

# Pharmacotherapy of Alcohol Use Disorders in the Veterans Health Administration

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**Objective:** Acamprosate, oral and long-acting injectable naltrexone, and disulfiram are approved for treatment of alcohol dependence. Their availability and consideration of their use in treatment are now standards of high-quality care. This study determined rates of medication initiation among Veterans Health Administration (VHA) patients. **Methods:** VHA pharmacy and administrative data were used to identify patients with alcohol use disorder diagnoses in fiscal years (FY) 2006 and 2007 and the proportion (nationally and by facility) who received each medication. Patient characteristics associated with receipt were also examined. **Results:** Among more than a quarter-million patients with alcohol use disorder diagnoses, the percentage receiving any of the medications increased from 2.8% in FY 2006 to 3.0% in FY 2007. Receipt of these medications was more likely among patients who received specialty addiction care, those with alcohol dependence (compared with abuse), those younger than 55 years, and females. In the patient subgroups examined, the largest proportion to receive any of the medications was 11.6%. Across 128 VHA facilities, rates of use among patients in the sample who had received past-year specialty addiction treatment ranged from 0% to 20.5%; rates ranged from 0% to 4.3% among those with no specialty treatment. Patient preferences and medical contraindications could not be determined from the data. **Conclusions:** Findings suggest the need to better understand systemwide variation in use of these medications and their use as a rough proxy for availability and consideration of pharmacotherapy—a standard of care with strong organizational support. (*Psychiatric Services* 61:392–398, 2010)

Until 1995 the U.S. Food and Drug Administration (FDA) had approved only one medication (disulfiram) for the treatment of alcohol dependence. In 1995 the FDA approved oral naltrexone. Acamprosate received approval in 2004 and long-acting injectable naltrexone in 2006. A recent study of U.S. prescription data found that although overall

sales of these medications have grown rapidly in recent years, only a small proportion of Americans with alcohol use disorders are treated with medication therapy (1).

Of the roughly 19 million people in the United States who meet diagnostic criteria for an alcohol use disorder (about 8.5 million with alcohol dependence), it has been estimated that

only 139,000 annually receive pharmacotherapy with approved medications—.07% overall and 5.8% of those seeking specialty treatment (2,3). Other estimates of prescription rates among persons with alcohol use disorders vary from less than 1% to 13%, depending on sample definitions, setting of care, and specific medication, with the highest rates found for naltrexone among alcohol-dependent patients in specialty addiction treatment settings (4,5). Several large surveys of addiction treatment programs have found far from universal adoption of pharmacotherapy for alcohol use disorders (3,6). To put this in perspective, the one-year prevalence of alcohol dependence is roughly half that of major depression (3.8% and 7.2%, respectively) (7,8); however, 336 times as many prescriptions were written in 2006 for antidepressants as for alcohol dependence medications (226,886,000 compared with 674,000) and the sales volume was 241 times as great (\$15,064,827,000 compared with \$62,383,000) (1,5,9).

The American Psychiatric Association's Physician Consortium for Performance Improvement and the National Committee for Quality Assurance recently adopted performance measures related to the management of alcohol dependence that include counseling regarding psychosocial and pharmacologic treatment options as one of the three measures related to substance use disorders (10). In a similar vein and consistent with consensus standards for evidence-based treatment of substance use disorders approved by the National Quality Fo-

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rum, availability of FDA-approved pharmacologic treatments for alcohol dependence and consideration of their use in treating alcohol-dependent patients were recently mandated for all facilities of the Veterans Health Administration (VHA) (11). In its recently revised Clinical Practice Guideline for Management of Substance Use Disorder (12), VHA clearly supports the availability and active consideration of these pharmacologic treatments.

Although the availability and consideration of pharmacotherapy are now considered important components of high-quality care for alcohol use disorders, clinical data describing whether and to what extent such pharmacotherapy is considered are either nonexistent or buried in the text of progress notes. Furthermore, the proportion of patients who should receive these drugs, determined on the basis of clinical judgments, medical contraindications, and patient preferences, is not known. Therefore, from a quality measurement standpoint, it is difficult to determine where and when these newly promulgated standards are being met. For patients with alcohol use disorders who do not receive pharmacotherapy, it is difficult to determine whether pharmacotherapy was actively considered, either by the clinician or patient. However, at the facility level it may be possible to use prescription data as a rough proxy for availability and consideration. If no treatment-seeking patients receive pharmacotherapy, it might be concluded that the medications are either not available or not being actively considered.

Knowing the extent to which these medications are utilized can help motivate implementation and quality improvement efforts and provide a baseline to judge the effects of these efforts. Although patient preferences, contraindications, cost, and other clinical and patient factors (perhaps including pharmacogenetics) should influence patients' receipt of pharmacotherapy for alcohol use disorders, adoption of these new policies and performance measures may motivate efforts to increase what has been historically low use of these medications.

In this study we sought to deter-

mine the extent to which these medications are initiated in the treatment of the almost 300,000 patients with alcohol use disorders in the VHA and to examine patient characteristics associated with receipt of these medications. We focused on receipt of pharmacotherapy for alcohol use disorders (yes or no), not on duration of use as studied previously (13,14). In addition to conducting patient-level analyses, we sought to describe variability in facility-level utilization of pharmacotherapy for alcohol use disorders. These data will establish baseline statistics that might be used to evaluate the effects of future implementation efforts. Finally, for comparison purposes, we determined which patients in our sample also had indications for and received selective serotonin reuptake inhibitors (SSRIs).

### Methods

To define a group of potential candidates for pharmacotherapy, we included patients with either alcohol abuse or dependence diagnoses, even though the medications are approved only for alcohol dependence. This decision was based on several factors, including the lack of fidelity with which these diagnostic distinctions are applied (for example, many patient have both diagnoses) and the appreciable percentage of patients taking these medications who have only a diagnosis of alcohol abuse. Using the VHA National Patient Care Database, we identified all patients who received an alcohol use disorder diagnosis (*ICD-9-CM* codes 303.9x or 305.0x) in fiscal years (FY) 2006 and 2007. We included "in remission" diagnoses because some patients in treatment are incorrectly diagnosed as having disorders in full remission.

We then used the VHA Decision Support System (DSS) inpatient and outpatient pharmacy benefits files to determine the proportion of patients with alcohol use disorders who received any of the four medications: acamprosate, naltrexone oral, injectable naltrexone, and disulfiram). Receipt of medication was operationalized as at least one pharmacy record for the medication. No attempt was made to define a minimum

efficacious course of medication or to characterize adherence to medication or duration of use.

We also examined administrative data on patient characteristics, such as age, gender, and a recent history of specialty addiction treatment as well as clinical diagnoses—alcohol abuse or dependence—to determine their associations with receipt of each of these medications. A recent history of specialty addiction treatment was defined as receipt of care during the fiscal year within one of VHA's specialty substance use disorder clinics or inpatient or residential programs (identified by DSS stop codes and bed section codes). Addiction care that may have occurred in other settings, such as psychiatric wards or primary care settings, was not included in this definition. Other potentially predictive demographic variables were not included because they were either not available (for example, income) or are notoriously unreliable in VHA administrative data (for example, race) (15). All patient-level analyses were done with mixed-effects logistic regression with a random effect to account for the clustering of patients within VHA facilities (128 major VHA facilities), which is the level of analysis for most VHA quality measures; facilities were identified by their three-digit station code. All statistical analyses were conducted with the R statistical program (version 2.9.2).

To explore variability in facility-level utilization of pharmacotherapy, we calculated the rates of receipt of medication for alcohol use disorders (that is, the number of patients receiving medication divided by the number with an alcohol use disorder diagnosis) in each of the 128 major VHA facilities; rates were also calculated for patients with and without a history of specialty addiction treatment. This analysis was purely descriptive. Chart documentation was not reviewed, and thus no data were available for prescriptions that were offered but declined by the patient or for medications that the clinician decided were contraindicated for other reasons. Institutional review boards of Stanford University and VA Palo Alto Health Care System approved all aspects of this study.

**Table 1**

Patients who received medication treatment for alcohol use disorders in the Veterans Health Administration in two fiscal years

Medication	2006 (N=267,982) <sup>a</sup>		2007 (N=281,353) <sup>a</sup>	
	N	%	N	%
Acamprosate	1,330	.5	1,592	.6
Oral naltrexone	3,658	1.4	4,520	1.6
Injectable naltrexone	0	—	70	<.1
Disulfiram	3,111	1.2	3,082	1.1
Any medication	7,520	2.8	8,492	3.0

<sup>a</sup> Ns represent unique patients with either alcohol abuse or dependence diagnoses as recorded in the yearly census of over five million patients.

## Results

Table 1 presents data on the proportion of patients with alcohol use disorders who received acamprosate, oral naltrexone, injectable naltrexone, or disulfiram. In FY 2006, among more than five million VA patients, 267,982 had a diagnosed alcohol use disorder, of which .5% received acamprosate, 1.4% received oral naltrexone, and 1.2% received disulfiram. Injectable naltrexone was approved by the FDA during FY 2006 but was not dispensed in VHA. Overall, 2.8% of patients with an alcohol use disorder received at least one of these medications from VHA during

FY 2006. In FY 2007, a total of 281,353 patients had an alcohol use disorder diagnosis, of which .6% received acamprosate, 1.6% received oral naltrexone, <.1% received injectable naltrexone, and 1.1% received disulfiram. Overall, 3.0% of patients with an alcohol use disorder received at least one of these medications from VHA during FY 2007.

Several patient and setting factors predicted receipt of any of these medications and of each medication. Table 2 presents FY 2007 data on the use of these medications stratified by gender, age, alcohol use disorder diagnosis (abuse or dependence), and

receipt of VHA specialty care for substance use disorders during the fiscal year. Women with an alcohol use disorder were almost twice as likely as men to receive these medications (5.2% compared with 3.0%). Patients older than 55 years were less likely to receive these medications (2.2%) than patients in the 30- to 55-year group (4.0%) and than those younger than 30 years (3.2%). Patients with an alcohol abuse diagnosis were half as likely as those with an alcohol dependence diagnosis to receive these medications (1.8% compared with 3.9%). Patients who received no substance use disorder specialty care during the fiscal year were much less likely to receive these medications (1.2%) than those who received only outpatient specialty care (6.4%), only residential care (11.2%), and both residential and outpatient specialty care (11.6%). As noted in Table 2, all of these comparisons were significant in single-predictor, mixed-effects logistic regression models with a random effect for VHA facility and receipt of any medication (yes or no) as the outcome.

To examine the conditional independence of these bivariate associations, we constructed a multivariate mixed-effects logistic regression model

**Table 2**

Predictors of medication use and receipt of specialty care for alcohol use disorders in the Veterans Health Administration in fiscal year 2007

Variable	Total N	Acamprosate (N=1,594)		Naltrexone (N=4,520)		Disulfiram (N=3,082)		Any medication (N=8,492)	
		N	%	N	%	N	%	N	%
Gender									
Male (reference)	270,774	1,499	.6	4,246	1.6	2,912	1.1	8,009	3.0
Female	9,319	95	1.0*	274	2.9*	170	1.8*	483	5.2*
Age									
>55 (reference)	141,511	584	.4	1,614	1.1	1,093	.8	3,063	2.2
30–55	126,694	969	.8*	2,662	2.1*	1,859	1.5*	5,045	4.0*
<30	11,888	41	.3	244	2.1*	130	1.1*	384	3.2*
Alcohol diagnosis									
Dependence (reference)	167,643	1,267	.8	3,440	2.1	2,367	1.4	6,510	3.9
Abuse	113,710	327	.3*	1,084	1.0*	719	.6*	1,992	1.8*
Addiction specialty care									
None (reference)	190,974	323	.2	1,127	.6	953	.5	2,305	1.2
Outpatient only	82,843	1,107	1.3*	2,872	3.5*	1,825	2.2*	5,318	6.4*
Residential only	296	4	1.4*	12	.1*	19	6.4*	33	11.2*
Both <sup>a</sup>	7,240	160	2.2*	509	7.0*	288	4.0*	841	11.6*

<sup>a</sup> Patients could have received medication in outpatient care, residential care, or both settings.

\*  $p < .05$  for the difference between the indicated group and the reference group in a single-predictor, mixed-effects logistic regression model with a random effect for facility

el predicting receipt of any of the four medications, using data on gender, age, alcohol use disorder diagnosis (abuse or dependence), and receipt of specialty care for substance use disorders. Consistent with the bivariate associations described above, these results indicated that all variables had independent associations with medication receipt (Table 3). The Nagelkerke  $R^2$  was .10 for the usual (non-mixed-effects) version of this logistic regression model. Receipt of substance use disorder specialty care had the largest adjusted odds ratios, indicating minimal use of these medications for patients who did not receive treatment in specialty settings.

#### Medication use by patients without alcohol use disorders

Some patients who did not have an alcohol use disorder received these medications, although they were not included in our main analyses. It is unknown to what extent such use represents treatment for undocumented alcohol use disorders or, especially in the case of naltrexone, treatment for other indications. In FY 2006, 6.3% (N=107) of patients receiving acamprosate, 19.3% (N=970) of those receiving naltrexone, and 16.2% (N=682) of those

**Table 3**

Multivariate model predicting receipt of any medication for alcohol use disorders in the Veterans Health Administration in fiscal year 2007<sup>a</sup>

Variable	Estimate	SE	z	OR	95% CI
Female (reference: male)	.459	.049	9.24	1.58	1.43–1.74
Age (reference: >55)					
30–55	.174	.024	7.15	1.19	1.13–1.25
<30	.186	.056	3.31	1.20	1.08–1.35
Abuse diagnosis (reference: dependence)	–.529	.026	–19.92	.59	.56–.62
Type of addiction care (reference: no specialty care)					
Outpatient only	1.600	.026	61.28	4.96	4.71–5.22
Residential only	2.187	.186	11.73	8.91	6.18–12.84
Both	2.195	.043	50.71	8.89	8.25–9.78
Intercept	–4.286	.025	–169.19		

<sup>a</sup> Results are from a mixed-effects logistic regression model with a random effect for facility. Nagelkerke  $R^2$  = .10 for non-mixed effects version of this model

receiving disulfiram did not have an alcohol use disorder diagnosis.

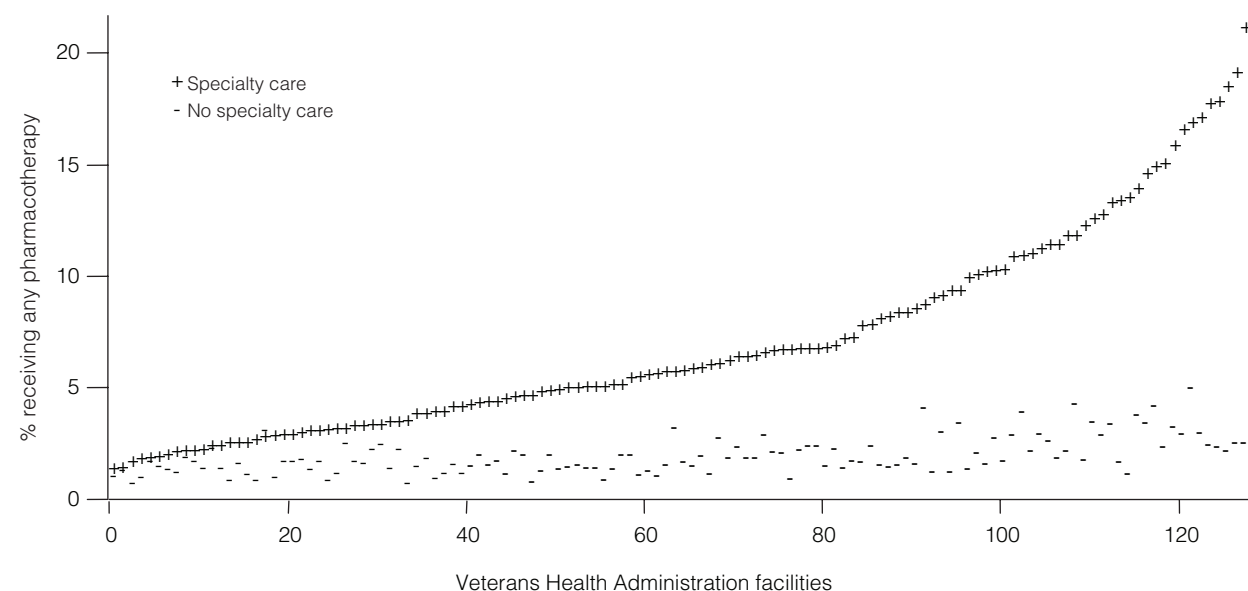
#### Facility rates of medication use for alcohol use disorders

Figure 1 presents data on the facility-level prevalence of pharmacotherapy for patients with alcohol use disorders who did and did not have contact with the specialty addiction treatment system. Across 128 VHA facilities, the proportion of patients with a history of specialty addiction treatment who

received pharmacotherapy ranged from 0% to 20.5%; at two facilities the rate was less than 1%. Across the same facilities, only 0% to 4.3% of patients who did not receive specialty treatment received pharmacotherapy; at 66 facilities the rate was less than 1%. Such data can be used to identify facilities at the high and low end of the utilization continuum in order to target implementation efforts. If the data were available, which they are not for VHA, these metrics

**Figure 1**

Percentage of patients at 128 facilities receiving pharmacotherapy for an alcohol use disorder in fiscal year 2007, by receipt of specialty care





might be calculated for specific programs or individual providers as feedback to clinical and quality managers.

### *Comparison with use of SSRIs*

A possible explanation for the low utilization rates of these medications in the treatment of alcohol use disorders is patients' reluctance to take any psychiatric medications among those with alcohol use disorders or clinicians' reluctance to prescribe them for these patients. To explore this possibility, we determined which patients in our sample had co-occurring psychiatric diagnoses that are indications for SSRIs, such as depression, anxiety disorders, posttraumatic stress disorder, and eating disorders. Of the 281,353 patients with an alcohol use disorder diagnosis in FY 2007, a total of 161,938 also had a diagnosis that is an indication for an SSRI. Of these, 52.6% (N=85,179) received an SSRI and 4.3% (N=6,963) received at least one medication for an alcohol use disorder. Thus these patients were much more likely to receive medication for their co-occurring disorder than for their alcohol use disorder. Of interest, of the 119,415 patients in the sample who did not have a psychiatric indication for an SSRI, 7.3% (N=8,817) received an SSRI and 1.2% received an alcohol use disorder medication (N=1,433). Apparently, patients with an alcohol use disorder who did not have an indication for an SSRI were more likely to receive an SSRI than an indicated medication for alcohol use disorder.

### **Discussion**

Approximately 3% of the more than quarter-million VHA patients with alcohol use disorders received pharmacotherapy for these disorders in FY 2006 and FY 2007. The rates of medication initiation were higher for patients who received care in one of the VHA substance use disorder specialty treatment settings in that fiscal year (6.4% of outpatients and 11.2% of patients who received residential specialty care in FY 2007). These rates represent patients who filled at least one prescription for these medications. Therefore, the rate of receipt of an adequate, efficacious course of medication must have been even low-

er, although this proportion was not examined directly.

The optimal percentage of patients with an alcohol use disorder who should be receiving each of these medications has not been established. Not every patient with an alcohol use disorder needs, wants, or will accept medication treatment. Furthermore, evidence supporting use of these medications is equivocal and varies by medication. VHA clinicians' potential enthusiasm for naltrexone may have been reduced by the null result obtained in a large VA multisite trial, even though reanalyses of data from the trial identified a subset of responders who may benefit (16,17) and despite the emerging possibility of genetic identification of likely responders (18).

Given the large number of patients with an alcohol use disorder who are either uninterested in or who have not benefited sufficiently from psychosocial treatment, we suggest that pharmacotherapy should, at a minimum, be available and considered for all patients with an alcohol use disorder and that the 3% prescription rate observed in this study represents an underutilization of medications for alcohol use disorders in VHA. The recommendation regarding availability and consideration is consistent with recently approved consensus standards that all patients with alcohol dependence should have clinical documentation that these medications were available and considered if they were not clinically contraindicated (10–12).

Perhaps more important, we found that at some facilities no patients, even those who sought treatment for addiction, were receiving pharmacotherapy for alcohol use disorders. To the extent that receipt of medication can be used as a rough proxy for availability and consideration of alcohol use disorder pharmacotherapy, these facilities appear not to be providing the standard of care. Quality managers might target implementation efforts at facilities (or other organizational units) that provide no alcohol use disorder pharmacotherapy or fail to exceed some minimal threshold of provision.

Certain patient characteristics were

associated with a greater likelihood of medication receipt. Patients over age 55 were somewhat less likely than younger patients to receive these medications. In this sample, only 23% of patients in the over-55 age group received any specialty addiction care during FY 2007, compared with 46% of the 30- to 55-year group and 38% of patients under age 30. Older patients may be less likely to seek any type of addiction treatment, including pharmacotherapy, because of higher perceived stigma or other cohort-related factors. Furthermore, disulfiram is not recommended for use among older adults, which may partly explain this finding (19,20).

Female patients with an alcohol use disorder in VHA were somewhat more likely than male patients to receive both specialty addiction care (43% compared with 40% in FY 2007) and treatment with any of the four medications (5.2% compared with 3.0%). Although we cannot disentangle the nature of these correlations with cross-sectional data, one treatment modality may facilitate (mediate) the other, or both correlations may result from an unobserved factor, such as a greater likelihood among women of having a co-occurring psychiatric diagnosis that brings them into contact with psychiatrists, a preference for psychoactive medications, and possible site differences, such as gender-specific programs at larger sites.

Patients who had a diagnosis of alcohol dependence were more likely than those with an alcohol abuse diagnosis to receive pharmacotherapy, which is not surprising given that these medications are approved for alcohol dependence. Use of these medications to treat alcohol abuse could technically be considered off label. FY 2007 rates of use of these medications among patients seen in specialty care for substance use disorders were higher but still modest—6.4% of patients in outpatient care for substance use disorders and 11.6% of patients seen in both residential and outpatient settings, compared with 1.2% of patients who did not receive addiction specialty care.

The fact that SSRIs were used about five times as often as medica-

tions for alcohol use disorders among patients with an alcohol use disorder but without a co-occurring psychiatric diagnosis raises questions. Although preliminary observational data suggest possible synergies between SSRIs and naltrexone in the treatment of alcohol dependence (21), there is no empirical support for SSRIs as a monotherapy for alcohol dependence. It is possible that the SSRIs were prescribed for other off-label indications. Or it may be that clinicians have more experience and greater comfort prescribing SSRIs, even in cases for which the drugs have no proven efficacy. More detailed examination of these cases is necessary to better understand this phenomenon.

### **Limitations**

This study has several limitations. We focused on initial receipt of medications but did not determine whether patients received an adequate course of therapy (for example, several months of refills). Clearly, the proportion of patients who received an adequate course of pharmacotherapy must be lower than the proportion of patients who received any medication. Also, we had data on filled prescriptions only, not on whether the medications were taken (with the exception of injectable naltrexone). Furthermore, we did not have data on prescriptions written by VHA clinicians that were either not filled or filled elsewhere. Although some patients may have obtained alcohol use disorder medications from other sources, the generally low copayments for VHA pharmacy benefits makes this less likely.

Another limitation is the unknown sensitivity and specificity of alcohol use disorder diagnoses in VHA, especially the extent to which patients without diagnoses meet diagnostic criteria and therefore might benefit from pharmacotherapy. In FY 2006 and 2007 roughly 5.5% of VHA patients had an alcohol use disorder diagnosis. This prevalence estimate is similar to other VHA estimates but not directly analogous. Kinder and colleagues (22) reported that 6.2% of a sample of 34,292 male VHA outpatients had scores greater than 8 on the Alcohol

Use Disorder Identification Test–Consumption, which indicates a high probability of meeting criteria for an alcohol use disorder. Wagner and colleagues (23) have estimated that 6.2% of veterans nationally, only some of whom are VHA patients, meet criteria for alcohol abuse or dependence. These diagnostic uncertainties led us to explore the use of these medications for patients without alcohol use disorder diagnoses, and we found that from 6% to 19% of all patients receiving these medications did not have these diagnoses. Without chart review, it is difficult to know what proportion of these patients was being treated for undiagnosed alcohol disorders or whether the medications were being prescribed for other indications, such as cocaine dependence or skin picking.

### **Barriers to implementation**

Patients with chronic and severe alcohol use disorders have high rates of relapse, readmission, and treatment attrition. Therefore, it is surprising that these medications are not more widely used. This apparent underutilization is not unique to VHA. Utilization rates for these medications at VHA are within the range of rates reported in other settings (4,5). Several authors have posited explanations for the apparent underutilization, including clinicians' lack of knowledge, perceived ineffectiveness, belief that medications might reduce motivation for psychosocial treatment and mutual-help group attendance, concerns about side effects, cost, lack of sufficient time allocated for management of patients, and patients' reluctance to take medications (4, 24–27). Mark and colleagues (5) asked 1,388 physicians what implementation efforts are most likely to result in greater use of medications to treat alcohol use disorders. The physicians cited more research to develop new medications (33%), more physician education about existing medications (17%), and increased physician involvement in alcoholism treatment (17%). An educational intervention to increase knowledge and acceptance of naltrexone in community-based addiction treatment settings has recently been

developed (28). However, education alone is rarely sufficient to produce meaningful changes in physicians' behaviors (29,30).

Two of the medications analyzed in this study, acamprosate and long-acting injectable naltrexone, have non-formulary status in VHA, which does not preclude use but attaches stipulations to prescriptions, which may act as a barrier to use. Other researchers have examined facility-level barriers, rather than patient- or clinician-level barriers, to pharmacotherapy for alcohol use disorders (31). Oser and Roman (6) found that having 12-step meetings on the premises, a lower level of education among administrators, a physician on the payroll, an employee handbook, a hospital affiliation, and for-profit status were significantly associated with greater likelihood of adoption of naltrexone treatment. Fuller and colleagues (32) found, among other things, that clinics that provided only substance use disorder services were less likely to utilize naltrexone than more general clinics. Ducharme and colleagues (26) found that adoption of disulfiram and naltrexone was significantly more likely in programs that were accredited, employed at least one physician, offered care for patients with co-occurring psychiatric conditions, derived more revenue from commercial insurance payers, and had fewer links with the criminal justice system.

If discussing all treatment options is now considered the standard of care for patients with alcohol use disorders (10–12), then all patients with these disorders should be apprised of the spectrum of self-help, mutual-help, psychosocial, and medication treatment options. If physicians are held accountable to provide knowledgeable and unbiased information to patients with these disorders, patient demand may drive utilization to its proper level.

### **Conclusions**

At VHA, the use of FDA-approved medications for the treatment of alcohol use disorders is generally low but highly variable. At some VHA sites, medications were prescribed to one in five patients seeking treatment for an alcohol use disorder, and

other sites were found to rarely use these treatment options. Therefore, examining facility-level barriers and supports for pharmacotherapy for alcohol use disorders is a priority in the VHA system. In light of these data, we are initiating a research program to identify facility-level predictors of pharmacotherapy for alcohol use disorders and surveying and interviewing staff at the high- and low-use facilities.

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The authors report no competing interests.

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