

Expanded HIV Testing: Benefits May Warrant Costs

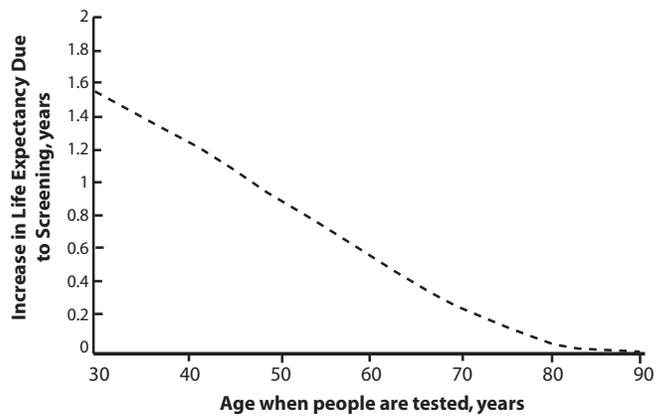
By Lori Whitten, NIDA NOTES Staff Writer

Offering voluntary HIV testing on a routine basis in outpatient health care settings would slow the spread of HIV and improve the survival of many of the estimated 280,000 Americans who are unaware that they are infected. The value of extending HIV screening to relatively low-risk populations in outpatient settings would be on par with the value of routine screening for other common conditions, such as colon cancer, according to two studies funded by NIDA.

In the United States, about one-quarter of the 1.04 million people estimated to be HIV infected do not know they have the virus. Under current testing guidelines, many of these individuals are likely to remain ignorant of their status for as long as they remain relatively healthy, because they do not belong to any of the high-prevalence subgroups to whom testing is recommended, and only those who live in areas with high infection rates will be screened as hospital inpatients. Meanwhile, their disease advances undiagnosed, compromising their prospects for future health and survival. They remain unaware of the need to take precautions against spreading the infection, and according to estimates from the Centers for Disease Control and Prevention (CDC), transmit the virus to 27,000 others each year.

Lead investigators in the two studies, Dr. A. David Paltiel of Yale University School of Medicine and Dr. Gillian Sanders of Duke University's Clinical Research Institute, used computer models to determine whether it would be

Study Predicts Routine Voluntary HIV Testing Would Extend Survival



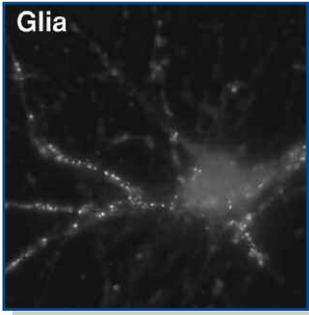
Compared with HIV detection based on symptoms, routine voluntary HIV testing would enhance the life expectancy of people with the infection by getting them into life-prolonging care earlier. Estimates are based on the assumption that state-of-the-art therapy would be initiated when patients had a relatively favorable CD4 count of 350 cells/m³ as opposed to 175 cells/m³, the average count associated with detection based on symptoms. The CD4 count is a measure of immune system health.

cost-effective to extend routine voluntary screening to subpopulations with moderate prevalence of infection or to the whole population. The models use data on the estimated cost associated with an HIV test, the number of additional people who would be tested and the number of cases likely to be diagnosed sooner (and how much sooner), the greater benefits of therapy in earlier as opposed to later stages of infection, and the number of new infections that will be avoided when people who find out they are infected take precautions against transmission. Their work updates previous cost analyses by incorporating the use of state-of-the-art antiretroviral treatment (HAART) for HIV. The analyses yield estimates of the cost of each

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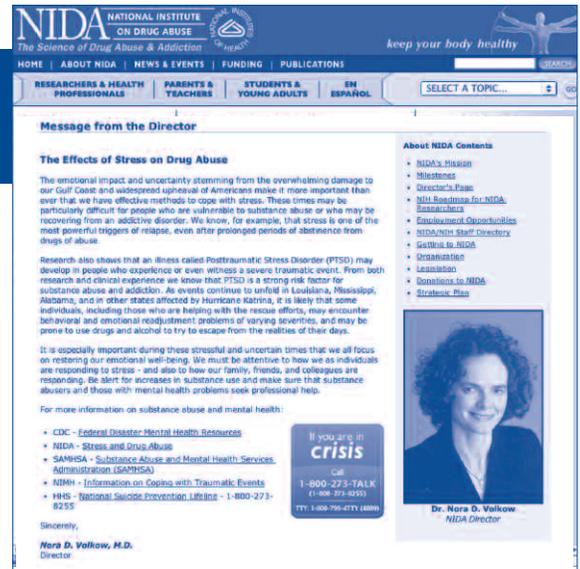
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NIDA Web Page Provides Mental Health Services Information to Katrina Victims

Even as recovery efforts provide relief from the physical devastation wrought by Hurricane Katrina, many survivors, aid workers, and others continue to wrestle with the mental and emotional toll of the disaster. Recognizing that disaster-related trauma and stress could trigger an increase in substance abuse, NIDA has published a list of mental health resources and a toll-free suicide prevention hotline on its Web site.

“These times may be particularly difficult for people who are vulnerable to substance abuse or who may be recovering from an addictive disorder,” says NIDA Director Dr. Nora D. Volkow. “We know, for example, that stress is one of the most powerful triggers of relapse, even after prolonged periods of abstinence from drugs of abuse.” Posttraumatic stress disorder (PTSD), another strong risk factor for substance abuse and addiction, may develop in people who experience or even witness a severe traumatic event, she adds.

NIDA’s Katrina Web page, <http://drugabuse.gov/about/welcome/messagestress905.html>, provides links to mental health resources from the Centers for Disease Control and Prevention, the National Institute of Mental Health, and the Substance Abuse and Mental Health Services Administration as well as to NIDA’s own resources on stress and drug abuse. There also is a link to the toll-free National Suicide Prevention Lifeline (1-800-273-TALK or 1-800-799-4TTY). **NN**



Inhalant Abuse: Danger Under the Kitchen Sink

By NIDA Director Nora D. Volkow, M.D.



Drug abuse among the Nation's young people declined substantially in the past three years, with 600,000 fewer teens abusing drugs, according to the most recent NIDA-University of Michigan Monitoring the Future (MTF) survey. Abuse of inhalants, however, is an exception. The percentage of eighth-graders who have at least once sought intoxication by inhaling spray paints, nail polish remover, lighter fluid, glue, marking pens, aerosols, cleaning fluid, or other volatile substances has increased 2 years in a row and now stands at 17.3 percent. This trend is alarming and unacceptable.

Why would anyone empty a container of lighter fluid into a cup and inhale the fumes, or repeatedly sniff marking pens? Inhalant abusers breathe in a substance's vapors for effects resembling alcohol inebriation, including mild stimulation, loss of inhibition, and distorted perceptions. Inhalants generally affect the same areas of the brain as alcohol and other addictive drugs, so it is not surprising that abusers experience intoxication in addition to nausea, vomiting, slurred speech, and loss of coordination. Older children and young adolescents may seek out inhalants as an easily obtainable substitute for alcohol. Intoxication occurs quickly and usually lasts only a few minutes, making abuse of inhalants easier to conceal than abuse of alcohol or marijuana.

We cannot take lightly even one-time experimentation with these toxic chemicals. For some unlucky children, just a single session of repeated inhalations has caused permanent organ damage or death. Organs at risk from inhalant abuse include the lungs, brain, liver, heart, and kidneys. From 2001 to 2002, the Nation's emergency departments reported a near tripling of the number of people requiring medical treatment after inhalant abuse (from 522 to 1,496). Some abusers experience restlessness, nausea, sweating, anxiety, and other symptoms of withdrawal when they stop taking the drug. Like any other drug when abused, inhalants can also lead to accidents and injuries.

NIDA is concerned that the latest MTF survey shows that the percentage of eighth-graders who believe it is dangerous to try inhalants once or twice has declined for three years and is now only 38.7 percent. These survey results parallel and may help to explain the current rise in abuse. Evidence shows that the public's perception of the risk involved in drug taking can affect rates of drug abuse. For example, an earlier peak in inhalant abuse occurred in 1995, when only 42 percent of 10th-graders believed that trying these substances was dangerous and 21.6 percent of eighth-graders had abused inhalants at least once. That trend reversed after a national media campaign, sponsored by the Partnership for a Drug-Free America, highlighted the health consequences associated with inhalant abuse. The abuse of inhalants dropped in tandem with a rise in the perception of risk.

Parents of teenagers may be unaware of the risks of inhalant abuse. Even those who are watchful for signs of alcohol or drug abuse may not realize the risk associated with products found under the kitchen sink and in the garage. For this reason, NIDA is offering science-based information on inhalant abuse to today's parents and young people at a new Web site, <http://inhalants.drugabuse.gov>. Adults don't have to clear out cabinets, utility closets, and garage shelves to keep young people safe from inhalant abuse. Rather, they should be aware of the problem, learn the facts, and communicate with children in a way that guides them toward healthy life choices.

In January, NIDA joined leaders of the Community Anti-Drug Coalitions of America to discuss the magnitude of youth inhalant abuse, underlying reasons, effects on the brain, and strategies to convince susceptible youth of the danger. The Institute participated in the National Inhalant Prevention Coalition's National "Inhalants & Poisons Awareness Week" in March. We will continue to work and collaborate to alert youth and the public that inhalants—often the first drugs that young people abuse—are addictive and dangerous. **NN**

Modafinil Improves Behavioral Therapy Results In Cocaine Addiction

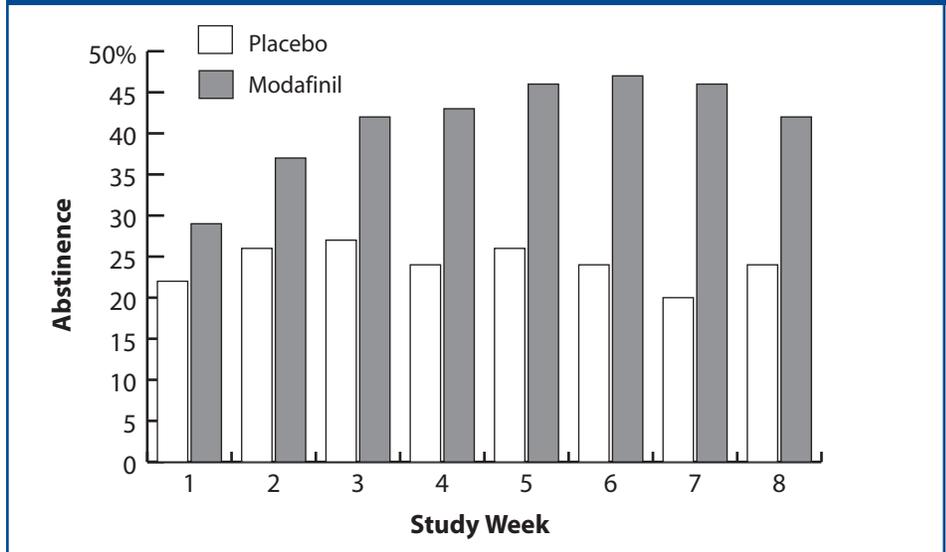
By Patrick Zickler, *NIDA NOTES* Staff Writer

NIDA-supported researchers evaluating modafinil's potential to enhance behavioral treatment for cocaine addiction have reported a second successful clinical efficacy trial. The new results affirm and extend the promising findings of the earlier, smaller, and less stringent "open label" trial, and they set the stage for large-scale multisite trials that could definitively establish the medication's usefulness.

Dr. Charles Dackis and colleagues at the University of Pennsylvania Treatment Research Center recruited 62 individuals (44 male, 18 female; mean age, 44.5 years) for their double-blind study. All had come to the Center seeking treatment for cocaine addiction, had ingested at least \$200 worth of cocaine in the 30 days prior to presenting for treatment, and met the cocaine-dependence criteria of the *Diagnostic and Statistical Manual of Mental Disorders, 4th Edition* (DSM-IV). The patients agreed to visit the clinic twice a week for individual sessions of cognitive-behavioral therapy (CBT) and provide urine samples 3 times a week for the 8-week course of the study. Once each week, the clinic staff dispensed a week's supply of pills, either modafinil in daily doses of four 100 mg pills (30 patients) or an equal number of identical-looking placebo pills (32 patients).

Throughout the study, modafinil-treated patients gave fewer cocaine-positive urine samples than the placebo group. "More impressive, though, is the fact that more than twice as many modafinil patients as placebo patients (33 percent compared with 13 percent) were able to attain abstinence for 3 weeks or more," Dr. Dackis says. "Maintaining abstinence for a prolonged period

Combining Modafinil with Behavioral Therapy in Cocaine Addiction Treatment Increases Likelihood of Abstinence



Abstinence rates among patients who received modafinil plus behavioral therapy during 8-week cocaine addiction treatment were consistently higher than rates among patients who received placebo.

during treatment is an important clinical threshold. Cocaine is a binge drug, and it is common in outpatient treatment for a patient to go 4 or 5 days without using, relapse, then have another clean week. The long continuous abstinence we saw with modafinil is a strong and encouraging signal that this medication can help patients avoid relapse during the critical first weeks of treatment." Both groups of patients attended the same average number of CBT sessions, he adds, further supporting the likelihood that modafinil was the factor accounting for reduced cocaine abuse in those who received it.

Modafinil, a medication currently used to treat narcolepsy, enhances levels of glutamate, a chemical that influences the activity of cells throughout

the brain. Animal research has shown that repeated exposure to cocaine depletes glutamate levels in brain regions associated with development of dependence and addiction, and that increasing glutamate concentrations will block reinstatement of cocaine self-administration in rats—a model of relapse to drug abuse in humans (see "Brain Glutamate Concentrations Affect Cocaine Seeking," *NIDA NOTES*, Vol. 19, No. 3, p. 1).

Modafinil's modulation of glutamate transmission may account for a striking effect reported by patients: "The mechanism for this isn't clear, but some patients receiving modafinil told us that if they did use cocaine it did not produce the irresistible urge to use more, which they had always felt before," Dr. Dackis says. "Some of

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NIDA Research Identifies Proteins That Direct Formation of the Brain's Communication Circuits

By Patrick Zickler, NIDA NOTES Staff Writer

NIDA-supported investigators have identified a pair of proteins that direct the formation of cell-to-cell connections—called synapses—that control the flow of information through the brain. An understanding of normal synapse formation may lead to improved treatment of conditions, such as epilepsy and drug addiction, that are characterized in part by too many synapses.

Research by Dr. Ben Barres, Dr. Karen Christopherson, and colleagues at Stanford University shows that proteins called thrombospondins, which are produced by cells called glia, are essential for the development of the circuitry that connects the brain's nerve cells, or neurons. Although glial cells comprise 90 percent of the cells in an adult brain, their role remains largely a mystery, Dr. Barres says. "We knew that neurons would not survive without glia to support them. Now we see that very few synapses will form without the thrombospondins produced by glial cells." Thrombospondins are produced most abundantly during mammalian brain development, especially during the surge in brain growth that begins after birth and continues through infancy. Low levels of the protein in the mature brain correspond with a poor ability to form new synapses.

To study the role of glial cells in neuron growth and maintenance, the investigators first identified a type of nerve cell that would grow in a laboratory dish without a supporting culture of glial cells. They discovered that one type of rat neuron—retinal ganglion cells, which transmit visual information from the retina to visual centers of the brain—survived and divided under these conditions. The researchers then added a layer of glial

cells to the culture, and noted the changes. They found that retinal cells formed very few synapses when no glial cells were present, but synaptic formation increased seven-fold when glial cells were added.

The researchers next isolated individual proteins produced by glial cells. When they added two of the proteins, called thrombospondin 1 and thrombospondin 2, to retinal cell cultures with no supporting glial cells present, the retinal cells formed synapses just as efficiently as when they were exposed to a supporting culture of whole glial cells.

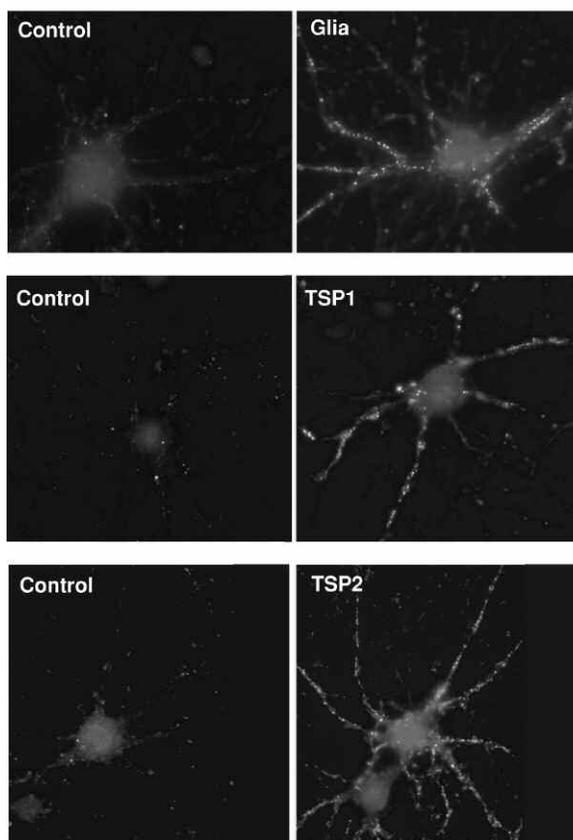
To confirm the role of thrombospondins in synaptic formation in living animals, the investigators developed a strain of mice lacking the genes necessary to produce thrombospondins 1 and 2. When investigators compared the adult brains of these mice to those of normal mice, they found 40 percent fewer synapses.

It is likely that other, as-yet-unidentified factors are necessary for the development of fully functional synapses, Dr. Barres says. A functional synapse consists of structures on two neurons: One is a sending (pre-synaptic) neuron that releases

messenger chemicals called neurotransmitters; the second (postsynaptic) neuron is a receiver that detects the neurotransmitter and responds to the chemical message. The synapses Dr. Barres and his colleagues developed by exposure to thrombospondins 1 and 2 were structurally normal but functionally "silent"—the postsynaptic cells did not respond to neurotransmitters. Research continues with a

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Proteins Produced by Glial Cells Are Crucial to Development of Synapses



Rat retinal nerve cells grown in a culture containing no glial cells (Control) develop very few synaptic structures (indicated by bright staining). Nerve cells grown in culture containing glial cells and in cultures containing glial proteins thrombospondin 1 (TSP1) and thrombospondin 2 (TSP2) developed extensive synaptic structures.

Reproduced with permission from Christopherson et al., 2005.

Expanded HIV Testing: Benefits May Warrant Costs

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additional year of life expectancy that would be gained by expanded testing. Policymakers use such analyses to decide how to allocate funds for health.

Benefits of Early Detection

Dr. Sanders, Dr. Douglas Owens of the Veterans Affairs Palo Alto Health Care System, and their colleagues analyzed a hypothetical group of patients typical of those in general health care settings. The researchers assumed the patients' average age was 43 and their rate of unknown HIV infection was 1 percent, the level at which the CDC recommends routine testing. A 1 percent prevalence of unknown infection is probably high compared with the overall U.S. population (0.1 percent), but lower than high-risk populations currently screened (3 percent). By comparing three different scenarios of HIV detection—symptom-based diagnosis, with a one-time voluntary test, and through testing every 5 years—the researchers were able to assess the lifetime benefits to patients and their partners, as well as the costs, of expanded testing.

The analysis found that one-time HIV testing would increase the life expectancies of individuals in the hypothetical population by an average of 4.7 quality-adjusted days and cost about \$15,078 for every year of life gained. Patients whose HIV was discovered earlier and treated sooner would live on average 1.5 years longer as a result of the testing.

The \$15,078 figure assumes that earlier HIV detection would reduce the spread of infection by 20 percent. Some such reduction would be likely because once people know they have HIV, they tend to change their behavior to avoid infecting others, and when they start antiretroviral treatment their body fluids become less infectious. If transmission were not

reduced, one-time HIV testing in the hypothetical population would cost \$41,736 per year of life gained—comparable to the cost-effectiveness of routine testing for colon cancer, hypertension, and type 2 diabetes. The researchers further suggested that one-time testing might be justified in terms of value in a hypothetical population with an HIV infection prevalence as low as 0.05 percent.

In the second study, Dr. Paltiel and his colleagues compared current practice with routine voluntary HIV testing among high-risk communities (3 percent prevalence), communities with 1 percent prevalence, and the general population of the United States (0.1 percent prevalence). They estimated that adding a one-time voluntary HIV test to current care

for people at high risk of infection would cost \$36,000 per life-year gained. Testing a population that meets the 1 percent threshold raises the cost to \$38,000—a figure similar to the \$41,736 estimate of Dr. Sanders and colleagues. In the high-risk population, testing every 5 years would cost \$50,000 per added life-year, rising to \$63,000 if testing were done every 3 years. The findings suggest that voluntary testing every 3 to 5 years in all populations except those with the lowest prevalence would increase survival at a comparatively attractive cost by U.S. standards, says Dr. Paltiel. A one-time voluntary screening in the general population may also be cost-effective, but merits further investigation, he adds.

“Expanding voluntary HIV testing will require an investment—but it

delivers better value for money than many other chronic disease testing programs that are routinely used in the United States today,” says Dr. Paltiel. Neither research project addressed who should pay for expanded HIV screening, but the findings serve as a springboard for policy discussions involving all people with a stake in the decision. “Cost-effectiveness is just one consideration in policy decisions. Implementing expanded HIV testing also will require people believing it’s an important use of limited resources,” says Dr. Sanders.

The findings have made an impact in the state with the largest HIV caseload in the nation. Citing the research, the New York State

HIV Testing and Other Routine Tests: Cost-Effectiveness Compared	
Test	\$/QALY* Gained
HIV test: All inpatients†	38,600
HIV test every 5 years: People at high risk (3% prevalence)†	50,000
HIV test one time (1% prevalence)‡ Individual benefit only	41,736
Including benefit to others	15,078
HIV test one time: U.S. general population (0.1% prevalence)†	113,000
Breast cancer test: Annual mammogram, age 50-69§	57,500
Colon cancer test: FOBT + SIG every 5 years, age 50-85§	57,700
Type 2 diabetes test: Fasting blood glucose, age >25§	70,000
Hypertension testing§	48,000
FOBT indicates fecal occult blood test; SIG, sigmoidoscopy. *In quality-adjusted life years (QALYs), which account for both longevity and health-related quality of life. †Paltiel et al (2005); ‡Sanders et al (2005); §Adapted from personal communication, Sanders and Paltiel, 2005.	

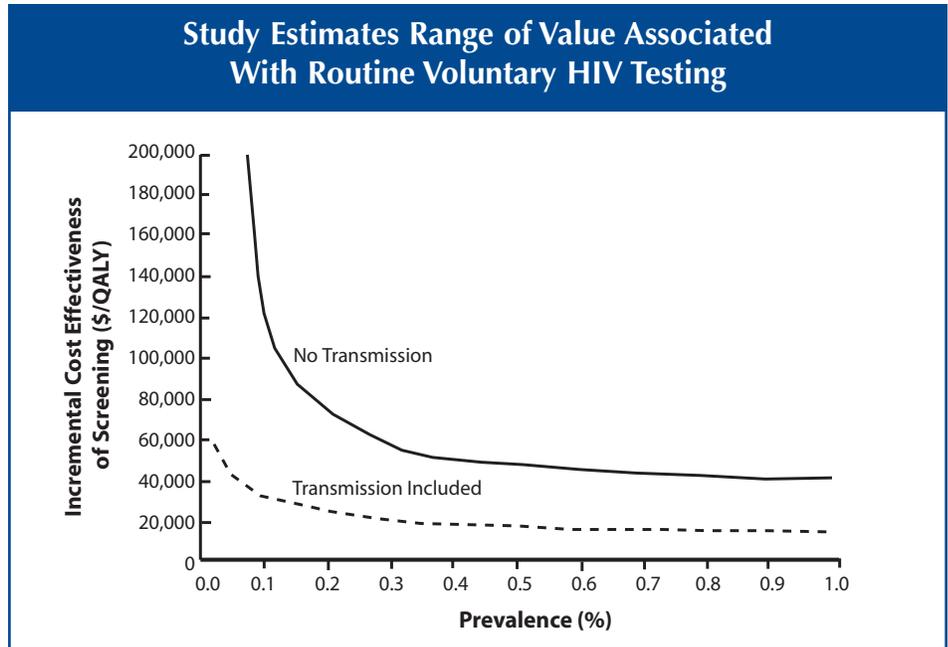
The cost-effectiveness of various HIV testing approaches compared with that of common routine tests.

Department of Health has revised its HIV guidelines, urging State health care providers to integrate routine testing into their medical care, use rapid HIV testing, and refer patients with positive test results to care, among other things.

“People may think of computer-based analyses as isolated and abstract, but this AIDS modeling program encourages researchers to use findings from a wide range of relevant disciplines and incorporate advice from clinicians,” says Dr. Peter Hartsock of NIDA’s Division of Epidemiology, Services and Prevention Research. “These two studies integrated data from many perspectives, and their results provide rigorous but practical information that can guide the societal discussion of what to do about the problem.”

Sources

• Paltiel, A.D., et al. Expanded screening for HIV in the United States—an analysis of cost-effectiveness. *New England Journal of Medicine* 352(6):586–595, 2005.



Dr. Sanders and colleagues estimated that routine HIV testing would be relatively economical even if the prevalence rates of undiagnosed infection were as low as 0.05 percent (half that of the U.S. general population estimate) when reduced transmission to partners is considered (dashed line). Even when transmission is not considered (solid line), HIV testing might be a financially attractive option at prevalence rates well below 1 percent.

• Sanders, G.D., et al. Cost-effectiveness of screening for HIV in the era of highly active antiretroviral therapy.

New England Journal of Medicine 352(6):570–585, 2005. **NN**

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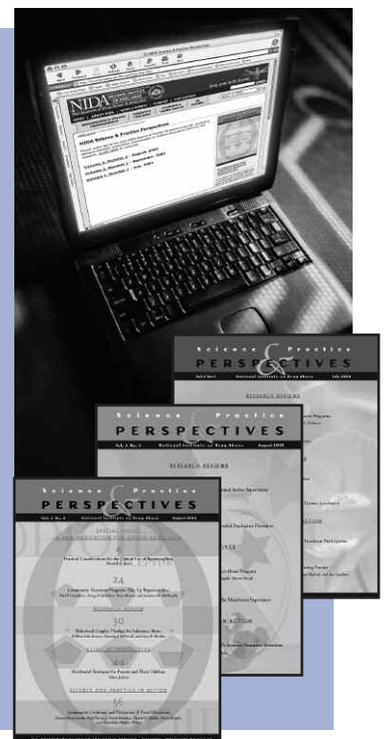
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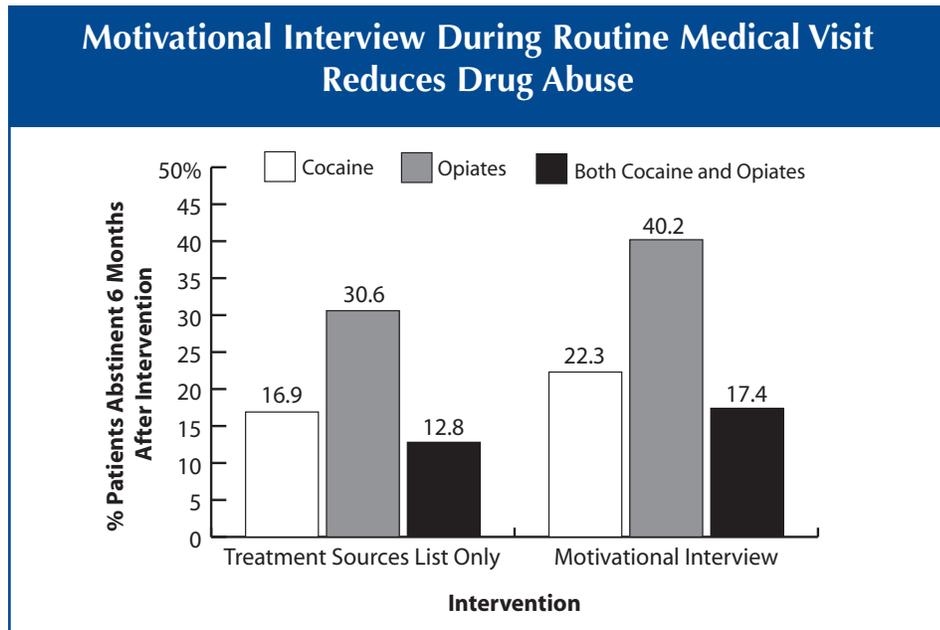
A Brief Encounter With Peer Educator Can Motivate Abstinence

By Lori Whitten, NIDA NOTES Staff Writer

A single meeting with a peer addiction educator during a routine medical visit has helped out-of-treatment cocaine and opiate abusers attain abstinence, report NIDA-funded researchers who conducted a study at three Boston clinics. The peer educators were bilingual individuals in long-term recovery recruited from the same ethnically mixed community as the out-of-treatment drug abusers. The meeting consisted of a structured motivational interview that culminated in a plan for recovery and referrals.

“Talking with a person like yourself—someone who knows your language and culture and views you as an equal, who has successfully recovered from addiction—shows that change is possible and seems to motivate people to get off drugs. It’s not a substitute for treatment, but it is a good first step,” says Dr. Edward Bernstein of Boston University School of Medicine, one of the lead investigators of the study.

Dr. Bernstein and his coinvestigator Dr. Judith Bernstein hired and trained individuals who had been in recovery for at least 3 years to serve as peer educators and research assistants. This staff then screened 23,669 outpatients who were seeking routine medical care at Boston Medical Center walk-in clinics between May 1998 and November 2000. Altogether 1,175 patients (about 5 percent of those screened) met the criteria for study participation—they reported abusing cocaine, opiates, or both drugs during the past 30 days; scored 3 or higher on the Drug Abuse Severity Test; and were not in addiction treatment or protective custody—and agreed to participate. A research assistant met with each participant to administer further assessments, including an



Six months after meeting with a peer addiction educator during a routine medical care visit, patients who participated in a motivational interview had higher rates of abstinence than patients who received a treatment sources list only.

abbreviated Addiction Severity Index (ASI), and an educator then randomly assigned each patient to either an intervention or a control group. Similar proportions of patients in the two groups had abused cocaine (about half), opiates (about 10 percent), or both drugs (33 to 40 percent) during the month before the study (see “Demographic Characteristics of 1,175 Study Participants”).

An educator conducted a motivational interview with each patient in the intervention group. This lasted from 10 to 45 minutes, engaging the patient in a discussion of drug abuse, its consequences, the gap between his or her actual and desired quality of life, and readiness to seek help. The educator concentrated on a few of the patient’s problems as identified by the ASI, negotiated a plan for behavioral change, and provided a handout

listing treatment resources in the community. The educator was able to convey personal knowledge about the community programs and mention particular people for patients to contact, having visited the organizations as part of his or her training. Ten days after the motivational interview, the educators telephoned patients to review the action plan, ask what happened, and provide additional referrals, if necessary. These calls reached less than a third of patients (31 percent).

Participants assigned to the control group received written advice—“based on your screening responses, you would benefit from help with drug abuse”—along with the handout listing treatment resources. They were not given a motivational interview, and those who expressed interest in the treatment programs were merely

encouraged to call a number from the handout. No followup call was attempted with these patients.

Results at Six Months

All participants, both the intervention group and controls, were given appointments to return to the clinic for followup 6 months after their original assessments. The team's research assistants tracked down no-shows by using the clinic's appointment system and visiting shelters and sites frequented by drug abusers. Altogether, they reached 962 (82 percent) of the 1,175 participants. Ultimately, 184 of these patients were excluded from the data analysis, either because hair samples taken at study entry did not confirm their initial reports of drug abuse, or because they did not give samples at followup.

Among the remaining 778 (66 percent of the original sample), 22.3 percent of those who had participated in the motivational interview had been abstinent from cocaine for at least 30 days at the time of the followup interview, compared with 16.9 percent of those who had received just the referral list. The motivational

intervention was associated with superior abstinence rates among the subgroups of participants who abused opiates (40.2 percent versus 30.6 percent) and both cocaine and opiates (17.4 percent versus 12.8 percent). These differences occurred even though patients in the motivational interview group had more severe medical and drug-related problems and reported more psychiatric conditions at the beginning of the study.

About 40 percent of patients in each group reported that they had participated in formal treatment with a health care professional during the 6 months between the initial assessment and followup. This similarity in rates of treatment suggests that the brief motivational encounter with the peer educator was beneficial in itself, and not because it prompted participants to seek therapy. Ninety percent of the patients who said they received professional help underwent detoxification but did not enter ongoing addiction therapy to prevent relapse, a finding the researchers attribute in part to lack of access. "During the study, our patients had very limited access to public methadone treatment,

which many had requested," says Dr. Edward Bernstein.

About half the patients in each group who achieved abstinence cited the peer educator as a source of help. The investigators believe patients viewed these individuals as role models for abstinence, which may prompt some to reduce drug abuse even without a motivational interview. "Doctors and patients are not equal, especially when there are language, class, and culture differences. Add drug abuse to the mix, and you usually get 'shaming and should-ing,' which makes

patients feel inferior and close down," says Dr. Judith Bernstein. Because of their combination of training and life experiences, peers seemed to inspire optimism about the prospect for recovery, even in patients who felt that others had given up on them. Other sources of support included family, mentioned by 50 percent of patients who achieved abstinence, and self-help groups (68 percent).

Peer Educators Welcomed

Clinic staff at the Boston Medical Center welcomed the study's structured effort to deal with drug abuse, which is a serious problem in the community. They appreciated the fact that the program fit unobtrusively into routine care. "Most doctors don't feel they have the time or training to deal with substance abuse and are happy to suggest that patients see the peer counselor," says Dr. Edward Bernstein. An emergency room physician, Dr. Bernstein plans next to implement and evaluate a peer counseling intervention at five emergency centers.

"It's promising to see reduced drug abuse among these vulnerable patients, many of whom were homeless and unemployed," says Dr. Dorynne Czechowicz of NIDA's Division of Clinical Neuroscience, Development and Behavioral Treatment. Previous studies have demonstrated that alcohol-addicted patients benefit from screening and brief motivational interviews in primary-care settings, but few investigations have involved drug abusers. "More research is needed, but these findings suggest that peer educators can play an important role in busy clinical environments and enhance outreach to abusers of cocaine, opiates, and perhaps other drugs," she says.

Source

- Bernstein, J., et al. Brief motivational intervention at a clinic visit reduces cocaine and heroin use. *Drug and Alcohol Dependence* 77(1):49–59, 2005. **NN**

Demographic Characteristics of 1,175 Study Participants	
Characteristic	%
Female	29
Race	
African-American	62
Hispanic	23
White	14
Born in the United States	82
Homeless	46
Reported psychiatric problems	24
Education less than high school	38
Employed	17
Had health insurance coverage	66
Never participated in substance abuse treatment	54

The research team worked with outpatients seeking routine medical care at Boston Medical Center walk-in clinics.

Study Points to Acetaldehyde-Nicotine Combination in Adolescent Addiction

By Patrick Zickler, *NIDA NOTES* Staff Writer

The teen years are when most smokers first light up, and adolescents become addicted to tobacco faster than adults. Research has suggested that young people are particularly vulnerable to smoking addiction in part because their brains are more sensitive to nicotine, but that other factors also contribute. Now, NIDA-funded investigators have produced evidence pointing to another chemical constituent of tobacco smoke, acetaldehyde, as one of those factors. A recent study demonstrated that in adolescent but not adult laboratory rats, acetaldehyde and nicotine together produce a much stronger pleasure-producing, or reinforcing, effect than either chemical alone.

Dr. James Belluzzi and colleagues at the Transdisciplinary Tobacco Use Research Center at the University of

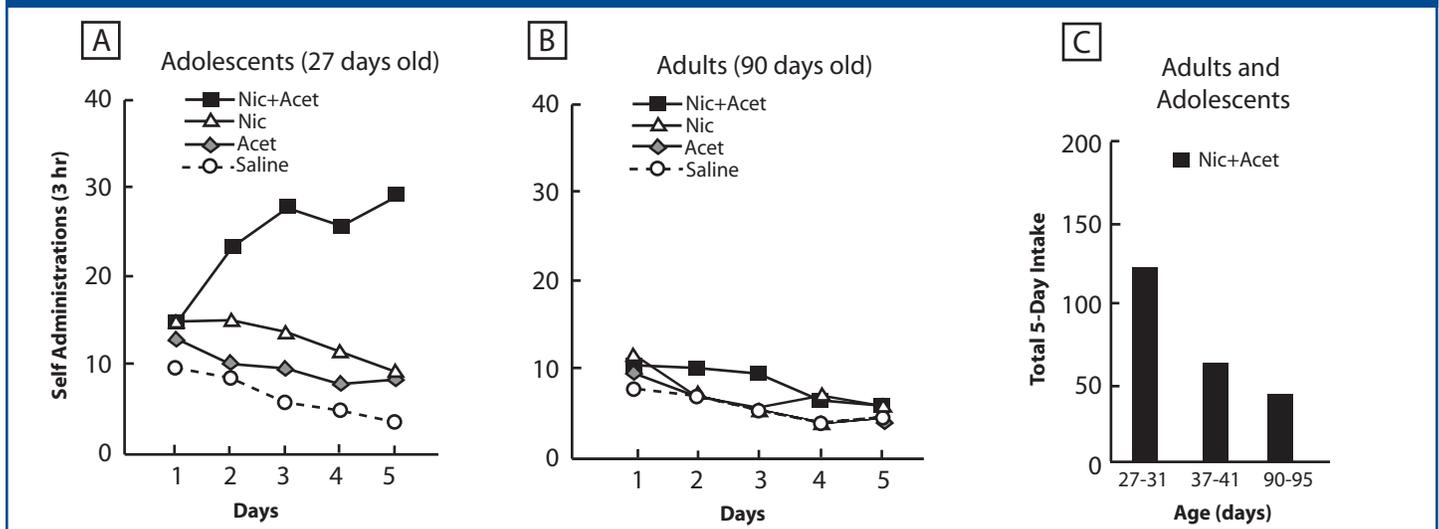
California at Irvine hypothesized that acetaldehyde might play a role in smoking addiction for several reasons. Among them:

- Smokers exhibit more drive to take another puff on a cigarette than laboratory animals do to push a lever for another nicotine infusion, a difference that might be explained if smoke contains an additional reinforcing constituent besides nicotine;
- Smokers are abundantly exposed to acetaldehyde, which occurs naturally in tobacco leaves and also is formed as a combustion product of sugars added to tobacco during cigarette manufacture;
- Research has suggested that acetaldehyde, which also is produced during alcohol metabolism, contributes to alcohol reinforce-

ment and withdrawal symptoms, raising the possibility that it might play a similar role in tobacco dependence.

To test their hypothesis that acetaldehyde contributes to tobacco addiction, particularly in adolescents, Dr. Belluzzi's research team conducted an animal self-administration study with early-adolescent (27-day-old), adolescent (37-day-old), and adult (90-day-old) rats. The researchers placed the animals in cages where they could poke their noses through holes in the cage wall to obtain injections of nicotine (30 $\mu\text{g}/\text{kg}$) plus acetaldehyde (16 $\mu\text{g}/\text{kg}$), nicotine or acetaldehyde alone, or saline. In such studies, the frequency and persistence with which animals nose-poke for a particular substance is a measure of how rewarding it is for them, which in turn may correspond

Adolescent Rats, but Not Adults, Increase Intake of Nicotine When it Is Combined With Acetaldehyde, a Component of Tobacco Smoke



(A) Adolescent rats self-administered nicotine combined with acetaldehyde—but not nicotine alone, acetaldehyde alone, or saline—with increasing frequency over 5 days. (B) Adult rats did not demonstrate any preference for nicotine, acetaldehyde, or the combination over saline. (C) Total 5-day intake of nicotine plus acetaldehyde was greatest for the youngest group of animals, suggesting that vulnerability to tobacco addiction decreases with age.

to how addictive it is for people. Over the course of five daily 3-hour sessions, the youngest rats worked up to poking their noses for nicotine plus acetaldehyde roughly three times as frequently than for either chemical alone or saline. The older adolescent rats also demonstrated a preference for the two-drug combination, but a less-marked one than the 27-day old animals. The adult rats responded no differently to the drugs, alone or in combination, than they did to the saline solution.

“Our results show that acetaldehyde, at the same relative concentration found in cigarette smoke, dramatically increases the reinforcing properties of nicotine,” says Dr. Belluzzi. “Furthermore, the effect is age-related, with adolescent animals far more sensitive than adults.”

To buttress their interpretation of their results, the researchers tested a potential alternative explanation for

the rats’ behavior: The animals might not be seeking pleasure when they poked their noses into the holes for nicotine and acetaldehyde, but simply exhibiting random activity due to chemically induced locomotor stimulation. To evaluate this possibility, the researchers put a control group of rats into the test cages and gave them injections of nicotine plus acetaldehyde at the test dosage. They predicted that these rats should nose-poke less than the original animals if pleasure-seeking was a main motivation for the behavior (because they were getting the chemicals’ reinforcing effects automatically without having to work for them), or nose-poke the same amount if locomotor stimulation was the primary cause (because the test animals and control animals received similar doses of the chemicals). The data showed that the control rats nose-poked less than the original animals.

“This research underscores the point that nicotine alone may not cause the intensity of dependence seen in smokers, and nicotine replacement does not, by itself, eliminate withdrawal or craving for people trying to quit. Other factors clearly are at play,” says Dr. Allison Chausmer of NIDA’s Division of Basic Neurosciences and Behavioral Research. “Dr. Belluzzi’s experiment strongly suggests that acetaldehyde is one of those factors, and it offers a potential explanation for age-related differences that we observe in epidemiological studies of the impact of tobacco.”

Source

• Belluzzi, J.D.; Wang, R.; and Leslie, F.M. Acetaldehyde enhances acquisition of nicotine self-administration in adolescent rats. *Neuropsychopharmacology* 30(4):705–712, 2005. **NN**

Modafinil Improves Behavioral Therapy Results In Cocaine Addiction

continued from page 4

the patients told me they had flushed cocaine away. In 25 years of treating addiction, no one ever told me they threw away cocaine.”

“The body of research suggesting that modafinil is effective in treating cocaine addiction is growing,” says Dr. Ivan Montoya of NIDA’s Division of

Pharmacotherapies and Medical Consequences of Drug Abuse. “Animal research supports the assumption that modafinil reverses the cocaine-induced neurochemical disruptions of glutamate and of dopamine-containing neurons in the brain’s reward centers. Clinically, modafinil has effects that are opposite to the symptoms of cocaine withdrawal, which usually include oversleeping, depression, poor concentration, and craving.”

Dr. Dackis and his colleagues are now planning the next test for

modafinil: a multisite clinical trial that will include more than 650 participants. The study will evaluate modafinil’s efficacy in doses of 200 mg and 400 mg per day in combination with CBT, and results may be available by mid-2006, Dr. Montoya says.

Source

• Dackis, C.A., et al. A double-blind, placebo-controlled trial of modafinil for cocaine dependence. *Neuropsychopharmacology* 30(1):205–211, 2005. **NN**

NIDA Research Identifies Proteins That Direct Formation of the Brain’s Communication Circuits

continued from page 5

search for factors that activate the postsynaptic terminals, Dr. Barres says. “We know that glia produce at least one other protein, which we

have not yet identified, that is necessary for a fully functional synapse.”

“Addictive drugs disrupt communication in the brain in part by altering the synapses,” observes Dr. Jonathan Pollock of NIDA’s Division of Basic Neurosciences and Behavior Research. “Identifying and fully understanding the contribution made by thrombospondins could make possible the development of thrombo-

spondin-based therapies to act on synapses and reverse or control the effects of drug addiction or other neurologic disorders.”

Source

• Christopherson, K.S., et al. Thrombospondins are astrocyte-secreted proteins that promote CNS synaptogenesis. *Cell* 120(3):421–33, 2005. **NN**

Telephone-Based Continuing Care Sustains Abstinence

By Lori Whitten, NIDA NOTES Staff Writer

Telephone-based continuing care, in which an addiction counselor supports patient recovery with 15-minute calls once a week, can be as good as or better than face-to-face care at helping most patients maintain abstinence after intensive outpatient treatment (IOP). In a recent NIDA-funded study, the benefits of a telephone support protocol were evident nearly 2 years after the last call for all but the 20 percent of patients with severe addiction problems that did not resolve during IOP.

“Telephone-based continuing care does not require transportation or interfere much with work or childcare responsibilities, and this flexibility may help patients stay engaged in recovery and maintain the gains achieved during initial inpatient or outpatient treatment,” says Dr. James McKay, lead researcher of the study.

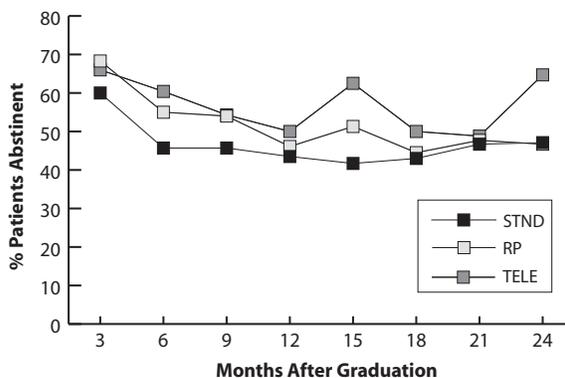
Dr. McKay and colleagues at the University of Pennsylvania, the Treatment Research Institute in Philadelphia, and Brandeis University worked with two Philadelphia-area outpatient addiction programs. Patients seeking treatment in these programs received about 9 hours of outpatient group therapy each week for 1 month, on average. The therapy concentrated on overcoming denial of substance abuse, learning about the addiction process and cues to relapse, and beginning self-help participation. Dr. McKay and colleagues recruited patients who “graduated” from therapy—that is, continued in the IOP and achieved abstinence in the last week—to receive 12 weeks of continuing care and followup for 2 years.

The patients, 359 men and women aged 18 to 65, were typical, in terms of demographics and problem severity, of individuals seeking treatment at publicly funded outpatient addiction

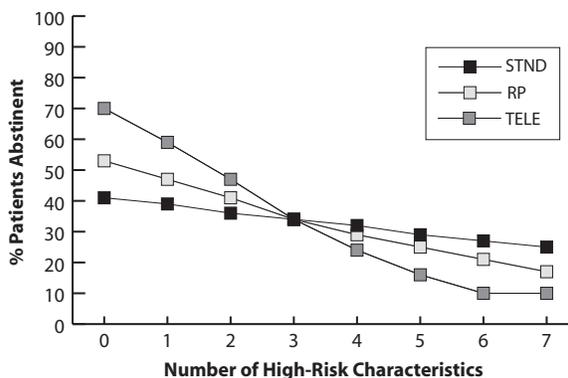
programs. Half met the *Diagnostic and Statistical Manual of Mental Disorders, 4th Edition* (DSM-IV) criteria for co-

occurring cocaine and alcohol dependence, 87 were dependent on cocaine only, and 91 were alcoholic. Thirty

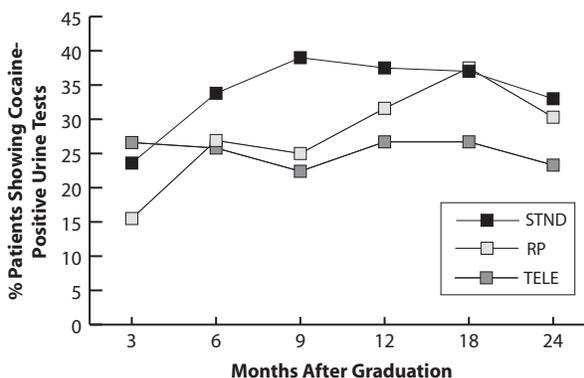
Telephone Counseling Helps Outpatient Treatment Graduates Stay Abstinent



Two years after graduating from intensive outpatient treatment, more patients who participated in telephone-based continuing care (TELE) had maintained abstinence during the previous 3 months than those receiving standard group counseling (STND). The percentage of abstinent patients did not differ between TELE and relapse prevention (RP) continuing care.



Throughout the study, patients with four or more characteristics reflecting severe addiction were better able to maintain abstinence if they participated in STND compared with TELE.



The percentage of cocaine-positive urine samples did not increase as quickly during the followup for TELE patients as it did for those who participated in RP, with a similar trend for TELE compared with STND.

All patients participated in 12 weeks of continuing care after completing a month of intensive outpatient treatment, and reported outcomes every 3 months during the 2-year followup.

percent had met the criteria for a diagnosis of major depression at some time in their lives. When they began treatment, they reported 8 years of cocaine and 18 years of alcohol abuse, on average, and multiple attempts to quit.

Regular Contact With a Therapist Is Crucial

The investigators randomly assigned each patient to one of three continuing care therapies: a face-to-face therapy, either standard group (STND) or relapse prevention (RP); or telephone-based (TELE) counseling. In STND care, the most common approach to continuing care for addiction, 122 patients attended twice-weekly counseling sessions that emphasized overcoming denial and engaging in mutual- and self-help activities. In RP therapy, 135 patients attended an individual session of cognitive-behavioral therapy and then group sessions once a week. In this approach, patients identify situations that prompt substance abuse and work to improve coping responses using structured activities and homework exercises.

In TELE care, 102 patients met with counselors in person the week before beginning the telephone phase to discuss the therapy and receive a workbook with exercises that structured subsequent calls. At a scheduled time each week, they telephoned counselors and talked for 15 to 20 minutes about progress during the previous week, any episodes of substance abuse, participation in self-help and other pro-recovery activities, plans for achieving the next week's goals, and any concerns. Counselors contacted patients who did not call and discussed in a supportive way their reasons for not doing so. To ease the transition from outpatient to continuing care, therapists offered the TELE patients group counseling once a week for a month. Patients struggling with relapse at that point could continue with group sessions; more than a third (35 percent) exercised this option.

The researchers followed up with patients every 3 months throughout the study and contacted 86 percent 2 years

after graduation from IOP. At this point, about two-thirds of TELE patients reported abstinence during the previous 3 months, compared with about half of those who had participated in STND. An analysis of urine samples from the cocaine-addicted patients showed an overall increase in the percentage of cocaine-positive samples during the followup period, but the increase was more rapid among RP participants than TELE participants. The TELE group had higher abstinence rates than STND throughout followup. Patients who participated in TELE maintained the gains of IOP even though they received about half as much therapeutic contact (428 minutes) as those receiving STND or RP (845 and 861 minutes, respectively).

“Continuing care benefits people in recovery in several ways, but regular contact with a therapist is crucial for patients with a chronic condition, and especially helps patients who have relapsed get back into treatment,” says Dr. Dorynne Czechowicz of NIDA’s Division of Clinical Neuroscience, Development, and Behavioral Treatment. Although larger studies with more diverse patients are needed, Dr. McKay and his colleagues laid important groundwork, she says.

Face-to-Face Care for Severe Problems

Some patients need more contact with a counselor than telephone-based continuing care affords to maintain recovery. To identify these patients, Dr. McKay and his colleagues examined the link between outcomes and seven patient characteristics: co-occurring addiction to alcohol and cocaine at the beginning of IOP; any alcohol use, any abuse of cocaine, minimal attendance at self-help meetings, below-average social support during IOP; and a lack of commitment to complete abstinence, and low self-efficacy for recovery at the end of IOP.

Patients who demonstrated three or fewer of the characteristics—about 80 percent of the study population—did at least as well with TELE continuing care as with the other two

approaches. But the remaining patients, those who met the criteria for co-occurring addiction at the beginning of treatment and did not achieve the main goals of IOP—abstinence from cocaine and alcohol during treatment, commitment to abstinence, and participation in self-help programs—were at high risk for relapse and showed better outcomes with STND continuing care, relative to TELE, during most of the followup. The findings suggest that TELE may be inappropriate for patients with more severe addiction problems until they demonstrate stable abstinence from drugs and alcohol, says Dr. McKay.

Flexible Continuing Care

“Some practitioners are developing flexible arrangements to engage and retain more patients in continuing care,” says Dr. McKay. Flexibility in the practical sense—the ability to call one’s counselor from any location—extends participation in continuing care, not only to busy people, but also to those living in rural areas or who have lost driver’s licenses.

Telephone-based care is one way that a treatment intervention can respond to each patient’s progress during recovery; it gives counselors the flexibility to intensify care if the patient is struggling to maintain abstinence. “Clinicians managing other chronic disorders—for example, hypertension and cancer—are using progress during initial treatment to determine subsequent care. It’s not a new therapeutic approach, but it is novel to addiction treatment,” Dr. McKay says.

Sources

- McKay, J.R.; Lynch, K.G.; Shepard, D.S.; and Pettinati, H.M. The effectiveness of telephone-based continuing care for alcohol and cocaine dependence. *Archives of General Psychiatry* 62(2):199-207, 2005.
- McKay, J.R., et al. Do patient characteristics and initial progress in treatment moderate the effectiveness of telephone-based continuing care for substance use disorders? *Addiction* 100(2):216-226, 2005. **NN**

Ray, Jamie Foxx Among Winners of 9th Annual PRISM Awards

The movie *Ray* and actor Jamie Foxx are two of the winners in the 9th annual PRISM Awards, which recognize accurate depictions of drug and alcohol abuse in television, film, video, music, and comic book entertainment.

NIDA Deputy Director Timothy Condon participated in the awards ceremony in Los Angeles on April 28. NIDA is a sponsor of the awards, in partnership with the Entertainment Industries Council, Inc., The Robert Wood Johnson Foundation, and FX Networks.

Ray won the award in the “wide release feature film” category for its realistic portrayal of musician Ray Charles’s addiction to drugs. Jamie Foxx won for his performance in the film’s title role. The winning limited-release feature film was *A Love Song for Bobby Long*, in which a teenager returns to her childhood home in Florida to find two down-and-out men living there. Alcoholism plays a prominent role in the film.

All My Children (daytime drama multi-episode), *Desperate Housewives* (comedy multi-episode), *Dr. Phil* (talk show episode), *ER* (drama episode), and *Lost* (drama multi-episode) were among the TV programs that received awards for accurately depicting drug abuse. Actors who received top honors for their performances include Ray Liotta (drama episode), Christine Lahti (drama storyline), Katey Sagal (comedy series), and Justine Waddell (TV movie).

Winners in other categories include:

- NBC’s *The More You Know*, for community service effort;
- *Bright Leaves*, for the PRISM film festival;
- *Untold*, for its “Darryl Strawberry” TV biographical series episode or special;
- *Gracie’s Choice*, for TV movie or miniseries;
- *Relative Evil*, for direct-to-video production; and



NIDA Deputy Director Tim Condon (third from left) with (from left) Dwayne Proctor and Kristin Schubert of The Robert Wood Johnson Foundation, actors Gerald McRaney and Michele Lee, and Brian Dyak of the Entertainment Industries Council at the 9th annual PRISM awards in Los Angeles.

- Brad Paisley and Alison Krauss for the music recording and music video *Whiskey Lullaby*. “These productions give our findings faces and lives, and this broadening of scientific knowledge throughout the public is critical to improving the overall health of the nation,” NIDA Director Dr. Nora D. Volkow said in a statement published in the awards program.

A list of all PRISM Award winners is available at <http://www.prismawards.com>. The awards ceremony aired September 4 on the FX cable network. **NN**

Breaking the Cycle of Drugs and Crime

Drug abuse among convicts could be reduced significantly if criminal justice supervision and drug treatment were better integrated, NIDA Director Dr. Nora D. Volkow told a gathering on Capitol Hill.

Dr. Volkow spoke at a March 15 briefing before congressional staff and members of organizations active in drug abuse research and treatment. The briefing was sponsored by the Friends of NIDA (FNIDA), a coalition of private-sector organizations in the drug abuse field that support NIDA’s mission.

Research demonstrates that treatment for individuals in the criminal justice system decreases their future drug use and criminal behavior and



Speakers at a Capitol Hill briefing on drugs and crime included (clockwise from center bottom) NIDA Director Dr. Nora D. Volkow, Dr. Dwayne Simpson of Texas Christian University, Mr. Dexter Manley of Second Genesis Inc., and Representative Patrick Kennedy.

improves social functioning.

“Treatment works, even when it is not voluntary,” Dr. Volkow said.

Many of the 6.9 million adults in the U.S. criminal justice system need treatment—by one estimate, up to 85 percent of State inmates—but relatively few receive treatment while incarcerated. Legal pressure is an effective mechanism for getting offenders to enter treatment and stick with it, Dr. Volkow said. “Aftercare”—community-based treatment upon release, along with case management and referral to medical and social services—is a crucial component of treatment, she emphasized. **NN**

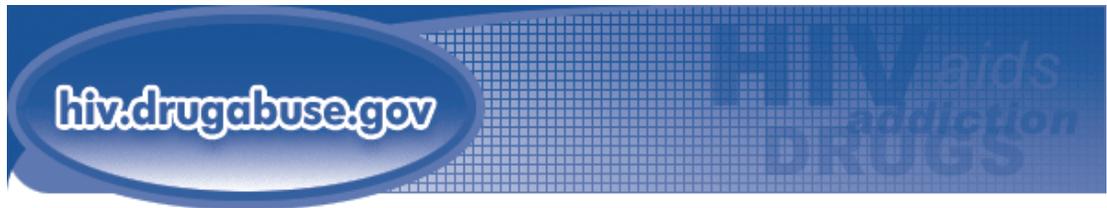
HIV/AIDS Research and Education Are Crucial to Drug Abuse Prevention

Behavior associated with drug abuse is the single largest factor in the spread of HIV infection in the United States, where about one-third of HIV/AIDS cases are related to injection drug abuse.

NIDA's Web site, <http://hiv.drugabuse.gov>, provides research-based information about HIV/AIDS and its relationship to drug abuse. A compendium of NIDA publications and public service announcements, the Web site is a valuable resource for care providers as well as parents and teens looking for information. Visitors to the site will find a list of drugs that are commonly abused, a phone number and Web site for treatment referrals, up-to-date research findings, and announcements in English and Spanish about special events.

Using or sharing drug paraphernalia such as unsterile needles, cotton swabs, rinse water, and cookers to inject heroin, cocaine, or other drugs places drug abusers at risk for contracting or transmitting HIV. Drug abuse without the use of needles and syringes can also foster the spread of HIV. Research sponsored by NIDA and the National Institute on Alcohol Abuse and Alcoholism has shown that drug and alcohol use can interfere with judgment about sexual behavior and thereby affect the likelihood of engaging in unplanned and unprotected sex. This increases the risk for contracting HIV from infected sex partners.

In the past 15 years, NIDA has sponsored a



comprehensive research program in response to the dynamic nature of the co-occurring epidemics of drug abuse and HIV/AIDS. This research has yielded science-based principles that should prove useful to community planners, policymakers, service providers, and medical practitioners as they develop and implement programs to prevent the spread of HIV and other infections among injecting and noninjecting drug users and their sexual partners. To foster widespread use of these principles, NIDA has produced a number of publications, such as *Principles of HIV/AIDS Prevention in Drug-Using Populations* and *The NIDA Community-Based Outreach Model: A Manual To Reduce the Risk of HIV and Other Blood-Borne Infections in Drug Users*.

The Web site also offers the "Jack & Jill" public service announcements,

which are geared toward teens and provide information about substance abuse and risky sexual behavior. "Jack & Jill" was the first installment in NIDA's "Keep Your Body Healthy" campaign, and deals with the connection between drug abuse and contracting HIV/AIDS. It has been estimated that at least half of all new HIV infections in the United States are among people under age 25, and most of these young people are infected sexually.

NIDA's Web sites, including <http://hiv.drugabuse.gov>, help bring the Institute's research and policies to a wide audience; by disseminating material online, parents, teens, and providers have an accessible resource for the latest in drug abuse research.

NN

AIDS Cases By Exposure Category and Sex Through 2002

Exposure category	Males		Females		Overall total	
	No.	%	No.	%	No.	%
Male-to-Male Sexual Contact	384,784	55	—	—	384,784	55
Injection Drug Abuse	151,367	22	58,552	39	209,919	30
Heterosexual Contact	36,692	5	63,379	42	100,071	14

Source: CDC. *HIV/AIDS Surveillance Report: Cases of HIV infection and AIDS in the United States, Vol. 14, 2002*. Atlanta, Georgia: U.S. Department of Health and Human Services.

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