Lisdexamfetamine versus placebo for ADHD in adults

Review information

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Dates

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Review First Published:	Not specified
Last Citation Issue:	Not specified

What's new

Date / Event	Description

History

Date / Event	Description

Characteristics of studies

Characteristics of included studies

Adler 2008

Methods	Randomized, double-blind, placebo-controlled, parallel-group 4-week with forced-dose escalation study. Randomly asssigned 2:2:2:1 to 30,50,70mg LDX or placebo
Participants	420 adults with ADHD aged 18-55 an required to meet 6 of the 9 DSM-IV-TR subtype criteria and to have a moderate or severe ADHD with ADHD-RS-IV score at least on >28. Normal ECG. Exclusion critria were comobid psychaitric diagnosis with significant symptoms that, in the judgement of investigator, migth preclude treatment with LDX. History of seizures. Medication that affect CNS or blood pressure or cadrdiac structural abnormality. History of hypertension. Pregnancy or lactation. Positive urine drugs.

Interventions	30, 50, 70 mg LDX and placebo in 4 weeks
Outcomes	ADHD core symptoms, functioning, adverse events.
Notes	ref ID 1523

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not descibed sufficient (2:2:2:1) not futher specified.
Allocation concealment (selection bias)	Unclear risk	Not descibed
Blinding of participants and personnel (performance bias)	Low risk	Double blind
Blinding of outcome assessment (detection bias)	Low risk	Double blind
Incomplete outcome data (attrition bias)	Low risk	Attrition descibed. Same for LDX and PBO
Selective reporting (reporting bias)	Low risk	None detected
Other bias	Low risk	None detected

Adler 2009 A

Methods	Randomized double-blind, placebo-controlled, parallel-group, forced dose, escalation study. (Randomly asssigned 2:2:2:1 to 30,50,70mg LDX or placebo. From Adler 2008 ref ID 1605).
Participants	420 adults with ADHD aged 18-55 with ADHD-RS-IV score at least on >28. excluded if comorbid psychiatric diagnosis with significant symptoms, hyperyension, significant abnomality on ECG, history of seizure or significant underweigth or morbbidly obese. Medication that affect CNS or blood pressure. History of drug dependence or substance abuse.
Interventions	4 weeks LDX 30, 50, 70mg. forced-dosed.
Outcomes	Sleep, adverse events
Notes	ref ID 1605

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not descibed
Allocation concealment (selection bias)	Unclear risk	Not descibed
Blinding of participants and personnel (performance bias)	Low risk	Double blind
Blinding of outcome assessment (detection bias)	Low risk	Double blind

Incomplete outcome data (attrition bias)	Low risk	Attrition descibed. Same for LDX and PBO.
Selective reporting (reporting bias)	Low risk	None detected
Other bias	Low risk	None detected

Adler 2009 B

Methods	Randomized, double-blind, multicenter, placebo-controlled parallel-group forced-dose titration study. Randomization was achived using block-randomization schedule with a block siza of 7 with a 2:2:2:1 allocation ratio of each of the 3 active doses versus palcebo.
Participants	Adults with ADHD, aged 18-55 years, with ADHD-RS-IV total score of >28 with moderate or severe symptoms. Normal ECG. exclusion criteria were a history of hypertension, known cardiac structrural abnomality. Any comobid psychiatric diagnosis with significant symptoms, that would contraindicate Lisdexamfetamine. History of seizure. or recent history of within the last 6 month of substance abuse. Taking any prohibed medication within 30 days of scenning visit including drugs CNS effects, affect blood pressure.
Interventions	30 or 50 or 70 mg LDX or placebo i 4 weeks
Outcomes	Cardiovaskular adverse events
Notes	ref ID 1522

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomization was achived using block-randomization schedule with a block siza of 7 with a 2:2:2:1 allocation ratio of each of the 3 active doses versus palcebo.
Allocation concealment (selection bias)	Unclear risk	Not descibed
Blinding of participants and personnel (performance bias)	Low risk	Double blinded
Blinding of outcome assessment (detection bias)	Low risk	Double blinded
Incomplete outcome data (attrition bias)	Low risk	Attribution descibed. Are nearly the same for LDX and PBO
Selective reporting (reporting bias)	Low risk	None detected
Other bias	Low risk	None detected

Adler 2013 A

Methods	Randomized, double-blind, multicenter, placebo-controlled parallel-group study. Randomized 1:1 blinded assignment of treament groups was acomplipliched though an interactive voice/web response system.
Participants	161 Adults with ADHD, aged 18-55 years, with ADHD-RS-IV total score of >28 and significant EFD assesses using a self-reported BRIEF-A GEC-T-score>65 at baseline. Exclusion criteria; adults who exhibed comorbid psychiatric conditions, controlled with prohibed medications or uncontrolled with significant symptoms, including axis 1 or 2 disorders including severe axid 1 or 2 disorders, cardiovaskular diseases, a history of moderately orr severe hypertension, ADHD that were velcontrolled on current ADHD therapy or a history of failure to respond to amphetamine therapy
Interventions	30, 50 70mg LDX or placebo i 10 weeks
Outcomes	ADHD core symptoms, function, advese events
Notes	Ref ID 1521

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Interactive voice web respons system was used for randomizing
Allocation concealment (selection bias)	Unclear risk	Not descibed
Blinding of participants and personnel (performance bias)	Low risk	Double blinded
Blinding of outcome assessment (detection bias)	Low risk	Double blinded
Incomplete outcome data (attrition bias)	Low risk	Minimal attriton eqaul attrition in both LDX and PBO
Selective reporting (reporting bias)	Low risk	None detected
Other bias	High risk	exclusion criteria: history of failure to respond to amphetamin therapy

Adler 2013 B

Methods	Randomized, double-blind, multicenter, placebo-controlled parallel-group study. Randomized 1:1 blinded assignment of treament groups was acomplipliched though an interactive voice/web response system.
Participants	161 Adults with ADHD, aged 18-55 years, with ADHD-RS-IV total score of >28 and significant EFD assesses using a self-reported BRIEF-A GEC-T-score>65 at baseline. Exclusion criteria; adults who exhibed comorbid psychiatric conditions, controlled or uncontrolled, including severe axid 1 or 2 disorders, cardiovaskular diseases, a history of moderately orr severe hypertension, current ADHD therapy or a history of failure to respond to amphetamine therapy

Interventions	10 weeks LDX 30 or 50 or 70mg as tolerated. Not specificed futher.
Outcomes	ADHD core symtomps. QoL. Adverse events
Notes	ref ID 1573

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Interactive voice web respons system was used for randomizing
Allocation concealment (selection bias)	Unclear risk	Not descibed
Blinding of participants and personnel (performance bias)	Low risk	Double blinded
Blinding of outcome assessment (detection bias)	Low risk	Double blinded
Incomplete outcome data (attrition bias)	Low risk	Minimal attrition and equal in both LDX and PBO group
Selective reporting (reporting bias)	Low risk	None detected
Other bias	High risk	excluded if ealier history of failure to respond to amphetamine

Kollins 2012

Methods	Randomized, double-blinded, placebo-controlled, parallel-group trial. Randomizing not futher descibed.
Participants	32 adults regular smokers with ADHD (DSM-IV-TR) between 18-50 years of age. Express interest in quiting smoking and smoke at leat 10 cigarettes/day. IQ >80. exclusion criteria: any other psychiatric condition, use of illicit drugs confimirmed by urine screen. Pragnancy. Taking psychoactive midication inclusiv for ADHD
Interventions	30, 50, 70 mg. LDX or placebo. in 28 days
Outcomes	ADHD core symptoms, safety
Notes	ref ID 1538

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not sufficient descibed
Allocation concealment (selection bias)	Unclear risk	Not descibed
Blinding of participants and personnel (performance bias)	Low risk	Double blinded

Blinding of outcome assessment (detection bias)	Low risk	Double blinded
Incomplete outcome data (attrition bias)	Low risk	Attrition descibed
Selective reporting (reporting bias)	High risk	There are missing data (self-rating ADHD core symptoms).
Other bias	Low risk	None detected

Mattingly 2013

Methods	Randomized placebo-controlled, multicenter, double-blind, parallel-group, forced dose escalation study. randomly assigned 2:2:2:1 to 30, 50, 70 mg LDX or placebo in 4 weeks.
Participants	Adults ≥ 18 to 55 years of age with a primary diagnosis of ADHD, based on the DSM-IV-TR criteria for the predominantly inattention subtype or the predominantly hyperactive/ impulsive and combined subtypes. Exclusion criteria included individuals with comorbid psychiatric disorders; history of seizures, hypertension, tic disorder; Tourette disorder; pregnant or lactating women; positive urine drug result at screening or baseline; current medication use that might confound the results of the study or increase risk to the participant; clinically significant ECG; and any concurrent chronic or acute illness, or unstable medical condition.
Interventions	Forced-dose excalation titration to an optimal dose on 30, 50, 70 mg LDX or placebo in 4 weeks.
Outcomes	Core symptoms
Notes	ref ID 1539

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not descibed
Allocation concealment (selection bias)	Unclear risk	Not descibed
Blinding of participants and personnel (performance bias)	Low risk	Double blinded
Blinding of outcome assessment (detection bias)	Low risk	Double blinded
Incomplete outcome data (attrition bias)	Low risk	Attrition descibed. Same for LDX and PBO.
Selective reporting (reporting bias)	Low risk	None detected
Other bias	Low risk	None detected

Wigal 2010

Methods	Randomized double-blind, placebo-controlled, 2 way crossover study. Randomized by a fixed-block randomization schedule to receive either their optimized dose of LDX or Placebo..
Participants	142 Adults (aged 18 to 55 years) with a primary diagnosis of ADHD based on DSM-IV-TR an d validated by comprehensive psychiatric evaluation that included semi-structured interview based on Adlut ADHD Clinical Diagnostic Scale version 1.2 (ASDS v1.2) and ADHD-RS-Iv score >28. Intellectual function >80. Excluded if comobid psychiatric diagnosis with significant symptoms. History of or percived risk for future suicide attempt. Recent history of substance abuse. Other medical conditions that would contraindicate psychostimulants. History of seizures, hypertension, cardiovascular disease. Lack of respond to previous amphetamine therapy. Concorminant CNS or blood pressure medication
Interventions	30, 50, 70mg LDX or placebo in 1 week. Then crossover 1 week more. The dose optimizing phase was opel label.
Outcomes	Core symptoms, functioning, advese events.
Notes	ref Id 1545

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Only descibed by fixed-block randomization schedule.
Allocation concealment (selection bias)	Unclear risk	Not descibed
Blinding of participants and personnel (performance bias)	Low risk	Double blinded
Blinding of outcome assessment (detection bias)	Low risk	Double blinded
Incomplete outcome data (attrition bias)	Low risk	Attrition equal for LDX and PBO in crossover fase. Seem to be due to natural disaster
Selective reporting (reporting bias)	Low risk	None detected
Other bias	High risk	Excluded if ealier lack of response to previous amphetamine therapy

Footnotes

Characteristics of excluded studies

Footnotes

Characteristics of studies awaiting classification

Footnotes

Characteristics of ongoing studies

Footnotes

Summary of findings tables

Additional tables

References to studies

Included studies

Adler 2008

[Other: Ref ID 1523]

[Empty]

Adler 2009 A

[Other: Ref ID 1605]

[Empty]

Adler 2009 B

[Other: ; Other: Ref ID 1522]

[Empty]

Adler 2013 A

[Other: ref ID 1521]

[Empty]

Adler 2013 B

[Other: ; Other: Ref ID 1573]

[Empty]

Kollins 2012

[Other: ref ID 1538]

[Empty]

Mattingly 2013

[Other: ref ID 1539]

[Empty]

Wigal 2010

[Other: Ref ID 1545]

[Empty]

Excluded studies

Studies awaiting classification

Ongoing studies

Other references

Additional references

Other published versions of this review

Data and analyses

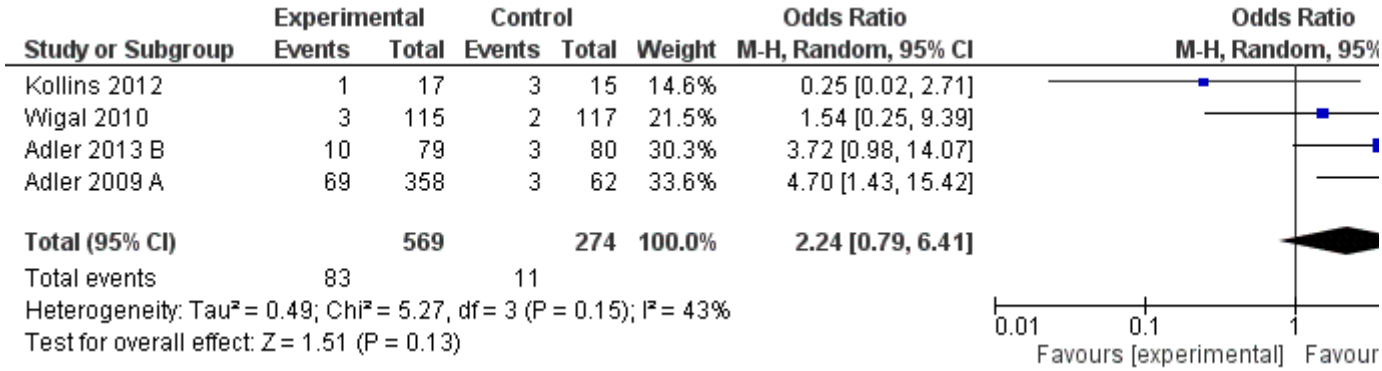
1 Lisdexamphetamine versus placebo

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
1.1 Insomnia	4	843	Odds Ratio (M-H, Random, 95% CI)	2.24 [0.79, 6.41]
1.2 Anorexia	2	579	Risk Ratio (M-H, Fixed, 95% CI)	7.46 [0.98, 56.70]
1.3 Increased heart rate	2	579	Odds Ratio (M-H, Fixed, 95% CI)	2.26 [0.51, 9.95]
1.4 Anxiety	3	684	Odds Ratio (M-H, Fixed, 95% CI)	4.27 [0.88, 20.60]
1.5 Irritability	3	423	Odds Ratio (M-H, Fixed, 95% CI)	2.16 [0.76, 6.14]
1.6 Decreased appetite	4	843	Odds Ratio (M-H, Fixed, 95% CI)	9.36 [4.35, 20.17]
1.7 Fatigue	4	843	Odds Ratio (M-H, Fixed, 95% CI)	0.50 [0.25, 0.97]
1.8 Headache	3	423	Odds Ratio (M-H, Fixed, 95% CI)	3.15 [1.37, 7.23]
1.9 Nausea	4	843	Odds Ratio (M-H, Fixed, 95% CI)	1.80 [0.70, 4.63]
1.10 Dry mouth	4	843	Odds Ratio (M-H, Fixed, 95% CI)	6.96 [3.33, 14.55]
1.11 Feeling jittery	3	567	Odds Ratio (M-H, Fixed, 95% CI)	11.52 [1.57, 84.73]

1.12 ADHD kernesymptomer	4	943	Std. Mean Difference (IV, Fixed, 95% CI)	-0.80 [-0.93, -0.66]
1.13 Pulse	2	703	Mean Difference (IV, Fixed, 95% CI)	3.65 [2.28, 5.03]
1.14 Systolic blood pressure	2	703	Mean Difference (IV, Fixed, 95% CI)	1.21 [-0.12, 2.54]
1.15 Diastolic blood pressure	2	703	Mean Difference (IV, Fixed, 95% CI)	0.04 [-1.06, 1.14]

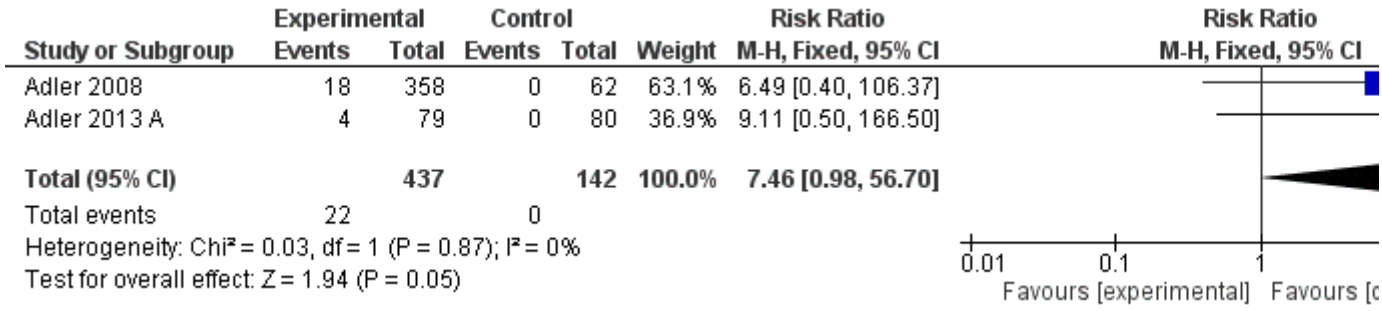
Figures

Figure 1 (Analysis 1.1)



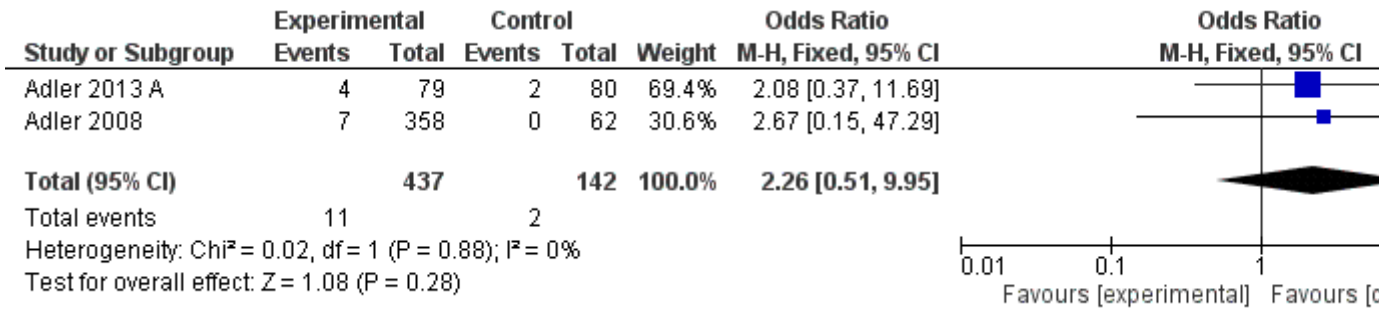
Forest plot of comparison: 1 Lisdexamphetamine versus placebo, outcome: 1.1 Insomnia.

Figure 2 (Analysis 1.2)



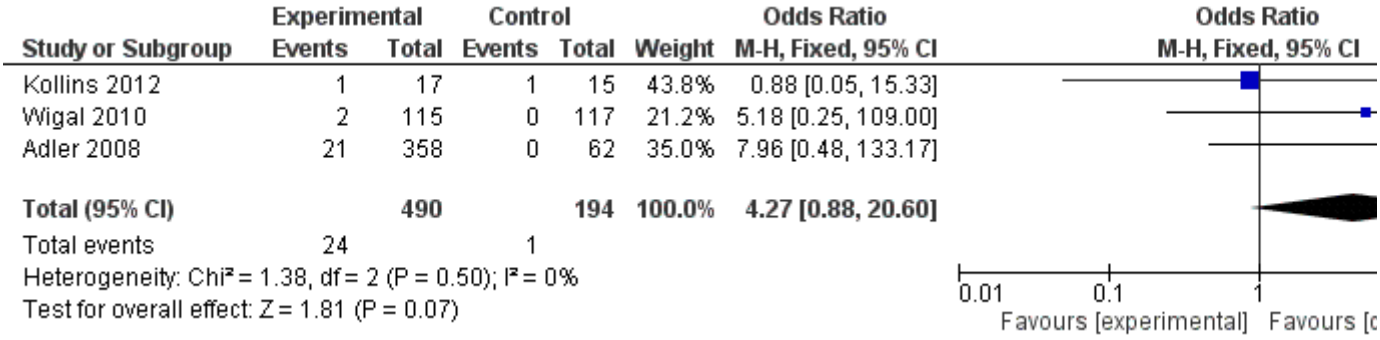
Forest plot of comparison: 1 Lisdexamphetamine versus placebo, outcome: 1.2 Anorexia.

Figure 3 (Analysis 1.3)



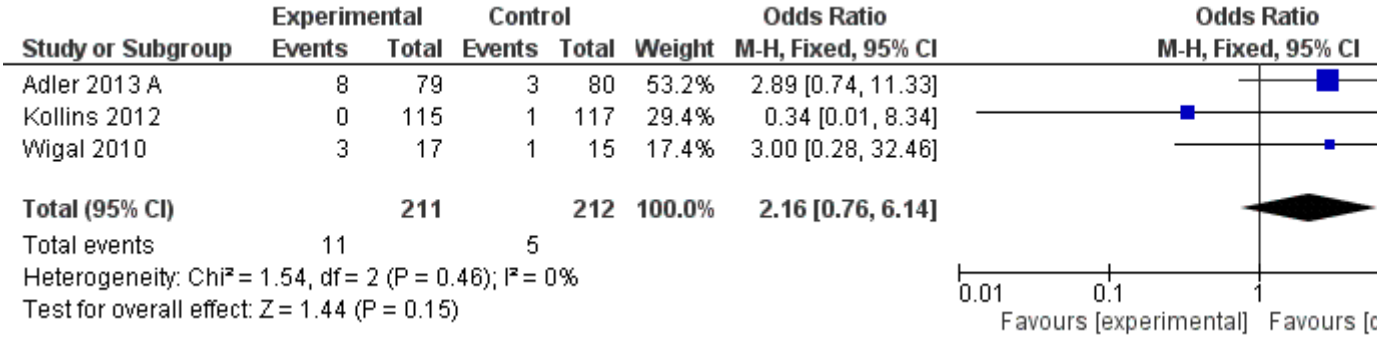
Forest plot of comparison: 1 Lisdexamphetamine versus placebo, outcome: 1.3 Increased heart rate.

Figure 4 (Analysis 1.4)



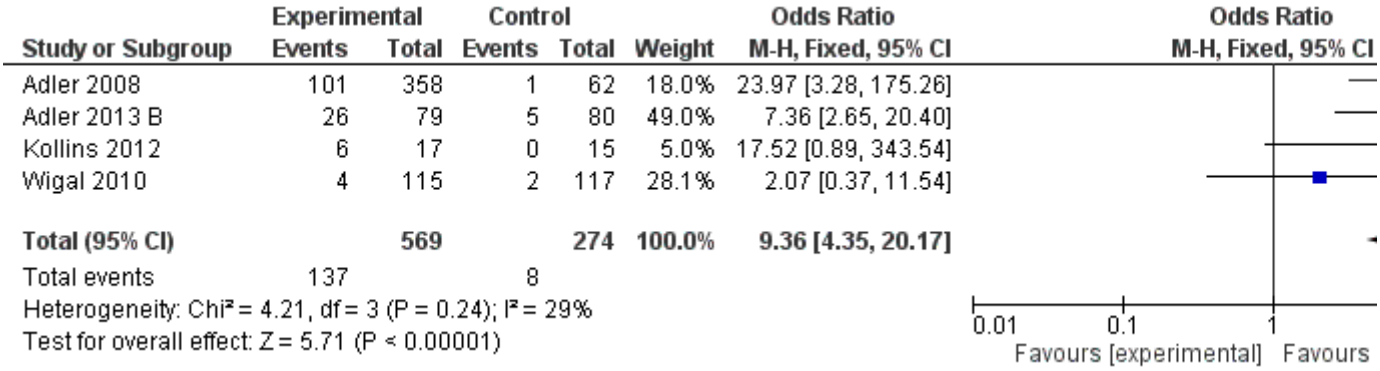
Forest plot of comparison: 1 Lisdexamphetamine versus placebo, outcome: 1.4 Anxiety.

Figure 5 (Analysis 1.5)



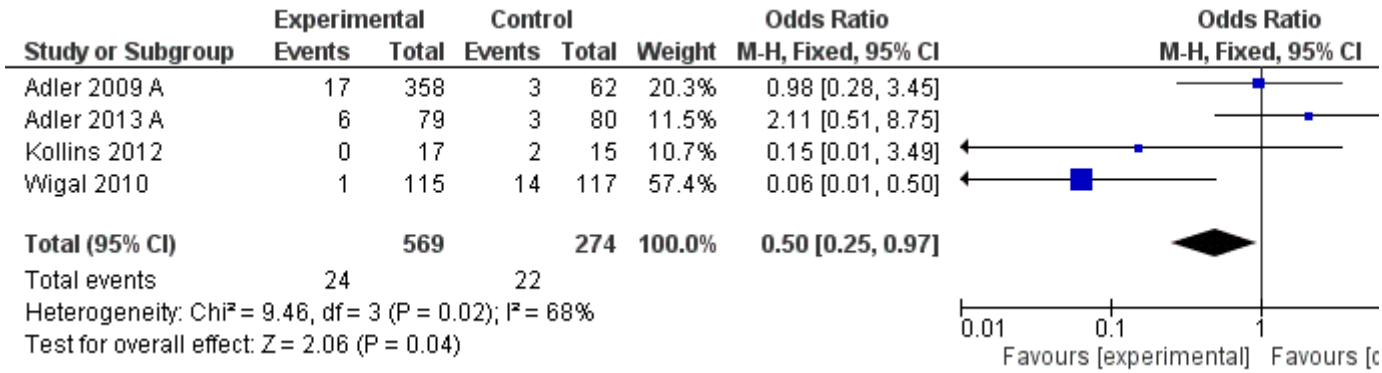
Forest plot of comparison: 1 Lisdexamphetamine versus placebo, outcome: 1.5 Irritability.

Figure 6 (Analysis 1.6)



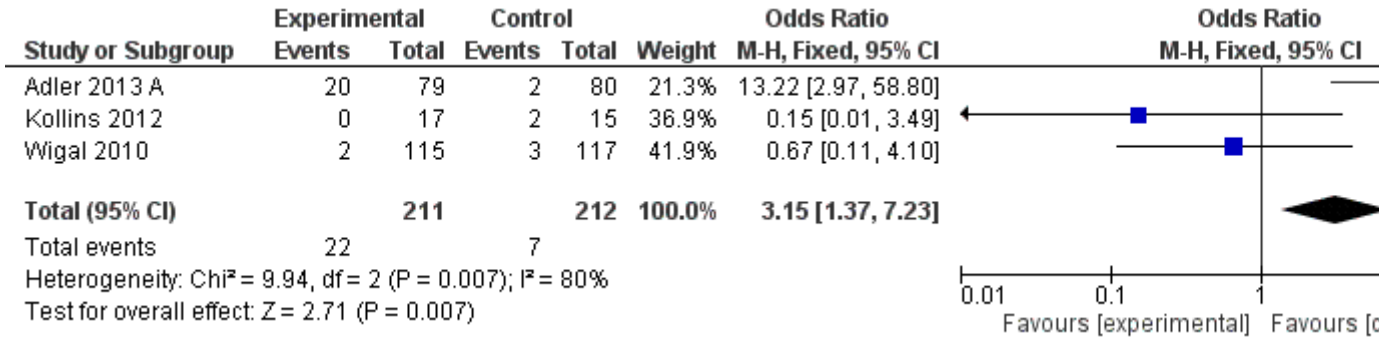
Forest plot of comparison: 1 Lisdexamphetamine versus placebo, outcome: 1.6 Decreased appetite.

Figure 7 (Analysis 1.7)



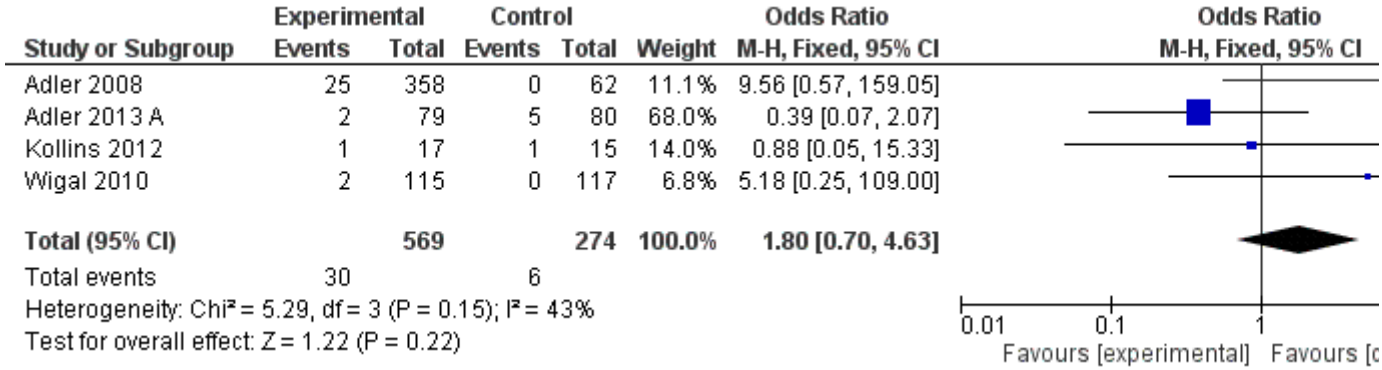
Forest plot of comparison: 1 Lisdexamphetamine versus placebo, outcome: 1.7 Fatigue.

Figure 8 (Analysis 1.8)



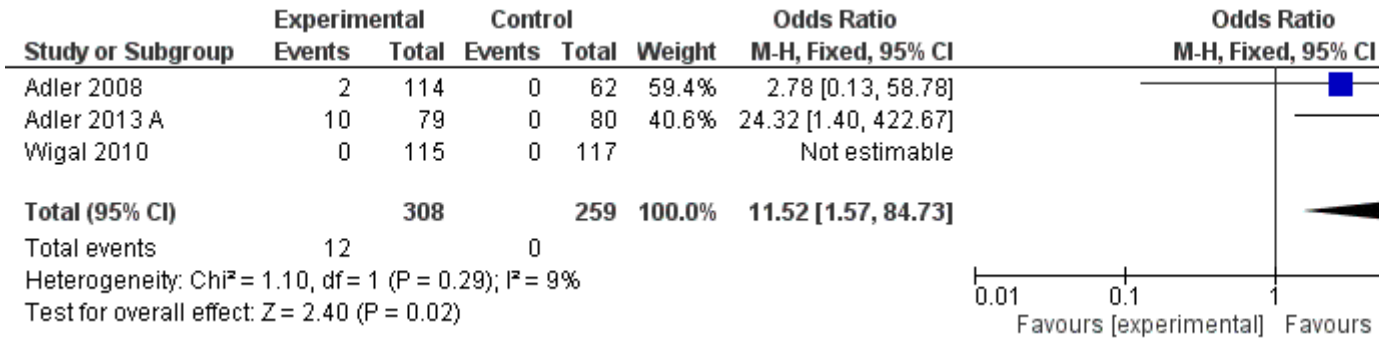
Forest plot of comparison: 1 Lisdexamphetamine versus placebo, outcome: 1.8 Headache.

Figure 9 (Analysis 1.9)



Forest plot of comparison: 1 Lisdexamphetamine versus placebo, outcome: 1.9 Nausea.

Figure 10 (Analysis 1.11)

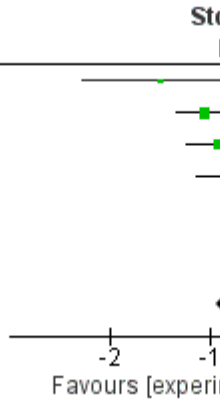


Forest plot of comparison: 1 Lisdexamphetamine versus placebo, outcome: 1.11 Feeling jittery.

Figure 11 (Analysis 1.12)

Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
Kollins 2012	17.5	4.8624	17	26	6.3202	15	3.0%	-1.48 [-2.28, -0.69]
Wigal 2010	18	10	104	29	11	104	22.3%	-1.04 [-1.33, -0.75]
Adler 2013 A	-21.4	11.9991	79	-10.3	12.3431	80	17.6%	-0.91 [-1.23, -0.58]
Adler 2008	22	10	122	31	13	62	18.7%	-0.81 [-1.12, -0.49]
Adler 2008	23	15	119	31	13	62	19.2%	-0.56 [-0.87, -0.24]
Adler 2008	23	16	117	31	13	62	19.2%	-0.53 [-0.84, -0.22]
Total (95% CI)			**558**			**385**	**100.0%**	**-0.80 [-0.93, -0.66]**

Heterogeneity: Chi² = 11.15, df = 5 (P = 0.05); I² = 55%
Test for overall effect: Z = 11.38 (P < 0.00001)

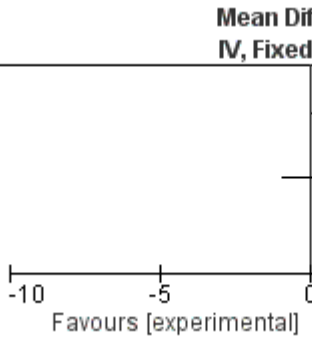


Forest plot of comparison: 1 Lisdexamphetamine versus placebo, outcome: 1.12 ADHD kernesymptomer.

Figure 12 (Analysis 1.13)

Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Adler 2009 B	5.2	8.9266	122	0	8.663	62	26.3%	5.20 [2.52, 7.88]
Adler 2009 B	2.8	8.8139	119	0	8.663	62	26.4%	2.80 [0.12, 5.48]
Adler 2009 B	4.2	8.738	117	0	8.663	62	26.4%	4.20 [1.52, 6.88]
Adler 2013 A	5.4	10.79	79	3.3	8.35	80	20.9%	2.10 [-0.90, 5.10]
Total (95% CI)			**437**			**266**	**100.0%**	**3.65 [2.28, 5.03]**

Heterogeneity: Chi² = 2.86, df = 3 (P = 0.41); I² = 0%
Test for overall effect: Z = 5.22 (P < 0.00001)

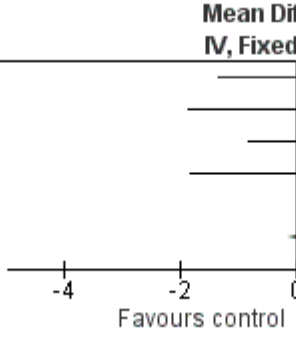


Forest plot of comparison: 1 Lisdexamphetamine versus placebo, outcome: 1.13 Pulse.

Figure 13 (Analysis 1.14)

Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Adler 2009 B	0.8	6.6968	119	-0.5	9.4365	62	25.4%	1.30 [-1.34, 3.94]
Adler 2009 B	0.3	6.6968	117	-0.5	9.4365	62	25.3%	0.80 [-1.84, 3.44]
Adler 2009 B	1.3	6.6968	122	-0.5	9.4365	62	25.6%	1.80 [-0.83, 4.43]
Adler 2013 A	2.6	8.39	79	1.7	9.2	80	23.7%	0.90 [-1.84, 3.64]
Total (95% CI)			**437**			**266**	**100.0%**	**1.21 [-0.12, 2.54]**

Heterogeneity: Chi² = 0.34, df = 3 (P = 0.95); I² = 0%
Test for overall effect: Z = 1.78 (P = 0.08)

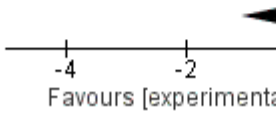


Forest plot of comparison: 1 Lisdexamphetamine versus placebo, outcome: 1.14 Systolic blood pressure.

Figure 14 (Analysis 1.15)

Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Adler 2009 B	1.6	11.1583	122	1.1	6.3004	62	19.0%	0.50 [-2.03, 3.03]
Adler 2009 B	0.8	6.6104	119	1.1	6.3004	62	31.3%	-0.30 [-2.27, 1.67]
Adler 2009 B	1.1	6.5535	117	1.1	6.3004	62	31.3%	0.00 [-1.97, 1.97]
Adler 2013 A	1.7	7.6	79	1.5	8.85	80	18.4%	0.20 [-2.36, 2.76]
Total (95% CI)			**437**			**266**	**100.0%**	**0.04 [-1.06, 1.14]**

Heterogeneity: Chi² = 0.26, df = 3 (P = 0.97); I² = 0%
Test for overall effect: Z = 0.07 (P = 0.95)



Forest plot of comparison: 1 Lisdexamphetamine versus placebo, outcome: 1.15 Diastolic blood pressure.

Sources of support

Internal sources

- No sources of support provided

External sources

- No sources of support provided

Feedback

Appendices