

Public release date: 2-May-2006

Contact: Ann Bradley
abradley@mail.nih.gov
301-443-3860
NIH/National Institute on Alcohol Abuse and Alcoholism

Effective Alcohol Dependence Treatments Defined

Combine study reports in JAMA

The medication naltrexone and up to 20 sessions of alcohol counseling by a behavioral specialist are equally effective treatments for alcohol dependence when delivered with structured medical management, according to results from "Combining Medications and Behavioral Interventions for Alcoholism" (The COMBINE Study). Results from the National Institutes of Health-supported study show that patients who received naltrexone, specialized alcohol counseling, or both demonstrated the best drinking outcomes after 16 weeks of outpatient treatment. All patients also received Medical Management (MM), an intervention consisting of nine brief, structured outpatient sessions provided by a health care professional. Contrary to expectations, the researchers found no effect on drinking of the medication acamprosate and no additive benefit from adding acamprosate to naltrexone. Effect of Combined Pharmacotherapies and Behavioral Interventions for Alcohol Dependence appears in the current issue of the Journal of the American Medical Association, Volume 295, Number 17, pages 2003-2017.

NIH's National Institute on Alcohol Abuse and Alcoholism (NIAAA) launched COMBINE in 2001 to identify the most effective current treatments and treatment combinations for alcohol dependence. The largest clinical trial ever conducted of pharmacologic and behavioral treatments for alcohol dependence, COMBINE was carried out at 11 academic sites that recruited and randomly assigned 1383 recently abstinent, alcohol-dependent patients to one of nine treatment groups.

Eight treatment groups received MM; four of these received naltrexone (100 milligrams a day), acamprosate (3 grams a day), both naltrexone and acamprosate, or placebo pills. The other four groups received in addition received specialized alcohol counseling. Termed Combined Behavioral Intervention (CBI), the counseling integrated cognitive-behavioral therapy, motivational enhancement, and techniques to enhance mutual help group participation--all treatments shown in earlier studies to be beneficial. Patients assigned to the specialized alcohol counseling could receive up to twenty 50-minute sessions in addition to medical management; the median number received was 10 sessions. To test for any effects of pill taking (placebo), the researchers assigned some patients to a ninth group that received specialized alcohol counseling, but no pills, and no more than four visits with a health professional for general medical advice.

During the 16 weeks of treatment and 1 year after the treatment, the researchers assessed the patients for the percentage of days abstinent from alcohol and time to the first heavy drinking day, defined as 4 or more drinks per day for women and 5 or more drinks per

day for men. They also assessed the odds of good clinical outcome, defined as abstinence or moderate drinking without alcohol-related problems. As in other large clinical trials, the researchers found that most patients showed substantial improvement during treatment and that both the overall level of improvement and the differences between treatment groups diminished during the follow-up period. In the COMBINE study, however, naltrexone continued to show a small advantage for preventing relapse at 1 year after the end of active treatment.

"These results demonstrate that either naltrexone or specialized alcohol counseling--with structured medical management--is an effective option for treating alcohol dependence," said Mark L. Willenbring, M.D., Director, Division of Treatment and Recovery Research, NIAAA. "Although MM is somewhat more intensive than the alcohol dependence interventions offered in most of today's health care settings, it is not unlike other patient care models such as initiating insulin therapy in patients with diabetes mellitus. MM's application in primary care and general mental health care settings would expand access to effective treatment dramatically, while offering patients greater choice." To expand its application, NIAAA will develop an abbreviated version of MM to be available in early summer. Print copies of the treatment manuals used in COMBINE are available by order from <http://www.niaaa.nih.gov/Publications/EducationTrainingMaterials>.

The COMBINE results provide guidance for applying today's treatment tools. NIAAA continues to explore new treatment tools in more than 50 current medication trials, in studies to better understand the mechanisms of action in behavioral treatments, and in our search for new molecular targets and novel compounds for clinical testing," according to Raye Z. Litten, Ph.D., COMBINE's government director and co-leader of NIAAA medications development team.

COMBINE chairpersons Raymond F. Anton, M.D., Department of Psychiatry, Medical University of South Carolina, and Stephanie O'Malley, Ph.D., Yale University School of Medicine, and Drs. Willenbring and Litten will discuss the COMBINE results in a news teleconference, to be held May 1, 2006, from 1:00 to 2:00 PM. To request the call-in code, please telephone Ann Bradley (301/443-3860 or 301/443-0595) before 12:00 PM on May 1; to join the call, please telephone 1-877-807-5706 between 12:50 and 1:00 PM.

For interviews with Drs. Anton and O'Malley, telephone 301/443-3860 through May 2. For interviews with the COMBINE study authors, please see author list that follows. For interviews with Drs. Willenbring and Litten, please telephone the NIAAA Press Office, 301/443-3860.

The National Institute on Alcohol Abuse and Alcoholism, part of the National Institutes of Health, is the primary U.S. agency for conducting and supporting research on the causes, consequences, prevention, and treatment of alcohol abuse, alcoholism, and alcohol problems and disseminates research findings to general, professional, and academic audiences. Additional alcohol research information and publications are available at www.niaaa.nih.gov.

The National Institutes of Health (NIH) - The Nation's Medical Research Agency - includes 27 Institutes and Centers and is a component of the U. S. Department of Health and Human Services. It is the primary Federal agency for conducting and supporting basic, clinical, and translational medical research, and it investigates the causes, treatments, and cures for both common and rare diseases. For more information about NIH and its programs, visit <http://www.nih.gov>.

###

COMBINE Study Authors Raymond F. Anton, M.D., Chair (2000-2006) Medical University of South Carolina 843-792-2626
Stephanie S. O'Malley, Ph.D., Chair (1997-1999) Yale University School of Medicine 203-500-5889

Domenic A. Ciraulo, M.D. Boston University School of Medicine 617-638-8491
Ron A. Cisler, Ph.D. University of Wisconsin-Milwaukee 414-699-8554

David Couper, Ph.D. University of North Carolina 919-962-3229
Dennis M. Donovan, Ph.D. University of Washington 206-543-0937/206-616-3192
James D. Hosking, Ph.D. University of North Carolina 919-962-3085
Bankole A. Johnson, M.D., Ph.D. University of Virginia Health System
University of Texas Health Science Center 434-924-9241

Joseph LoCastro, Ph.D. Veterans Affairs Boston Health Care System/
Boston University School of Medicine 617-278-4488

Richard Longabaugh, Ed.D. Roger Williams Medical Center/Brown University 401-465-4116

Barbara J. Mason, Ph.D. University of Miami School of Medicine
The Scripps Research Institute 858-504-0905
Margaret E. Mattson, Ph.D. Staff Collaborator, NIAAA 301-443-0638
William R. Miller, Ph.D.
University of New Mexico 505-277-1821/508-710-3633
Helen M. Pettinati, Ph.D. University of Pennsylvania 215-547-0311
Carrie L. Randall, Ph.D. Medical University of North Carolina
Robert Swift, M.D. Roger Williams Medical Center/Brown University 401-965-1708

Roger D. Weiss, M.D.
Harvard University/McLean Hospital 617-855-2110

Lauren D. Williams, M.D. University of Miami School of Medicine c/o 858-504-0905

Allen Zweben, D.S.W.
Columbia University School of Social Work
University of Wisconsin-Milwaukee/Columbia 212-851-2887

414-732-7337

COMBINE FINDINGS: HIGHLIGHTS

At 16 weeks

All groups substantially reduced drinking during treatment. Overall percent days abstinent tripled, from 25 to 73 percent, and alcohol consumption per week decreased from 66 to 13 drinks, a decrease of 80 percent.

Patients who received medical management plus either naltrexone or specialized counseling showed similarly improved outcomes (PDA= 80.6 percent and 79.2 percent, respectively), compared with patients who received medical management and placebo pills (PDA=75.1 percent).

Patients who received naltrexone reported less craving for alcohol.

The odds of a good composite clinical outcome relative to patients who received medical management and placebo were 1.82 for patients who received MM plus CBI (but no naltrexone), 1.92 for patients who received MM, CBI, and naltrexone, and 2.16 for patients who received MM and naltrexone (but no CBI). That is, adding either naltrexone or specialized alcohol counseling to medical management almost doubled the chance to do well.

About 6 to 7 patients need to be treated with medical management and either specialized alcohol counseling or naltrexone for one additional patient to have a good clinical outcome. This "number needed to treat" is similar to that for other chronic conditions such as depression, Crohn disease, or type 2 diabetes.