Integrated psychosocial and opioid-antagonist treatment for alcohol dependence: A systematic review of controlled evaluations

Michael G. Vaughn and Matthew O. Howard

Methodological characteristics and outcomes of 14 controlled clinical investigations of integrated psychosocial and opioid-antagonist alcohol dependence treatment were evaluated. The 14 studies were identified through computerized bibliographic and manual literature searches. Clients receiving integrated psychosocial and opioid-antagonist treatment had outcomes superior to those of clients receiving monotherapy (generally placebo and standard psychosocial treatment). Rates of relapse, levels of self-reported alcohol craving, and extent of posttreatment alcohol consumption were significantly reduced in clients receiving integrated therapy relative to controls. However, the long-term efficacy of integrated psychosocial and opioid-antagonist alcohol dependence treatment was not established, and client factors associated with the differential effectiveness of integrated interventions were not identified.

Key words: **alcohol dependence; evidence-based practice; integrated treatments; naltrexone; systematic review**

Michael G. Vaughn, MA, MALS, is a NIDA fellow and doctoral student, and ***Matthew O. Howard, PhD,*** *is associate professor, Comorbidity and Addictions Center, George Warren Brown School of Social Work, Washington University, One Brookings Drive, Campus Box 1196, St. Louis, MO 63130-4899. Please send all correspondence to Dr. Howard; e-mail: howard@gwbmail.wustl.edu.*

Effective treatments for alcohol abuse and dependence are critically needed given the substantial prevalence of these disorders nationally and the manifold deleterious consequences attending habitual alcohol use (Sammons & Schmidt, 2001). Epidemiological findings indicate that approximately 9.3% to 13.4% of men and 3.0% to 4.4% of women meet *Diagnostic and Statistical Manual of Mental Disorders* criteria for alcohol use disorders in any given year (DSM-IV-TR) (American Psychiatric Association [APA], 2000; Caetano & Tam, 1995; Grant, Harford, Dawson, et al., 1994; Grant, Harford, Hasin, Chou, & Pickering, 1992). Annual costs of alcohol-related health and social problems in the United States exceed $185 billion (National Institute on Alcohol Abuse and Alcoholism, 2000).

Alcohol use disorders are especially debilitating to the vulnerable client populations social workers serve (Hester & Miller, 2002). Thus, it is important that practitioners be aware of the most effective approaches to alcohol dependence treatment (Nathan, Gorman, & Salkind, 1999). In a seminal study attempting to identify treatments that work for this population, Miller and colleagues (1995) found little or no empirical support for nearly three-quarters of the 43 alcohol dependence treatment modalities they evaluated. Among the most effective interventions they identified were a variety of psychosocial and cognitive–behavioral approaches, including brief interventions, skills training, behavior contracting, motivational enhancement therapy, and the community reinforcement approach. Opioid-antagonist medications had not emerged as potential treatments for alcohol dependence at the time Miller and colleagues conducted their comprehensive review.

Early studies indicating that the opioid-antagonist naltrexone was nontoxic and appeared to reduce craving for alcohol and posttreatment alcohol

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consumption led to more widespread application of naltrexone pharmacotherapy with alcoholics. Increasingly, psychosocial and opioid-antagonist treatments are considered complementary (Volpicelli, Pettinati, McLellan, & O'Brien, 2001), and growing support for integrated treatments has emerged for a range of mental health disorders (Sammons & Schmidt, 2001). Psychosocial interventions used in association with opioid-antagonist medications include individualized manual-based cognitive–behavioral therapies focusing on coping skills, relapse prevention training, and abstinence reinforcement. Psychosocial and behavioral interventions have also been used to help alcohol-dependent clients initiate behavior change, be compliant with pharmacotherapeutic regimens, manage negative emotions, and increase environmental supports.

The best known and most widely researched opioid-antagonist medications are naltrexone and nalmefene (Volpicelli et al., 1997). These agents are nonaddictive, produce few side effects, and appear to reduce craving for alcohol and the pleasurable effects associated with alcohol's stimulation of the endogenous opioid system and related reward systems should drinking occur (Greenstein, Fudala, & O'Brien, 1997). Naltrexone (ReVia) is the primary opioid-antagonist medication in clinical use. Standard oral dosage is 50 mg per day; however, doses of 25 to 100 mg or higher can be used. In principle, opioid antagonists can help clients achieve periods of abstinence from alcohol during which newly learned skills can be consolidated. Many supporters of opioid-antagonist treatment view these agents as adjunctive therapies and emphasize the key role of psychosocial interventions in integrated treatment protocols. This systematic review critically evaluated the methodological quality and outcomes of controlled studies that evaluated integrated psychosocial and opioid-antagonist alcohol dependence treatment.

METHOD

Search Strategy

The initial study objective was to identify all published controlled trials of integrated psychosocial and opioid-antagonist treatment for alcohol-dependent clients. No evaluations of acamprosate, disulfiram, or nonopioid-antagonist medications used for alcohol dependence treatment were included unless groups treated with these agents served as controls for comparisons with groups receiving opioid antagonists. Only treatment, as opposed to safety, outcomes were examined, and all study participants met DSM-IV-TR criteria for alcohol dependence (APA, 2000).

The databases searched included *Medline* (1966–June 2002), *PsychInfo* (1964–June 2002), the Cochrane Library of Systematic Reviews and the Cochrane Controlled Trials Register. Also, a National Library of Medicine computerized bibliographic search using 38 lines of code used in an earlier Cochrane review of opiate-antagonist treatment (that did not examine the effectiveness of integrated therapies) was conducted. Web sites such as those of the National Institute of Alcohol Abuse and Alcoholism (www.niaaa.nih.gov), National Clearinghouse for Alcohol and Drug Information (www.health.org), ClinicalTrials.gov (www.clinicaltrials.gov), and the former Agency for Health Care Policy and Research (www.ahcpr.gov) were also searched. We also conducted manual searches of the reference sections of identified studies, other relevant articles, reference sections of recent pertinent book titles, and government documents related to this area. Key word searches included the following descriptors: "naltrexone," "nalmefene," "alcohol dependence," "alcohol use disorders," "alcoholism," "psychosocial interventions," "psychosocial treatments," "behavioral interventions," "behavioral treatments," "psychotherapy," "community-based interventions," "randomized controlled trials," and "controlled clinical trials." Abstracts of 278 articles were retrieved and screened for relevance. Findings from 14 investigations published between 1992 and 2001 in 18 journal articles constituted the final study sample.

Methodological Quality of Integrated Alcohol Dependence Treatment Studies

Miller and colleagues' (1995; 2002) Methodological Quality Rating Scale (MQRS) was used to assess the methodological characteristics of studies of integrated alcohol dependence treatment; this instrument measures 12 dimensions of methodological quality assessed by the MQRS (see Table 1). Each study was assessed for the presence (+1 or +2 points) or absence (0 points) of the 12 methodological attributes. The total number of points a study could receive ranged from 0 (very poor quality) to 16 (exceptionally high quality). Study methodological characteristics, intervention protocols, sample descriptions, and outcome findings were coded on an intervention review form. A subsample of seven (50%) controlled trials was assessed by the second author across the 12 MQRS dimensions; only four

TABLE 1—Methodological Quality Rating Scale

Methodological Attribute	Points Assigned
A. Study design	1 = Single group pretest–posttest
	2 = Quasi-experimental (nonequivalent control group)
	3 = Randomization with control group
B. Replicability	0 = Intervention/follow-up descriptions insufficiently detailed
	1 = Procedures contain sufficient detail
C. Baseline	0 = No baseline scores, client characteristics or measures reported
	1 = Baseline scores, client characteristics or measures reported
D. Quality control	0 = No intervention standardization specified
	1 = Intervention standardization by manual, procedures, specific training, and so forth
E. Follow-up length	0 = Less than 6 months
	1 = 6–11 months
	2 = 12 months or longer
F. Follow-up rate	0 = Less than 70% completion
	1 = 70–84.9% completion
	2 = 85–100% completion
G. Collaterals	0 = No collateral verification of participant self-report
	1 = Collaterals interviewed
H. Objective verification	0 = No objective verification of participant self-report
	1 = Verification of records (paper records, blood, materials, and so forth)
I. Dropouts	0 = No discussion or enumeration of dropouts or dropouts excluded from analysis
	1 = Intervention dropouts enumerated
J. Independent	0 = Follow-up conducted non-blind or by an unspecified method
	1 = Follow-up by person blind to participants' treatment condition
K. Analyses	0 = No statistical analyses conducted or clearly inappropriate analyses
	1 = Appropriate statistical analyses (group differences, characteristics comparable)
L. Multisite	0 = Single site study
	1 = Parallel replications at two or more sites

NOTE: Scores could range from 0 (low) to 16 (high).
SOURCE: Adapted from Miller, W. R., Brown, J. M., Simpson, T. L., Handmaker, N. S., Bien, T. H., Luckie, L. H., Montgomery, H. A., Hester, R. K., & Tonigan, J. S. (1995). What works? A methodological analysis of the alcohol treatment outcome literature. In R. K. Hester & W. R. Miller (Eds.), *Handbook of alcoholism treatment approaches: Effective alternatives* (2nd ed., pp. 12–44). Needham Heights, MA: Allyn & Bacon.

of 84 ratings of the two raters differed, yielding a Kappa statistic of .76.

RESULTS

Methodological Characteristics of Identified Reports

Of the 14 studies examined, 13 were randomized controlled trials (Table 2). Feeney, Young, and colleagues (2001) and Feeney, Conner, and colleagues (2001) used a quasi-experimental pretest–posttest design. Twelve studies provided sufficient methodological detail to permit replication; two studies did not report sufficient information about the psychosocial intervention (that is, Chick et al., 2000; Landabaso et al., 1999). Across studies, pharmacological interventions were described in greater detail than psychosocial interventions. However, most studies provided descriptions of psychosocial interventions adequate to support replication efforts. Baseline client characteristics were reported in every study but one (compare Landabaso et al.). Twelve studies implemented standardized intervention protocols using manuals, training, and prescribed dosage regimens.

Follow-up intervals ranged from three (10 studies) to 24 (1 study) months. Two studies reported six-month outcomes and two studies reported 12-months

TABLE 2—Methodological Characteristics of Studies of Integrated Psychosocial and Opiate Antagonist Treatment for Alcohol Dependence (*N* = 14 studies reported in 18 journal articles)

Study No.	Authors	Study Design	Replicability[a]	Baseline Score	Quality Control	Follow-up Length	Follow-up Rate (%)	Collaterals	Objective Records	Dropouts	Independent Follow-up	Analyses	Single or Multisite
1a	Anton et al. (1999)	RCT	Sufficient detail	Yes	Standardized	3 months	97.7	Yes	Yes	Enumerated	Follow-up non-blind	Appropriate statistical analyses	Single site
1b	Anton et al. (2001)	RCT	Sufficient detail	Yes	Standardized	6 months	94.6	Yes	Yes	Enumerated	Follow-up non-blind	Appropriate statistical analyses	Single site
2	Chick et al. (2000)	RCT	Insufficient detail (psychosocial component)	Yes	No standardization (psychosocial component)	3 months	81.1	No	Yes	Enumerated	Follow-up non-blind	Appropriate statistical analyses	Six sites
3a	Feeney, Young, et al. (2001)	Quasi-experimental	Sufficient detail	Yes	Standardized	3 months	100.0	No	Yes	Enumerated	Follow-up non-blind	Appropriate statistical analyses	Single site
3b	Feeney, Conner, et al. (2001)	Single group pretest–posttest	Sufficient detail	Yes	Standardized	3 months	100.0	No	Yes	Enumerated	Follow-up non-blind	Appropriate statistical analyses	Single site
4	Heinala et al. (2001)	RCT	Sufficient detail	Yes	Standardized	8 months	100.0	Yes	Yes	Enumerated	Follow-up non-blind	Appropriate statistical analyses	Single site
5	Kranzler et al. (2000)	RCT	Sufficient detail	Yes	Standardized	3 months	99.0	Yes	Yes	Enumerated	Follow-up non-blind	Appropriate statistical analyses	Single site
6	Landabaso et al. (1999)	RCT	Insufficient detail (psychosocial component)	No	No standardization	24 months	70.0	No	No	Enumerated	Follow-up non-blind	Appropriate statistical analyses	Single site
7	Mason et al. (1999)	RCT	Sufficient detail	Yes	Standardized	3 months	100.0	Yes	Yes	Enumerated	Follow-up blind	Appropriate statistical analyses	Single site
8	Monti et al. (2001)	RCT	Sufficient detail	Yes	Standardized	12 months	87.0	Yes	Yes	Enumerated	Follow-up non-blind	Appropriate statistical analyses	Single site

(continued)

TABLE 2—Continued

Study No.	Authors	Study Design	Replicability[a]	Baseline Score	Quality Control	Follow-up Length	Follow-up Rate (%)	Collaterals	Objective Records	Dropouts	Independent Follow-up	Analyses	Single or Multisite
9a	O'Malley, Jaffe, Rode, & Rounsaville (1992)	RCT	Sufficient detail	Yes	Standardized	3 months	93.2	Yes	Yes	Enumerated	Follow-up blind	Appropriate statistical analyses	Single site
9b	O'Malley, Jaffe, Chang, et al. (1996)	RCT	Sufficient detail	Yes	Standardized	6 months	82.4	Yes	Yes	Enumerated	Follow-up blind	Appropriate statistical analyses	Single site
9c	O'Malley, Jaffe, Rode, & Rounsaville (1996)	RCT	Sufficient detail	Yes	Standardized	3 months	97.6	No	Yes	Enumerated	Follow-up blind	Appropriate statistical analyses	Single site
10	Oslin et al. (1997)	RCT	Sufficient detail	Yes	Standardized	3 months	61.3	No	Yes	Enumerated	Follow-up non-blind	Appropriate statistical analyses	Single site
11	Pettinati et al. (2000)[b]	RCT	Sufficient detail	Yes	Standardized	3 months	100.0	Yes	Yes	Enumerated	Follow-up blind	Appropriate statistical analyses	Single site
12	Rubio et al. (2001)	RCT	Sufficient detail	Yes	Standardized	12 months	83.4	Yes	Yes	Enumerated	Follow-up blind	Appropriate statistical analyses	Single site
13	Volpicelli et al. (1992)	RCT	Sufficient detail	Yes	Standardized	3 months	92.8	No	Yes	Enumerated	Follow-up blind	Appropriate statistical analyses	Single site
14	Volpicelli et al. (1997)	RCT	Sufficient detail	Yes	Standardized	3 months	100.0	No	Yes	Enumerated	Follow-up blind	Appropriate statistical analyses	Single site

NOTE: RCT = randomized controlled trial.
[a]If psychosocial or medication aspect of intervention did not contain sufficient detail then insufficient was marked on table.
[b]Partly included data from studies 13, 14.

outcomes. Follow-up rates generally exceeded 85.0% and ranged from 61.3% to 100.0% (six studies). Collateral informants were used in eight (57.1%) studies to validate participants' reports. Thirteen studies (92.8%) used objective verification (for example, records, urine, blood) to validate clients' self-reports of alcohol use. Eight studies (57.1%) had follow-up measures collected by study workers blind to participants' treatment condition. All studies enumerated dropouts and used appropriate statistical analyses. Only one study (that is, Chick et al., 2000) used a multisite design.

Methodological Quality Ratings of Integrated Alcohol Dependence Treatment Studies

MQRS scores of the 14 studies of integrated treatment ranged from 8 to 15 ($M = 11.9$, $SD = 2.0$). The median and mode MQRS scores were 13. Overall, the methodological quality of integrated alcohol dependence treatment studies was high, with only a few notable deficiencies in a small number of reports. Few long-term follow-ups or multisite investigations were conducted, and most studies examined homogeneous white samples.

Integrated Alcohol Dependence Interventions

Overall, there was greater variance with regard to the psychosocial intervention component than the pharmacological. All but one study used naltrexone (Table 3) (Mason, Salvato, Williams, Rituo, & Cutler, 1999). The standard dose used was 50 mg of naltrexone taken once daily (10 studies). The remaining three studies used naltrexone at either 100 mg and 150 mg on alternating days (compare Oslin, Liberto, O'Brien, Krois, & Noreck, 1997), 25 mg twice a day (compare Monti et al., 2001), or 25 mg once daily (compare Landabaso et al., 1999). Eleven studies (78.5%) compared medication with a placebo-only group condition. The remaining three investigations compared naltrexone to nefazodone and placebo (compare Kranzler, Modesto-Lowe, & von Kirk, 2000), an aversive agent (compare Landabaso et al.), or acamprosate (compare Rubio, Jimènez-Arriero, Ponce, & Palomo, 2001). Although many of the psychosocial treatments were highly detailed and standardized cognitive–behavioral interventions (compare Kranzler et al.), others were nonstandardized and poorly described (compare Chick et al., 2000; Landabaso et al.). Four studies (28.5%) used manualized psychosocial interventions. Psychosocial interventions included coping skills training, supportive therapy, relapse prevention training, abstinence training, standard alcoholism group therapy, cue-exposure training, and a combined medication management and clinical care approach. Many of the studies (for example, O'Malley et al., 1992; O'Malley, Jaffe, Chang, et al., 1996; O'Malley, Jaffe, Rode, & Rounsaville, 1996) used several of the psychosocial treatments conjointly.

Study Outcomes

Clinical outcomes examined in more than one study included level of craving for alcohol (eight studies), rate of relapse (eight studies), alcohol consumption level (six studies), percentage of total days abstinent from alcohol (four studies), medication adherence and compliance (four studies), time (days) to first relapse (four studies), number of drinks per drinking day (three studies), percentage of total days abstinent (three studies), percentage of total days drinking (three studies), number of heavy drinking days (two studies), program attendance and completion (two studies), time (days) to first drink (two studies), and time (days) to first heavy drinking (two studies). Common measures used in these studies included alcohol breathalyzer tests, the Alcohol Dependence Scale (Skinner & Allen, 1982), Addiction Severity Index (McLellan, Luborsky, Woody, & O'Brien, 1980), Michigan Alcoholism Screening Test (Selzer, 1971), Obsessive–Compulsive Drinking Scale (Anton, Moak, & Latham, 1995), serum gamma-glutamy/transferase, time-line follow-back method, urinalysis, as well as various self-report alcohol consumption measures.

Two or more studies identified statistically significant positive effects of integrated treatment across 10 outcome measures. Relapse rates and level of craving were significantly reduced in clients receiving integrated treatments in seven of eight studies in which they were examined. Abstinence rates were significantly increased in clients receiving integrated treatments in three of four studies. Finally, measures of time to relapse, alcohol consumption, program attendance and completion, medication adherence and compliance, percentage of days drinking, and extent of drinking on drinking days reflected positive findings in two reports.

As time passed beyond the initial treatment period, subsequent treatment gains diminished and group differences were not significant in three studies (that is, Anton et al., 2001; Monti et al., 2001; & O'Malley, Jaffe, Chang, et al., 1996). No differences on most outcome variables were observed in three 12-week trials (compare, Chick et al., 2000; Kranzler et al., 2000; & Oslin et al., 1997). Table 4 displays the total number of studies that evaluated

TABLE 3—Overview of Studies of Integrated Psychosocial and Opioid-Antagonist Treatment for Alcohol Dependence (*N* = 14 studies reported in 18 journal articles)

No.	Study	Psychosocial Component	Pharmacological Component	Sample	Outcomes Measured	Findings	Duration of Study
1a	Anton et al. (1999)	12-week sessions of individual manual-guided, cognitive–behavioral therapy.	50 mg of naltrexone daily (1 dose) or identical capsule for placebo group	131 subjects age (*M*) = 42.5; 71% male; 85.5% white	• Time to first relapse (days) • % of days abstinent • Number of drinks per drinking day	Overall survival for naltrexone-treated group was significantly better than placebo (62% versus 40%). Naltrexone group had significantly greater percentage of time abstinent, longer time intervals between relapses, and, when drinking, consumed fewer drinks per drinking day.	12 weeks
1b	Anton et al. (2001)	12-week sessions of individual manual-guided, cognitive–behavioral therapy.	50 mg of naltrexone daily (1 dose) or identical capsule for placebo group	131 subjects age (*M*) = 42.5; 71% male; 85.5% white	• Time to first relapse (days) • Percentage of days abstinent • Number of drinks per drinking day	During posttreatment phase, naltrexone group was superior to placebo group on outcome measures. However, differences were no longer statistically significant. As time elapsed, the naltrexone group converged toward the placebo/CBT group.	12 weeks; follow-up at week 26
2	Chick et al. (2000)	Psychosocial treatment in terms of type and amount was free of protocol constraints. Subjects were also free to attend AA or other support groups.	50 mg of naltrexone daily (1 dose) or identical placebo preparation for 12 weeks	175 subjects between ages 18–65	• Time to first episode of heavy drinking • Time to first drink • Alcohol consumption • Craving	No significant difference between groups on time to first heavy drinking or time to first drink outcomes. Alcohol consumption for naltrexone group was lower in last 4 weeks but not significantly. Naltrexone group reported significantly less craving for alcohol.	12 weeks
3a	Feeney, Young, et al. (2001)	Weekly hour-long sessions of a standardized cognitive–behavioral therapy (contract-based).	50 mg of naltrexone daily (1 dose) for 12 weeks	100 subjects (50 current and 50 matched historical controls); age (*M*) = 42; primarily white and male	• Program attendance rate • Time to relapse • Rate of relapse • Program completion rate • Rate of continuous abstinence	The naltrexone/CBT group had significantly greater attendance and a longer time to relapse, greater program completion rate (88% versus 36%), and significantly higher rates of abstinence (76% versus 18%) at follow-up.	12 weeks
3b	Feeney, Conner, et al. (2001)	Weekly hour-long sessions of a standardized cognitive–behavioral therapy (contract-based).	50 mg of naltrexone daily (1 dose) for 12 weeks	50 subjects, age (*M*) = 42; primarily white and male	• Adherence to program attendance • Adherence to naltrexone • Relapse • Psychological state	27 of 50 subjects (54%) filled naltrexone prescriptions; 44 of 50 subjects (88%) attended all 8 program sessions, and of the 44 who attended, 33 remained abstinent for the duration of treatment.	12 weeks

(continued)

TABLE 3—Continued

No.	Study	Psychosocial Component	Pharmacological Component	Sample	Outcomes Measured	Findings	Duration of Study
4	Heinala et al. (2001)	Coping skills training (manual-based, cognitive–behavioral therapy) or general supportive therapy encouraging abstinence.	50 mg of naltrexone daily (1 dose) or identical placebo capsule	121 subjects, age (M) = 45; 71% male; 88% married; Finnish sample	• Rate of relapse to heavy drinking • Alcohol consumption • Craving • Adverse events	In the coping groups, naltrexone was significantly superior to placebo and produced a lower rate of relapse to heavy drinking. No significant differences between supportive-naltrexone group and supportive-placebo group were identified, although supportive-naltrexone group exhibited less craving.	32 weeks
5	Kranzler et al. (2000)	Weekly coping skills training, structured and manual-guided, consisting of presentation, rehearsal, and homework.	50 mg of naltrexone daily (1 dose) or identical placebo. 100 mg of nefazodone (2 doses) or identical placebo	183 subjects; age (M) = 41; 77% male; 93% white	• Alcohol consumption • Abstinence rates • Time to first drink • Time to first heavy drinking • Compliance	No significant difference on outcome measures. Neither agent in this study was superior to placebo. In general, among all groups, treatment compliance predicted slightly less drinking (no significant differences between groups).	12 weeks
6	Landabaso et al. (1999)	Identical general supportive psychotherapy.	Aversion agent (disulfiram) and 25 mg of naltrexone per day for 6 months (1 year for aversion agent). Control group received aversion agent for 1 year.	30 subjects, age (M) = 30; 73% male	• Relapse • Abstinence • Alcohol consumption • Percentage of days using alcohol during treatment	At six months, 13.3% of the naltrexone group had relapsed, compared with 53.3% of the control group. Throughout the study period, 46.7% of the naltrexone group versus 86.7% of the control group drank. Average days per week of drinking: 1.3 for naltrexone group versus 2.3 for control group.	104 weeks
7	Mason et al. (1999)	Individual-guided, manual-based cognitive–behavioral therapy.	20 mg of nalmefene (10 mg twice daily or 40 mg twice a day or identical placebo	105 subjects, age (M) = 42; 65% male; 82% white	• Rate of relapse to heavy drinking • Percentage of days abstinent • Number of drinks consumed per drinking day	Clients receiving nalmefene were 2.5 times more likely than those receiving placebo not to relapse to heavy drinking. The nalmefene group experienced significantly fewer heavy drinking episodes and a significantly lower rate of relapse to heavy drinking (37.8% for nalmefene group versus 60.9% for placebo). Both groups displayed an increase in percentage of days abstinent.	12 weeks
8	Monti et al. (2001)	Cue exposure with coping skills and communication skills training (2 groups); education and relaxation control (2 groups).	25 mg of naltrexone twice a day or identical placebo twice a day	128 subjects, age (M) = 39; 76% male; 97% white; 84% employed	• Relapse rates • Number of heavy drinking days • Number of drinks on drinking days • Craving	Naltrexone showed results superior to placebo, while subjects took medication. However, the effects did not persist. Overall, cue exposure training with coping and communication skills training showed better long-term outcomes.	52 weeks

(continued)

TABLE 3—Continued

No.	Study	Psychosocial Component	Pharmacological Component	Sample	Outcomes Measured	Findings	Duration of Study
9a	O'Malley et al. (1992)	Coping skills training with relapse prevention—manual-based cognitive–behavioral therapy (2 groups) Supportive therapy encouraging abstinence but without specific skills (2 groups).	50 mg of naltrexone daily (1 dose) or identical placebo	97 subjects, age (*M*) = 40.5; 93% white; 74% male; 73% employed	• Abstinence rates • Relapse rates • Frequency and quantity of drinking • Craving	Abstinence rates were as follows: 61% of naltrexone-supportive, 28% of naltrexone-coping, 21% of placebo-coping, 19% of placebo-supportive. Naltrexone groups had a 67% reduced chance of relapse compared with placebo groups, and naltrexone groups drank less frequently (naltrexone-coping drank the least on drinking days). Craving was least in the naltrexone-coping group.	12 weeks
9b	O'Malley, Jaffe, Chang, et al. (1996)	Coping skills training with relapse prevention—manual-based cognitive–behavioral therapy (2 groups) Supportive therapy encouraging abstinence but without specific skills (2 groups).	50 mg of naltrexone daily (1 dose) or identical placebo	80 subjects of original 97 (see above)	• Abstinence • Light-to-moderate drinking • Heavy drinking • Alcohol-related diagnosis at follow-up	During follow-up period: no significant differences between groups vis-a-vis abstinence or rates of drinking. Groups were similar except for the supportive therapy-placebo group, which exhibited higher levels of heavy drinking. At follow-up, 13% of naltrexone-treated groups met criteria for alcohol abuse and 18% for dependence. Placebo groups were 24% and 39%, respectively.	12 weeks; follow-up at 6 weeks
9c	O'Malley, Jaffe, Rode, & Rounsaville (1996)	Coping skills training with relapse prevention—manual-based cognitive–behavioral therapy (2 groups) Supportive therapy encouraging abstinence but without specific skills (2 groups).	50 mg of naltrexone daily (1 dose) or identical placebo	43 subjects of original 97 (see above)	• Craving modification	The naltrexone group reported significantly lower levels of craving compared with the placebo group.	12 weeks
10	Oslin et al. (1997)	Psychosocial treatment aimed at abstinence and including peer support with education.	100 mg of naltrexone on Monday, Wednesday, and 150 mg on Friday or identical placebo	44 subjects, age (*M*) = 57; 63% African American; 36% white	• Relapse • Treatment compliance • Craving	14.3% of subjects in the naltrexone group relapsed versus 34.8% in the placebo group. No significant differences in treatment compliance or reported craving.	12 weeks

(continued)

TABLE 3—Continued

No.	Study	Psychosocial Component	Pharmacological Component	Sample	Outcomes Measured	Findings	Duration of Study
11	Pettinati et al. (2000)	BRENDA framework (combined medication management and motivational enhancement to individualized clinical care while monitoring pharmacotherapy) or individualized counseling.	50–100 mg of naltrexone daily or identical placebo (pills given on weekly basis in bottles or blisterpacks)	196 subjects from previous study and 100 subjects from new study (combined analyses); age (*M*) = 45; 78% male; 66% white	• Compliance effect on outcome • Pill compliance rates • Treatment completion	For compliant subjects, much lower relapse rates experienced in naltrexone group (10% versus 38% for placebo). For noncompliant subjects there was no advantage to naltrexone over placebo. Compliance with BRENDA method significantly higher than with individualized counseling (83% versus 55% for trial completion and 77% versus 60% for medication compliance.	12 weeks
12	Rubio et al. (2001)	Supportive group therapy once weekly consisting of basic relapse prevention and abstinence reinforcement.	50 mg of naltrexone daily (1 dose) or 6 tablets of acamprosate daily (2 tablets three times a day)	157 subjects, age (*M*) = 43.5; 100% male; 90% married; 75% full-time employed	• Cumulative days of abstinence • Days to first relapse • Number of drinks consumed per week • Number of drinks consumed at a time • Craving	At the study's end, 41% of naltrexone group had not relapsed and 54% were abstinent versus 17%, and 27%, respectively, for the acamprosate group. In the naltrexone group, there was a trend toward fewer dropouts, higher medication compliance, greater attendance at psychotherapy sessions, less craving, and fewer drinks on drinking days.	52 weeks
13	Volpicelli et al. (1992)	Group therapy twice per week.	50 mg of naltrexone daily (1 dose) or identical placebo	70 subjects, age (*M*) = 43; 78% black; 100% male; 41% employed; all veterans	• Alcohol craving • Relapse rates • Drinking days	Naltrexone group experienced significantly less craving and less drinking once drinking was initiated. Naltrexone group drank 1.6% of study days versus 8.3% for placebo group. Naltrexone subjects experienced a 23% relapse rate versus 54% for placebo.	12 weeks
14	Volpicelli et al. (1997)	Individual psychotherapy based on Gorski and Miller relapse prevention program twice weekly.	50 mg of naltrexone daily (1 dose) or identical placebo (technician monitored pill counts)	97 subjects, age (*M*) = 38; 78% male; 41% African American; 37% white; 59% other; 67% employed	• Time to relapse • Alcohol craving • Percentage drinking days	The naltrexone group experienced one-third less craving, lower relapse rates (27% versus 52%), and fewer drinking days (5.4% versus 12.6%) than the placebo group.	12 weeks

NOTE: CBT = cognitive behavioral therapy.

TABLE 4—Major Outcomes across Studies of Integrated Psychosocial and Opiate-Antagonist Treatment for Alcohol Dependence, Number of Studies Assessing Each Outcome, and Number of Studies Reporting Positive Findings vis-à-vis Outcomes

Outcome	Number	Number positive	%
Craving for alcohol	8	7	87.5
Rate of relapse	8	7	87.5
Alcohol consumption level	6	2	33.3
Percentage of total days abstinent	4	3	75.0
Medication adherence/compliance	4	2	50.0
Time to first relapse (days)	4	2	50.0
Number of drinks per drinking day	3	2	66.6
Percentage of total days abstinent	3	1	33.3
Percentage of total days drinking	3	2	66.6
Number of heavy drinking days	2	1	50.0
Program attendance/completion	2	2	100.0
Time (days) to first drink	2	1	50.0
Time (days) to first heavy drinking	2	2	100.0
Totals	51	34	66.6

an outcome and the number of studies reporting statistically significant positive findings for that outcome. Eleven of 13 outcomes examined yielded positive findings in at least one-half of the studies in which they were examined. Seven of 13 outcomes yielded significant positive findings in at least two-thirds of the studies in which they were examined. Although the time to first heavy-drinking episode and program attendance and completion outcomes reflected statistically significant positive treatment effects in all studies in which they were examined, only two studies evaluated these outcomes. As mentioned, the two outcomes reflecting positive treatment effects most consistently were rate of relapse and level of craving for alcohol, with both showing positive results in seven of eight (87.5%) studies in which they were assessed. A total of 51 individual outcome analyses were conducted in relation to the 13 outcomes that appeared more than once across studies, 34 (66.6%) were associated with statistically significant positive findings.

DISCUSSION AND PRACTICE IMPLICATIONS

Rigorous studies of combined psychosocial and opioid-antagonist treatment of alcohol-dependent clients suggest that integrated therapy is effective in producing a range of positive short-term outcomes. Most of the studies we reviewed were randomized controlled trials, used standardized intervention protocols, were sufficiently explicit in their reporting to permit replication, and evidenced good to excellent follow-up rates. More multisite, long-term follow-ups with ethnically and socioeconomically heterogeneous clients are needed. Opioid-antagonist pharmacotherapy in conjunction with psychosocial–behavioral interventions reliably reduces rates of relapse and diminishes alcohol craving at least during the first three months of treatment. Positive outcome findings associated with integrated therapies also included reductions in the average number of drinks per drinking day, proportion of total days spent drinking, and time to first heavy-drinking episode.

Although many positive outcomes were achieved over a 12-week period, when treatment ended there was a corresponding diminution of treatment gains. These findings suggest that long-term administration of opioid antagonists may be justified given the apparent nontoxicity and efficacy of these agents. This raises the central issue of compliance. Recent research has shown that demographic or pretreatment alcohol use variables have not predicted compliance (Feeney, Conner, et al. 2001; Rohsenow et al., 2000) and that adherence to naltrexone is similar to that of other medications in use for chronic illnesses (Feeney, Conner, et al.). Future investigations should evaluate the effectiveness of long-term combined therapy and identify client characteristics associated with the need for extended medication as well as continued psychosocial intervention. On the basis of research to date, practitioners should routinely consider integrated opioid-antagonist and psychosocial intervention, preferably using one of the empirically supported psychosocial treatments identified by Hester and Miller (1995, 2002). Volpicelli and colleagues (2001) proposed a case management–based integrated treatment approach that might be particularly appealing to social workers.

The conclusions of our review are, to some extent, limited by the number of published clinical trials of integrated treatments for alcohol dependence. Additional limitations derive from the systematic review process itself. These limitations, all of which potentially alter the conclusions of a review, include the uncertainty of identifying all studies, the subjective aspects of assessing methodological rigor, and the scope of conditions related to study inclusion

criteria. Future studies should address several key issues related to integrated treatments in this area. More studies experimentally manipulating the psychosocial treatments delivered in conjunction with opioid antagonists are needed. To date, most studies have compared groups receiving naltrexone to those given placebo, all of whom received standard agency-based psychosocial interventions. Future studies should include longer follow-up periods, ensure that they evaluate treatment effects in patients who are compliant with treatment, and examine the effects of treatment on the extent of drinking in patients who relapse.

Integrated therapies are being applied with increasing regularity in addictions and mental health practice settings (Sammons & Schmidt, 2001). Social work practitioners need to be aware of effective pharmacotherapies for the treatment of diverse health and mental health conditions and the psychosocial interventions with which they might fruitfully be combined. Integrated treatments widen the practice arena for social workers in the addictions, and practical knowledge of medications needs to be attained. Social work educators should foster in their students a preference for evidence-based practice approaches, teach empirically supported interventions, and ensure that future practitioners learn how to locate, evaluate, and apply relevant clinical research to the issues they confront in practice (Howard, McMillen, & Pollio, 2003). Referring to the future of social work practice in the addictions, Gordis (2001), past director of the National Institute on Alcohol Abuse and Alcoholism, contended that

> the era of a "brain free" behavioral approach is coming to an end. This does not mean that the important things that social workers do to help people straighten out their lives will disappear. What will change is that clinicians will have to be aware of things happening in branches of science other than their own clinical area in order to maintain a practice that is rational, intelligent, and exciting. (p. 19)

Because they are multisystemic and emphasize professional teamwork in the provision of client care, integrated alcohol dependence treatments accord well with social work's ecological approach and offer new opportunities for professional collaboration. However, combined approaches require increasing sophistication on the part of social workers with regard to knowledge of pharmacological and psychosocial approaches to alcohol dependence treatment. ■

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