



What are the long-term effects of methamphetamine abuse?

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from the director:

The abuse of methamphetamine—a potent and highly addictive stimulant—remains an extremely serious problem in the United States. According to data from the 2012 National Survey on Drug Use and Health (NSDUH), over 12 million people (4.7 percent of the population) have tried methamphetamine at least once. NSDUH also reports that approximately 1.2 million people used methamphetamine in the year leading up to the survey.

The consequences of methamphetamine abuse are terrible for the individual—psychologically, medically, and socially. Abusing the drug can cause memory loss, aggression, psychotic behavior, damage to the cardiovascular system, malnutrition, and severe dental problems. Methamphetamine abuse has also been shown to contribute to increased transmission of infectious diseases, such as hepatitis and HIV/AIDS.

Beyond its devastating effects on individual health, methamphetamine abuse threatens whole communities, causing new waves of crime, unemployment, child neglect or abuse, and other social ills. A 2009 report from the RAND Corporation noted that methamphetamine abuse cost the Nation approximately \$23.4 billion in 2005.

But the good news is that methamphetamine abuse can be prevented and addiction to the drug can be treated. People can and do recover over time if they have ready access to effective treatments that address the multitude of problems resulting from their abuse of methamphetamine.

The primary goals of the National Institute on Drug Abuse (NIDA) are to apply what our scientists learn from drug abuse research to develop new treatment approaches and enhance existing ones, and to bring these effective treatments to the communities that need them.

In this newly updated Research Report, we provide an overview of the latest scientific information on methamphetamine. Our intent is to illustrate for readers the damaging effects of methamphetamine abuse and to inform them about effective prevention and treatment interventions.

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Research Report Series

Methamphetamine

What is Methamphetamine?

Methamphetamine is a powerful, highly addictive stimulant that affects the central nervous system. Also known as meth, chalk, ice, and crystal, among many other terms, it takes the form of a white, odorless, bitter-tasting crystalline powder that easily dissolves in water or alcohol.

Methamphetamine was developed early in the 20th century from its parent drug, amphetamine, and was used originally in nasal decongestants and bronchial inhalers. Like amphetamine, methamphetamine causes increased activity and talkativeness, decreased appetite, and a pleasurable sense of well-being or euphoria. However, methamphetamine differs from amphetamine in that, at comparable doses, much greater amounts of the drug get into the brain, making it a more potent stimulant. It also has longer-lasting and more harmful effects on the central nervous system. These characteristics make it a drug with high potential for widespread abuse.

Methamphetamine has been classified by the U.S. Drug Enforcement Administration as a Schedule II stimulant, which makes it legally available only through a nonrefillable prescription. Medically it may be indicated for the treatment of attention deficit hyperactivity disorder (ADHD) and as a short-term component of weight-loss treatments, but these uses are limited and it is rarely prescribed; also, the prescribed doses are far lower than those typically abused.

continued inside

What is the scope of methamphetamine abuse in the United States?

According to the 2012 National Survey on Drug Use and Health (NSDUH), approximately 1.2 million people (0.4 percent of the population) reported using methamphetamine in the past year, and 440,000 (0.2 percent) reported using it in the past month. This represents a decrease from previous years: In 2006 731,000 (0.3 percent) reported past-month use. In 2012, there were 133,000 new users of methamphetamine age 12 or older—the same as the previous year but continuing a general downward trend across the past decade. The average age of new methamphetamine users in 2012 was 19.7 years old.

The 2012 Monitoring the Future (MTF) survey of adolescent drug use and attitudes reported that about 1 percent of 8th, 10th, and 12th graders had used methamphetamine within the past year. These data indicate that 10th and 12th graders are using methamphetamine less than they did 5 years ago, but that use by 8th graders has not dropped significantly in that time. Overall, however, use of methamphetamine by adolescents has declined significantly since 1999, when this drug was first added to the survey.

According to the Drug Abuse Warning Network (DAWN), which collects information on drug-related episodes from hospital emergency departments (EDs) throughout the Nation, methamphetamine accounted for about 103,000 ED visits in 2011; it was the fourth most mentioned illicit drug in ED visits following cocaine, marijuana, and heroin. While still high, this number represents a decrease from the 132,576 ED visits for methamphetamine abuse measured in 2004.

The Treatment Episode Data Set (TEDS) provides information on admissions to substance abuse treatment facilities that are licensed or certified by State substance abuse agencies. According to TEDS data, nationwide treatment admissions for methamphetamine abuse dropped from 8.1 percent in 2005 to 5.6 percent in 2011. The majority of primary methamphetamine admissions were male (53 percent), and about two-thirds (68 percent) were non-Hispanic Whites.



While national trends are showing declines, methamphetamine abuse continues to exhibit regional variability. The strongest effects are felt in the West and parts of the Midwest, according to the National Institute on Drug Abuse's (NIDA's) Community Epidemiology Work Group (CEWG), a network of researchers that provides information about the nature and patterns of drug abuse across the United States. For example, in the first half of 2012, methamphetamine ranked first in drug-related treatment admissions in Hawaii and San Diego, second in San Francisco, and third in Denver and Phoenix.

How is methamphetamine abused?

Methamphetamine comes in several forms and can be smoked, inhaled (snorted), injected, or orally ingested. The preferred method of abusing the drug varies by geographical region and has changed over time. Smoking methamphetamine is currently the most common way of ingesting it, according to CEWG data.

Smoking or injecting methamphetamine puts the drug very quickly into the bloodstream and brain, causing an immediate, intense “rush” and amplifying the drug’s addiction potential and adverse health consequences. The rush, or “flash,” lasts only a few minutes and is described as extremely pleasurable. Snorting or oral ingestion produces euphoria—a high, but not an intense rush. Snorting produces effects within 3 to 5 minutes, and oral ingestion produces effects within 15 to 20 minutes.

As with many stimulants, methamphetamine is most often abused in a “binge and crash” pattern. Because the pleasurable effects of methamphetamine disappear even before the drug concentration in the blood falls significantly, users try to maintain the high by taking more of the drug. In some cases, abusers indulge in a form of bingeing known as a “run,” foregoing food and sleep while continuing to take the drug for up to several days.

How Is Methamphetamine Manufactured?

Most of the methamphetamine abused in this country is manufactured in “superlabs” here or, usually, in Mexico. But the drug is also easily made in small clandestine laboratories, with relatively inexpensive over-the-counter ingredients such as pseudoephedrine, a common ingredient in cold medications. To curb production of methamphetamine, Congress passed the Combat Methamphetamine Epidemic Act in 2005, which requires that pharmacies and other retail stores keep logs of purchases of products containing pseudoephedrine and limits the amount of those products an individual can purchase per day. A few States have even made pseudoephedrine available only with a prescription. Mexico has also tightened its restrictions on this and other methamphetamine precursor chemicals. But manufacturers adapt to these restrictions via small- or large-scale “smurfing”

operations: obtaining pseudoephedrine from multiple sources, below the legal thresholds, using multiple false identifications. Manufacturers in Mexico are also increasingly using a different production process (called P2P, from the precursor chemical phenyl-2-propanone) that does not require pseudoephedrine.

Methamphetamine production also involves a number of other easily obtained chemicals that are hazardous, such as acetone, anhydrous ammonia (fertilizer), ether, red phosphorus, and lithium. Toxicity from these chemicals can remain in the environment around a methamphetamine production lab long after the lab has been shut down, causing a wide range of damaging effects to health. Because of these dangers, the U.S. Environmental Protection Agency has provided guidance on cleanup and remediation of methamphetamine labs.

How is methamphetamine different from other stimulants, such as cocaine?

The methamphetamine molecule is structurally similar to amphetamine and to the neurotransmitter dopamine, a brain chemical that plays an important role in the regulation of reward, but it is quite different from cocaine. Although these stimulants have similar behavioral and physiological effects, there are some major differences in the basic mechanisms of how they work.

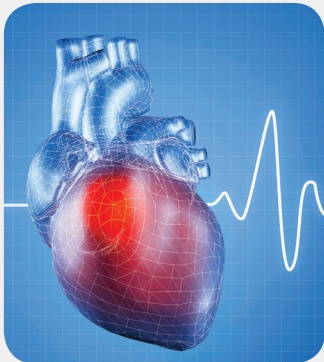
In contrast to cocaine, which is quickly removed from and almost completely metabolized in

the body, methamphetamine has a much longer duration of action, and a larger percentage of the drug remains unchanged in the body. Methamphetamine therefore remains in the brain longer, which ultimately leads to prolonged stimulant effects. Although both methamphetamine and cocaine increase levels of dopamine, administration of methamphetamine in animal studies leads to much higher levels of dopamine, because nerve cells respond differently to the two drugs. Cocaine prolongs dopamine

actions in the brain by blocking the re-absorption (re-uptake) of the neurotransmitter by signaling nerve cells. At low doses, methamphetamine also blocks the re-uptake of dopamine, but it also increases the release of dopamine, leading to much higher concentrations in the synapse (the gap between neurons), which can be toxic to nerve terminals.

Figure 1. Methamphetamine versus Cocaine

Methamphetamine	Cocaine
Stimulant	Stimulant and local anesthetic
Man-made	Plant-derived
Smoking produces a long-lasting high	Smoking produces a brief high
50% of the drug is removed from the body in 12 hours	50% of the drug is removed from the body in 1 hour
Increases dopamine release and blocks dopamine re-uptake	Blocks dopamine re-uptake
Limited medical use for ADHD, narcolepsy, and weight loss	Limited medical use as a local anesthetic in some surgical procedures



Short-Term Effects May Include:

- Increased attention
- Decreased fatigue
- Increased activity and wakefulness
- Decreased appetite
- Euphoria and rush
- Increased respiration
- Rapid/irregular heartbeat
- Hyperthermia

Long-Term Effects May Include:

- Addiction
- Psychosis, including:
 - paranoia
 - hallucinations
 - repetitive motor activity
- Changes in brain structure and function
- Deficits in thinking and motor skills
- Increased distractibility
- Memory loss
- Aggressive or violent behavior
- Mood disturbances
- Severe dental problems
- Weight loss

What are the immediate (short-term) effects of methamphetamine abuse?

As a powerful stimulant, methamphetamine, even in small doses, can increase wakefulness and physical activity and decrease appetite. Methamphetamine can also cause a variety of cardiovascular problems, including rapid heart rate, irregular heartbeat, and increased blood pressure. Hyperthermia (elevated body temperature) and convulsions may occur with methamphetamine overdose and, if not treated immediately, can result in death.

Most of the pleasurable effects of methamphetamine are believed to result from the release of very high levels of dopamine in the brain. Dopamine is involved in motivation, the experience of pleasure, and motor function, and most drugs of abuse work in part by affecting levels of this neurotransmitter. The elevated release of dopamine produced by methamphetamine is also thought to contribute to the drug's harmful effects on terminals of dopamine-producing neurons in the brain.

What are the long-term effects of methamphetamine abuse?

Long-term methamphetamine abuse has many negative consequences, including addiction. Addiction is a chronic, relapsing disease, characterized by compulsive drug seeking and use and accompanied by functional and molecular changes in the brain.

As is the case with many drugs, tolerance to methamphetamine's pleasurable effects develops when it is taken repeatedly. Abusers often need to take higher doses of the drug, take it more frequently, or change how they take it in an effort to get the desired effect. Chronic methamphetamine abusers may develop difficulty feeling any pleasure other than that provided by the drug, fueling further abuse. Withdrawal from methamphetamine occurs when a chronic abuser stops taking the drug; symptoms of withdrawal include depression, anxiety, fatigue, and an intense craving for the drug.

In addition to being addicted to methamphetamine, chronic abusers may exhibit symptoms that can include significant anxiety, confusion, insomnia, mood disturbances, and violent behavior. They also may display a number of psychotic features,

including paranoia, visual and auditory hallucinations, and delusions (for example, the sensation of insects creeping under the skin). Psychotic symptoms can sometimes last for months or years after a person has quit abusing methamphetamine, and stress has been shown to precipitate spontaneous recurrence of methamphetamine psychosis in formerly psychotic methamphetamine abusers.

These and other problems reflect significant changes in the brain caused by abuse of methamphetamine. Neuroimaging studies have demonstrated alterations in the activity of the dopamine system that are associated with reduced motor speed and impaired verbal learning. Studies in chronic methamphetamine abusers have also revealed severe structural and functional changes in areas of the brain associated with emotion and memory, which may account for many of the emotional and cognitive problems observed in chronic methamphetamine abusers.

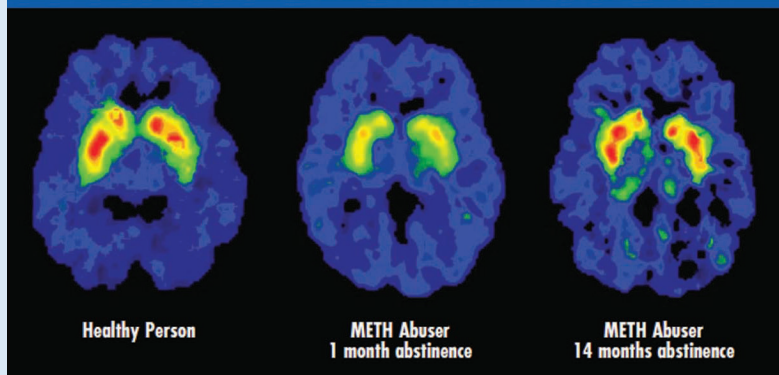
Methamphetamine abuse also has been shown to have negative effects on non-neural brain cells

called microglia. These cells support brain health by defending the brain against infectious agents and removing damaged neurons. Too much activity of the microglial cells, however, can assault healthy neurons. A study using brain imaging found more than double the levels of microglial cells in former methamphetamine abusers compared to people with no history of methamphetamine abuse, which could explain some of the neurotoxic effects of methamphetamine.

Some of the neurobiological effects of chronic methamphetamine abuse appear to be at least partially reversible. In the aforementioned study, abstinence from methamphetamine resulted in less excess microglial activation over time, and abusers who had remained methamphetamine-free for 2 years exhibited microglial activation levels similar to the study's control subjects. Another neuroimaging study showed neuronal recovery in some brain regions following prolonged abstinence (14 but not 6 months). This recovery was associated with improved performance on motor and verbal memory tests. But function in other brain regions did not recover even after 14 months of abstinence, indicating that some methamphetamine-induced changes are very long lasting. Moreover, methamphetamine use can increase one's risk of stroke, which can cause irreversible damage to the brain. A recent study even showed higher incidence of Parkinson's disease among past users of methamphetamine.

In addition to the neurological and behavioral consequences of methamphetamine abuse, long-term users also suffer physical effects, including weight loss, severe tooth decay and tooth loss ("meth mouth"), and skin sores. The dental problems may be caused by a combination of poor nutrition and dental hygiene as well as dry mouth and teeth grinding caused by the drug. Skin sores are the result of picking and scratching the skin to get rid of insects imagined to be crawling under it.

BRAIN RECOVERY WITH PROLONGED ABSTINENCE



Recovery of Brain Dopamine Transporters in Chronic Methamphetamine (METH) Abusers

Methamphetamine abuse greatly reduces the binding of dopamine to dopamine transporters (highlighted in red and green) in the striatum, a brain area important in memory and movement. With prolonged abstinence, dopamine transporters in this area can be restored.

What are the risks of methamphetamine abuse during pregnancy?



Our knowledge of the effects of methamphetamine abuse during pregnancy is limited because studies of this issue have used small samples and have not been able to account for the possibility that mothers used other drugs besides methamphetamine. But the available research points to increased rates of premature delivery, placental abruption (separation of the placental lining from the uterus), and

various effects on babies prenatally exposed to methamphetamine, including small size, lethargy, and heart and brain abnormalities. A large ongoing NIDA-funded study is examining developmental outcomes in children born to mothers who abused methamphetamine. Thus far, researchers have found neurobehavioral problems such as decreased arousal and increased stress and subtle but significant attention impairments in these children.

Are people who abuse methamphetamine at risk for contracting HIV/AIDS and hepatitis B and C?

Methamphetamine abuse raises the risk of contracting or transmitting HIV and hepatitis B and C—not only for individuals who inject the drug but also for noninjecting methamphetamine abusers. Among injecting drug users, HIV and other infectious diseases are spread primarily through the re-use or sharing of contaminated syringes, needles, or related paraphernalia. But regardless of how methamphetamine is taken, its intoxicating effects can alter judgment and inhibition and lead people to engage in unsafe behaviors like unprotected sex.

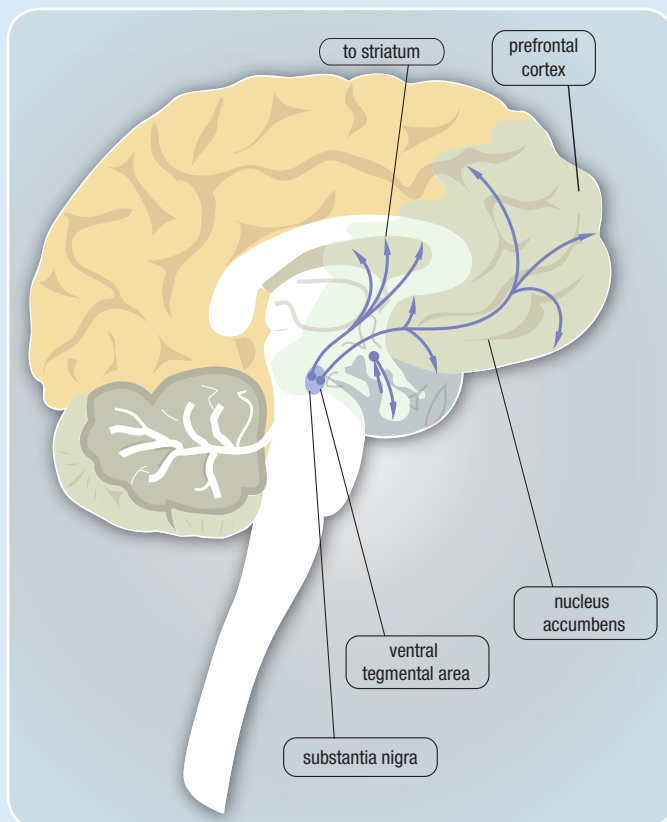
Methamphetamine abuse is associated with a culture of risky sexual behavior, both among men who have sex with men and in heterosexual populations, a link that may be attributed to the fact that methamphetamine and related stimulants can increase libido.

(Although paradoxically, long-term methamphetamine abuse may be associated with decreased sexual functioning, at least in men.) The combination of injection practices and sexual risk-taking may result in HIV becoming a greater problem among methamphetamine abusers than among other drug abusers, and some epidemiologic reports are already showing this trend. For example, while the link between HIV infection and methamphetamine abuse has not yet been established for heterosexuals, data show an association between methamphetamine abuse and the spread of HIV among men who have sex with men.

Methamphetamine abuse may also worsen the progression of HIV disease and its consequences. In animal studies, methamphetamine has been shown to increase viral replication. Clinical

studies in humans suggest that current methamphetamine users taking highly active antiretroviral therapy (HAART) to treat HIV may be at greater risk of developing AIDS than non-users, possibly as a result of poor medication adherence. Methamphetamine abusers with HIV also have shown greater neuronal injury and cognitive impairment due to HIV, compared with those who do not abuse the drug.

NIDA-funded research has found that, through drug abuse treatment, prevention, and community-based outreach programs, drug abusers can change their HIV risk behaviors. Drug abuse and drug-related risk behaviors, such as needle sharing and unsafe sexual practices, can be reduced significantly, thus decreasing the risk of exposure to HIV and other infectious diseases. Therefore, drug abuse treatment *is* HIV prevention.



Dopamine Pathways

In the brain, dopamine plays an important role in the regulation of reward and movement. As a major chemical messenger in the reward pathway, dopamine is manufactured in nerve cell bodies located within a group of neurons called the ventral tegmental area and is released in the nucleus accumbens, sometimes called the “pleasure center” because of its role in producing rewarding feelings, as well as in the prefrontal cortex, which is responsible for higher cognitive functions like decision-making and self-control. Dopamine’s regulation of motor functions is linked to a separate pathway: Cell bodies in the substantia nigra manufacture and release dopamine into the striatum, which is involved in executing and inhibiting movements and reward-seeking behavior.



What treatments are effective for people who abuse methamphetamine?

The most effective treatments for methamphetamine addiction at this point are behavioral therapies, such as cognitive-behavioral and contingency-management interventions. For example, the Matrix Model, a 16-week comprehensive behavioral treatment approach that combines behavioral therapy, family education, individual counseling, 12-Step support, drug testing, and encouragement for non-drug-related activities, has been shown to be effective in reducing methamphetamine abuse. Contingency management interventions, which provide tangible incentives in exchange for engaging in treatment and maintaining abstinence, have also been shown to be effective. Motivational Incentives for Enhancing Drug Abuse Recovery (MIEDAR), an incentive-

based method for promoting cocaine and methamphetamine abstinence, has demonstrated efficacy in methamphetamine abusers through NIDA's National Drug Abuse Clinical Trials Network.

Although medications have proven effective in treating some substance use disorders, there are currently no medications that counteract the specific effects of methamphetamine or that prolong abstinence from and reduce the abuse of methamphetamine by an individual addicted to the drug. NIDA has made research in the development of medications to treat addiction to stimulants and other drugs a priority, however. One approach being tried is to target the activity of glial cells. A drug called AV411 (ibudilast) that suppresses the neuroinflammatory

actions of glial cells has been shown to inhibit methamphetamine self-administration in rats and is now being fast-tracked in clinical trials to establish its safety and effectiveness in humans with methamphetamine addiction. Also under study are approaches that use the body's immune system to neutralize the drug in the bloodstream before it reaches the brain. These approaches include injecting a user with anti-methamphetamine antibodies or with vaccines that would stimulate the body to produce its own such antibodies. Researchers have begun a clinical study to establish the safety of an anti-methamphetamine monoclonal antibody known as mAb7F9 in human methamphetamine users.

Glossary

Addiction: A chronic, relapsing disease characterized by compulsive drug seeking and use despite serious adverse consequences, and by long-lasting changes in the brain.

Anesthetic: An agent that causes insensitivity to pain and is used for surgeries and other medical procedures.

Attention deficit hyperactivity disorder (ADHD):

A disorder that typically presents in early childhood, characterized by inattention, hyperactivity, and impulsivity.

Central nervous system (CNS): The brain and spinal cord.

Craving: A powerful, often uncontrollable desire for drugs.

Dopamine: A brain chemical, classified as a neurotransmitter, found in regions that regulate movement, emotion, motivation, and pleasure.

Neurotransmitter: A chemical produced by neurons that carry messages from one nerve cell to another.

Psychosis: A mental disorder characterized by delusional or disordered thinking detached from reality; symptoms often include hallucinations.

Rush: A surge of pleasure (euphoria) that rapidly follows the administration of some drugs.

Stimulants: A class of drugs that enhance the activity of monoamines (such as dopamine and norepinephrine) in the brain, increasing arousal, heart rate, blood pressure, and respiration, and decreasing appetite; includes some medications used to treat attention deficit hyperactivity disorder (e.g., methylphenidate and amphetamines), as well as cocaine and methamphetamine.

Tolerance: A condition in which higher doses of a drug are required to produce the same effect achieved during initial use; often associated with physical dependence.

Toxic: Causing temporary or permanent effects detrimental to the functioning of a body organ or group of organs.

Withdrawal: Symptoms that occur after chronic use of a drug is reduced abruptly or stopped.

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Where can I get further information about methamphetamine?

To learn more about methamphetamine and other drugs of abuse, visit the NIDA Web site at **www.drugabuse.gov** or contact the *DrugPubs* Research Dissemination Center at 877-NIDA-NIH (877-643-2644; TTY/TDD: 240-645-0228).

NATIONAL INSTITUTE ON DRUG ABUSE



RESEARCH DISSEMINATION CENTER

What's on the NIDA Web Site

- Information on drugs of abuse and related health consequences
- NIDA publications, news, and events
- Resources for health care professionals
- Funding information (including program announcements and deadlines)
- International activities
- Links to related Web sites (access to Web sites of many other organizations in the field)

NIDA Web Sites

www.drugabuse.gov
www.backtoschool.drugabuse.gov
www.smoking.drugabuse.gov
www.hiv.drugabuse.gov
www.marijuana-info.org
www.clubdrugs.gov
www.steroidabuse.gov
www.teens.drugabuse.gov
www.inhalants.drugabuse.gov

Other Web Sites

Information on drug abuse and other mental illnesses is also available through these other Web sites:

- National Institute of Mental Health: www.nimh.nih.gov
- National Institute on Alcohol Abuse and Alcoholism: www.niaaa.nih.gov
- Substance Abuse and Mental Health Services Administration Publications Ordering: www.store.samhsa.gov/home



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