NKA Demens PICO 3 antipsykotika vs benzodiazepin ved BPSD

Review information

Authors

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[1][Empty affiliation]

Citation example: [Empty name]. NKA Demens PICO 3 antipsykotika vs benzodiazepin ved BPSD. Cochrane Database of Systematic Reviews [Year], Issue [Issue].

Characteristics of studies

Characteristics of included studies

Coccaro 1990

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Antipsychotics, halperidol ● *Age in years, mean (range)*: 76.5 (58-96) ● *Females (%)*: 10/20 (50%) ● *Numbers (%) with BPSD*: 20/20 (100%) ● *Alzheimer´s disease, number (%)*: NI ● *Vascular demnetia, number (%)*: NI ● *Levy Body dementia, number (%)*: NI ● *Frontotemporal dementia, number (%)*: NI ● *Other types of dementia, number (%)*: NI ● *Nursing home recidients, number (%)*: 100% ● *Inpatients, number (%)*: 0% ● *Living in their own homes, number (%)*: 0% ● *Non farmacological/psychosocial interventions have been tried*: NI ● *Possible somatic reasons for BPSD have been examined/treated*: NI ● *Numbers with mild dementia*: NI ● *Numbers with moderate dementia*: NI ● *Numbers with severe dementia*: NI Benzodiazepines, oxazepam ● *Age in years, mean (range)*: 73.3 (59-97) ● *Females (%)*: 7/19 (37%) ● *Numbers (%) with BPSD*: 19/19 (100%) ● *Alzheimer´s disease, number (%)*: 19/19 (100%) ● *Vascular demnetia, number (%)*: NI ● *Levy Body dementia, number (%)*: NI ● *Frontotemporal dementia, number (%)*: NI ● *Other types of dementia, number (%)*: NI ● *Nursing home recidients, number (%)*: 100% ● *Inpatients, number (%)*: 0% ● *Living in their own homes, number (%)*: 0%

	● *Non farmacological/psychosocial interventions have been tried*: NI ● *Possible somatic reasons for BPSD have been examined/treated*: NI ● *Numbers with mild dementia*: NI ● *Numbers with moderate dementia*: NI ● *Numbers with severe dementia*: NI **Included criteria:** >55 years old. Met DSM-III criteria for dementia, and showed signs of agitation.Patients were considered agitated if they received a rating of at least 4 (moderate) on the tension or excitement items of the Brief Psychiatric Rating Scale (BPRS) or at least 3 (moderate) on one of the following items from the 40-item version of Alzheimer's Disease Assesment Scale: verbal aggressiveness, physical aggressiveness, pacing, fidgeting, and increased motor activity. These criteria were met on two successive ratings, separated by at least 1 week, and agreed on by two independt experienced clinical raters. **Excluded criteria:** Patients with a history of schizophrenia, convulsive disorder, Parkinson's disorder, delirium, and decompensated or poorly compensated cardiac, pulmonary, or renal diseases were excluded. **Pretreatment:** After screening, all psychotropic medication was discontinued for a 2 week single blind placebo wash out period
Interventions	**Intervention Characteristics** Antipsychotics, halperidol ● *Desciption*: After screening, all psychotropic medication was discontinued for a 2 week single blind placebo wash out period. p.o. halperidol up to 5 mg/day ● *Dose*: Halperidol (0,5 mg/capsules). Begining with one or two capsules, for the first two weeks the dose was adjustet daily to an optimal clinical response. Maximum dose was 5 mg. Halpridol. After the first two weeks the patients recieved a constant dose for a maximum of four additional weeks, the mean daily dose was 1.5 mg. ● *Duration*: 2 weeks wash out followed by up to 6 weeks of treatment ● *Time point for short time follow-up*: 8 weeks Benzodiazepines, oxazepan ● *Desciption*: Oral capsule ● *Dose*: Oxazepam(10 /capsules) Begining with one or two capsules, for the first two weeks the dose was adjustet daily to an optimal clinical response. Maximum dose was 60 mg. oxazepam. After the first two weeks the patients recieved a constant dose for a maximum of four additional weeks. The mean daily dose was 30 mg. ● *Duration*: ● *Time point for short time follow-up*: 8 weeks
Outcomes	Agitation/udadreagerende adfærd målt med modified Modified Alzheimer's Disease Assessment Scale (ADAS), mean final,SD ● **Outcome type**: Continuous Outcome ● **Reporting**: Fully reported ● **Scale**: Modified Alzheimer's Disease Assessment Scale (ADAS) ● **Range**: 0-25 ● **Unit of measure**: points ● **Direction**: Lower is better ● **Data value**: Endpoint BPSD (adfærdsændringer) målt med Brief Psychiatric Rating Scale (BPRS) mean final,SD ● **Outcome type**: Continuous Outcome ● **Reporting**: Fully reported ● **Scale**: Brief Psychiatric Rating Scale (BPRS) ● **Range**: 18-126 ● **Unit of measure**: points ● **Direction**: Lower is better ● **Data value**: Endpoint ADL målt med Physical and Self Maintenance Scale for activities of daily living, mean final, SD ● **Outcome type**: Continuous Outcome ● **Reporting**: Fully reported ● **Scale**: Physical and Self Maintenance Scale for activities of daily living ● **Range**:

	● **Unit of measure**: points ● **Direction**: Lower is better ● **Data value**: Endpoint
Identification	**Sponsorship source:** Alzheimer's Disease Research Center grant AG-05138 from the National Institute on Agigng.Medications and placebo capsules were provided by McNeil Pharmaceuticals (haloperidol), Wyeth Laboratories (oxazepam), and Parke-Davis (diphenhydramine and placebo). **Country:** USA **Setting:** Chronic care wards. Jewish Home and Hospital for the Aged, New York; the VA Medical Center, Montrose, N.Y.; the VA Medical Center, Lyons, N.J. **Authors name:** Emil F. Coccaro
Notes	

Risk of bias table

Covington 1975

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Antipsychotics, thioridazine ● *Age in years, mean (SD)*: 80 years approximately ● *Females (%)*: 18/20 (90%) ● *Numbers (%) with BPSD*: 20/20 (100%) ● *Alzheimer´s disease, number (%)*: NI ● *Vascular demnetia, number (%)*: NI ● *Levy Body dementia, number (%)*: NI ● *Frontotemporal dementia, number (%)*: NI ● *Other types of dementia, number (%)*: NI ● *Nursing home recidients, number (%)*: 20/20 (100%) ● *Inpatients, number (%)*: 0% ● *Living in their own homes, number (%)*: 0% ● *Non farmacological/psychosocial interventions have been tried*: NI ● *Possible somatic reasons for BPSD have been examined/treated*: NI ● *Numbers with mild dementia*: NI ● *Numbers with moderate dementia*: NI ● *Numbers with severe dementia*: NI Benzodiazepines, diazepam ● *Age in years, mean (SD)*: 80 years approximately ● *Females (%)*: 16/20 (80%) ● *Numbers (%) with BPSD*: 20/20 (100%) ● *Alzheimer´s disease, number (%)*: NI ● *Vascular demnetia, number (%)*: NI ● *Levy Body dementia, number (%)*: NI ● *Frontotemporal dementia, number (%)*: NI ● *Other types of dementia, number (%)*: NI ● *Nursing home recidients, number (%)*: 20/20 (100%) ● *Inpatients, number (%)*: 0% ● *Living in their own homes, number (%)*: 0% ● *Non farmacological/psychosocial interventions have been tried*: NI ● *Possible somatic reasons for BPSD have been examined/treated*: NI

	● *Numbers with mild dementia*: NI ● *Numbers with moderate dementia*: NI ● *Numbers with severe dementia*: NI **Included criteria: senile.** All had varying degrees of confusion, lack of mental alertness, disorientation for time or place, merory loss for recent events, emotional lability and difficultiy in coping with dayly living tasks such as bathing, dressing and eating. In addition they had at least some of the following: agitation, anxiety, tension, apprehension, depressed mood or sleep disturbances **Excluded criteria:** Psychotic. None had recieved major tranquilizers for at least two weeks or minor tranquilizers ofr at least 3 days before the study began
Interventions	**Intervention Characteristics** Antipsychotics, thioridazine ● *Desciption*: P.o. thioridazine, up to 200 mg. per day ● *Dose*: Up to 200 mg. thioridazine. Patients recieved between 10-80 mg per day, mean 32.9 mg ● *Duration*: 4 weeks ● *Time point for short time follow-up*: 1-4 weeks Benzodiazepines ● *Desciption*: P.o. diazepam, ip to 40 mg. per day ● *Dose*: Up to 40 mg. diazepam. Patients recived between 4-18 mg per day, mean 7,2 mg ● *Duration*: 4 weeks ● *Time point for short time follow-up*: 1-4 weeks
Outcomes	Agitation/udadreagerende adfærd målt med Modified Hamilton Anxiety Scale (agitation), mean change, no var ● **Outcome type**: Continuous Outcome ● **Reporting**: Partially reported, nor var ● **Scale**: Modified Hamilton Anxiety Scale (agitation) ● **Range**: 0-5 ● **Unit of measure**: points ● **Direction**: Lower is better ● **Data value**: Change BPSD (adfærdsændringer) målt med NOISE total, mean change, no var ● **Outcome type**: Continuous Outcome ● **Reporting**: Partially reported, nor var ● **Scale**: NOISE total ● **Range**: ● **Unit of measure**: points ● **Direction**: Lower is better ● **Data value**: Change Alvorlige hændelser, Serious adverse advents (SAE) ● **Outcome type**: Dichotomous Outcome ● **Reporting**: Fully reported ● **Unit of measure**: Antal personer med alvorlige hændelser ● **Direction**: Lower is better ● **Data value**: Endpoint
Identification	**Sponsorship source:** **Country:** USA **Setting:** Geriatric patients, *Nursing home recidients,* **Authors name:** Covington **Institution:** Kings Daugters and Sons Nursing Home, Meridian, Miss.

Notes	

Risk of bias table

Meehan 2002

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Antipsychotics, olanzapine 2.5 mg ● *Numbers (%) with BPSD*: 100% ● *Alzheimer´s disease, number (%)*: NI ● *Vascular demnetia, number (%)*: NI ● *Levy Body dementia, number (%)*: 0% ● *Frontotemporal dementia, number (%)*: 0% ● *Other types of dementia, number (%)*: NI ● *Nursing home recidients, number (%)*: NI ● *Inpatients, number (%)*: NI ● *Living in their own homes, number (%)*: 0% ● *Non farmacological/psychosocial interventions have been tried*: NI ● *Possible somatic reasons for BPSD have been examined/treated*: NI ● *Numbers with mild dementia*: NI ● *Numbers with moderate dementia*: NI ● *Numbers with severe dementia*: NI Benzodiazepines, Lorazepam ● *Numbers (%) with BPSD*: 100% ● *Alzheimer´s disease, number (%)*: NI ● *Vascular demnetia, number (%)*: NI ● *Levy Body dementia, number (%)*: 0% ● *Frontotemporal dementia, number (%)*: 0% ● *Other types of dementia, number (%)*: NI ● *Nursing home recidients, number (%)*: NI ● *Inpatients, number (%)*: NI ● *Living in their own homes, number (%)*: 0% ● *Non farmacological/psychosocial interventions have been tried*: NI ● *Possible somatic reasons for BPSD have been examined/treated*: NI ● *Numbers with mild dementia*: NI ● *Numbers with moderate dementia*: NI ● *Numbers with severe dementia*: NI Antipsychotics olanzapine 5.0 mg ● *Numbers (%) with BPSD*: 100% ● *Alzheimer´s disease, number (%)*: NI ● *Vascular demnetia, number (%)*: NI ● *Levy Body dementia, number (%)*: 0% ● *Frontotemporal dementia, number (%)*: 0% ● *Other types of dementia, number (%)*: NI ● *Nursing home recidients, number (%)*: NI ● *Inpatients, number (%)*: NI

	● *Living in their own homes, number (%)*: 0% ● *Non farmacological/psychosocial interventions have been tried*: NI ● *Possible somatic reasons for BPSD have been examined/treated*: NI ● *Numbers with mild dementia*: NI ● *Numbers with moderate dementia*: NI ● *Numbers with severe dementia*: NI Overall ● *Age in years, mean (SD)*: 77.6 (9.7) ● *Females (%)*: 166/272 (61%) ● *Numbers (%) with BPSD*: 272/272 (100%) ● *Alzheimer´s disease, number (%)*: NI ● *Vascular demnetia, number (%)*: NI ● *Levy Body dementia, number (%)*: 0% ● *Frontotemporal dementia, number (%)*: 0% ● *Other types of dementia, number (%)*: NI ● *Nursing home recidients, number (%)*: 63/272 (23%) ● *Inpatients, number (%)*: 209/272 (77%) ● *Living in their own homes, number (%)*: 0% ● *Non farmacological/psychosocial interventions have been tried*: NI ● *Possible somatic reasons for BPSD have been examined/treated*: NI ● *Numbers with mild dementia*: NI ● *Numbers with moderate dementia*: NI ● *Numbers with severe dementia*: NI **Included criteria:** Patients in this study were clinically agitated inpatients, hospitalized or nursing home residents, aged 55 or older, who met either National Institute of Neurological and Communicative Disorders and Stroke—Alzheimer's Disease and Related Disorders Association or DSM-IV (American Psychiatric Association 1994) criteria for possible or probable Alzheimer's disease (AD), vascular dementia, or a combination of both ("mixed dementia"). Patients were initially screened on the basis of chart reviews, staff interviews, and recommendations by the investigators and patients' family members. For study inclusion, patients must have scored 14 on the Excited Component of the Positive and Negative Syndrome Scale (PANSS; Kay et al. 1986); for description of Excited Component, see Assessments section), have at least one individual PANSS item score 4 on a scale of 1–7, and be diagnosed with clinically significant agitation for which treatment with a parenteral agent is indicated. **Excluded criteria:** Patients were excluded if they received benzodiazepines, antipsychotics, or anticholinergics within 4 h prior to the first injection of study drug, if they received psychostimulants or reserpine within one week prior to study drug administration, or an injectable depot neuroleptic within less than one dosing interval of study initiation, if they had been diagnosed with any serious neurological condition other than AD or vascular dementia that could contribute to psychosis or dementia, if they had laboratory or ECG abnormalities with clinical implications for the patient's participation in the study, or if they were judged to be at serious risk of suicide.
Interventions	**Intervention Characteristics** Antipsychotics, olanzapine 2.5 mg ● *Desciption*: Intramuscular olanzapine. Up to three injections with-in 20 hours. Injection 2, if deemedclinically necessary, was given at least 2 h after injection 1. Injection 1 and 2 was of 2.5 mg.The doses of injection 3, if deemed necessary, were 1.25 mg. Injection 3 was given at least 1h after injection 2 ● *Dose*: 2.5 mg ● *Duration*: 24 hours ● *Time point for short time follow-up*: After 24 hours Benzodiazepines, Lorazepam ● *Desciption*: Intramuscular Lorazepam. Up to three injections with-in 20 hours. Injection 2, if deemedclinically necessary, was given at least 2 h after injection 1. The doses of injection 3, if deemed necessary, were 0.5 mg. Inhectin 1 and 2 was of 1.0 mg. Injection 3 was given at least 1h after injection 2 ● *Dose*: 1.0 mg ● *Duration*: 24 hours ● *Time point for short time follow-up*: After 24 hours Antipsychotics olanzapine 5.o mg

	● *Desciption*: Intramuscular olanzapine. Up to three injections with-in three hours. Injection 2, if deemedclinically necessary, was given at least 2 h after injection 1. The doses of injection 3, if deemed necessary, were 2.5 mg. Injection 1 and 2 was of 5 mg. Injection 3 was given at least 1h after injection 2 ● *Dose*: 5.0 mg ● *Duration*: 24 hours ● *Time point for short time follow-up*: After 24 hours
Outcomes	Agitation/udadreagerende adfærd målt med CMAI, mean change, SD ● **Outcome type**: Continuous Outcome ● **Reporting**: Fully reported ● **Scale**: CMAI ● **Range**: 29-203 ● **Unit of measure**: points ● **Direction**: Lower is better ● **Data value**: Change BPSD (adfærdsændringer) målt med Brief Psychiatric Rating Scale (BPRS) mean final,SD ● **Outcome type**: Continuous Outcome ● **Reporting**: Fully reported ● **Scale**: Brief Psychiatric Rating Scale (BPRS) ● **Range**: 18-126 ● **Unit of measure**: points ● **Direction**: Lower is better ● **Data value**: Endpoint Somnolence ● **Outcome type**: Dichotomous Outcome ● **Reporting**: Fully reported ● **Unit of measure**: Antal personer med somnolence ● **Direction**: Lower is better ● **Data value**: Endpoint Mortalitet ● **Outcome type**: Dichotomous Outcome ● **Reporting**: Fully reported ● **Unit of measure**: Antal personer der dør ● **Direction**: Lower is better ● **Data value**: Endpoint
Identification	**Sponsorship source:** This work was sponsored by Eli Lilly and Company. **Country:** USA, russia and Romania **Setting:** Multicenter, 33 sites in USA, 2 in Russia and 3 in Rimania, Inpatients hospitalized or nursing home residents **Authors name:** Meehan et al. **Address:** Address correspondence to: Dr. Alan Breier, Lilly Research Laboratories, Eli Lilly and Company, Lilly Corporate Center, Indianapolis, IN 46285, Tel.: (317) 277-9222; Fax: (317) 433-5101
Notes	

Risk of bias table

Footnotes

Characteristics of excluded studies

Ancill 1991

Reason for exclusion	Wrong comparator

Footnotes

References to studies

Included studies

Coccaro 1990

Coccaro, E. F.; Kramer, E.; Zemishlany, Z.; Thorne, A.; Rice, C. M. 3rd; Giordani, B.; Duvvi, K.; Patel, B. M.; Torres, J.; Nora, R.. Pharmacologic treatment of noncognitive behavioral disturbances in elderly demented patients. The American Journal of Psychiatry 1990;147(12):1640-1645. [DOI: 10.1176/ajp.147.12.1640]

Covington 1975

Covington, J. S.. Alleviating agitation, apprehension, and related symptoms in geriatric patients: A double-blind comparison of a phenothiazine and a benzodiazepien. Southern medical journal 1975;68(6):719-724. [DOI: 10.1097/00007611-197506000-00015]

Meehan 2002

Meehan, Karena M.; Wang, Huei; David, Stacy R.; Nisivoccia, Jennifer R.; Jones, Barry; Beasley, Charles M. Jr; Feldman, Peter D.; Mintzer, Jacobo E.; Beckett, Louise M.; Breier, Alan. Comparison of rapidly acting intramuscular olanzapine, lorazepam, and placebo: a double-blind, randomized study in acutely agitated patients with dementia. Neuropsychopharmacology : official publication of the American College of Neuropsychopharmacology 2002;26(4):494-504. [DOI: 10.1016/S0893-133X(01)00365-7]

Excluded studies

Ancill 1991

Ancill, R. J.; Carlyle, W. W.; Liang, R. A.; Holliday, S. G.. Agitation in the demented elderly: a role for benzodiazepines? International clinical psychopharmacology 1991;6(3):141-146. [DOI: 10.1097/00004850-199100630-00002]

Data and analyses

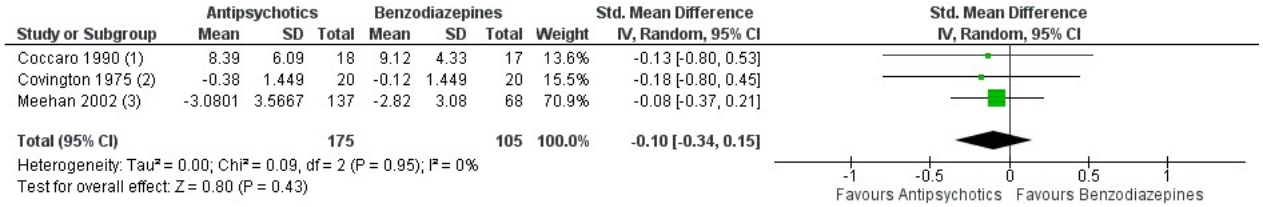
1 Antipsychotics vs Benzodiazepines

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
1.1 Agitation/out -reacting behaviour	3	280	Std. Mean Difference (IV, Random, 95% CI)	-0.10 [-0.34, 0.15]
1.2 BPSD (adfærdsændringer)	3	280	Std. Mean Difference (IV, Random, 95% CI)	-0.13 [-0.46, 0.20]
1.3 ADL	1	35	Mean Difference (IV, Fixed, 95% CI)	-5.79 [-14.74, 3.16]
1.4 SAE	1		Risk Difference (IV, Fixed, 95% CI)	No totals
1.5 Somnolence	1		Risk Ratio (IV, Fixed, 95% CI)	No totals

1.6 Mortality	1		Risk Difference (IV, Fixed, 95% CI)	No totals

Figures

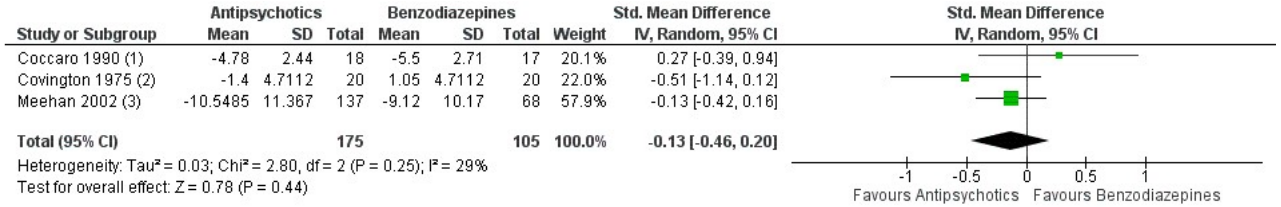
Figure 1 (Analysis 1.1)



Footnotes
(1) P.o haloperidol up to 5 mg. per day (mean 1.5 mg) vs p.o. oxazepam p.o. up to 60 mg. per day(mean 30 mg.)
(2) P.o. thioridazine, up to 200 mg. per day (mean 32.9 mg.) vs p.o diazepam up to 40 mg per day (mean 7,2 mg)
(3) i.m. olanzapine 2,5 mg/5.0 mg vs i.m. lorazepam 1.0 mg (up to 3 injections with in 24 hours (3. injection 1.25/2.5 mg olanzapine or 0,5 mg. lorazepam)

Forest plot of comparison: 1 Antipsychotics vs Benzodiazepines, outcome: 1.1 Agitation/out -reacting behaviour.

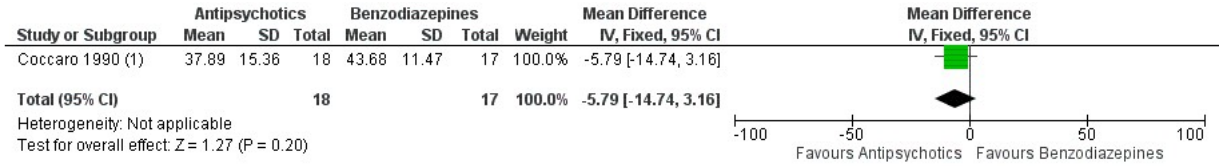
Figure 2 (Analysis 1.2)



Footnotes
(1) P.o haloperidol up to 5 mg. per day (mean 1.5 mg) vs p.o. oxazepam p.o. up to 60 mg. per day(mean 30 mg.)
(2) P.o. thioridazine, up to 200 mg. per day (mean 32.9 mg.) vs p.o diazepam up to 40 mg per day (mean 7,2 mg)
(3) i.m. olanzapine 2,5 mg/5 mg vs i.m. lorazepam 1.0 mg (up to 3 injections with in 24 hours (3. injection 1.25 mg/2.5 mg olanzapine or 0,5 mg. lorazepam)

Forest plot of comparison: 1 Antipsychotics vs Benzodiazepines, outcome: 1.2 BPSD (adfærdsændringer).

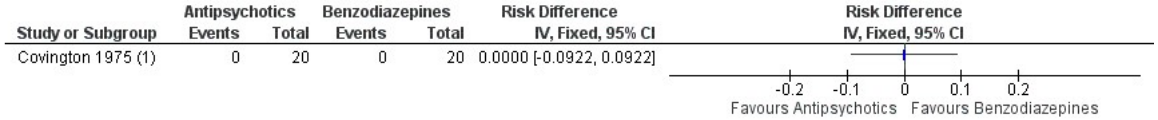
Figure 3 (Analysis 1.3)



Footnotes
(1) P.o haloperidol up to 5 mg. per day (mean 1.5 mg) vs p.o. oxazepam p.o. up to 60 mg. per day(mean 30 mg.)

Forest plot of comparison: 1 Antipsychotics vs Benzodiazepines, outcome: 1.3 ADL.

Figure 4 (Analysis 1.4)

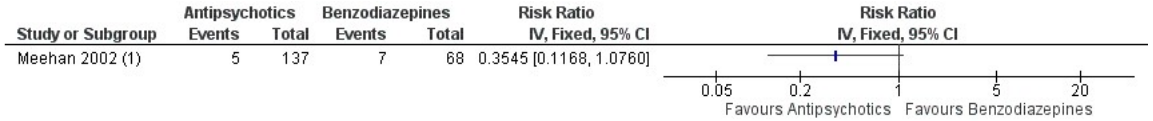


Footnotes

(1) P.o. thioridazine, up to 200 mg. per day (mean 32.9 mg.) vs p.o diazepam up to 40 mg per day (mean 7,2 mg)

Forest plot of comparison: 1 Antipsychotics vs Benzodiazepines, outcome: 1.4 SAE.

Figure 5 (Analysis 1.5)

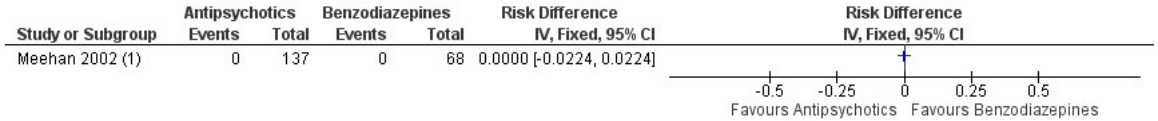


Footnotes

(1) i.m. olanzapine 2.5 mg/5.0 mg vs i.m. lorazepam 1.0 mg (up to 3 injections with in 24 hours (3. injection 1.25mg/2.5 mg olanzapine or 0,5 mg....

Forest plot of comparison: 1 Antipsychotics vs Benzodiazepines, outcome: 1.5 Somnolence.

Figure 6 (Analysis 1.6)



Footnotes

(1) i.m. olanzapine 2,5 mg/5 mg vs i.m. lorazepam 1.0 mg (up to 3 injections with in 24 hours (3. injection 1.25 mg/2.5 mg olanzapine or 0,5 mg. lorazepam)

Forest plot of comparison: 1 Antipsychotics vs Benzodiazepines, outcome: 1.6 Mortality.