

**The following are abstracts of studies looking at the efficacy of several pharmacological treatments approved by the FDA in the treatment of alcohol dependence. The research over the past decade appears to be very conflicting. These are just a select number of the more recent studies and reviews.**

### **Update on neuropharmacological treatments for alcoholism: scientific basis and clinical findings.**

[Johnson BA.](#)

1: [Biochem Pharmacol.](#) 2008 Jan 1;75(1):34-56.

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The past decade has seen an expansion of research and knowledge on pharmacotherapy for the treatment of alcohol dependence. The Food and Drug Administration (FDA)-approved medications naltrexone and Acamprosate have shown mixed results in clinical trials. Oral naltrexone and naltrexone depot formulations have generally demonstrated efficacy at treating alcohol dependence, but their treatment effect size is small, and more research is needed to compare the effects of different doses on drinking outcome. Acamprosate has demonstrated efficacy for treating alcohol dependence in European trials, but with a small effect size. In U.S. trials, Acamprosate has not proved to be efficacious. Research continues to explore which types of alcohol-dependent individual would benefit the most from treatment with naltrexone or Acamprosate. The combination of the two medications demonstrated efficacy for treating alcohol dependence in one European study but not in a multi-site U.S. study. Another FDA-approved medication, Disulfiram, is an aversive agent that does not diminish craving for alcohol. Disulfiram is most effective when given to those who are highly compliant or who are receiving their medication under supervision. Of the non-approved medications, topiramate is among the most promising, with a medium effect size in clinical trials. Another promising medication, baclofen, has shown efficacy in small trials. Serotonergic agents such as selective serotonin reuptake inhibitors and the serotonin-3 receptor antagonist, ondansetron, appear to be efficacious only among certain genetic subtypes of alcoholic. As neuroscientific research progresses, other promising medications, as well as medication combinations, for treating alcohol dependence continue to be explored.

PMID: 17880925 [PubMed - indexed for MEDLINE]

### **Acamprosate supports abstinence, naltrexone prevents excessive drinking: evidence from a meta-analysis with unreported outcomes.**

[Rösner S](#), [Leucht S](#), [Lehert P](#), [Soyka M](#).

1: [J Psychopharmacol.](#) 2008 Jan;22(1):11-23.

Two pharmacological agents have repeatedly been shown to be efficacious for relapse prevention in alcohol dependence: The putative glutamate-antagonist Acamprosate and the opioid-antagonist naltrexone. Clinical evidence for both drugs is based on various outcome criteria. Whereas for Acamprosate primarily abstinence maintenance has been demonstrated, studies with naltrexone have mostly emphasized the prevention of heavy drinking. The remaining effects of both drugs are not always reported; accordingly the corresponding database is fragmentary. Thus, the primary objective of the present meta-analysis was to complete the efficacy profiles for Acamprosate and naltrexone and to compare them with each other. Unreported results, requested from the study investigators and the drug manufacturers, were integrated in the computation of effect sizes. For the meta-analysis, emphasis was placed on the conceptual distinction between having a first drink and returning to heavy drinking. Naltrexone was found to have a significant effect on the maintenance of abstinence as well as the prevention of heavy drinking. Acamprosate was shown only to support abstinence; it did not influence alcohol consumption after the first drink. When the efficacy profiles of the two drugs were compared, Acamprosate was found to be more effective in preventing a lapse, whereas naltrexone was better in preventing a lapse from becoming a relapse. The superiority of either one drug or over the other one cannot be determined as a general rule, it rather depends on the therapeutic target. Benefits in the treatment of alcohol dependence might be optimized by matching the efficacy profiles of specific antidipsotropics with the motivational status of alcohol-dependent patients.

PMID: 18187529 [PubMed - indexed for MEDLINE]

## **A randomized, multicentre, open-label, comparative trial of Disulfiram, naltrexone and Acamprosate in the treatment of alcohol dependence.**

[Laaksonen E](#), [Koski-Jännes A](#), [Salaspuro M](#), [Ahtinen H](#), [Alho H](#).

1: [Alcohol Alcohol](#). 2008 Jan-Feb;43(1):53-61. Epub 2007 Oct 27.

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**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-behavioral 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-behavioral 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 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 behavioral intervention significantly reduce their alcohol

consumption and report improved QL. Supervised DIS appeared superior, especially during the continuous medication period, to NTX and ACA.

PMID: 17965444 [PubMed - indexed for MEDLINE]

## **Do Acamprosate or naltrexone have an effect on daily drinking by reducing craving for alcohol?**

[Richardson K](#), [Baillie A](#), [Reid S](#), [Morley K](#), [Teesson M](#), [Sannibale C](#), [Weltman M](#), [Haber P](#).

1: [Addiction](#). 2008 Jun;103(6):953-9.

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AIM: To explore the effect of Acamprosate and naltrexone on craving and alcohol consumption in the treatment of alcohol dependence. DESIGN: A randomized, double-blind, single-dummy, placebo-controlled trial. SETTING: Three treatment centers in Sydney, Australia. PARTICIPANTS: A total of 169 alcohol-dependent subjects were given naltrexone (50 mg/day), Acamprosate (1998 mg/day) or placebo for 12 weeks, in conjunction with manualized medication compliance therapy. INTERVENTION: During the course of the trial, participants kept a daily diary which included the number of standard drinks they consumed and their peak craving for alcohol that day rated on a 0-10 scale. MEASUREMENTS: Subjective ratings of daily craving and daily drinking for the first 6 weeks of treatment. FINDINGS: Mixed/hierarchical linear models were employed on an intention-to-treat basis. Analyses revealed that craving was a significant predictor of daily drinking and baseline levels of depression were the best predictor of daily craving. There was no significant improvement in model fit when treatment group was added both in models of daily craving and daily drinking. Daily alcohol consumption was best predicted by a model incorporating baseline dependence and depression scores, and daily craving, entered as a time-varying covariate. However, there was a significant craving x time x treatment interaction ( $t = -3.365$ ,  $df = 4413.712$ ,  $P < 0.001$ ), suggesting that at higher levels of craving drinking was reduced at a significantly greater rate with naltrexone compared to Acamprosate. CONCLUSIONS: Naltrexone had a greater effect on drinking when craving was high. These results support the role of naltrexone in reducing craving when that craving is highly salient. The role of Acamprosate in reducing craving was not supported by these findings.

PMID: 18482418 [PubMed - in process]

## **Using Topiramate or Naltrexone for the Treatment of Alcohol-Dependent Patients.**

[Flórez G](#), [García-Portilla P](#), [Alvarez S](#), [Saiz PA](#), [Nogueiras L](#), [Bobes J](#)

1: [Alcohol Clin Exp Res](#). 2008 May 14

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Background: To compare topiramate versus naltrexone in the treatment of alcohol dependence. Methods: A 6-month naturalistic, randomized and open-label, trial of topiramate versus naltrexone,

with assessments at enrollment and after 3 and 6 months of treatment. The setting was an outpatient alcohol clinic. One hundred and two alcohol-dependent patients who had been drinking heavily during the past month were included. Two randomized groups were created. In one, naltrexone was used as the therapeutic agent and, in the other, topiramate was chosen as the therapeutic agent. Both groups received psychological relapse prevention therapy. Outcome was measured using tools that assessed alcohol intake, cravings, disability, and quality of life; changes in biomarkers of alcohol intake were also used. With all the data, a secondary composite measure was created in order to assess each patient's global alcohol intake and its consequences. Results: Both groups showed substantial reduction in their drinking. Naltrexone patients had higher nicotine consumption throughout the study. Topiramate was better at reducing alcohol-related cravings throughout the study. Both treatments had a similar mean cost throughout the study. Conclusions: Both topiramate and naltrexone were efficacious in the treatment of alcohol dependence, and the treatment costs were similar. There is a trend for topiramate to be superior to naltrexone on critical measures of drinking; however, the study did not have adequate statistical power to establish this fact.

PMID: 18482157 [PubMed - as supplied by publisher]

## **Naltrexone and cognitive behavioral therapy for the treatment of alcohol dependence: do sex differences exist?**

[Baros AM](#), [Latham PK](#), [Anton RF](#).

1: [Alcohol Clin Exp Res](#). 2008 May;32(5):771-6.

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**BACKGROUND:** Sex differences in regards to pharmacotherapy for alcoholism is a topic of concern following publications suggesting naltrexone, one of the longest approved treatments of alcoholism, is not as effective in women as in men. This study was conducted by combining 2 randomized placebo controlled clinical trials utilizing similar methodologies and personnel in which the data was amalgamated to evaluate sex effects in a reasonable sized sample. **METHODS:** A total of 211 alcoholics (57 female and 154 male) were randomized to the naltrexone/cognitive behavioral therapy (CBT) or placebo/CBT arm of the 2 clinical trials analyzed. Baseline variables were examined for differences between sex and treatment groups via ANOVA for continuous variable or chi-squared test for categorical variables. All initial outcome analysis was conducted under an intent-to-treat analysis plan. Effect sizes for naltrexone over placebo were determined by Cohen's D (d). **RESULTS:** The effect size of naltrexone over placebo for the following outcome variables was similar in men and women [% days abstinent (PDA)  $d = 0.36$ , % heavy drinking days (PHDD)  $d = 0.36$ , and total standard drinks (TSD)  $d = 0.36$ ]. Only for men were the differences significant secondary to the larger sample size (PDA  $p = 0.03$ ; PHDD  $p = 0.03$ ; TSD  $p = 0.04$ ). There were a few variables (GGT at week-12 change from baseline to week-12: men  $d = 0.36$ ,  $p = 0.05$ ; women  $d = 0.20$ ,  $p = 0.45$  and drinks per drinking day: men  $d = 0.36$ ,  $p = 0.05$ ; women  $d = 0.28$ ,  $p = 0.34$ ) where the naltrexone effect size for men was greater than women. In women, naltrexone tended to increase continuous abstinent days before a first drink (women  $d = 0.46$ ,  $p = 0.09$  and men  $d = 0.00$ ,  $p = 0.44$ ). **CONCLUSIONS:** The effect size of naltrexone over placebo appeared similar in women and men in our hands suggesting the findings of sex differences in naltrexone response might have to do with sample size and/or endpoint drinking variables rather than any inherent pharmacological or biological differences in response.

PMID: 18336635 [PubMed - indexed for MEDLINE]

## **Moderators of naltrexone's effects on drinking, urge, and alcohol effects in non-treatment-seeking heavy drinkers in the natural environment.**

[Tidey JW](#), [Monti PM](#), [Rohsenow DJ](#), [Gwaltney CJ](#), [Miranda R Jr](#), [McGeary JE](#), [MacKillop J](#), [Swift RM](#), [Abrams DB](#), [Shiffman S](#), [Paty JA](#).

1: [Alcohol Clin Exp Res](#). 2008 Jan;32(1):58-66

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**BACKGROUND:** Naltrexone (NTX) has proven to be effective with alcoholics in treatment, with most controlled clinical trials showing beneficial effects on heavy drinking rates. However, little is known about the behavioral mechanisms underlying the effects of NTX on drinking, or about patient characteristics that may moderate NTX's effects on drinking. In this study, ecological momentary assessment (EMA) techniques were used to investigate some of the putative mechanisms of naltrexone's effects on drinking in heavy drinkers who were not seeking treatment for alcohol problems. Polymorphisms in the D4 dopamine receptor (DRD4) gene and the mu-opiate receptor (OPRM1) gene, family history of alcohol problems, age of onset of alcoholism and gender were explored as potential moderators of NTX's effects. **METHODS:** After a 1-week placebo lead-in period, heavy drinkers (n = 180), 63% of whom were alcohol-dependent, were randomized to 3 weeks of daily naltrexone (50 mg) or placebo. Throughout the study, participants used EMA on palm-pilot computers to enter, in real time, drink data, urge levels, and subjective effects of alcohol consumption. **RESULTS:** Naltrexone reduced percentage drinking days in all participants and reduced percent heavy drinking days in DRD4-L individuals; NTX decreased urge levels in participants with younger age of alcoholism onset; NTX increased time between drinks in participants who had more relatives with alcohol problems; and NTX reduced the stimulating effects of alcohol in women. OPRM1 status did not moderate any of NTX's effects. **CONCLUSIONS:** These results confirm earlier findings of NTX's effects on drinking and related subjective effects, and extend them by describing individual difference variables that moderate these effects in the natural environment, using data collected in real time.

PMID: 18028530 [PubMed - indexed for MEDLINE]

## **Acamprosate efficacy in alcohol-dependent patients: summary of results from three pivotal trials.**

[Kranzler HR](#), [Gage A](#).

1: [Am J Addict](#). 2008 Jan-Feb;17(1):70-6.

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In 2004, the United States Food and Drug Administration (FDA) approved acamprosate for use in conjunction with psychosocial support in the maintenance of abstinence in alcohol-dependent patients who are abstinent at treatment initiation. That approval was based primarily on a re-analysis of three European double-blind, placebo-controlled trials in which complete abstinence was the primary outcome measure. The current report presents data from the re-analysis of the pivotal trials, which were 13-, 48-, and 52-week studies. A total of 998 DSM-III-R alcohol-dependent patients were included in the studies, with the majority abstinent at

randomization. Using a more stringent definition of abstinence, re-analysis of the rate of complete abstinence, percent days abstinent, and the time to first drink confirmed the original findings for the efficacy of Acamprosate in the treatment of alcohol dependence. Rate of complete abstinence was significantly higher with Acamprosate than placebo ( $p < .05$ ); both percent days abstinent and time to first drink were also significantly greater among Acamprosate-treated than placebo-treated patients ( $p < .01$ ). These findings support the use of Acamprosate in the treatment of alcohol dependence and illustrate some of the issues that can arise in the FDA process for approval of medications to treat the disorder.

PMID: 18214726 [PubMed - indexed for MEDLINE]

### **Effectiveness and safety of baclofen for maintenance of alcohol abstinence in alcohol-dependent patients with liver cirrhosis: randomized, double-blind controlled study.**

[Addolorato G](#), [Leggio L](#), [Ferrulli A](#), [Cardone S](#), [Vonghia L](#), [Mirijello A](#), [Abenavoli L](#), [D'Angelo C](#), [Caputo F](#), [Zambon A](#), [Haber PS](#), [Gasbarrini G](#).

1: [Lancet](#). 2007 Dec 8;370(9603):1915-22

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**BACKGROUND:** Intervention to achieve alcohol abstinence represents the most effective treatment for alcohol-dependent patients with liver cirrhosis; however, anticraving drugs might worsen liver disease. We aimed to investigate the effectiveness and safety of baclofen in achieving and maintaining alcohol abstinence in patients with liver cirrhosis. **METHODS:** Between October, 2003, and November, 2006, 148 alcohol-dependent patients with liver cirrhosis were referred to the Institute of Internal Medicine, Rome, Italy. 84 were randomly allocated either oral baclofen or placebo for 12 weeks. Primary outcome was proportion of patients achieving and maintaining alcohol abstinence. Measures of this outcome were total alcohol abstinence and cumulative abstinence duration, which were assessed at outpatient visits. Relapse was defined as alcohol intake of more than four drinks per day or overall consumption of 14 or more drinks per week over a period of at least 4 weeks. Analysis was by intention to treat. This study is registered with ClinicalTrials.gov, number NCT00525252. **FINDINGS:** Of 42 patients allocated baclofen, 30 (71%) achieved and maintained abstinence compared with 12 (29%) of 42 assigned placebo (odds ratio 6.3 [95% CI 2.4-16.1];  $p=0.0001$ ). The number of dropouts (termination of treatment) did not differ between the baclofen (6/42 [14%]) and placebo (13/42 [31%]) groups ( $p=0.12$ ). Cumulative abstinence duration was about twofold higher in patients allocated baclofen than in those assigned placebo (mean 62.8 [SE 5.4] vs 30.8 [5.5] days;  $p=0.001$ ). No hepatic side-effects were recorded. **INTERPRETATION:** Baclofen is effective at promoting alcohol abstinence in alcohol-dependent patients with liver cirrhosis. The drug is well tolerated and could have an important role in treatment of these individuals.

PMID: 18068515 [PubMed - indexed for MEDLINE]

### **Prescription procedures in medication for relapse prevention after inpatient treatment for alcohol use disorders in Switzerland.**

[Buri C](#), [Moggi F](#), [Giovanoli A](#), [Strik W](#).

1: [Alcohol Alcohol](#). 2007 Jul-Aug;42(4):333-9.

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**AIMS:** In randomized controlled trials with high internal validity, pharmacotherapy using acamprosate, naltrexone, and, to a somewhat lesser extent, disulfiram has proved effective in preventing relapse in patients with alcohol use disorders (AUD). There remains, however, a paucity of studies with sufficient external validity in which the effectiveness of pharmacotherapy in clinical practice is investigated. This study aimed to make a contribution to close this gap in research. **METHODS:** In this naturalistic, prospective study, a comparison on indices of substance use, psychiatric symptoms, and treatment service utilization was carried out using samples of 92 patients who received pharmacotherapy and 323 patients who did not receive pharmacotherapy following discharge from 12 residential AUD programmes (index stay). **RESULTS:** Patients that received pharmacotherapy were more likely to use alcohol during the index stay and at the 1-year follow-up. Moreover, this patient group more readily utilized treatment services during a 2-year period prior to and a 1-year period following index stay than patients who were not given pharmacotherapy. Nevertheless, when pharmacotherapy was prescribed before first post-treatment alcohol use, it was associated with delay of alcohol use, fewer relapses, and a reduced need for inpatient treatment. In many cases, however, medication was not prescribed until alcohol use and relapse had occurred. The length of time to first alcohol use was longer, and the cumulative abstinence rate higher, for disulfiram than for acamprosate, the latter being generally prescribed for more severely alcohol-dependent patients. **CONCLUSIONS:** There is a need for further studies to probe the reasons why medication for relapse prevention is not prescribed upon discharge from residential treatment and for less severely alcohol-dependent patients.

PMID: 17517820 [PubMed - indexed for MEDLINE]

## **An open randomized study comparing Disulfiram and Acamprosate in the treatment of alcohol dependence.**

[de Sousa A](#), [de Sousa A](#).

1: [Alcohol Alcohol](#). 2005 Nov-Dec;40(6):545-8. Epub 2005 Jul 25.

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**AIMS:** To compare the efficacy of acamprosate (ACP) and disulfiram (DSF) for preventing alcoholic relapse in routine clinical practice. **METHODS:** One hundred alcoholic men with family members who would encourage medication compliance and accompany them for follow-up were randomly allocated to 8 months of treatment with DSF or ACP. Weekly group psychotherapy was also available. The psychiatrist, patient, and family member were aware of the treatment prescribed. Alcohol consumption, craving, and adverse events were recorded weekly for 3 months and then fortnightly. Serum gamma glutamyl transferase was measured at the start and the end of the study. **RESULTS:** At the end of the trial, 93 patients were still in contact. Relapse (the consumption of >5 drinks/40 g of alcohol) occurred at a mean of 123 days with DSF compared to 71 days with ACP (P = 0.0001). Eighty-eight per cent of patients on DSF remained abstinent compared to 46% with ACP (P = 0.0002). However, patients allocated to ACP had lower craving than those on DSF (P = 0.002). **CONCLUSION:** DSF is superior to ACP for preventing relapse in alcohol-dependent men with good family support. Further comparisons between these two drugs in different treatment settings and populations are warranted.

## **A one-year pragmatic trial of naltrexone vs disulfiram in the treatment of alcohol dependence.**

[De Sousa A](#), [De Sousa A](#).

1: [Alcohol Alcohol](#). 2004 Nov-Dec;39(6):528-31.

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AIMS: To compare the efficacy of naltrexone and disulfiram in preventing an alcoholic relapse in routine clinical practice in an Indian metropolis. METHODS: Hundred alcohol-dependent men, for whom a family member would accompany the patient to follow-up appointments, were randomly allocated to a year of treatment with either naltrexone or disulfiram. Patients, the accompanying family member and the treating psychiatrist were aware of the nature of treatment given. Alcohol consumption, craving and adverse events were recorded weekly for the first three months, then fortnightly for the rest of the year, by the treating psychiatrist. Serum gamma-glutamyl transferase (GGT) was measured at the start and the end of the study. RESULTS: At the end of the year, 97 patients were still in contact. Relapse, the consumption of >5 drinks (40 g of ethanol) in a 24 h period, occurred at a mean of 119 days with disulfiram and at 63 days with naltrexone ( $P = 0.020$ ). Mean serum GGT, which had not differed between the two groups initially, was 117 U/l with naltrexone and 85 U/l with disulfiram ( $P = 0.038$ ) at the end of the study. Eighty-six per cent of the patients remained abstinent throughout the study with disulfiram compared to 44% with naltrexone ( $P = 0.0009$ ). However, patients allocated to naltrexone had significantly lower craving than those allocated to disulfiram. CONCLUSIONS: Disulfiram is superior to naltrexone in preventing a relapse among alcohol-dependent men with family support. Comparison between these treatments in other settings and in different types of alcoholics is warranted.

PMID: 15525790 [PubMed - indexed for MEDLINE]

## **Naltrexone versus acamprosate: one year follow-up of alcohol dependence treatment.**

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1: [Alcohol Alcohol](#). 2001 Sep-Oct;36(5):419-25.

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Naltrexone and Acamprosate reduce relapse in alcohol dependence. They have not yet been compared in a published trial. The aim of this study was to compare the efficacy of these compounds in conditions similar to those in routine clinical practice. Random allocation to a year of treatment with naltrexone (50 mg/day) or Acamprosate (1665-1998 mg/day) was made in 157 recently detoxified alcohol-dependent men with moderate dependence (evaluated using the Addictions Severity Index and Severity of Alcohol Dependence Scale). All were patients whom a member of the family would accompany regularly to appointments. Alcohol

consumption, craving and adverse events were recorded weekly for the first 3 months, and then bi-weekly, by the treating psychiatrist who was not blinded. At 3-monthly intervals, investigators who were blinded to the treatment documented patients' alcohol consumption based on patients' accounts, information given by the psychiatrists when necessary, and reports from patients' families. Serum gamma-glutamyltransferase (GGT) was also measured. Efforts were made to sustain the blindness of the investigators. The same investigator did not assess the same patient twice. The integrity of the blindness was not checked. There was no difference between treatments in mean time to first drink (naltrexone 44 days, acamprosate 39 days) but the time to first relapse (five or more drinks in a day) was 63 days (naltrexone) versus 42 days (acamprosate) ( $P = 0.02$ ). At the end of 1 year, 41% receiving naltrexone and 17% receiving acamprosate had not relapsed ( $P = 0.0009$ ). The cumulative number of days of abstinence was significantly greater, and the number of drinks consumed at one time and severity of craving were significantly less, in the naltrexone group compared to the acamprosate group, as was the percentage of heavy drinking days ( $P = 0.038$ ). More patients in the acamprosate than the naltrexone group were commenced on disulfiram during the study. Naltrexone patients attended significantly more group therapy sessions, though this could not explain their better outcome. There were non-significant trends for the naltrexone group to comply better with medication, to stay in the study longer, and to show greater improvement over baseline in serum GGT.

PMID: 11524308 [PubMed - indexed for MEDLINE]

## **Acamprosate in Korean alcohol-dependent patients: a multi-centre, randomized, double-blind, placebo-controlled study.**

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1: [Alcohol Alcohol](#). 2003 Mar-Apr;38(2):135-41.

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**AIMS:** A multi-centre, randomized, double-blind, placebo-controlled trial was conducted to evaluate the efficacy and the safety of acamprosate over 8 weeks in Korean alcohol-dependent patients. **METHODS:** One hundred and forty-two alcohol-dependent patients in 12 centres were randomized to 8 weeks treatment with either acamprosate ( $n = 72$ ) or a placebo ( $n = 70$ ) in combination with out-patient psychosocial intervention. They were predominantly male (95.8%), with a mean age of 44.3 +/- 8.3 years; 76.1% were married; 59.9% were employed; 58.5% had received previous alcoholism treatment (previous mean number of admissions in alcoholism in-patient programmes 4.6 +/- 6.9). At visits to the clinic (weekly for 4 weeks, then biweekly for 4 weeks), a record was made of alcohol use (Time-Line Follow-Back), alcohol craving using a Korean version of the Obsessive Compulsive Drinking Scale and a visual analogue scale, and adverse events. Serum aspartate aminotransferase, alanine aminotransferase, gamma-glutamyltransferase (GGT), blood urea nitrogen and creatinine levels were measured on weeks 0, 2, 4 and 8. **RESULTS:** In the acamprosate group (A), 71.4% had had alcohol within the 2 days prior to starting medication, against 65.2% of patients in the placebo group (P); ( $P > 0.05$ ). One hundred and one subjects (71.1%) completed 8-weeks of treatment (A, 73.6%; P, 68.6%;  $P > 0.05$ ). During the 8-week treatment period, 37, (A) ( $n = 72$ ) and 32% (P) ( $n = 70$ ) achieved continuous abstinence ( $P > 0.05$ ), and 40, (A) and 39% (P) remained without relapse ( $P > 0.05$ ) (defined as a day when a man consumed five or more drinks or a woman four or more drinks). The percentage of days abstinent during the 8-week treatment period was 81.2, (A) and 78.5% (P) ( $P > 0.05$ ), and the percentage of days without heavy drinking 86.1 (A) and 84.9% (P) ( $P > 0.05$ ). The mean amount drunk per drinking occasion was 7.2, (A) and 8.6 standard drinks (P) ( $P > 0.05$ ). No statistically significant differences in changes in the serum GGT level or craving scores from baseline to the end-point of treatment were found between the two groups. Recency of drinking prior to commencing study drug predicted percentage of days abstinent in the first 2 weeks on treatment; however, when ANOVAs were conducted using treatment outcomes as a dependent variable, medication condition as an independent variable and the period of abstinence prior to treatment as a covariate,

a significant effect of medication condition was still not seen. CONCLUSIONS: Acamprosate was ineffective in reducing drinking in this Korean sample. The result differs from that of most European acamprosate trials. This might be explained by our sample's relatively severe alcohol dependence, and low social support, or the fact that many patients were still drinking near to their first medication. The variability of the psychosocial support, ethnicity (which might also affect acamprosate pharmacokinetics) and the Korean drinking style, which differs from that of Europeans, might have contributed to our negative result.

PMID: 12634260 [PubMed - indexed for MEDLINE]

### **Naltrexone versus acamprosate in the treatment of alcohol dependence: A multi-centre, randomized, double-blind, placebo-controlled trial.**

[Morley KC](#), [Teesson M](#), [Reid SC](#), [Sannibale C](#), [Thomson C](#), [Phung N](#), [Weltman M](#), [Bell JR](#), [Richardson K](#), [Haber PS](#).

1: [Addiction](#). 2006 Oct;101(10):1451-62.

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AIM: To compare the efficacy of acamprosate and naltrexone in the treatment of alcohol dependence.

DESIGN: A double-blind, placebo-controlled trial. SETTING: Three treatment centres in Australia.

PARTICIPANTS: A total of 169 alcohol dependent subjects were given naltrexone (50 mg/day), acamprosate (1998 mg/day) or placebo for 12 weeks. INTERVENTION: All subjects were offered manualized compliance therapy, a brief intervention that targets problems that may affect treatment compliance such as ambivalence and misperceptions about medication. MEASUREMENTS: Time to the first drink, time to first relapse, drinks per drinking day and cumulative abstinence. FINDINGS: In intention-to-treat analyses, there were no differences between groups on outcome measures of drinking, craving or biochemical markers. Similarly, analyses of the 94 subjects that completed the study in full and demonstrated 80% compliance, revealed no significant treatment effects. Differential treatment effects were identified after stratification according to scores on the Alcohol Dependence Scale (ADS) and Depression Anxiety and Stress Scale (DASS). A significant beneficial treatment effect on time to first relapse was revealed for subjects with 'no depression' allocated to naltrexone (n = 56; P < 0.01). In addition, a significant beneficial treatment effect was revealed in subjects with 'low dependence' allocated to naltrexone (n = 34; P < 0.05). CONCLUSIONS: The results of this study support the efficacy of naltrexone in the relapse prevention of alcoholism amongst those with low levels of clinical depression and alcohol dependence severity. No effect of acamprosate was found in our sample.

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