

Library Watch

substance use
medical aspects

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A review of the clinical pharmacology of methamphetamine. (review).

Cruickshank CC; Dyer KR. *Addiction* 104(7): 1085-1099, 2009. (182 refs.)

To examine the literature regarding clinical pharmacokinetics, direct effects and adverse clinical outcomes associated with methamphetamine use. Relevant literature was identified through a PubMed search. Additional literature was obtained from relevant books and monographs. The mean elimination half-life for methamphetamine is approximately 10 hours, with considerable inter-individual variability in pharmacokinetics. Direct effects at low-to-moderate methamphetamine doses (5-30 mg) include arousal, positive mood, cardiac stimulation and acute improvement in cognitive domains such as attention and psychomotor coordination. At higher doses used typically by illicit users (≥ 50 mg), methamphetamine can produce psychosis. Its hypertensive effect can produce a number of acute and chronic cardiovascular complications. Repeated use may induce neurotoxicity, associated with prolonged psychiatric symptoms, cognitive impairment and an increased risk of developing Parkinson's disease. Abrupt cessation of repeated methamphetamine use leads to a withdrawal syndrome consisting of depressed mood, anxiety and sleep disturbance. Acute withdrawal lasts typically for 7-10 days, and residual symptoms associated with neurotoxicity may persist for several months. Copyright 2009, Society for the Study of Addiction to Alcohol and Other Drugs.

Alcohol consumption and male erectile dysfunction: An unfounded reputation for risk?

Chew KK; Bremner A; Stuckey B; Earle C; Jamrozik K. *Journal of Sexual Medicine* 6(5): 1386-1394, 2009. (24 refs.)

Alcohol consumption is a contentious social topic and is often assumed to have deleterious effects on sexual performance. There is a lack of consensus on whether alcohol consumption may in fact be beneficial to erectile function. We examined the data from a population-based cross-sectional study of men's health to assess the association between usual alcohol consumption and erectile dysfunction (ED). Reply-paid questionnaires were posted to a randomly selected

age-stratified male population sample obtained from the Western Australian (WA) Electoral Roll. The survey questionnaire included sociodemographic details, self-reported clinical information, and drinking habits. The 5-item International Index of Erectile Function (IIEF-5) was used to assess erectile function. Most (87%) participants were current alcohol drinkers, with binge drinking, as defined by the Australian National Health and Medical Research Council (NHMRC), reported by 20% of drinkers. Compared with never-drinkers, the age-adjusted odds of ED were lower among current, weekend, and binge drinkers and higher among ex-drinkers. Among current drinkers, the odds were lowest for consumption within the NHMRC guidelines of between 1 and 20 standard drinks a week. On further adjustment for cardiovascular disease (CVD) or for cigarette smoking, age-adjusted odds of ED were reduced by 25-30% among alcohol drinkers. Our findings suggest a modest negative association between alcohol consumption and ED and confounding of the association by CVD and cigarette smoking. The Western Australia Men's Health Study certainly provides no justification for advising men with ED whose drinking habits are consistent with NHMRC guidelines that they should cease or reduce their consumption of alcohol. Copyright 2009, Wiley-Blackwell Publishing.

Alcohol screening scores predict risk of subsequent fractures.

Harris AHS; Bryson CL; Sun HL; Blough D; Bradley KA. *Substance Use & Misuse* 44(8): 1055-1069, 2009. (39 refs.)

The Alcohol Use Disorders Identification Test-Consumption (AUDIT-C; 0-12 points) was included on health surveys in a cohort (if 32,622 general medicine outpatients from seven US Department of Veterans Affairs (VA) hospitals. Cox proportional hazards models were used to estimate the risk of fracture (mean follow-up = 1.6 years) by AUDIT-C category. After adjusting for confounders, AUDIT-C scores of 8-9 and 10-12 were associated with significantly increased risks for subsequent fractures, HR (95% CI) = 1.37 (1.03 to 1.83) and 1.79 (1.38 to 2.33) respectively. These results can be used to

provide feedback to patients linking their alcohol screening scores to medical outcomes—a critical component of evidence-based brief counseling for alcohol misuse. The study's limitations are noted. Copyright 2009, Taylor & Francis.

Buprenorphine for the management of opioid withdrawal. (review).

Gowing L; Ali R; White JM. *Cochrane Database of Systemic Reviews* 3: article CD002025, 2009. (142 refs.)

Background: Managed withdrawal is a necessary step prior to drug-free treatment or as the end point of substitution treatment. **Objectives:** To assess the effectiveness of interventions involving the use of buprenorphine to manage opioid withdrawal, for withdrawal signs and symptoms, completion of withdrawal and adverse effects. **Search strategy:** We searched the Cochrane Central Register of Controlled Trials (The Cochrane Library, Issue 3, 2008), MEDLINE (January 1966 to July 2008), EMBASE (January 1985 to 2008 Week 31), PsycINFO (1967 to 7 August 2008) and reference lists of articles. **Selection criteria:** Randomised controlled trials of interventions involving the use of buprenorphine to modify the signs and symptoms of withdrawal in participants who were primarily opioid dependent. **Comparison interventions** involved reducing doses of methadone, alpha2-adrenergic agonists, symptomatic medications or placebo, or different buprenorphine-based regimes. **Data collection and analysis:** One author assessed studies for inclusion and methodological quality, and undertook data extraction. **Inclusion decisions** and the overall process was confirmed by consultation between all authors. **Main results:** Twenty-two studies involving 1736 participants were included. The major comparisons were with methadone (5 studies) and clonidine or lofexidine (12 studies). Five studies compared different rates of buprenorphine dose reduction. Severity of withdrawal is similar for withdrawal managed with buprenorphine and withdrawal managed with methadone, but withdrawal symptoms may resolve more quickly with buprenorphine. It appears that completion of withdrawal treatment may be more likely with buprenorphine relative to methadone (RR 1.18; 95% CI 0.93 to 1.49, $P = 0.18$) but more studies are required to confirm this. Relative to clonidine or lofexidine, buprenorphine is more effective in ameliorating the symptoms of withdrawal, patients treated with buprenorphine stay in treatment for longer (SMD 0.92, 95% CI 0.57 to 1.27, $P < 0.001$), and are more likely to complete withdrawal treatment (RR 1.64; 95% CI 1.31 to 2.06, $P < 0.001$). At the same time

there is no significant difference in the incidence of adverse effects, but drop-out due to adverse effects may be more likely with clonidine. **Authors' conclusions:** Buprenorphine is more effective than clonidine or lofexidine for the management of opioid withdrawal. Buprenorphine may offer some advantages over methadone, at least in inpatient settings, in terms of quicker resolution of withdrawal symptoms and possibly slightly higher rates of completion of withdrawal. Copyright 2009, John Wiley & Sons.

Can prenatal ultrasound detect the effects of in-utero alcohol exposure? A pilot study.

Kfir M; Yevtushok L; Onishchenko S; Wertenlecker W; Bakhireva L; Chambers CD et al. *Ultrasound in Obstetrics and Gynecology* 33(6): 683-689, 2009. (16 refs.)

Objectives The aim of this pilot study was to explore possible ultrasound parameters for the early detection of alcohol-mediated fetal somatic and central nervous system (CNS) maldevelopment. Maternal alcohol ingestion during pregnancy may lead to fetal alcohol spectrum disorders (FASD), which encompass a broad range of structural abnormalities including growth impairment, specific craniofacial features and CNS abnormalities. Early detection of fetuses at risk of FASD would support earlier interventions. **Methods** We performed a longitudinal prospective pilot study, from 2004 to 2006 at two sites in Ukraine. A sample of pregnant women who reported consuming moderate-to-heavy amounts of alcohol participated in a comprehensive maternal interview, and received ultrasound evaluation of fetal growth and specific fetal brain measurements during the second and third trimesters. These measurements were compared with those collected from a group of pregnant women who consumed little-to-no alcohol during pregnancy, and who were recruited and followed in the same manner. **Results:** From 6745 screened women, 84 moderate-to-heavy alcohol users and 82 comparison women were identified and ultrasound examinations performed. After controlling for maternal smoking, alcohol-exposed fetuses had shorter mean femur length, calvarial distance and frontothalamic measurements in the second trimester ($P < 0.05$), and alcohol-exposed fetuses also had shorter frontothalamic distance measurements in the third trimester relative to comparison fetuses ($P < 0.05$). In addition, after controlling for maternal smoking, both mean orbital diameter and biparietal diameter measurements were significantly smaller on average in the alcohol-exposed group in the third trimester relative to comparison fetuses ($P < 0.05$). **Conclusions:**

Significant differences in selected somatic and brain measurements were noted between alcohol-exposed and comparison fetuses, suggesting these markers may be further explored for clinical utility in prenatal identification of affected children. Further study correlating these findings with alcohol-related physical features of the newborn and subsequent comparisons of neuro-developmental outcomes will help define potential uses of prenatal ultrasound for intervention and prevention of FASD. Copyright 2009, John Wiley & Sons.

Can serotonin transporter genotype predict craving in alcoholism?

Ait-Daoud N; Roache JD; Dawes MA; Liu L; Wang XQ et al. *Alcoholism: Clinical and Experimental Research* 33(8): 1329-1335, 2009. (47 refs.)

Background: We hypothesize that functional control of the serotonergic system is regulated in part by differential expression of the serotonin (5-HT) transporter (5-HTT). Alcohol-dependent individuals with the LL/LS genotype (L-carriers), compared with those with the SS genotype, have a lower 5-HT neurotransmission, which we hypothesize would be associated with higher craving for alcohol among L-carriers. We hypothesize further that acute peripheral depletion of tryptophan (5-HT's precursor), while further reducing 5-HT function, might decrease auto-inhibition of 5-HT neuronal firing, thereby increasing 5-HT neurotransmission transiently and lowering alcohol craving. Methods: We tested these hypotheses by examining whether in 34 Hispanic alcohol-dependent individuals subjective and physiological cue craving for alcohol differed by genotype, age of onset of problem drinking, and tryptophan availability. Results: On subjective "urge to drink" and "crave for a drink," we found a significant ($p < 0.05$) main effect of genotype and cue, as well as an interaction among genotype, age of onset of problem drinking, and tryptophan depletion. For the physiological measure of pulse, there was a main effect of genotype. L-carriers had higher craving than their SS counterparts, an effect that decreased under tryptophan depletion. While craving in L-carriers increased with an earlier age of onset of problem drinking, the opposite effect was seen in those with the SS genotype. Conclusion: These results not only provide support for the hypothesis that alcoholics who are L-carriers have greater alcohol craving and possibly greater propensity for drinking but also propose that there is an important 5-HTT gene-by-environment interaction that alters cue craving response for alcohol. Copyright 2009, Research Society on Alcoholism.

Cannabinoids inhibit the respiration of human sperm.

Badawy ZS; Chohan KR; Whyte DA; Penefsky HS; Brown OM; Souid AK. *Fertility and Sterility* 91(6): 2471-2476, 2009. (24 refs.)

Objective: To investigate the effects of the psychotropic compounds Delta(9)-tetrahydrocannabinol (Delta(9)-THC) and, Delta(8)-tetrahydrocannabinol (Delta(8)-THC) on sperm mitochondrial O-2 consumption (respiration). Setting: State University of New York Upstate Medical University, Syracuse, New York. Patient(s): Forty-one men who visited the andrology laboratory for fertility evaluation. Intervention(s): None. Main Outcome Measure(s): A phosphorescence analyzer that measures O-2 concentration in sperm suspensions as a function of time was used to measure respiration. Result(s): An immediate decline in the rate of respiration was observed when Delta(9)-THC or Delta(8)-THC was added to washed sperm. The inhibition was concentration dependent, and Delta(9)-THC was the more potent of the two compounds. Respiration was much less affected when Delta(9)-THC or Delta(8)-THC was added to neat semen, suggesting the presence of protective factors in seminal plasma. Both compounds inhibited the respiration of isolated mitochondria, illustrating that direct mitochondrial damage is likely the primary mechanism of action. Conclusion(s): The two main active cannabinoids of the marijuana plant, Delta(9)- and Delta(8)-THC, are potent inhibitors of mitochondrial O-2 consumption in human sperm. These findings emphasize the adverse effects of these toxins on male fertility. The cytoprotective capacity of seminal plasma deserves further investigation. Copyright 2009, American Society for Reproductive Medicine.

Ethyl glucuronide in hair. A sensitive and specific marker of chronic heavy drinking.

Morini L; Politi L; Poletti A. *Addiction* 104(6): 915-920, 2009. (20 refs.)

This study aims to define a cut-off concentration for ethyl glucuronide in hair to determine if there was a history of heavy drinking. Pavia, Italy. We analysed hair samples from 98 volunteers among teetotallers, social drinkers and heavy drinkers, whose ethanol daily intake (EDI) was estimated by means of a written questionnaire. Ethyl glucuronide hair concentration (HEtG) was measured by liquid chromatography-tandem mass spectrometry (lower limit of quantification: 3 pg/mg) using a fully validated method. The HEtG level providing the best compromise between sensitivity (0.92) and specificity (0.96) at detecting an EDI of 60 g or higher during the

last 3 months was 27 pg/mg. None of the factors examined among those known to affect ethanol metabolism and/or the diagnostic power of other markers of ethanol use or hair analyses, including age, gender, body mass index, tobacco smoke, prevalent beverage, hair colour, cosmetic treatments and hygienic habits was found to influence marker performance significantly. However, the slight differences in HETG performance observed for some factors (e.g. body mass index, smoke and hair treatments) require further studies on larger groups of individuals in order to assess their influence more precisely. Our results confirm further that HETG is a sensitive and specific marker of chronic heavy drinking. Copyright 2009, Society for the Study of Addiction to Alcohol and Other Drugs.

Genetics of alcohol dependence. (review).

Gelernter J; Kranzler HR. *Human Genetics* 126(1): 91-99, 2009. (79 refs.)

Alcohol dependence (AD), a genetically influenced phenotype, is extremely costly to individuals and to society in the United States and throughout the world, contributing to morbidity and mortality and a host of economic, interpersonal, and societal problems. Although until recently the only genes established to affect risk for AD were those encoding several alcohol metabolizing enzymes, there are now several other genes that can be regarded as confirmed risk loci, discovered through linkage and candidate gene association studies. While the mechanism of action of the effects of alcohol-metabolizing enzymes on AD risk is thought to be well understood, we are still in the early stages of understanding the physiology of other risk loci. Further, it is clear that only a small number of the many genes that influence risk for AD have been identified. Newer methodologies (e.g., genomewide association, study of copy number variation, and deep sequencing of candidate loci to identify rare risk variants) that have improved our understanding of other complex traits hold the promise of identifying a greater set of AD susceptibility loci. Copyright 2009, Springer-Verlag.

Lower diffusion in white matter of children with prenatal methamphetamine exposure.

Cloak CC; Ernst T; Fujii L; Hedemark B; Chang L. *Neurology* 72(24): 2068-2075, 2009. (27 refs.)

Background: Methamphetamine use is a common problem among women of childbearing age, leading to an increasing number of children with prenatal methamphetamine exposure. Whether microstructural brain changes associated with prenatal methamphetamine exposure can be detected with

diffusion tensor imaging (DTI) is unknown. Method: Twelve-direction DTI was performed in 29 methamphetamine-exposed and 37 unexposed children ages 3-4 years on a 3-T MRI scanner. Fractional anisotropy (FA) and apparent diffusion coefficient (ADC) were determined in the corpus callosum (genu and splenium) and bilaterally in the frontal and parietal white matter (WM), basal ganglia (caudate, putamen, globus pallidus), and thalamus. Results: Children with prenatal methamphetamine exposure had lower ADC in the frontal (right: -2.1%, $p = 0.04$; left: -2.0%, $p = 0.09$) and parietal WM (right: -3.9%, $p = 0.002$; left: -3.3%, $p = 0.02$) compared to unexposed children. The methamphetamine-exposed children also showed a trend for higher FA in the left frontal WM (-4.9%, $p = 0.06$) compared to the unexposed children. Conclusion: Since less myelination and higher dendritic or spine density have been reported in animals exposed to methamphetamine, lower diffusion in our children may reflect more compact axons or greater dendritic or spine density associated with prenatal methamphetamine exposure. These findings suggest alterations in white matter maturation in these children exposed to methamphetamine in utero. Copyright 2009, Lippincott, Williams & Wilkins.

Maternal smoking, alcohol, and coffee use during pregnancy and son's risk of testicular cancer.

Mongraw-Chaffin ML; Cohn BA; Anglemeyer AT; Cohen RD; Christianson RE. *Alcohol* 43(3): 241-245, 2009. (38 refs.)

It has been suggested that increased risk for testicular cancer occurring worldwide may be due to exposures during fetal development. Lifestyle or environmental exposures may be the most important predictors of risk. However, few studies have directly examined these exposures prospectively. The Child Health and Development Studies is a 40-year follow-up of 20,530 pregnancies occurring between 1959 and 1967. There were 20 cases of testicular cancer diagnosed through 2003 among sons with a maternal interview in early pregnancy. Cases were matched to three controls on birth year and race. Odds ratios and 95% confidence intervals were calculated with exact conditional logistic regression. Compared to controls, mothers of testicular cancer cases were more likely to drink alcohol (unadjusted odds ratio, 3.2; 95% confidence interval, 0.83-15.48 for above vs. below the median for controls) and less likely to drink coffee (unadjusted odds ratio, 0.19; 95% confidence interval, 0.02-1.02 for above vs. below the median). Case mothers were neither more nor less likely to smoke. Although low power may limit interpretation of negative results, the prospective design minimizes bias. In this cohort,

maternal serum testosterone in pregnancy was previously reported to be lower in women who drank alcohol. Because populations with high testicular cancer risk also have lower maternal testosterone, we suggest that testosterone could play a role in explaining the higher risk of son's testicular cancer among mothers who drank alcohol during pregnancy. Copyright 2009, Elsevier Science.

Opioid maintenance treatment during pregnancy: Occurrence and severity of neonatal abstinence syndrome.

Bakstad B; Sarfi M; Welle-Strand GK; Ravndal E. *European Addiction Research* 15(3): 128-134, 2009. (38 refs.)

Background: Opioid maintenance treatment (OMT) is widely used to treat pregnant women with a history of opioid dependence. This study investigated whether maternal methadone/buprenorphine dose and nicotine use in pregnancy affects the occurrence and duration of neonatal abstinence syndrome (NAS) in the infant. Methods: Forty-one pregnant women from OMT programmes in Norway who gave birth between January 2005 and January 2007 were enrolled in a national prospective study. Thirty-eight women (81% of the population) were interviewed in the last trimester of pregnancy and 3 months after delivery. Data from the European Addiction Severity Index and a questionnaire measuring enrolled birth information were compared with medical records and urine analyses. Results: Treatment requiring NAS occurred in 58% of the methadone-exposed and in 67% of the buprenorphine-exposed infants. There was no significant relationship between a maternal dose of methadone or buprenorphine in pregnancy and NAS treatment duration for the infant. The mean number of cigarettes consumed correlated significantly with NAS treatment duration for the methadone group. Birth weight for the methadone group was approximately 200 g above international findings despite high doses during pregnancy. Conclusions: Maternal methadone /buprenorphine dose predicted neither the occurrence nor the need for NAS treatment for the infant. Copyright 2009, Karger AG.

Transfer of buprenorphine into breast milk and calculation of infant drug dose.

Lindemalm S; Nydert P; Svensson JO; Stahle L; Sarman I. *Journal of Human Lactation* 25(2): 199-205, 2009. (28 refs.)

Little is known about the safety of buprenorphine (BUP) in breastfeeding. The aim of this work was to investigate the transfer of buprenorphine and its main active metabolite, norbuprenorphine (n-BUP), into

human milk and to determine the drug dose and effects in exposed infants. Seven lactating women, who were maintained on BUP treatment because of previous opiate addiction, were studied in an open observational study. All mothers had a strong wish to breastfeed their newborn infants. Buprenorphine samples for analysis were collected from the urine of 6 infants together with breast milk, blood, and urine from their mothers during a 24-hour period in the week after birth. One mother-infant pair was studied at 9 months of age. Buprenorphine and n-BUP were analyzed by a liquid chromatography/ mass spectrometry method suitable for handling different matrices. Buprenorphine and n-BUP were found in low levels in the infants' urine. Breastfed infants were exposed to a calculated BUP dose per kg bodyweight less than 1%, with an average milk/plasma area under the curve of 1.7 (range, 1.1-2.8) for BUP and 0.7 (range, 0.4-1.2) for n-BUP. These data support the use of BUP during breastfeeding. However, the authors recommend that infants be monitored closely. Copyright 2009, Sage Publications.

Treatment for amphetamine withdrawal. (review).

Shoptaw SJ; Kao U; Heinzerling K; Ling W. *Cochrane Database of Systemic Reviews* 2009(2): article CD003021, 2009. (32 refs.)

Background: Few studies examined treatments for amphetamine withdrawal, although it is a common problem among amphetamine users. Its symptoms, in particular intense craving, may be a critical factor leading to relapse to amphetamine use. In clinical practice, medications for cocaine withdrawal are commonly used to manage amphetamine withdrawal although the pharmacodynamic and pharmacokinetic properties of these two illicit substances are different. Objectives: To assess the effectiveness of pharmacological alone or in combination with psychosocial treatment for amphetamine withdrawals on discontinuation rates, global state, withdrawal symptoms, craving, and other outcomes. Search strategy: MEDLINE (1966 - 2008), CINAHL (1982 - 2008), PsycINFO(1806 - 2008), CENTRAL (Cochrane Library 2008 issue 2), references of obtained articles. Selection criteria: All randomised controlled and clinical trials evaluating pharmacological and or psychosocial treatments (alone or combined) for people with amphetamine withdrawal symptoms. Data collection and analysis Two authors evaluated and extracted data independently. The data were extracted from intention-to-treat analyses. The Relative Risk (RR) with the 95% confidence interval (95% CI) was used to assess dichotomous outcomes. The Weighted Mean Difference (WMD) with 95% CI was used to

assess continuous outcomes. Main results: Four randomised controlled trials (involving 125 participants) met the inclusion criteria for the review. Two studies found that amineptine significantly reduced discontinuation rates and improved overall clinical presentation, but did not reduce withdrawal symptoms or craving compared to placebo. The benefits of mirtazapine over placebo for reducing amphetamine withdrawal symptoms were not as clear. One study suggested that mirtazapine may reduce hyperarousal and anxiety symptoms associated with amphetamine withdrawal. A more recent study failed to find any benefit of mirtazapine over placebo on retention or on amphetamine withdrawal symptoms. Authors' conclusions: No medication is effective for treatment of amphetamine withdrawal. Amineptine showed reduction in discontinuation rates and improvement in clinical presentation compared to placebo, but had no effect on reducing withdrawal symptoms or craving. In spite of these limited benefits, amineptine is not available for use due to concerns over abuse liability when using the drug. The benefits of mirtazapine as a withdrawal agent are less clear based on findings from two randomised controlled trials: one report showed improvements in amphetamine withdrawal symptoms over placebo; a second report showed no differences in withdrawal symptoms compared to placebo. Further potential treatment studies should examine medications that increase central nervous system activity involving dopamine, norepinephrine and/or serotonin neurotransmitters, including mirtazapine. Copyright 2009, John Wiley & Sons.

Vaccines for cocaine abuse. (review).

Orson FM; Kinsey BM; Singh RAK; Wu Y; Kosten TR. *Human Vaccines* 5(4): 194-199, 2009. (56 refs.) Treatments for cocaine abuse have been disappointingly ineffective, especially in comparison with those for some other abused substances. A new approach, using vaccination to elicit specific antibodies to block the access of cocaine to the brain, has shown considerable promise in animal models, and more recently in human trials. The mechanism of action for the antibody effect on cocaine is very likely

to be the straightforward and intuitive result of the binding of the drug in circulation by antibodies, thereby reducing its entry into the central nervous system and thus its pharmacological effects. The effectiveness of such antibodies on drug pharmacodynamics is a function of both the quantitative and the qualitative properties of the antibodies, and this combination will determine the success of the clinical applications of anti-cocaine vaccines in helping addicts discontinue cocaine abuse. This review will discuss these issues and present the current developmental status of cocaine conjugate vaccines. Copyright 2009, Landes Bioscience.

Targeted naltrexone for problem drinkers.

Kranzler HR; Tennen H; Armeli S; Chan G; Covault J; Arias A et al. *Journal of Clinical Psychopharmacology* 29(4): 350-357, 2009. (23 refs.) This study aimed to replicate and extend prior research showing that the targeted use of naltrexone is a useful strategy to reduce heavy drinking. We compared the effects of naltrexone with those of placebo in a sample of 163 individuals (58.3% male) whose goal was to reduce their drinking to safe limits. Patients received study medication (ie, naltrexone 50 mg or placebo) and were instructed to use it daily or targeted to situations identified by them as being high risk for heavy drinking. An interactive voice response system was used to obtain daily reports of drinking and medication use during the 12-week trial. Analyses were conducted using hierarchical linear modeling, with sex as a potential moderator variable. On the primary outcome measure, mean drinks per day, at week 12, men in the targeted naltrexone group drank significantly less than patients in the other groups did. On a secondary outcome measure, drinks per drinking day, during week 12, the targeted naltrexone group drank significantly less than the other groups did, with no moderating effect of sex. These results support the use of a targeted approach to reduce drinking among heavy drinkers, particularly men), but argue for the use of additional strategies or more efficacious medications than naltrexone to increase the effects of such an intervention. Copyright 2009, Lippincott, Williams & Wilkins.