

Alcoholism and Pathways to Recovery: New Survey Results on Views and Treatment Options CME

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Target Audience

This article is intended for primary care physicians, addiction medicine specialists, psychiatrists, and other physicians who care for patients at risk of problem drinking.

Goal

The goal of this article is to review the epidemiology of alcohol problems vis a vis attitudes from physicians and the population in general. Physicians should also understand the mechanism of pharmacotherapies for alcohol abuse.

Learning Objectives for This Educational Activity

Upon completion of this activity, participants will be able to:

1. Describe the epidemiology and health risks of problem drinking.
2. List risk factors for alcohol abuse among adolescents.
3. Identify attitudes regarding problem drinking among the general public as well as physicians.
4. Describe obstacles in the identification and treatment of alcoholism.
5. Specify the mechanism of action and contraindications for medical treatments of alcoholism.

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Contents of This CME Activity

Approximately 8% of Americans require treatment for an alcohol problem, but this significant disorder remains poorly understood by both the general public and physicians. The current report reviews attitudes and truths regarding alcoholism as well as current pharmacotherapy for alcohol abuse.

1. Alcoholism and Pathways to Recovery: New Survey Results on Views and Treatment Options
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Alcoholism and Pathways to Recovery: New Survey Results on Views and Treatment Options CME

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Abstract and Introduction

Abstract

Almost 19 million Americans require treatment for an "alcohol problem"; however, only 2.4 million have been diagnosed and just 139,000 receive medication to treat it. Chronic heavy drinking contributes to cardiovascular illnesses, liver disease, cancer, and psychiatric disorders. Imaging studies demonstrate structural changes in the human brain with prolonged exposure to alcohol. Alcoholism can thus be described as an acquired brain dysfunction with specific neurochemical and neuroanatomic pathways. There is a need to intervene early because the average age of alcohol experimentation is 11-13 years -- delaying onset reduces the rate of alcoholism. A survey sponsored by the Community

Anti-Drug Coalitions of America (CADCA) set out to measure the attitudes and misperceptions of 1000 adults from the general population plus 300 physicians and 503 individuals in recovery from alcohol use disorder (AUD) to better understand approaches toward alcohol treatment. In these surveys, 74% of the general public indicated that alcoholism affects their daily lives, with 41% reporting having to encourage a loved one to seek help for an alcohol problem. The vast majority ($\geq 80\%$) indicated a stigma toward alcoholics. Denial or refusal to admit severity and fear of social embarrassment were the top 2 reasons for not seeking help. The majority of the general population believes that alcoholism is caused partly by moral weakness. The survey revealed that most Americans are open to medications to treat alcoholism if physician-recommended and if it could reduce alcohol cravings and maintain abstinence. In the past 55 years, only 3 medications (disulfiram, naltrexone, and acamprosate) have been US Food and Drug Administration (FDA)-approved for the treatment of AUD, each with unique mechanisms of action.

Introduction

On September 29, 2004, a panel of experts presented on topics related to alcoholism in a science media briefing in Pittsburgh, Pennsylvania. The main highlight of this meeting was the presentation of results from a survey, conducted by the Community Anti-Drug Coalitions of America (CADCA) and sponsored by a grant from Forest Laboratories, as part of National Alcohol and Drug Addiction Recovery Month. This survey included 1000 men and women, 300 general practitioners/internists, and 503 people in recovery from alcohol addiction. The panel included the following:

- Alan Leshner, PhD, Chief Executive Officer, American Association for the Advancement of Science; Executive Publisher of Science; and a member of the CADCA Board of Directors;
- David Kessler, MD, Dean, University of California, San Francisco School of Medicine; and former US FDA Commissioner;
- Alan Rivlin, Senior Vice President, Peter D. Hart Research Associates; and
- Drew Pinsky, MD, Medical Director, Department of Chemical Dependency Services at Las Encinas Hospital, Los Angeles, California.

What Is Alcoholism, Really?

Alcoholism is defined by the American Society of Addiction Medicine as the following:

... a primary, chronic disease with genetic, psychosocial, and environmental factors influencing its development and manifestations. The disease is often progressive and fatal. It is characterized by continuous or periodic impaired control over drinking, preoccupation with the drug alcohol, use of alcohol despite adverse consequences, and distortions in thinking, most notably denial.^[1]

Alcohol dependence is characterized by persistent high levels of alcohol use that is uncontrolled, is automatic, has compulsive features, and develops over a long period of time. Many of these behaviors have a neurobehavioral basis. Alcoholism, therefore, can be described as an acquired brain dysfunction with specific neurochemical and neuroanatomic pathways playing crucial roles.^[2]

Alcohol is a central nervous system depressant that acts on at least 6 separate neurotransmitter systems. Acute intake leads to increased levels of dopamine, serotonin, and norepinephrine as well as increased activity in the inhibitory transmitter system involving gamma-aminobutyric acid (GABA) and inhibition of the *N*-methyl-D-aspartate (NMDA) receptor. Chronic alcohol use can lead to depletion of these neurotransmitters and downregulation of the GABA and NMDA receptors. The acute effects range from impaired coordination to memory lapses, coma, and death (Table 1).^[1]

Its Effect

Dr. Leshner described the current situation of alcohol dependency. Nearly 19 million Americans (8% of the US population) require treatment for an "alcohol problem," and 16 million drink heavily.^[3] However, according to Dr. Leshner, only 2.4 million have been diagnosed with the disease, and just 139,000 receive medication to treat it. One in 4 children lives with a parent who is dependent on, or abuses, alcohol.^[4] Alcohol dependence is responsible for approximately 100,000 deaths each year.^[5] Chronic heavy drinking is a leading cause of cardiovascular illnesses, such as cardiomyopathy, coronary artery disease, high blood pressure, dangerous heart rhythms, and stroke. It is a leading cause of illness and death from liver disease in the United States.^[6] Consuming ≥ 4 alcoholic beverages a day statistically significantly increases the risk of developing any type of cancer.^[7] Psychiatric disorders, such as depression, anxiety disorders, and antisocial personality disorder, occur more often among alcoholics than in the general population (Table 2).^[8] Harmful and hazardous drinking is involved in about one third of suicides, one half of homicides, and one third of child abuse cases.^[9] In a 2003 National Survey on Drug and Health by the US Department of Health and Human Services, among heavy alcohol users, 61.7% smoked cigarettes in the past month, whereas only 17.4% of nondrinkers were current smokers.^[3] Alcoholism abuse and dependence costs the US \$185 billion in direct and indirect social costs per year,^[4] with more than 70% of the cost attributed to lost productivity.^[6]

Physical Changes

The neurocircuitry of alcohol use disorder (AUD) is beginning to be understood. Dr. Leshner explained that via functional magnetic resonance imaging (fMRI) and positron emission tomography (PET), structural changes in the human brain are evident with prolonged exposure to alcohol. Controlled studies have revealed compelling evidence for alcohol-related brain structural and functional modification -- some long-standing, some transient, and some compensatory.^[10] MRI studies suggest a central role for degradation of the frontocerebellar neuronal nodes and connecting circuitry affecting widespread brain regions and contributing to alcoholism's salient, enduring, and debilitating cognitive

and motor deficits.^[10] In chronic heavy drinkers, significant gray matter volume loss was observed compared with light drinkers. Within heavy drinkers, smaller gray matter volumes were associated with higher current levels of drinking, whereas a positive family history of problem drinking was associated with smaller cerebrospinal fluid volumes.^[11] In laboratory animals, alcohol exposure for weeks leads to increased alcohol consumption. Dahchour and De Witte^[12] demonstrated that in rats exposed and made dependent on alcohol, increases in amino acids -- glutamate, taurine, and aspartate -- were detected in the hippocampus during periods of alcohol withdrawal. These amino acid imbalances are behaviorally expressed in the form of alcohol withdrawal.^[12,13] AUD, therefore, can be described as an acquired brain dysfunction with specific neurochemical and neuroanatomic pathways playing crucial roles.^[2] Does the brain recover if alcohol exposure ceases? Gross structural changes in the brain do; however, the behavior that is associated with the changes does not -- implicating other factors within the brain that are affected by alcohol. With these newer molecular understandings, the groundwork for potential pharmacotherapeutic compounds for treating AUD can begin. Although there are promising medications available, there is no pharmacologic cure for alcohol abuse or dependence.

Pathophysiology

Dr. Kessler described the disease pathophysiology and comorbidity with other diseases. As shown in Figure 1, the prevalence of alcohol dependence peaks at an early age, from 18 to 24 years of age, but decreases markedly from age 25 onward; the earlier the onset, the more likely that one develops an AUD. According to Dr. Kessler, there is the need to intervene early because the average age of alcohol experimentation is 11-13 years. Each year, alcohol onset is delayed and reduces the rate of alcoholism by 5%. There are 3 predictors of alcohol abuse disorder in adolescence:

- Family history of dependence^[14]
- Psychological dysregulation^[15]
- Neurobehavioral disinhibition^[16]
 - Poor parenting and maltreatment
 - Psychiatric disorders:
 - Mood and anxiety disorders (Table 2)
 - Attention-deficit/hyperactivity disorder
 - Oppositional defiant disorder.

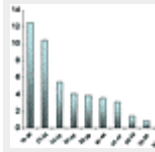


Figure 1. (click image to zoom) The prevalence of alcohol dependence, as defined by the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV)*, peaks in individuals between ages 18 and 20 years and then decreases with increasing age.^[4,17,25] Reproduced with permission from Fleishman-Hillard Inc., on behalf of the Community Anti-Drug Coalitions of America media briefing.

Although brief interventions in the medical care settings, various self-help groups (Alcoholics Anonymous), and counseling techniques (relapse prevention therapies) are successful in a number of individuals, it is becoming increasingly clear that pharmacologic intervention combined with efforts at behavioral change offer the highest rates of success.^[2]

Results of a Newly Completed Survey on Attitudes Toward Alcoholism

Survey Methods

Allan Rivlin presented results from 3 recently completed Internet surveys of adults from the general population, physicians, and individuals in recovery. This survey was sponsored by CADCA and conducted by Peter D. Hart Research Associates in August 2005.^[17] The surveys were conducted to assess perceptions about alcoholism as a public health issue, attitudes toward alcoholics and those in recovery, and awareness of pathways to treatment. Internet surveys were conducted among the following populations:

- 1000 adults ≥ 20 years of age (margin of error, ± 3.2 percentage points)
- 300 physicians (margin of error, ± 5.7 percentage points)
 - 60% general practitioners and 40% internists
- 503 people in recovery from alcohol addiction (margin of error, ± 4.4 percentage points)
 - Sample included adults aged 25-50 recruited by CADCA
 - 46% say that they struggled with alcohol problems for ≥ 10 years
 - 32% say that they struggled with alcohol for 5-10 years
 - 47% have been in recovery for ≥ 10 years.

Survey Results

Figure 2 demonstrates the most important health issues to physicians and the general public. Obesity and heart disease are considered the 2 top health priorities among those physicians who were surveyed, 71% and 57%, respectively. This trend was also reflected in members of the general public who were surveyed, 45% and 31%, respectively. Alcoholism ranked behind obesity, cancer, heart disease, drug addiction, AIDS, and depression in a list of the most important health-related issues facing the nation. Alcoholism was considered a top health priority by only 4% and 6% of surveyed physicians and the general public, respectively. Despite this, 74% of the general public who were surveyed indicated that alcoholism affects their daily lives, whether their own addiction, addiction of a friend or family member, or any other experience (Figure 3). Additionally, 41% of the public reported having encouraged a loved one to seek help for an alcohol problem.

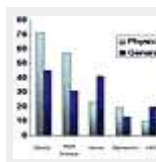


Figure 2. (click image to zoom) In both physician and general public survey respondents, alcoholism was considered a top priority in only a very small percentage of these 2 survey populations.^[17] Reproduced with permission from Fleishman-Hillard Inc., on behalf of the Community Anti-Drug Coalitions of America media briefing.

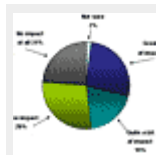


Figure 3. (click image to zoom) The relative impact that alcoholism has on the general public. About three quarters of the survey respondents indicated that they were affected in some way by alcoholism, either directly or indirectly.^[17] Reproduced with permission from Fleishman-Hillard Inc., on behalf of the Community Anti-Drug Coalitions of America media briefing.

Among the 3 survey groups, there were differences as to what was perceived as the most important factors contributing to alcohol addiction. For example, the general public and physician groups both indicated that stress, anxiety, and insecurity about work, family, and other problems were the most important factors contributing to alcohol addiction, whereas people in recovery believed that genetics or family history played the predominate role.

Table 3 lists the other factors contributing to alcohol addiction and the respective attitudes held by each of the 3 survey groups.

Stigma Persists as a Barrier to Seeking and Receiving Treatment

Despite advances in the scientific understanding of alcoholism, the stigma surrounding this disease is still pervasive; these misperceptions may prevent people from seeking and

receiving treatment. The vast majority of those surveyed (91% of primary care physicians, 89% of people in alcohol addiction recovery, and 80% of the general public) say that there is a stigma toward alcoholics. That stigma extends to people in recovery. About three quarters (73%) of primary care physicians and individuals in recovery (71%) believe that there is a stigma toward alcoholics in recovery, compared with 51% in the general public survey sample. As a side comparison, when an obese person is losing weight, it is often viewed in a positive light -- not so for recovering alcoholics. In all 3 survey populations, denial or refusal to admit severity of the problem and fear of social embarrassment were the top 2 reasons for not seeking help with alcohol addiction ([Table 4](#)). In the general public, 66% believe that social embarrassment and fear of discrimination are major barriers to treatment for people with alcohol addiction. The majority of the general public (63%) believes that alcoholism is caused, at least in part, by moral weakness, compared with 43% of physicians and 11% of individuals in recovery.

Obstacles to Screening for Alcoholism

About 50% of the physicians who were surveyed reported asking about drinking habits during routine patient office visits half the time or less. The reasons cited as to why patients are not asked about their drinking habits more often are inadequate resources (48%), denial of any problem with alcohol (41%), and lack of expertise (24%). Forty-nine percent of the primary care physicians reported that they would refer a patient with alcohol addiction to a treatment facility, counselor, another physician, or addiction specialist. Another 20% would refer a patient to support groups, and 13% would recommend a combination of medication and counseling. The survey also revealed opportunities for physicians to drive treatment:

- Sixty-five percent of the general public would turn to doctors or healthcare providers for help if they or their loved ones had a problem with alcohol;
- However, only 13% of the general public are asked about their drinking habits at every visit to the doctor; and
- Forty-seven percent of primary care physicians suspect that $\geq 10\%$ of their patients have a problem with alcohol.

Attitudes on Treatment Medications

The survey revealed that most Americans are open to medications to treat alcoholism. The general public and people in recovery would recommend medications for themselves or their loved ones:

- Eighty-three percent of the general public said that they would encourage a loved one to take a physician-recommended medication to treat alcoholism;
- Seventy percent of people in recovery for ≤ 1 year indicated that they would take a medication to keep them alcohol-free or to reduce their cravings for alcohol;

- Forty percent of people in recovery for ≤ 1 year indicated that they would be likely to try a physician-recommended medication in conjunction with a treatment program, if such a medication were available; and
- Only 26% of primary care physicians think that medication would be very or fairly effective in treating alcoholism.

Pathways to Recovery for Alcoholics

Dr. Pinsky discussed the approaches to treating AUD. The criteria for identifying AUD should involve 3 or more of the following characteristics during a 1-year period:

- Alcohol tolerance;
- Alcohol withdrawal signs or symptoms;
- Drinking more than intended;
- Unsuccessful efforts to stop or reduce drinking;
- Use despite physical or psychological consequences;
- Excessive time spent drinking or recovering; and
- Impaired social or work activities due to alcohol.

Some commonly overlooked signs and symptoms include family complaints about drinking, work problems, medical problems, and arrests. The most effective screening method for detecting alcohol problems is to elicit an alcohol history by asking quantity and frequency questions and using a standardized screening instrument.^[18] A variety of questionnaires can be used to identify hazardous or harmful drinking. The Alcohol Use Disorders Identification Test (AUDIT) is a 10-item questionnaire developed by the World Health Organization to aid in the identification of harmful alcohol consumption in healthcare settings. It is the most studied screening tool for detecting alcohol-related problems in primary care settings. It is sensitive for detecting alcohol misuse and abuse or dependence and can be used alone or embedded in broader health risk or lifestyle assessments. Then there is the CAGE questionnaire, whose acronym is derived from the words taken from each question -- Cut down, Annoyed, Guilty, and Eye-opener:

- Have you ever believed that you should Cut down on your drinking?
- Have people Annoyed you by criticizing your drinking?
- Have you ever felt Guilty about your drinking?
- Have you ever had a drink the first thing in the morning to steady your nerves or get rid of a hangover (*Eye-opener*)?

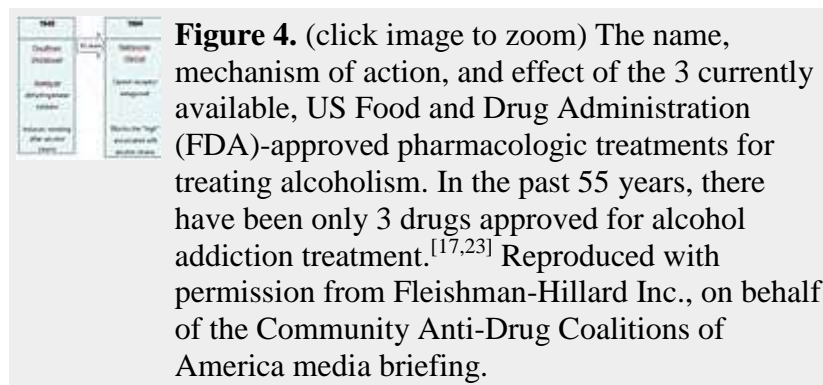
It is the most popular screening test for detecting alcohol abuse or dependency in primary care. Screening tools are available at the National Institute on Alcohol Abuse and Alcoholism Web site. Although not very sensitive, biochemical tests, such as the carbohydrate-deficient transferrin and the gamma-glutamyl transferase tests, can be combined with other information to support the need for treatment.^[2,18]

Evolving Treatment Goals

Treatment goals for AUD are evolving based on emerging science. For example, according to the American Psychiatric Association, the goal of treatment is for alcoholics to stop drinking altogether -- complete abstinence. The National Institute on Alcohol Abuse and Alcoholism defines treatment goals as relapse prevention once the drinking has stopped.^[19] In light of the emerging science involving the mechanism of action of new pharmacotherapies, normalizing imbalanced brain systems is becoming a goal. Dr. Pinsky indicated that rats exposed to alcohol developed a 6-fold increase in alcohol consumption by the equivalent age of 15, ruling out the argument of moral weakness being the main cause of this disease. Although brief interventions in medical care settings, various self-help groups (Alcoholics Anonymous), and counseling techniques (relapse prevention therapies) are successful in a number of individuals, it is becoming increasingly clear that pharmacologic intervention, combined with efforts at behavioral change, offer the highest rates of success.^[2]

Pharmacotherapy for Alcoholism

There are only 3 FDA-approved drug treatments for alcoholism, each with a different mode of action. These 3 drugs (disulfiram, naltrexone, and acamprosate) are the only drugs that have been developed and FDA-approved in the past 55 years for the treatment of alcoholism (Figure 4).^[20-22]



Disulfiram (*Antabuse*), developed over 55 years ago, is an aversive agent that inhibits the metabolism of alcohol. The usual dose of disulfiram is 250 mg once daily. Disulfiram produces a sensitivity to alcohol that results in a highly unpleasant reaction when the patient under treatment ingests even small amounts of alcohol. Drinking while taking disulfiram produces flushing, palpitations, nausea, and vomiting. It should not be prescribed for patients with cirrhosis or other chronic medical conditions, such as heart

disease.^[1] Because of these caveats, disulfiram has limited effectiveness because only very compliant individuals may benefit from its use. Although information is scarce, disulfiram is unlikely to reduce cravings; therefore, people often discontinue its use, especially because people feel ill if they consume alcohol while on disulfiram.^[2] According to Dr. Pinsky, some physicians are reluctant to prescribe disulfiram due to its dangerous reactions of nausea and vomiting as a means of inducing alcohol avoidance.

Naltrexone (*ReVia*), available since 1995, is an opioid receptor antagonist. It is most efficacious when used along with relapse prevention counseling techniques. After a few days of abstinence, naltrexone can be started at 25 mg/day and, after several days, maintained at 50-100 mg/day. A reduction in both craving and relapse drinking is reported when used over 3-6 months. Because naltrexone blocks central nervous system opiate receptors, individuals who are dependent on opiates could experience severe withdrawal symptoms. It is because of this antagonism of the opiate receptors that naltrexone blocks the "high" that is associated with alcohol intake.^[2]

Acamprosate (*Campral*) is the most recent drug to enter the armamentarium of alcohol dependence treatment. It was FDA-approved in July 2004 for the maintenance of alcohol abstinence in patients with AUD who are abstinent at treatment initiation. Its mechanism of action is not completely understood; however, recent evidence suggests that acamprosate's main interaction is with the glutamate system. It appears to modulate the excitatory glutamate amino acid system via the NMDA receptor in the brain.^[2] Chronic alcohol exposure is hypothesized to alter the normal balance between neuronal excitation and inhibition. Acamprosate is believed to *reset* this neurochemical system after alcohol withdrawal to reduce craving and relapse drinking. This mechanism of action is different from that ascribed to disulfiram and naltrexone, which induce vomiting if alcohol is ingested or block the "high" that is associated with alcohol.

Prescribing Trends of AUD Treatments

Table 5 compares and summarizes the safety of disulfiram, naltrexone, and acamprosate. Looking back at the survey conducted by Peter D. Hart Associates, 51% of primary care physicians have prescribed disulfiram at some point; however, only 22% are currently doing so. Only 26% of primary care physicians have experience with naltrexone. Less (15%) have experience with acamprosate, despite the survey indicating that 45% of those prescribing acamprosate believed that it would lead to recovery compared with 25% among those not prescribing acamprosate. These percentages indicate that physicians have not been totally accepting of pharmacotherapeutic treatments.

Conclusion

Patients' personal motivations to change strongly influence whether they seek, comply with, and complete treatment.^[24] Behavioral studies show that patients often go through several cycles of abstinence followed by relapse before quitting for good.^[25] These attempts at abstinence are complicated by the comorbid psychiatric disorders that are seen in many patients.^[26] Many patients who enter treatment under pressure from others

may not be ready to change their drinking behavior and will not actively participate in treatment. Pivotal studies have shown that readiness to change at the start of treatment makes it much more likely that the treatment will be effective.^[24] To be effective, patients need to receive behavioral Counseling, be Committed to treatment, and be Compliant with prescribed pharmacologic treatment regimens -- the 3 C's. The survey by Peter D. Hart Associates has revealed the stigmas and attitudes of the general public, physicians, and those in recovery, which need to be addressed. The survey also indicates unmet educational needs for physicians in the areas of diagnostic training and on available FDA-approved treatments. Through education and better understandings into the biological mechanisms of alcoholism, we can finally view AUD as a medical disease and not just a psychological or moral weakness.

Tables

Table 1. Impairment by Blood Alcohol Level^[1]

Blood Alcohol Level (mg/100 mL Blood)	Effect
20-99	Impaired coordination
100-199	Ataxia, impaired judgment
200-299	Slurred speech, difficulty ambulating, labile mood, nausea, and vomiting
300-399	Blackouts, reduced level of consciousness
> 400	Coma and death

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Table 2. Co-occurrence of Current (12-Month) (Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition) Alcohol Dependence and Mood/Anxiety Disorders/Personality Disorders^[26]

Disorder	Alcohol-Dependence Risk
Major depression	3.7 times
Dysthymia	2.8 times
Manic disorder	5.7 times
Hypomania	5.2 times
Panic (with agoraphobia)	3.6 times

Panic (without agoraphobia)	3.4 times
Social phobia	2.5 times
Specific phobia	2.2 times
Generalized anxiety	3.1 times
Antisocial	7.1 times
Avoidant	3.8 times
Dependent	6.1 times
Histrionic	7.5 times
Obsessive-compulsive disorder	2.2 times
Paranoid	4.6 times
Schizoid	2.9 times

Table 3. Perceived Causes of Alcohol Addiction^[17]

Most Important Factors Contributing to Alcohol Addiction			
	General Public	Physician	People in Recovery
Stress, anxiety, and insecurity about work, family, and other problems	52%	66%	55%
Genetics and family history	44%	63%	68%
Emotional disorders or mental illness, depression/fear	37%	58%	50%
Lack of willpower/self-control	30%	23%	4%

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Table 4. Obstacles to Getting Help for Alcoholism^[17]

Which Do You Believe Are the Biggest Obstacles That Keep People From Getting Help?	General Public	Physicians	People in Recovery
Denial, refusal to admit severity of problem	68%	69%	73%
Fear of social embarrassment, shame	38%	42%	34%
Fear of being fired/discriminated against in employment, housing, etc	28%	31%	16%

Cost of treatment, lack of insurance	27%	38%	18%
Lack of information about how/where to get help	17%	23%	26%
Treatment programs not effective	11%	18%	7%
Lack of treatment programs	7%	16%	7%
All of these obstacles	22%	14%	4%

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Table 5. Comparative Safety of Disulfiram, Naltrexone, and Acamprosate^[17,20-22]

	Disulfiram	Naltrexone	Acamprosate
Safe for use during relapses?	No	Yes	Yes
Safe for use in patients with hepatic impairment?	No	No	Yes
Drug-drug interactions	? Alcohol or alcohol-containing preparations	? Opioids	? None known
		? Opioid-containing products	
Contraindicated in patients with these conditions	? Hepatic cirrhosis	? Opioid dependence	? Severe renal impairment
	? Hepatic insufficiency	? Opioid analgesic treatment	
		? Acute liver failure	
Possible severe adverse events	? Optic neuritis	? Hepatocellular injury	? None known
	? Peripheral neuritis		
	? Polyneuritis		
	? Peripheral neuropathy		

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