors	Unclear risk	Judgement Comment: The authors describe that it is a double-blind study, however, it is not specified who is blinded. It is unclear whether the participants, personnel or outcome assessors were blinded. In this case, it is supposed that the participants and the personnel were blinded, however, this is not clear.

Kurlan 2007

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group **Other:**
Participants	**Baseline Characteristics** Intervention 1 ● *Age in years, mean (SD)*: 73.5 (5.8) ● *Females (%)*: 9 (45) ● *Numbers (%) with BPSD*: 20 (100) ● *Alzheimer´s disease, number (%)*: 4 (20) ● *Vascular demnetia, number (%)*: ● *Levy Body dementia, number (%)*: 11 (55) ● *Frontotemporal dementia, number (%)*: ● *Nursing home recidents, number (%)*: ● *Inpatients, number (%)*:

- *Living in their own homes, number (%)*:

Control
- *Age in years, mean (SD)*: 74.1 (6.1)
- *Females (%)*: 6 (30)
- *Numbers (%) with BPSD*: 20 (100)
- *Alzheimer´s disease, number (%)*: 4 (20)
- *Vascular demnetia, number (%)*:
- *Levy Body dementia, number (%)*: 12 (60)
- *Frontotemporal dementia, number (%)*:
- *Nursing home recidents, number (%)*:
- *Inpatients, number (%)*:
- *Living in their own homes, number (%)*:

Overall
- *Age in years, mean (SD)*:
- *Females (%)*: 15 (37.5)
- *Numbers (%) with BPSD*: 40 (100)
- *Alzheimer´s disease, number (%)*: 8 (20)
- *Vascular demnetia, number (%)*:
- *Levy Body dementia, number (%)*: 23 (57.5)
- *Frontotemporal dementia, number (%)*:
- *Nursing home recidents, number (%)*:
- *Inpatients, number (%)*:
- *Living in their own homes, number (%)*:

Included criteria: Eligible subjects inciuded men or women of any ethnicity. Inclusion criteria were 1) fluent in English or Spanish, 2) age 50 years or older, 3) presence of dementia as defined in the Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSM-IV), 4) meets National Institute of Neurological and Communicative Disorders and Stroke—Alzheimer's Disease and Related Disorders Association diagnostic criteria for probable AD or Consortium diagnostic criteria for DLB or UK Brain Bank criteria for PD, 5) presence of psychosis (as defined in Jeste and Finkel , 2000, and the DSM-1V10) or agitation (as defined in Cohen-Mansfield and Billig, 1986) (theduration of psychosis or agitation prior to enroliment was not recorded), 6) presence of extrapyramidal motor features (defined by having two or more of the following four signs: restingtremor, bradykinesia, limb rigidity, shuffling gait), 7) sum ofratings for the tremor at rest, rigidity (highest one of the fourrigidity items), bradykinesia, and gait items of the Unified PDRating Scale greater than or equal to 2, 8) Brief PsychiatricRating Scale (BPRS) score greater than or equal to 12, 9) atleast one of the following BPRS items scored greater than orequal to 3 (moderate): hostility, suspiciousness, hallucinatorybehavior, uncooperativeness, unusual thought content, excitement, 10) presence of a caregiver/informant who is willing to accompany the subject to all evaluation visits and to report on the subject's activities and behavior, 11) on a stable dosage of non-excluded medications for at least 4 weeks, 12) in stable medical condition for at least 4 weeks, 13) physically acceptable for the study as confirmed by medical history, physical examination, and screening clinical laboratory tests (blood counts, serum chemistries, electrocardiogram), 14) able to ingest study medications (confirmed using placebo pills), and 15) supervision available for administration of study medications.
Excluded criteria: Exclusion criteria were 1) Mini-Mental State Examination (MMSE) score <8, 2) use of a classic or atypical antipsychotic drug in theprior 3 weeks, 3) a history of a severe adverse reaction to anyatypical antipsychotic drug, 4) a serious medical illness that would preclude the safe administration of quetiapine, 5) known pregnancy, and 6) current evidence or history in the prior 2 years of epilepsy, focal brain lesions, head injury

	with loss of consciousness or immediate confusion after the injury. Patients thought to be experiencing a toxic, metabolic, or infectious encephalopathy (delirium) were excluded. Excluded concomitant medications included any classic or atypical antipsychotic, anxiolytic, or hypnotic drug. **Pretreatment:** **Total sample size:** 40 were randomized **Other:**
Interventions	**Intervention Characteristics** Intervention 1 ● *Number of participants allocated*: 20 ● *Dose*: Quetiapine 25 mg/day ● *Length of treatment*: 10 weeks ● *Other*: Control ● *Number of participants allocated*: 20 ● *Dose*: ● *Length of treatment*: 10 weeks ● *Other*:
Outcomes	*Serious adverse events* ● **Outcome type**: DichotomousOutcome *Mortality* ● **Outcome type**: DichotomousOutcome *BPSD* ● **Outcome type**: ContinuousOutcome *Agitation* ● **Outcome type**: ContinuousOutcome *Cognition* ● **Outcome type**: ContinuousOutcome *Activity of Daily Living (ADL)* ● **Outcome type**: ContinuousOutcome *Quality of life* ● **Outcome type**: ContinuousOutcome *BPSD_dikotom* ● **Outcome type**: DichotomousOutcome

Identification	**Sponsorship source:** Supported by the National Institute on Aging (#R01 AG020086). Study drug and matching placebo was supplied by AstraZeneca, LP. **Country:** USA **Setting:** Multicenter, own residence and nursing homes **Comments:** **Authors name:** Roger Kurlan **Institution:** University of Rochester **Email:** Roger_Kurlan@urmc.rochester.edu **Address:** Mt. Hope Professional Building, 1351 Mt. Hope Avenue, Suite 100, Rochester, NY 14620, USA **Start date:** September 2002 **End date:** September 2005 **Other:**
Notes	*NKA Demens 2023* on 26/04/2024 20:52 **Select** P: personer med demens og adfærssymptomerI: quetiapinC: placebo *Kasper Jørgensen* on 08/05/2024 18:17 **Select** 10 ugers behandling

Risk of bias table

Bias	Authors' judgement	Support for judgement
Selective outcome reporting	Unclear risk	Judgement Comment: The study protocol is available (NCT00043849), however, there are no outcome measures reported in the study protocol. Therefore, the occurence of selective outcome reporting is not known.
Blinding of participants and personnel	Low risk	Judgement Comment: Study participants, investigators administering study medications, and those assessing the outcomes were blinded to group assignment. No formal assessment of the success of blinding was carried out.
Allocation concealment	Unclear risk	Judgement Comment: The method used to conceal the allocation sequence is not described. Therefore it is unclear if allocations could have been foreseen in advance of, or during, enrolment.
Incomplete outcome data	Low risk	Judgement Comment: The reasons for study discontinuation and exclusions from the ITT analysis are given. There were four exclusions from the ITT analysis (1 in the quetiapine group and 3 in the placebo group) because they didn't have a post-baseline visit.The missing outcome data is not very imbalanced between the groups and there are similar reasons for discontinuation.
Sequence Generation	Low risk	Judgement Comment: Patients were randomly allocated using a permuted block design stratified by study site with equal probability of being assigned to the treatment arm or placebo.
Other sources of bias	Low risk	

Blinding of outcome assessors	Low risk	Judgement Comment: Those assessing the outcomes were blinded to group assignment. No formal assessment of the success of blinding was carried out, but it is unlikely that the blinding could have been broken.

Lee 2023

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group **Other:**
Participants	**Baseline Characteristics** Intervention 1 ● *Age in years, mean (SD)*: 74.5 (7.7) ● *Females (%)*: 135 (59.2) ● *Numbers (%) with BPSD*: 228 (100) ● *Alzheimer´s disease, number (%)*: 228 (100) ● *Vascular demnetia, number (%)*: ● *Levy Body dementia, number (%)*: ● *Frontotemporal dementia, number (%)*: ● *Nursing home recidents, number (%)*: 228 (100) ● *Inpatients, number (%)*: ● *Living in their own homes, number (%)*: Control ● *Age in years, mean (SD)*: 73.0 (7.0) ● *Females (%)*: 60 (51.3) ● *Numbers (%) with BPSD*: 117 (100) ● *Alzheimer´s disease, number (%)*: 117 (100) ● *Vascular demnetia, number (%)*: ● *Levy Body dementia, number (%)*: ● *Frontotemporal dementia, number (%)*: ● *Nursing home recidents, number (%)*: 117 (100) ● *Inpatients, number (%)*: ● *Living in their own homes, number (%)*: Overall ● *Age in years, mean (SD)*: 74.0 (7.5) ● *Females (%)*: 195 (56.5) ● *Numbers (%) with BPSD*: 345 (100) ● *Alzheimer´s disease, number (%)*: 345 (100) ● *Vascular demnetia, number (%)*: ● *Levy Body dementia, number (%)*: ● *Frontotemporal dementia, number (%)*: ● *Nursing home recidents, number (%)*: 345 (100)

	● *Inpatients, number (%)*: ● *Living in their own homes, number (%)*: **Included criteria:** Key inclusion criteria were age 55 to 90 years; diagnosis of probable Alzheimer disease, defined by the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association (NINCDS-ADRDA) criteria; Mini-Mental State Examination (MMSE) score of 5 to 22 at screening andbaseline; previous computed tomography or magnetic resonance imaging scan of the brain with findings consistent with a diagnosis of Alzheimer disease; a diagnosis of agitation that meets the International Psychogeriatric Association definition (which was a provisional definition at the time); onset of agitation at least 2 weeks prior to screening; Neuropsychiatric Inventory (NPI) or NPI–Nursing Home version (NPI-NH) Agitation/Aggression domain score(frequency × severity) of 4 or greater at screening and baseline; requiring pharmacotherapy for the treatment of agitation in the investigator'sjudgment after an evaluation for reversible factors (eg, pain, infection, polypharmacy) and a trial of nonpharmacological interventions (eg, redirecting behavior, group activities, music therapy); living in a care facility or community-based setting (not living alone); and having an identified caregiver who has sufficient contact to describe the patient's symptoms and behavior. An additional required inclusion criterion based on positivity for Cohen-Mansfield Agitation Inventory(CMAI) factor 1 (aggressive behavior [12 items: hitting, kicking, scratching, grabbing, pushing, hurting self or others, throwing things, cursing or verbal aggression, spitting, tearing things or destroying property, screaming, and biting]) was blinded to patients, caregivers, and investigators. To meet the CMAI factor 1 positivity criterion, 1 of the following must have been established at screening and baseline: 1 or more aggressive behaviors occurring several times per week, 2 or more aggressive behaviors occurring once or twice per week, or 3 or more aggressive behaviors occurring less than once per week. **Excluded criteria:** Key exclusion criteria were dementia or memory impairment due to a reason other than Alzheimer disease and any clinically significant neurological, psychiatric (except as specified), or unstable medicalcondition. **Pretreatment:** **Total sample size:** 345 were randomized **Other:**
Interventions	**Intervention Characteristics** Intervention 1 ● *Number of participants allocated*: 228 ● *Dose*: Brexpiprazole 2-3 mg/day ● *Length of treatment*: 12 weeks ● *Other*: Control ● *Number of participants allocated*: 117 ● *Dose*: ● *Length of treatment*: 12 weeks ● *Other*:
Outcomes	*Serious adverse events* ● **Outcome type**: DichotomousOutcome *Mortality* ● **Outcome type**: DichotomousOutcome *BPSD* ● **Outcome type**: ContinuousOutcome

	Agitation ● **Outcome type**: ContinuousOutcome *Cognition* ● **Outcome type**: ContinuousOutcome *Activity of Daily Living (ADL)* ● **Outcome type**: ContinuousOutcome *Quality of life* ● **Outcome type**: ContinuousOutcome
Identification	**Sponsorship source:** This study was supported by Otsuka Pharmaceutical Development &Commercialization and H. Lundbeck. **Country:** Bulgaria, Hungary, Serbia, Slovakia, Spain, Ukraine and USA **Setting:** Multicenter, care facilities and community-based settings (not living alone) in Europe and the USA **Comments:** **Authors name:** Daniel Lee **Institution:** Otsuka Pharmaceutical Development & Commercialization, Princeton, New Jersey **Email:** george.grossberg@health.slu.edu **Address:** Department of Psychiatry and Behavioral Neuroscience, St Louis University School of Medicine, 1438 South Grand Blvd, St Louis, MO 63104 **Start date:** May 16, 2018 **End date:** June 1, 2022 **Other:**
Notes	*NKA Demens 2023* on 06/05/2024 19:15 **Select** P: personer med demensI: brexipiprazolC: placebo *NKA Demens 2023* on 05/06/2024 23:28 **Included** Obs: er den endelige afrapportering for NCT03548584 (2018) som ligger i "anden litt." mappen

Risk of bias table

Bias	Authors' judgement	Support for judgement
Selective outcome reporting	Low risk	Judgement Comment: The study protocol is available (NCT03548584) and all of the study's pre-specified primary and secondary outcomes have been reported in the pre-specified way.
Blinding of participants and personnel	Low risk	Judgement Comment: Treatment assignments were blinded to patients, caregivers, investigators, and sponsor personnel, including those involved in data analysis.
Allocation concealment	Low risk	Judgement Comment: Treatments were assigned to patients using an eSource

Incomplete outcome data	Low risk	Judgement Comment: The missing outcome data are balanced between the groups with similar reasons for discontinuation. The reasons for discontinuation and numbers can be seen in figure 1. The rate of discontinuation due to adverse events was low and comparable between groups.
Sequence Generation	Low risk	Judgement Comment: Treatments were assigned to patients using an eSource method via a fixed-block (block size 3) computer-generated randomization code provided by the sponsor and stratified by site.
Other sources of bias	Low risk	
Blinding of outcome assessors	Low risk	Judgement Comment: Treatment assignments were blinded to patients, caregivers, investigators, and sponsor personnel, including those involved in data analysis.The outcome assessors were blinded.

Mintzer 2006

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group **Other:**
Participants	**Baseline Characteristics** Intervention 1 ● *Age in years, mean (SD)*: 83.4 (7.2) ● *Females (%)*: 183 (77.9) ● *Numbers (%) with BPSD*: 235 (100) ● *Alzheimer´s disease, number (%)*: 235 (100) ● *Vascular demnetia, number (%)*: ● *Levy Body dementia, number (%)*: ● *Frontotemporal dementia, number (%)*: ● *Nursing home recidents, number (%)*: 235 (100) ● *Inpatients, number (%)*: ● *Living in their own homes, number (%)*: Control ● *Age in years, mean (SD)*: 83.2 (7.38) ● *Females (%)*: 181 (76.1) ● *Numbers (%) with BPSD*: 238 (100) ● *Alzheimer´s disease, number (%)*: 238 (100) ● *Vascular demnetia, number (%)*: ● *Levy Body dementia, number (%)*: ● *Frontotemporal dementia, number (%)*: ● *Nursing home recidents, number (%)*: 238 (100) ● *Inpatients, number (%)*: ● *Living in their own homes, number (%)*: Overall

	● *Age in years, mean (SD)*: ● *Females (%)*: 364 (77) ● *Numbers (%) with BPSD*: 473 (100) ● *Alzheimer´s disease, number (%)*: 473 (100) ● *Vascular demnetia, number (%)*: ● *Levy Body dementia, number (%)*: ● *Frontotemporal dementia, number (%)*: ● *Nursing home recidents, number (%)*: 473 (100) ● *Inpatients, number (%)*: ● *Living in their own homes, number (%)*: **Included criteria:** Patients with AD eligible for enroilment were 55 years old, residents of nursing homes or long-term care facilities, and mobile (ambulatory, walked with assistance, or used a wheelchair independently). They met the criteria for psychosis of AD and were deemed to be in need of treatment with an atypical antipsychotic in accordance with OBRA guidelines. Enrolled patients also scored ≥2 on any item of the Behavioral pathology in Alzheimer's Disease (BEHAVE-AD) Psychosis subscale and between 5 to 23 on a Mini-Mental Status Examination (MMSE). **Excluded criteria:** Patients excluded had recently been treated with neuroleptic injections, had other medical conditions that diminish cognition, or had other psychiatric disorders that produce psychotic symptoms. Patients with epilepsy, recent diagnoses of cancer (except nonmelanoma skin cancers), unstable medical conditions, changes in prescription medications 30 days before screening, or significant baseline laboratory or electrocardiographic abnormalities were also excluded. Patients were withdrawn if their behavior worsened considerably, they withdrew consent, or their randomization code was broken. **Pretreatment:** **Total sample size:** 473 were randomized **Other:**
Interventions	**Intervention Characteristics** Intervention 1 ● *Number of participants allocated*: 235 ● *Dose*: Risperidone 0.5-1.5 mg ● *Length of treatment*: 8 weeks ● *Other*: Control ● *Number of participants allocated*: 238 ● *Dose*: ● *Length of treatment*: 8 weeks ● *Other*:
Outcomes	*Serious adverse events* ● **Outcome type**: DichotomousOutcome *Mortality* ● **Outcome type**: DichotomousOutcome *BPSD*

	● **Outcome type**: ContinuousOutcome *Agitation* ● **Outcome type**: ContinuousOutcome *Cognition* ● **Outcome type**: ContinuousOutcome *Activity of Daily Living (ADL)* ● **Outcome type**: ContinuousOutcome *Quality of life* ● **Outcome type**: ContinuousOutcome *BPSD_dikotom* ● **Outcome type**: DichotomousOutcome
Identification	**Sponsorship source:** This study was sponsored by Johnson & Johnson Pharmaceutical Research & Development, L.L.C. **Country:** USA **Setting:** Multicenter, nursing homes and long-term care facilities **Comments:** **Authors name:** Jacobo Mintzer **Institution:** Medical University of South Carolina, Alzheimer's Research and Clinical Programs **Email:** mintzerjm@musc.edu **Address:** Medical University of South Carolina, Alzheimer's Research and Clinical Programs, 5900 Core Rd., Suite 203, N. Charleston, SC 29406-6076. **Start date:** December 2000 **End date:** January 2003 **Other:**
Notes	*NKA Demens 2023* on 26/04/2024 21:38 **Select** P: personer med diagnostiseret AD og vurderet behov for API: risperidonC: placebo

Risk of bias table

Bias	Authors' judgement	Support for judgement
Selective outcome reporting	Unclear risk	Judgement Comment: Many subanalyses with primary outcome, but adverse events reported in moredetail than usual.
Blinding of participants and personnel	Unclear risk	Judgement Comment: Placebo-controlled with identical tablets, double-blind, but no reference toblinding of participants and personel specifically.
Allocation concealment	Low risk	Judgement Comment: "Investigators received sealed envelopes for each patient containing codeddetails of the treatment in this phase."

Incomplete outcome data	High risk	Judgement Comment: Drop-out was high (>20%). Modified ITT (excluding patients without assessment after baseline). Handling of missing data not reported.
Sequence Generation	Unclear risk	Judgement Comment: No information
Other sources of bias	High risk	Judgement Comment: During the run-in phase, all patients received placebo for 1 week to wash outpreviously used psychotropic medications. The run-in length was reduced forpatients not using psychotropic medications and for patients whose psychosisor agitation worsened.
Blinding of outcome assessors	Unclear risk	Judgement Comment: No information

Mintzer 2007

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group **Other:**
Participants	**Baseline Characteristics** Intervention 1 ● *Age in years, mean (SD)*: 83.0 (range 62.0-95.0) ● *Females (%)*: 96 (81) ● *Numbers (%) with BPSD*: 118 (100) ● *Alzheimer´s disease, number (%)*: 118 (100) ● *Vascular demnetia, number (%)*: ● *Levy Body dementia, number (%)*: ● *Frontotemporal dementia, number (%)*: ● *Nursing home recidents, number (%)*: 118 (100) ● *Inpatients, number (%)*: ● *Living in their own homes, number (%)*: Intervention 1 ● *Age in years, mean (SD)*: ● *Females (%)*: ● *Numbers (%) with BPSD*: ● *Alzheimer´s disease, number (%)*: ● *Vascular demnetia, number (%)*: ● *Levy Body dementia, number (%)*: ● *Frontotemporal dementia, number (%)*: ● *Nursing home recidents, number (%)*: ● *Inpatients, number (%)*: ● *Living in their own homes, number (%)*: Intervention 1 ● *Age in years, mean (SD)*:

- *Females (%)*:
- *Numbers (%) with BPSD*:
- *Alzheimer´s disease, number (%)*:
- *Vascular demnetia, number (%)*:
- *Levy Body dementia, number (%)*:
- *Frontotemporal dementia, number (%)*:
- *Nursing home recidents, number (%)*:
- *Inpatients, number (%)*:
- *Living in their own homes, number (%)*:

Intervention 2

- *Age in years, mean (SD)*: 82.4 (range 60.0-97.0)
- *Females (%)*: 93 (76)
- *Numbers (%) with BPSD*: 122 (100)
- *Alzheimer´s disease, number (%)*: 122 (100)
- *Vascular demnetia, number (%)*:
- *Levy Body dementia, number (%)*:
- *Frontotemporal dementia, number (%)*:
- *Nursing home recidents, number (%)*: 122 (100)
- *Inpatients, number (%)*:
- *Living in their own homes, number (%)*:

Intervention 3

- *Age in years, mean (SD)*: 82.3 (range 56.0-94.0)
- *Females (%)*: 96 (76)
- *Numbers (%) with BPSD*: 126 (100)
- *Alzheimer´s disease, number (%)*: 126 (100)
- *Vascular demnetia, number (%)*:
- *Levy Body dementia, number (%)*:
- *Frontotemporal dementia, number (%)*:
- *Nursing home recidents, number (%)*: 126 (100)
- *Inpatients, number (%)*:
- *Living in their own homes, number (%)*:

Control

- *Age in years, mean (SD)*: 82.2 (range 56.0-96.0)
- *Females (%)*: 99 (82)
- *Numbers (%) with BPSD*: 121 (100)
- *Alzheimer´s disease, number (%)*: 121 (100)
- *Vascular demnetia, number (%)*:
- *Levy Body dementia, number (%)*:
- *Frontotemporal dementia, number (%)*:
- *Nursing home recidents, number (%)*: 121 (100)

	● *Inpatients, number (%)*: ● *Living in their own homes, number (%)*: Overall ● *Age in years, mean (SD)*: 82.5 (range 56.0 –97.0) ● *Females (%)*: 385 (79) ● *Numbers (%) with BPSD*: 487 (100) ● *Alzheimer´s disease, number (%)*: 487 (100) ● *Vascular demnetia, number (%)*: ● *Levy Body dementia, number (%)*: ● *Frontotemporal dementia, number (%)*: ● *Nursing home recidents, number (%)*: 487 (100) ● *Inpatients, number (%)*: ● *Living in their own homes, number (%)*: **Included criteria:** Patients eligible for enrollment in this study were men and women aged 55–95 years (inclusive), who were diagnosed with AD (defined by the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition [DSM–IV criteria]) and psychotic symptoms of delusions or hallucinations, who were living in nursing homes or residential assisted-living facilities for a minimum of four weeks before study entry. Patients were also required to be capable of self-locomotion (alone or with the aid of an assistive device) and have an identified or proxy caregiver. To be eligible for enrollment into the study, all patients had to undergo a screening period (maximum 28 days). Eligible patients had a Mini-MentalState Exam (MMSE) score of 6 –22 points (inclusive), and had experienced persistent or intermittent delusions, hallucinations or both for at least one month. Prior to randomization, patients underwent evaluations to determine eligibility for randomization and to establish baseline values for efficacy assessments. A minimum seven-day washout period of any psychotropic medication was required and the presence of psychotic symptoms was confirmed byscores of 6 or higher on either the delusions or hallucinations items of the NPI-NH Psychosis Subscale score. **Excluded criteria:** Patients were excluded from participation in the study if they had: an axis I diagnosis of delirium, amnestic disorder, bipolar disorder, schizophrenia or schizoaffective disorder, or mood disorder with psychotic features; non-AD; a current major depressive episode with psychotic symptoms of hallucinations or delusions; seizure disorders; history of refractoriness to antipsychotics; known hypersensitivity to aripiprazole or other quinolinones; suicidal ideation or history; unstable thyroid function; clinically significant abnormal laboratory findings; or previous participation in aripiprazole trials. Also excluded were women who were pregnant or nursing or of childbearing potential and not using adequate contraception. **Pretreatment:** **Total sample size:** 487 were randomized **Other:**
Interventions	**Intervention Characteristics** Intervention 1 ● *Number of participants allocated*: 118 ● *Dose*: Aripiprazole 2 mg/day ● *Length of treatment*: 10 weeks ● *Other*: Intervention 1 ● *Number of participants allocated*: 122 ● *Dose*: Aripiprazole 5 mg/day ● *Length of treatment*: 10 weeks

	● *Other*: Intervention 1 ● *Number of participants allocated*: 126 ● *Dose*: Aripiprazole 10 mg/day ● *Length of treatment*: 10 weeks ● *Other*: Intervention 2 ● *Number of participants allocated*: 122 ● *Dose*: Aripiprazole 5 mg/day ● *Length of treatment*: 10 weeks ● *Other*: Intervention 3 ● *Number of participants allocated*: 126 ● *Dose*: Aripiprazole 10 mg/day ● *Length of treatment*: 10 weeks ● *Other*: Control ● *Number of participants allocated*: 121 ● *Dose*: ● *Length of treatment*: 10 weeks ● *Other*:
Outcomes	*Serious adverse events* ● **Outcome type**: DichotomousOutcome *Mortality* ● **Outcome type**: DichotomousOutcome *BPSD* ● **Outcome type**: ContinuousOutcome *Agitation* ● **Outcome type**: ContinuousOutcome *Cognition* ● **Outcome type**: ContinuousOutcome *Activity of Daily Living (ADL)* ● **Outcome type**: ContinuousOutcome *Quality of life* ● **Outcome type**: ContinuousOutcome

	BPSD_dikotom ● **Outcome type**: DichotomousOutcome
Identification	**Sponsorship source:** Bristol-Myers Squibb Company and Otsuka Pharmaceutical Development & Commercialization (Princeton, NJ) provided funding for this support. **Country:** USA, Australia, Canada, South Africa, and Argentina. **Setting:** Multicenter, institutionalized patients (nursing homes or residential assisted-living facilities) **Comments:** **Authors name:** Jacobo E. Mintzer **Institution:** Medical University of South Carolina/Alzheimer's Research & Clinical Programs **Email:** mintzerj@musc.edu **Address:** Medical University of South Carolina/Alzheimer's Research & Clinical Programs, 5900 Core Rd., Suite 203, N. Charleston, SC 29406-6076 **Start date:** **End date:** **Other:**
Notes	*NKA Demens 2023* on 26/04/2024 21:36 **Select** P: personer med demens og psykotiske symptomerI: aripiprazol (3 forskellige doser)C: placebo *Anja Ussing* on 07/05/2024 19:14 **Select** inkluderet i NKR fra 2018

Risk of bias table

Bias	Authors' judgement	Support for judgement
Selective outcome reporting	High risk	Judgement Comment: Outcome was measured with several scales and presented for each drug groupseparately. Subanalyses of individual NPI items. No correction for multipletesting. % any adverse event per group missing. No study protocol available.
Blinding of participants and personnel	Unclear risk	Judgement Comment: No information
Allocation concealment	Unclear risk	Judgement Comment: No information
Incomplete outcome data	High risk	Judgement Comment: Drop-out was very high (42%). Modified ITT with exclusion of patients whodid not take at least one dose of study medication, and did not have at leastone postbaseline evaluation within 7 days after the last medication was taken.Handling of missing data with LOCF
Sequence Generation	Unclear risk	Judgement Comment: No information

Other sources of bias	High risk	Judgement Comment: Concomitant use of antipsychotics, mood stabilizers or sedatives (except trazodone [25–50 mg], zolpidem tartrate [2.5–5.0 mg] and temazepam [7.5–15.0mg]) was prohibited during the study treatment period and the seven days prior to randomization.
Blinding of outcome assessors	Unclear risk	Judgement Comment: No information

NCT00287742 2006

Methods	**Study design:** **Study grouping:** **Other:**
Participants	**Baseline Characteristics** Intervention 1 ● *Age in years, mean (SD)*: ● *Females (%)*: ● *Numbers (%) with BPSD*: ● *Alzheimer´s disease, number (%)*: ● *Vascular demnetia, number (%)*: ● *Levy Body dementia, number (%)*: ● *Frontotemporal dementia, number (%)*: ● *Nursing home recidents, number (%)*: ● *Inpatients, number (%)*: ● *Living in their own homes, number (%)*: Control ● *Age in years, mean (SD)*: ● *Females (%)*: ● *Numbers (%) with BPSD*: ● *Alzheimer´s disease, number (%)*: ● *Vascular demnetia, number (%)*: ● *Levy Body dementia, number (%)*: ● *Frontotemporal dementia, number (%)*: ● *Nursing home recidents, number (%)*: ● *Inpatients, number (%)*: ● *Living in their own homes, number (%)*: Overall ● *Age in years, mean (SD)*: ● *Females (%)*: ● *Numbers (%) with BPSD*: ● *Alzheimer´s disease, number (%)*: ● *Vascular demnetia, number (%)*:

	● *Levy Body dementia, number (%)*: ● *Frontotemporal dementia, number (%)*: ● *Nursing home recidents, number (%)*: ● *Inpatients, number (%)*: ● *Living in their own homes, number (%)*: **Included criteria:** **Excluded criteria:** **Pretreatment:** **Total sample size:** **Other:**
Interventions	**Intervention Characteristics** Intervention 1 ● *Number of participants allocated*: ● *Dose*: ● *Length of treatment*: ● *Other*: Control ● *Number of participants allocated*: ● *Dose*: ● *Length of treatment*: ● *Other*:
Outcomes	
Identification	**Sponsorship source:** **Country:** **Setting:** **Comments:** **Authors name:** **Institution:** **Email:** **Address:** **Start date:** **End date:** **Other:**
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Selective outcome reporting	High risk	Judgement Comment: Only BEHAVE-AD Psychotic Symptom Cluster Score reported. Results for ADLand MMSE not reported. Early terminated trial. No full article.
Blinding of participants and personnel	Unclear risk	Judgement Comment: "Double-blind" trial, but unclear who was blinded.
Allocation concealment	Unclear risk	Judgement Comment: No information provided
Incomplete outcome data	High risk	Judgement Comment: Dropout was 7 of 33 (21%) in total and differed for 18% between groups. Outcomes were provided for all participants at endpoin
Sequence Generation	Unclear risk	Judgement Comment: No information provided
Other sources of bias	High risk	Judgement Comment: Single-blind (with placebo) run-in of 1 week
Blinding of outcome assessors	Unclear risk	Judgement Comment: "Double-blind" trial, but unclear who was blinded.

Paleacu 2008

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group **Other:**
Participants	**Baseline Characteristics** Intervention 1 ● *Age in years, mean (SD)*: ● *Females (%)*: ● *Numbers (%) with BPSD*: 20 (100) ● *Alzheimer´s disease, number (%)*: 20 (100) ● *Vascular demnetia, number (%)*: ● *Levy Body dementia, number (%)*: ● *Frontotemporal dementia, number (%)*: ● *Nursing home recidents, number (%)*: ● *Inpatients, number (%)*: ● *Living in their own homes, number (%)*: Control ● *Age in years, mean (SD)*: ● *Females (%)*: ● *Numbers (%) with BPSD*: 20 (100) ● *Alzheimer´s disease, number (%)*: 20 (100) ● *Vascular demnetia, number (%)*: ● *Levy Body dementia, number (%)*:

	● *Frontotemporal dementia, number (%)*: ● *Nursing home recidents, number (%)*: ● *Inpatients, number (%)*: ● *Living in their own homes, number (%)*: Overall ● *Age in years, mean (SD)*: 82.2 (6.4) ● *Females (%)*: 26 (65) ● *Numbers (%) with BPSD*: 40 (100) ● *Alzheimer´s disease, number (%)*: 40 (100) ● *Vascular demnetia, number (%)*: ● *Levy Body dementia, number (%)*: ● *Frontotemporal dementia, number (%)*: ● *Nursing home recidents, number (%)*: ● *Inpatients, number (%)*: ● *Living in their own homes, number (%)*: **Included criteria:** Inclusion criteria were: age >50 years, dementia of the Alzheimer's type diagnosed according to DSM-IV criteria, Mini-Mental State Examination (MMSE) score <24 and a score >6 on any of the Neuropsychological Inventory (NPI) items. **Excluded criteria:** The exclusion criteria were: other types of dementia (e.g. vascular, frontotemporal lobe dementia), concomitant malignant disease, active ischemic heart disease or chronic heart failure, women of childbearing potential and alcohol or drug abuse. **Pretreatment:** **Total sample size:** 40 were randomized **Other:**
Interventions	**Intervention Characteristics** Intervention 1 ● *Number of participants allocated*: 20 ● *Dose*: Quetiapine 150-300 mg/day ● *Length of treatment*: 6 weeks ● *Other*: Control ● *Number of participants allocated*: 20 ● *Dose*: ● *Length of treatment*: 6 weeks ● *Other*:
Outcomes	*Serious adverse events* ● **Outcome type**: DichotomousOutcome ● **Data value**: Endpoint *Mortality* ● **Outcome type**: DichotomousOutcome

	● **Data value**: Endpoint *BPSD* ● **Outcome type**: ContinuousOutcome ● **Data value**: Endpoint *Agitation* ● **Outcome type**: ContinuousOutcome ● **Data value**: Endpoint *Cognition* ● **Outcome type**: ContinuousOutcome ● **Data value**: Endpoint *Activity of Daily Living (ADL)* ● **Outcome type**: ContinuousOutcome ● **Data value**: Endpoint *Quality of life* ● **Outcome type**: ContinuousOutcome ● **Data value**: Endpoint *BPSD_dikotom* ● **Outcome type**: DichotomousOutcome ● **Data value**: Endpoint
Identification	**Sponsorship source:** This study was supported by a grant from AstraZeneca. **Country:** Israel **Setting:** **Comments:** **Authors name:** D Paleacu **Institution:** Neurology Service and Memory Clinic, Abarbanel Mental Health Center, Bat-Yam, Israel, Affiliated with the Sackler School of Medicine, Tel Aviv University, Israel **Email:** paleacu@post.tau.ac.il **Address:** Neurological Service and Memory Clinic, Abarbanel Mental Health Center, 15 Keren Kayemet, 59110 Bat Yam, Israel. **Start date:** **End date:** **Other:**
Notes	*NKA Demens 2023* on 06/05/2024 17:30 **Select** P: personer med demens og BPSDI: quetiapinC: placebo

Risk of bias table

Bias	Authors' judgement	Support for judgement
Selective outcome reporting	Unclear risk	Judgement Comment: No detailed data for NPI total baseline to endpoint. For CGI-C no comparisondata with placebo. The study report fails to include results for a key outcome(NPI total) that would be expected to have been reported for in the usual way(baseline to endpoint). No study protocol available.
Blinding of participants and personnel	Unclear risk	Judgement Comment: No information
Allocation concealment	Unclear risk	Judgement Comment: No information
Incomplete outcome data	Unclear risk	Judgement Comment: Overall drop-out was 15%. Missing outcome data balanced in numbers acrossintervention groups, with similar reasons for missing data across groups. Buthigh discontinuation rate with a very small sample with a high rate of imputeddata. Results included patients that dropped-out (ITT analysis), with LOCF formissing data.
Sequence Generation	Unclear risk	Judgement Comment: No information
Other sources of bias	High risk	Judgement Comment: For those patients who received other antipsychotics before the trial a washout period of 2 weeks was mandatory.
Blinding of outcome assessors	Unclear risk	Judgement Comment: No information

RIS-INT-83 2003

Methods	**Study design:** **Study grouping:** **Other:**
Participants	**Baseline Characteristics** Intervention 1 ● *Age in years, mean (SD)*: ● *Females (%)*: ● *Numbers (%) with BPSD*: ● *Alzheimer´s disease, number (%)*: ● *Vascular demnetia, number (%)*: ● *Levy Body dementia, number (%)*: ● *Frontotemporal dementia, number (%)*: ● *Nursing home recidents, number (%)*: ● *Inpatients, number (%)*: ● *Living in their own homes, number (%)*: Control ● *Age in years, mean (SD)*: ● *Females (%)*: ● *Numbers (%) with BPSD*:

	● *Alzheimer´s disease, number (%)*: ● *Vascular demnetia, number (%)*: ● *Levy Body dementia, number (%)*: ● *Frontotemporal dementia, number (%)*: ● *Nursing home recidents, number (%)*: ● *Inpatients, number (%)*: ● *Living in their own homes, number (%)*: Overall ● *Age in years, mean (SD)*: ● *Females (%)*: ● *Numbers (%) with BPSD*: ● *Alzheimer´s disease, number (%)*: ● *Vascular demnetia, number (%)*: ● *Levy Body dementia, number (%)*: ● *Frontotemporal dementia, number (%)*: ● *Nursing home recidents, number (%)*: ● *Inpatients, number (%)*: ● *Living in their own homes, number (%)*: **Included criteria:** **Excluded criteria:** **Pretreatment:** **Total sample size:** **Other:**
Interventions	**Intervention Characteristics** Intervention 1 ● *Number of participants allocated*: ● *Dose*: ● *Length of treatment*: ● *Other*: Control ● *Number of participants allocated*: ● *Dose*: ● *Length of treatment*: ● *Other*:
Outcomes	

Identification	**Sponsorship source:** **Country:** **Setting:** **Comments:** **Authors name:** **Institution:** **Email:** **Address:** **Start date:** **End date:** **Other:**
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Selective outcome reporting	Low risk	All outcomes seem to be reported.
Blinding of participants and personnel	Unclear risk	Judgement Comment: It is stated that the study is a double-blind study, however, it is not known who the blinded parties are. It is assumed that the patients and the clinicians were blinded, but it is not known.
Allocation concealment	Unclear risk	Judgement Comment: There is no information regarding the allocation concealment.
Incomplete outcome data	High risk	Judgement Comment: 408 subjects were planned to be analyzed, however, only 18 subjects were included in the efficacy and safety analyses. This is due to the study being terminated early. There is not provided any reasons behind the early termination of the study.
Sequence Generation	Unclear risk	Judgement Comment: There is no information regarding the allocation sequence.
Other sources of bias	High risk	Judgement Comment: All eligible subjects first participated in a single-blind, placebo-controlled runin phase of 7 day
Blinding of outcome assessors	Unclear risk	Judgement Comment: It is stated that the study is a double-blind study, however, it is not known who the blinded parties are. It is now known whether the outcome assessors were blinded. No information

Schneider 2006

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group **Other:**
Participants	**Baseline Characteristics** Intervention 1 ● *Age in years, mean (SD)*: 78.8 (7.3) ● *Females (%)*: 55 (55)

- *Numbers (%) with BPSD*: 100 (100)
- *Alzheimer´s disease, number (%)*: 100 (100)
- *Vascular demnetia, number (%)*:
- *Levy Body dementia, number (%)*:
- *Frontotemporal dementia, number (%)*:
- *Nursing home recidents, number (%)*:
- *Inpatients, number (%)*:
- *Living in their own homes, number (%)*: 77 (77)

Intervention 1
- *Age in years, mean (SD)*:
- *Females (%)*:
- *Numbers (%) with BPSD*:
- *Alzheimer´s disease, number (%)*:
- *Vascular demnetia, number (%)*:
- *Levy Body dementia, number (%)*:
- *Frontotemporal dementia, number (%)*:
- *Nursing home recidents, number (%)*:
- *Inpatients, number (%)*:
- *Living in their own homes, number (%)*:

Intervention 1
- *Age in years, mean (SD)*:
- *Females (%)*:
- *Numbers (%) with BPSD*:
- *Alzheimer´s disease, number (%)*:
- *Vascular demnetia, number (%)*:
- *Levy Body dementia, number (%)*:
- *Frontotemporal dementia, number (%)*:
- *Nursing home recidents, number (%)*:
- *Inpatients, number (%)*:
- *Living in their own homes, number (%)*:

Intervention 2
- *Age in years, mean (SD)*: 77.3 (8.7)
- *Females (%)*: 50 (53)
- *Numbers (%) with BPSD*: 94 (100)
- *Alzheimer´s disease, number (%)*: 94 (100)
- *Vascular demnetia, number (%)*:
- *Levy Body dementia, number (%)*:
- *Frontotemporal dementia, number (%)*:
- *Nursing home recidents, number (%)*:
- *Inpatients, number (%)*:

- *Living in their own homes, number (%)*: 69 (73)

Intervention 3
- *Age in years, mean (SD)*: 78.4 (7.1)
- *Females (%)*: 49 (58)
- *Numbers (%) with BPSD*: 85 (100)
- *Alzheimer´s disease, number (%)*: 85 (100)
- *Vascular demnetia, number (%)*:
- *Levy Body dementia, number (%)*:
- *Frontotemporal dementia, number (%)*:
- *Nursing home recidents, number (%)*:
- *Inpatients, number (%)*:
- *Living in their own homes, number (%)*: 61 (72)

Control
- *Age in years, mean (SD)*: 77.3 (7.1)
- *Females (%)*: 81 (57)
- *Numbers (%) with BPSD*: 142 (100)
- *Alzheimer´s disease, number (%)*: 142 (100)
- *Vascular demnetia, number (%)*:
- *Levy Body dementia, number (%)*:
- *Frontotemporal dementia, number (%)*:
- *Nursing home recidents, number (%)*:
- *Inpatients, number (%)*:
- *Living in their own homes, number (%)*: 100 (70)

Overall
- *Age in years, mean (SD)*: 77.9 (7.5)
- *Females (%)*: 235 (56)
- *Numbers (%) with BPSD*: 421 (100)
- *Alzheimer´s disease, number (%)*: 421 (100)
- *Vascular demnetia, number (%)*:
- *Levy Body dementia, number (%)*:
- *Frontotemporal dementia, number (%)*:
- *Nursing home recidents, number (%)*:
- *Inpatients, number (%)*:
- *Living in their own homes, number (%)*: 307 (73)

Included criteria: Eligible participants fulfilled criteria for dementia of the Alzheimer's type (according to the Diagnostic and Statistical Manual of Mental Disorders, fourth edition) or probable Alzheimer's disease on the basis of the history, physical examination, results of structural brain imaging, and the score on the Mini–Mental State Examination (MMSE); the MMSE score had to be between 5 and 26 (on a scale from 0 to 30, with lower scores indicating poorer performance). To be eligible, patients had to be ambulatory and living at home or in an assisted-living facility. Eligible patients had delusions, hallucinations, aggression, or agitation that developed after the onset of dementia and was severe enough to disrupt their functioning and, in the opinion of the study physicians, to justify treatment with antipsychotic drugs. Signs and symptoms of psychosis, aggression, or agitation had to

	have occurred nearly daily during the previous week or at least intermittently for 4 weeks. During the week before they were randomly assigned to treatment, eligible patients also had a severity rating of at least “moderate” for conceptual disorganization, suspiciousness, or hallucinatory behavior on the Brief Psychiatric Rating Scale (BPRS). Alternatively, a frequency rating of “often” or “more frequently” and a severity rating of at least “moderate” were required for delusions, hallucinations, agitation, or “aberrant motor behavior” in the Neuropsychiatric Inventory. A study partner or caregiver who had regular contact with the patient was required to participate in the assessments. **Excluded criteria:** Patients were excluded if they had received a diagnosis of a primary psychotic disorder (e.g., schizophrenia), delirium, other dementia such as vascular dementia or Lewy-body dementia, or psychosis, agitation, or aggression that could be better accounted for by another medical condition, medication, or substance abuse. Patients were also excluded if they required psychiatric admission, were suicidal, were going to receive treatment with a cholinesterase inhibitor or antidepressant medication, had previously been treated with two of the three atypical antipsychotic drugs under study, or had contraindications to any of the study drugs. **Pretreatment:** **Total sample size:** 421 were randomized **Other:**
Interventions	**Intervention Characteristics** Intervention 1 ● *Number of participants allocated*: 100 ● *Dose*: Olanzapine 2.5 or 5 mg/day ● *Length of treatment*: 12 weeks ● *Other*: Intervention 1 ● *Number of participants allocated*: 94 ● *Dose*: Quetiapine 25 or 50 mg/day ● *Length of treatment*: 12 weeks ● *Other*: Intervention 1 ● *Number of participants allocated*: 85 ● *Dose*: Risperidone 0.5 or 1 mg/day ● *Length of treatment*: 12 weeks ● *Other*: Intervention 2 ● *Number of participants allocated*: 94 ● *Dose*: Quetiapine 25 or 50 mg/day ● *Length of treatment*: 12 weeks ● *Other*: Intervention 3 ● *Number of participants allocated*: 85 ● *Dose*: Risperidone 0.5 or 1 mg/day ● *Length of treatment*: 12 weeks ● *Other*:

	Control ● *Number of participants allocated*: 142 ● *Dose*: ● *Length of treatment*: 12 weeks ● *Other*:
Outcomes	*Serious adverse events* ● **Outcome type**: DichotomousOutcome ● **Data value**: Endpoint *Mortality* ● **Outcome type**: DichotomousOutcome ● **Data value**: Endpoint *BPSD* ● **Outcome type**: ContinuousOutcome ● **Data value**: Endpoint *Agitation* ● **Outcome type**: ContinuousOutcome ● **Data value**: Endpoint *Cognition* ● **Outcome type**: ContinuousOutcome ● **Data value**: Endpoint *Activity of Daily Living (ADL)* ● **Outcome type**: ContinuousOutcome ● **Data value**: Endpoint *Quality of life* ● **Outcome type**: ContinuousOutcome ● **Data value**: Endpoint *BPSD_dikotom* ● **Outcome type**: DichotomousOutcome ● **Data value**: Endpoint
Identification	**Sponsorship source:** Supported by a research contract from the National Institute of Mental Health (N01 MH9001) and supported in part by the Department of Veterans Affairs. Astra-Zeneca Pharmaceuticals, Forest Pharmaceuticals, Janssen Pharmaceutica, and Eli Lilly provided medications for the study.Dr. Sultzer has received research funding from Forest Research Institute and Pfizer; lecture honorarium from Forest Laboratories; and has consulted to Eli Lilly and AstraZeneca. **Country:** USA **Setting:** Multicenter, outpatients living at home or in an assisted-living facility in the USA **Comments:**

	Authors name: David L. Sultzer **Institution:** VA Greater Los Angeles Healthcare System/University of California, Los Angeles, CA **Email:** lschneid@usc.edu **Address:** Keck School of Medicine, University of Southern California, 1510 San Pablo St., HCC 600, Los Angeles, CA 90033 **Start date:** April 2001 **End date:** November 2004 **Other:**
Notes	*Anett Borg Kristensen* on 06/05/2024 04:54 **Select** varighed *NKA Demens 2023* on 06/05/2024 18:54 **Select** P: personer med alzheimersI: olanzapin, quetiapin, risperidonC: placebo *NKA Demens 2023* on 23/05/2024 18:51 **Screen** Wrong study design

Risk of bias table

Bias	Authors' judgement	Support for judgement
Selective outcome reporting	Unclear risk	Judgement Comment: Study protocol available but no outcomes prespecified.
Blinding of participants and personnel	Unclear risk	Judgement Comment: The trials was "double-blind" and "Medications were dispensed at each visit inthe form of identically appearing small and large capsules [...]". Persons blinded has not been specified.
Allocation concealment	Low risk	Judgement Comment: "Randomization was performed with the use of permuted blocks of nine persite without stratification and was implemented with the use of an interactivevoice-response telephone system."The use of blocks diminishes concealment,but the blocks are large and an interactive voice-response telephone system isused.
Incomplete outcome data	High risk	Judgement Comment: The overall rate of discontinuation of treatment at 12 weeks was 63% (primaryoutcome).Other outcomes are analysed with modified ITT (patients without anassessment after baseline are excluded).
Sequence Generation	Unclear risk	Judgement Comment: No information provided.
Other sources of bias	Low risk	Judgement Comment: Washout from previous treatment and run-in periods were not used becauseof the patients' acute clinical symptoms; instead, the study design allowedfor rapid assignment and initiation of treatment to be consistent with clinicalpractice.
Blinding of outcome assessors	Unclear risk	Judgement Comment: The trial was "double-blind" and "Medications were dispensed at each visit inthe form of identically appearing small and large capsules [...]". Persons blinded has not been specified.

Street 2000

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group **Other:**
Participants	**Baseline Characteristics** Intervention 1 ● *Age in years, mean (SD)*: 82.9 (6.5) ● *Females (%)*: 33 (58.9) ● *Numbers (%) with BPSD*: 56 (100) ● *Alzheimer´s disease, number (%)*: 56 (100) ● *Vascular demnetia, number (%)*: ● *Levy Body dementia, number (%)*: ● *Frontotemporal dementia, number (%)*: ● *Nursing home recidents, number (%)*: 56 (100) ● *Inpatients, number (%)*: ● *Living in their own homes, number (%)*: Intervention 1 ● *Age in years, mean (SD)*: ● *Females (%)*: ● *Numbers (%) with BPSD*: ● *Alzheimer´s disease, number (%)*: ● *Vascular demnetia, number (%)*: ● *Levy Body dementia, number (%)*: ● *Frontotemporal dementia, number (%)*: ● *Nursing home recidents, number (%)*: ● *Inpatients, number (%)*: ● *Living in their own homes, number (%)*: Intervention 1 ● *Age in years, mean (SD)*: ● *Females (%)*: ● *Numbers (%) with BPSD*: ● *Alzheimer´s disease, number (%)*: ● *Vascular demnetia, number (%)*: ● *Levy Body dementia, number (%)*: ● *Frontotemporal dementia, number (%)*: ● *Nursing home recidents, number (%)*: ● *Inpatients, number (%)*: ● *Living in their own homes, number (%)*:

Intervention 2
- *Age in years, mean (SD)*: 83.6 (6.5)
- *Females (%)*: 33 (66.0)
- *Numbers (%) with BPSD*: 50 (100)
- *Alzheimer´s disease, number (%)*: 50 (100)
- *Vascular demnetia, number (%)*:
- *Levy Body dementia, number (%)*:
- *Frontotemporal dementia, number (%)*:
- *Nursing home recidents, number (%)*: 50 (100)
- *Inpatients, number (%)*:
- *Living in their own homes, number (%)*:

Intervention 3
- *Age in years, mean (SD)*: 83.0 (6.7)
- *Females (%)*: 31 (58.5)
- *Numbers (%) with BPSD*: 53 (100)
- *Alzheimer´s disease, number (%)*: 53 (100)
- *Vascular demnetia, number (%)*:
- *Levy Body dementia, number (%)*:
- *Frontotemporal dementia, number (%)*:
- *Nursing home recidents, number (%)*: 53 (100)
- *Inpatients, number (%)*:
- *Living in their own homes, number (%)*:

Control
- *Age in years, mean (SD)*: 81.4 (6.7)
- *Females (%)*: 29 (61.7)
- *Numbers (%) with BPSD*: 47 (100)
- *Alzheimer´s disease, number (%)*: 47 (100)
- *Vascular demnetia, number (%)*:
- *Levy Body dementia, number (%)*:
- *Frontotemporal dementia, number (%)*:
- *Nursing home recidents, number (%)*: 47 (100)
- *Inpatients, number (%)*:
- *Living in their own homes, number (%)*:

Overall
- *Age in years, mean (SD)*: 82.8
- *Females (%)*: 126 (61.2)
- *Numbers (%) with BPSD*: 206 (100)
- *Alzheimer´s disease, number (%)*: 206 (100)
- *Vascular demnetia, number (%)*:
- *Levy Body dementia, number (%)*:

	● *Frontotemporal dementia, number (%)*: ● *Nursing home recidents, number (%)*: 206 (100) ● *Inpatients, number (%)*: ● *Living in their own homes, number (%)*: **Included criteria:** Patients met the National Institute of Neurological and Communicative Disorders and Stroke-Alzheimer's Disease and Related Disorders Association criteria for possible or probable AD. For study inclusion, patients must have scored 3 or higher on any of the Agitation/Aggression, Hallucinations, or Delusions items of the Neuropsychiatric Inventory-Nursing Home version (NPI/NH) at screening and following a single blind, placebo lead-in. A score of 3 or higher correlates with a clincially significant level of psychotic or behavioral symptoms, corresponding with moderate severity or frequency. **Excluded criteria:** Exclusion criteria included a history of a DSM-IV Axis I disorder (schizophrenia, bipolar disorder, severe or recurrent depression), any neurological condition other than AD that could contribute to psychosis or dementia, a Mini-Mental State Examination (MMSE) of greater than 24, and bedridden status. **Pretreatment:** **Total sample size:** 206 were randomized **Other:**
Interventions	**Intervention Characteristics** Intervention 1 ● *Number of participants allocated*: 56 ● *Dose*: Olanzapine 5 mg/day ● *Length of treatment*: 6 weeks ● *Other*: Intervention 1 ● *Number of participants allocated*: 50 ● *Dose*: Olanzapine 10 mg/day ● *Length of treatment*: 6 weeks ● *Other*: Intervention 1 ● *Number of participants allocated*: 53 ● *Dose*: Olanzapine 15 mg/day ● *Length of treatment*: 6 weeks ● *Other*: Intervention 2 ● *Number of participants allocated*: 50 ● *Dose*: Olanzapine 10 mg/day ● *Length of treatment*: 6 weeks ● *Other*: Intervention 3 ● *Number of participants allocated*: 53

	● *Dose*: Olanzapine 15 mg/day ● *Length of treatment*: 6 weeks ● *Other*: Control ● *Number of participants allocated*: 47 ● *Dose*: ● *Length of treatment*: 6 weeks ● *Other*:
Outcomes	*Serious adverse events* ● **Outcome type**: DichotomousOutcome ● **Data value**: Endpoint *Mortality* ● **Outcome type**: DichotomousOutcome ● **Data value**: Endpoint *BPSD* ● **Outcome type**: ContinuousOutcome ● **Data value**: Endpoint *Agitation* ● **Outcome type**: ContinuousOutcome ● **Data value**: Endpoint *Cognition* ● **Outcome type**: ContinuousOutcome ● **Data value**: Endpoint *Activity of Daily Living (ADL)* ● **Outcome type**: ContinuousOutcome ● **Data value**: Endpoint *Quality of life* ● **Outcome type**: ContinuousOutcome ● **Data value**: Endpoint *BPSD_dikotom* ● **Outcome type**: DichotomousOutcome ● **Data value**: Endpoint
Identification	**Sponsorship source:** This work was sponsored by Elli Lilly and Company, Indianapolis, Ind. Dr. Cummings is supported by a National Institute on Aging Alzheimer's Disease Center grant, Bethesda, Md; Alzheimer's Disease Research Center of California grant, Los Angeles, Calif; and the Sidell-Kagan Foundation, Los Angeles.

	Country: USA **Setting:** Multicenter, nursing home residents in the USA **Comments:** **Authors name:** Jamie S. Street **Institution:** Lilly Research Laboratories, Eli Lilly and Company, Indianapolis, Ind **Email:** **Address:** Lilly Research Laboratories, Eli Lilly and Company, Lilly Corporate Center, Drop Code 1758, Indianapolis, IN 46285 **Start date:** **End date:** **Other:**
Notes	*NKA Demens 2023* on 06/05/2024 19:02 **Select** P: personer med demens og agitationI: olanzapin (3 forskellige doser)C: placebo *Anja Ussing* on 07/05/2024 19:12 **Included** er inkluderet i oprindelig NKR

Risk of bias table

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

Streim 2008

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group **Other:**
Participants	**Baseline Characteristics** Intervention 1 ● *Age in years, mean (SD)*: 83.0 (range 61.0-96.0) ● *Females (%)*: 97 (74) ● *Numbers (%) with BPSD*: 131 (100) ● *Alzheimer´s disease, number (%)*: 131 (100) ● *Vascular demnetia, number (%)*: ● *Levy Body dementia, number (%)*: ● *Frontotemporal dementia, number (%)*: ● *Nursing home recidents, number (%)*: 131 (100) ● *Inpatients, number (%)*: ● *Living in their own homes, number (%)*: Control ● *Age in years, mean (SD)*: 83.0 (59.0-96.0) ● *Females (%)*: 98 (78) ● *Numbers (%) with BPSD*: 125 (100) ● *Alzheimer´s disease, number (%)*: 125 (100) ● *Vascular demnetia, number (%)*: ● *Levy Body dementia, number (%)*: ● *Frontotemporal dementia, number (%)*: ● *Nursing home recidents, number (%)*: 125 (100) ● *Inpatients, number (%)*: ● *Living in their own homes, number (%)*: Overall ● *Age in years, mean (SD)*: 83.0 (range 59.0-96.0) ● *Females (%)*: 195 (76) ● *Numbers (%) with BPSD*: 256 (100) ● *Alzheimer´s disease, number (%)*: 256 (100) ● *Vascular demnetia, number (%)*: ● *Levy Body dementia, number (%)*: ● *Frontotemporal dementia, number (%)*: ● *Nursing home recidents, number (%)*: 256 (100) ● *Inpatients, number (%)*: ● *Living in their own homes, number (%)*: **Included criteria:** Subjects eligible for enrollment were men and women aged 55-95 years (inclusive), diagnosed with AD (DSM-IV criteria), and who had psychotic symptoms of delusions or hallucinations (at least intermittently) for ≥1 month. Subjects had to be institutionalized (i.e., residing in a

	nursing home or residential assisted-living facility) for ≥4 weeks before study entry; capable of self-locomotion or locomotion with the aid of an assistive device; and have a caregiver or family member who could serve as a collateral informant for study assessments and, if necessary, provide proxy consent to participate. Subjects were required to have a Mini-Mental State Examination (MMSE) score between 6 and 22 at screening, and a score of ≥6 on either the delusions or hallucinations items of the Neuropsychiatric Inventory-Nursing Home Version (NPI-NH) at baseline (at the time of randomization). **Excluded criteria:** Subjects were excluded if they had an Axis I diagnosis of delirium or schizophrenia; a schizoaffective, mood, bipolar, or amnestic disorder; any reversible cause of dementia; continuous symptoms of psychosis (delusions/hallucination) before the onset of dementia; psychotic symptoms better accounted for by another medical condition or directs effects of a substance; a current episode og major depression with symptoms of psychosis; dementia resulting from vascular causes; any 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. Subjects were also excluded if they had previously been refractory to antipsychotic drug treatment for psychosis; had been randomized in an aripiprazole clinical study; 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-IV criteria for any significant substance use disorder (≤6 months before screening); were were deemed to be at significant risk of suicide; were likely to require prohibited concomitant therapy; were known to be allergic or hypersensitive to aripiprazole or quinolinones; had any laboratory test, vital sign, og ECG abnormalities that could indicate an elevated risk for significant adverse events, or any medical condtion that would make study participation unsafe. **Pretreatment:** **Total sample size:** 256 were randomized **Other:**
Interventions	**Intervention Characteristics** Intervention 1 ● *Number of participants allocated*: 131 ● *Dose*: Aripiprazole 2-15 mg/day ● *Length of treatment*: 10 weeks ● *Other*: Control ● *Number of participants allocated*: 125 ● *Dose*: ● *Length of treatment*: 10 weeks ● *Other*:
Outcomes	*Serious adverse events* ● **Outcome type**: DichotomousOutcome ● **Data value**: Endpoint *Mortality* ● **Outcome type**: DichotomousOutcome ● **Data value**: Endpoint *BPSD* ● **Outcome type**: ContinuousOutcome

	● **Data value**: Endpoint *Agitation* ● **Outcome type**: ContinuousOutcome ● **Data value**: Endpoint *Cognition* ● **Outcome type**: ContinuousOutcome ● **Data value**: Endpoint *Activity of Daily Living (ADL)* ● **Outcome type**: ContinuousOutcome ● **Data value**: Endpoint *Quality of life* ● **Outcome type**: ContinuousOutcome ● **Data value**: Endpoint *BPSD_dikotom* ● **Outcome type**: DichotomousOutcome ● **Data value**: Endpoint
Identification	**Sponsorship source:** This study was supported by Bristol-Myers Squibb Company and Otsuka Pharmaceutical Company, Ltd. **Country:** USA **Setting:** Multicenter, insitutionalízed (residing in a nursing home or assisted-living facility) men and women in the USA **Comments:** **Authors name:** Joel E Streim **Institution:** Section on Geriatric Psychiatry, University of Pennsylvania, Philadelphia, PA, USA **Email:** jstreim@mail.med.upenn.edu **Address:** Section on Geriatric Psychiatry, University of Pennsylvania, 3535 Market Street, Room 3053, Philadelphia, PA 19104-3309. **Start date:** **End date:** **Other:**
Notes	*Anett Borg Kristensen* on 06/05/2024 05:04 **Select** Varighed af intervention 10 uger *NKA Demens 2023* on 06/05/2024 18:58 **Select** P: personer med demensI: aripiprazolC: placebo *Anja Ussing* on 07/05/2024 19:20 **Select**

	er inkluderet i NKR fra 2018, lad os tage med her også

Risk of bias table

Bias	Authors' judgement	Support for judgement
Selective outcome reporting	Unclear risk	Judgement Comment: Insufficient information. Study protocol is available but no outcomes prespecified. Two coprimary outcomes. Multiple scales for NPS. Many additional analyses including OC comparisons. Unusual cut-oNs f.i. only weight increase of 7%or more included. Correction for multiple testing
Blinding of participants and personnel	Unclear risk	Judgement Comment: No information
Allocation concealment	Unclear risk	Judgement Comment: No information
Incomplete outcome data	High risk	Judgement Comment: Drop-out was high (41%). Modified ITT was used excluding patients that didnot receive one dose of study medication or an assessment after baseline(within 7 days after taking medication). Missing data was imputed with LOCF.
Sequence Generation	Unclear risk	Judgement Comment: No information
Other sources of bias	High risk	Judgement Comment: Following screening and a minimum 7-day psychotropic medication washoutperiod (...)
Blinding of outcome assessors	Unclear risk	Judgement Comment: No information

Tariot 2006

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group **Other:**
Participants	**Baseline Characteristics** Intervention 1 ● *Age in years, mean (SD)*: 81.92 (6.85) ● *Females (%)*: 66 (72.5) ● *Numbers (%) with BPSD*: 91 (100) ● *Alzheimer´s disease, number (%)*: 91 (100) ● *Vascular demnetia, number (%)*: ● *Levy Body dementia, number (%)*: ● *Frontotemporal dementia, number (%)*: ● *Nursing home recidents, number (%)*: 91 (100) ● *Inpatients, number (%)*: ● *Living in their own homes, number (%)*: Intervention 1 ● *Age in years, mean (SD)*:

- *Females (%)*:
- *Numbers (%) with BPSD*:
- *Alzheimer´s disease, number (%)*:
- *Vascular demnetia, number (%)*:
- *Levy Body dementia, number (%)*:
- *Frontotemporal dementia, number (%)*:
- *Nursing home recidents, number (%)*:
- *Inpatients, number (%)*:
- *Living in their own homes, number (%)*:

Intervention 2

- *Age in years, mean (SD)*: 83.55 (6.05)
- *Females (%)*: 63 (67.0)
- *Numbers (%) with BPSD*: 94 (100)
- *Alzheimer´s disease, number (%)*: 94 (100)
- *Vascular demnetia, number (%)*:
- *Levy Body dementia, number (%)*:
- *Frontotemporal dementia, number (%)*:
- *Nursing home recidents, number (%)*: 94 (100)
- *Inpatients, number (%)*:
- *Living in their own homes, number (%)*:

Control

- *Age in years, mean (SD)*: 83.93 (6.66)
- *Females (%)*: 79 (79.8)
- *Numbers (%) with BPSD*: 99 (100)
- *Alzheimer´s disease, number (%)*: 99 (100)
- *Vascular demnetia, number (%)*:
- *Levy Body dementia, number (%)*:
- *Frontotemporal dementia, number (%)*:
- *Nursing home recidents, number (%)*: 99 (100)
- *Inpatients, number (%)*:
- *Living in their own homes, number (%)*:

Overall

- *Age in years, mean (SD)*: 83.16 (6.56)
- *Females (%)*: 208 (73.24)
- *Numbers (%) with BPSD*: 284 (100)
- *Alzheimer´s disease, number (%)*: 284 (100)
- *Vascular demnetia, number (%)*:
- *Levy Body dementia, number (%)*:
- *Frontotemporal dementia, number (%)*:
- *Nursing home recidents, number (%)*: 284 (100)

	● *Inpatients, number (%)*: ● *Living in their own homes, number (%)*: **Included criteria:** Participants were >64 years old, not bedridden, nursing home residents for 2 weeks, expected to remain in the facility throughout the trial, and diagnosed with probable Alzheimer's dementia by Diagnostic and Statistical Manual ofMental Disorders, FourthEdition (DSM-IV) criteria or "possible" Alzheimer's dementia by National Institute of Neurological and Communicative Disorders & Stroke—Alzheimer's Disease and Related Disorders Association(NINCDS-ADRA) criteria. The presence of psychosis was required, defined as: Brief Psychiatric Rating Scale (BPRS) scores ≥ 24 and Clinical Global Impression—Severity of Illness (CGI-S) scores ≥ 4 at screening and baseline; scores of ≥ 3 on two or more of the following BPRS items: 4, conceptual disorganization; 11, suspiciousness; 12, hallucinatory behavior; 15, unusual thought content; and frequency scores of ≥ 3 on at least one of two psychosis items (delusions or hallucinations) of the Neuropsychiatric Inventory—Nursing Horne Version (NPI-NH).Scores of ≥ 5 on the Mini-Mental State Examination (MMSE) at screening and baseline were required, as was written informed consent from the participant, spouse, family member, or legal representative. **Excluded criteria:** Exclusion criteria included other clinicaily significant medical conditions, history of drug-induced agranulocytosis, acute orthostasis, clinically significant abnormal electrocardiogram, or concurrent other Axis I DSM—IV diagnosis. **Pretreatment:** **Total sample size:** 284 were randomized **Other:**
Interventions	**Intervention Characteristics** Intervention 1 ● *Number of participants allocated*: 91 ● *Dose*: Quetiapine 100 mg/day ● *Length of treatment*: 10 weeks ● *Other*: Intervention 1 ● *Number of participants allocated*: 94 ● *Dose*: Haloperidol 0.5 mg/day ● *Length of treatment*: 10 weeks ● *Other*: Intervention 2 ● *Number of participants allocated*: 94 ● *Dose*: Haloperidol 0.5 mg/day ● *Length of treatment*: 10 weeks ● *Other*: Control ● *Number of participants allocated*: 99 ● *Dose*: ● *Length of treatment*: 10 weeks ● *Other*:

Outcomes	*Serious adverse events* ● **Outcome type**: DichotomousOutcome ● **Data value**: Endpoint *Mortality* ● **Outcome type**: DichotomousOutcome ● **Data value**: Endpoint *BPSD* ● **Outcome type**: ContinuousOutcome ● **Data value**: Endpoint *Agitation* ● **Outcome type**: ContinuousOutcome ● **Data value**: Endpoint *Cognition* ● **Outcome type**: ContinuousOutcome ● **Data value**: Endpoint *Activity of Daily Living (ADL)* ● **Outcome type**: ContinuousOutcome ● **Data value**: Endpoint *Quality of life* ● **Outcome type**: ContinuousOutcome ● **Data value**: Endpoint *BPSD_dikotom* ● **Outcome type**: DichotomousOutcome ● **Data value**: Endpoint
Identification	**Sponsorship source:** This study was supported by AstraZeneca Pharmaceuticals LP.Pierre N. Tariot, M.D., has received consulting fees and research support from Abbott Laboratories, Bristol Myers Squibb, Janssen Pharmaceuticals, and Eli Lilly & Company. He has also received consulting fees, research support, and educational fees from AstraZeneca and Pfizer Inc.; and research support from the NIA, NIMH, Alzheimer's Association, Arizona Department of Health Services, and the Institute for Mental Health Research. **Country:** USA **Setting:** Multicenter, nursing home residents at 47 sites in the USA **Comments:** **Authors name:** Pierre N. Tariot **Institution:** Memory Disorders Center, Banner Alzheimer's Disease Institute, Phoenix, Arizona **Email:** pierre.tariot@bannerhealth.com **Address:** Memory Disorders Center, Banner Alzheimer's Disease Institute, 901 E.Willetta Street, Phoenix, AZ 85006 **Start date:** March 1998 **End date:** February 2000

	Other:
Notes	*NKA Demens 2023* on 06/05/2024 19:10 **Select** P: personer med demens og agitationI: quetiapin, haloperidolC: placebo *Anja Ussing* on 07/05/2024 21:43 **Select** Separate data på AD populationen, intervention 10 uger

Risk of bias table

Bias	Authors' judgement	Support for judgement
Selective outcome reporting	Unclear risk	Judgement Comment: No protocol available. Insufficient information. 'Any adverse events' and 'serious adverse events' were not reported.
Blinding of participants and personnel	Low risk	Judgement Comment: This was a "double-blind" trial. "Identically appearing capsules containing 25mg quetiapine, 0.5 mg haloperidol, or placebo" were used.
Allocation concealment	Unclear risk	Judgement Comment: No information
Incomplete outcome data	Unclear risk	Judgement Comment: Drop-out was high (29%), analyses were not based on all randomized, LOCF formissing data. However, it is a negative trial. In addition, missing outcome databalanced in numbers across intervention groups, with similar reasons for missing data across groups.
Sequence Generation	Unclear risk	Judgement Comment: No information
Other sources of bias	High risk	Judgement Comment: Participants underwent a washout of ≥48 hours
Blinding of outcome assessors	Unclear risk	Judgement Comment: No information

Teri 2000

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group **Other:**
Participants	**Baseline Characteristics** Intervention 1 ● *Age in years, mean (SD)*: 75.3 (6.9) ● *Females (%)*: 20 (59) ● *Numbers (%) with BPSD*: 34 (100) ● *Alzheimer´s disease, number (%)*: 34 (100) ● *Vascular demnetia, number (%)*:

	● *Levy Body dementia, number (%)*: ● *Frontotemporal dementia, number (%)*: ● *Nursing home recidents, number (%)*: 34 (100) ● *Inpatients, number (%)*: ● *Living in their own homes, number (%)*: Control ● *Age in years, mean (SD)*: 75.8 (6.2) ● *Females (%)*: 24 (67) ● *Numbers (%) with BPSD*: 36 (100) ● *Alzheimer´s disease, number (%)*: 36 (100) ● *Vascular demnetia, number (%)*: ● *Levy Body dementia, number (%)*: ● *Frontotemporal dementia, number (%)*: ● *Nursing home recidents, number (%)*: 36 (100) ● *Inpatients, number (%)*: ● *Living in their own homes, number (%)*: Overall ● *Age in years, mean (SD)*: ● *Females (%)*: 44 (62.9) ● *Numbers (%) with BPSD*: 70 (100) ● *Alzheimer´s disease, number (%)*: 70 (100) ● *Vascular demnetia, number (%)*: ● *Levy Body dementia, number (%)*: ● *Frontotemporal dementia, number (%)*: ● *Nursing home recidents, number (%)*: 70 (100) ● *Inpatients, number (%)*: ● *Living in their own homes, number (%)*: **Included criteria:** Key inclusion criteria were 1) diagnosis of probable or possible ADaccording to the criteria of the National Institute of Neurologic and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association (NINCDS-ADRDA); 2) at least a 2-week history of two or more agitated behaviors occurring at least once weekly, and rated by the caregiver as distressing or requiring help; 3) community residence with a responsible informant; 4) on stable doses of other medications. **Excluded criteria:** Key exclusion criteria were 1) presence of major psychiatric disorders within the last 2 years; 2) neurologic or systemic illness (e.g., delirium, hypoxia, or unstable thyroid dysfunction); 3) alcoholor drug abuse within the past year; 4) need for emergency treatment for agitation. **Pretreatment:** **Total sample size:** 149 were randomized **Other:**
Interventions	**Intervention Characteristics** Intervention 1 ● *Number of participants allocated*: 34 ● *Dose*: Haloperidol 0.5 mg/day

	● *Length of treatment*: 16 weeks ● *Other*: Control ● *Number of participants allocated*: 36 ● *Dose*: ● *Length of treatment*: 16 weeks ● *Other*:
Outcomes	*Serious adverse events* ● **Outcome type**: DichotomousOutcome ● **Data value**: Endpoint *Mortality* ● **Outcome type**: DichotomousOutcome ● **Data value**: Endpoint *BPSD* ● **Outcome type**: ContinuousOutcome ● **Data value**: Endpoint *Agitation* ● **Outcome type**: ContinuousOutcome ● **Data value**: Endpoint *Cognition* ● **Outcome type**: ContinuousOutcome ● **Data value**: Endpoint *Activity of Daily Living (ADL)* ● **Outcome type**: ContinuousOutcome ● **Data value**: Endpoint *Quality of life* ● **Outcome type**: ContinuousOutcome ● **Data value**: Endpoint *BPSD_dikotom* ● **Outcome type**: DichotomousOutcome ● **Data value**: Endpoint
Identification	**Sponsorship source:** Supported by a grant from the National Institute of Aging (AG-010483). Active study medications and corresponding placebos were provided by Purpac Pharmaceutical, Elizabeth, NJ. **Country:** USA **Setting:** Multicenter, community residents

	Comments: **Authors name:** Linda Teri **Institution:** From the University of Washington. **Email:** lteri@u.washington.edu **Address:** Department of Psychosocial and Community Health, Box 357263, University of Washington, Seattle, WA 98195-7263 **Start date:** **End date:** **Other:**
Notes	*NKA Demens 2023* on 06/05/2024 18:56 **Select** P: personer med alzheimers og agitationI: non-farmakologisk behandling, trazodon eller haloperidolC: placebo *Anja Ussing* on 07/05/2024 21:38 **Select** Halperidol vs placebo kunne være interessant, meninterventionen varer 16 uger og der er ikke umiddelbart data undervejs i stuidiet

Risk of bias table

Bias	Authors' judgement	Support for judgement
Selective outcome reporting	Low risk	Judgement Comment: All outcomes seem to be reported.
Blinding of participants and personnel	Unclear risk	Judgement Comment: Not completely blinded, because one arm (behaviour management techniques) could not be blinded.
Allocation concealment	Unclear risk	Judgement Comment: Not enough information provided.It was a "randomized" trial. "Treatmentswere assigned in randomized blocks of nine (for three arms) or 12 (for fourarms)." Restriction methods could potentially affect allocation concealment
Incomplete outcome data	Low risk	Judgement Comment: Overall drop-out was high (36%).ITT-analysis: "Missing scores at posttreatmentwere imputed with last observation carried forward from discontinuation visit scores or, if those were not available, from midpoint visit scores. If no ADCS-CGIC score [primary outcome, rev] was available, a value of “worse” was assigned (n=12). The rationale for doing this was to assume the worst case scenario: subjects who dropped out did so because they became worse. In addition,we reviewed the reasons caregivers cited for dropping out of the studyand in each instance our assignment of“worse” was confirmed. "
Sequence Generation	Unclear risk	Judgement Comment: No information
Other sources of bias	High risk	Judgement Comment: Subjects receiving psychotropic medications were required to discontinuethem at least 2 weeks before study enrolment.

Blinding of outcome assessors	Low risk	Judgement Comment: "Assessments were conducted [...] by interviewers blind to treatment assignment." "To insure that interviewers remained blind to treatment assignment,caregivers did not discuss any aspect of their treatment with the interviewer. In no instance was the blinding compromised.""Medication was providedin [...] identically appearing tablets." "The primary outcome measure was [...]completed by a trained clinician blind to treatment assignment."

Zhong 2007

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group **Other:**
Participants	**Baseline Characteristics** Intervention 1 ● *Age in years, mean (SD)*: 83.0 (7.2) ● *Females (%)*: 90 (72.6) ● *Numbers (%) with BPSD*: 124 (100) ● *Alzheimer´s disease, number (%)*: 94 (75.8) ● *Vascular demnetia, number (%)*: 16 (12.9) ● *Levy Body dementia, number (%)*: ● *Frontotemporal dementia, number (%)*: ● *Nursing home recidents, number (%)*: 124 (100) ● *Inpatients, number (%)*: ● *Living in their own homes, number (%)*: Intervention 1 ● *Age in years, mean (SD)*: ● *Females (%)*: ● *Numbers (%) with BPSD*: ● *Alzheimer´s disease, number (%)*: ● *Vascular demnetia, number (%)*: ● *Levy Body dementia, number (%)*: ● *Frontotemporal dementia, number (%)*: ● *Nursing home recidents, number (%)*: ● *Inpatients, number (%)*: ● *Living in their own homes, number (%)*: Intervention 2 ● *Age in years, mean (SD)*: 83.5 (8.0) ● *Females (%)*: 92 (78.6) ● *Numbers (%) with BPSD*: 117 (100) ● *Alzheimer´s disease, number (%)*: 96 (82.1) ● *Vascular demnetia, number (%)*: 13 (11.1) ● *Levy Body dementia, number (%)*:

- *Frontotemporal dementia, number (%)*:
- *Nursing home recidents, number (%)*: 117 (100)
- *Inpatients, number (%)*:
- *Living in their own homes, number (%)*:

Control

- *Age in years, mean (SD)*: 83.2 (7.2)
- *Females (%)*: 65 (70.7)
- *Numbers (%) with BPSD*: 92 (100)
- *Alzheimer´s disease, number (%)*: 73 (79.3)
- *Vascular demnetia, number (%)*: 9 (9.8)
- *Levy Body dementia, number (%)*:
- *Frontotemporal dementia, number (%)*:
- *Nursing home recidents, number (%)*: 92 (100)
- *Inpatients, number (%)*:
- *Living in their own homes, number (%)*:

Overall

- *Age in years, mean (SD)*: 83
- *Females (%)*: 247 (74.2)
- *Numbers (%) with BPSD*: 333 (100)
- *Alzheimer´s disease, number (%)*: 263 (79)
- *Vascular demnetia, number (%)*: 38 (11.4)
- *Levy Body dementia, number (%)*:
- *Frontotemporal dementia, number (%)*:
- *Nursing home recidents, number (%)*: 333 (100)
- *Inpatients, number (%)*:
- *Living in their own homes, number (%)*:

Included criteria: They had diagnoses of probable or possible AD or vascular dementia according to Diagnostic and Statistical Manual of Mental Disorders— fourth edition [DSM-IV] or the National Institute of Neurological and Communicative Disorders and Stroke/the Alzheimer's Disease and Related Disorders Association [NTNCDS/ADRDA]) criteria. Other inclusion criteria were as follows: minimum age of 55 years, ambulatory or ambulatory with assistance, documented clinical symptoms of agitation that did not result directly from the participant's medical condition and required treatment with antipsychotic medication in the opinion of the investigator, a total score of ≥14 on the PANSS-EC and a score of ≥4 on one of the 5 PANSS-EC items (hostility, tension, uncooperativeness, excitement, poor impulse control) both at screening and at randomization.
Excluded criteria: Key exclusion criteria included a history of schizophrenia, schizoaffective disorder or bipolar disorder, agitation that was judged not to be related to dementia, failure to respond to a prior adequate trial of atypical antipsychotics for the treatment of agitation, and unstable medical illness (this included but was not limited to: cardiovascular, renal, hepatic, hematological, endocrine, and cerebrovascular disorders). Any participants with abnormal ECG results that were considered clinically significant were also excluded from the study.
Pretreatment:
Total sample size: 333 were randomized
Other:

Interventions	**Intervention Characteristics** Intervention 1 ● *Number of participants allocated*: 124 ● *Dose*: Quetiapine 100 mg/day ● *Length of treatment*: 10 weeks ● *Other*: Intervention 1 ● *Number of participants allocated*: 117 ● *Dose*: Quetiapine 200 mg/day ● *Length of treatment*: 10 weeks ● *Other*: Intervention 2 ● *Number of participants allocated*: 117 ● *Dose*: Quetiapine 200 mg/day ● *Length of treatment*: 10 weeks ● *Other*: Control ● *Number of participants allocated*: 92 ● *Dose*: ● *Length of treatment*: 10 weeks ● *Other*:
Outcomes	*Serious adverse events* ● **Outcome type**: DichotomousOutcome ● **Data value**: Endpoint *Mortality* ● **Outcome type**: DichotomousOutcome ● **Data value**: Endpoint *BPSD* ● **Outcome type**: ContinuousOutcome ● **Data value**: Endpoint *Agitation* ● **Outcome type**: ContinuousOutcome ● **Data value**: Endpoint *Cognition* ● **Outcome type**: ContinuousOutcome ● **Data value**: Endpoint

	Quality of life ● **Outcome type**: ContinuousOutcome ● **Data value**: Endpoint *Activity of Daily Living (ADL)* ● **Outcome type**: ContinuousOutcome ● **Data value**: Endpoint *BPSD_dikotom* ● **Outcome type**: DichotomousOutcome ● **Data value**: Endpoint
Identification	**Sponsorship source:** AstraZeneca Pharmaceuticals supported this study (5077US/0046). **Country:** USA **Setting:** Multicenter, residents of nursing homes and assisted living facilities in the USA **Comments:** **Authors name:** Kate X. Zhong **Institution:** 1800 Concord Pike, Wilmington, DE 19850-5437, USA. **Email:** margaret.minkwitz@astrazeneca.com **Address:** 1800 Concord Pike, Wilmington, DE 19850-5437, USA **Start date:** September 2002 **End date:** November 2003 **Other:**
Notes	*NKA Demens 2023* on 06/05/2024 18:09 **Select** P: personer med demens og agitationI: quetiapinC: placebo *Anja Ussing* on 07/05/2024 19:16 **Select** inkluderet i NKR fra 2028

Risk of bias table

Bias	Authors' judgement	Support for judgement
Selective outcome reporting	High risk	Judgement Comment: Various scale for the outcome have been used. The least commonly used ispresented as the primary outcome. Results based on OC analyses and p-valuesare given undue attention f.i. in the abstract. Subgroup analyses for type of dementia. Protocol was submitted after publication and does not list pre-specified outcomes
Blinding of participants and personnel	Unclear risk	Judgement Comment: This was a "double-blind" trial. "Each [medication] kit contained 10 blisterwallets with the same number of tablets and the same configuration of color,size, and shape. Study medication was administered twice daily from blisterwallets."Personal not mentioned

Allocation concealment	Low risk	
Incomplete outcome data	High risk	Judgement Comment: Drop-out was high (35%). Modified ITT analysis excluding patients that did notreceive one dose of study medication or one assessment after baseline. LOCFwas used for imputing missing data.
Sequence Generation	Low risk	Judgement Comment: The centralized randomization schedule was generated using a random blocksize of 8 and was created using random seed and treatment allocation ratios of3:3:2 and maintained blinded by the sponsor's randomization group.
Other sources of bias	Low risk	Judgement Comment: No run-in period
Blinding of outcome assessors	Unclear risk	Judgement Comment: This was a "double-blind" trial. "Each [medication] kit contained 10 blisterwallets with the same number of tablets and the same configuration of color,size, and shape. Study medication was administered twice daily from blisterwallets."Personal not mentioned.

Footnotes

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Data and analyses

1 Antipsychotics vs placebo

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
1.1 BPSD - EoT	19	5624	Std. Mean Difference (IV, Random, 95% CI)	-0.17 [-0.25, -0.09]
1.2 BPSD - 4 uger	9	3031	Std. Mean Difference (IV, Random, 95% CI)	-0.23 [-0.32, -0.15]
1.3 BPSD - 6 uger	14	4635	Std. Mean Difference (IV, Random, 95% CI)	-0.18 [-0.26, -0.11]
1.4 BPSD - 12 uger	5	1371	Std. Mean Difference (IV, Random, 95% CI)	-0.34 [-0.45, -0.23]
1.5 BPSD_dikotom - EoT	3	547	Risk Ratio (IV, Random, 95% CI)	1.22 [0.87, 1.72]
1.6 Agitation - EoT	21	5882	Std. Mean Difference (IV, Random, 95% CI)	-0.14 [-0.23, -0.06]
1.7 Agitation - 4 uger	9	2987	Std. Mean Difference (IV, Random, 95% CI)	-0.12 [-0.27, 0.04]
1.8 Agitation - 12 uger	8	2282	Std. Mean Difference (IV, Random, 95% CI)	-0.22 [-0.36, -0.09]
1.9 Cognition - EoT	14	2638	Std. Mean Difference (IV, Random, 95% CI)	-0.07 [-0.18, 0.05]
1.10 Activity of Daily Living (ADL) - EoT	7	1210	Std. Mean Difference (IV, Random, 95% CI)	-0.14 [-0.28, -0.00]
1.11 Quality of life - EoT	2	935	Std. Mean Difference (IV, Random, 95% CI)	0.07 [-0.06, 0.20]
1.12 Serious adverse events - EoT	19	5750	Risk Ratio (IV, Random, 95% CI)	1.27 [1.08, 1.51]
1.13 Serious adverse events - 12 uger	8	3240	Risk Ratio (IV, Random, 95% CI)	1.36 [1.08, 1.72]
1.14 Mortality - EoT	23	7026	Risk Ratio (IV, Random, 95% CI)	1.41 [0.98, 2.03]
1.15 Mortality - 12 uger	8	3244	Risk Ratio (IV, Random, 95% CI)	1.19 [0.66, 2.15]

2 Antipsychotics vs placebo (subgruppe m. præparater)

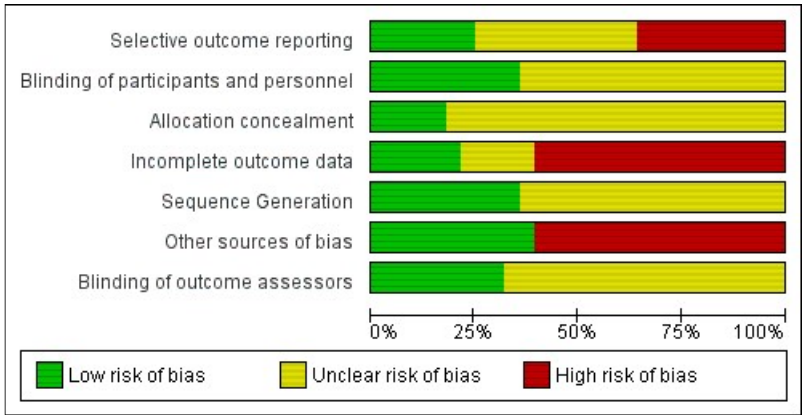
Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate

2.1 BPSD	19	5739	Std. Mean Difference (IV, Random, 95% CI)	-0.16 [-0.24, -0.09]
2.1.1 Risperidon	6	1605	Std. Mean Difference (IV, Random, 95% CI)	-0.22 [-0.44, -0.01]
2.1.2 Olanzapin	4	1136	Std. Mean Difference (IV, Random, 95% CI)	-0.11 [-0.25, 0.04]
2.1.3 Quetiapin	4	588	Std. Mean Difference (IV, Random, 95% CI)	-0.06 [-0.23, 0.11]
2.1.4 Aripiprazol	3	906	Std. Mean Difference (IV, Random, 95% CI)	-0.20 [-0.35, -0.05]
2.1.5 Haloperidol	3	302	Std. Mean Difference (IV, Random, 95% CI)	-0.07 [-0.30, 0.17]
2.1.6 Brexpiprazol	1	326	Std. Mean Difference (IV, Random, 95% CI)	-0.35 [-0.58, -0.12]
2.1.7 Pimavanserin	2	876	Std. Mean Difference (IV, Random, 95% CI)	-0.14 [-0.33, 0.06]
2.2 Agitation	21	5997	Std. Mean Difference (IV, Random, 95% CI)	-0.14 [-0.21, -0.06]
2.2.1 Risperidon	6	1603	Std. Mean Difference (IV, Random, 95% CI)	-0.24 [-0.39, -0.10]
2.2.2 Olanzapin	5	1405	Std. Mean Difference (IV, Random, 95% CI)	-0.11 [-0.32, 0.09]
2.2.3 Quetiapin	4	610	Std. Mean Difference (IV, Random, 95% CI)	-0.12 [-0.29, 0.05]
2.2.4 Aripiprazol	2	709	Std. Mean Difference (IV, Random, 95% CI)	-0.28 [-0.44, -0.12]
2.2.5 Haloperidol	4	502	Std. Mean Difference (IV, Random, 95% CI)	0.13 [-0.11, 0.37]
2.2.6 Brexpiprazol	3	1010	Std. Mean Difference (IV, Random, 95% CI)	-0.15 [-0.28, -0.02]
2.2.7 Pimavanserin	1	158	Std. Mean Difference (IV, Random, 95% CI)	0.04 [-0.27, 0.35]
2.6 Serious adverse events	19	5750	Risk Ratio (IV, Random, 95% CI)	1.27 [1.07, 1.51]
2.6.1 Risperidon	6	1615	Risk Ratio (IV, Random, 95% CI)	1.23 [0.94, 1.61]
2.6.2 Olanzapin	3	456	Risk Ratio (IV, Random, 95% CI)	1.49 [0.84, 2.62]
2.6.3 Quetiapin	4	726	Risk Ratio (IV, Random, 95% CI)	1.11 [0.71, 1.71]
2.6.4 Aripriprazol	3	944	Risk Ratio (IV, Random, 95% CI)	1.25 [0.84, 1.85]
2.6.5 Haloperidol	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
2.6.6 Brexpiprazol	3	1044	Risk Ratio (IV, Random, 95% CI)	1.49 [0.83, 2.65]
2.6.7 Pimavanserin	2	965	Risk Ratio (IV, Random, 95% CI)	1.45 [0.79, 2.67]

2.7 Mortality	23	7026	Risk Ratio (IV, Random, 95% CI)	1.37 [0.95, 1.97]
2.7.1 Risperidon	7	2036	Risk Ratio (IV, Random, 95% CI)	1.50 [0.87, 2.61]
2.7.2 Olanzapin	5	1356	Risk Ratio (IV, Random, 95% CI)	1.20 [0.43, 3.34]
2.7.3 Quetiapin	4	725	Risk Ratio (IV, Random, 95% CI)	1.43 [0.60, 3.38]
2.7.4 Aripriprazol	2	620	Risk Ratio (IV, Random, 95% CI)	1.41 [0.53, 3.77]
2.7.5 Haloperidol	3	276	Risk Ratio (IV, Random, 95% CI)	2.04 [0.19, 22.14]
2.7.6 Brexpiprazol	3	1048	Risk Ratio (IV, Random, 95% CI)	1.52 [0.26, 8.99]
2.7.7 Pimavanserin	2	965	Risk Ratio (IV, Random, 95% CI)	0.63 [0.14, 2.73]

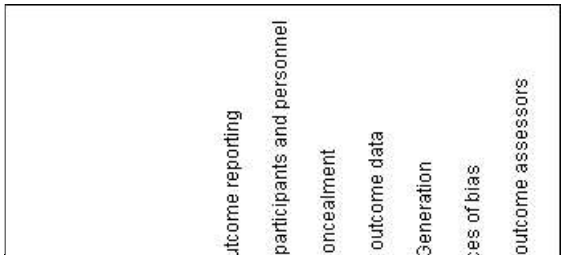
Figures

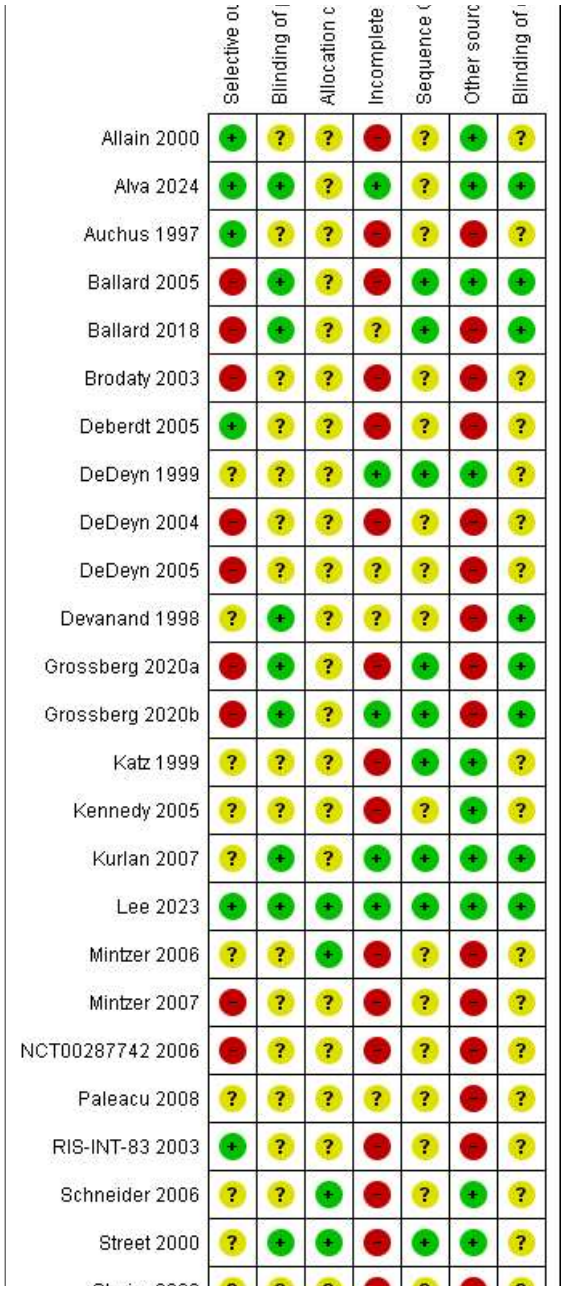
Figure 1



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

Figure 2




Selective ou
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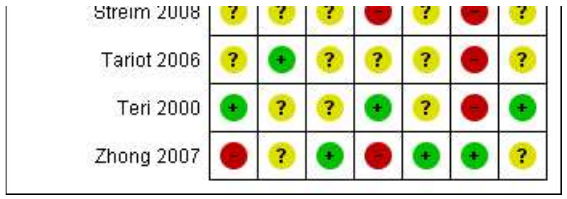
Allain 2000
Alva 2024
Auchus 1997
Ballard 2005
Ballard 2018
Brodaty 2003
Deberdt 2005
DeDeyn 1999
DeDeyn 2004
DeDeyn 2005
Devanand 1998
Grossberg 2020a
Grossberg 2020b
Katz 1999
Kennedy 2005
Kurlan 2007
Lee 2023
Mintzer 2006
Mintzer 2007
NCT00287742 2006
Paleacu 2008
RIS-INT-83 2003
Schneider 2006
Street 2000

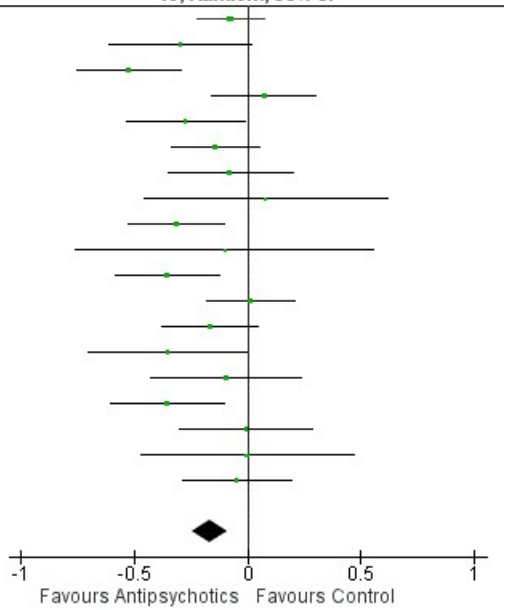


Risk of bias summary: review authors' judgements about each risk of bias item for each included study.

Figure 3 (Analysis 1.1)

Study or Subgroup	Antipsychotics Mean	SD	Total	Placebo Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
Alva 2024 (1)	3.14	2.68	361	3.34	2.68	358	9.2%	-0.07 [-0.22, 0.07]
Ballard 2018 (2)	-5.12	17.2842	76	0	17.2842	81	4.2%	-0.29 [-0.61, 0.02]
Brodaty 2003 (3)	-6.8	8.6301	149	-2.3	8.6301	152	6.2%	-0.52 [-0.75, -0.29]
Deberdt 2005 (4)	-10.75	21.15	383	-12.3	22	91	6.3%	0.07 [-0.16, 0.30]
DeDeyn 1999 (5)	-8.6	6.4	115	-6.2	10.6	114	5.4%	-0.27 [-0.53, -0.01]
DeDeyn 2004 (6)	-16.1	15.9	513	-13.7	20.3	129	7.4%	-0.14 [-0.34, 0.05]
DeDeyn 2005 (7)	-11.2	18.81	103	-9.75	18.81	100	5.0%	-0.08 [-0.35, 0.20]
Devanand 1998 (8)	50.48	9.58	40	49.65	11.25	20	1.8%	0.08 [-0.46, 0.62]
Katz 1999 (9)	-7.4	7.24	317	-5.2	6.52	118	6.8%	-0.31 [-0.52, -0.10]
Kurlan 2007 (10)	24.6	19.1	19	26.6	20.3	17	1.3%	-0.10 [-0.75, 0.56]
Lee 2023 (11)	-17.3	13.2	215	-12.7	12.64	111	6.2%	-0.35 [-0.58, -0.12]
Mintzer 2006 (12)	-4.9	8.23	201	-5	8.27	212	7.4%	0.01 [-0.18, 0.21]
Mintzer 2007 (13)	-15.9	18.2	337	-13	16.4	117	6.8%	-0.16 [-0.37, 0.05]
Schneider 2006 (14)	-15.5	17.4	103	-9	20.6	47	3.7%	-0.35 [-0.70, -0.00]
Street 2000 (15)	-5.7	8	155	-4.9	10.3	45	3.9%	-0.09 [-0.43, 0.24]
Streim 2008 (16)	-16.43	17.32	128	-10.01	18.83	121	5.6%	-0.35 [-0.60, -0.10]
Tariot 2006 (17)	-4.14	6.04	86	-4.11	5.99	94	4.7%	-0.00 [-0.30, 0.29]
Teri 2000 (18)	-5.35	22.41	34	-5.28	24.36	36	2.3%	-0.00 [-0.47, 0.47]
Zhong 2007 (19)	-9.3	23.2	234	-8.2	23	92	5.9%	-0.05 [-0.29, 0.19]
Total (95% CI)			**3569**			**2055**	**100.0%**	**-0.17 [-0.25, -0.09]**

Heterogeneity: Tau² = 0.01; Chi² = 30.99, df = 18 (P = 0.03); I² = 42%
Test for overall effect: Z = 4.24 (P < 0.0001)



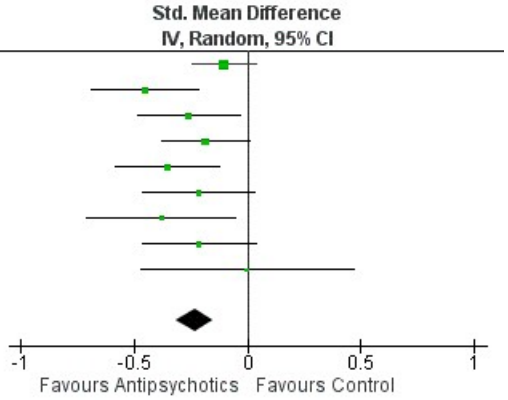
Footnotes
(1) 1. gen AP: Pimavanserin., CGI-I
(2) 1. gen AP: Pimavanserin. NPI-NH
(3) Risperidone, CGI-S
(4) Olanzapine & Risperidone, NPI-total
(5) Risperidone, Behave-AD
(6) Olanzapine 1 mg, 2.5 mg, 5 mg & 7.5 mg, NPI-NH
(7) Aripiprazole, NPI total
(8) 1. gen AP: Haloperidol., BPRS
(9) Risperidone 0.5 mg, 1 mg & 2 mg, Behave-AD
(10) Quetiapine, NPI total
(11) Brexpiprazole, NPI-NH
(12) Risperidone, Behave-AD
(13) Aripiprazole 2 mg/day, 5 mg/day & 10 mg/day, NPI-NH
(14) Olanzapine, Quetiapine & Risperidone, NPI-NH
(15) Olanzapine 5 mg, 10 mg & 15 mg, NPI-NH
(16) Aripiprazole, NPI-NH
(17) Quetiapine, NPI-NH
(18) 1. gen AP: Haloperidol, BRSD
(19) Quetiapine 100 mg & 200 mg, NPI-NH

Forest plot of comparison: 1 Antipsychotics vs placebo, outcome: 1.1 BPSD - EoT.

Figure 4 (Analysis 1.2)

Study or Subgroup	Antipsychotics Mean	SD	Total	Placebo Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
Alva 2024 (1)	3.46	0.58	373	3.53	0.77	372	23.2%	-0.10 [-0.25, 0.04]
Brodaty 2003 (2)	-6.33	8.55	141	-2.61	7.87	138	10.6%	-0.45 [-0.69, -0.21]
DeDeyn 1999 (3)	-5.03	7.299	230	-3.12	7.69	114	11.6%	-0.26 [-0.48, -0.03]
Katz 1999 (4)	-5.9754	7.2039	392	-4.68	6.52	141	15.0%	-0.18 [-0.38, 0.01]
Lee 2023 (5)	-17.3	13.2	215	-12.7	12.64	111	11.1%	-0.35 [-0.58, -0.12]
Schneider 2006 (6)	-10.5712	17.3689	185	-6.6	20.6	94	9.8%	-0.21 [-0.46, 0.04]
Street 2000 (7)	8.7374	7.8736	159	11.96	10.3	47	6.0%	-0.38 [-0.71, -0.05]
Streim 2008 (8)	-13.32	14.72	128	-10.09	15.47	121	9.7%	-0.21 [-0.46, 0.04]
Teri 2000 (9)	-5.35	22.41	34	-5.28	24.36	36	3.0%	-0.00 [-0.47, 0.47]
Total (95% CI)			**1857**			**1174**	**100.0%**	**-0.23 [-0.32, -0.15]**

Heterogeneity: Tau² = 0.00; Chi² = 9.42, df = 8 (P = 0.31); I² = 15%
Test for overall effect: Z = 5.46 (P < 0.00001)



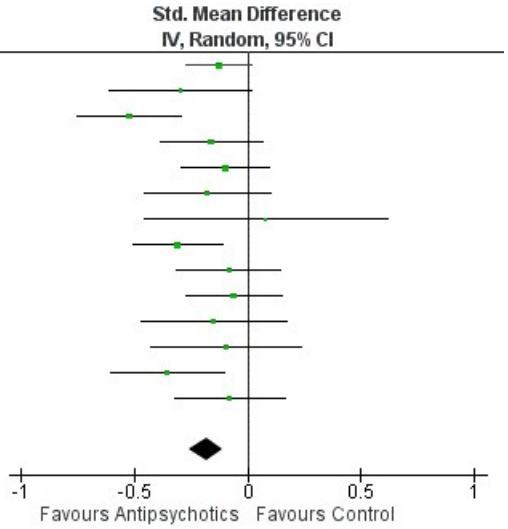
Footnotes
(1) 1. gen AP: Pimavanserin., *CGI-I*
(2) Risperidone, *BEHAVE-AD*
(3) Risperidone, *BEHAVE-AD*
(4) Risperidone 0.5 mg, 1 mg & 2 mg, *BEHAVE-AD*
(5) Brexpiprazole, *NPI-NH*
(6) Olanzapine, Quetiapine & Risperidone, *NPI-NH*
(7) Olanzapine 5 mg, 10 mg & 15 mg, *NPI-NH*
(8) Aripiprazole, *NPI-NH*
(9) 1. gen AP: Haloperidol, *BRSD*

Forest plot of comparison: 1 Antipsychotics vs placebo, outcome: 1.2 BPSD - 4 uger.

Figure 5 (Analysis 1.3)

Study or Subgroup	Antipsychotics Mean	SD	Total	Placebo Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
Alva 2024 (1)	3.3	0.77	365	3.41	0.97	374	13.8%	-0.13 [-0.27, 0.02]
Ballard 2018 (2)	-5.12	17.2842	76	0	17.2842	81	4.7%	-0.29 [-0.61, 0.02]
Brodaty 2003 (3)	-6.8	8.6301	149	-2.3	8.6301	152	7.7%	-0.52 [-0.75, -0.29]
DeDeyn 1999 (4)	-6.28	8.4506	230	-4.94	8.11	114	7.9%	-0.16 [-0.39, 0.06]
DeDeyn 2004 (5)	-5.35	4.9	513	-4.84	6.1	129	9.8%	-0.10 [-0.29, 0.09]
DeDeyn 2005 (6)	-6	6.29	103	-4.87	6.5	100	5.8%	-0.18 [-0.45, 0.10]
Devanand 1998 (7)	50.48	9.58	40	49.65	11.25	20	1.8%	0.08 [-0.46, 0.62]
Katz 1999 (8)	-6.3	7.19	372	-4.14	6.51	134	9.4%	-0.31 [-0.51, -0.11]
Lee 2023 (9)	-0.74	0.73	214	-0.68	0.74	112	7.7%	-0.08 [-0.31, 0.15]
Mintzer 2006 (10)	-3.1	3.42	166	-2.9	3.19	184	8.7%	-0.06 [-0.27, 0.15]
Schneider 2006 (11)	-11.73	22.3	185	-8.21	29.1	47	4.5%	-0.15 [-0.47, 0.17]
Street 2000 (12)	-5.7	8	155	-4.9	10.3	45	4.3%	-0.09 [-0.43, 0.24]
Streim 2008 (13)	-14.42	16.54	128	-8.28	17.99	121	6.7%	-0.35 [-0.61, -0.10]
Zhong 2007 (14)	2.73	2.14	234	2.89	1.92	92	7.1%	-0.08 [-0.32, 0.16]
Total (95% CI)			**2930**			**1705**	**100.0%**	**-0.18 [-0.26, -0.11]**

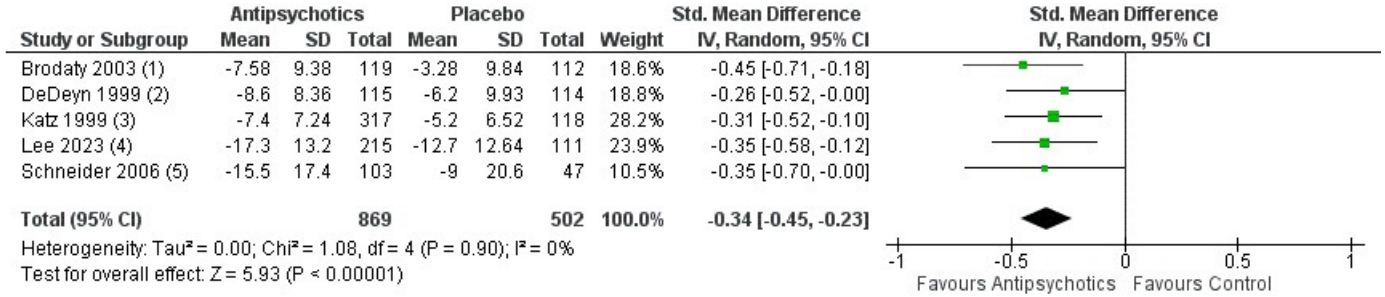
Heterogeneity: Tau² = 0.00; Chi² = 17.51, df = 13 (P = 0.18); I² = 26%
Test for overall effect: Z = 4.82 (P < 0.00001)



Footnotes
(1) 1. gen AP: Pimavanserin. CGI-I
(2) 1. gen AP: Pimavanserin. NPI-NH
(3) Risperidone, *Behave-AD*
(4) Risperidone, Behave-AD
(5) Olanzapine 1 mg, 2.5 mg, 5 mg & 7.5 mg, SD fra final change, *NPI Psychosis*
(6) Aripiprazole, *NPI Psychosis*
(7) 1. gen AP: Haloperidol., BPRS
(8) Risperidone 0.5 mg, 1 mg & 2 mg, Behave-AD
(9) Brexpiprazole, *CGI-S*
(10) Risperidone, Behave-AD
(11) Olanzapine, Quetiapine & Risperidone, NPI-NH
(12) Olanzapine 5 mg, 10 mg & 15 mg, NPI-NH
(13) Aripiprazole, NPI-NH
(14) Quetiapine 100 mg & 200 mg, *CGI-C*

Forest plot of comparison: 1 Antipsychotics vs placebo, outcome: 1.3 BPSD - 6 uger.

Figure 6 (Analysis 1.4)



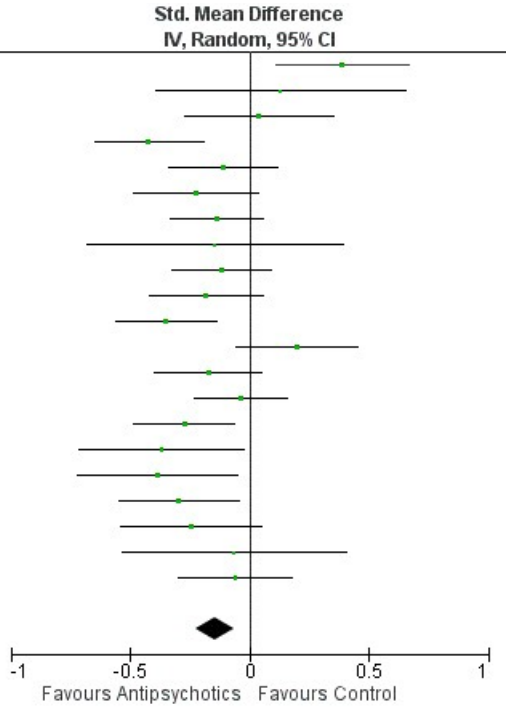
Footnotes
(1) Risperidone, Behave-AD
(2) Risperidone, Behave-AD
(3) Risperidone 0.5 mg, 1 mg & 2 mg, Behave-AD
(4) Brexpiprazole, NPI-NH
(5) Olanzapine, Quetiapine & Risperidone, NPI-NH

Forest plot of comparison: 1 Antipsychotics vs placebo, outcome: 1.4 BPSD - 12 uger.

Figure 7 (Analysis 1.6)

Study or Subgroup	Antipsychotics Mean	SD	Total	Placebo Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
Allain 2000 (1)	6.75	5.46	99	4.71	5.01	101	4.6%	0.39 [0.11, 0.67]
Ballard 2005	-4	15.4	27	-6.2	17.6	29	2.0%	0.13 [-0.39, 0.66]
Ballard 2018 (2)	0.3	7.5011	77	0	7.5011	81	4.1%	0.04 [-0.27, 0.35]
Brodaty 2003 (3)	-7.5	10.4004	149	-3.1	10.4004	152	5.6%	-0.42 [-0.65, -0.19]
Deberdt 2005	-1.4	4.8	382	-0.9	3.1	90	5.6%	-0.11 [-0.34, 0.12]
DeDeyn 1999	-8.3	13.9	115	-4.9	16.1	114	5.0%	-0.23 [-0.49, 0.03]
DeDeyn 2004	-1.75	3.1	513	-1.3	3.7	129	6.3%	-0.14 [-0.33, 0.05]
Devanand 1998 (4)	3.13	1.52	40	3.35	1.39	20	1.9%	-0.15 [-0.68, 0.39]
Grossberg 2020a	-19.6	15.3	272	-17.8	14.9	131	6.0%	-0.12 [-0.33, 0.09]
Grossberg 2020b	-18.9	13.7	131	-16.5	12.8	135	5.3%	-0.18 [-0.42, 0.06]
Katz 1999	-2.3	3.12	317	-1.2	3.26	118	5.9%	-0.35 [-0.56, -0.14]
Kennedy 2005	0.65	1.6	178	0.33	1.61	90	5.1%	0.20 [-0.06, 0.45]
Lee 2023	-16.2	13.65	225	-13.9	12.82	116	5.7%	-0.17 [-0.40, 0.05]
Mintzer 2006	-1.1	2.42	201	-1	2.83	212	6.4%	-0.04 [-0.23, 0.16]
Mintzer 2007	-10.2	13.3	347	-6.5	14.3	115	5.9%	-0.27 [-0.48, -0.06]
Schneider 2006	-7.7	10.5	102	-3.9	9.8	48	3.6%	-0.37 [-0.71, -0.02]
Street 2000	-3.7	4	156	-2.1	4.6	45	3.8%	-0.39 [-0.72, -0.05]
Streim 2008	-10.25	12.85	126	-6.16	14.56	121	5.1%	-0.30 [-0.55, -0.05]
Tariot 2006	-2.63	4.99	86	-1.49	4.33	94	4.4%	-0.24 [-0.54, 0.05]
Teri 2000	-7.26	22.51	34	-5.94	18.5	36	2.4%	-0.06 [-0.53, 0.41]
Zhong 2007	-10.1	22.1	234	-8.8	22.1	94	5.4%	-0.06 [-0.30, 0.18]
Total (95% CI)			**3811**			**2071**	**100.0%**	**-0.14 [-0.23, -0.06]**

Heterogeneity: Tau² = 0.02; Chi² = 41.79, df = 20 (P = 0.003); I² = 52%
Test for overall effect: Z = 3.41 (P = 0.0007)



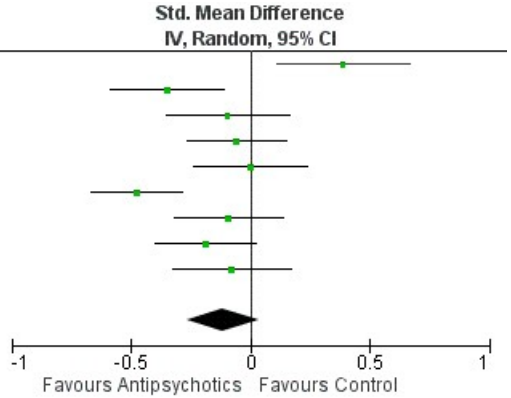
Footnotes
(1) 1. gen AP: Haloperidol.
(2) 1. gen AP: Pimavanserin. SD er estimeret fra konfidensinterval.
(3) SD er estimeret fra konfidensinterval.
(4) 1. gen AP: Haloperidol.

Forest plot of comparison: 1 Antipsychotics vs placebo, outcome: 1.6 Agitation - EoT.

Figure 8 (Analysis 1.7)

Study or Subgroup	Antipsychotics Mean	SD	Total	Placebo Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
Allain 2000 (1)	6.75	5.46	99	4.71	5.01	101	10.0%	0.39 [0.11, 0.67]
Brodaty 2003 (2)	-6.33	11.76	141	-2.34	11.04	138	11.0%	-0.35 [-0.59, -0.11]
DeDeyn 1999	-3.33	11.15	115	-2.34	9.29	114	10.5%	-0.10 [-0.36, 0.16]
Grossberg 2020a	-11.6879	12.8071	272	-10.98	11.67	131	11.7%	-0.06 [-0.27, 0.15]
Grossberg 2020b	-8.04	8.36	131	-8.04	8.48	135	10.9%	0.00 [-0.24, 0.24]
Katz 1999	-3.8245	3.12	396	-2.32	3.26	143	12.1%	-0.48 [-0.67, -0.28]
Lee 2023	-12.1	12.3	216	-11	11.42	114	11.3%	-0.09 [-0.32, 0.14]
Mintzer 2007	-7.5796	11.7882	347	-5.31	12.8	115	11.7%	-0.19 [-0.40, 0.02]
Schneider 2006	-0.3088	1.5096	185	-0.2	0.97	94	10.7%	-0.08 [-0.33, 0.17]
Total (95% CI)			**1902**			**1085**	**100.0%**	**-0.12 [-0.27, 0.04]**

Heterogeneity: Tau² = 0.04; Chi² = 30.88, df = 8 (P = 0.0001); I² = 74%
Test for overall effect: Z = 1.49 (P = 0.14)



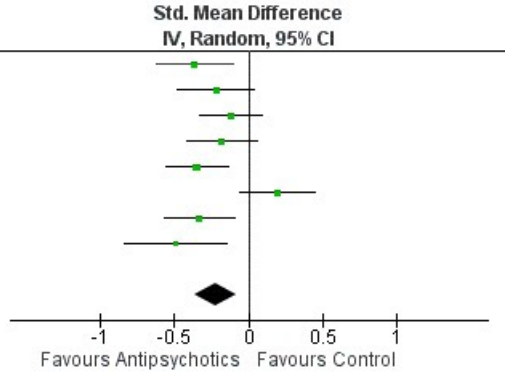
Footnotes
(1) 1. gen AP: Haloperidol.
(2) SD er estimeret fra konfidensinterval.

Forest plot of comparison: 1 Antipsychotics vs placebo, outcome: 1.7 Agitation - 4 uger.

Figure 9 (Analysis 1.8)

Study or Subgroup	Antipsychotics Mean	SD	Total	Placebo Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
Brodaty 2003	-8.6	12.44	119	-4.49	9.95	112	12.1%	-0.36 [-0.62, -0.10]
DeDeyn 1999	-8.3	14.37	115	-4.92	16.44	114	12.1%	-0.22 [-0.48, 0.04]
Grossberg 2020a	-19.6	15.3	272	-17.8	14.9	131	14.3%	-0.12 [-0.33, 0.09]
Grossberg 2020b	-18.9	13.73	131	-16.5	12.78	135	12.9%	-0.18 [-0.42, 0.06]
Katz 1999	-2.3	3.12	320	-1.2	3.26	120	14.2%	-0.35 [-0.56, -0.14]
Kennedy 2005	0.65	1.6	178	0.33	1.61	90	12.4%	0.20 [-0.06, 0.45]
Lee 2023	-22.6	16.2	192	-17.3	15.51	103	12.9%	-0.33 [-0.57, -0.09]
Schneider 2006 (1)	-0.6689	1.4989	103	0	0.97	47	9.0%	-0.49 [-0.84, -0.14]
Total (95% CI)			**1430**			**852**	**100.0%**	**-0.22 [-0.36, -0.09]**

Heterogeneity: Tau² = 0.02; Chi² = 17.13, df = 7 (P = 0.02); I² = 59%
Test for overall effect: Z = 3.17 (P = 0.001)



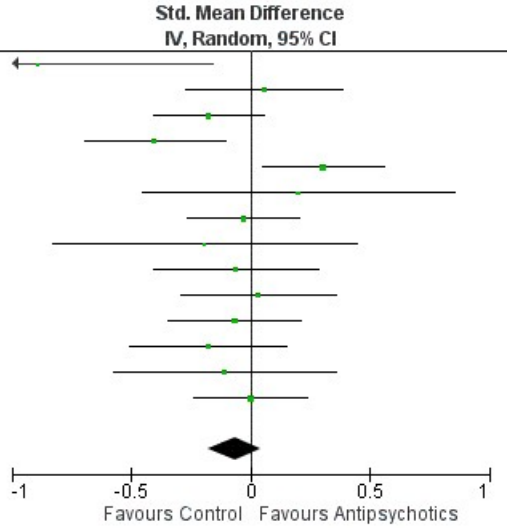
Footnotes
(1) BPRS Agitation, change

Forest plot of comparison: 1 Antipsychotics vs placebo, outcome: 1.8 Agitation - 12 uger.

Figure 10 (Analysis 1.9)

Study or Subgroup	Antipsychotics Mean	SD	Total	Placebo Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
Ballard 2005	-10.5	14.8	14	3.2	15.1	18	2.1%	-0.89 [-1.63, -0.16]
Ballard 2018 (1)	0.02	3.2741	67	-0.2	4.272	73	7.3%	0.06 [-0.27, 0.39]
Deberdt 2005	-1.05	3.75	362	-0.4	3.4	91	10.8%	-0.18 [-0.41, 0.05]
DeDeyn 2005 (2)	-0.81	3.5	94	0.53	3.1	86	8.4%	-0.40 [-0.70, -0.11]
Kennedy 2005	1.17	3.2	178	0.21	3.04	90	9.8%	0.30 [0.05, 0.56]
Kurlan 2007	18	6.2	19	16.6	7.5	17	2.6%	0.20 [-0.46, 0.86]
Mintzer 2007	-1	3.5	299	-0.9	3.1	92	10.7%	-0.03 [-0.26, 0.20]
Paleacu 2008	13.5	6.8	19	14.9	7.3	19	2.7%	-0.19 [-0.83, 0.44]
Schneider 2006	0.5	3.6	104	0.7	2.7	47	6.9%	-0.06 [-0.40, 0.29]
Street 2000	-0.2	3.5	159	-0.3	2.2	47	7.5%	0.03 [-0.29, 0.36]
Streim 2008	-0.77	2.99	106	-0.57	3.17	93	9.0%	-0.06 [-0.34, 0.21]
Tariot 2006	-1.58	2.98	69	-0.9	4.42	72	7.3%	-0.18 [-0.51, 0.15]
Teri 2000	-0.61	2.69	34	-0.28	3.35	36	4.5%	-0.11 [-0.58, 0.36]
Zhong 2007	0	2.7	241	0	2	92	10.4%	0.00 [-0.24, 0.24]
Total (95% CI)			**1765**			**873**	**100.0%**	**-0.07 [-0.18, 0.05]**

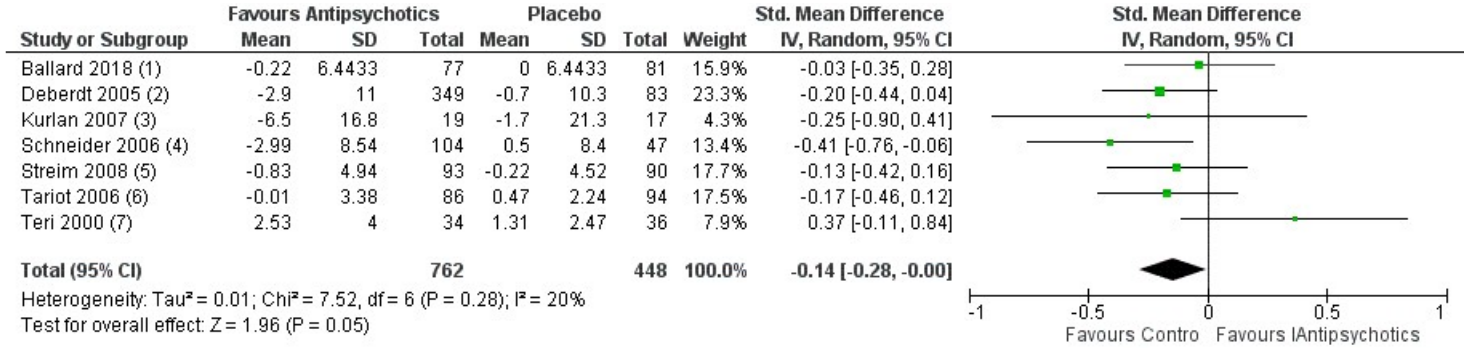
Heterogeneity: Tau² = 0.02; Chi² = 21.28, df = 13 (P = 0.07); I² = 39%
Test for overall effect: Z = 1.15 (P = 0.25)



Footnotes
(1) 1. gen AP: Pimavanserin. Aflæst fra figur.
(2) Brugt SD fra Mintzer 2007

Forest plot of comparison: 1 Antipsychotics vs placebo, outcome: 1.9 Cognition - EoT.

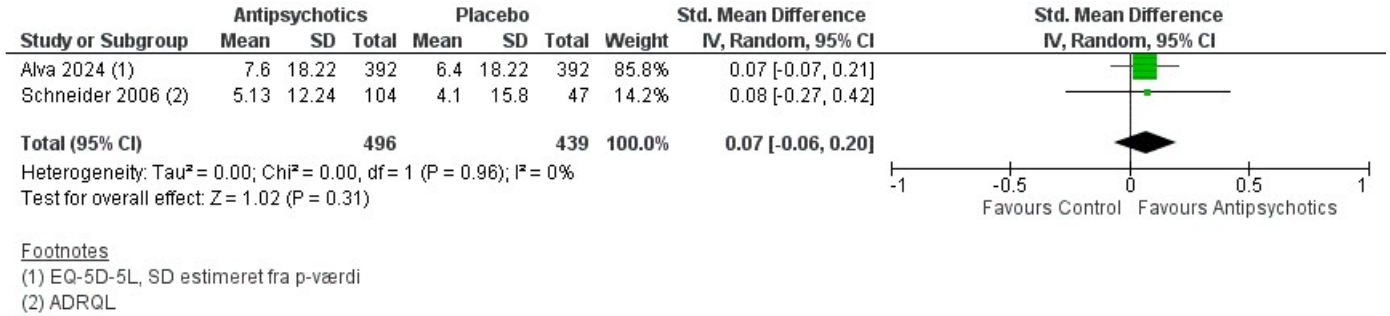
Figure 11 (Analysis 1.10)



Footnotes
(1) ADCS-ADL. Mean difference, SD er estimeret fra konfidensinterval, højere=bedre
(2) PDS, lavere=bedre, change
(3) ADCS-ADL, højere=bedre
(4) ADCS-ADL, højere=bedre
(5) ADCS-ADL, højere=bedre, change
(6) Physical Self_maintainance Scale PSMS, højere=bedre
(7) Physical Self_maintainance Scale PSMS, højere=bedre

Forest plot of comparison: 1 Antipsychotics vs placebo, outcome: 1.10 Activity of Daily Living (ADL) - EoT.

Figure 12 (Analysis 1.11)



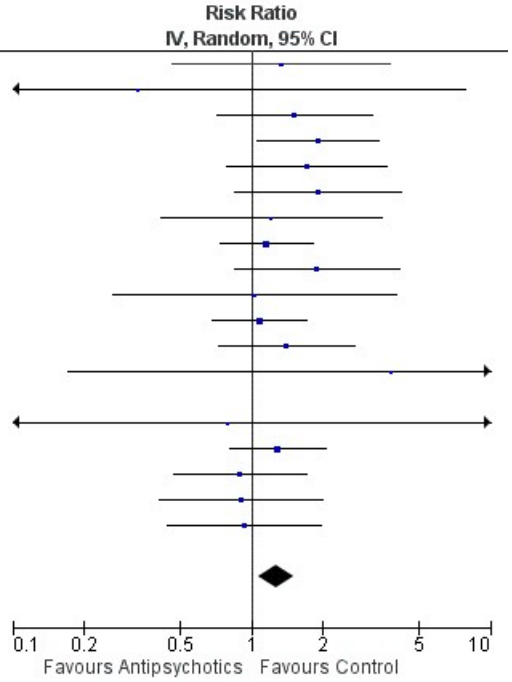
Footnotes
(1) EQ-5D-5L, SD estimeret fra p-værdi
(2) ADRQL

Forest plot of comparison: 1 Antipsychotics vs placebo, outcome: 1.11 Quality of life - EoT.

Figure 13 (Analysis 1.12)

Study or Subgroup	Antipsychotics Events	Total	Placebo Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Alva 2024 (1)	8	392	6	392	2.6%	1.33 [0.47, 3.81]
Ballard 2005 (2)	0	31	1	31	0.3%	0.33 [0.01, 7.88]
Ballard 2018 (3)	15	90	10	91	5.2%	1.52 [0.72, 3.20]
Brodaty 2003 (4)	28	167	15	170	8.3%	1.90 [1.05, 3.43]
DeDeyn 2005 (5)	16	106	9	102	4.9%	1.71 [0.79, 3.69]
Grossberg 2020a (6)	29	297	7	136	4.5%	1.90 [0.85, 4.22]
Grossberg 2020b (7)	7	132	6	137	2.5%	1.21 [0.42, 3.51]
Katz 1999 (8)	69	462	21	163	13.9%	1.16 [0.74, 1.83]
Kennedy 2005 (9)	26	178	7	90	4.6%	1.88 [0.85, 4.16]
Lee 2023 (10)	6	226	3	116	1.5%	1.03 [0.26, 4.03]
Mintzer 2006 (11)	33	235	31	238	13.9%	1.08 [0.68, 1.70]
Mintzer 2007 (12)	42	360	10	120	6.7%	1.40 [0.73, 2.70]
NCT00287742 2006 (13)	1	13	0	17	0.3%	3.86 [0.17, 87.65]
Paleacu 2008 (14)	0	20	0	20		Not estimable
RIS-INT-83 2003 (15)	1	10	1	8	0.4%	0.80 [0.06, 10.89]
Schneider 2006 (16)	53	279	21	142	13.4%	1.28 [0.81, 2.04]
Streim 2008 (17)	16	131	17	125	7.1%	0.90 [0.47, 1.70]
Tariot 2006 (18)	10	91	12	99	4.6%	0.91 [0.41, 2.00]
Zhong 2007 (19)	22	241	9	92	5.3%	0.93 [0.45, 1.95]
Total (95% CI)		**3461**		**2289**	**100.0%**	**1.27 [1.08, 1.51]**
Total events	382		186			

Heterogeneity: Tau² = 0.00; Chi² = 9.13, df = 17 (P = 0.94); I² = 0%
Test for overall effect: Z = 2.80 (P = 0.005)



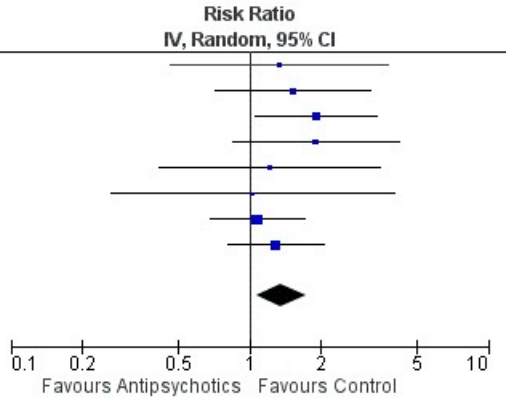
Footnotes
(1) 1. gen AP: Pimavanserin
(2) Quetiapine
(3) 1. gen AP: Haloperidol
(4) Risperidone
(5) Aripiprazole
(6) AP data stammer fra tre interventionsgrupper: Brexpiprazole 0.5 mg/day, Brexpiprazole 1 mg/day & Brexpiprazole 2 mg/day
(7) Brexpiprazole
(8) AP data stammer fra tre interventionsgrupper: Risperidone 0.5 mg, Risperidone 1 mg & Risperidone 2 mg
(9) Olanzapine
(10) Brexpiprazole
(11) Risperidone
(12) AP data stammer fra tre interventionsgrupper: Aripiprazole 2 mg/day, Aripiprazole 5 mg/day & Aripiprazole 10 mg/day
(13) Risperidone
(14) Quetiapine
(15) Risperidone
(16) tre 2. gen AP interventionsgrupper: Olanzapine, Quetiapine & Risperidone
(17) Aripiprazole
(18) Quetiapine
(19) Quetiapine 100 mg/day & Quetiapine 200 mg/day

Forest plot of comparison: 1 Antipsychotics vs placebo, outcome: 1.12 Serious adverse events - EoT.

Figure 14 (Analysis 1.13)

Study or Subgroup	Antipsychotics Events	Total	Placebo Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Alva 2024 (1)	8	392	6	392	5.0%	1.33 [0.47, 3.81]
Ballard 2018 (2)	15	90	10	91	10.0%	1.52 [0.72, 3.20]
Brodaty 2003 (3)	28	167	15	170	15.9%	1.90 [1.05, 3.43]
Grossberg 2020a (4)	29	297	7	136	8.7%	1.90 [0.85, 4.22]
Grossberg 2020b (5)	7	132	6	137	4.9%	1.21 [0.42, 3.51]
Lee 2023 (6)	6	226	3	116	3.0%	1.03 [0.26, 4.03]
Mintzer 2006 (7)	33	235	31	238	26.7%	1.08 [0.68, 1.70]
Schneider 2006 (8)	53	279	21	142	25.8%	1.28 [0.81, 2.04]
Total (95% CI)		**1818**		**1422**	**100.0%**	**1.36 [1.08, 1.72]**
Total events	179		99			

Heterogeneity: Tau² = 0.00; Chi² = 3.25, df = 7 (P = 0.86); I² = 0%
Test for overall effect: Z = 2.57 (P = 0.01)

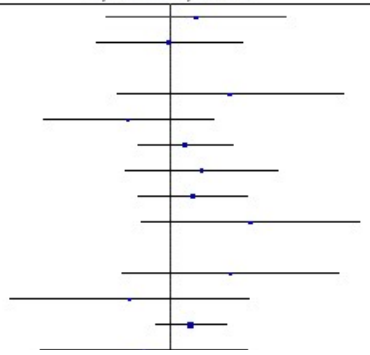


Footnotes
(1) 1. gen AP: Pimavanserin
(2) 1. gen AP: Haloperidol
(3) Risperidone
(4) AP data stammer fra tre interventionsgrupper: Brexpiprazole 0.5 mg/day, Brexpiprazole 1 mg/day & Brexpiprazole 2 mg/day
(5) Brexpiprazole
(6) Brexpiprazole
(7) Risperidone
(8) tre 2. gen AP interventionsgrupper: Olanzapine, Quetiapine & Risperidone

Forest plot of comparison: 1 Antipsychotics vs placebo, outcome: 1.13 Serious adverse events - 12 uger.

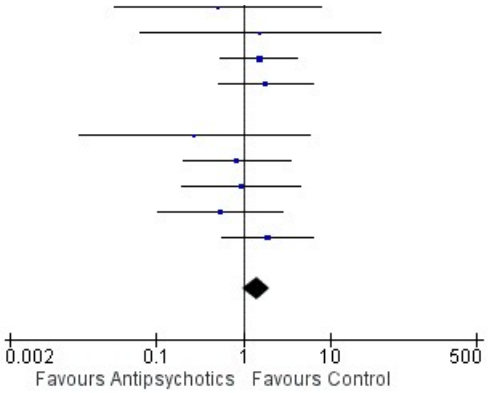
Figure 15 (Analysis 1.14)

Study or Subgroup	Antipsychotics Events	Total	Placebo Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Allain 2000 (1)	2	101	1	103	2.4%	2.04 [0.19, 22.14]
Alva 2024 (2)	2	392	2	392	3.5%	1.00 [0.14, 7.06]
Auchus 1997 (3)	0	6	0	6		Not estimable
Ballard 2005 (4)	2	31	0	31	1.5%	5.00 [0.25, 100.08]
Ballard 2018 (5)	1	90	3	91	2.7%	0.34 [0.04, 3.18]
Brodaty 2003 (6)	6	167	4	170	8.7%	1.53 [0.44, 5.31]
Deberdt 2005 (7)	10	400	1	94	3.2%	2.35 [0.30, 18.13]
DeDeyn 2004 (8)	15	520	2	129	6.3%	1.86 [0.43, 8.03]
DeDeyn 2005 (9)	4	106	0	102	1.6%	8.66 [0.47, 158.91]
Devanand 1998 (10)	0	40	0	20		Not estimable
Grossberg 2020a (11)	5	297	0	136	1.6%	5.06 [0.28, 90.81]
Grossberg 2020b (12)	0	133	1	137	1.3%	0.34 [0.01, 8.35]
Katz 1999 (13)	25	462	5	163	15.1%	1.76 [0.69, 4.53]



Kennedy 2005 (14)	1	178	1	90	1.8%	0.51 [0.03, 7.99]
Lee 2023 (15)	1	228	0	117	1.3%	1.55 [0.06, 37.66]
Mintzer 2006 (16)	9	235	6	238	13.0%	1.52 [0.55, 4.20]
Mintzer 2007 (17)	11	244	3	120	8.5%	1.80 [0.51, 6.34]
Paleacu 2008 (18)	0	20	0	20		Not estimable
RIS-INT-83 2003 (19)	0	10	1	8	1.4%	0.27 [0.01, 5.92]
Schneider 2006 (20)	5	279	3	142	6.7%	0.85 [0.21, 3.50]
Streim 2008 (21)	3	131	3	125	5.4%	0.95 [0.20, 4.64]
Tariot 2006 (22)	2	91	4	98	4.8%	0.54 [0.10, 2.87]
Zhong 2007 (23)	15	241	3	92	9.1%	1.91 [0.57, 6.44]
Total (95% CI)		**4402**		**2624**	**100.0%**	**1.41 [0.98, 2.03]**
Total events	119		43			

Heterogeneity: Tau² = 0.00; Chi² = 10.10, df = 19 (P = 0.95); I² = 0%
Test for overall effect: Z = 1.83 (P = 0.07)



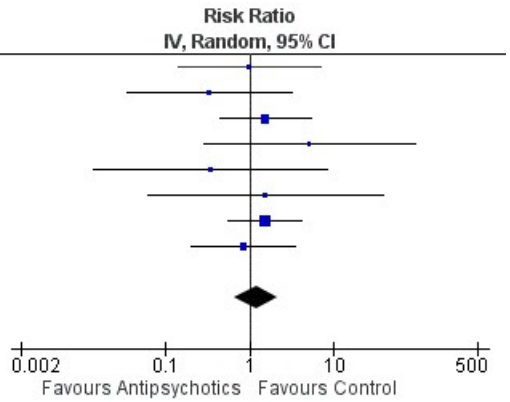
Footnotes
(1) 1. gen AP: Haloperidol.
(2) 1. gen AP: Pimavanserin.
(3) 1. gen AP: Haloperidol.
(4) Quetiapine
(5) 1. gen AP: Pimavanserin.
(6) Risperidone
(7) Olanzapine & Risperidone
(8) Olanzapine 1 mg, 2.5 mg, 5 mg & 7.5 mg
(9) Aripiprazole
(10) 1. gen AP: Haloperidol.
(11) Brexpiprazole 0.5 mg, 1 mg & 2 mg
(12) Brexpiprazole
(13) Risperidone 0.5 mg, 1 mg & 2 mg
(14) Olanzapine
(15) Brexpiprazole
(16) Risperidone
(17) Aripiprazole 2 mg/day, 5 mg/day & 10 mg/day
(18) Quetiapine
(19) Risperidone
(20) Olanzapine, Quetiapine & Risperidone
(21) Aripiprazole
(22) Quetiapine
(23) Quetiapine 100 mg & 200 mg

Forest plot of comparison: 1 Antipsychotics vs placebo, outcome: 1.14 Mortality - EoT.

Figure 16 (Analysis 1.15)

Study or Subgroup	Antipsychotics Events	Total	Placebo Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Alva 2024 (1)	2	392	2	392	9.1%	1.00 [0.14, 7.06]
Ballard 2018 (2)	1	90	3	91	6.9%	0.34 [0.04, 3.18]
Brodaty 2003 (3)	6	167	4	170	22.3%	1.53 [0.44, 5.31]
Grossberg 2020a (4)	5	297	0	136	4.2%	5.06 [0.28, 90.81]
Grossberg 2020b (5)	0	133	1	137	3.4%	0.34 [0.01, 8.35]
Lee 2023 (6)	1	228	0	117	3.4%	1.55 [0.06, 37.66]
Mintzer 2006 (7)	9	235	6	238	33.5%	1.52 [0.55, 4.20]
Schneider 2006 (8)	5	279	3	142	17.3%	0.85 [0.21, 3.50]
Total (95% CI)		**1821**		**1423**	**100.0%**	**1.19 [0.66, 2.15]**
Total events	29		19			

Heterogeneity: Tau² = 0.00; Chi² = 3.41, df = 7 (P = 0.84); I² = 0%
Test for overall effect: Z = 0.59 (P = 0.56)



Footnotes
(1) 1. gen AP: Pimavanserin.
(2) 1. gen AP: Pimavanserin.
(3) Risperidone
(4) Brexpiprazole 0.5 mg, 1 mg & 2 mg
(5) Brexpiprazole
(6) Brexpiprazole
(7) Risperidone
(8) Olanzapine, Quetiapine & Risperidone

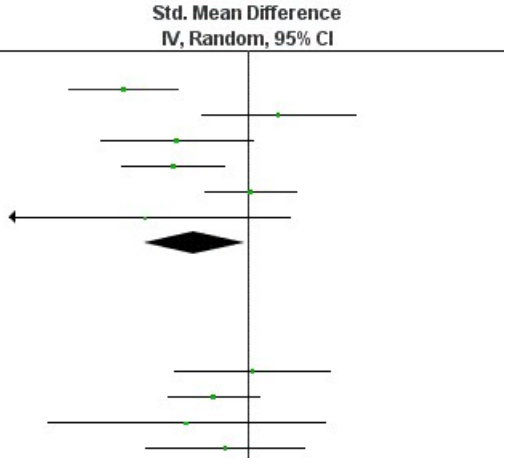
Forest plot of comparison: 1 Antipsychotics vs placebo, outcome: 1.15 Mortality - 12 uger.

Figure 17 (Analysis 2.1)

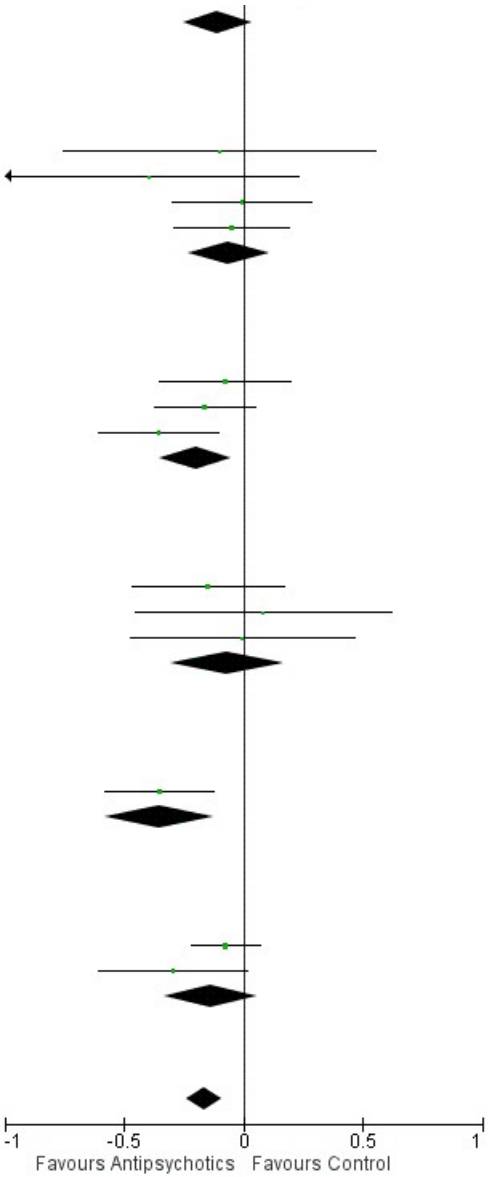
Study or Subgroup	Antipsychotics Mean	SD	Total	Placebo Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
2.1.1 Risperidon								
Brodaty 2003 (1)	-6.8	8.6301	149	-2.3	8.6301	152	6.0%	-0.52 [-0.75, -0.29]
Deberdt 2005 (2)	-9.7	19.5	190	-12.3	22	46	3.7%	0.13 [-0.19, 0.45]
DeDeyn 1999 (3)	-8.6	6.4	115	-6.2	10.6	57	3.8%	-0.30 [-0.62, 0.02]
Katz 1999 (4)	-7.4	7.24	317	-5.2	6.52	118	6.6%	-0.31 [-0.52, -0.10]
Mintzer 2006 (5)	-4.9	8.23	201	-5	8.27	212	7.3%	0.01 [-0.18, 0.21]
Schneider 2006 (6)	-16.4	15	32	-9	20.6	16	1.3%	-0.43 [-1.03, 0.18]
Subtotal (95% CI)			**1004**			**601**	**28.6%**	**-0.22 [-0.44, -0.01]**

Heterogeneity: Tau² = 0.05; Chi² = 18.00, df = 5 (P = 0.003); I² = 72%
Test for overall effect: Z = 2.04 (P = 0.04)

2.1.2 Olanzapin								
Deberdt 2005	-11.8	22.8	193	-12.3	22	45	3.7%	0.02 [-0.30, 0.35]
DeDeyn 2004 (7)	-16.1	15.9	513	-13.7	20.3	129	7.3%	-0.14 [-0.34, 0.05]
Schneider 2006 (8)	-14	18.7	40	-9	20.6	16	1.4%	-0.26 [-0.84, 0.33]
Street 2000 (9)	-5.7	8	155	-4.9	10.3	45	3.6%	-0.09 [-0.43, 0.24]



Subtotal (95% CI)			**901**			**235**	**15.9%**	**-0.11 [-0.25, 0.04]**
Heterogeneity: Tau² = 0.00; Chi² = 0.99, df = 3 (P = 0.80); I² = 0%								
Test for overall effect: Z = 1.47 (P = 0.14)								
2.1.3 Quetiapin								
Kurlan 2007 (10)	24.6	19.1	19	26.6	20.3	17	1.1%	-0.10 [-0.75, 0.56]
Schneider 2006 (11)	-16.6	18.3	31	-9	20.6	15	1.2%	-0.39 [-1.01, 0.23]
Tariot 2006 (12)	-4.14	6.04	86	-4.11	5.99	94	4.3%	-0.00 [-0.30, 0.29]
Zhong 2007 (13)	-9.3	23.2	234	-8.2	23	92	5.6%	-0.05 [-0.29, 0.19]
Subtotal (95% CI)			**370**			**218**	**12.2%**	**-0.06 [-0.23, 0.11]**
Heterogeneity: Tau² = 0.00; Chi² = 1.25, df = 3 (P = 0.74); I² = 0%								
Test for overall effect: Z = 0.71 (P = 0.48)								
2.1.4 Aripiprazol								
DeDeyn 2005 (14)	-11.2	18.81	103	-9.75	18.81	100	4.7%	-0.08 [-0.35, 0.20]
Mintzer 2007 (15)	-15.9	18.2	337	-13	16.4	117	6.6%	-0.16 [-0.37, 0.05]
Streim 2008 (16)	-16.43	17.32	128	-10.01	18.83	121	5.3%	-0.35 [-0.60, -0.10]
Subtotal (95% CI)			**568**			**338**	**16.7%**	**-0.20 [-0.35, -0.05]**
Heterogeneity: Tau² = 0.00; Chi² = 2.34, df = 2 (P = 0.31); I² = 15%								
Test for overall effect: Z = 2.59 (P = 0.010)								
2.1.5 Haloperidol								
DeDeyn 1999 (17)	-7.5	7.5	115	-6.2	10.6	57	3.8%	-0.15 [-0.47, 0.17]
Devanand 1998 (18)	50.48	9.58	40	49.65	11.25	20	1.6%	0.08 [-0.46, 0.62]
Teri 2000 (19)	-5.35	22.41	34	-5.28	24.36	36	2.0%	-0.00 [-0.47, 0.47]
Subtotal (95% CI)			**189**			**113**	**7.4%**	**-0.07 [-0.30, 0.17]**
Heterogeneity: Tau² = 0.00; Chi² = 0.62, df = 2 (P = 0.73); I² = 0%								
Test for overall effect: Z = 0.56 (P = 0.57)								
2.1.6 Brexpiprazol								
Lee 2023 (20)	-17.3	13.2	215	-12.7	12.64	111	5.9%	-0.35 [-0.58, -0.12]
Subtotal (95% CI)			**215**			**111**	**5.9%**	**-0.35 [-0.58, -0.12]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 3.00 (P = 0.003)								
2.1.7 Pimavanserin								
Alva 2024 (21)	3.14	2.68	361	3.34	2.68	358	9.5%	-0.07 [-0.22, 0.07]
Ballard 2018 (22)	-5.12	17.2842	76	0	17.2842	81	3.9%	-0.29 [-0.61, 0.02]
Subtotal (95% CI)			**437**			**439**	**13.3%**	**-0.14 [-0.33, 0.06]**
Heterogeneity: Tau² = 0.01; Chi² = 1.55, df = 1 (P = 0.21); I² = 35%								
Test for overall effect: Z = 1.39 (P = 0.17)								
Total (95% CI)			**3684**			**2055**	**100.0%**	**-0.16 [-0.24, -0.09]**
Heterogeneity: Tau² = 0.01; Chi² = 31.55, df = 22 (P = 0.09); I² = 30%								
Test for overall effect: Z = 4.53 (P < 0.00001)								
Test for subgroup differences: Chi² = 5.61, df = 6 (P = 0.47), I² = 0%								

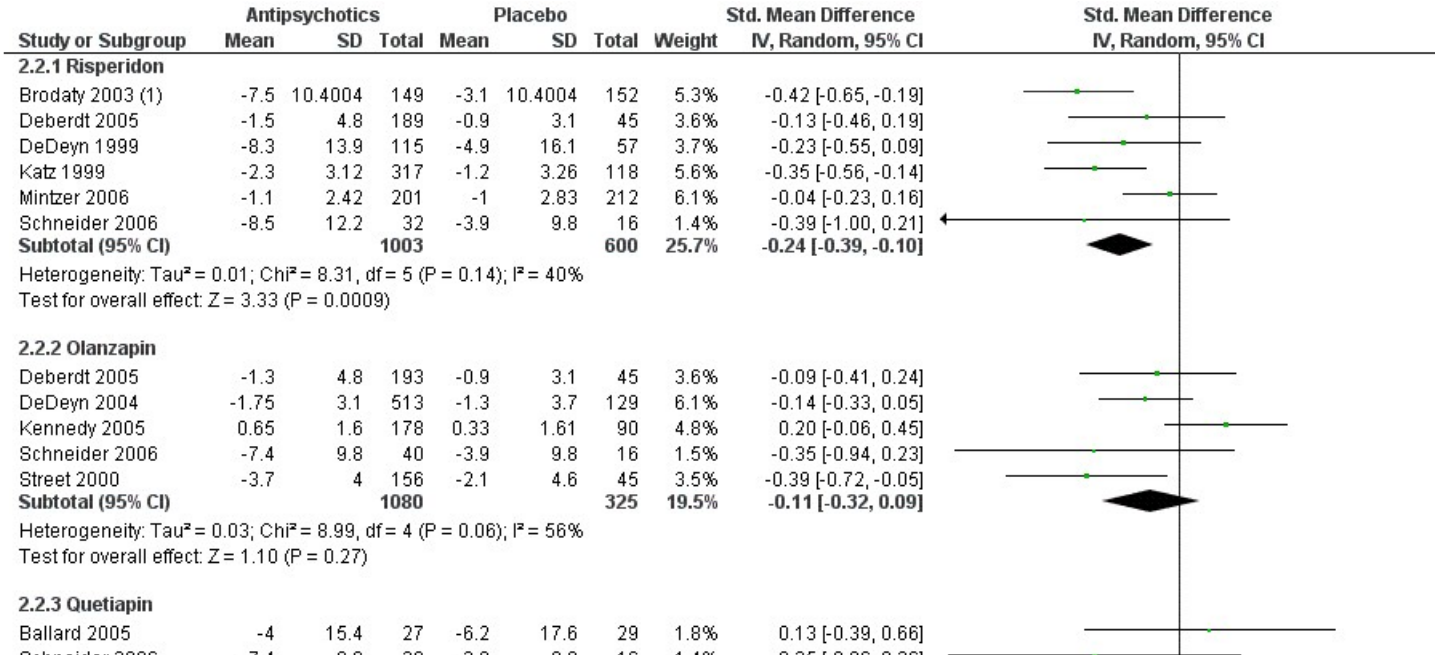


Footnotes
(1) CGI-S
(2) NPI-total
(3) Behave-AD

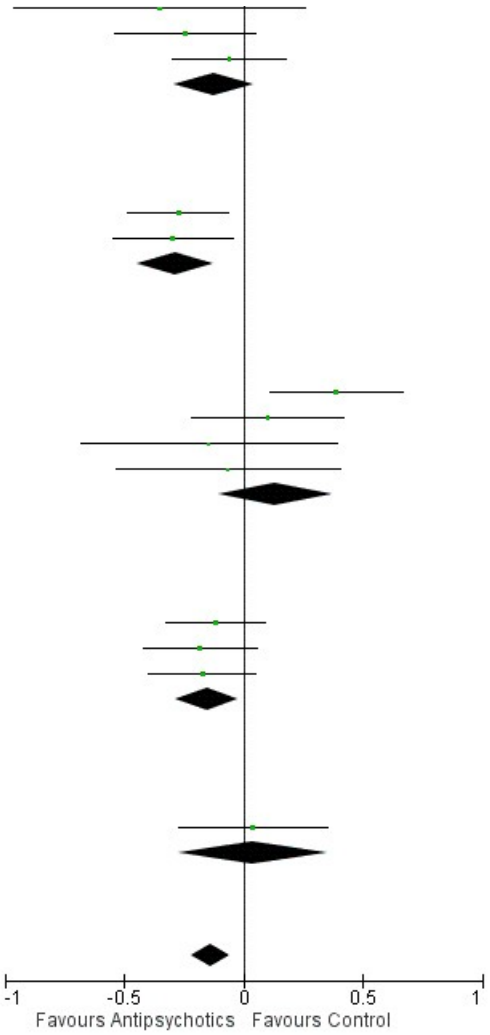
(4) Behave-AD
(5) Behave-AD
(6) NPI-NH
(7) NPI-NH
(8) NPI-NH
(9) NPI-NH
(10) NPI total
(11) NPI-NH
(12) NPI-NH
(13) NPI-NH
(14) NPI total
(15) NPI-NH
(16) NPI-NH
(17) Behave-AD
(18) BPRS
(19) BRSD
(20) NPI-NH
(21) CGI-I
(22) NPI-NH

Forest plot of comparison: 2 Antipsychotics vs placebo (subgruppe m. præparater), outcome: 2.1 BPSD.

Figure 18 (Analysis 2.2)



Schneider 2006	-7.4	9.8	30	-3.9	9.8	16	1.4%	-0.35 [-0.96, 0.26]
Tariot 2006	-2.63	4.99	86	-1.49	4.33	94	4.1%	-0.24 [-0.54, 0.05]
Zhong 2007	-10.1	22.1	234	-8.8	22.1	94	5.1%	-0.06 [-0.30, 0.18]
Subtotal (95% CI)			**377**			**233**	**12.4%**	**-0.12 [-0.29, 0.05]**
Heterogeneity: Tau² = 0.00; Chi² = 2.36, df = 3 (P = 0.50); I² = 0%								
Test for overall effect: Z = 1.42 (P = 0.15)								
2.2.4 Aripiprazol								
Mintzer 2007	-10.2	13.3	347	-6.5	14.3	115	5.6%	-0.27 [-0.48, -0.06]
Streim 2008	-10.25	12.85	126	-6.16	14.56	121	4.8%	-0.30 [-0.55, -0.05]
Subtotal (95% CI)			**473**			**236**	**10.5%**	**-0.28 [-0.44, -0.12]**
Heterogeneity: Tau² = 0.00; Chi² = 0.02, df = 1 (P = 0.88); I² = 0%								
Test for overall effect: Z = 3.43 (P = 0.0006)								
2.2.5 Haloperidol								
Allain 2000	6.75	5.46	99	4.71	5.01	101	4.3%	0.39 [0.11, 0.67]
DeDeyn 1999	-3.6	10.7	115	-4.9	16.1	57	3.7%	0.10 [-0.22, 0.42]
Devanand 1998	3.13	1.52	40	3.35	1.39	20	1.7%	-0.15 [-0.68, 0.39]
Teri 2000	-7.26	22.51	34	-5.94	18.5	36	2.2%	-0.06 [-0.53, 0.41]
Subtotal (95% CI)			**288**			**214**	**12.0%**	**0.13 [-0.11, 0.37]**
Heterogeneity: Tau² = 0.02; Chi² = 4.80, df = 3 (P = 0.19); I² = 37%								
Test for overall effect: Z = 1.09 (P = 0.28)								
2.2.6 Brexpiprazol								
Grossberg 2020a	-19.6	15.3	272	-17.8	14.9	131	5.7%	-0.12 [-0.33, 0.09]
Grossberg 2020b	-18.9	13.7	131	-16.5	12.8	135	5.0%	-0.18 [-0.42, 0.06]
Lee 2023	-16.2	13.65	225	-13.9	12.82	116	5.4%	-0.17 [-0.40, 0.05]
Subtotal (95% CI)			**628**			**382**	**16.1%**	**-0.15 [-0.28, -0.02]**
Heterogeneity: Tau² = 0.00; Chi² = 0.18, df = 2 (P = 0.91); I² = 0%								
Test for overall effect: Z = 2.34 (P = 0.02)								
2.2.7 Pimavanserin								
Ballard 2018 (2)	0.3	7.5011	77	0	7.5011	81	3.8%	0.04 [-0.27, 0.35]
Subtotal (95% CI)			**77**			**81**	**3.8%**	**0.04 [-0.27, 0.35]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.25 (P = 0.80)								
Total (95% CI)			**3926**			**2071**	**100.0%**	**-0.14 [-0.21, -0.06]**
Heterogeneity: Tau² = 0.02; Chi² = 44.03, df = 24 (P = 0.008); I² = 45%								
Test for overall effect: Z = 3.40 (P = 0.0007)								
Test for subgroup differences: Chi² = 11.24, df = 6 (P = 0.08), I² = 46.6%								



Footnotes

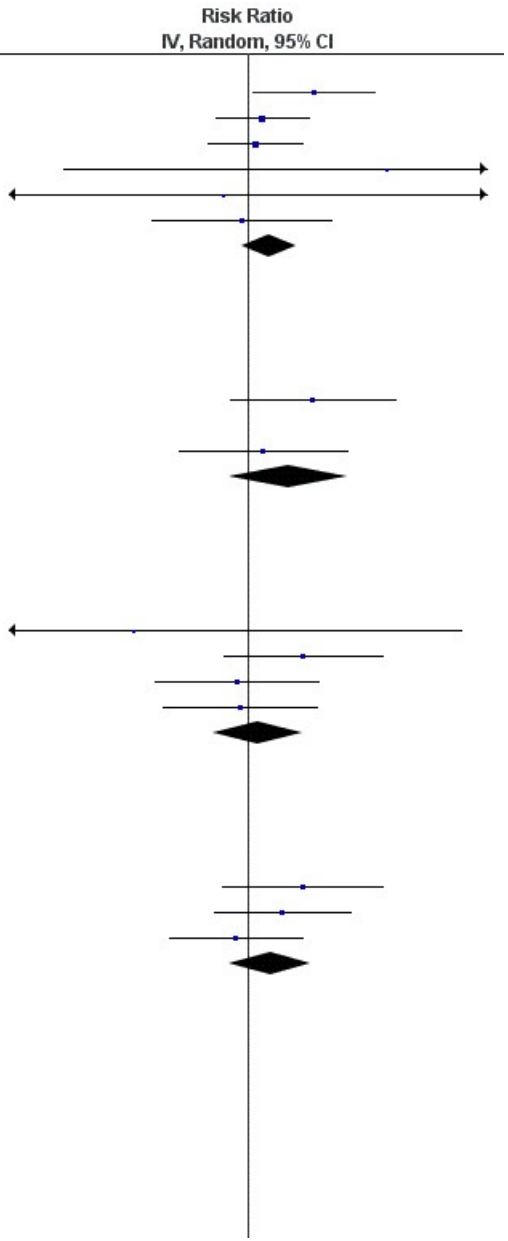
(1) SD er estimeret fra konfidensinterval.

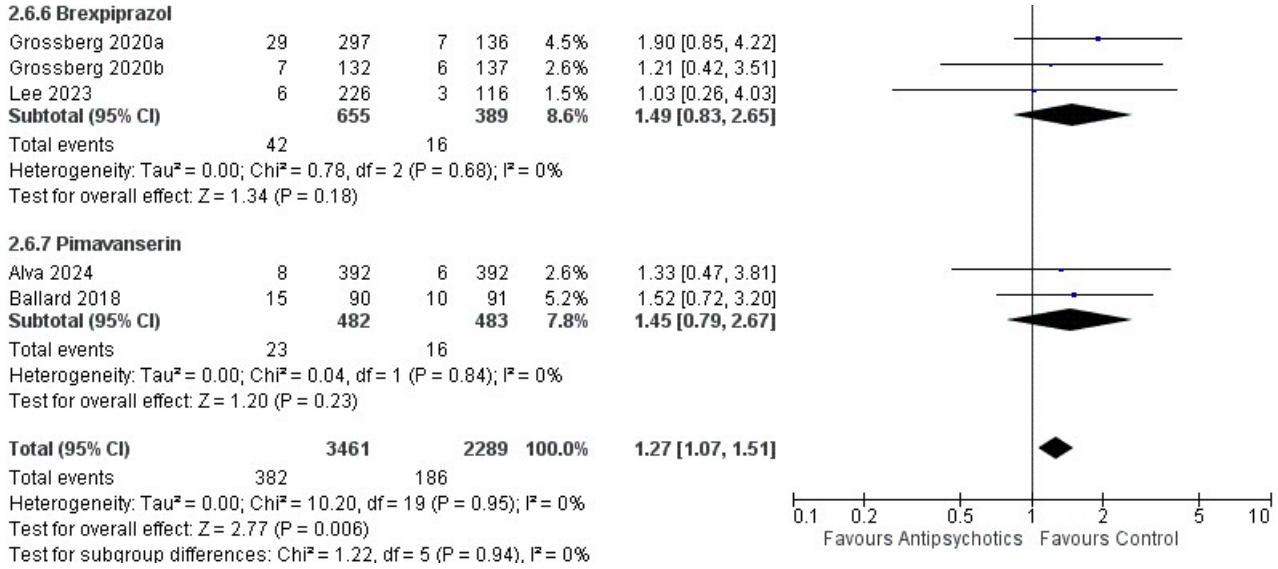
(2) SD er estimeret fra konfidensinterval.

Forest plot of comparison: 2 Antipsychotics vs placebo (subgruppe m. præparater), outcome: 2.2 Agitation.

Figure 19 (Analysis 2.6)

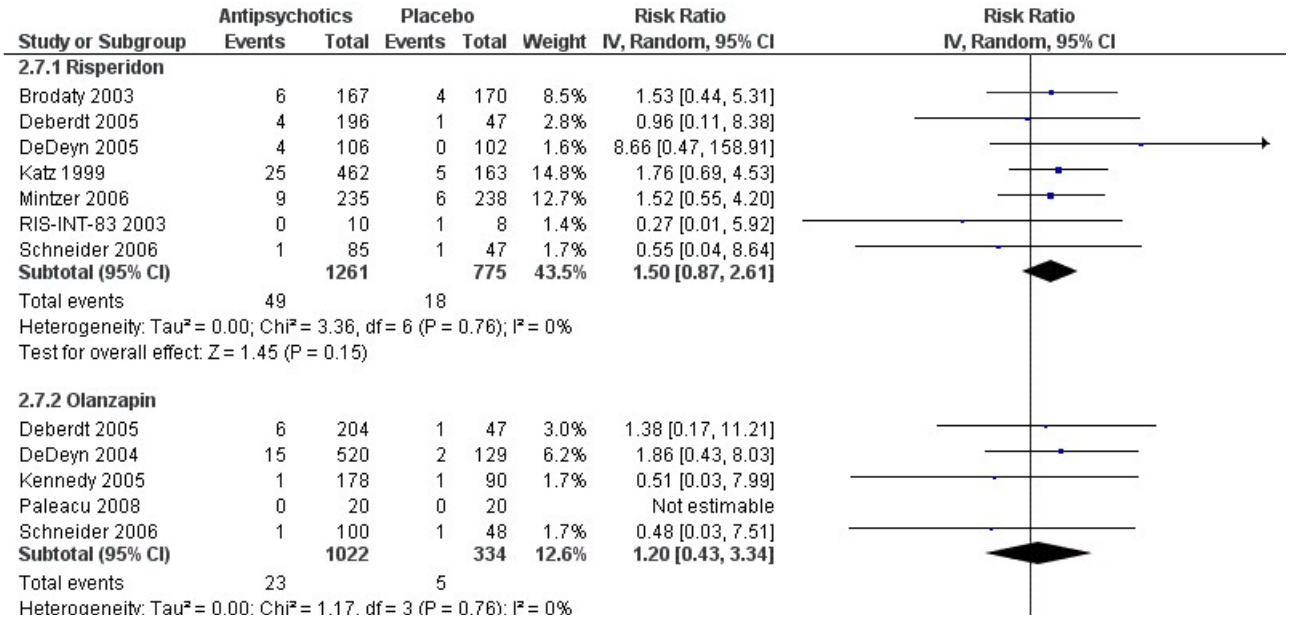
Study or Subgroup	Antipsychotics Events	Total	Placebo Events	Total	Weight	Risk Ratio IV, Random, 95% CI
2.6.1 Risperidon						
Brodaty 2003	28	167	15	170	8.3%	1.90 [1.05, 3.43]
Katz 1999	69	462	21	163	14.0%	1.16 [0.74, 1.83]
Mintzer 2006	33	235	31	238	13.9%	1.08 [0.68, 1.70]
NCT00287742 2006	1	13	0	17	0.3%	3.86 [0.17, 87.65]
RIS-INT-83 2003	1	10	1	8	0.4%	0.80 [0.06, 10.89]
Schneider 2006	12	85	7	47	3.9%	0.95 [0.40, 2.24]
Subtotal (95% CI)		**972**		**643**	**40.8%**	**1.23 [0.94, 1.61]**
Total events	144		75			
Heterogeneity: Tau² = 0.00; Chi² = 3.45, df = 5 (P = 0.63); I² = 0%						
Test for overall effect: Z = 1.54 (P = 0.12)						
2.6.2 Olanzapin						
Kennedy 2005	26	178	7	90	4.6%	1.88 [0.85, 4.16]
Paleacu 2008	0	20	0	20		Not estimable
Schneider 2006	17	100	7	48	4.4%	1.17 [0.52, 2.62]
Subtotal (95% CI)		**298**		**158**	**9.0%**	**1.49 [0.84, 2.62]**
Total events	43		14			
Heterogeneity: Tau² = 0.00; Chi² = 0.68, df = 1 (P = 0.41); I² = 0%						
Test for overall effect: Z = 1.37 (P = 0.17)						
2.6.3 Quetiapin						
Ballard 2005	0	31	1	31	0.3%	0.33 [0.01, 7.88]
Schneider 2006	24	94	7	47	4.9%	1.71 [0.80, 3.69]
Tariot 2006	10	91	12	99	4.6%	0.91 [0.41, 2.00]
Zhong 2007	22	241	9	92	5.3%	0.93 [0.45, 1.95]
Subtotal (95% CI)		**457**		**269**	**15.2%**	**1.11 [0.71, 1.71]**
Total events	56		29			
Heterogeneity: Tau² = 0.00; Chi² = 2.26, df = 3 (P = 0.52); I² = 0%						
Test for overall effect: Z = 0.45 (P = 0.65)						
2.6.4 Aripriprazol						
DeDeyn 2005	16	106	9	102	4.9%	1.71 [0.79, 3.69]
Mintzer 2007	42	360	10	120	6.7%	1.40 [0.73, 2.70]
Streim 2008	16	131	17	125	7.1%	0.90 [0.47, 1.70]
Subtotal (95% CI)		**597**		**347**	**18.7%**	**1.25 [0.84, 1.85]**
Total events	74		36			
Heterogeneity: Tau² = 0.00; Chi² = 1.79, df = 2 (P = 0.41); I² = 0%						
Test for overall effect: Z = 1.09 (P = 0.27)						
2.6.5 Haloperidol						
Subtotal (95% CI)		**0**		**0**		**Not estimable**
Total events	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						

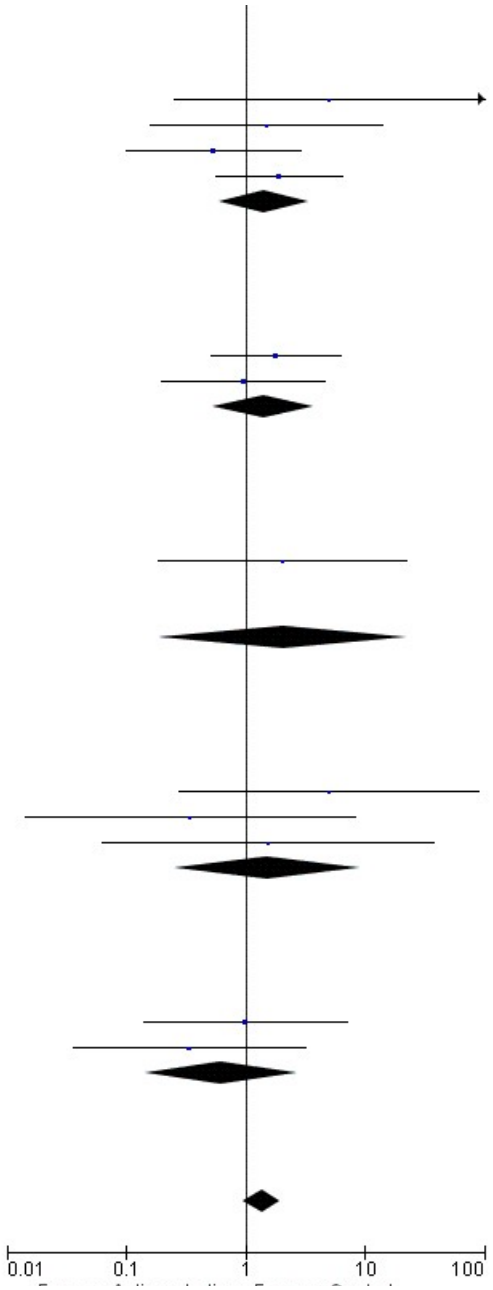




Forest plot of comparison: 2 Antipsychotics vs placebo (subgruppe m. præparater), outcome: 2.6 Serious adverse events.

Figure 20 (Analysis 2.7)





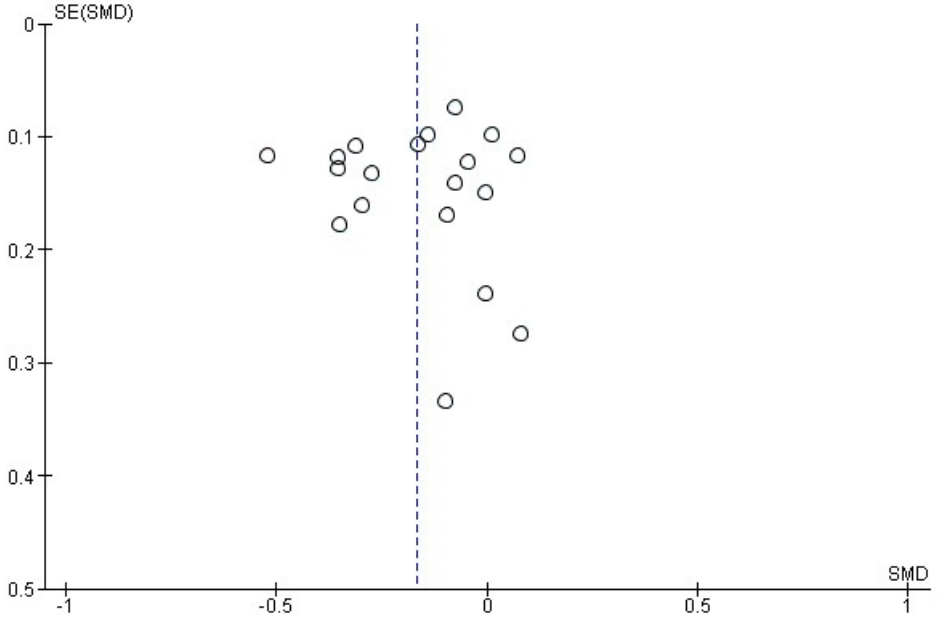
Test for overall effect: Z = 0.36 (P = 0.72)						
2.7.3 Quetiapin						
Ballard 2005	2	31	0	31	1.5%	5.00 [0.25, 100.08]
Schneider 2006	3	94	1	47	2.6%	1.50 [0.16, 14.03]
Tariot 2006	2	91	4	98	4.7%	0.54 [0.10, 2.87]
Zhong 2007	15	241	3	92	8.9%	1.91 [0.57, 6.44]
Subtotal (95% CI)		**457**		**268**	**17.7%**	**1.43 [0.60, 3.38]**
Total events	22		8			
Heterogeneity: Tau² = 0.00; Chi² = 2.20, df = 3 (P = 0.53); I² = 0%						
Test for overall effect: Z = 0.81 (P = 0.42)						
2.7.4 Aripriprazol						
Mintzer 2007	11	244	3	120	8.3%	1.80 [0.51, 6.34]
Streim 2008	3	131	3	125	5.3%	0.95 [0.20, 4.64]
Subtotal (95% CI)		**375**		**245**	**13.6%**	**1.41 [0.53, 3.77]**
Total events	14		6			
Heterogeneity: Tau² = 0.00; Chi² = 0.38, df = 1 (P = 0.54); I² = 0%						
Test for overall effect: Z = 0.68 (P = 0.49)						
2.7.5 Haloperidol						
Allain 2000	2	101	1	103	2.3%	2.04 [0.19, 22.14]
Auchus 1997	0	6	0	6		Not estimable
Devanand 1998	0	40	0	20		Not estimable
Subtotal (95% CI)		**147**		**129**	**2.3%**	**2.04 [0.19, 22.14]**
Total events	2		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.59 (P = 0.56)						
2.7.6 Brexpiprazol						
Grossberg 2020a	5	297	0	136	1.6%	5.06 [0.28, 90.81]
Grossberg 2020b	0	133	1	137	1.3%	0.34 [0.01, 8.35]
Lee 2023	1	228	0	117	1.3%	1.55 [0.06, 37.66]
Subtotal (95% CI)		**658**		**390**	**4.2%**	**1.52 [0.26, 8.99]**
Total events	6		1			
Heterogeneity: Tau² = 0.00; Chi² = 1.50, df = 2 (P = 0.47); I² = 0%						
Test for overall effect: Z = 0.46 (P = 0.65)						
2.7.7 Pimavanserin						
Alva 2024	2	392	2	392	3.4%	1.00 [0.14, 7.06]
Ballard 2018	1	90	3	91	2.6%	0.34 [0.04, 3.18]
Subtotal (95% CI)		**482**		**483**	**6.1%**	**0.63 [0.14, 2.73]**
Total events	3		5			
Heterogeneity: Tau² = 0.00; Chi² = 0.51, df = 1 (P = 0.47); I² = 0%						
Test for overall effect: Z = 0.62 (P = 0.53)						
Total (95% CI)		**4402**		**2624**	**100.0%**	**1.37 [0.95, 1.97]**
Total events	119		44			
Heterogeneity: Tau² = 0.00; Chi² = 10.51, df = 22 (P = 0.98); I² = 0%						
Test for overall effect: Z = 1.70 (P = 0.09)						

Favours Antipsychotics Favours Control

Test for subgroup differences: Chi² = 1.39, df = 6 (P = 0.97), I² = 0%

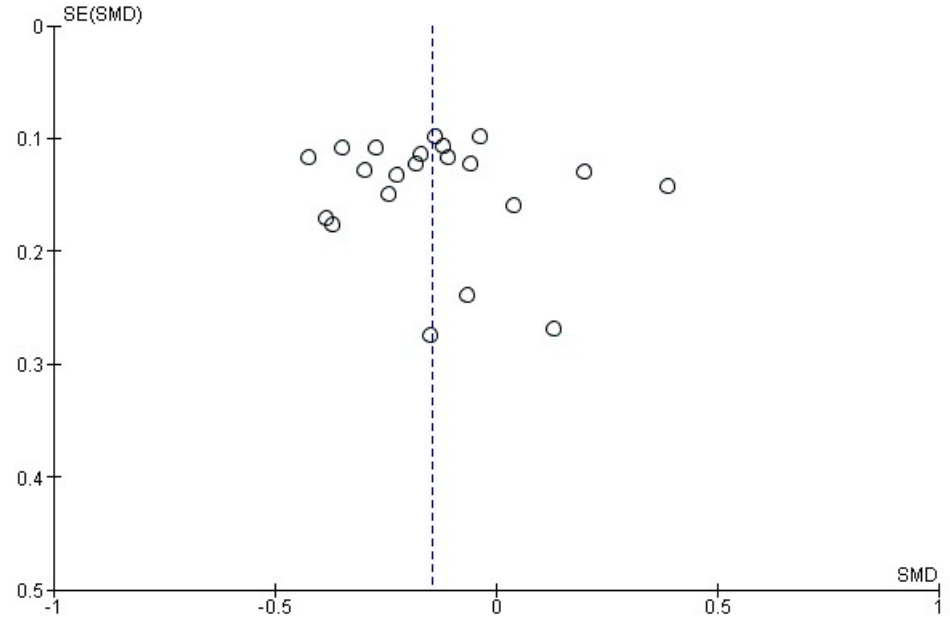
Forest plot of comparison: 2 Antipsychotics vs placebo (subgruppe m. præparater), outcome: 2.7 Mortality.

Figure 21 (Analysis 1.1)



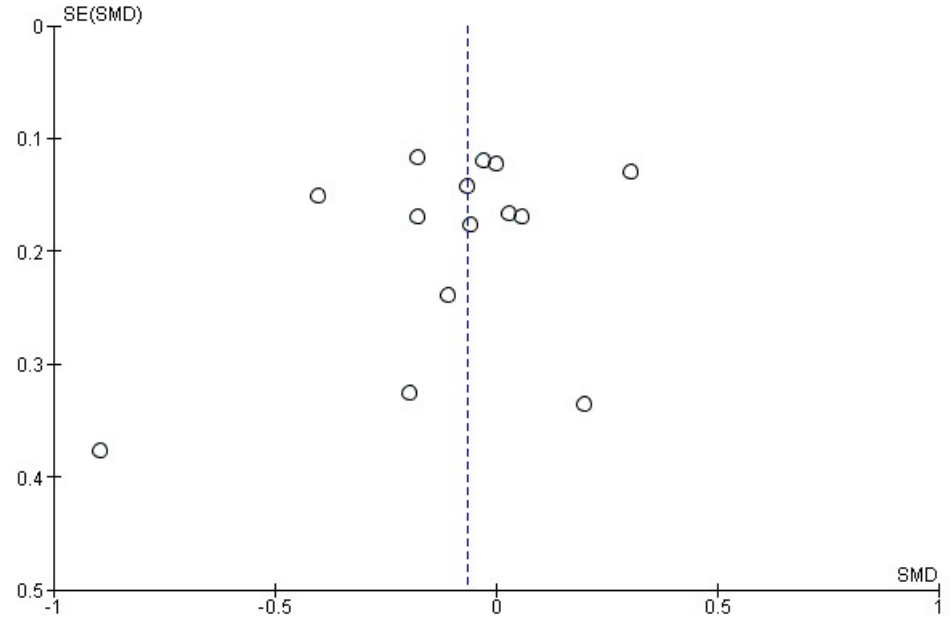
Funnel plot of comparison: 1 Antipsychotics vs placebo, outcome: 1.1 BPSD - EoT.

Figure 22 (Analysis 1.6)



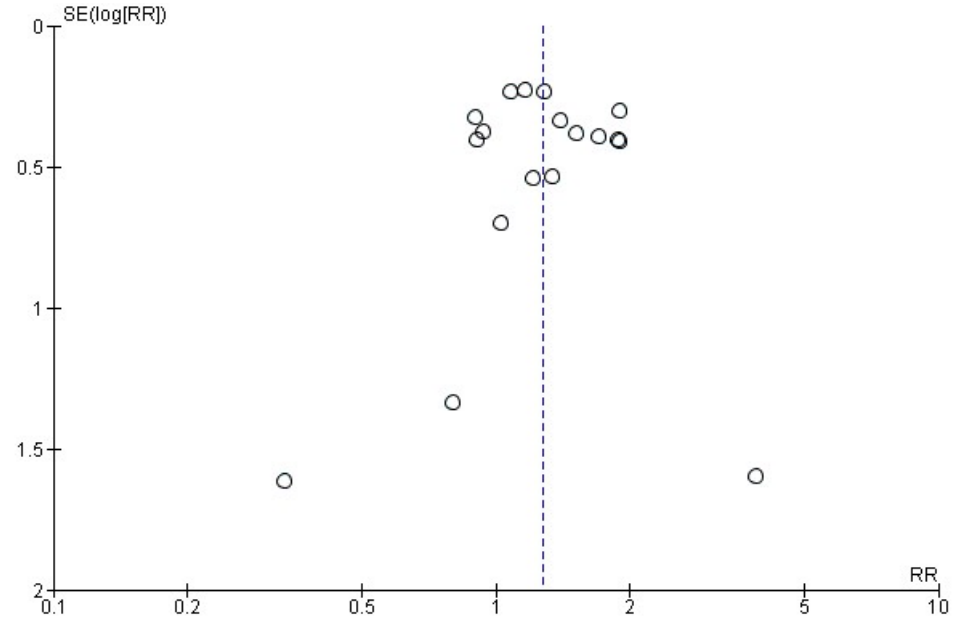
Funnel plot of comparison: 1 Antipsychotics vs placebo, outcome: 1.6 Agitation - EoT.

Figure 23 (Analysis 1.9)



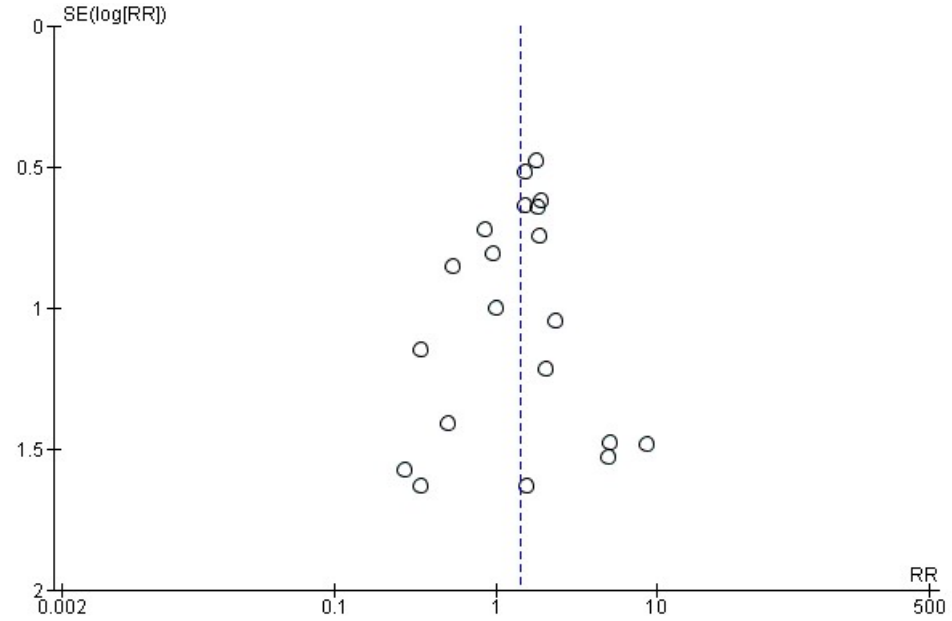
Funnel plot of comparison: 1 Antipsychotics vs placebo, outcome: 1.9 Cognition - EoT.

Figure 24 (Analysis 1.12)



Funnel plot of comparison: 1 Antipsychotics vs placebo, outcome: 1.12 Serious adverse events - EoT.

Figure 25 (Analysis 1.14)



Funnel plot of comparison: 1 Antipsychotics vs placebo, outcome: 1.14 Mortality - EoT.