NKR1_ADHD_PICO11_atomoxetine vs amfetamine

Characteristics of studies

Characteristics of included studies

Dittmann 2013

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Atomoxetine ● *Age*: 10.4 mean ● *% boys*: 76.9 Lisdexamfetamine ● *Age*: 10.9 mean ● *% boys*: 73.4 **Included criteria:** 1. An inadequate response to previous MPH treatment. This included, but was not limited to, one or more of the following:•The presence of some residual ADHD symptoms•Inadequate duration of action•Variable symptom control•If, based on the investigator's judgement, the patient maybenefit clinically from an alternative to MPH **Excluded criteria:** 1. Intolerable adverse events from previous MPH treatment2. Previous exposure to amfetamine or ATX3. Previous treatment with more than one MPH medication•This did not include patients who had received immediaterelease MPH for dose titration on a short-term basis (B4 weeks)provided that they experienced an adequate response4. Failure to respond to more than one previous course of MPHmedication•Failure to respond was defined as a worsening, no change orminimal improvement of symptoms5. Good control of ADHD symptoms with acceptable tolerabilityon current ADHD medication **Pretreatment:** No apparent differences at baseline
Interventions	**Intervention Characteristics** Atomoxetine ● *Description*: ATXwas available in 10-, 18-, 25-, 40- and 60-mg capsules. Allpatients in the ATX group who weighed less than 70 kgwere started on a daily dose of approximately 0.5 mg/kgbody weight, the final target daily dose being 1.2 mg/kg,with a maximum permitted daily dose of 1.4 mg/kg.Patients who weighed 70 kg or more initially received40 mg and, if required, were titrated to 80 mg and then to100 mg daily. Some patients treated with ATX would needtwo capsules to achieve the required dose (e.g. 80 and100 mg were achieved using two capsules). Therefore, allpatients weighing more than 64.5 kg who were titrated to ahigher dose were instructed to take two capsules (the sec-ond capsule could be either active drug or placebo, asappropriate) to maintain the double-blind study design ● *Length of intervention*: 9 weeks Lisdexamfetamine ● *Description*: LDX was provided in a single capsule of 30, 50 or70 mg, with patients initially receiving a 30-mg dose. ● *Length of intervention*: 9 weeks
Outcomes	*ADHD kernesymptomer, observatør/kliniker bedømt, SD* ● **Outcome type**: ContinuousOutcome *Alvorlige bivirkninger-totalt, n* ● **Outcome type**: DichotomousOutcome *Frafald pga. bivirkninger, n* ● **Outcome type**: DichotomousOutcome *Appetitforstyrrelser* ● **Outcome type**: DichotomousOutcome *Vægttab, n* ● **Outcome type**: DichotomousOutcome *Søvnforstyrrelser, n* ● **Outcome type**: DichotomousOutcome
Identification	**Sponsorship source:** **Country:** Germany **Setting: NA** **Comments:** ClinicalTrials.gov NCT01106430. **Authors name:** Ralf W. Dittmann **Institution:** Paediatric Psychopharmacology, Department of Child andAdolescent Psychiatry and Psychotherapy **Email:** ralf.dittmann@zi-mannheim.de **Address:** Paediatric Psychopharmacology, Department of Child andAdolescent Psychiatry and Psychotherapy, Central Instituteof Mental Health, Medical Faculty Mannheim, Universityof Heidelberg, 68072 Mannheim, German
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "a 4-week, stepwise, dose-optimization stage. Randomization of patients was stratified by country, and an automated interactive response system was used to generate the ran- dom (concealed) allocation sequence and assign partici- pants to study treatments; patients, caregivers and investigators were blinded to the treatment allocation. All study drugs were over-encapsulated so they appeared identical. The dose-optimization phase involved adjustment"
Allocation concealment (selection bias)	Low risk	Quote: "(concealed) allocation sequence and assign partici- pants to study treatments; patients, caregivers and investigators were blinded to the treatment allocation. All study drugs were over-encapsulated"
Blinding of participants and personnel (performance bias)	Low risk	Judgement Comment: Patients, caregivers and invedstigators are blinded
Blinding of outcome assessment (detection bias)	Low risk	Judgement Comment: Participants and investigators are blinded
Incomplete outcome data (attrition bias)	Low risk	Judgement Comment: Dropuouts have been accounted for
Selective reporting (reporting bias)	Low risk	Judgement Comment: Not all the secondary outcomes are reported in the study, however they are reported at clinicaltrials.gov
Other bias	Low risk	Judgement Comment: No other apparent sources of bias.

Footnotes

Summary of findings tables

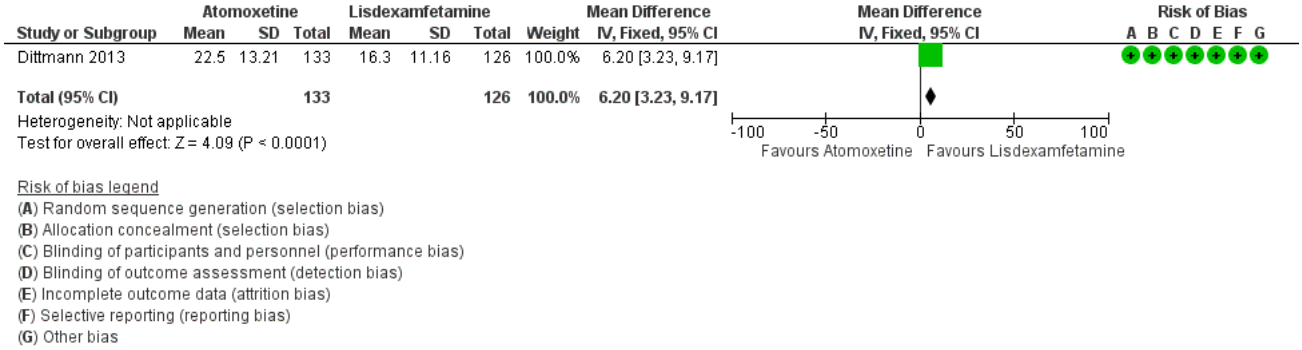
Data and analyses

1 Atomoxetine vs Lisdexamfetamine

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
1.1 ADHD core symptoms, observerrated, Final (ADHD-RS, total)	1	259	Mean Difference (IV, Fixed, 95% CI)	6.20 [3.23, 9.17]
1.2 Severe adverse events - total	1	262	Risk Ratio (IV, Fixed, 95% CI)	0.55 [0.16, 1.82]
1.3 Dropout due to adverse events	1	262	Risk Ratio (IV, Fixed, 95% CI)	1.19 [0.49, 2.93]
1.4 Decreased appetite	1	262	Risk Ratio (IV, Fixed, 95% CI)	0.41 [0.23, 0.72]
1.5 Decreased weight	1	262	Risk Ratio (IV, Fixed, 95% CI)	0.31 [0.15, 0.63]
1.6 Insomnia	1	262	Risk Ratio (IV, Fixed, 95% CI)	0.51 [0.22, 1.16]

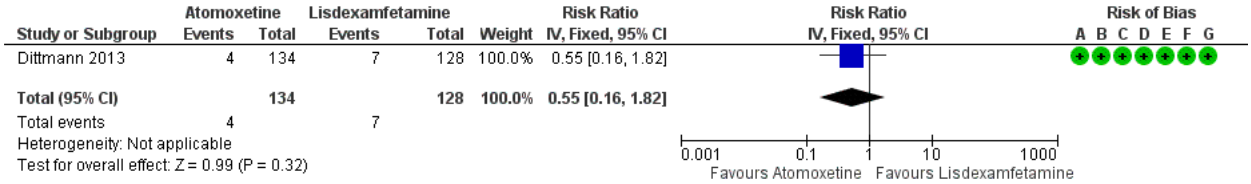
Figures

Figure 1 (Analysis 1.1)



Forest plot of comparison: 1 Atomoxetine vs Lisdexamfetamine, outcome: 1.1 ADHD core symptoms, observerrated, Final (ADHD-RS, total).

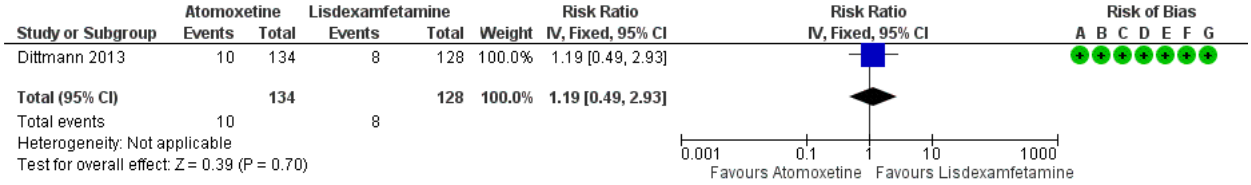
Figure 2 (Analysis 1.2)



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

Forest plot of comparison: 1 Atomoxetine vs Lisdexamfetamine, outcome: 1.2 Severe adverse events - total.

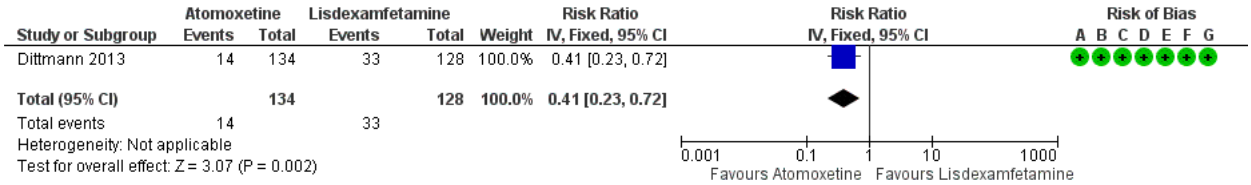
Figure 3 (Analysis 1.3)



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

Forest plot of comparison: 1 Atomoxetine vs Lisdexamfetamine, outcome: 1.3 Dropout due to adverse events.

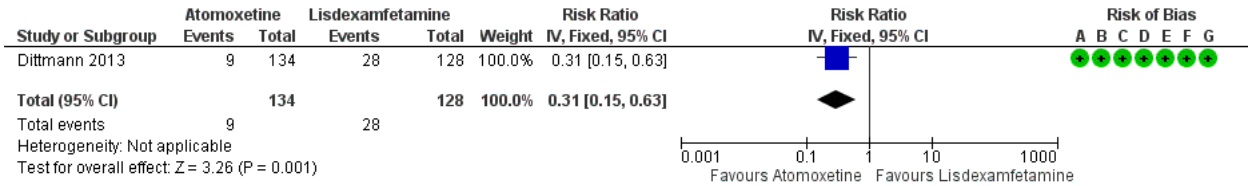
Figure 4 (Analysis 1.4)



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

Forest plot of comparison: 1 Atomoxetine vs Lisdexamfetamine, outcome: 1.4 Decreased appetite.

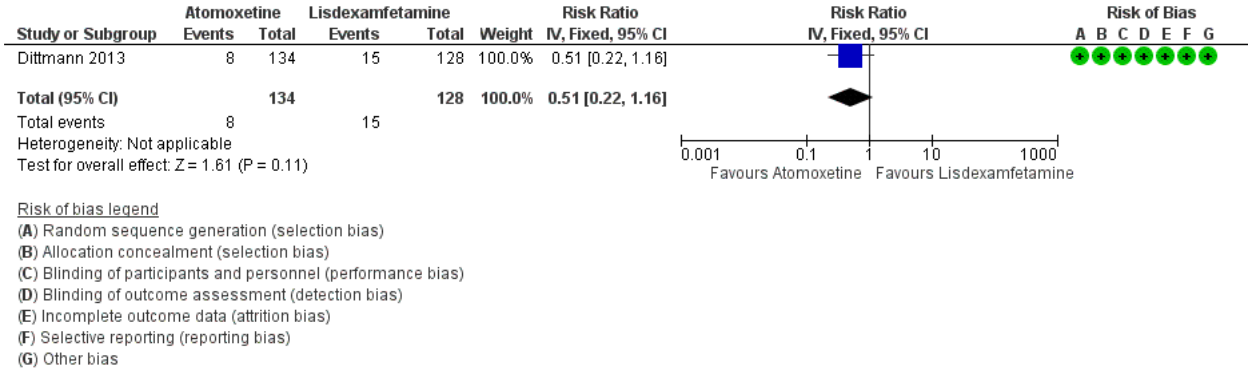
Figure 5 (Analysis 1.5)



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

Forest plot of comparison: 1 Atomoxetine vs Lisdexamfetamine, outcome: 1.5 Decreased weight.

Figure 6 (Analysis 1.6)



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

Forest plot of comparison: 1 Atomoxetine vs Lisdexamfetamine, outcome: 1.6 Insomnia.