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The Impact of Alcohol Treatment on Social Costs of Alcohol Dependence: Results from the COMBINE Study

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Abstract

Background—The COMBINE (Combined Pharmacotherapies and Behavioral Intervention) clinical trial recently evaluated the efficacy of pharmacotherapies, behavioral therapies, and their combinations for the treatment of alcohol dependence. Previously, the cost and cost-effectiveness of COMBINE have been studied. Policy makers, patients, and nonalcohol-dependent individuals may be concerned not only with alcohol treatment costs but also with the impact of alcohol interventions on broader social costs and outcomes.

Objectives—To estimate the sum of treatment costs plus the costs of health care utilization, arrests, and motor vehicle accidents for the 9 treatments in COMBINE 3 years post-randomization.

Research Design—A cost study based on a randomized controlled clinical trial.

Subjects—786 participants 3 years post-randomization.

Results—Multivariate results show no significant differences in mean costs between any of the treatment arms as compared to medical management (MM) + placebo for the 3-year post-randomization sample. The *median* costs of MM + acamprosate, MM + naltrexone, MM +

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acamprosate + naltrexone, and MM + acamprosate + combined behavioral intervention were significantly lower than the median cost for MM + placebo.

Conclusions—The results show that social cost savings are generated relative to MM + placebo by 3 years post-randomization, and the magnitude of these cost savings is greater than the costs of the COMBINE treatment received 3 years prior. Our study suggests that several alcohol treatments may indeed lead to reduced *median* social costs associated with health care, arrests, and motor vehicle accidents.

Keywords

alcohol treatment; social costs; cost offsets

INTRODUCTION

Alcohol abuse and dependence impose significant costs to society, estimated at \$184 billion in 1998,¹ and alcohol use is the third leading preventable cause of death.² Altogether, 8.5% of adults in the United States meet clinical criteria for alcohol abuse (4.7% or 9.7 million adults) or alcohol dependence (3.8% or 7.9 million adults).³ The impact of alcohol use, abuse, and dependence on society has led researchers to seek out treatments that reduce the negative consequences of alcohol use disorders.

COMBINE was a multicenter, randomized controlled clinical trial (RCT) of alcohol treatments sponsored by the National Institute on Alcohol Abuse and Alcoholism. The study examined whether combinations of pharmacotherapies (acamprosate and naltrexone) and behavioral therapies (medical management [MM] and combined behavioral intervention [CBI]) treated alcohol dependence better than monotherapies. COMBINE participants at 11 sites were randomized into 9 treatment groups. Eight of the treatment groups (all receiving MM) form a 2×2×2 factorial design in which patients were randomized to receive acamprosate (active or placebo form), naltrexone (active or placebo form), and either CBI or no additional behavioral therapy. The ninth treatment group received only CBI (no medication, placebo, or MM).⁴

A separate study was funded to estimate the costs and cost-effectiveness of COMBINE in 9 of the 11 treatment sites.^{5,6} Zarkin and colleagues⁶ estimated the treatment costs and cost-effectiveness of COMBINE at the end of 16 weeks of treatment from the treatment provider's perspective. Dunlap et al.⁷ added patient time costs to the treatment costs and re-evaluated the costs and cost-effectiveness of COMBINE from the patient's perspective.

In this paper, we expand the perspective of the analysis to include broader social outcomes and costs over three years. Policy makers, patients, and nonalcohol-dependent individuals may be concerned not only with alcohol treatment costs but also with the impact of alcohol interventions on social costs, such as the costs of health care utilization, crime, and motor vehicle accidents. An initially costly treatment intervention may incur smaller future social costs, making the sum of treatment and social costs similar to or even less than other treatment choices.

Despite the enormous social costs imposed by alcohol abuse, only a few studies have examined the impact of alcohol treatment on these broader social costs in the context of RCTs. Holder et al.⁸ examined the cost of medical care following 3 behavioral treatments as part of the Project MATCH RCT. They found that total medical care declined post-treatment for all 3 modalities, but there were no significant differences across the treatment modalities. More recently, the UKATT Research Team⁹ evaluated the cost and cost-effectiveness of 2 behavioral treatments in an RCT. Both therapies showed similar and substantial savings of

approximately 5 times the cost of treatment in terms of reduced expenditures for health care, social services, and criminal justice services. This paper takes advantage of COMBINE's RCT design and the large number of behavioral and pharmacological treatment therapies studied in COMBINE.

METHODS

Zarkin and colleagues designed a cost and cost-effectiveness study of COMBINE.^{5,6} The social costs analyzed here are the sum of treatment costs and the economic costs of health care utilization, arrests, and motor vehicle accidents. The costs of treatment are the same as those estimated in Zarkin et al.⁶ and include pharmaceutical, labor, and laboratory and nonlaboratory assessment costs for delivering the 9 COMBINE treatments through 16 weeks.

Broader social costs were measured using the following economic outcomes recorded on the Economic Form-90:¹⁰ health care utilization, arrests, and motor vehicle accidents. Health care utilization includes nights spent in a hospital and whether these were mental health or substance abuse (MH/SA) related, nights in another MH/SA treatment facility, emergency room (ER) visits, and other health care visits and whether these were MH/SA related. Arrests are categorized as driving under the influence, other traffic violations, disorderly conduct or public drunkenness, assault, motor vehicle theft, burglary, robbery, or other arrests.

We recognize that intensity of care may vary in inpatient, outpatient, or ER settings. Furthermore, variability exists in the extent of injuries incurred as a result of crimes or motor vehicle accidents. Because we did not collect detailed information on the complexity or the actual costs of these outcomes, we multiplied the economic outcomes by a corresponding average unit cost, which was derived from the literature and updated to 2007 dollars with the medical services consumer price index. Unit costs for health care utilization were mostly derived from French and Martin,¹¹ the exception is the cost for a night in a nonhospital MH/SA treatment facility, which was derived from Roebuck et al.¹² We used Miller et al.¹³ for costs per arrest by crime type. To be conservative, we used the "monetary subtotal costs" for the unit costs for assault, robbery, motor vehicle theft, and burglary. Monetary costs include policing costs, property damage/loss, health care costs, lost future earnings, and adjudication and sanctioning costs. For the arrest categories not specifically covered by Miller et al.—driving under the influence, other traffic violations, disorderly conduct and public drunkenness, and other arrests—we used the "adjudication and sanctioning" unit cost because health care costs, property damage, and earnings losses typically would not be incurred in these cases. Finally, costs of motor vehicle accidents were from Blincoc et al.¹⁴ To estimate the unit cost of an accident, we used the economic costs of accidents excluding medical costs. For COMBINE participants, health care utilization associated with accidents is captured in the Form-90 health care utilization measures. Our accident unit cost, which is sizeable, represents a conservative estimate because it does not include accident-related medical costs for those involved in reported accidents who are not patients in the COMBINE trial.

The COMBINE treatment and social costs were summed through 3 years post-randomization. This 3-year sample includes only the 9 sites that were part of the cost-effectiveness follow-up study and patients with at least 1 follow-up record of the Economic Form-90 both before and after the main trial stopped following patients (1 year after treatment). Of 1,144 participants who were randomized in the main trial from the 9 sites, 1053 participants (92% of those randomized) had a Form-90 after week 16 when treatment ended, and 786 participants (75% of those completing treatment) were included in the 3-year

economic study. No differential attrition existed across the treatment arms from either the randomized group or the week 16 sample.

In the 3-year sample, 71% of patients have complete records for the 11 interview dates. To mitigate attrition bias, we included individuals with complete and incomplete data. Individuals with missing interview dates have lower cumulative costs, all else equal. To account for these cost differences, we included a covariate in our regression analyses for the total number of reporting days represented by the costs.

Because of the skewness of the data, the mean, median, and 90th percentile of costs were estimated for 3-year post-randomization sample. Ordinary least squares (OLS) and median regression models were estimated with covariates for treatment intervention, treatment sites, days of cost reporting (measured as the deviation from the number of days in the entire follow-up period), and baseline costs (measured as the deviation from the baseline mean). We focused on individual coefficient estimates that compare the mean or median cost of each treatment arm to the mean or median cost of the reference category, MM + placebo; *t*-tests of individual coefficient estimates indicate whether the treatment has significantly different total costs compared to MM + placebo. In addition, we performed *F*-tests of the hypotheses that the treatment coefficients are jointly equal to each other and that the treatment coefficients are jointly equal to zero, which is equivalent to testing whether the treatment coefficients as a group are jointly equal to the coefficient on MM + placebo.

When reporting multivariate regression results, we note coefficients that are significantly different from zero at the 1% and 5% levels. We also included *p*-values of the coefficient estimates so that readers who have a concern about the number of treatment intervention comparisons (9) may use a more stringent significance level.

RESULTS

Unit cost estimates used in the study are presented in Table 1. As shown, motor vehicle accidents are the most expensive economic outcome, due in large part to the cost of motor vehicle repair, and any arrest is more expensive than a day or night of health care utilization. The most expensive arrest is robbery, followed by motor vehicle theft and assault.

Because the unit cost for each outcome is the same across the treatment arms, cost differences across arms reflect differences in the number of events that occur. As shown in Table 2, the mean cost across all treatment arms 3 years post-randomization was \$13,965; the median cost was \$5,861; and the 90th percentile was \$34,391. Health care costs represented 52% of total costs, and motor vehicle accident costs represented 33% of total costs. Arrest costs accounted for less than 10% of total costs (7.9%), and COMBINE treatment costs represented less than 10% of total costs (6.3%). MM + acamprosate + naltrexone had the lowest mean cost (\$11,742), and MM + acamprosate + CBI had the lowest median cost (\$4,639). CBI only had the largest mean cost (\$14,938), and MM + placebo had the largest median cost (\$8,637). Health care, arrest, and motor vehicle accident costs were skewed as shown by the mean exceeding the median and by the large values for the 90th percentile. This skewness arose because expensive events such as inpatient care, arrests, and auto accidents occurred rarely, but when they did, they added substantially to costs. For example, for several treatments, the 90th percentile of motor vehicle costs was \$14,576, the cost of 1 auto accident, but the median number of accidents for all treatments is zero.

COMBINE treatment costs do not appear to be positively related to total social costs and, in fact, are suggestive of a negative relationship. For example, MM + placebo had the lowest mean (\$406) and median (\$410) treatment costs and yet had the third largest mean total

costs (\$14,865) and the largest median total costs (\$8,637); MM + acamprosate + naltrexone + CBI had the largest mean (\$1,379) and median (\$1,492) treatment costs but only the fifth largest mean total costs and the second largest median total costs.

The OLS results in Table 3 show that point estimates were negative, which indicated that the interventions had lower mean treatment + social costs (but not significantly so) 3 years post-randomization compared with MM + placebo. We cannot reject the null hypothesis that the coefficients on the treatment arms were jointly equal to each other ($F(7,767) = 0.28, P = .96$), nor can we reject the null hypothesis that the coefficients on the treatment arms were jointly equal to zero ($F(8,767) = 0.36, P = .94$), implying that there were no significant differences in mean costs between the treatment arms as a group compared with MM + placebo for the 3-year post-randomization sample.

The median regressions in Table 3 show several treatment interventions that had statistically significant (at the .05 level or lower) median cost differences relative to MM + placebo. At 3 years post-randomization, the median costs of MM + acamprosate, MM + naltrexone, MM + acamprosate + naltrexone, and MM + acamprosate + CBI were significantly lower than the median cost for MM + placebo ($P < .05$). These median cost differences ranged from \$2,500 to \$3,800 lower than the median costs of MM + placebo. The F -test on the median model shows that we fail to reject the null hypothesis that the treatment coefficients were jointly equal to each other ($F(7,767) = 1.34, P = 0.23$). An F -test also shows that we reject the hypothesis that the coefficients were jointly equal to zero at the .10 level but not at the .05 level ($F(8,767) = 1.85, P = 0.07$). This latter F -test provides some evidence, although not definitive, that the treatment interventions as a group reduced median 3-year costs relative to MM + placebo.

The coefficients on days of cost reporting and baseline costs for the OLS and median regressions were significant ($P < .01$ for all but the days coefficient in the OLS model) and have the expected signs: individuals with interviews covering more reporting days had greater mean and median costs post-randomization, and individuals with greater baseline costs had greater mean and median costs post-randomization.

DISCUSSION

We estimated the sum of the COMBINE treatment costs plus the social costs of health care use, arrests, and motor vehicle accidents over three years for the 9 alcohol dependence treatments in the COMBINE study.⁴ If alcohol treatment interventions generate future social cost savings, then these treatment interventions are more attractive from the social perspective because they generate social benefits that are not limited to alcohol-dependent patients. Furthermore, adding social costs to treatment costs may change the relative attractiveness of costly interventions—an initially costly treatment intervention may result in lower future social costs, increasing its attractiveness relative to other alternatives.

Our multivariate results show no significant differences in mean costs between any of the treatment arms as compared to MM + placebo for the 3-year post-randomization sample. We hypothesize that this lack of statistical significance was largely caused by the skewness of the data, which in turn was caused by the occurrence of rare but expensive inpatient hospital stays, arrests, and motor vehicle accidents. These high cost outliers increased both the mean and variance of costs and typically a larger sample size is required to show significant cost differences between treatment interventions.

Because our sample size was predetermined by the design of COMBINE and could not be increased, we addressed the skewness by estimating median regression models. In contrast to mean costs, the medians are less affected by high cost outliers. At 3 years post-

randomization, the *median* costs of MM + acamprosate, MM + naltrexone, MM + acamprosate + naltrexone, and MM + acamprosate + CBI were significantly lower than the median cost for MM + placebo. Median cost differences ranged from \$2,500 to \$3,800 less than the median costs of MM + placebo. These results show that social cost savings are generated relative to MM + placebo by 3 years post-randomization and, importantly, the magnitude of these cost savings is greater than the costs of the COMBINE treatment received 3 years prior. Qualitatively, this result is similar to the UKATT⁹ results, although it is difficult to make a definitive comparison because UKATT did not have a placebo condition, as was the case here.

To explore our results in more detail, we re-ran our mean and median regression analyses with just the initial treatment costs plus health care expenses (i.e., excluding arrests and motor vehicle accidents). We found that the 3-year post-randomization median results were very different from Table 3: no treatment intervention was individually significant, only 4 of the coefficients were negative in sign, and we could not reject the null that the coefficients were jointly equal to zero ($P = .37$). Thus, we concluded that there are no offsetting health care costs 3 years post-randomization and that including arrests and motor vehicle accident outcomes had a substantial effect on our estimated social cost differences.

As an alternative to our OLS specification, we transformed our model to account for the skewness of our cost data. We followed the methodology described by Manning and Mullahy¹⁵ to determine the appropriate data transformation. This process suggested a generalized linear model with a log-link and gamma distribution. With this model, the differences in costs represented by the treatment arm coefficients and the costs of MM + placebo were the same in sign (with one exception) and generally of a similar magnitude as the differences in means shown in Table 3 for the OLS models. These results highlight the robustness of the OLS model to our skewed data distribution, and we report the OLS specification along with the median regression model.

A related literature examines the potential cost-offset of alcohol treatment by evaluating whether alcohol treatment as compared to no treatment reduces subsequent medical utilization and health care costs (e.g., 16–21). The results of this literature vary widely due in part to differences in study population, study design, and comparison group. For example, Parthasarathy et al.¹⁸ found that inpatient, ER, and total medical costs declined 18 months after intake into the outpatient chemical dependency program at Sacramento Kaiser Permanente; non-ER outpatient costs were unchanged. Booth et al.¹⁹ found differences in the use of inpatient and outpatient care as alcohol treatment varied in intensity from short detox to extended detox to incomplete treatment and completed treatment. In their study of male alcoholics in the VA, Booth et al. found that inpatient days and outpatient visits increased post-alcohol treatment for all treatment groups; however, inpatient medical care decreased and substance abuse inpatient care increased for most treatment groups; overall, the use of inpatient services increased for these groups. In a study of adults receiving benefits from a behavioral managed care company and its parent medical care insurance company, Kane et al.¹⁶ found that the pattern of outpatient and inpatient medical utilization before and after alcoholism treatment was symmetric: utilization increased gradually in the year before treatment and then decreased post-treatment. Their results suggested that alcoholism treatment did not reduce subsequent health care utilization.

In contrast to previous cost offset papers of which we are aware, our paper takes advantage of the COMBINE trial's RCT design. Related papers typically create an untreated alcohol-dependent group from health care records. Weaknesses of this design include the potential regression to a lower mean utilization post-treatment and potential selection bias caused by the inability to control for unobserved differences between alcohol-dependent patients who

do and do not go to alcohol treatment. Our RCT design does not have these weaknesses and thus our conclusions have more internal validity.

Our paper has several limitations. First, our analysis examines only a subset of possible social costs: health care utilization, arrests, and motor vehicle accidents. We did not examine labor market outcomes because of the difficulty of placing a dollar value on all the outcomes, such as the value of being “unemployed.” But because a majority of the COMBINE patients were not unemployed (approximately 75% were employed at intake and at weeks 52 and 156), excluding this variable is unlikely to change our conclusions. Second, although we drew on peer-reviewed literature for our unit cost estimates, we exercised some judgment in selecting the unit cost components to include. For example, in selecting the unit costs of arrests, we used the monetary subtotal of arrest costs, but we adopted a conservative approach and did not include accident-related medical costs for those involved in accidents who were not patients in the COMBINE trial or nonmonetary cost estimates of pain and suffering, which would have increased our unit cost estimates substantially. Although the size of the cost differences would increase with larger unit cost estimates, there is no reason to believe that our conservative approach affects our comparisons across the alternative treatment interventions because the unit costs were applied consistently to all treatment arms. Third, all treatment interventions are compared to MM + placebo, which is not a “no treatment” group as MM plays an important treatment role. If the comparison group did not include MM, an active treatment, the estimated cost differences may have been even larger than estimated here. Fourth, we recognize that expensive rare events such as lengthy hospital stays, arrests, and motor vehicle accidents may greatly affect mean costs especially given the size of our sample. Our analysis of *median* costs, which are less affected by outliers, is one way to address this concern. In the future, additional RCT studies with larger sample sizes are needed to confirm the joint and individual impact of alcohol treatment on mean and median costs.

Finally, while it is reasonable to compare the clinical outcomes with the cost results reported here, we are reluctant to make causal statements about the relationship between specific clinical therapies and the impact on costs 3 years post-randomization because COMBINE was not designed for that analysis. We do note, however, that MM + acamprosate + naltrexone had the highest mean effectiveness⁶ for all 3 clinical outcomes (percent days absent, proportion of patients who avoid heavy drinking, and proportion of patients with good clinical outcomes) and also the largest estimated decrease in median costs 3 years post-randomization. Similarly, MM + acamprosate + CBI and MM + naltrexone had the next largest estimated median cost reductions and the second or third largest mean effectiveness estimates across the clinical outcomes. Additional analyses with larger clinical and economic samples and/or analyses that develop structural relationships between clinical outcomes and cost would be required to be more definitive about the relationship. In the meantime, our study suggests that several alcohol treatments—MM + acamprosate, MM + naltrexone, MM + acamprosate + naltrexone, and MM + acamprosate + CBI—may indeed lead to reduced median social costs associated with health care, arrests, and motor vehicle accidents.

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Table 1

Unit Costs

Variable	Unit Cost (2007 \$)	Source
Health care utilization		
Hospital night	1,592	French and Martin (1996) ¹¹
Mental health/substance abuse (MH/SA)	1,481	French and Martin (1996) ¹¹
Nights in other MH/SA treatment facility	132	Roebuck et al. (2003) ¹²
Emergency department visit	793	French and Martin (1996) ¹¹
Other health care (outpatient/counseling)	142	French and Martin (1996) ¹¹
MH/SA	93	French and Martin (1996) ¹¹
Arrests		
Driving under the influence	2,971	Miller et al. (2006) ¹³
Other traffic	2,971	Miller et al. (2006) ¹³
Public drunkenness	2,971	Miller et al. (2006) ¹³
Assault	8,261	Miller et al. (2006) ¹³
Motor vehicle theft	8,874	Miller et al. (2006) ¹³
Burglary	4,587	Miller et al. (2006) ¹³
Robbery	12,171	Miller et al. (2006) ¹³
Not specified in list above	2,971	Miller et al. (2006) ¹³
Motor vehicle accidents	14,576	Blincoe et al. (2002) ¹⁴

Table 2

Mean, Median, and 90th Percentile of Costs at 3 Years Post-Randomization

	Medical Management (No CBI)							Medical Management + CBI				Total
	MM + Placebo	MM + Acamprostate	MM + Naltrexone	MM + Acamprostate + Naltrexone	MM + Placebo + CBI	MM + Acamprostate + CBI	MM + Naltrexone + CBI	MM + Acamprostate + Naltrexone + CBI	MM + CBI Only	MM + Naltrexone + CBI Only	MM + Acamprostate + Naltrexone + CBI Only	
Num. obs.	88	92	83	86	85	92	87	86	87	86	86	786
Treatment costs ^a												
Mean	\$406	\$734	\$702	\$1,038	\$766	\$1,202	\$1,061	\$553	\$1,379	\$553	\$873	\$873
Median	\$410	\$799	\$745	\$1,123	\$787	\$1,235	\$1,101	\$573	\$1,492	\$573	\$819	\$819
90th percentile	\$481	\$997	\$875	\$1,404	\$998	\$1,469	\$1,287	\$764	\$1,833	\$764	\$1,420	\$1,420
Social costs												
Health care costs												
Mean	\$7,268	\$5,969	\$9,752	\$7,364	\$7,391	\$6,108	\$6,199	\$9,803	\$6,301	\$9,803	\$7,318	\$7,318
Median	\$3,006	\$2,330	\$2,678	\$2,310	\$2,154	\$2,484	\$2,556	\$2,996	\$2,433	\$2,996	\$2,514	\$2,514
90th percentile	\$15,304	\$13,593	\$25,345	\$21,585	\$22,322	\$16,184	\$17,637	\$28,603	\$14,718	\$28,603	\$18,457	\$18,457
Arrest costs												
Mean	\$897	\$1,159	\$1,320	\$798	\$1,451	\$542	\$823	\$2,040	\$934	\$2,040	\$1,101	\$1,101
Median	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0
90th percentile	\$2,971	\$2,971	\$2,971	\$2,971	\$2,971	\$2,971	\$2,971	\$8,261	\$2,971	\$8,261	\$2,971	\$2,971
Motor vehicle accident costs												
Mean	\$6,294	\$5,862	\$3,161	\$2,542	\$5,144	\$4,753	\$6,031	\$2,542	\$5,529	\$2,542	\$4,673	\$4,673
Median	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0
90th percentile	\$14,576	\$29,152	\$14,576	\$14,576	\$14,576	\$14,576	\$14,576	\$14,576	\$14,576	\$14,576	\$14,576	\$14,576
Total social costs ^b												
Mean	\$14,459	\$12,991	\$14,233	\$10,705	\$13,987	\$11,402	\$13,053	\$14,385	\$12,763	\$14,385	\$13,092	\$13,092
Median	\$8,166	\$5,110	\$4,552	\$3,804	\$4,828	\$3,373	\$5,807	\$5,326	\$6,691	\$5,326	\$4,852	\$4,852
90th percentile	\$33,039	\$32,070	\$37,798	\$26,213	\$35,216	\$33,294	\$41,241	\$39,862	\$28,265	\$39,862	\$33,294	\$33,294
Total costs												
Mean	\$14,865	\$13,725	\$14,935	\$11,742	\$14,752	\$12,604	\$14,115	\$14,938	\$14,142	\$14,938	\$13,965	\$13,965
Median	\$8,637	\$5,895	\$5,352	\$4,884	\$5,704	\$4,639	\$6,757	\$5,871	\$7,869	\$5,871	\$5,861	\$5,861

	Medical Management (No CBI)					Medical Management + CBI					Total
	MM + Placebo	MM + Acamprosate	MM + Naltrexone	MM + Acamprosate + Naltrexone	MM + Placebo + CBI	MM + Acamprosate + CBI	MM + Naltrexone + CBI	MM + Acamprosate + Naltrexone + CBI	MM + Placebo + CBI	MM + Acamprosate + Naltrexone + CBI	
90th percentile	\$33,424	\$32,910	\$38,583	\$27,332	\$35,567	\$34,705	\$41,511	\$30,238	\$40,559	\$34,391	

Note: MM = medical management; CBI = combined behavioral intervention

^aTreatment costs are the treatment costs from the provider perspective as covered in the cost methodology of COMBINE in Zarkin et al. (2005)⁵ and presented in Zarkin et al. (2008).⁶

^bExcludes treatment costs.

Table 3

Regression Coefficients

Variables	3 Years Post-Randomization	
	OLS (1)	Median Regression (2)
Constant	14,049.07	10,204.39
	(2,843.98)**	(1,325.35)**
MM + acamprosate	p < 0.01 -1,979.77 (2,792.78)	p < 0.01 -2,547.31 (1,290.97)*
MM + naltrexone	p = 0.48 -763.18 (2,863.35)	p = 0.05 -2,991.12 (1,329.52)*
MM + acamprosate + naltrexone	p = 0.79 -3,739.66 (2,837.07)	p = 0.03 -3,871.26 (1,321.55)**
MM + placebo + CBI	p = 0.19 -764.05 (2,847.06)	p < 0.01 -1,897.29 (1,326.87)
MM + acamprosate + CBI	p = 0.79 -3,062.88 (2,791.10)	p = 0.15 -3,276.55 (1,293.45)*
MM + naltrexone + CBI	p = 0.27 -2,522.16 (2,839.71)	p = 0.01 -1,176.21 (1,319.85)
MM + acamprosate + naltrexone + CBI	p = 0.38 -1,863.15 (2,834.27)	p = 0.37 -734.56 (1,320.53)
CBI only	p = 0.51 -1,230.32 (2,843.80)	p = 0.58 -1,690.61 (1,317.97)
Days	p = 0.67 12.78 (4.96)*	p = 0.20 9.37 (2.28)**
Baseline costs	p = 0.01 0.44 (0.12)**	p < 0.01 0.49 (0.05)**
	p < 0.01	p < 0.01

Notes: MM = medical management; CBI = combined behavioral intervention.

Standard errors in parentheses.

* Significant at 5%;

** Significant at 1%.

Coefficients on treatment arms compare to MM + placebo.

Number of observations is 786 for 3-year sample.

Regressions controlled for difference in costs between the 9 sites in the 3-year sample.