NKR 13 Alkoholbehandling Naltrexon for alcohol dependece

Review information

Authors

Sundhedsstyrelsen[1]

[1][Empty affiliation]

Citation example: S. NKR 13 Alkoholbehandling Naltrexon for alcohol dependece. Cochrane Database of Systematic Reviews [Year], Issue [Issue].

Characteristics of studies

Characteristics of included studies

Ahmadi 2002

Methods	
Participants	
Interventions	
Outcomes	
Notes	For more information see Rösner S, Hackl-Herrwerth A, Leucht S, Vecchi S, Srisurapanont M, Soyka M. Opioid antagonists for alcohol dependence. Cochrane Database of Systematic Reviews 2010, Issue 12. Art. No.: CD001867. DOI: 10.1002/14651858.CD001867.pub3.

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	
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Incomplete outcome data (attrition bias)	Unclear risk	
Selective reporting (reporting bias)	Unclear risk	
Other bias	Unclear risk	

Anton 1999

Methods	
Participants	
Interventions	
Outcomes	
Notes	For more information see Rösner S, Hackl-Herrwerth A, Leucht S, Vecchi S, Srisurapanont M, Soyka M. Opioid antagonists for alcohol dependence. Cochrane Database of Systematic Reviews 2010, Issue 12. Art. No.: CD001867. DOI: 10.1002/14651858.CD001867.pub3.

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Anton 2005

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Anton 2006

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Balldin 2003

Methods	
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Notes	For more information see Rösner S, Hackl-Herrwerth A, Leucht S, Vecchi S, Srisurapanont M, Soyka M. Opioid antagonists for alcohol dependence. Cochrane Database of Systematic Reviews 2010, Issue 12. Art. No.: CD001867. DOI: 10.1002/14651858.CD001867.pub3.

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Baltieri 2008

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BALTIERI2008

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Chick 2000

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Interventions	
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Selective reporting (reporting bias)	Unclear risk	
Other bias	Unclear risk	

Garbutt 2016

Methods	**Study design:** **Study grouping:**
Participants	**Baseline Characteristics** Intervention: naltrexone 50 mg/day Control: placebo tablets Overall **Included criteria:** **Excluded criteria:** **Pretreatment:**
Interventions	**Intervention Characteristics** Intervention: naltrexone 50 mg/day ● *Description*: ● *Duration (weeks) 12 weeks*: ● *50 mg daily*: ● *Follow-up time 12 weeks = by end of treatment period*: ● *all received BRENDA alcohol psycho social counseling*: Control: placebo tablets ● *Description*: ● *Duration (weeks) 12 weeks*: ● *50 mg daily*: ● *Follow-up time 12 weeks = by end of treatment period*: ● *all received BRENDA alcohol psycho social counseling*:
Outcomes	*Drop out due to all causes* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Fully reported ● **Direction**: Lower is better ● **Data value**: Endpoint *Procent dage afholdende*

	● **Outcome type**: DichotomousOutcome ● **Reporting**: Fully reported ● **Direction**: Higher is better ● **Data value**: Endpoint *Frafald pga. bivirkninger* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Fully reported ● **Direction**: Lower is better ● **Data value**: Endpoint
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	hydrochloride, 50 mg/d, or to matching placebo, with randomization balanced by SL vs SDL status and high vs low levels of craving (dichotomized for randomization only on median PACS scores from prior trials 22) based on a 1:1 algorithm assignment (SAS software; SAS Institute Inc) within the 4 respective blocks provided by one of us (R.J.G.) The University of North Carolina In- vestigational Drug Service assigned participants to interven- tions based on the randomization schedule.
Allocation concealment (selection bias)	Low risk	The University of North Carolina In- vestigational Drug Service assigned participants to interven- tions based on the randomization schedule. Participants
Blinding of participants and personnel (performance bias)	Low risk	identical pills
Blinding of outcome assessment (detection bias)	Unclear risk	I assume that the outcome assessors were not able to tell the difference between intervention and placebo, but it is not clearly described
Incomplete outcome data (attrition bias)	Low risk	intention to treat analysis, Outcomes according to study protocol and few drop outs
Selective reporting (reporting bias)	Low risk	similar to pretreatment protocol

Other bias	Low risk	broad inclusion criteria. No role of sponsor

Gastpar 2002

Methods	
Participants	
Interventions	
Outcomes	
Notes	For more information see Rösner S, Hackl-Herrwerth A, Leucht S, Vecchi S, Srisurapanont M, Soyka M. Opioid antagonists for alcohol dependence. Cochrane Database of Systematic Reviews 2010, Issue 12. Art. No.: CD001867. DOI: 10.1002/14651858.CD001867.pub3.

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Other bias	Unclear risk	

Guardia 2002

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Other bias	Unclear risk	

Heinälä 2001

Methods	
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Notes	For more information see Rösner S, Hackl-Herrwerth A, Leucht S, Vecchi S, Srisurapanont M, Soyka M. Opioid antagonists for alcohol dependence. Cochrane Database of Systematic Reviews 2010, Issue 12. Art. No.: CD001867. DOI: 10.1002/14651858.CD001867.pub3.

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Other bias	Unclear risk	

Huang 2005

Methods	
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Notes	For more information see Rösner S, Hackl-Herrwerth A, Leucht S, Vecchi S, Srisurapanont M, Soyka M. Opioid antagonists for alcohol dependence. Cochrane Database of Systematic Reviews 2010, Issue 12. Art. No.: CD001867. DOI: 10.1002/14651858.CD001867.pub3.

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Other bias	Unclear risk	

Kiefer 2003

Methods	
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Other bias	Unclear risk	

Killeeen 2004

Methods	
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Other bias	Unclear risk	

Kranzler 2000

Methods	
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Other bias	Unclear risk	

Krystal 2001

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Other bias	Unclear risk	

Latt 2002

Methods	
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Notes	For more information see Rösner S, Hackl-Herrwerth A, Leucht S, Vecchi S, Srisurapanont M, Soyka M. Opioid antagonists for alcohol dependence. Cochrane Database of Systematic Reviews 2010, Issue 12. Art. No.: CD001867. DOI: 10.1002/14651858.CD001867.pub3.

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Other bias	Unclear risk	

Lee 2001

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Other bias	Unclear risk	

Mann2013

Methods	RCT 12 weeks naltrexon, "support" for 6 months
Participants	alcohol dependent, admitted for alcohol detoxification, no major psychiatric illness
Interventions	naltrexon and medical manegement biweekly
Outcomes	drop-out due to all reasons, time to heavy drinking (not a outcome for the NKR group)
Notes	Federal Government of Germany + medication donated by Bristol Meyer Squibb and MERCK Serono

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	p681 of Mann et al., 2009 ("Searching for Responders to Acamprosate and Naltrexone in Alcoholism Treatment: Rationale and Design of the Predict Study") states "For allocating these patients to the 3 treatment arms, an imbalanced randomization algorithm is used ensuring proportions of 2:2:1 between acamprosate, naltrexone, and placebo, respectively." It is unclear how this was done and by whom.
Allocation concealment (selection bias)	Unclear risk	p681 of Mann et al., 2009 ("Searching for Responders to Acamprosate and Naltrexone in Alcoholism Treatment: Rationale and Design of the Predict Study") states "For allocating these patients to the 3 treatment arms, an imbalanced randomization algorithm is used ensuring proportions of 2:2:1 between acamprosate, naltrexone, and placebo, respectively." It is unclear how this was done and by whom.
Blinding of participants and personnel (performance bias)	Low risk	p 939-940: "To ensure double-blind treatment, each patient had to take seven pills daily (three in the morning, tow at noon and two in the late afternoon), regardless of the drug they were taking. Each blister pack contained a 1-week supply of medication". There was no information in the text to state whether the tablets for both active treatments and for placebo all look identical - but I presume they did. The protocol (Mann et al., 2009 -Searching for Responders to Acamprosate and Naltrexone in Alcoholism Treatment: Rationale and Design of the Predict Study) does not provide any further details.
Blinding of outcome assessment (detection bias)	Unclear risk	There were no details in the actual paper and no further details in the protocol
Incomplete outcome data (attrition bias)	Low risk	Figure 1 clearly states number of patients who discontinued, and the number of patients that were included in the analyses. The number of patients included in the analyses in figure 1 agrees with data in table 1
Selective reporting (reporting bias)	Low risk	Primary outcome and primary efficacy analysis are same in protocol and paper.
Other bias	Unclear risk	No other types of bias noted

Monti 2001

Methods	
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Notes	For more information see Rösner S, Hackl-Herrwerth A, Leucht S, Vecchi S, Srisurapanont M, Soyka M. Opioid antagonists for alcohol dependence. Cochrane Database of Systematic Reviews 2010, Issue 12. Art. No.: CD001867. DOI: 10.1002/14651858.CD001867.pub3.

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Morley 2006

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Morris 2001

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O'Malley 1992

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Oslin 1997

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Oslin 2008

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Volpicelli 1992

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Volpicelli 1997

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Footnotes

Characteristics of excluded studies

Bold 2016

Reason for exclusion	Wrong study design

Bujarski 2017

Reason for exclusion	Wrong study design

Busch 2017

Reason for exclusion	Wrong comparator

Canidate 2017

Reason for exclusion	Wrong study design

Chen 2016

Reason for exclusion	Wrong comparator

Chen 2017

Reason for exclusion	Wrong study design

DeMartini 2014

Reason for exclusion	Wrong study design

DeMartini 2016

Reason for exclusion	Wrong study design

DeSousa 2014

Reason for exclusion	Wrong study design

Harris 2015

Reason for exclusion	Wrong study design

Jonas 2014

Reason for exclusion	Wrong study design

McCormack 2017

Reason for exclusion	Wrong study design

Miranda 2014

Reason for exclusion	Wrong study design

Mouaffak 2017

Reason for exclusion	Wrong study design

O'Malley 2015

Reason for exclusion	Wrong study design

Oslin 2015

Reason for exclusion	Wrong study design

Palpacuer 2017

Reason for exclusion	Wrong study design

Footnotes

Characteristics of studies awaiting classification

Footnotes

Characteristics of ongoing studies

Footnotes

References to studies

Included studies

Ahmadi 2002

[Empty]

Anton 1999

[Empty]

Anton 2005

[Empty]

Anton 2006

[Empty]

Balldin 2003

[Empty]

BALTIERI2008

[Empty]

Baltieri 2008

[Empty]

Chick 2000

[Empty]

Garbutt 2016

Garbutt, James C.; Kampov-Polevoy, Alexey B.; Kalka-Juhl, Linda S.; Gallop, Robert J.. Association of the Sweet-Liking Phenotype and Craving for Alcohol With the Response to Naltrexone Treatment in Alcohol Dependence: A Randomized Clinical Trial.. JAMA Psychiatry 2016;73(10):1056-1063. [DOI:]

Gastpar 2002

[Empty]

Guardia 2002

[Empty]

Heinälä 2001

[Empty]

Huang 2005

[Empty]

Kiefer 2003

[Empty]

Killeeen 2004

[Empty]

Kranzler 2000

[Empty]

Krystal 2001

[Empty]

Latt 2002

[Empty]

Lee 2001

[Empty]

Mann2013

[Empty]

Monti 2001

[Empty]

Morley 2006

[Empty]

Morris 2001

[Empty]

O'Malley 1992

[Empty]

O'Malley 2008

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Oslin 1997

[Empty]

Oslin 2008

[Empty]

Volpicelli 1992

[Empty]

Volpicelli 1997

[Empty]

Excluded studies

Bold 2016

Bold, Krysten W.; Fucito, Lisa M.; Corbin, William R.; DeMartini, Kelly S.; Leeman, Robert F.; Kranzler, Henry R.; O'Malley, Stephanie S.. Daily relations among affect, urge, targeted naltrexone, and alcohol use in young adults.. Experimental & Clinical Psychopharmacology 2016;24(5):367-375. [DOI:]

Bujarski 2017

Bujarski S.; Green R.; Roche D.J.O.; Ray, L. A.. Naltrexone and subjective responses to alcohol: A systematic reviewand meta-analysis. 2017;(Conference Proceedings). [DOI: http://dx.doi.org/10.1111/acer.13391]

Busch 2017

Busch A.C.; Denduluri M.; Glass J.; Hetzel S.; Gugnani S.P.; Gassman M.; Krahn D.; Deyo B.; Brown, R.. Predischarge Injectable Versus Oral Naltrexone to Improve Postdischarge Treatment Engagement Among Hospitalized Veterans with Alcohol Use Disorder: A Randomized Pilot Proof-of-Concept Study.. Alcoholism: Clinical and Experimental Research 2017;41(7):1352-1360. [DOI: http://dx.doi.org/10.1111/acer.13410]

Canidate 2017

Canidate, Shantrel S.; Carnaby, Giselle D.; Cook, Christa L.; Cook, Robert L.. A Systematic Review of Naltrexone for Attenuating Alcohol Consumption in Women with Alcohol Use Disorders.. Alcoholism: Clinical & Experimental Research 2017;41(3):466-472. [DOI:]

Chen 2016

Chen J.; Obi R.; Wong S.; Flannery M.; McDonald R.; Tofighi B.; Kermack A.; Laska E.; Rotrosen J.; Gourevitch, M. N.. Extended-release naltrexone versusoral naltrexone for alcohol use disorder treatment in primary care. 2016;(Conference Proceedings). [DOI: http://dx.doi.org/10.1111/acer.13084]

Chen 2017

Chen J.; McDonald R.D.; Obi R.; Wong S.; Flannery M.; Tofighi B.; Kermack A.; Rotrosen J.; Gourevitch M.; Lee, J. D.. Extended-release vs. oral naltrexone for alcohol dependence treatment in primary care. 2017;(Conference Proceedings). [DOI: http://dx.doi.org/10.1016/j.drugalcdep.2016.08.120]

DeMartini 2014

DeMartini K.S.; Gueorguiva R.; Leeman R.F.; Corbin W.R.; Fucito L.M.; Kranzler H.R.; O'Malley, S. S.. Naltrexone for non-treatment seeking young adult drinkers: One-year outcomes. 2014;(Conference Proceedings). [DOI:]

DeMartini 2016

DeMartini, Kelly S.; Gueorguieva, Ralitza; Leeman, Robert F.; Corbin, William R.; Fucito, Lisa M.; Kranzler, Henry R.; O'Malley, Stephanie S.. Longitudinal findings from a randomized clinical trial of naltrexone for young adult heavy drinkers.. Journal of Consulting & Clinical Psychology 2016;84(2):185-190. [DOI:]

DeSousa 2014

De Sousa, A.. A comparative study using Disulfiram and Naltrexone in alcohol-dependent adolescents.. Journal of Substance Use 2014;19(5):341-345. [DOI: http://dx.doi.org/10.3109/14659891.2013.813084]

Harris 2015

Harris, Alex H. S.; Bowe, Thomas; Del Re, Aaron C.; Finlay, Andrea K.; Oliva, Elizabeth; Myrick, Hugh L.; Rubinsky, Anna D.. Extended release naltrexone for alcohol use disorders: quasi-experimental effects on mortality and subsequent detoxification episodes.. Alcoholism: Clinical & Experimental Research 2015;39(1):79-83. [DOI:]

Jonas 2014

Jonas, Daniel E.; Amick, Halle R.; Feltner, Cynthia; Bobashev, Georgiy; Thomas, Kathleen; Wines, Roberta; Kim, Mimi M.; Shanahan, Ellen; Gass, C. Elizabeth; Rowe, Cassandra J.; Garbutt, James C.. Pharmacotherapy for adults with alcohol use disorders in outpatient settings: a systematic review and meta-analysis. JAMA 2014;311(18):1889-1900. [DOI:]

McCormack 2017

McCormack R.P.; Gonzalez M.T.; Rotrosen J.; Gragui D.A.; Carmona R.K.; Demuth M.K.; D'Onofrio, G.. Initiating extended-release naltrexone in frequent emergency department users with severe alcohol use disorders is feasible and acceptable. 2017;(Conference Proceedings). [DOI: http://dx.doi.org/10.1111/acer.13391]

Miranda 2014

Miranda, Robert; Ray, Lara; Blanchard, Alexander; Reynolds, Elizabeth K.; Monti, Peter M.; Chun, Thomas; Justus, Alicia; Swift, Robert M.; Tidey, Jennifer; Gwaltney, Chad J.; Ramirez, Jason. Effects of naltrexone on adolescent alcohol cue reactivity and sensitivity: an initial randomized trial.. Addiction Biology 2014;19(5):941-954. [DOI:]

Mouaffak 2017

Mouaffak, Faycal; Leite, Claudio; Hamzaoui, Sonia; Benyamina, Amine; Laqueille, Xavier; Kebir, Oussama. Naltrexone in the Treatment of Broadly Defined Behavioral Addictions: A Review and Meta-Analysis of Randomized Controlled Trials.. European addiction research 2017;23(4):204-210. [DOI:]

O'Malley 2015

O'Malley, Stephanie S.; Corbin, William R.; Leeman, Robert F.; DeMartini, Kelly S.; Fucito, Lisa M.; Ikomi, Jolomi; Romano, Denise M.; Wu, Ran; Toll, Benjamin A.; Sher, Kenneth J.; Gueorguieva, Ralitza; Kranzler, Henry R.. Reduction of alcohol drinking in young adults by naltrexone: a double-blind, placebo-controlled, randomized clinical trial of efficacy and safety.. Journal of Clinical Psychiatry 2015;76(2):e207-13. [DOI:]

Oslin 2015

Oslin, David W.; Leong, Shirley H.; Lynch, Kevin G.; Berrettini, Wade; O'Brien, Charles P.; Gordon, Adam J.; Rukstalis, Margaret. Naltrexone vs Placebo for the Treatment of Alcohol Dependence: A Randomized Clinical Trial.. JAMA Psychiatry 2015;72(5):430-437. [DOI:]

Palpacuer 2017

Palpacuer, Clement; Duprez, Renan; Huneau, Alexandre; Locher, Clara; Boussageon, Remy; Laviolle, Bruno; Naudet, Florian. Pharmacologically controlled drinking in the treatment of alcohol dependence or alcohol use disorders: a systematic review with direct and network meta-analyses on nalmefene, naltrexone, acamprosate, baclofen and topiramate. Addiction 2017;(Journal Article). [DOI:]

Data and analyses

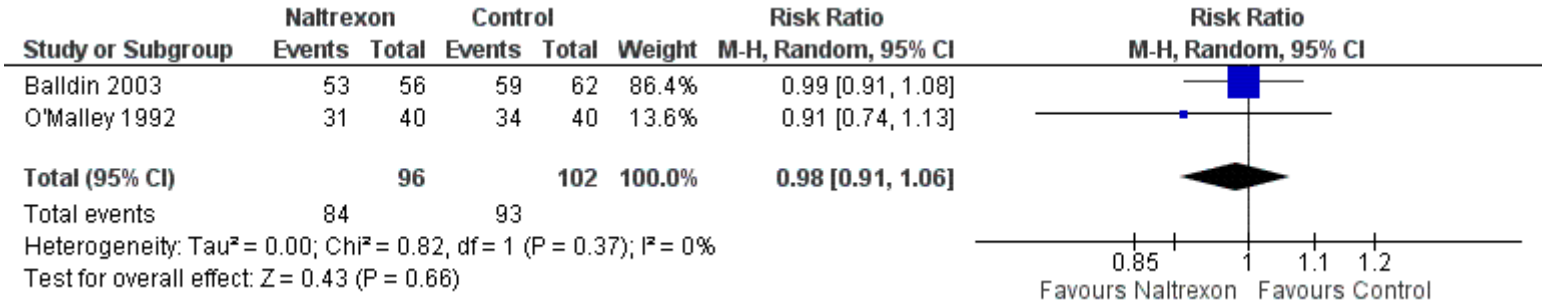
1 naltrexon versus placebo for alcohol dependence

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
1.1 Number of individuals non-abstinent (lapsed) 6-12 months after baseline	2	198	Risk Ratio (M-H, Random, 95% CI)	0.98 [0.91, 1.06]
1.2 Number individuals non-abstinent (lapsed) after 3 months treatment	16	1847	Risk Ratio (M-H, Random, 95% CI)	0.92 [0.86, 1.00]
1.3 Number of individuals non-abstinent (lapsed) 6-12 month FU	1	80	Risk Ratio (M-H, Random, 95% CI)	0.91 [0.74, 1.13]
1.4 Percentage days abstinent at 3 month after baseline	9	1607	Mean Difference (IV, Random, 95% CI)	-3.83 [-6.25, -1.40]
1.5 Percentage days abstinent at 6-12 months after baseline	2	742	Mean Difference (IV, Random, 95% CI)	-4.55 [-9.20, 0.10]
1.6 Drinks per drinking day 3 month after baseline	9	1526	Mean Difference (IV, Random, 95% CI)	-1.16 [-1.84, -0.48]
1.39 Side effect: Diarrhea	7	1366	Risk Ratio (M-H, Random, 95% CI)	0.97 [0.54, 1.75]

1.46 Side effect: Nausea	15	2729	Risk Ratio (M-H, Random, 95% CI)	1.57 [1.35, 1.82]
1.54 Side effect: Serious adverse events	4	877	Risk Ratio (M-H, Random, 95% CI)	1.23 [0.68, 2.23]
1.55 Drop-outs due to adverse events	16	2266	Risk Ratio (M-H, Random, 95% CI)	1.55 [1.01, 2.38]
1.57 Drop-outs	26	4135	Risk Ratio (M-H, Random, 95% CI)	0.91 [0.80, 1.03]

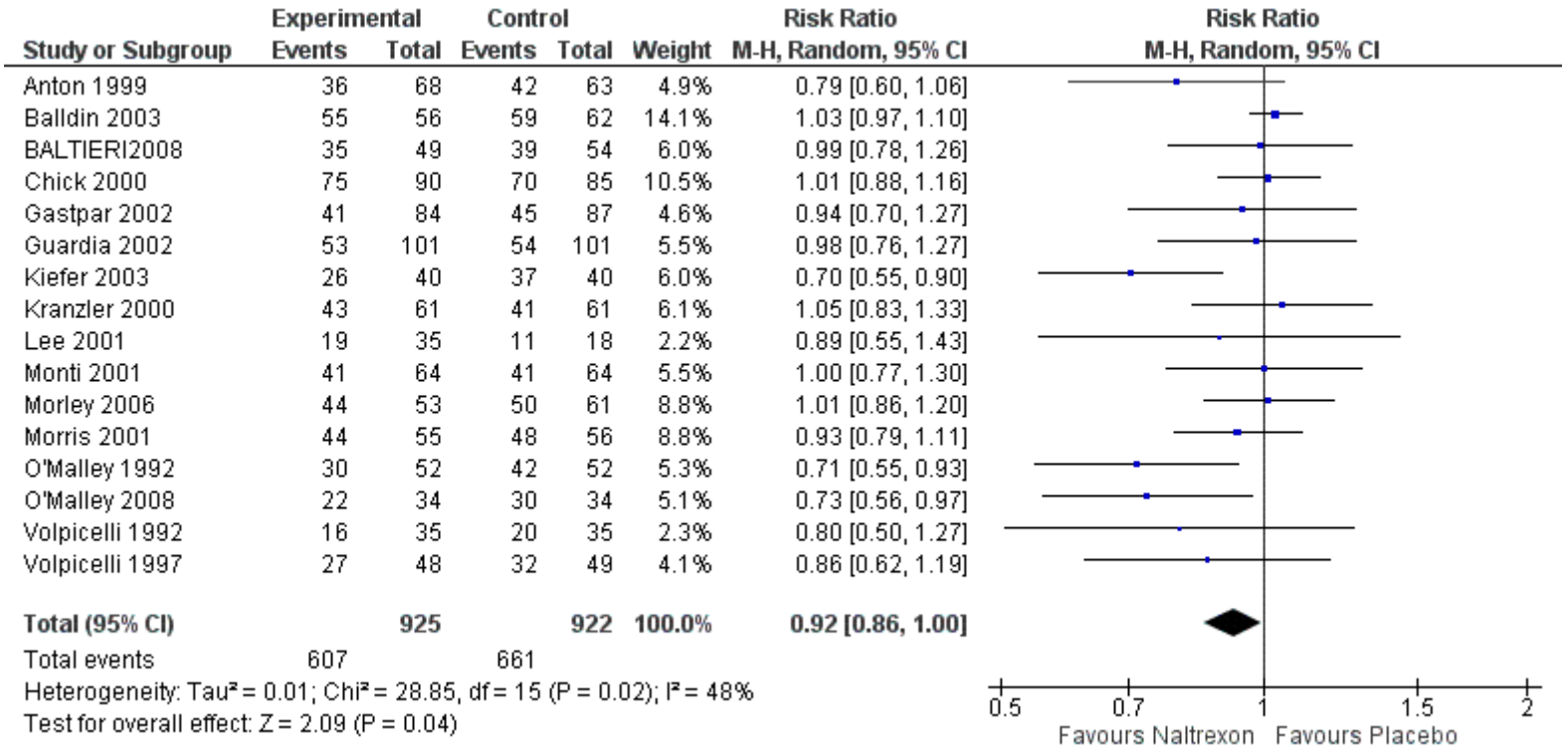
Figures

Figure 1 (Analysis 1.1)



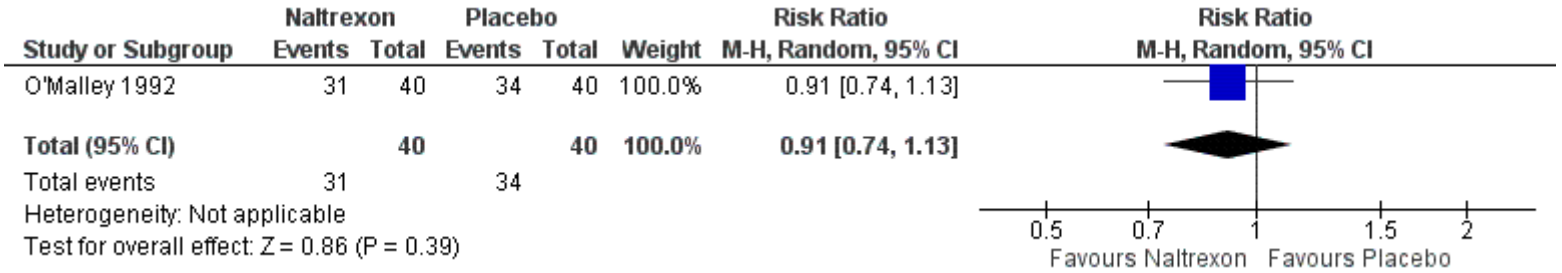
Forest plot of comparison: 1 naltrexon versus placebo for alcohol dependence, outcome: 1.1 Number of individuals non-abstinent (lapsed) 6-12 months after baseline.

Figure 2 (Analysis 1.2)



Forest plot of comparison: 1 naltrexon versus placebo for alcohol dependence, outcome: 1.2 Number individuals non-abstinent (lapsed) after 3 months treatment.

Figure 3 (Analysis 1.3)

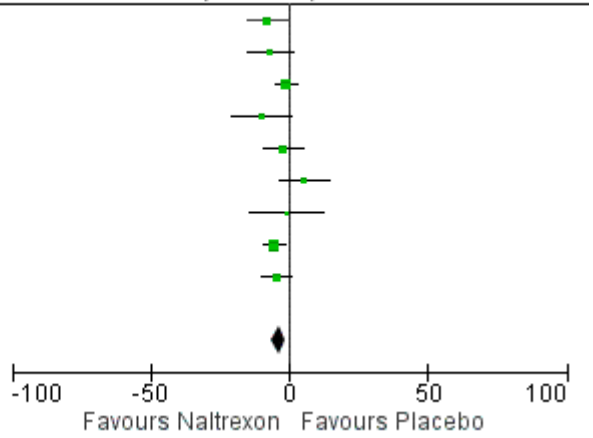


Forest plot of comparison: 1 naltrexon versus placebo for alcohol dependence, outcome: 1.3 Number of individuals non-abstinent (lapsed) 6-12 month FU.

Figure 4 (Analysis 1.4)

Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Anton 1999	-90	18.9	68	-82	22.9	63	9.4%	-8.00 [-15.22, -0.78]
Anton 2005	-83.825	25.0684	80	-77.05	28.9635	80	7.3%	-6.78 [-15.17, 1.62]
Anton 2006	-77.9434	26.0686	309	-76.8291	25.9416	309	21.6%	-1.11 [-5.21, 2.99]
Balldin 2003	-61.3571	26.1766	56	-51.4516	32.8891	62	4.7%	-9.91 [-20.58, 0.77]
Guardia 2002	-65.3	22.64	93	-63	26.9	99	9.9%	-2.30 [-9.32, 4.72]
Kranzler 2000	-78.8	28.9	60	-84.3	21.3	63	6.4%	5.50 [-3.51, 14.51]
Morris 2001	-75	28	38	-74	30	33	3.0%	-1.00 [-14.57, 12.57]
O'Malley 1992	-95.7626	10.0232	46	-90.1294	9.2512	51	23.3%	-5.63 [-9.48, -1.78]
Volpicelli 1997	-93.8	11.13	48	-89.24	16.07	49	14.5%	-4.56 [-10.05, 0.93]
Total (95% CI)			**798**			**809**	**100.0%**	**-3.83 [-6.25, -1.40]**

Heterogeneity: Tau² = 2.73; Chi² = 10.06, df = 8 (P = 0.26); I² = 20%
Test for overall effect: Z = 3.09 (P = 0.002)

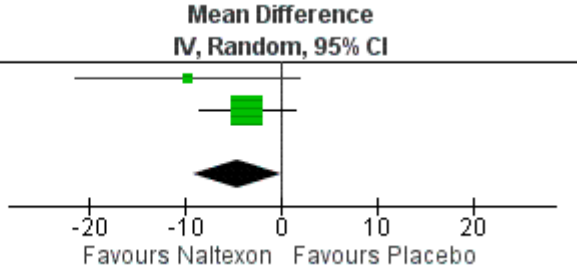


Forest plot of comparison: 1 naltrexon versus placebo for alcohol dependence, outcome: 1.4 Percentage days abstinent at 3 month after baseline.

Figure 5 (Analysis 1.5)

Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Anton 1999	-77.8	29.7	66	-68	35.7	58	15.9%	-9.80 [-21.45, 1.85]
Anton 2006	-67.0466	31.4114	309	-63.4893	32.8464	309	84.1%	-3.56 [-8.62, 1.51]
Total (95% CI)			**375**			**367**	**100.0%**	**-4.55 [-9.20, 0.10]**

Heterogeneity: Tau² = 0.00; Chi² = 0.93, df = 1 (P = 0.34); I² = 0%
Test for overall effect: Z = 1.92 (P = 0.05)

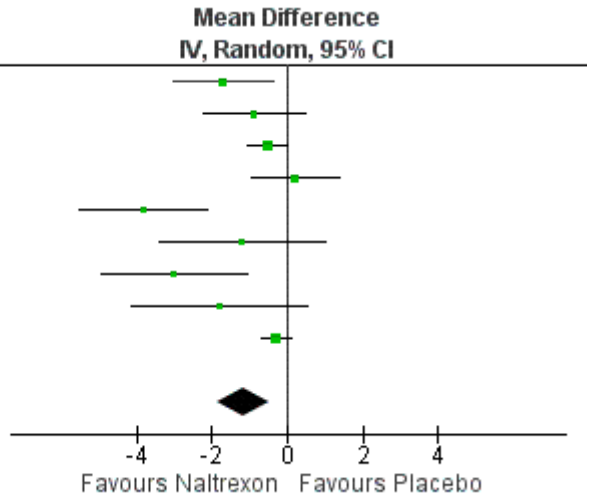


Forest plot of comparison: 1 naltrexon versus placebo for alcohol dependence, outcome: 1.5 Percentage days abstinent at 6-12 months after baseline.

Figure 6 (Analysis 1.6)

Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Anton 1999	2.5	3.3	68	4.2	4.3	63	11.4%	-1.70 [-3.02, -0.38]
Anton 2005	3.51	4.2095	80	4.4	4.5744	80	11.1%	-0.89 [-2.25, 0.47]
Guardia 2002	0.71	1.64	93	1.22	2.12	99	17.8%	-0.51 [-1.04, 0.02]
Krystal 2001	9.2	8	378	9	6	187	12.5%	0.20 [-0.98, 1.38]
Monti 2001	4.94	3.36	64	8.77	6.17	64	8.8%	-3.83 [-5.55, -2.11]
Morley 2006	5.9	6.1	53	7.1	6	61	6.4%	-1.20 [-3.43, 1.03]
Morris 2001	6	3	38	9	5	33	7.5%	-3.00 [-4.95, -1.05]
O'Malley 1992	4.9913	6.5314	46	6.7824	5.0196	51	5.9%	-1.79 [-4.13, 0.55]
O'Malley 2008	3.6	0.85	34	3.9	0.82	34	18.7%	-0.30 [-0.70, 0.10]
Total (95% CI)			**854**			**672**	**100.0%**	**-1.16 [-1.84, -0.48]**

Heterogeneity: Tau² = 0.60; Chi² = 27.51, df = 8 (P = 0.0006); I² = 71%
Test for overall effect: Z = 3.34 (P = 0.0008)

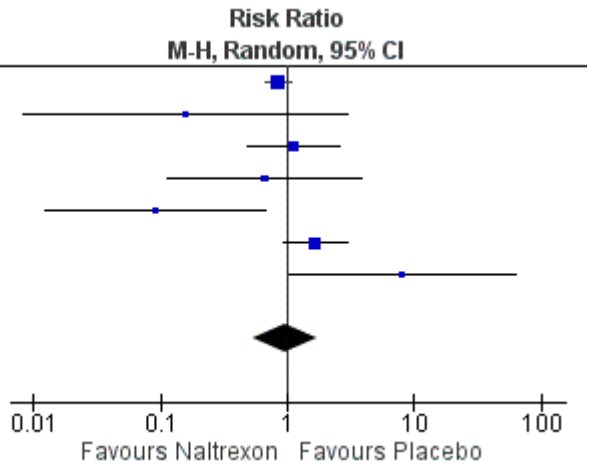


Forest plot of comparison: 1 naltrexon versus placebo for alcohol dependence, outcome: 1.6 Drinks per drinking day 3 month after baseline.

Figure 7 (Analysis 1.39)

Study or Subgroup	Naltrexone Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Anton 2006	92	309	108	309	30.9%	0.85 [0.68, 1.07]
Baltieri 2008	0	49	3	54	3.6%	0.16 [0.01, 2.97]
Chick 2000	11	85	9	78	19.7%	1.12 [0.49, 2.56]
Gastpar 2002	2	82	3	82	8.3%	0.67 [0.11, 3.89]
Kiefer 2003	1	40	11	40	6.8%	0.09 [0.01, 0.67]
Kranzler 2000	21	61	13	63	24.3%	1.67 [0.92, 3.03]
Morley 2006	7	53	1	61	6.5%	8.06 [1.02, 63.38]
Total (95% CI)		**679**		**687**	**100.0%**	**0.97 [0.54, 1.75]**
Total events	134		148			

Heterogeneity: Tau² = 0.28; Chi² = 15.44, df = 6 (P = 0.02); I² = 61%
Test for overall effect: Z = 0.10 (P = 0.92)

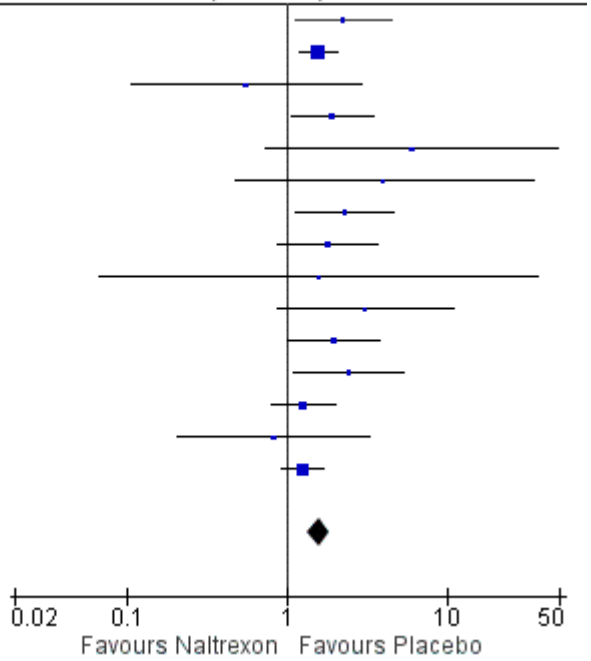


Forest plot of comparison: 1 naltrexon versus placebo for alcohol dependence, outcome: 1.39 Side effect: Diarrhea.

Figure 8 (Analysis 1.46)

Study or Subgroup	Naltrexone Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Ahmadi 2002	20	58	9	58	4.6%	2.22 [1.11, 4.46]
Anton 2006	101	309	65	309	31.3%	1.55 [1.19, 2.03]
Baltieri 2008	2	49	4	54	0.8%	0.55 [0.11, 2.88]
Chick 2000	27	85	13	78	6.6%	1.91 [1.06, 3.42]
Gastpar 2002	6	82	1	82	0.5%	6.00 [0.74, 48.74]
Kiefer 2003	4	40	1	40	0.5%	4.00 [0.47, 34.24]
Kranzler 2000	20	61	9	63	4.6%	2.30 [1.14, 4.64]
Krystal 2001	32	418	9	209	4.4%	1.78 [0.86, 3.65]
Lee 2001	1	35	0	18	0.2%	1.58 [0.07, 37.02]
Morley 2006	8	53	3	61	1.4%	3.07 [0.86, 10.98]
Morris 2001	19	55	10	56	5.0%	1.93 [0.99, 3.78]
O'Malley 1992	17	52	7	52	3.6%	2.43 [1.10, 5.36]
O'Malley 2008	20	34	16	34	11.0%	1.25 [0.79, 1.97]
Oslin 1997	3	21	4	23	1.2%	0.82 [0.21, 3.25]
Oslin 2008	55	120	44	120	24.3%	1.25 [0.92, 1.70]
Total (95% CI)		**1472**		**1257**	**100.0%**	**1.57 [1.35, 1.82]**
Total events	335		195			

Heterogeneity: Tau² = 0.00; Chi² = 13.32, df = 14 (P = 0.50); I² = 0%
Test for overall effect: Z = 5.86 (P < 0.00001)

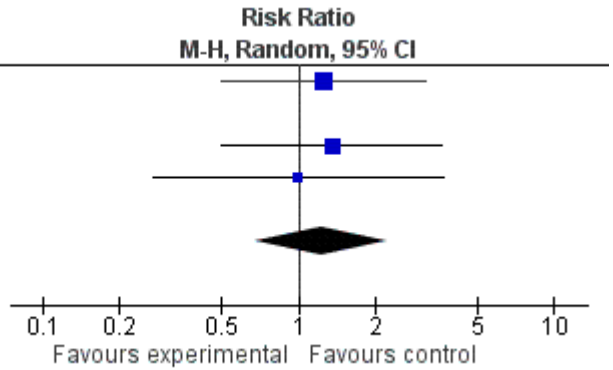


Forest plot of comparison: 1 naltrexon versus placebo for alcohol dependence, outcome: 1.46 Side effect: Nausea.

Figure 9 (Analysis 1.54)

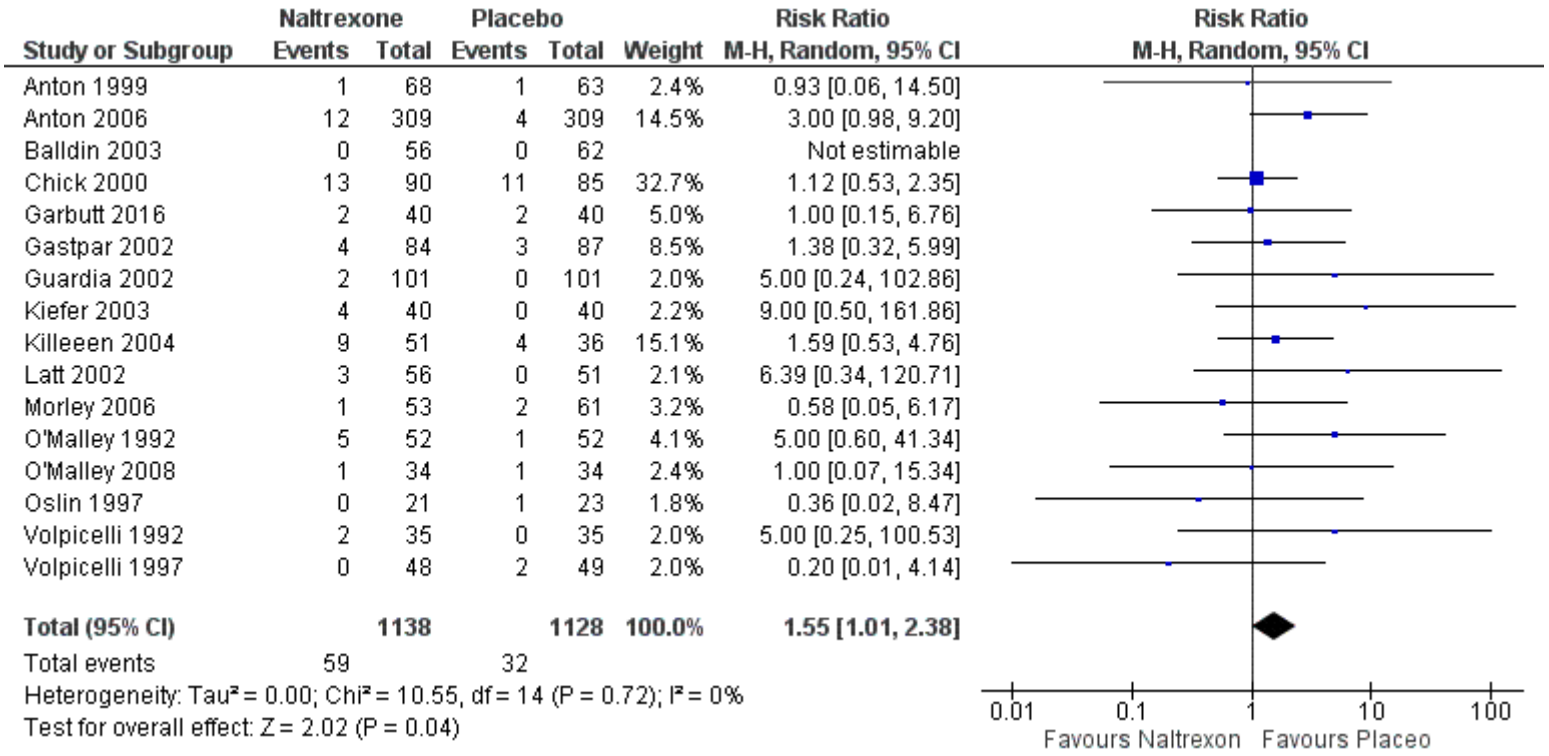
Study or Subgroup	Naltrexone Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Anton 2006	10	309	8	309	42.5%	1.25 [0.50, 3.12]
Kiefer 2003	0	40	0	40		Not estimable
Morris 2001	8	55	6	56	36.4%	1.36 [0.50, 3.66]
O'Malley 2008	4	34	4	34	21.1%	1.00 [0.27, 3.68]
Total (95% CI)		**438**		**439**	**100.0%**	**1.23 [0.68, 2.23]**
Total events	22		18			

Heterogeneity: Tau² = 0.00; Chi² = 0.14, df = 2 (P = 0.93); I² = 0%
Test for overall effect: Z = 0.68 (P = 0.50)



Forest plot of comparison: 1 naltrexon versus placebo for alcohol dependence, outcome: 1.54 Side effect: Serious adverse events.

Figure 10 (Analysis 1.55)

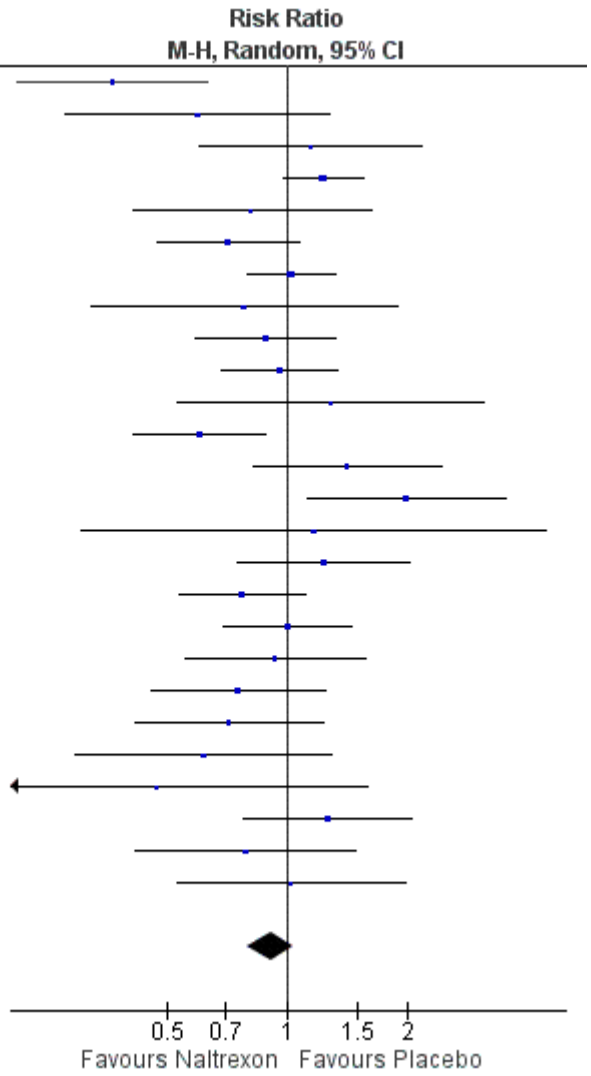


Forest plot of comparison: 1 naltrexon versus placebo for alcohol dependence, outcome: 1.55 Drop-outs due to adverse events.

Figure 11 (Analysis 1.57)

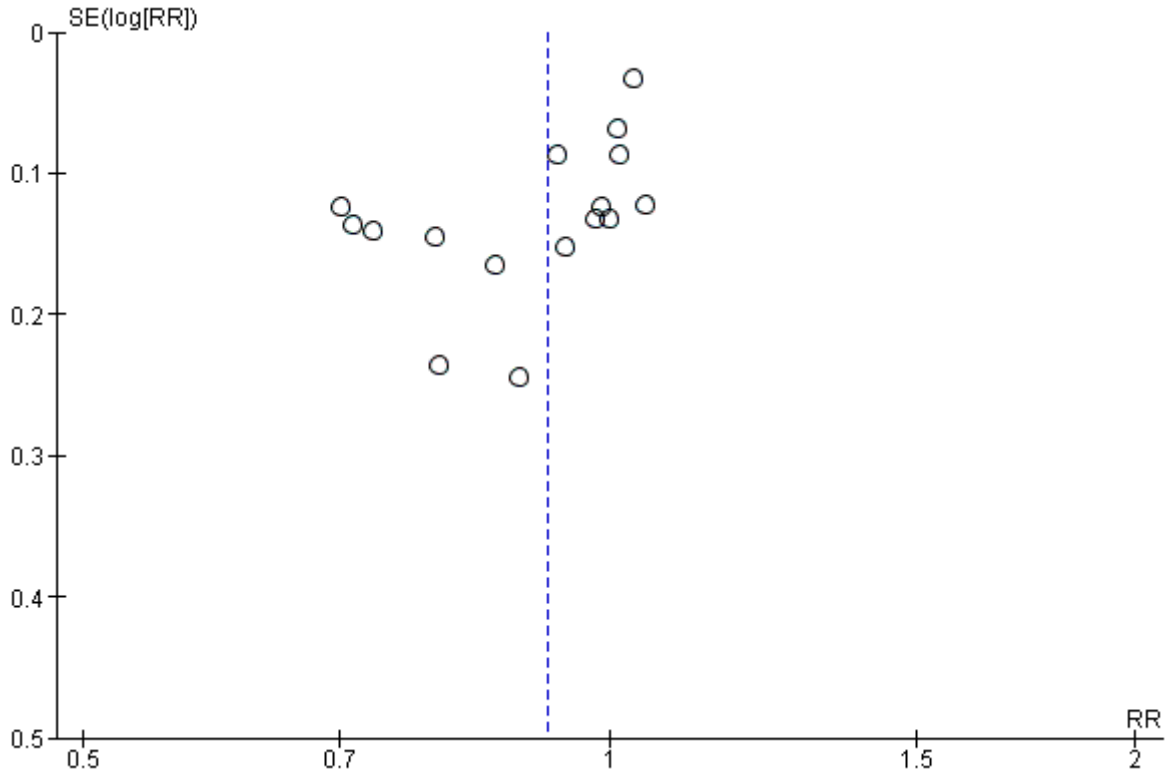
Study or Subgroup	Naltrexone Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Ahmadi 2002	12	58	33	58	3.6%	0.36 [0.21, 0.63]
Anton 1999	9	68	14	63	2.3%	0.60 [0.28, 1.28]
Anton 2005	16	80	14	80	2.9%	1.14 [0.60, 2.18]
Anton 2006	108	309	88	309	7.7%	1.23 [0.97, 1.55]
Balldin 2003	11	56	15	62	2.6%	0.81 [0.41, 1.62]
Baltieri 2008	20	49	31	54	5.1%	0.71 [0.47, 1.07]
Chick 2000	53	90	49	85	7.4%	1.02 [0.79, 1.31]
Garbutt 2016	7	40	9	40	1.8%	0.78 [0.32, 1.88]
Gastpar 2002	28	84	33	87	5.1%	0.88 [0.59, 1.32]
Guardia 2002	40	101	42	101	6.1%	0.95 [0.68, 1.33]
Huang 2005	9	40	7	40	1.8%	1.29 [0.53, 3.12]
Kiefer 2003	18	40	30	40	5.4%	0.60 [0.41, 0.88]
Killeeen 2004	24	51	12	36	3.6%	1.41 [0.82, 2.44]
Kranzler 2000	25	61	13	63	3.4%	1.99 [1.12, 3.51]
Krystal 2001	7	418	3	209	0.9%	1.17 [0.30, 4.47]
Latt 2002	23	56	17	51	4.1%	1.23 [0.75, 2.03]
Lee 2001	21	35	14	18	5.6%	0.77 [0.53, 1.11]
Mann2013	55	169	28	86	5.5%	1.00 [0.69, 1.45]
Morley 2006	17	53	21	61	3.9%	0.93 [0.55, 1.57]
Morris 2001	17	55	23	56	4.0%	0.75 [0.45, 1.25]
O'Malley 1992	15	52	21	52	3.7%	0.71 [0.42, 1.23]
O'Malley 2008	8	34	13	34	2.4%	0.62 [0.29, 1.29]
Oslin 1997	3	21	7	23	1.0%	0.47 [0.14, 1.58]
Oslin 2008	29	120	23	120	4.2%	1.26 [0.78, 2.05]
Volpicelli 1992	11	35	14	35	3.0%	0.79 [0.42, 1.48]
Volpicelli 1997	13	48	13	49	2.8%	1.02 [0.53, 1.97]
Total (95% CI)		**2223**		**1912**	**100.0%**	**0.91 [0.80, 1.03]**
Total events	599		587			

Heterogeneity: Tau² = 0.04; Chi² = 43.76, df = 25 (P = 0.01); I² = 43%
Test for overall effect: Z = 1.48 (P = 0.14)



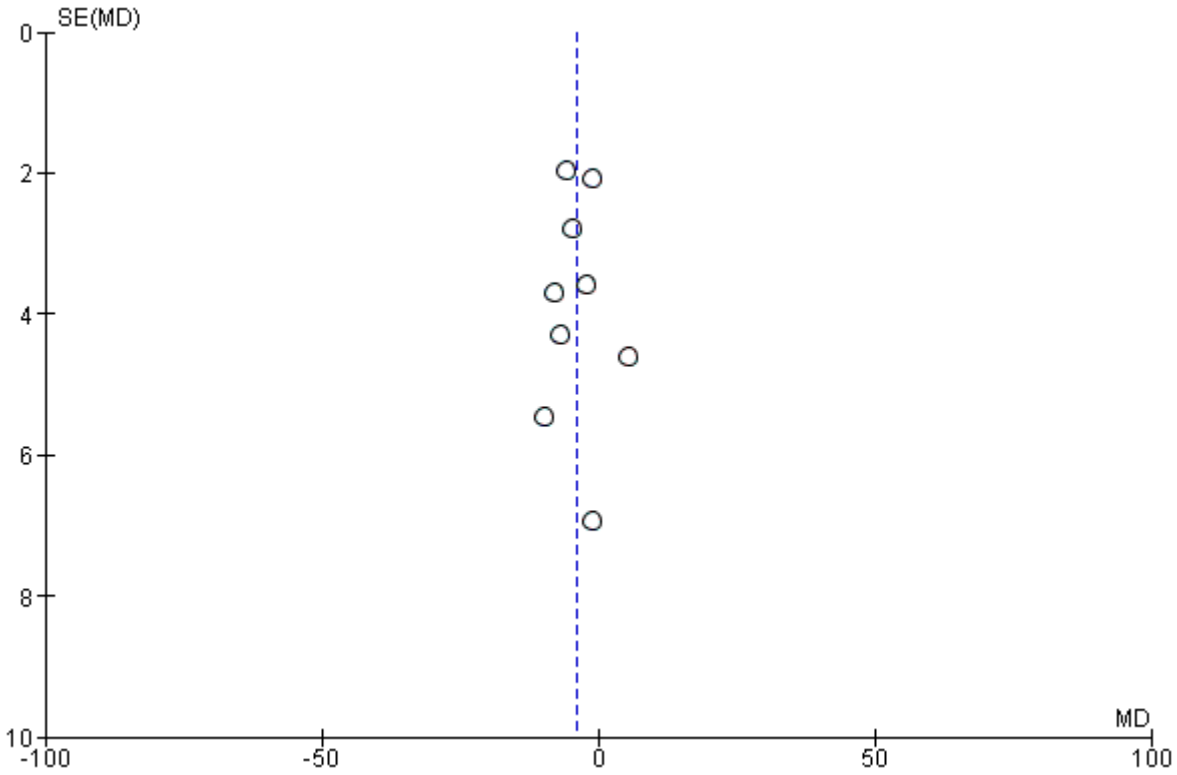
Forest plot of comparison: 1 naltrexon versus placebo for alcohol dependence, outcome: 1.57 Drop-outs.

Figure 12 (Analysis 1.2)



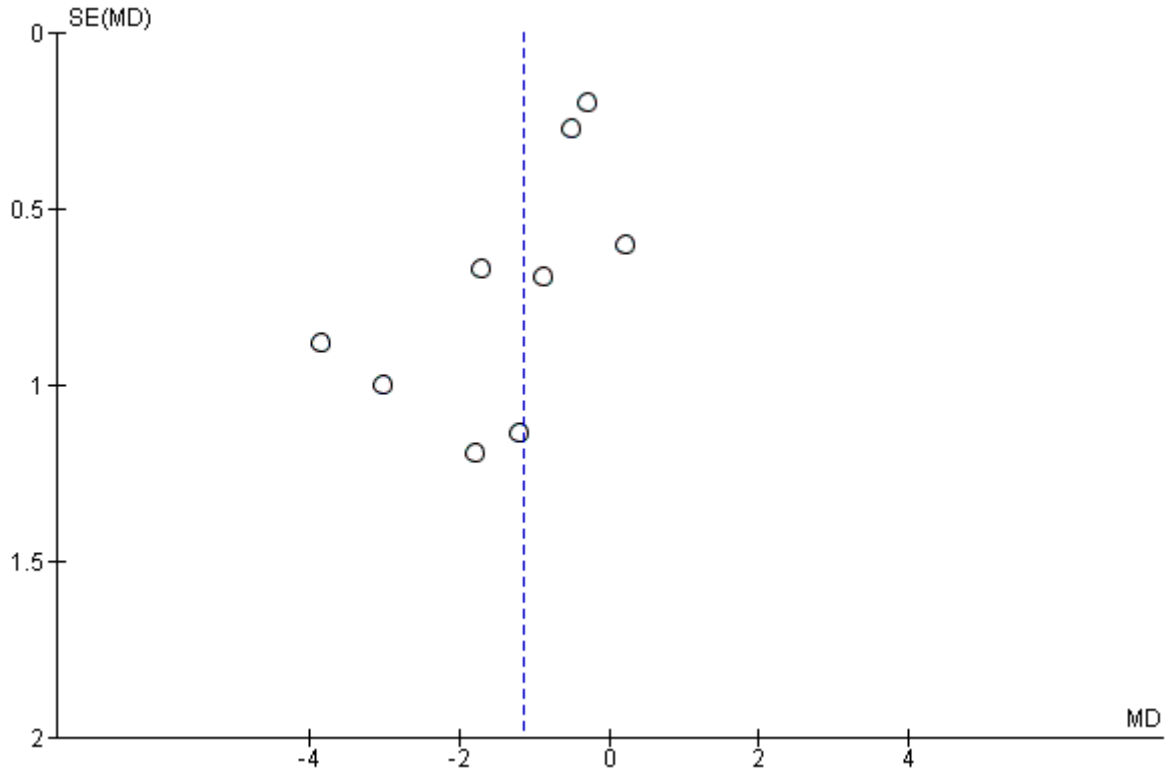
Funnel plot of comparison: 1 naltrexon versus placebo for alcohol dependence, outcome: 1.2 Number individuals non-abstinent (lapsed) after 3 months treatment.

Figure 13 (Analysis 1.4)



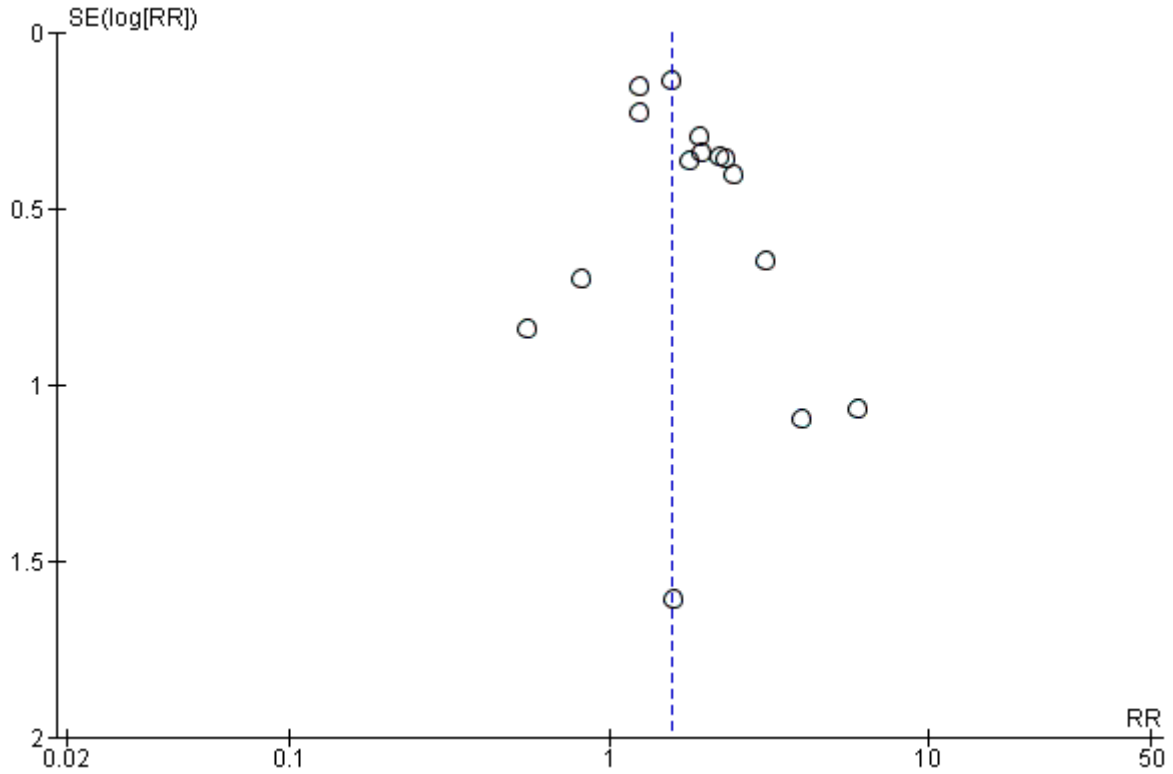
Funnel plot of comparison: 1 naltrexon versus placebo for alcohol dependence, outcome: 1.4 Percentage days abstinent at 3 month after baseline.

Figure 14 (Analysis 1.6)



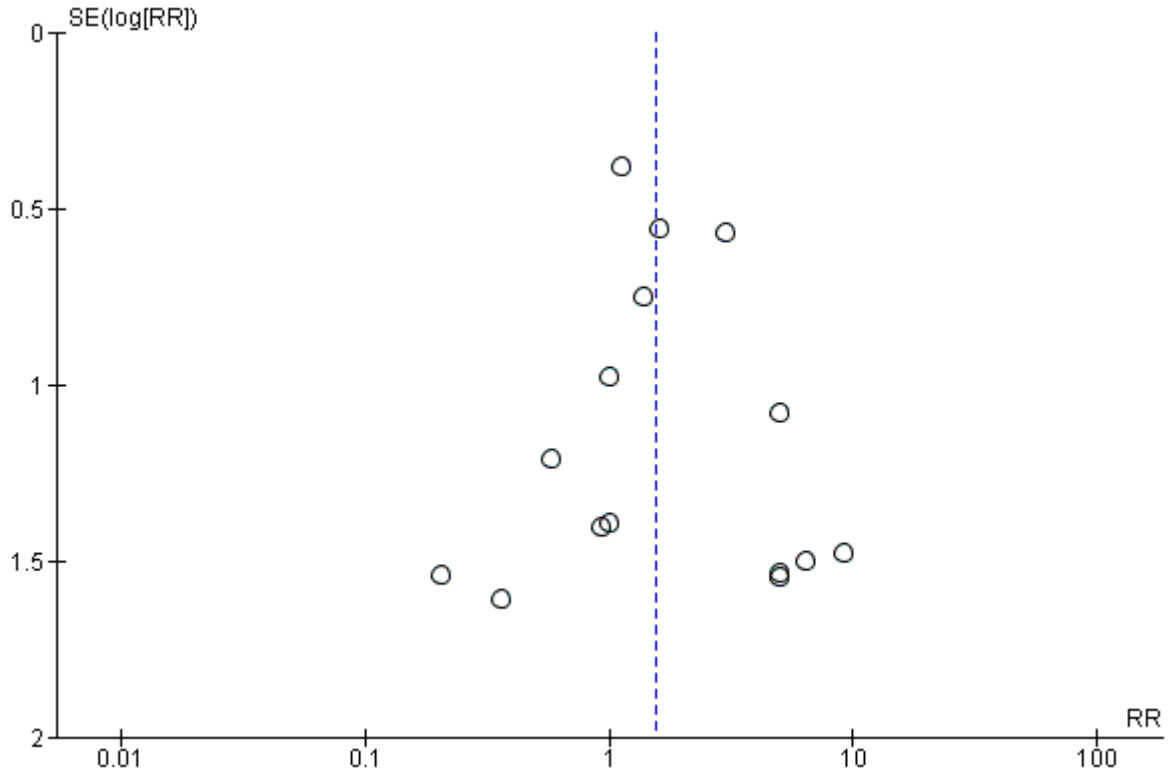
Funnel plot of comparison: 1 naltrexon versus placebo for alcohol dependence, outcome: 1.6 Drinks per drinking day 3 month after baseline.

Figure 15 (Analysis 1.46)



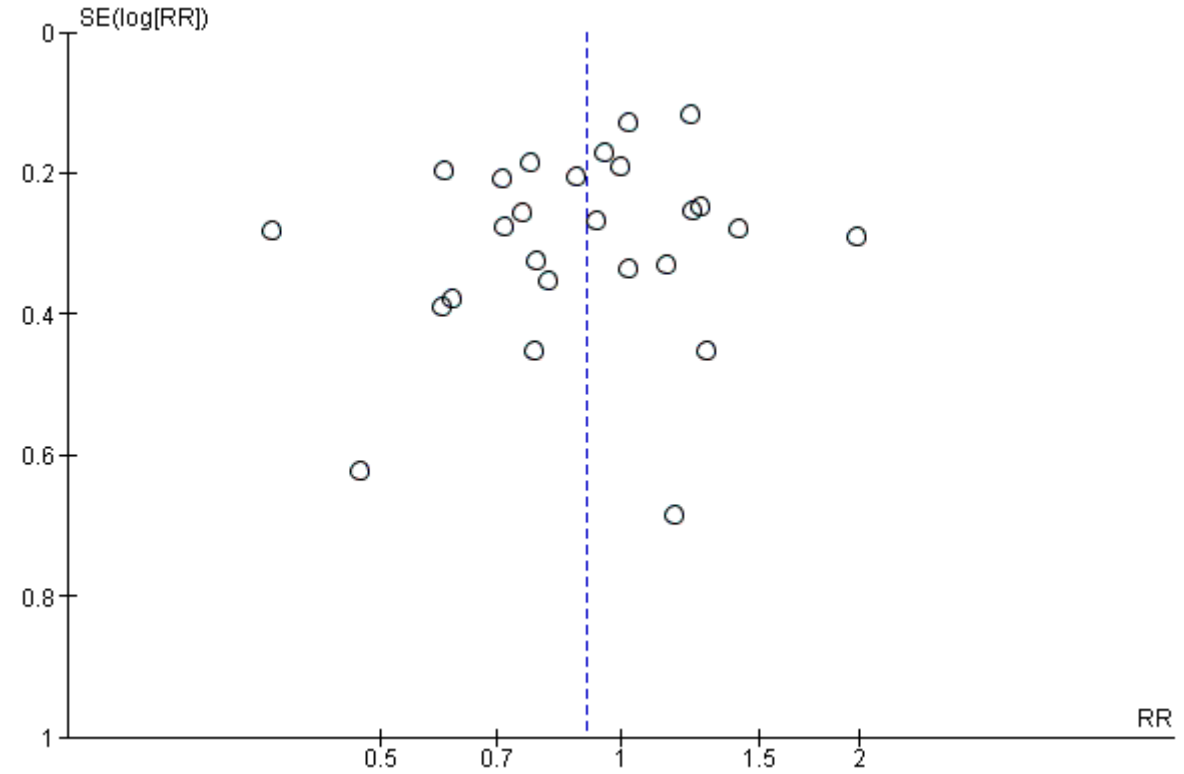
Funnel plot of comparison: 1 naltrexon versus placebo for alcohol dependence, outcome: 1.46 Side effect: Nausea.

Figure 16 (Analysis 1.55)



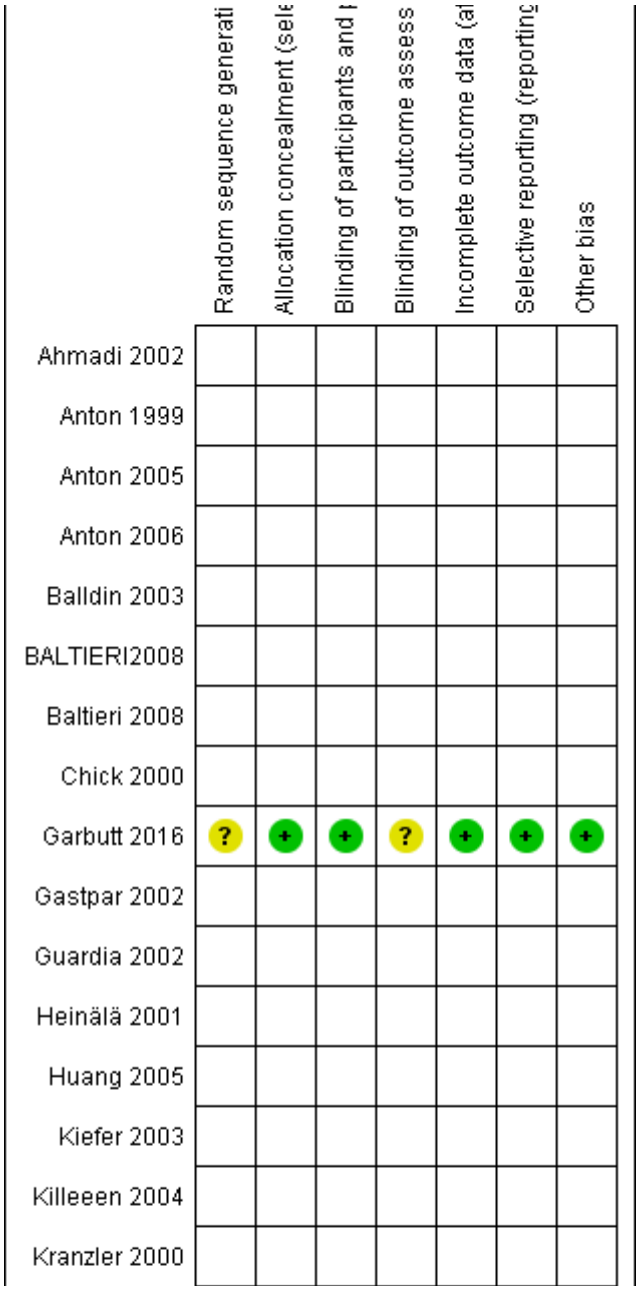
Funnel plot of comparison: 1 naltrexon versus placebo for alcohol dependence, outcome: 1.55 Drop-outs due to adverse events.

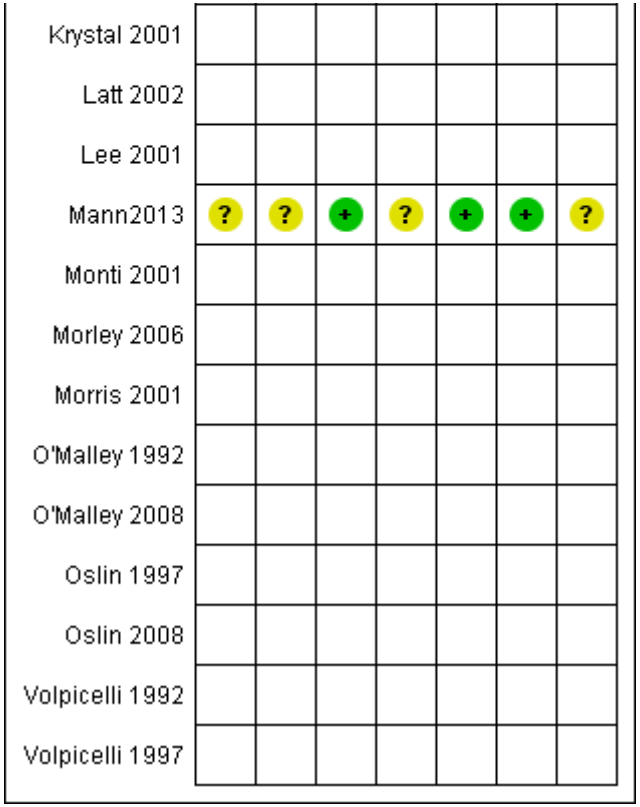
Figure 17 (Analysis 1.57)



Funnel plot of comparison: 1 naltrexon versus placebo for alcohol dependence, outcome: 1.57 Drop-outs.

Figure 18


Random sequence generati
Allocation concealment (sele
Blinding of participants and
Blinding of outcome assess
Incomplete outcome data (at
Selective reporting (reporting
Other bias
Ahmadi 2002
Anton 1999
Anton 2005
Anton 2006
Balldin 2003
BALTIERI2008
Baltieri 2008
Chick 2000
Garbutt 2016
Gastpar 2002
Guardia 2002
Heinälä 2001
Huang 2005
Kiefer 2003
Killeeen 2004
Kranzler 2000



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

Sources of support

Internal sources

- No sources of support provided

External sources

- No sources of support provided