

Dissemination, Adoption, and Implementation of Acamprosate for Treating Alcohol Use Disorders

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ABSTRACT. Objective: Acamprosate has been available in the United States for treating alcohol use disorders (AUDs) for nearly a decade, yet few studies have examined its use within AUD treatment organizations. In addition to describing dissemination and adoption of acamprosate, this study provides novel data regarding organizational processes that underlie its implementation within adopting programs. **Method:** Data were drawn from interviews with leaders of a nationally representative sample of 307 organizations delivering AUD treatment. Quantitative indicators of organizational characteristics, dissemination, adoption, and implementation of acamprosate, as well as qualitative measures of implementation processes, were measured during face-to-face interviews. **Results:** Only 18.0% ($n = 55$) of sampled organizations had adopted acamprosate for treating AUDs, and adoption was positively associated with accreditation, having a physician on staff, receiving information about

acamprosate via pharmaceutical representatives, and learning about this medication from other treatment providers. Within adopting programs, an average of 6.0% of AUD patients were currently receiving acamprosate. Numerous implementation challenges were identified, including appropriate patient selection, patient reluctance to be prescribed acamprosate, suboptimal adherence, its costs, and limited counselor training. **Conclusions:** The limited adoption and implementation of acamprosate likely limits the potential public health impact of this adjunct to AUD treatment. Research integrating the perspectives of organizational leaders, medical professionals, and patients is needed to determine whether specific strategies can address the implementation challenges identified in the current study and increase use of acamprosate in specialty AUD treatment settings. (*J. Stud. Alcohol Drugs*, 75, 467–475, 2014)

INNOVATIONS FOR TREATING ALCOHOL USE disorders (AUDs) have marked the past two decades as this specialty treatment sector has become increasingly integrated into mainstream medical care in terms of organization, accreditation, and reimbursement (Samet et al., 2001; Sorensen et al., 2009). Both psychosocial and pharmacological therapies have been developed and diffused (McLellan and McKay, 2009; National Institute on Drug Abuse, 2009), although rates of adoption have fallen short of expectations (Manuel et al., 2011; Roman et al., 2011). In pharmacotherapy for AUDs, the approval of acamprosate (calcium acetylamino propane sulfonate [Campral]) by the U.S. Food and Drug Administration (FDA) in 2004 significantly expanded therapeutic choices, which had previously been limited to naltrexone and disulfiram (Boothby and Doering, 2005).

Given the potential impact of medications on the efficiency of delivering AUD treatment through possible expansion within primary care medicine, the body of re-

search on acamprosate has been both modest and partially contradictory. Research conducted in the 1990s and early 2000s demonstrated superior outcomes for acamprosate relative to placebo (Kiefer et al., 2003; Whitworth et al., 1996) and confirmed its safety (Carmen et al., 2004). Other research, including an Australian study (Morley et al., 2006; Richardson et al., 2008) and the large U.S. COMBINE Study (Combined Pharmacotherapies and Behavioral Interventions for Alcohol Dependence; Anton et al., 2006; Donovan et al., 2008), did not find improvements in drinking outcomes. Overall, however, meta-analyses of randomized clinical trials show that, relative to placebo, acamprosate improves both the rate and duration of continuous abstinence (Carmen et al., 2004) and may be more beneficial than naltrexone for these specific outcomes (Maisel et al., 2013).

Several studies have explored the integration of delivering acamprosate to patients in specialty AUD treatment. Improved treatment outcomes are found when acamprosate is prescribed to patients who have completed detoxification (Maisel et al., 2013), a service delivered by some AUD programs. Second, effectiveness is enhanced by combining this medication with psychosocial treatments typically available in AUD specialty care (Maisel et al., 2013); combining pharmacotherapy with psychosocial interventions has emerged as a general principle in medication-related research (Carroll et al., 2004).

Despite the potential value of pairing acamprosate with psychosocial treatment, previous studies have shown both limited rates of adoption (i.e., any use) and implementation

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(i.e., extent of use) within specialty treatment settings. In the first year after FDA approval, about 7% of substance use disorder (SUD) treatment programs offered acamprosate, and in the adopting programs an average of only 11% of AUD patients actually received this medication (Ducharme et al., 2006). More recent studies have reported rates of adoption ranging from 6% to 32% depending on the type of treatment organization (Abraham et al., 2010; Knudsen et al., 2010, 2011), with generally greater adoption occurring in privately funded organizations relative to those reliant on public funding, such as government block grants and contracts (Roman et al., 2011). In addition to funding, acamprosate adoption is associated with such organizational characteristics as workforce professionalism (e.g., availability of physicians, more educated counseling staff) and structural characteristics (e.g., location in a hospital, accreditation) (Abraham et al., 2010; Ducharme et al., 2006). Recent data still show limited implementation, with an average of only 17.5% of AUD patients in adopting programs receiving this medication (Knudsen et al., 2011).

The present study expands on previous health services research on acamprosate in specialty SUD treatment in three ways. First, this study presents more recent data collected from a national sample of specialty treatment organizations. Second, we consider the roles of specific mechanisms of dissemination (i.e., sources of information about acamprosate) in a model of adoption that controls for organizational characteristics. These dissemination mechanisms have not been previously examined as correlates of acamprosate adoption. Finally, we provide novel data regarding acamprosate implementation in terms of the organizational processes and procedures that underlie its use within adopting programs. We address critical implementation issues, such as the roles of program staff in patient selection, education, and adherence. This consideration of how acamprosate is being implemented, beyond simply the rate of patients receiving it, has not previously been reported for acamprosate or other SUD medications.

Method

Sample

This research draws on data from a larger study of service delivery within a newly established nationally representative sample of U.S. treatment organizations that offer specialty treatment for AUDs. Organizations were randomly sampled from the 2008 Substance Abuse Treatment Services Locator, a directory supported by the Substance Abuse and Mental Health Services Administration (SAMHSA; <http://findtreatment.samhsa.gov/>). Telephone screening established eligibility using the following inclusion criteria: (a) at least 25% of a treatment organization's patients had a primary AUD diagnosis; (b) at least two full-time equivalent employees were

employed by the treatment center; (c) the organization offered a minimum level of AUD treatment at least equivalent to structured outpatient services, as defined by the American Society of Addiction Medicine (Mee-Lee et al., 1996); and (d) treatment services were open to the general public. These criteria excluded opioid treatment programs that exclusively dispense pharmacotherapy (e.g., methadone), counselors in private practice, driving under the influence/driving while intoxicated programs, detoxification-only programs, halfway houses, services located within the Veterans Health Administration, corrections-based programs, military facilities, and services operated by the Indian Health Service.

Sampled treatment centers were then scheduled for a face-to-face interview with the administrator and/or clinical director of the organization. Before the interviewer's arrival at the organization's location, potential participants received a study packet with a description of the study and informed consent forms, which were collected before the interview began. Interviews were conducted by trained interviewers who had attained at least a bachelor's level of education. On assignment to this study, interviewers received multiday training from the research team on study-specific interviewing procedures. Most interviewers had multiple years of experience in interviewing leaders of SUD organizations from the team's prior studies. Program leaders of 307 SUD treatment organizations were interviewed from mid-2009 to January 2012, representing a 65% response rate among eligible organizations. These research procedures were approved by the Institutional Review Boards of the University of Georgia and the University of Kentucky.

Measures

Structured interviews measured organizational characteristics, dissemination sources specific to acamprosate, current use of this medication, implementation rate, and organizational processes supporting its implementation. Organizational characteristics included the structure of the treatment center, its levels of care (i.e., treatment and detoxification), and staffing (e.g., medical personnel and counselors); these measures appear in Table 1. With regard to dissemination, respondents were asked if they had heard or read about acamprosate (1 = yes, 0 = no). Additional dichotomous items (Table 2) asked whether respondents had learned about acamprosate from publications, conferences, direct mailings, pharmaceutical detailing via telephone or office visits, and other providers. For each specific source of dissemination, respondents who had never heard or read about acamprosate were coded as "no." Adoption of acamprosate was a dichotomous variable indicating whether the prescription of this medication was current practice within the organization. In programs that reported adoption, a series of closed-ended and open-ended questions were asked about implementation; interviewers recorded responses to open-ended questions on

the interview form. The implementation rate was defined as the percentage of AUD patients receiving acamprosate. Other items addressed organizational processes related to implementation (e.g., patient selection, patient education, delivery of other therapeutic services, and efforts to address medication compliance); some measures were closed-ended whereas others were open-ended to allow for more detailed responses. Respondents in adopting organizations also rated the perceived sustainability of continued acamprosate use.

Data analysis

Descriptive statistics were calculated for all quantitative variables. To compare adopters of acamprosate to nonadopters on organizational characteristics, chi-square tests and *t* tests were used to identify statistically significant differences between these two groups ($p < .05$, two-tailed tests). Open-ended responses to questions about organizational processes related to the implementation of acamprosate were examined for key themes, and frequencies of response consistent with these themes were counted.

For our multivariate model of acamprosate adoption, we used logistic regression in Stata Version 13 (StataCorp LP, College Station, TX). Before estimating the logistic regression model, we implemented multiple imputation by chained equations using the “mi impute chained” command; this approach avoids the methodological limitations associated with listwise deletion (Allison, 2002, 2009). Listwise deletion would have resulted in the loss of 8.1% ($n = 25$) of organizations in the sample. The mi impute chained command draws extensively on the earlier work of Royston (2004, 2005a, 2005b) and estimates a series of iterative univariate imputation models based on the other variables in the model. A key strength of mi impute chained is that the appropriate link function can be specified for each variable with missing data (e.g., logistic regression for dichotomous variables, linear regression for continuous variables). Variables with the least missing data are imputed before variables with greater proportions of missing data (StataCorp, 2011). Our use of “mi impute chained” resulted in 20 data sets. The “mi estimate” command was used during estimation of the logistic regression model of acamprosate adoption to pool the results from each of the 20 imputed data sets.

Results

Organizational characteristics for the sample of AUD treatment organizations appear in Table 1. Few organizations were owned by governmental agencies or located within hospitals, and only about one in five organizations operated on a for-profit basis. More intensive levels of care, such as inpatient or residential, were less likely to be offered than intensive outpatient or standard outpatient treatment. The average number of physicians on staff was less than one, and

nearly 40% of centers lacked access to physicians through either employment or contractual relationships. Other structural and staffing characteristics are presented in Table 1.

Information dissemination, adoption, and rate of implementation of acamprosate

As seen in Table 2, the majority of treatment organizations (70.7%) reported that they had heard or read about acamprosate for treating AUDs. When queried about specific sources of information, none of the dissemination sources was endorsed by more than one third of organizations. The average treatment organization endorsed slightly more than one of the five dissemination sources ($M = 1.4$, $SD = 1.5$).

The adoption of acamprosate, defined as the current use of this medication to treat AUDs, was reported by 18.0% ($n = 55$) of 305 sampled organizations that provided data on medication adoption. Nonadoption of acamprosate generally reflected the absence of pharmacological treatment in the center (57.4%; $n = 175$). The remaining nonadopters were programs that offered other SUD medications but not acamprosate (19.0%; $n = 58$) and “discontinuers,” or those reporting use of acamprosate in the past but not currently (5.6%; $n = 17$).

Comparisons of adopters and nonadopters revealed several differences in organizational characteristics (Table 1). Differences (e.g., location in a hospital setting, provision of inpatient detoxification, and employment of physicians and medical extenders) suggested a more medicalized orientation among acamprosate adopters. Adopting organizations were also more likely to be accredited and to employ a greater proportion of master’s-level counselors. Organizations that offered acamprosate reported less reliance on public (non-Medicaid) funding than nonadopters.

Adopters and nonadopters also differed significantly in their contact with dissemination sources about acamprosate (Table 2). Adopters were more likely than nonadopters to have heard or read about acamprosate from each of the five dissemination sources, resulting in a mean number of dissemination sources that was significantly greater. Although all five of the dissemination sources differed between adopters and nonadopters, the difference in pharmaceutical detailing through telephone or office visits between these two groups was particularly large, reflecting a nearly fourfold difference.

Variables that differed between adopters and nonadopters were entered into a multivariate logistic regression model of acamprosate adoption (Table 3). Four variables were significantly associated with adoption. First, the likelihood of acamprosate adoption was more than three times greater in organizations that had received accreditation from an external body (e.g., Joint Commission, Commission on the Accreditation of Rehabilitation Facilities, Commission on Accreditation) than nonaccredited organizations (odds ratio

TABLE 1. Organizational characteristics of alcohol use disorder treatment organizations

Variable	All centers % (n) or M (SD)	Adopters % (n) or M (SD)	Nonadopters % (n) or M (SD)
Structural characteristics			
Government owned	9.1% (28)	12.7% (7)	8.4% (21)
For profit	21.2% (65)	14.6% (8)	22.8% (57)
Located in a hospital setting*	11.7% (36)	20.0% (11)	10.0% (25)
Operates additional locations	59.2% (180)	64.8% (35)	57.7% (143)
Accredited***	38.8% (119)	69.1% (38)	32.0% (80)
% past-year revenues from Medicaid	18.6 (26.0)	22.6 (24.7)	17.0 (25.8)
% past-year revenues from other public sources (block grant, other federal/state/local government, criminal justice)**	48.3 (35.3)	35.8 (35.6)	52.2 (34.5)
Levels of care			
Offers inpatient detoxification**	16.3% (50)	30.9% (17)	13.2% (33)
Offers inpatient treatment	11.4% (35)	18.2% (10)	10.0% (25)
Offers residential treatment	27.8% (85)	23.6% (13)	28.8% (72)
Offers partial hospitalization/day treatment**	10.1% (31)	21.8% (12)	7.6% (19)
Offers intensive outpatient treatment	48.4% (148)	54.6% (30)	46.8% (117)
Offers outpatient treatment	73.5% (225)	76.4% (42)	72.8% (182)
Number of levels of care (range: 0–6)**	1.8 (1.2)	2.3 (1.2)	1.8 (1.1)
Staffing characteristics			
Number of physicians on staff***	0.7 (2.1)	2.0 (3.7)	0.4 (1.4)
Typology of physician employment***			
At least 1 medical doctor on staff	28.2% (86)	63.0% (34)	20.5% (51)
At least 1 medical doctor on contract	32.5% (99)	27.8% (15)	33.3% (83)
No access to physicians	39.3% (120)	9.3% (5)	46.2% (115)
Employs any medical extenders with prescribing privileges***	18.2% (55)	40.7% (22)	12.6% (31)
Number of counselors on staff	12.1 (51.7)	13.5 (20.0)	11.9 (56.6)
Percentage of counselors with master's-level degree or higher**	45.6 (35.0)	57.8 (33.0)	42.8 (35.0)

Notes: Adopters and nonadopters were compared using *t* tests and chi-square tests depending on the level of measurement.

* $p < .05$; ** $p < .01$; *** $p < .001$ (two-tailed tests).

[OR] = 3.14, 95% CI [1.38, 7.14], $p < .01$). Second, organizations with at least one physician on staff were significantly more likely than those with contracted physician(s) to have adopted acamprosate (OR = 2.58, 95% CI [1.09, 6.12], $p < .05$); the difference in acamprosate adoption between organizations with contracted physician(s) and those with no access to physicians was not significant. Finally, two dissemination sources were positively associated with acamprosate adoption. Organizations reporting any pharmaceutical detailing (e.g., office visits, telephone calls) were nearly six times more likely to have adopted acamprosate than programs reporting no pharmaceutical detailing (OR = 5.76, 95% CI [2.42, 13.60], $p < .001$). The odds of acamprosate adoption were also significantly greater in programs reporting that they had heard about this medication from other treatment providers (OR = 3.41, 95% CI [1.52, 7.66], $p < .01$).

Within adopting organizations, the average rate of implementation, defined as the percentage of AUD patients who were receiving acamprosate on the day of the interview, was quite low, encompassing just 6.0% of AUD patients ($SD = 10.0$). To further understand implementation, we asked respondents about the percentage of AUD patients who were considered to be candidates for receiving acamprosate; in the average program, about half of the AUD caseload was

considered to be candidates for acamprosate ($M = 47.5$, $SD = 38.4$). Of those candidates, less than a quarter actually received acamprosate at some point during their treatment episode ($M = 22.7$, $SD = 28.1$). Multiplying the percentage of AUD patients who were potential candidates by the percentage who actually received acamprosate at some point during treatment resulted in a treatment episode-level rate of implementation ($M = 8.5$, $SD = 13.2$) that was not significantly different from the average implementation reported for the day of the interview, paired $t(49) = 1.84$, $p = .07$.

Associations between the implementation rate on the day of the interview and organizational characteristics from Table 1 were examined (results not shown). Programs offering partial hospitalization reported significantly greater implementation ($M = 11.1$, $SD = 11.6$) than programs without this level of care ($M = 4.4$, $SD = 9.0$), $t(50) = -2.09$, $p < .05$. Other organizational characteristics were not associated with acamprosate implementation. Comparisons of implementation rate by the five sources of dissemination yielded no significant differences.

To consider whether the low rate of acamprosate implementation among adopters resulted from programs placing greater emphasis on implementing other medications for AUDs, we examined adoption and implementation of disul-

TABLE 2. Dissemination of information about acamprosate to alcohol use disorder treatment organizations

Variable	Full sample % (N) or M (SD)	Adopters % (N) or M (SD)	Nonadopters % (N) or M (SD)
Has heard or read about acamprosate***	70.7% (215)	100.0% (55)	64.3% (160)
Sources of information about acamprosate			
Journal articles or trade magazines***	33.2% (101)	54.6% (30)	28.5% (71)
Conferences or meetings**	32.9% (100)	52.7% (29)	28.5% (71)
Direct mailing***	14.5% (44)	30.9% (17)	10.8% (27)
Pharmaceutical detailing (telephone or office visits)***	24.3% (74)	63.6% (35)	15.7% (39)
Other treatment providers or physicians***	32.9% (100)	63.6% (35)	26.1% (65)
Number of sources of information endorsed***	1.4 (1.5)	2.7 (1.6)	1.1 (1.3)

Notes: Differences between adopters and nonadopters were tested with chi-square tests or *t* tests depending on the level of measurement.

p* < .01; *p* < .001 (two-tailed tests).

firm (Antabuse), tablet naltrexone, and extended-release depot naltrexone (Vivitrol) in this subset of organizations. Among the 55 acamprosate adopters, 45.5% (*n* = 25) also used disulfiram, 57.7% (*n* = 30) offered tablet naltrexone, and 35.3% (*n* = 18) had adopted extended-release depot naltrexone. Despite these seemingly high rates of adoption, the average level of implementation of these medications within adopting programs was actually quite low. Implementation of disulfiram in the subset of disulfiram adopters averaged 2.6% (*SD* = 5.0), naltrexone adopters averaged an implementation rate of 8.3% (*SD* = 18.4), and extended-release depot naltrexone adopters implemented this medication with just 4.5% of their AUD patients (*SD* = 8.7)

Despite the small proportion of AUD patients receiving acamprosate during their treatment episodes, treatment organizations reported strong intentions to sustain their adoption. About 76.4% (*n* = 42) of current adopters indicated that

they were very likely to continue to offer acamprosate in the future; an additional 16.4% (*n* = 9) indicated that they were somewhat likely to sustain acamprosate as a treatment option. Only 7.3% (*n* = 4) reported that they were undecided or unlikely to sustain their adoption of acamprosate over time.

Implementation issues for acamprosate

To further describe the implementation of acamprosate, respondents from adopting organizations were asked a series of closed- and open-ended questions focused on organizational processes related to the use of this medication. Key organizational processes included candidate selection, patient education, and counselor training. The majority of respondents (77.8%; *n* = 42) reported that at least some AUD patients were reluctant to add acamprosate to their treatment plan. About 63.5% (*n* = 33) of respondents indi-

TABLE 3. Multivariate logistic regression model organizational characteristics on acamprosate adoption

Variable	<i>b</i> (SE)
Organizational characteristics	
Located in a hospital setting	-0.24 (0.56)
Accredited	1.14 (0.42)**
Number of treatment levels of care	0.11 (0.16)
% past-year revenues from other public sources	-0.01 (0.01)
Staffing characteristics	
Typology of physician employment	
At least 1 medical doctor on staff	0.95 (0.44)*
At least 1 medical doctor on contract	ref.
No access to physicians	-0.91 (0.60)
Employs any medical extenders with prescribing privileges	0.70 (0.44)
Percentage of counselors with master's-level degree or higher	0.00 (0.01)
Sources of information about acamprosate	
Journal articles or trade magazines	0.02 (0.48)
Conferences or meetings	0.06 (0.49)
Direct mailing	-0.39 (0.53)
Pharmaceutical detailing (telephone or office visits)	1.75 (0.44)***
Other treatment providers or physicians	1.23 (0.41)**
Constant	-3.52 (0.71)***

Note: Ref. = reference.

p* < .05; *p* < .01; ****p* < .001 (two-tailed tests).

cated that certain types of patients were considered to be “poor candidates” for receiving acamprosate. When asked to qualitatively describe such patients, the most common responses could be characterized as descriptions of patients with potential medical complications (e.g., pregnancy, allergy, interactions with other medications; $n = 14$). In contrast, about 38.5% ($n = 20$) of respondents reported that there were certain types of patients for whom acamprosate was “more successful.” There were two themes in the responses to an open-ended question about the characteristics of these “more successful” patients. The first theme consisted of responses regarding motivation ($n = 6$) in which respondents mentioned that successful patients were those who were motivated and could comply with the regimen (e.g., thrice daily dosing). The other theme ($n = 7$) revolved around responses that had an element of temporality, such as patients who were older, had a longer history of AUDs, or had a history of prior treatment failures. In addition to these descriptions of potential candidates, the cost associated with implementing acamprosate was frequently cited as a factor in patient selection for this medication (63.6% of respondents; $n = 35$).

The implementation of acamprosate also includes formal processes that support its use in clinical practice. Two formal processes with an educational focus were patient education and requiring counselors to be trained about acamprosate. Most organizations (81.8%; $n = 45$) that had adopted acamprosate reported that they provided AUD patients with written materials regarding this medication. However, only about half of the respondents in adopting programs indicated that counselors were provided with training about acamprosate (50.9%; $n = 28$), and even fewer required all counselors to participate in this training (20.4%; $n = 11$).

Such training has increased significance given that, in some programs, counselors may provide clinical support in implementing acamprosate. In response to an open-ended question regarding how patients were introduced to acamprosate as a treatment option, mentions of the involvement of counselors or medical providers in introducing acamprosate were counted. Although discussions with medical providers (e.g., psychiatrist, physician, nurse practitioner) were mentioned in the majority of responses (69.1%; $n = 38$), about 34.5% of respondents ($n = 17$) specifically noted that counselors were involved in the process of introducing acamprosate to patients.

For respondents who indicated that some patients were reluctant to receive acamprosate ($n = 42$; 76.4% of adopters), an additional open-ended question asked how patient reluctance was addressed. The most common responses referred to patient education about this treatment option ($n = 16$; e.g., providing information about acamprosate, describing how other patients have benefited from it) and interactive discussions ($n = 15$; e.g., counseling, discussing concerns, offering supportive guidance, using interventions to enhance motivation). A few respondents mentioned that

patient reluctance was linked to the cost of acamprosate ($n = 3$) or philosophical resistance to pharmacotherapy ($n = 3$).

Perceived patient compliance with acamprosate and clinical processes to support adherence were also measured. Respondents were asked to rate the extent to which patient compliance was an issue in implementing acamprosate on a scale in which 0 represented *no extent* and 5 represented *a very great extent*. The average response approached the midpoint of this scale ($M = 2.7$, $SD = 1.6$), indicating that medication compliance was perceived as somewhat problematic. When asked an open-ended question about what types of efforts were made to enhance compliance, the predominant theme ($n = 32$) centered on additional education, support, and motivational enhancement through discussions with the patient; 12 respondents specifically noted that this role was performed by counselors or occurred within therapy sessions. Some respondents ($n = 16$) described examples of intensifying treatment through supervised dosing, increased frequency of appointments with medical staff, or reminder calls. Finally, a minority of respondents ($n = 6$) indicated that the program made no specific efforts to increase medication compliance.

The implementation of acamprosate generally occurred within the context of other SUD treatments. About 90.9% ($n = 50$) of respondents indicated that acamprosate was delivered in conjunction with other treatments, such as therapy or psychotropic medications. When asked to further describe the other treatments, nearly all ($n = 49$) described counseling services—group counseling, individual counseling, or specific types of therapy—delivered by staff at the treatment center. The specific therapy most commonly mentioned was behavioral or cognitive-behavioral therapy ($n = 32$). Less frequently mentioned therapies included motivational interviewing ($n = 9$) or 12-step counseling ($n = 5$). Other medications (e.g., antidepressant and anti-anxiety medications) were mentioned by 10 respondents.

Discussion

Adoption and implementation of acamprosate continues to be limited within the specialty AUD treatment sector. Despite the promise indicated by clinical trials and by FDA approval, fewer than one in five treatment programs has adopted acamprosate for treating AUDs. Acamprosate-adopting organizations differed significantly from nonadopters on a range of organizational characteristics, but our multivariate model indicated that adoption was associated with two key organizational variables: access to physicians and accreditation.

The finding regarding physicians on staff is consistent with prior work on the diffusion of medications to treat SUDs; clearly, physicians are a necessary resource for delivering this service. In addition to prescribing acamprosate, our qualitative information indicates that physicians are key

catalysts for introducing acamprosate as a treatment option to patients.

Our analysis was also novel in its consideration of medical extenders with prescribing privileges as a potential mechanism for acamprosate adoption. At the bivariate level, the employment of medical extenders with prescribing privileges also differed between adopters and nonadopters but was not significant in the multivariate model. Closer examination of the data revealed that the presence of medical extenders was most common in programs with at least one physician on staff and relatively rare in programs with no access to physicians. Thus, there is little evidence that medical extenders are being used as a strategy to overcome limited access to physicians.

We also expanded on prior models of medication adoption to consider whether specific mechanisms of dissemination were associated with the availability of acamprosate. Our multivariate analysis indicated that active, interpersonal methods of dissemination, specifically detailing by pharmaceutical representatives and communication with other providers, were positively associated with adoption. The finding about pharmaceutical detailing is consistent with prior studies in which we examined detailing and adoption of any medications to treat SUDs (Knudsen et al., 2010) as well as the broader literature on detailing in health care (Ching and Ishihara, 2012; Fischer et al., 2009; Huddle, 2008; Katz et al., 2010; Mizik and Jacobson, 2004; Narayanan et al., 2004; Velasco et al., 2011). The positive association between communication with other providers and acamprosate adoption aligns with Rogers's classic Diffusion of Innovations (2003) theory, which noted the value of interpersonal networks of relationships in furthering innovation adoption. What remains to be seen is whether these findings about the potential value of interpersonal methods of dissemination could be used to inform the development of strategies that could be subjected to rigorous testing of their impact on medication adoption decisions by treatment organizations.

This study also revealed that more passive forms of information dissemination (e.g., publications, conferences, mailings) were not significantly associated with adoption once other variables were controlled. This finding is not altogether unexpected, given prior research in other health care settings about the limitations of passive types of dissemination in achieving innovation adoption (Colditz, 2012). It may raise a question about the types of dissemination that should be emphasized and supported by key stakeholders, such as SAMHSA (including the Center on Substance Abuse Treatment's Addiction Technology Transfer Centers), the National Institute on Drug Abuse, and the National Institute on Alcohol Abuse and Alcoholism. However, additional research is needed regarding the impact of these less intensive and less expensive methods of dissemination, because their effect on adoption and implementation decisions has not been rigorously tested within SUD treatment organizations.

Within adopting programs, the rate of implementation was less than 10% of AUD patients, a finding that is consistent with prior studies about the limited implementation of medications in SUD treatment. Qualitative findings suggest that limited implementation may reflect processes of patient selection that exclude nearly half of AUD patients from consideration as candidates for this medication. Even among those AUD patients considered candidates, only a quarter receive acamprosate at some point during their treatment episode.

To some extent, this limited rate of implementation may reflect the lack of empirical guidance regarding patient selection and strategies for improving medication adherence. Our qualitative data suggest a degree of floundering, confusion, and inconsistency in decision-making about acamprosate use on the front lines, despite the availability of clinical practice guidelines (Center for Substance Abuse Treatment, 2009; Fishman et al., 2010). Research regarding the optimal pairings of psychosocial interventions and medication adherence strategies, and subsequent dissemination of such findings to the field, may improve implementation within treatment programs. Furthermore, there is an urgent need for implementation research that explicitly tests the impact of specific approaches to increase the reach of this medication.

An additional caveat is the necessary recognition that although acamprosate may constitute an evidence-based practice, the magnitude of its effect on abstinence is somewhat limited. A recent meta-analysis notes that the number of persons required to be treated with acamprosate to achieve one additional case of abstinence is between seven and eight people (Maisel et al., 2013); this result is similar to those of prior reviews (Rösner et al., 2010, 2011). The extent to which this limited effectiveness is perhaps reducing the likelihood of prescribing decisions is unknown. At the same time, the broader medical literature shows that, to achieve a desired outcome or to prevent an undesirable one in a single person, many individuals may need to undergo treatment (Kumana et al., 1999; Omorphos et al., 2004; Suissa, 2013). Nonetheless, the coupling of needing to treat a significant number of patients with low levels of acamprosate implementation has likely circumscribed the public health impact of this medication.

These data did not indicate that limited implementation of acamprosate reflected greater reliance on other AUD medications. Within programs that had adopted acamprosate and other AUD medications, the rates of implementation for those alternative medications was also quite low. Taken together, these findings highlight the need for additional research to expand our understanding about why implementation of acamprosate and other AUD medications is so limited within treatment organizations that have overcome the barriers to medication adoption. An important avenue for future research is to gather information from physicians regarding the decision to prescribe acamprosate to AUD patients.

Seminal work by Mark and colleagues (2003) collected physician-level data about naltrexone and disulfiram, but their work was conducted before the availability of acamprosate. Qualitative methods may offer an opportunity to gain considerable information about the factors that physicians consider before prescribing medications to AUD patients. Much could be learned about acamprosate implementation by addressing the perspectives of prescribers as well as patients.

There are a number of limitations related to the study design that should be noted. First, these data were collected at a single point in time, so causal relationships could not be examined. We are in the midst of collecting longitudinal data from this panel of programs, which will improve our ability to test causal relationships in future research. However, these cross-sectional data make novel contributions, particularly with regard to descriptive information about how acamprosate is implemented as a treatment adjunct within AUD organizations. In addition to the limitation of cross-sectional data, another limitation is that all measures were framed at the organizational level and were obtained from a single key informant; no data were collected directly from patients, physicians, or medical records. Reviewing medical records, in particular, could identify patterns of prescription of acamprosate (or lack thereof) that would expand our understanding of medication implementation. Consideration of these other sources of data represents an important direction for future research. Finally, although our sample was nationally representative with regard to facilities offering specialty AUD treatment to the general public, these findings may not generalize to organizations that are embedded within other sectors (e.g., the Veterans Affairs system, treatment programs in correctional organizations, or practitioners in private practice).

Despite the many efforts aimed at expanding the use of evidence-based practices in SUD treatment in the past decade, adoption and implementation of acamprosate for treating AUDs in specialty treatment organizations remains limited. Acamprosate may not work for all patients, but the generally limited access to this medication for patients in specialty care likely limits the potential public health impact of this adjunct to treatment. Future research should examine whether there are implementation strategies that can increase the use of this medication and others as part of the treatment process while integrating the perspectives of organizational leaders, medical professionals, and patients.

References

Abraham, A. J., Knudsen, H. K., Rothrauff, T. C., & Roman, P. M. (2010). The adoption and implementation of alcohol pharmacotherapies in the Clinical Trials Network: The influence of research network participation. *Journal of Substance Abuse Treatment, 38*, 275–283.

Allison, P. D. (2002). *Missing data*. Thousand Oaks, CA: Sage.

Allison, P. D. (2009). Missing data. In R. E. Millsap & A. Maydeu-Olivares

(Eds.), *The SAGE handbook of quantitative methods in psychology* (pp. 72–89). Thousand Oaks, CA: Sage.

Anton, R. F., O'Malley, S. S., Ciraulo, D. A., Cisler, R. A., Couper, D., Donovan, D. M., . . . Zweben, A., for the COMBINE Study Research Group. (2006). Combined pharmacotherapies and behavioral interventions for alcohol dependence—The COMBINE study: A randomized controlled trial. *Journal of the American Medical Association, 295*, 2003–2017.

Boothby, L. A., & Doering, P. L. (2005). Acamprosate for the treatment of alcohol dependence. *Clinical Therapeutics, 27*, 695–714.

Carmen, B., Angeles, M., Ana, M., & Maria, A. J. (2004). Efficacy and safety of naltrexone and acamprosate in the treatment of alcohol dependence: A systematic review. *Addiction, 99*, 811–828.

Carroll, K. M., Kosten, T. R., & Rounsaville, B. J. (2004). Choosing a behavioral therapy platform for pharmacotherapy of substance users. *Drug and Alcohol Dependence, 75*, 123–134.

Center for Substance Abuse Treatment. (2009). *Incorporating alcohol pharmacotherapies into medical practice (Treatment Improvement Protocol #49)*. Rockville, MD: Substance Abuse and Mental Health Services Administration.

Ching, A. T., & Ishihara, M. (2012). Measuring the informative and persuasive roles of detailing on prescribing decisions. *Management Science, 58*, 1374–1387.

Colditz, G. A. (2012). The promise and challenge of dissemination and implementation research. In R. C. Brownson, G. A. Colditz, & E. K. Proctor (Eds.), *Dissemination and implementation research in health* (pp. 3–22). New York, NY: Oxford University Press.

Donovan, D. M., Anton, R. F., Miller, W. R., Longabaugh, R., Hosking, J. D., & Youngblood, M. (2008). Combined pharmacotherapies and behavioral interventions for alcohol dependence (The COMBINE Study): Examination of posttreatment drinking outcomes. *Journal of Studies on Alcohol and Drugs, 69*, 5–13.

Ducharme, L. J., Knudsen, H. K., & Roman, P. M. (2006). Trends in the adoption of medications for alcohol dependence. *Journal of Clinical Pharmacology, 26*, S13–S19.

Fischer, M. A., Keough, M. E., Baril, J. L., Saccoccio, L., Mazor, K. M., Ladd, E., . . . Gurwitz, J. H. (2009). Prescribers and pharmaceutical representatives: Why are we still meeting? *Journal of General Internal Medicine, 24*, 795–801.

Fishman, M. J., Shulman, G. D., Mee-Lee, D., Kolodner, G., & Wilford, B. B. (Eds.). (2010). *ASAM patient placement criteria: Supplement on pharmacotherapies for alcohol use disorders*. Philadelphia, PA: Lippincott Williams & Wilkins.

Huddle, T. S. (2008). Drug reps and the academic medical center—a case for management rather than prohibition. *Perspectives in Biology and Medicine, 51*, 251–260.

Katz, D., Caplan, A. L., & Merz, J. F. (2010). All gifts large and small: Toward an understanding of the ethics of pharmaceutical industry gift-giving. *American Journal of Bioethics, 10*, 11–17.

Kiefer, F., Jahn, H., Tarnaske, T., Helwig, H., Briken, P., Holzbach, R., . . . Wiedemann, K. (2003). Comparing and combining naltrexone and acamprosate in relapse prevention of alcoholism: A double-blind, placebo-controlled study. *Archives of General Psychiatry, 60*, 92–99.

Knudsen, H. K., Abraham, A. J., & Roman, P. M. (2011). Adoption and implementation of medications in addiction treatment programs. *Journal of Addiction Medicine, 5*, 21–27.

Knudsen, H. K., Roman, P. M., & Oser, C. B. (2010). Facilitating factors and barriers to the use of medications in publicly funded addiction treatment organizations. *Journal of Addiction Medicine, 4*, 99–107.

Kumana, C. R., Cheung, B. M., & Lauder, I. J. (1999). Gauging the impact of statins using number needed to treat. *Journal of the American Medical Association, 282*, 1899–1901.

Maisel, N. C., Blodgett, J. C., Wilbourne, P. L., Humphreys, K., & Finney, J. W. (2013). Meta-analysis of naltrexone and acamprosate for treating

- alcohol use disorders: When are these medications most helpful? *Addiction*, 108, 275–293.
- Manuel, J. K., Hagedorn, H. J., & Finney, J. W. (2011). Implementing evidence-based psychosocial treatment in specialty substance use disorder care. *Psychology of Addictive Behaviors*, 25, 225–237.
- Mark, T. L., Kranzler, H. R., Song, X., Bransberger, P., Poole, V. H., & Crosse, S. (2003). Physicians' opinions about medications to treat alcoholism. *Addiction*, 98, 617–626.
- McLellan, A. T., & McKay, J. R. (2009). Integrating evidence-based components into a functional continuum of care. In R. K. Ries, D. A. Fiellin, S. C. Miller, & R. Saitz (Eds.), *Principles of addiction medicine* (4th ed., pp. 361–378). Baltimore, MD: Lippincott, Williams, and Wilkins.
- Mee-Lee, D., Gartner, L., Miller, M. M., Shulman, G. R., & Wilford, B. B. (1996). *Patient placement criteria for the treatment of substance-related disorders* (2nd ed.). Chevy Chase, MD: American Society of Addiction Medicine.
- Mizik, N., & Jacobson, R. (2004). Are physicians "easy marks"? Quantifying the effects of detailing and sampling on new prescriptions. *Management Science*, 50, 1704–1715.
- Morley, K. C., Teesson, M., Reid, S. C., Sannibale, C., Thomson, C., Phung, N., . . . Haber, P. S. (2006). Naltrexone versus acamprosate in the treatment of alcohol dependence: A multi-centre, randomized, double-blind, placebo-controlled trial. *Addiction*, 101, 1451–1462.
- Narayanan, S., Desiraju, R., & Chintagunta, P. K. (2004). Return on investment implications for pharmaceutical promotional expenditures: The role of marketing-mix interactions. *Journal of Marketing*, 68, 90–105.
- National Institute on Drug Abuse. (2009). *Principles of drug addiction treatment: A research-based guide* (NIH Publication No. 09-4180). Rockville, MD: Author.
- Omorpos, S., Hanif, M., & Dunning, J. (2004). Are prophylactic beta-blockers of benefit in reducing the incidence of AF following coronary bypass surgery? *Interactive Cardiovascular and Thoracic Surgery*, 3, 641–646.
- Richardson, K., Baillie, A., Reid, S., Morley, K., Teesson, M., Sannibale, C., . . . Haber, P. (2008). Do acamprosate or naltrexone have an effect on daily drinking by reducing craving for alcohol? *Addiction*, 103, 953–959.
- Rogers, E. M. (2003). *Diffusion of innovations* (5th ed.). New York, NY: Free Press.
- Roman, P. M., Abraham, A. J., & Knudsen, H. K. (2011). Using medication-assisted treatment for substance use disorders: Evidence of barriers and facilitators of implementation. *Addictive Behaviors*, 36, 584–589.
- Rösner, S., Hackl-Herrwerth, A., Leucht, S., Leher, P., Vecchi, S., & Soyka, M. (2011). Acamprosate for alcohol dependence. *Cochrane Database of Systematic Reviews, Issue 9*, Article No. CD004332.
- Rösner, S., Hackl-Herrwerth, A., Leucht, S., Vecchi, S., Srisurapanont, M., & Soyka, M. (2010). Opioid antagonists for alcohol dependence. *Cochrane Database of Systematic Reviews, Issue 12*, Article No. CD001867.
- Royston, P. (2004). Multiple imputation of missing values. *The Stata Journal*, 4, 227–241.
- Royston, P. (2005a). Multiple imputation of missing values: Update. *The Stata Journal*, 5, 188–201.
- Royston, P. (2005b). Multiple imputation of missing values: Update of ice. *The Stata Journal*, 5, 527–536.
- Samet, J. H., Friedmann, P., & Saitz, R. (2001). Benefits of linking primary medical care and substance abuse services: Patient, provider, and societal perspectives. *Archives of Internal Medicine*, 161, 85–91.
- Sorensen, J. L., Hetteima, J. E., & Larios, S. (2009). What is evidence-based treatment? In P. M. Miller (Ed.), *Evidence-based addiction treatment* (pp. 3–20). Burlington, MA: Academic Press.
- StataCorp. (2011). *Stata multiple-imputation reference manual: Release 12*. College Station, TX: Stata Press.
- Suissa, S. (2013). Number needed to treat in COPD: Exacerbations versus pneumonias. *Thorax*, 68, 540–543.
- Velasco, E., Espelage, W., Faber, M., Noll, I., Ziegelmann, A., Krause, G., . . . Eckmanns, T. (2011). A national cross-sectional study on socio-behavioural factors that influence physicians' decisions to begin antimicrobial therapy. *Infection*, 39, 289–297.
- Whitworth, A. B., Fischer, F., Lesch, O. M., Nimmerrichter, A., Oberbauer, H., Platz, T., . . . Fleischhacker, W. W. (1996). Comparison of acamprosate and placebo in long-term treatment of alcohol dependence. *The Lancet*, 347, 1438–1442.