Kliiniline küsimus nr 12

Kas kõigil aversiivseid ravimeid saavatel alkoholisõltuvusega patsientidel rakendada abstinentsi säilitamiseks tablettravi (jälgitud kasutamine vs mittejälgitud kasutamine) vs subkutaanset implantaati?

Kriitilised tulemusnäitajad:
abstinents, tagasilangus, alkoholi tarvitamise vähenemine, patsiendi rahulolu, patsiendi elukvaliteet, kvaliteetselt elatud eluaastate lisandumine, haiguse/vaegurluse tõttu kaotatud päevade arv, ravisoostumus, ravi katkestamine mistahes põhjusel, ravi katkestamine ravimite kõrvaltoimete tõttu, juhuslik alkoholi tarvitamine

Ravijuhendid

Kokkuvõte tõendusmaterjali kvaliteedist

Tablettravi vs implantaat:

Põhjalik metaanalüüs, mis käsitleb implanteeritava disulfiraami efektiivust on toodud Austraalia 2011 ülevaates „farmakoteraapia alkoholisõltuvuse ravis" vt täpsemalt allpool. Meta-analüüsi kvaliteedi määravad ära selles kasutatud kliinilised uuringud. Kvaliteeti hinnati GRADE põhimõttel.

Jälgitud kasutamine vs mittejälgitud kasutamine:

Skinner et al 2014 hea kvaliteediga süstemaatiline ülevaade analüüsis superviseeritud vs mitte superviseeritud disulfiraami efektiivsust. Efektiivsus oli mõõdetud "Hedge g "efekti suurusega:

Efekti suurus 0.2 to 0.3 ''small'' effect

around 0.5 a''medium'' effect

0.8 to infinity, a ''large'' effect

Subgrupi analüüs näitas, et superviseeritud disulfiraam vs kontrollgrupp oli palju efektiivsem g = 0.82, 95%CI

= .59–1.05 (Figure 4). Kui disulfiraamiga ravi ei olnud jälgitud, siis ei leitud olulist erinevust aktiivravi ja kontrollgrupi vahel g = 0.26 (95%CI =2 .02–.53). Vt allolev joonis (Skinner 2014, figure 4)

When combining the 22 RCTs, our meta-analysis showed a

significant success rate of disulfiram compared to controls: g = 0.58

(95%CI = .35–.82). The subgroup analysis comparing blind and open-label RCTs

indicated that only the open-label trials showed a significant

superiority of disulfiram over controls: g = .70 (95%CI = .46–.93),

whereas the RCTs with blind designs showed no efficacy of

disulfiram as compared to controls: g = .01 (95%CI = . 2.29–.32)

Veel üks oluline tähelepanek selles meta-analüüsis: disulfiraami efektiivsus avaldub vaid avatud disainiga uuringutes. Pimendatud uuringutes ei leitud efekti disulfiraami ja kontrollgrupi vahel. Pimendatud disainiga disulfiraami uuringud kaotavad olulise psühholoogilse efekti (hirm alkoholi ja ravimi koostoime ees) gruppide vahel. Ehk nii disulfiraami kui kontrollgrupiga patsiendid kõik kardavad ravimi ja alkoholi koostoimeid ning seetõttu hoiduvad alkoholist ja gruppide erinevust ei esine.

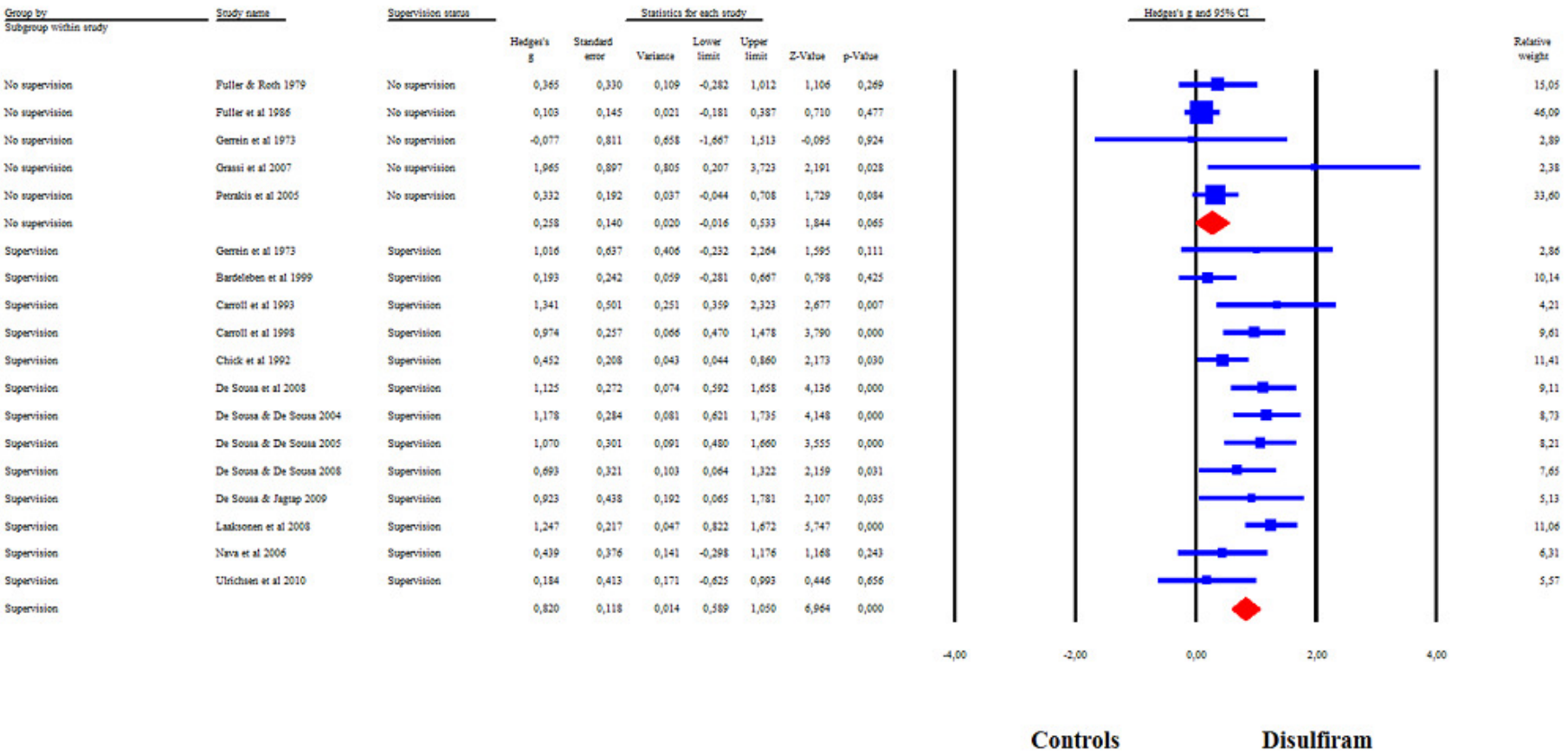


Figure 4. Meta-analysis of RCTs with supervision versus no supervision. Meta-analysis of Hedges' g effect-size comparing the efficacy of disulfiram and controls in RCTs with supervision versus no supervision.
doi:10.1371/journal.pone.0087366.g004

Australia 2009 ravijuhendi tõendusmaterjali kokkuvõte jälgitud vs mittejälgitud disulfiraami kohta põhineb 2 RCT-l ja 1 ülevaateartiklil (Chick et al. 1992; Hughes and Cook 1997; Laaksonen et al. 2008). Need uuringud annavad kinnitust, et superviseeritud disulfiraam on efektiivsem kui mittejälgitud ravii võtmine. Laaksonen et al 2008 tõdeb, et kehvad tulemused disulfiraamraviga võivad tuleneda halvast ravisoostumusest, kui patsiendid võtavad disulfiraami mittejälgitult. Mitmeid uuringuid on kritiseeritud selle eest, et disulfiraami anti mittesuperviseeritult (Brewer, 1987; Anton, 2001). Laaksonen et al 2008 uuringusse kaasati 25-65 aastased alkoholisõltuvuse diagnoosiga (RHK-10) patsiendid. Uuringus osalejad jaotati 3 gruppi: 81 patsienti naltreksooni, 81 akamprosaadi ja 81 patsienti disulfiraami rühma.Uuringu esimesed 3 kuud olid regulaarne ravimi tarbimine (disulfiraam 400mg 2x nädalas), pärast seda võeti ravimit vajadusel riskiolukorras, seda ka disulfiraami korral. Selle uuringu primaarsed tulemusnäitajad on ära toodud tabelis 2 ja 3.

Table 2. Drinking outcomes during continuous medication period (up to 12 weeks)

	ACA	DIS	NTX
Time (days) to first HDD, mean ± SD (n)	17.6 ± 22.0 (44)	46.6 ± 27.5 (33)**	22.0 ± 22.0 (47)
Time (days) to first drinking, mean ± SD (*N*)	11.4 ± 17.0 (50)	30.4 ± 27.8 (39)*	16.2 ± 20.2 (50)
Abstinence days/week, mean ± SD (*N*)	4.5 ± 2.1 (52)	6.3 ± 0.9 (54 ***)	4.6 ± 2.0 (53)

* Significance DIS > NTX and ACA; $P = 0.0002$.
** Significance DIS > NTX and ACA ($P < 0.0001$).
*** Significance DIS > NTX and ACA ($P < 0.0001$); difference between weeks ($P = 0.001$).

Table 3. Average alcohol (g/ethanol per week) intake during the study period (0–52 weeks)

	ACA	DIS	NTX
Baseline, mean ± SD (*N*)	570.8 ± 333.8 (71)	591.2 ± 325.8 (69)	561.8 ± 286.2 (75)
Continuous medication (weeks 1–12), mean ± SD (*N*)	203.2 ± 180.2 (58)	52.0 ± 90.7 (60)*	183.7 ± 174.1 (64)
Targeted medication (weeks 13–52), mean ± SD (*N*)	194.9 ± 148.4 (39)	109.2 ± 103.7 (37)**	229.3 ± 199.6 (41)

Significant reduction in alcohol intake in all groups between the baseline and weeks 1–12 and 13–52.
* Significance DIS > NTX and ACA ($P < 0.0001$).
** Significance DIS. > NTX ($P = 0.0005$) and ACA ($P = 0.0097$).

Põhjalikumalt on analüüsitud superviseeritud disulfiraami uuringuid Australia 2011 meta-analüüsis, kus tõdetakse et ravisoostumus on kriitiline ravitulemuse saavutamiseks ning ravisoostumus on rohkem tõenäoline superviseeritud ravimi võtmisega ja kui patsiendil on stabiilsed lähisuhted. Siiski üleüldine dislufiraami efekt kohe peale 6-11 kuud kestnud ravi oli väikene (efekti suurus +0.15) ja 12-23 kuud peale ravi lõpetamist + 0.10. Meta-analüüsis on

analüüsitud disulfiraami efekti totaalsele abstinentsile ning on leitud, et abstinents ravi ajal või ravi lõppedes ei ole olulist erinevust järgmistes võrdlustes:

- Per os disulfiraam vs platseebo (RR 1.08, 95% Cll 0.88, 1.31; P=0.47) (very low strength of evidence)

- Implanteeritud disulfiraam vs platseebo (RR 1.39, 95% Cl 0.79, 2.44; P=0.25) (very low strength of evidence)

- per os disulfiraam vs mitte ravimid (RR1.29, 95% Cl 0.97, 1.70; P=0.08) (very low strength of evidence)

Kokkuvõte ravijuhendites leiduvatest soovitustest

Kümnest ravijuhendist kolmes (Austraalia 2009, Soome 2010, WFSBP 2008) leidus infot K12 küsimuse kohta. WSFBP ravijuhend mainib, et Johnsen and Morland 1991 uuring ei näidanud disulfiraami implantaadi efektiivsust.

Soome ravijuhend tõdeb samuti, et implanteeritava disulfiraami efekt ei erine platseebost.

Kõige põhalikumalt on implanteeritava disulfiraami efekte hinnatud Austraalia 2011 meta-analüüsis.

Erinevalt teistest allikatest on seal välja toodud ka see, et platseboefekt on implanteeritava disulfiraami uuringutes olnud väga tugev ning eraldi on refereeritud Wilsoni (1980) uuringu tulemusi kus platseebo (sham operatsioon) rühmas oli abstsinents 307 päeva ja disulfiraami puhul 361 päeva võrreldes tavaolukorraga kus enamik sellistest patsientides hakkab 1 kuu jooksul uuesti alkoholi tarvitama.

Kontrollimata andmed viitavad sellele, et osade patsientide rahulolu püsiva abstsinentsi saavutamise osas implanteeritava disulfiraamiga on väga kõrge (vt. allpool).

Ravijuhendite soovituste tekstid (inglise keeles):

SIGN 2003
Ei käsitle implanteeritavat disulfiraami

NICE 2011
For naltrexone and disulfiram, only the oral delivery preparations of these drugs was considered for meta-analysis due to the lack of available evidence and the uncommon usage of the extended-release and subcutaneous implantation preparations of these drugs.

NSW Psychosocial interventions 2008
There is less evidence for the use of disulfiram among people with alcohol dependence. It is most commonly indicated for clients who are highly motivated to abstain from alcohol, and good outcomes can be achieved with close supervision. Disulfiram works by interacting with alcohol to create an intensely aversive reaction when alcohol is consumed (28), however is not currently subsidised by the pharmaceutical benefits scheme.

Austraalia 2009
Ei käsitle implanteeritavat disulfiraami, kuid
käsitleb superviseeritud per os disulfirami ja annab järgmise soovituse:

Disulfiram is recommended in closely supervised alcohol-dependent patients motivated for abstinence and with no contraindications.

Supervision
Based on the outcomes of the recent studies discussed above, disulfiram treatment is best suited to individuals with social supports (e.g. family) who will help supervise medication adherence (Chick et al. 1992; Hughes and Cook 1997; Laaksonen et al. 2008). Supervision has a marked effect on adherence and may greatly improve the effectiveness of this intervention.
A spouse/partner is an obvious choice for married/de facto patients. It is important to stress that the spouse cannot be expected to control the other person's drinking. A

written 'disulfiram contract' should be considered between a carer and patient. This contract should include an outline of the likely effects of drinking and products that may need to be avoided (e.g. facial products), the recognition that the patient will allow the medication to be supervised, that the carer will be the supervisor and that the supervisory role includes contacting the health professional if medication compliance becomes a problem.

Soome 2010

With disulfiram implants inadequate blood levels are achieved, and the effect is therefore no greater than that of a placebo «Disulfiraami-implantteja käytettäessä lääkkeen pitoisuus veressä ei ole riittävä, ja tästä syystä sen vaikutus on enintään lumelääkkeen veroinen.»A.

With disulfiram implants inadequate blood levels are achieved, and the effect is therefore no greater than that of a placebo.

Currently available disulfiram implants are incapable of providing therapeutically sufficient blood levels. In one trial, only, a positive treatment result was achieved using the implant product «Wilson A, Davidson WJ, Blanchard R. Disulfiram implantation: a trial using placebo implants and two types of controls. J Stud Alcohol 1980;41:429-36»1. In four controlled studies (n = 76, 120, 12, 36) the results were negative «Borg S, Halldin J, Kuhlhorn E et al. Disulfiram implantation – en placebokontrollerad multicenter studie stödjer inte dess terapeutiska effekt. Läkartidningen 1984;81:4381-7»2, «Johnsen J, Mörland J. Disulfiram implant: a double-blind placebo-controlled follow-up on treatment outcome. Alcohol Clin Exp Res 1991;15:532-6»3, «Wilson A, Davidson WJ, White J. Disulfiram implantation: placebo, psychological deterrent, and pharmacological deterrent effects. Br J Psychiatry 1976;129:277-80»4, «Wilson A, Davidson WJ, Blanchard R, White J. Disulfiram implantation. A placebo-controlled trial with two-year followup. J Stud Alcohol 1978;39:809-19»5.

- Quality of study: acceptable
- Applicability to the Finnish population: good

BAP 2012

Ei käsitle implanteeritavat disulfiraami

WFSBP 2008

Efforts have been made to develop long-lasting, implantable formulations of disulfiram to improve adherence. There are few studies of this approach. A placebo-controlled trial (Johnsen and Morland 1991) failed to show efficacy of the disulfiram implant. At present, this treatment cannot be recommended.

APA 2006

Ei käsitle implanteeritavat disulfiraami

SAMHSA 2009

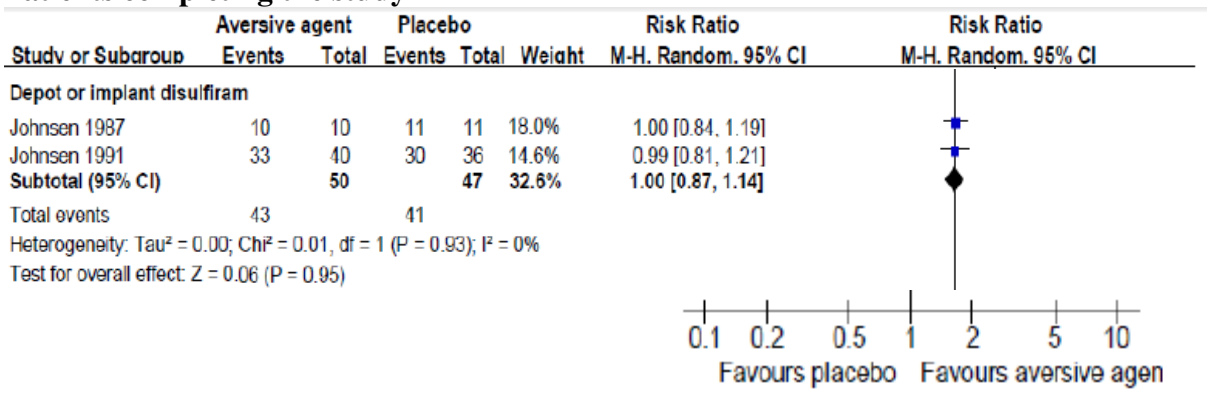
Ei käsitle implanteeritavat disulfiraami

Meta-analüüs: Pharmacotherapies for relapse prevention in alcohol dependence, Drug and Alcohol Services South Australia, Linda R.Gowing, 2011:

Time to firs drink and time to relapse

Implant disulfiram is no more effective than placebo in delaying recommencement of drinking but there is a strong placebo effect.* Studies cited used implant disufliram – Johnsen 1987; Johnsen 1991; Wislon 1976; Wilson 1980.
There are limitations to all data, with further studies needed to confirm findings
Adverse effects
Factros affecting treatment response
Available evidcence does not support significantly improved outcomes with implanted compared to oral disulfiram.
The implants used in fours studies comprised eight to ten 100 mg tablets of disulfiram.

Patients completing the study



There is no significant difference in the proportion of participants abstinent at the end of treatment, or continuously abstinent during treatment with:

- Implant disulfiram compared with placebo (Fig 3.5. RR 1.08; 95% CI 0.79, 2.44, P=0.25

Fig3.5 Aversive agent compared with placebo, participants at end of treatment continuously abstinent during treatment

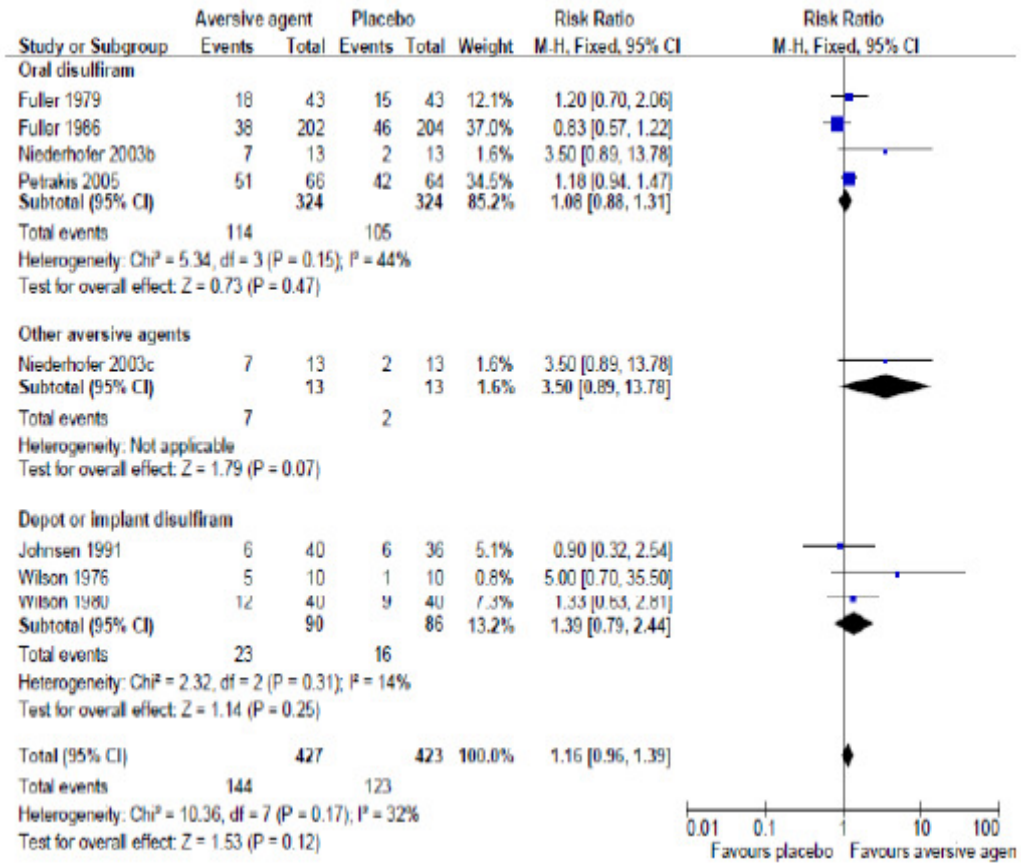


Fig 3.6. Aversive agent compared with no medication, participants abstinent at the end of treatment of continuously abstinent during treatment.

Figure 3.6: Aversive agent compared with no medication, participants abstinent at end of treatment or continuously abstinent during treatment

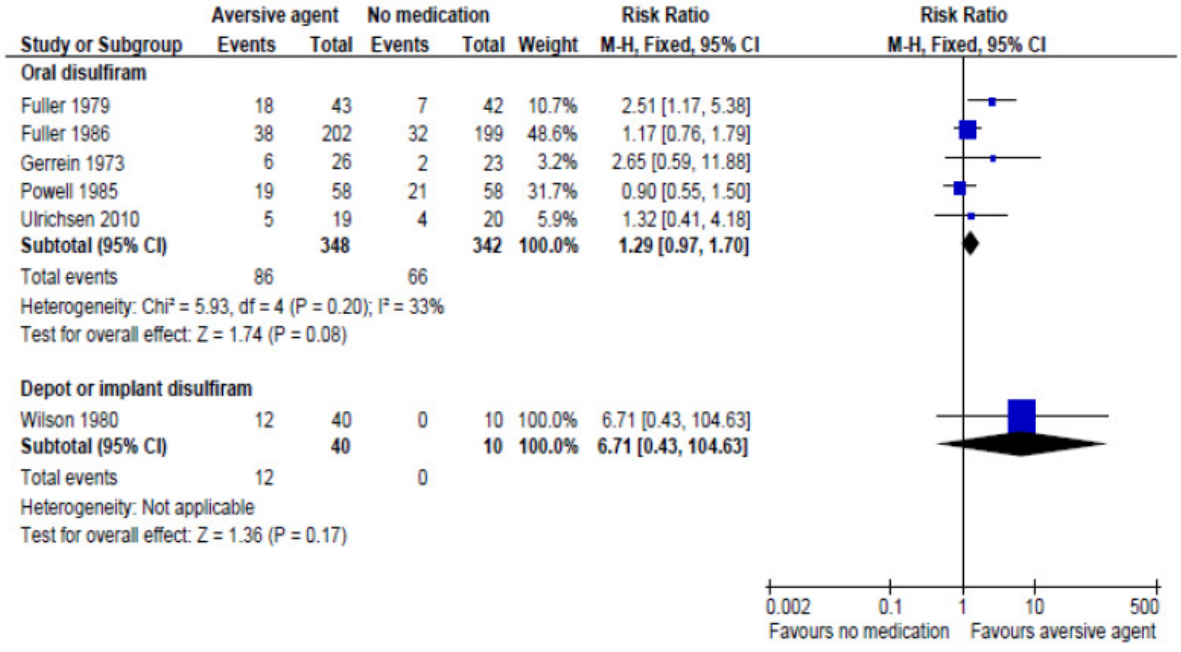
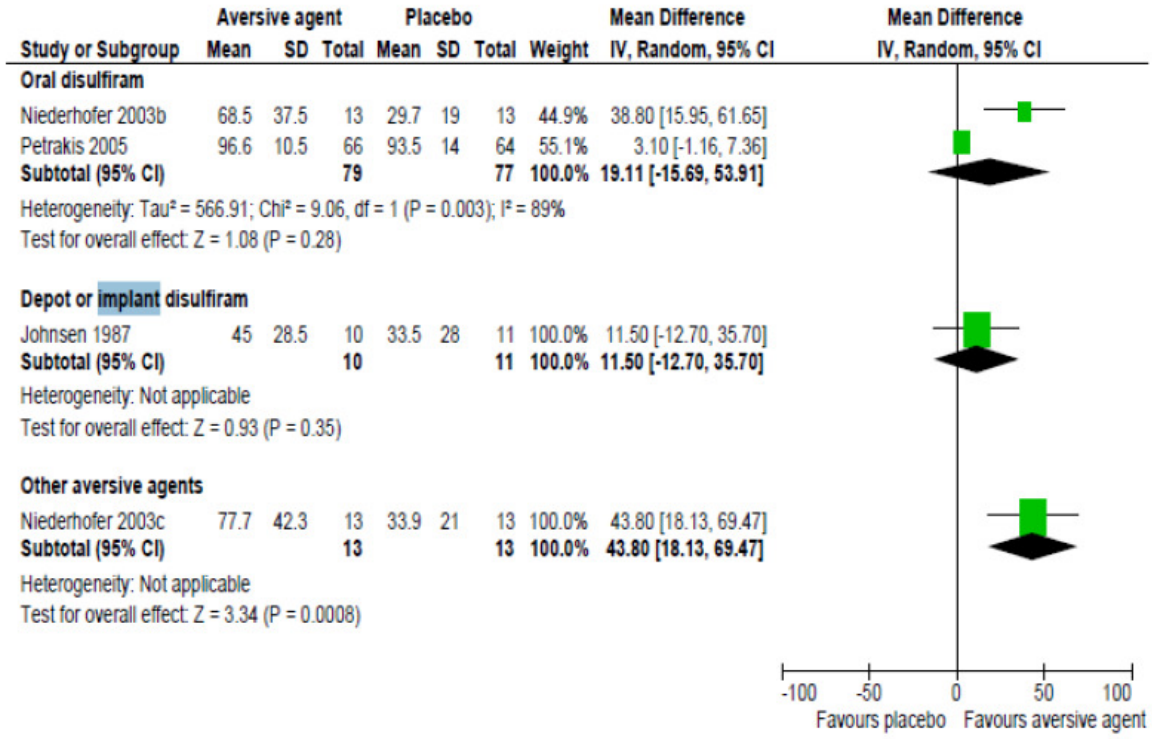


Figure 3.10: Aversive agent compared with placebo, % treatment days abstinent (cumulative abstinence duration)

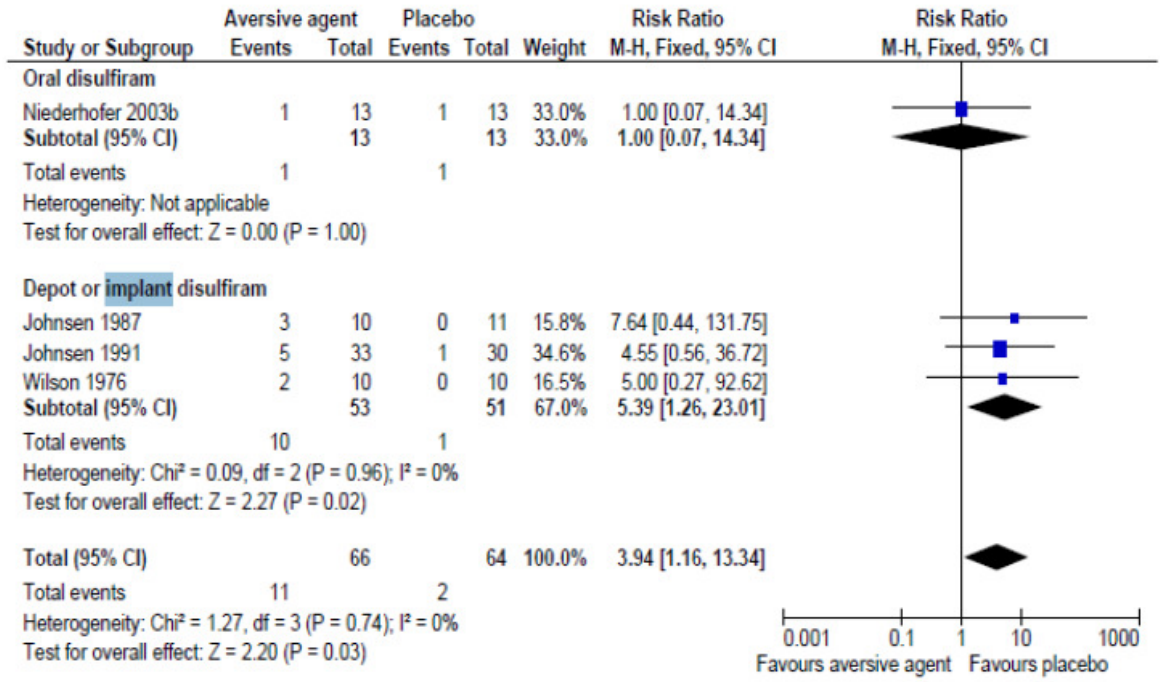


Time to first drink and time to relapse

- Implant disfulfiram is no more effective than placebo in delaying recommencement of drinking, but there is strong placebo effect.
- In Wilson 1980, the disulfiram patients were abstinent for a mean of 361 days, placebo patients 307 days and no-operation controls 24 days. The latter finding shows the presence of a strong placebo effect.

The implantation of disulfirsam tablets as performed by the studies included in this review appears to be associated with significantly greater risk of wound complications.

Figure 3.16: Aversive agent compared with placebo, participants experiencing any adverse effects



Based on three studies, implant preparations of disulfiram are associated with significantly more adverse effects than placebo (Figure 3.16: RR 5.39, 95% CI 1.26, 23.01; P=0.02)*. Adverse effects of implants are largely due to a greater risk of wound complications. Allen and Litten 231 commented that implants are frequently problematic due to inadequate release of the drug as well as infections and other adverse physiological consequences of the surgical procedure.

In Wilson 1976, five patients with disulfiram implants resumed drinking after an ethanol challenge. Two of the five required emergency treatment for disulfiram-ethanol reactions, and the others experienced mild reactions. In Wilson 1980, on resumption of drinking, seven patients with disulfiram implants did not experience a disulfiram-ethanol reaction, six experienced mild reactions, and four experienced severe reactions requiring hospitalisation for up to three days.

Compliance

Available evidence does not support significantly improved outcomes with implanted compared to oral disulfiram.

Factors affecting treatment effectiveness

Studies of disulfiram implants did not support increased effectiveness from this route of administration, with complications around the point of implant insertion comprising a significant source of adverse effects.

Johnsen 1987 [210]	Norway	Alcoholism by Short Michigan Screening Test. Mean age 40, all male.	Disulfiram or calcium phosphate (placebo) implant (10x100mg tablet). No adjunct treatment reported – participants not told some would receive placebo. 20 week study.
Johnsen 1991 [220]	Norway	Alcohol dependent by DSM-III, requested disulfiram implant. Mean age 42, male and female (proportions not reported).	Disulfiram (10x100mg) or placebo (9x100mg calcium phosphate, 1x100mg disulfiram) tablet implant. No adjunct treatment reported. Participants not told some would receive placebo. 10 month study.
Wilson 1976 [223;224]	Canada	"Alcoholic", 17/20 from "Skid Row", mean age 34, 85% male.	Disulfiram 8 x 100mg tablets implanted, or sham operation. Alcohol challenge 120 hours after operation, monthly interviews.
Wilson 1980 [214]	Canada	"Alcoholic", weighted heavily towards "Skid Row". Mean age 36, 89% male	Disulfiram or placebo implant or no operation. No adjunct treatment reported. Follow-up interval mean 18 months.

Viited

Ravijuhendid

The management of harmful drinking and alcohol dependence in primary care, a national clinical guideline, Scottish Intercollegiate Guidelines Network, 2003	SIGN 2003
Treatment of Alcohol Abuse, Current Care Guideline**,** The Finnish Medical Society Duodecim and the Finnish Society of Addiction Medicine,2010	Soome 2010
Guidelines for the Treatment of Alcohol Problems, Australian Government Department of Health and Ageing, 2009	Austraalia 2009
Incorporating Alcohol Pharmacotherapies Into Medical Practice . Treatment Improvement Protocol (TIP) Series, Substance Abuse and Mental Health Services Administration, 2009.	SAMHSA 2009
Practice Guideline For The Treatment of Patients With Substance Use Disorders, 2nd Edition, American Psychiatric Association, 2006	APA 2006
Alcohol-Use Disorders: Diagnosis, Assessment and Management of Harmful Drinking and Alcohol Dependence, National Institute for Health & Clinical Excellence, 2011	NICE 2011
World Federation of Societies of Biological Psychiatry (WFSBP) Guidelines for Biological Treatment of Substance Use and Related Disorders, Part 1: Alcoholism, 2008	WFSBP 2008
Evidence-based guidelines for the pharmacological management of substance abuse, harmful use, addiction and comorbidity: recommendations from The British Association for Psychopharmacology,2012	BAP 2012

Viited süstemaatilised ülevaated ja RCT-d

Kokkuvõtte (abstract või kokkuvõtlikum info)	**Viide kirjandusallikale**
To assess the efficacy of supervised disulfiram as an adjunct to out-patient treatment of alcoholics, a randomised, partially blind, six-month follow-up study was conducted in which 126 patients received 200 mg disulfiram or 100 mg vitamin C under the supervision of a nominated informant. In the opinion of the (blinded) independent assessor, patients on disulfiram increased average total abstinent days by 100 and patients on vitamin C by 69, thus enhancing by one-third this measure of treatment outcome. Mean weekly alcohol consumption was reduced by 162 units with disulfiram, compared with 105 units with vitamin C, and the disulfiram patients reduced their total six-month alcohol consumption by 2572 units compared with an average reduction of 1448 units in the vitamin C group. Serum gamma-GT showed a mean fall of 21 IU/l in patients on disulfiram but rose by a mean of 13 IU/l with vitamin C. Unwanted effects in the disulfiram group led to a dose reduction in seven patients and to treatment withdrawal in four (and in one vitamin C patient). Two-thirds of the disulfiram group asked to continue the treatment at the end of the study. There were no medically serious adverse reactions.	Chick, J, Gough K, Falkowski W et al.1992, Disulfiram treatment of alcoholism. Br J Psychiatry 161: 84–89. **Osaliselt pimendatud RCT**

Twenty-four studies of outcome following oral disulfiram and 14 following implanted disulfiram were identified for review from MEDLINE and PsycINFO databases and by manual searching for the period 1967-95. The methodological rigour of these studies was generally poor, albeit not as poor as that of earlier studies (not reviewed here). An overall assessment of the results of research in this field is hampered by the diversity of both the methods used and the subject populations studied. However, it is clear that support for the general use of oral disulfiram is equivocal, mostly being found in the form of reduced quantity of alcohol consumed and a reduced number of drinking days. Evidence for an effect in increasing the proportion of patients who achieve abstinence is surprisingly lacking. Where it is prescribed, disulfiram use should be supervised and it should be employed as one part of a comprehensive treatment programme. There is no good evidence in favour of implanting disulfiram tablets, but the possibility of a depot injection is intriguing.	Hughes, J and C Cook 1997, The efficacy of disulfiram: a review of outcome studies. Addiction 92: 381–395. **Ülevaade**
AIM: To compare the effects in alcohol-dependent patients of three pharmacotherapies, disulfiram (DIS), naltrexone (NTX), and acamprosate (ACA), when used with a brief manual-based cognitive-behavioural intervention. **METHOD:** We conducted a randomized, open label, multicentre naturalistic study in two phases; first, a 12-week continuously supervised medication, followed by targeted medication (TM) up to 52 weeks in addition to a 67-week follow-up period; altogether 119 weeks (2.5 years), in 243 voluntary treatment-seeking alcohol-dependent adult outpatients. Subjects were randomized 1:1:1 to receive supervised NTX, ACA or DIS, 50, 1998, or 200 mg, respectively, per day, plus a brief manual-based cognitive-behavioural intervention. The patients were met in the second and sixth weeks, and then after 3, 6, and 12 months. The primary outcome measures were the time (days) to first heavy drinking day (HDD), and time during the first 3 months to the first drinking day after medication started. Secondary variables were abstinent days/week (0 drinks/day), average weekly alcohol intake, Alcohol Use Disorder Identification Test (AUDIT), Severity of Alcohol Dependence Data (SADD), and quality of life (QL) measures. **RESULTS:** All three study groups showed marked reduction in drinking, from baseline to the end of the study. During the continuous medication phase, treatment with DIS was more effective in reducing HDDs and average weekly alcohol consumption, and increasing time to the first drink, as well as the number of abstinent days. During the TM period, there were no significant differences between the groups in time to first HDD and days to first drinking, but the abstinence days were significantly more frequent in the DIS group than ACA and NTX. There were no	Laaksonen, E, Koski-Jannes A, Salaspuro M et al. 2008, A randomized, multicentre, open-label, comparative trial of disulfiram, naltrexone and acamprosate in the treatment of alcohol dependence. Alcohol Alcohol 43(1): 53-61. **Open Lable RCT**

differences between the NTX and ACA groups in either phase of the study of drinking outcomes. However, SADD scores improved more in the NTX group than the ACA group. **CONCLUSIONS:** Patients allocated to ACA, NTX and DIS combined with brief manual-based cognitive behavioural intervention significantly reduce their alcohol consumption and report improved QL. Supervised DIS appeared superior, especially during the continuous medication period, to NTX and ACA.	
The review covers all pharmacotherapies for which a RCT investigating effectiveness in treatment of alcohol dependence has been located.	Pharmacotherapies for relapse prevention in alcohol dependence, Drug and Alcohol Services South Australia, 2011 Meta-analysis (full version in dropbox)
BACKGROUND: Despite its success with compliant or supervised patients, disulfiram has been a controversial medication in the treatment of alcoholism. Often, study designs did not recognize a pivotal factor in disulfiram research, the importance of an open-label design. Our objectives are: (1) to analyze the efficacy and safety of disulfiram in RCTs in supporting abstinence and (2) to compare blind versus open-label studies, hypothesizing that blinded studies would show no difference between disulfiram and control groups because the threat would be evenly spread across all groups. **METHODS AND FINDINGS:** We searched PubMed, EMBASE and the Cochrane Central Register for RCTs on disulfiram use with alcoholics in comparison to any alcoholic control group. The primary outcome was defined by the authors of each trial. Additional analyses included: blind vs. open-label, with or without supervision, cocaine study or not, and type of control. Overall, the 22 included studies showed a higher success rate of disulfiram compared to controls Hedges'g =.58 (95%CI =.35-.82). When comparing blind and open-label RCTs, only open-label trials showed a significant superiority over controls g =.70 (95%CI =.46-.93). RCTs with blind designs showed no efficacy of disulfiram compared to controls. Disulfiram was also more effective than the control condition when compared to naltrexone g =.77, 95%CI =.52-1.02, to acamprosate g =.76, 95%CI =.04-1.48, and to the no disulfiram groups g =.43, 95%CI =.17-.69. LIMITS INCLUDE: (1) a population of 89% male subjects and (2) a high but unavoidable heterogeneity of the studies with a substantial I-square in most subgroups of studies. **CONCLUSIONS:** Blinded studies were incapable of distinguishing a difference	Skinner MD, Lahmek P, Pham H, Aubin H-J (2014) Disulfiram Efficacy in the Treatment of Alcohol Dependence: A Meta-Analysis. PLoS ONE 9(2): e87366. doi:10.1371/journal.pone.0087366 Systematic review

between treatment groups and thus are incompatible with disulfiram research. Based on results with open-label studies, disulfiram is a safe and efficacious treatment compared to other abstinence supportive pharmacological treatments or to no disulfiram in supervised studies for problems of alcohol abuse or dependence.	

Muu: Raamatud:

Jon Eister, Ulysses Unbound: Studies in Rationality, Precommitment and Constraints. 2000.

"As with other deterrents, disulfiram works best when it is never triggered. If the fear is strong enough, it may never be triggered. Subcutaneously implanted disulfiram may in fact provide a benign instance of what Gerry Mackie calls a "belief trap."155. In some countries, it has been widely believed that anyone who drinks when using implanted disulfiram will die156. As a matter of fact, implanted disulfiram is pharmacologically inert157. The belief bolstered by the fact that some alcoholics have died when using disulfiram, though not because they used it – could nevertheless deter people from testing it. Although false, the belief might be therapeutically useful. Thus "following the publication of a controlled study in Norway which found no difference in outcome between placebo and allegedly active disulfiram implants, one of the authors received much criticism from patients who had had implants,!158