



## Missed Opportunities: The Limited Utilization of Alcohol Abstinence Medications

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### Abstract

**Background:** There is a high rate of alcohol use disorders (AUDs) in the United States and this poses a substantial burden on the medical system due to health complications. Medications to treat AUDs have been proven to have efficacy in reducing the number of drinking days, amount of alcohol consumed at a time, and in achieving overall abstinence from alcohol. Medicare studies, as well as other researchers, have shown that alcohol abstinence medications (AAMs) are underutilized.

**Method:** A retrospective chart review of records from a large urban hospital system was undertaken to establish the number of patients discharged with a AUDs as well as the prescription rate for AAMs. This was followed by a 17-item questionnaire distributed hospital-wide to attending and resident physicians that aimed to identify barriers to prescribing AAMs.

**Results:** In the Department of Psychiatry during the year reviewed, out of 3,402 admissions, 759 patients were diagnosed with an AUD at the time of discharge from the hospital. Only 100 prescriptions for AAMs were ordered in the entire hospital system; 83% of these orders were written by psychiatrists. The commonly cited barriers to prescribing AAMs identified by the survey were patient medication adherence, lack of knowledge about the medications, cost, and lack of consideration for utilizing AAMs.

**Conclusions:** AAM utilization remains very low for the treatment of AUDs. Education about AUDs, the various treatments and their efficacy, the impact of under-treating, and reimbursement would improve the quality of care for this patient population and would help to reduce comorbidity and the financial burden associated with AUDs.

### Keywords

Alcohol Abstinence Medications, Alcohol Use Disorder, Disulfiram, Naltrexone, Acamprostate

### Abbreviations

AAMs: alcohol abstinence medications; AUDs: alcohol use disorders; FDA: Federal Drug Administration; EMR: electronic medical record

### Introduction

The estimated prevalence of alcohol use disorder (AUD) in the general population over a 12-month period is 8.46% [1]. It has been estimated that 52% of the general population reports current

use of alcohol and that 17.6 million Americans have an AUD [2]. The utilization of alcohol abstinence medications (AAMs) is limited. Currently, the United States Food and Drug Administration (FDA) has approved four AAMs: disulfiram, acamprostate, naltrexone, and naltrexone long-acting formulation. Although not yet formally approved by the FDA, topiramate has shown promising results in treating AUD [3-5]. Baclofen, ondansetron, and gabapentin have also been used off-label for treatment of AUD [5-9]. Many peer-reviewed journal articles support the efficacy of the aforementioned medications across various treatment settings [1,3-9]. Despite a variety of medication options for treatment of AUD and published research on their utility, the actual rate of prescriptions for AAMs for AUD remains low [6].

Mark et al. [1] surveyed members of the American Academy of Addiction Psychiatry and the American Society of Addiction Medicine about the use of disulfiram and naltrexone for the treatment of AUDs. Nearly all physicians who responded to the survey reported that they had heard of the two medications, but felt that their knowledge about utilization and efficacy was limited compared to the use of antidepressants (the most commonly prescribed class of medications as of 2010). Respondents indicated a need for more extensive research into the development of AAMs, more education about existing AAMs, and the pattern of use of these medications by alcohol treatment programs.

### Background

Traditionally, the treatment of AUD has utilized primarily counseling and support groups. Disulfiram was first developed in the 1940s, but did not see wide-spread use for more than 40 years. Disulfiram inhibits acetaldehyde dehydrogenase, which blocks the metabolism of alcohol. Drinking alcohol while taking disulfiram produces unpleasant side effects including headache, facial flushing, nausea, and vomiting. The idea behind the use of disulfiram was that these side effects would be aversive and noxious enough to deter the patient from further drinking. Its wide-spread utilization was compromised by the fact that patients could avoid side effects by not taking the medication. Further, there is a potential for significant medical complications from drinking while taking disulfiram. Caution must be used when prescribing disulfiram to patients who are experiencing psychosis, impulsivity, and cognitive deficits [5,10]. Studies have shown that patients taking disulfiram report fewer

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days of drinking after a relapse, but this medication does not appear to improve abstinence or length of time before the first drink once abstinent [5,10].

Naltrexone was approved for use as an AAM in 1994. As an opioid antagonist, it is thought to decrease the reinforcing aspects of alcohol, which then diminishes the desire and craving to drink via disruption of the dopamine reward pathway. Naltrexone has been shown to be safe and efficacious for treating AUD. There is some indication that use of naltrexone in patients with depression and AUD is more effective than treating the two mental health conditions separately [11]. Several studies have shown that naltrexone is an effective short-term treatment for alcoholism as demonstrated by increasing the number of days of abstinence, reducing the number of “heavy” drinking days, and significantly decreasing the number of relapses [5,10].

Acamprosate was approved by the FDA in 2004 for the promotion of abstinence from alcohol. It has been found to be efficacious. Minor gastrointestinal discomfort is the only adverse effect that has been described. Acamprosate is metabolized by the kidneys, so caution should be used when treating patients with renal disease. The mechanism of action is not yet clear, but the medication appears to modulate over-activity of the glutamergic system. There is evidence that acamprosate modulates NMDA receptor function as well. Studies show that there are few interactions of acamprosate with psychiatric medications, making it useful for patients with co-morbid AUD and psychiatric disorders. Use of acamprosate promotes higher rates of continuous abstinence, and may mitigate the severity of a relapse [2,5,10]. The dosage frequency is three times a day, which makes adherence problematic.

Topiramate decreases the extracellular release of dopamine in the midbrain and antagonizes glutamate activity therefore counteracting chemical changes that are induced by the intake of alcohol. Topiramate can be used while the patient is still drinking. This medication has demonstrated efficacy for the treatment of AUD and comorbid mood disorders, but has a side effect profile that includes cognitive deficits (which may limit its use) [3-5]. Topiramate appears to decrease the number of heavy drinking days as well as the number of drinks taken per day (“safe drinking”) [3-5].

In individuals with chronic, long-term AUD, the gabaminergic system’s transmission is lowered. Baclofen is a GABAb receptor agonist. Baclofen is excreted through the kidneys and therefore is safe for patients with liver disease [5,7]. Studies have shown that baclofen diminishes cravings and decreases concomitant anxiety, reducing the number of drinks taken a day [5,7]. As a muscle relaxant, Baclofen carries the potential for a tolerance and a withdrawal syndrome that must be considered in its use in treatment of AUD.

Ondansetron affects the serotonergic system, specifically serotonin receptor type 3 (5-HT3). It is believed that 5-HT3 receptors play a role in the rewarding effects of alcohol use. Studies have shown that patients taking ondansetron reported a reduced number of drinks taken per day, an increased number of abstinent days, and reduced cravings for alcohol [5,8]. Ondansetron is contraindicated in patients with QTc prolongation on EKG or with liver impairment.

Gabapentin is purported to balance dysregulation of GABA/ glutamate activity that is present during the early stages of alcohol abstinence, thereby reducing the risk of relapsing [5,9]. Research has demonstrated that patients on gabapentin reported reduced number of drinks taken each day and fewer days of heavy drinking, and increased number of days of abstinence [5,9]. This medication is also excreted by the kidneys so is safe in patients with liver impairment.

## Study Goals

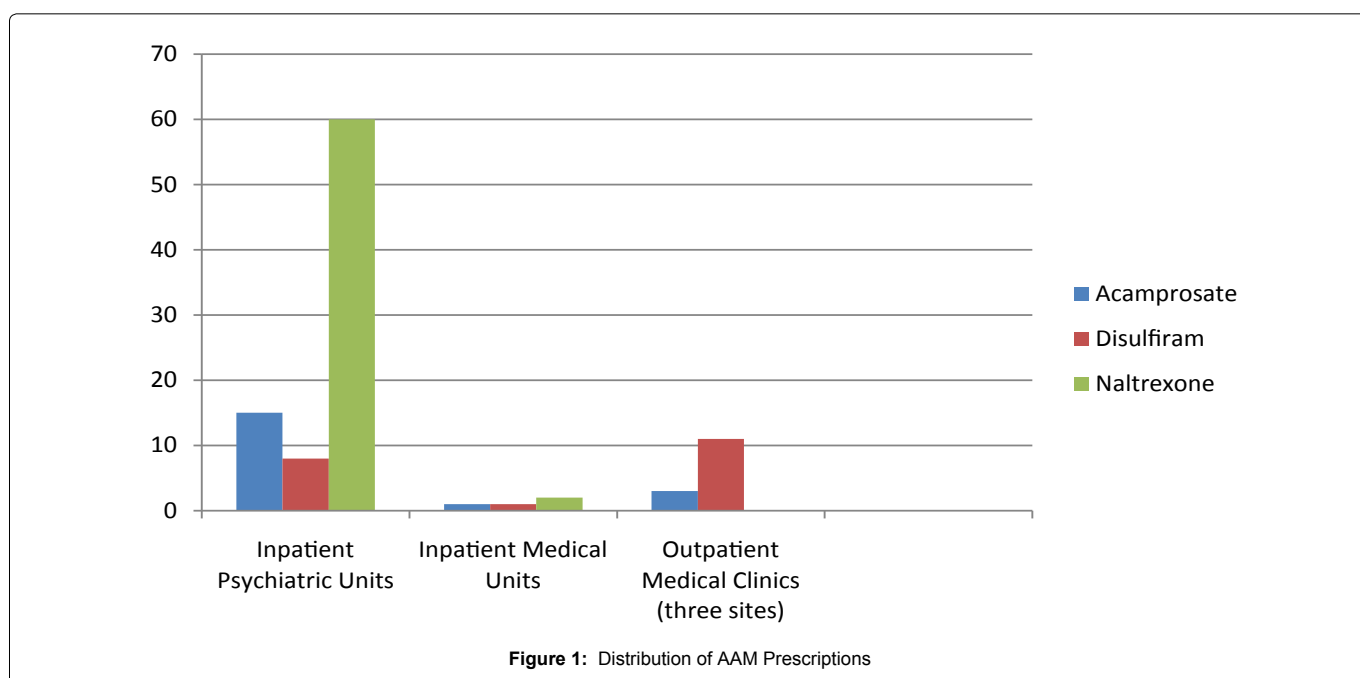
The aim of this study was to ascertain barriers faced by physicians in prescribing AAMs to their patients with AUD. Maricopa Integrated Health System (MIHS) is a county-based medical program in Phoenix, Arizona that includes a large inpatient medical hospital, two psychiatric hospitals, a Level 1 trauma center, the state’s only Burn Center, Arizona Children’s Center, HIV/AIDS clinic, Comprehensive Health Center (outpatient services), and 11 family health clinics. There are 20,000 admissions to the hospital per year, which includes approximately 3,600 psychiatric admissions and 300,000 outpatient visits per year [12].

## Methods

Using a retrospective chart review of electronic medical records (EMR), the author determined the number of AUD encounters in the inpatient psychiatric department as well as AAM utilization history in the hospital system. A 17-item survey was distributed to attending and resident physicians in the hospital network. The cross-sectional survey targeted practitioners’ issues and concerns about prescribing AAMs to their AUD patients. Examples of questions on the survey included routine demographic information, estimates of the number of AUD patients seen and AAM prescriptions written monthly, reasons for not prescribing AAMs, and beliefs about AAM efficacy.

## Results

A review of medical records from June 1, 2013 to June 1, 2014 indicated that 759 patients out of a total of 3,402 admissions were discharged from the psychiatry inpatient service with AUD as a diagnosis. AUDs were identified from the problem list in the EMR



and included diagnoses of alcohol abuse, alcoholic cirrhosis or hepatitis, alcohol withdrawal, alcohol-related polyneuropathy, alcohol-induced amnesia or dementia, alcohol-induced psychosis, alcohol dependence, and other alcohol-induced conditions. Alcohol abuse was noted in 416 out of 759 records, and 238 of the identified patients in this one-year time frame were noted to meet diagnostic criteria for alcohol dependence.

Pharmacy records for the same time frame revealed that a total of only 100 prescriptions for FDA-approved AAMs (acamprosate, disulfiram, and naltrexone) were written in the entire hospital system (Figure 1). All patients received only one AAM. These medications are on the hospital system formulary and are available through the state's Medicaid program. Eighty-three of these prescriptions were written by attending physicians employed by the Department of Psychiatry in the inpatient treatment setting, versus only 18 prescriptions written by all other disciplines and departments.

With only 100 prescriptions written by psychiatrists and a potential of 739 patients with AUDs, only 11% of potential patients with AUDs were prescribed AAMs. If only those with an alcohol dependence diagnosis were considered as possible candidates for AAMs, then the rate of prescribing rose to 35%.

A total of 52 physicians (44 attending physicians and eight residents) completed the AAM survey. Among respondents, 20 physicians (38%) were from the Department of Psychiatry and 42 (62%) were from other disciplines (family medicine, internal medicine, surgery and OB/GYN) (Figure 2). Forty of the responding physicians (77%) indicated that they are involved in the care of AUD patients. Almost two-thirds of respondents reported that they recommend AAMs to their patients. Only 31% of survey participants reported actually prescribing AAMs.

The survey asked respondents to identify barriers to prescribing AAM. The survey covered areas such as access to AAMs, patient adherence to medication, knowledge about AAMs, lack of support from the medical system for prescribing AAMs, medication side effects, drug-drug interactions, and medical comorbidity. Forty six percent of respondents reported that the primary reason for not prescribing AAMs was the inability of patients to pay for the prescription and limited insurance coverage. Patient medication adherence (42%), physician lack of knowledge about AAMs (35%), physicians not considering use of AAMs (31%), and AUD not being the primary focus of care (29%) were the most frequently cited reasons for not prescribing AAMs. The three least important

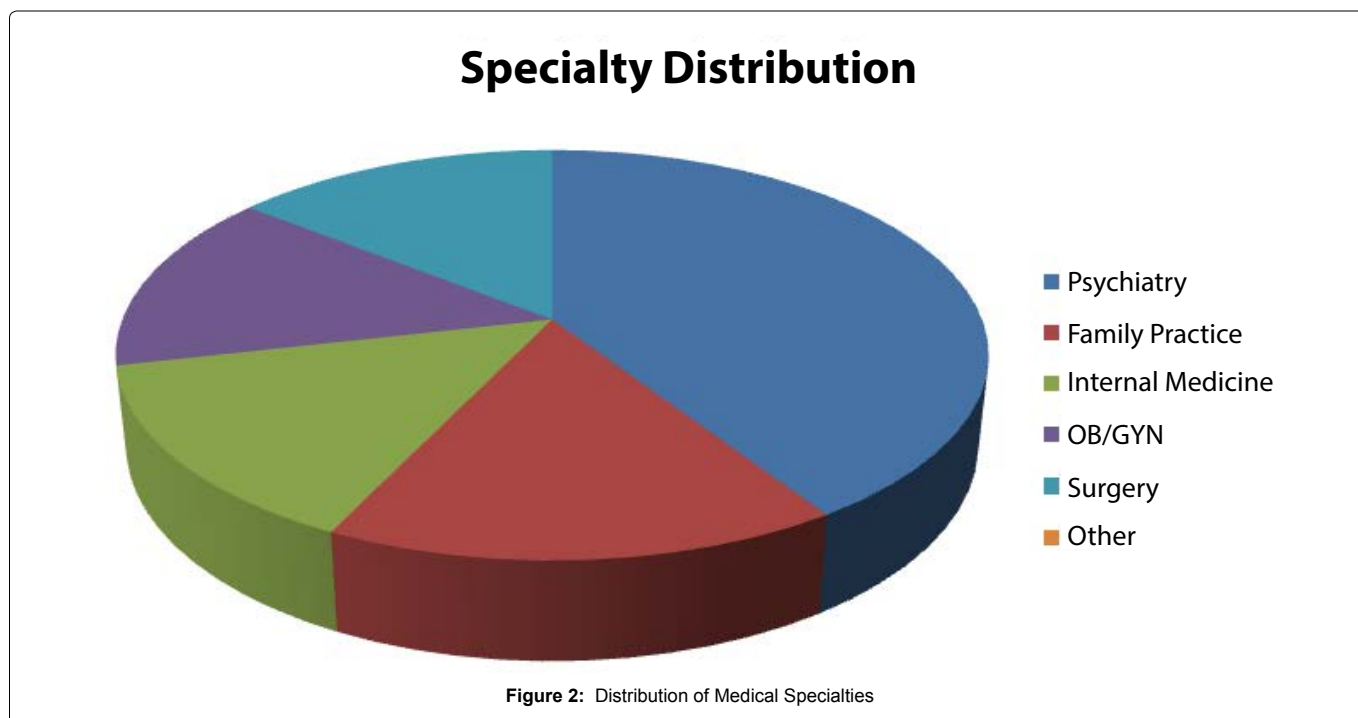
obstacles were lack of institutional support for the physician's use of AAMs in treatment of patients (2%), lack of social supports for the patient (4%), and AAM inefficacy (8%).

## Discussion

In 2008, Mark et al. published an article on prescribing trends for alcohol and opioid dependence medications [13]. Despite the growth in pharmaceutical sales of AAMs (and those for opioid dependence), the number of patients receiving AAM treatment was relatively small in relation to the large number of substance users. Studies have shown that sales of AAMs rose from about \$30 million to \$78 million in 2007 [13]. In comparison to antidepressants, \$15 billion in sales in 2006, this is still a relatively small market. Grant et al. noted that during the period from 2001 to 2002, only 9% of the population with AUD received prescription medication to treat their disorder [13]. In this study, 11% of the potential patients received AAM. Other papers published in 2010 by Mark et al. [1] and in 2011 by Oliva et al. [14] documented the very low utilization of AAMs, demonstrating that even in 2014, prescription of AAMs remained low in relation to the number of patients who might benefit from their use. This finding is of interest, especially in light of increasing evidence-based research demonstrating the efficacy of these medications.

Barriers to prescribing AAMs in 2008 were described by Mark et al. [13] as medication efficacy, lack of knowledge about AAMs, medication side effects, and cost. Just a few years later, Oliva et al. [14] discussed barriers such as cost, support for use, identifying providers who prescribe AAMs, and lack of knowledge about the medications. The current study continues to show that all of these same obstacles still exist for physicians who interact with patients with AUD.

Cost of AAM was the primary reason given by survey respondents for not prescribing these drugs. It is interesting to note that acamprosate and naltrexone are both on the government approved formulary used by the hospital system referenced in this study. The vast majority of patients who utilize the hospital system are covered by government insurance. Specifically, Arizona administers its own federal Medicaid dollars in a program called Arizona Health Care Cost Containment System. Many major private insurers also cover FDA-approved AAMs; however, these medications often require a co-pay from the patient. Since prescribers are using these medications very rarely, it is not surprising that they would not have investigated whether or not the AAMs were covered by a patient's insurance. The Chair of the Department of Psychiatry at the study's location has educated psychiatrists about the insurance coverage of AAMs, which



likely had an influence on the increased number of prescriptions written by the department as a whole.

AUD rehabilitation programs in the United States typically emphasize complete abstinence as the goal of treatment, especially as promoted by Alcoholics Anonymous. Although the debate has waxed and waned over the past 50 years, studies completed in the United Kingdom by Davies in 1962 [15] and in 2008 in a Rand Report [16] suggested that alcohol use reduction or controlled drinking resulted in overall improvement of the patient's health and reduction of that patient's health risks. A survey of addiction professionals in the United States found that 50% of respondents believed that non-abstinence (controlled drinking) was somewhat or completely acceptable for persons with alcohol abuse as an intermediate or final goal of treatment. In contrast, only 28% of respondents felt that controlled drinking was acceptable for alcohol dependent patients [17].

The current survey did not ascertain if the controversy over abstinence and moderation in drinking impacted providers' consideration of utilizing AAMs for their patients. General lack of knowledge about these medications was cited as a barrier to their use in this study, as was the issue of cost. Therefore, if a provider knows little about AAMs, he/she will not be able to appreciate the debate between reduction and abstinence. The AAMs reviewed in this paper all demonstrated efficacy in reducing the amount of alcohol consumed, but not necessarily abstinence. It is possible that providers may view the impact of AAMs as questionable because data indicates that AAMs reduce alcohol use, but do not eliminate drinking entirely.

## Limitations

This study is limited in scope. The findings shed light on the prescription patterns of AAMs in a large, urban medical center that included inpatient and outpatient settings. The survey return rate was about 25%. There was a much higher return rate for the Department of Psychiatry (an internal survey) than for other areas of the hospital system (external survey). As a safety-net medical system, serving mostly indigent or low income patients, patient characteristics and medical needs may have influenced the rate of identified AUDs and prescription patterns of the providers. All of these factors may make the data difficult to generalize to other populations.

## Conclusions

Despite recent evidence-based research on the efficacy of FDA-approved and off-label use of AAMs and the availability of AAMs on insurance formularies (even government funded programs), utilization of these medications is very low. Similar barriers to the use of AAMs are cited today as were reported eight years ago, when these medications became widely available. Educating physicians is the key to expanding utilization of AAMs in the treatment of individuals with AUDs. Although somewhat controversial, but wide-spread in the US, pharmaceutical representatives' sponsored education can be one of the best mechanisms for disseminating information about newly introduced medications. Unfortunately, the FDA-approved AAMs are now generic, and pharmaceutical representatives cannot endorse off-label usage of any medications. Currently, physicians must obtain information about AAMs on their own. Unless a physician has a particular interest in substance abuse, he/she often lacks incentive to evaluate new treatment approaches or attend seminars on the topic of AUD. In recent years, there has been an increased focus on opioid treatment options, with the health care crisis of narcotic abuse and the introduction of buprenorphine and naloxone. As a result, AUD is receiving less attention than in the past. It is interesting to note that The Joint Commission on Accreditation of Healthcare Organizations added a new core component on the Hospital-Based Inpatient Psychiatric Service measure for 2016 that requires physicians to document that a discussion about alcohol use and intervention was provided to patients with an AUD.

Even if a physician feels comfortable prescribing AAMs, a variety of other barriers remain with which to contend. Limited research has been undertaken to assess patient-level barriers and perceptions

of AAMs. Within the medical community, the trend of separating medical and psychiatric treatment from substance abuse treatment remains a common standard of care. This division of care adversely affects the identification and treatment of patients with AUD. Due to time constraints in the provision of medical care in this age, even the most conscientious physician finds it difficult to fully assess patients' substance use, especially when it is not the primary focus of treatment. Often, physicians encounter limited patient adherence to recommended treatment and medication for the patient's primary medical condition. Adding another medication to the treatment regimen may seem fruitless or counterproductive. Integration of medical, psychiatric and substance abuse treatment and improving patient care interventions are necessary to improve outcomes and decrease risks for patients with AUD. Ultimately, we as a medical community are missing a valuable opportunity to treat patients with AUD optimally.

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