NKR 13 Alkoholbehandling. Disulfiram for alcohol dependency

Review information

Authors

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[1][Empty affiliation]

Characteristics of studies

Characteristics of included studies

Chick 1992

Methods	RCT
Participants	outpatients who had relapsed from earlier treatment
Interventions	supervised disulfiram and counselling
Outcomes	
Notes	funded by Fisons Pic Pharma devision

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	not described
Allocation concealment (selection bias)	Low risk	applied by pharmacist at participating centres
Blinding of participants and personnel (performance bias)	High risk	not blinded
Blinding of outcome assessment (detection bias)	Low risk	assessor blinded
Incomplete outcome data (attrition bias)	High risk	about 1/3 stopped treatment in both groups
Selective reporting (reporting bias)	Low risk	not detected
Other bias	Low risk	not detected

Fuller 1986

Methods	RCT
Participants	men yonger than 60 years presenting for alcohol treatment, excluded if living alone
Interventions	disulfiram and counselling
Outcomes	
Notes	USA, NA, propably VA programme

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	randomisation list likely open
Allocation concealment (selection bias)	High risk	numbered envelopes not described as opaque
Blinding of participants and personnel (performance bias)	Low risk	blinded, tablets of identical type
Blinding of outcome assessment (detection bias)	Low risk	blinded
Incomplete outcome data (attrition bias)	Low risk	only 28 out of 202 did not complete 1 year follow-up
Selective reporting (reporting bias)	Low risk	not detected
Other bias	Low risk	not detected

Gerrein 1973

Methods	RCT
Participants	alcoholics in an outpatient clinic
Interventions	disulfiram supervised plus counselling
Outcomes	
Notes	Fisons Plc Pharma division

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	not decribed
Allocation concealment (selection bias)	Low risk	applied by pharmacist in attending centres
Blinding of participants and personnel (performance bias)	High risk	not blinded
Blinding of outcome assessment (detection bias)	Low risk	assessor blinded
Incomplete outcome data (attrition bias)	High risk	about 1/3 dropped out
Selective reporting (reporting bias)	Low risk	not detected
Other bias	Low risk	not detected

Ulrichsen 2010

Methods	RCT
Participants	patinets admitted for withdrawal treatment
Interventions	supervised disulfiram + kognitive therapy
Outcomes	
Notes	Denmark, foundation for the advancement of science

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	secretary instructed to arrange envelopes in random order
Allocation concealment (selection bias)	Unclear risk	sealed envelopes not described as opaque
Blinding of participants and personnel (performance bias)	High risk	not blinded
Blinding of outcome assessment (detection bias)	High risk	not blinded
Incomplete outcome data (attrition bias)	Low risk	low number of drop-outs
Selective reporting (reporting bias)	Low risk	none detected
Other bias	Low risk	none detected

Footnotes

Characteristics of excluded studies

DeSousa 2014

Reason for exclusion	Wrong study design

Donoghue 2015

Reason for exclusion	Wrong study design

Venkata 2017

Reason for exclusion	Wrong study design

Yoshimura 2014

Reason for exclusion	Wrong intervention

Footnotes

Characteristics of studies awaiting classification

Footnotes

Characteristics of ongoing studies

Footnotes

References to studies

Included studies

Chick 1992

[Empty]

Fuller 1986

[Empty]

Gerrein 1973

[Empty]

Ulrichsen 2010

[Empty]

Excluded studies

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:]

Donoghue 2015

Donoghue, Kim; Elzerbi, Catherine; Saunders, Rob; Whittington, Craig; Pilling, Stephen; Drummond, Colin. The efficacy of acamprosate and naltrexone in the treatment of alcohol dependence, Europe versus the rest of the world: a meta-analysis. Addiction 2015;110(6):920-930. [DOI:]

Venkata 2017

Venkata K.V.; Chhoda A.; Halanych J.H.; Singal, A.. Pharmacological treatment of alcohol abstinence: A systematic review and network meta-analysis.. Gastroenterology 2017;Conference(Journal Article):geste. [DOI:]

Yoshimura 2014

Yoshimura, Atsushi; Kimura, Mitsuru; Nakayama, Hisakazu; Matsui, Toshifumi; Okudaira, Fukiko; Akazawa, Shigeru; Ohkawara, Masao; Cho, Tetsuji; Kono, Yoshihiro; Hashimoto, Koji; Kumagai, Masayuki; Sahashi, Yukiko; Roh, Sungwon; Higuchi, Susumu. Efficacy of disulfiram for the treatment of alcohol dependence assessed with a multicenter randomized controlled trial.. Alcoholism: Clinical & Experimental Research 2014;38(2):572-578. [DOI:]

Data and analyses

1 Disulfiram vs control post treatment

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
1.1 All cause drop-out	3	563	Risk Ratio (M-H, Random, 95% CI)	0.59 [0.27, 1.29]
1.3 Number of patients abstinent 6-12 month from baseline	1	401	Risk Ratio (M-H, Random, 95% CI)	1.17 [0.76, 1.79]
1.4 Number of days abstinent after 6 month treatment (Final)	1	39	Mean Difference (IV, Random, 95% CI)	0.00 [-46.76, 46.76]
1.5 Number of days abstinent in last 6 month (change)	1	93	Mean Difference (IV, Random, 95% CI)	-31.00 [-58.85, -3.15]
1.6 Number of patients abstinent 3 month after baseline	0	0	Odds Ratio (M-H, Fixed, 95% CI)	Not estimable
1.7 Remaining abstinent at 8 weeks EoT	1	36	Risk Ratio (M-H, Random, 95% CI)	4.42 [0.99, 19.67]
1.8 Number of patients abstinent 6-12 month FU	0	0	Odds Ratio (M-H, Fixed, 95% CI)	Not estimable
1.9 Time to first drink (days)	2	440	Mean Difference (IV, Random, 95% CI)	2.42 [-28.48, 33.31]
1.10 Drinks pr week after 6 month of treatment (Change)	1	97	Mean Difference (IV, Random, 95% CI)	-57.00 [-120.63, 6.63]

1.11 Drinks pr drinkings day 6-12 months FU	0	0	Std. Mean Difference (IV, Random, 95% CI)	Not estimable
1.12 Serious adverts events	2	165	Risk Ratio (M-H, Random, 95% CI)	0.32 [0.01, 7.78]
1.13 Drop out due to adverse events	2	165	Risk Ratio (M-H, Random, 95% CI)	3.88 [0.45, 33.71]
1.14 Adverse events - diarrhea	0	0	Risk Ratio (M-H, Random, 95% CI)	Not estimable
1.15 Adverts Events - nausea	1	126	Risk Ratio (M-H, Random, 95% CI)	0.97 [0.14, 6.66]

Figures

Figure 1 (Analysis 1.1)
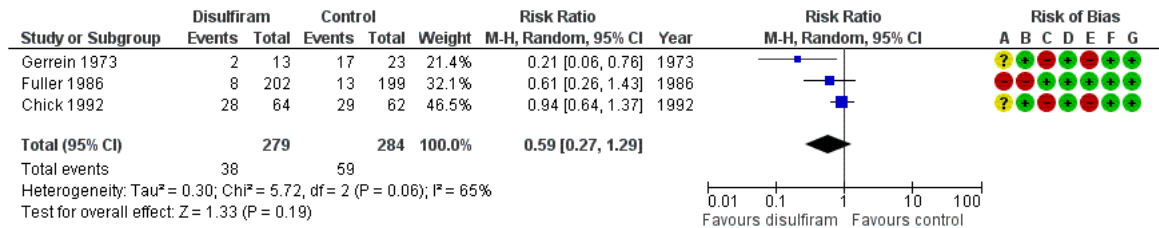
Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Forest plot of comparison: 1 Disulfiram vs control post treatment, outcome: 1.1 All cause drop-out.
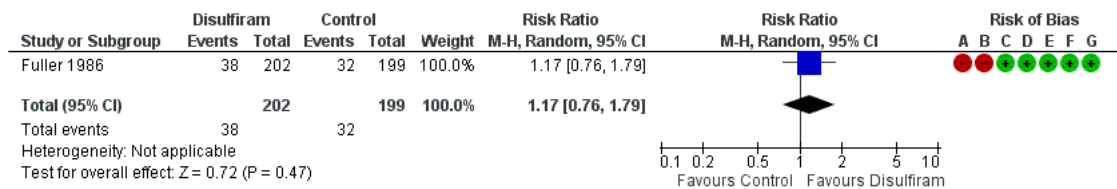
Figure 2 (Analysis 1.3)

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 Disulfiram vs control post treatment, outcome: 1.3 Number of patients abstinent 6-12 month from baseline.

Figure 3 (Analysis 1.4)

Study or Subgroup	Disulfiram Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI	Risk of Bias A B C D E F G
Ulrichsen 2010	100	72	19	100	77	20	100.0%	0.00 [-46.76, 46.76]		? ? ● ● − ● ●
Total (95% CI)			19			20	100.0%	0.00 [-46.76, 46.76]		

Heterogeneity: Not applicable
Test for overall effect: Z = 0.00 (P = 1.00)
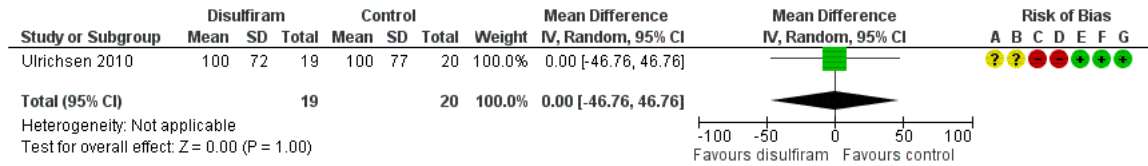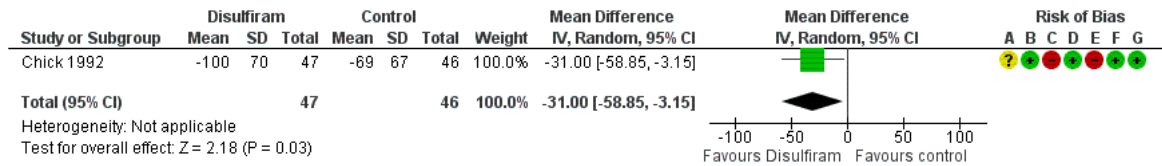
-100 -50 0 50 100
Favours disulfiram   Favours control

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 Disulfiram vs control post treatment, outcome: 1.4 Number of days abstinent after 6 month treatment (Final).

Figure 4 (Analysis 1.5)

Study or Subgroup	Disulfiram Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI	Risk of Bias A B C D E F G
Chick 1992	-100	70	47	-69	67	46	100.0%	-31.00 [-58.85, -3.15]		? ● ● ● ● ● ●
Total (95% CI)			47			46	100.0%	-31.00 [-58.85, -3.15]		

Heterogeneity: Not applicable
Test for overall effect: Z = 2.18 (P = 0.03)

-100 -50 0 50 100
Favours Disulfiram   Favours control

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 Disulfiram vs control post treatment, outcome: 1.5 Number of days abstinent in last 6 month (change).

Figure 5 (Analysis 1.7)

Study or Subgroup	Disulfiram Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI	Risk of Bias A B C D E F G
Gerrein 1973	5	13	2	23	100.0%	4.42 [0.99, 19.67]		?➕➖➕➖➕➕
Total (95% CI)		13		23	100.0%	4.42 [0.99, 19.67]		
Total events	5		2					

Heterogeneity: Not applicable
Test for overall effect: Z = 1.95 (P = 0.05)

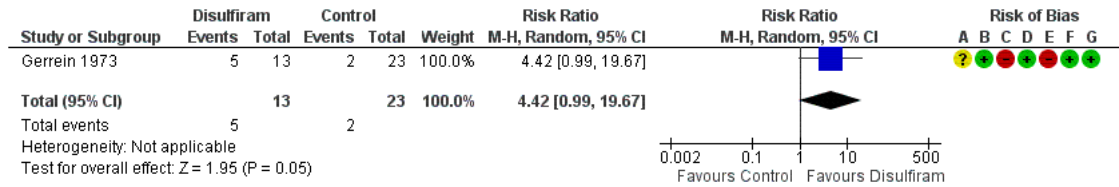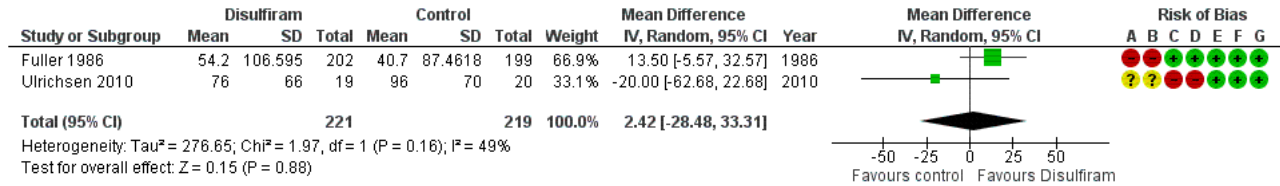0.002   0.1   1   10   500
Favours Control   Favours Disulfiram

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 Disulfiram vs control post treatment, outcome: 1.7 Remaining abstinent at 8 weeks EoT.
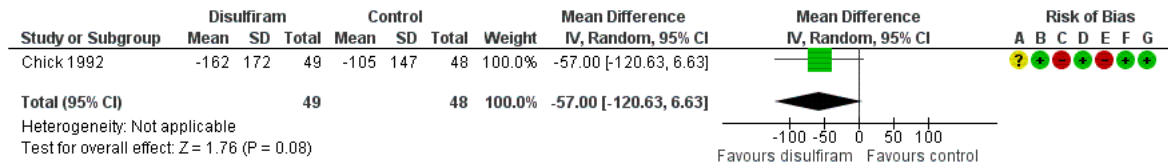
Figure 6 (Analysis 1.9)

Study or Subgroup	Disulfiram Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI	Year	Mean Difference IV, Random, 95% CI	Risk of Bias A B C D E F G
Fuller 1986	54.2	106.595	202	40.7	87.4618	199	66.9%	13.50 [-5.57, 32.57]	1986		➖➖➕➕➕➕➕
Ulrichsen 2010	76	66	19	96	70	20	33.1%	-20.00 [-62.68, 22.68]	2010		??➖➖➕➕➕
Total (95% CI)			221			219	100.0%	2.42 [-28.48, 33.31]			

Heterogeneity: Tau² = 276.65; Chi² = 1.97, df = 1 (P = 0.16); I² = 49%
Test for overall effect: Z = 0.15 (P = 0.88)

-50   -25   0   25   50
Favours control   Favours Disulfiram

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 Disulfiram vs control post treatment, outcome: 1.9 Time to first drink (days).
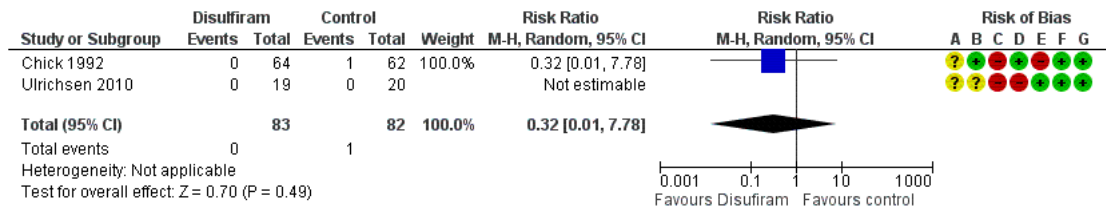
Figure 7 (Analysis 1.10)

	Disulfiram			Control				Mean Difference	Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	A B C D E F G
Chick 1992	-162	172	49	-105	147	48	100.0%	-57.00 [-120.63, 6.63]		? + – + – + +
Total (95% CI)			49			48	100.0%	-57.00 [-120.63, 6.63]		

Heterogeneity: Not applicable
Test for overall effect: Z = 1.76 (P = 0.08)

-100 -50 0 50 100
Favours disulfiram   Favours control

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 Disulfiram vs control post treatment, outcome: 1.10 Drinks pr week after 6 month of treatment (Change).
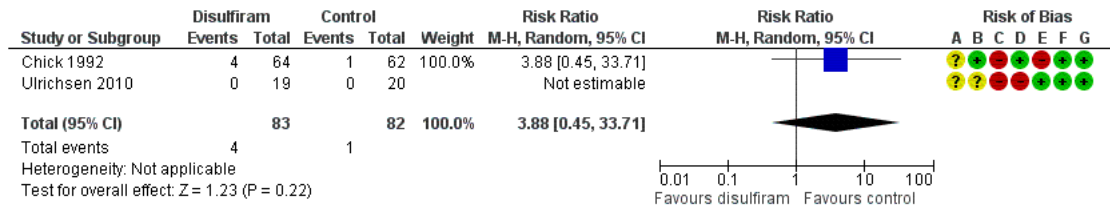
Figure 8 (Analysis 1.12)

	Disulfiram		Control			Risk Ratio	Risk Ratio	Risk of Bias
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI	A B C D E F G
Chick 1992	0	64	1	62	100.0%	0.32 [0.01, 7.78]		? + – + – + +
Ulrichsen 2010	0	19	0	20		Not estimable		? ? – + – + +
Total (95% CI)		83		82	100.0%	0.32 [0.01, 7.78]		
Total events	0		1					

Heterogeneity: Not applicable
Test for overall effect: Z = 0.70 (P = 0.49)

0.001 0.1 1 10 1000
Favours Disufiram   Favours control

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 Disulfiram vs control post treatment, outcome: 1.12 Serious adverts events.
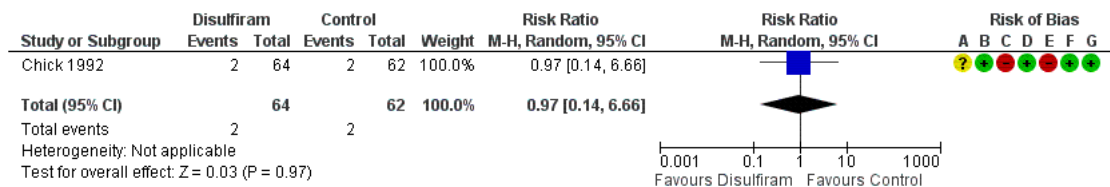
Figure 9 (Analysis 1.13)

Study or Subgroup	Disulfiram Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Chick 1992	4	64	1	62	100.0%	3.88 [0.45, 33.71]
Ulrichsen 2010	0	19	0	20		Not estimable
Total (95% CI)		83		82	100.0%	3.88 [0.45, 33.71]
Total events	4		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.23 (P = 0.22)						

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 Disulfiram vs control post treatment, outcome: 1.13 Drop out due to adverse events.

Figure 10 (Analysis 1.15)

Study or Subgroup	Disulfiram Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Chick 1992	2	64	2	62	100.0%	0.97 [0.14, 6.66]
Total (95% CI)		64		62	100.0%	0.97 [0.14, 6.66]
Total events	2		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.03 (P = 0.97)						

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 Disulfiram vs control post treatment, outcome: 1.15 Adverts Events - nausea.

Figure 11

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