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A Pilot Study of Naltrexone and BASICS for Heavy Drinking Young Adults

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Abstract

Heavy drinking young adults often have limited motivation to change their drinking behavior. Adding pharmacotherapy to brief counseling is a novel approach to treating this population. A small open-label pilot study was conducted to assess the feasibility of offering eight weeks of daily and targeted (i.e., taken as needed in anticipation of drinking) naltrexone with BASICS (brief motivational) counseling to heavy drinking young adults; to assess the tolerability of the medication in this population and to obtain preliminary efficacy data. The sample (N = 14) showed strong adherence to study appointments and medication taking, supporting the feasibility of this approach. Overall, the medication was well-tolerated. Significant reductions from baseline were observed in drinks per drinking day and in percent heavy drinking days and these gains were maintained one month after treatment ended. A significant decrease in alcohol-related consequences was also observed. Findings from this small pilot study suggest that naltrexone in combination with BASICS represents a promising strategy to reduce heavy drinking among young adults.

Keywords

Naltrexone; young adult drinking; undergraduate drinking; heavy drinking; alcohol-related consequences; BASICS

1. Introduction

Heavy episodic drinking, defined as 5 or more drinks in a single occasion for men and 4 or more for women, is common among undergraduates. In a national survey, just under 44% of undergraduates in the United States reported at least one heavy episodic drinking occasion in the prior two weeks (Wechsler, Lee, Nelson & Kuo, 2002). Findings from the National Epidemiologic Survey of Alcohol and Related Conditions (NESARC) showed comparable levels of heavy drinking among both young adult students and non-students in the U. S. (Dawson et al., 2004). Although the natural history of young adult drinking suggests that the majority reduce consumption as they reach their mid-to-late twenties, a considerable minority will continue to experience clinically significant problems (Jackson, Sher, Gotham & Wood,

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2001). Even among young adults who eventually "mature out" of heavy alcohol consumption, these high levels of alcohol use are associated with increased risk for consequences such as unsafe sexual practices and accidents (White, Labouvie & Papadaratsakis, 2005).

Several aspects of young adults' lives support heavy alcohol use and other risky behaviors. Relative to adolescents, young adults are less frequently monitored by parents, yet have fewer responsibilities than older adults (Arnett, 2000). It is not surprising then that they tend to report low motivation to change their drinking behavior and that only a small minority report interest in quitting drinking (Dimeff, Baer, Kivlahan & Marlatt, 1999; Epler, Sher, Loomis, O'Malley, in press). Brief interventions, such as Brief Alcohol Screening and Intervention for College Students (BASICS; Dimeff et al., 1999), which include face-to-face contact, motivational interviewing techniques, personalized normative feedback and strategies to reduce drinking, have been associated with significant but small reductions in heavy drinking (Carey, Scott-Sheldon, Carey & DeMartini, 2007). The addition of pharmacotherapy could potentiate the effects of brief interventions to ameliorate heavy alcohol use in this population.

The opiate antagonist naltrexone may represent the best option presently. A meta-analysis showed a significant advantage of naltrexone over placebo in the number of participants relapsing/returning to heavy drinking, a near significant trend for decreasing the number of drinks consumed and weaker support for decreasing any drinking days in short-term treatment for alcohol dependence (Srisurapanont and Jarusuraisin, 2005). In a recently-published multi-site trial, naltrexone was associated with an increase in abstinent days and decreased risk of a heavy drinking day (Anton et al., 2006). Evidence suggests that naltrexone might be particularly well suited for the treatment of heavy drinking young adults, who may be unwilling to abstain from alcohol. Naltrexone is safe to take while consuming alcohol and has been shown to be efficacious for reducing drinking in heavy drinkers not interested in stopping (Mitchell, Fields, White, Meadoff, Joslyn, & Rowbotham, 2007; Tidey et al., 2008; but see Davidson, Saha, Seifres, Fyffe, O'Connor & Selzer, 2004 for negative results). In a recent open-label pilot study involving five alcohol dependent adolescents, naltrexone treatment was found to be safe, well tolerated and associated with significant decreases in drinks per drinking day (Deas, May, Randall, Johnson, & Anton, 2005). Human laboratory research involving non-treatment-seeking heavy drinkers suggests that naltrexone reduces cue-induced craving (Monti et al., 1999), slows the rate of consumption and shortens the duration of drinking sessions compared with placebo (Anton, Drobes, Voronin, Durazo-Avizu & Moak, 2004; O'Malley, Krishnan-Sarin, Farren, Sinha & Kreek, 2002). Given these mechanisms of action, naltrexone may make it easier to implement the strategies taught in BASICS such as drinking more slowly.

A recent trend in the naltrexone literature has supported the efficacy of targeted dosing (i.e., taken as needed in anticipation of drinking situations, Heinala, Alho, Kiianmaa, Lonnqvist, Kuoppasalmi & Sinclair, 2001; Kranzler, Tennen, Penta & Bohn, 1997; Kranzler et al., 2003). In a 4-week open-label pilot study (Kranzler et al., 1997), targeted naltrexone combined with brief coping skills therapy was associated with significant decreases from baseline in drinks per drinking day, any drinking days and heavy drinking days. In a subsequent placebo-controlled trial, targeted administration (active or placebo) reduced the frequency of any drinking and naltrexone, particularly the daily dose, reduced the frequency of heavy drinking in comparison with placebo (Kranzler et al., 2003). These findings suggest that daily dosing and targeted dosing may serve different functions in reducing alcohol consumption.

Given high levels of heavy drinking and limited motivation to quit among young adults and naltrexone's efficacy and mechanisms of action, we pursued naltrexone in conjunction with BASICS as a therapeutic approach in this population. We conducted a small open-label pilot study in a sample of heavy drinking young adults with three main objectives: 1) to evaluate the feasibility of this approach (i.e., to assess our ability to recruit in this population and to

gauge the extent to which heavy drinking young adults would attend study appointments and adhere to the medication regimen); 2) to assess the tolerability of the medication in this population (i.e., whether adverse effects would be limited to the mild-to-moderate range and whether dose reductions due to adverse effects would be infrequent) and 3) to obtain preliminary efficacy data on drinking-related outcomes. To our knowledge, this is the first study in which pharmacotherapy was administered as a component of non-abstinence based treatment for heavy drinking young adults.

2. Method

2.1 Participants

Young adults ages 18–25 were recruited primarily through flyers posted in and around local college campuses. Inclusion criteria included at least three days of heavy episodic drinking in the prior two weeks and the ability to read English and complete assessments. Females could not be pregnant or lactating and were required to agree to the use of reliable birth control. Exclusion criteria included current, clinically significant physical disease or abnormality; current serious psychiatric illness and/or use of psychotropic drugs (other than Selective Serotonin Reuptake Inhibitors); a urine drug test positive for any illegal drug other than marijuana; current diagnosis of DSM-IV drug dependence other than nicotine; lifetime history of DSM-IV opiate dependence; current serious alcohol dependence as evidenced by clinically significant withdrawal symptoms; or a history of hypersensitivity to naltrexone. The inclusion of participants taking a stable dose of an SSRI was allowed due to findings supporting the safety of combining naltrexone with SSRI's (Croop et al., 1997).

2.2 Procedures

This trial was approved by the institutional review board of Yale University School of Medicine. Prospective participants were screened by telephone with those meeting preliminary eligibility criteria scheduled for an intake. These individuals provided informed consent and then completed the drug and alcohol portions of the Structured Clinical Interview for DSM-IV-TR, Axis I disorders (First et al., 2002), a 30-day Timeline Followback interview (TLFB; Sobell & Sobell, 2003), self-report measures and a physical exam including blood and urine analysis.

One to two weeks following the intake, eligible participants returned for a BASICS session provided by a doctoral-level psychologist and manual-guided medication-oriented counseling provided by a nurse practitioner. The medication counseling entailed instruction in the use of naltrexone as prescribed for targeted dosing and/or daily dosing, emphasized medication adherence, and highlighted links between the skills offered in BASICS and use of naltrexone. For instance, as part of BASICS, participants are counseled to space their drinks out over the course of a drinking session. Based on human laboratory findings in which naltrexone reduced drinking when access to alcohol following an initial drink was delayed but not when it was immediate (Anton et al., 2004), participants were advised to wait at least 45 minutes to an hour before consuming a second drink. Following initial counseling, participants began an 8-week course of naltrexone during which they attended biweekly appointments with the study nurse. At these appointments, medication adherence and adverse events were monitored; aspects of BASICS and the medication-oriented counseling were reinforced and study medications were dispensed. Liver function tests were repeated at Weeks 4 and 8 and urine pregnancy tests for women were repeated at each appointment. Between intake and end of treatment, participants were asked to complete a daily survey on the internet including items on their drinking behavior and medication use the prior day. A follow-up was conducted approximately four weeks after the end of treatment (Week 12). Participants were paid $20 for attending each appointment,

$2 for each daily survey and a bonus payment of $6 each week in which all surveys were completed.

The dosing protocol for the initial cohort of participants was 25 mg of targeted naltrexone (half the FDA-approved daily dose) for four weeks. After four weeks, participants who reported two or fewer heavy-drinking days during the prior two weeks of treatment remained on this dose while those not meeting this criterion were randomized to either 25 mg daily + 25 mg targeted or a 50 mg targeted dose. Given that most participants in the initial cohort did not meet the criterion to remain on the 25mg targeted dose, the protocol was amended so that the final cohort of participants was treated with 25 mg daily + 25 mg targeted naltrexone throughout. This was thought to be the optimal dosing strategy because it provides both a targeted dose in anticipation of high-risk situations and a daily dose to ensure consistency of treatment.

2.3 Measures

Demographic information including age and racial/ethnic identity was obtained as part of the intake survey. The Family Tree Questionnaire (FTQ; Mann, Sobell, Sobell, & Pavan, 1985) was used to obtain information regarding family history of alcohol problems. The authors reported evidence of reliability of reports according to a two week test-retest assessment.

Motivation to change at intake was assessed using the contemplation ladder (Biener & Abrams, 1991), which was adapted for this study. The authors demonstrated both construct and predictive validity for the original version of their measure. The 10-point scale was anchored at “1” with “no thought of reducing my alcohol use,” at “5” with “Think I should reduce my alcohol use but not quite ready” and at “10” with “Taking action to reduce my alcohol use.” The frequency with which participants utilized protective behavioral strategies (i.e., engaging in specific behaviors or skills to moderate their level of intoxication before or during drinking occasions) was assessed with the 16-item Protective Strategies Questionnaire (PSQ; Palmer, 2004) using a Likert-type scale (“1” = *never*, “7” = *always*). Items on the PSQ are introduced with “When I am drinking, I…” and example items include: “count the number of drinks I have over the course of the night” and “alternate alcoholic drinks with non-alcoholic beverages.” The PSQ total score was calculated by recoding the scale to range from 0 to 6 and summing all items. Internal consistency reliability in the baseline administration in the present study was .75.

Alcohol consumption (frequency and quantity) was assessed at baseline, at Week 0 and at Week 12 using the TLFB (Sobell & Sobell, 2003), which makes use of a calendar including memory prompts to facilitate recall of the number of standard drinks consumed on each day during a specified period. Data obtained with the TLFB have been shown to be valid for periods of up to 12 months. During treatment, alcohol use data were obtained primarily through reports of the number of drinks consumed on the daily web surveys. When a daily survey was missed, the TLFB was used to obtain the missing information at the subsequent biweekly appointment.

Medication use for the prior day was also queried in the daily web survey. When a daily survey was not completed, this was queried at the next appointment. Blister packs including unused medication were returned at each appointment. Each blister was dated and earmarked for daily or targeted use, which allowed for easy verification of self-reported medication use.

Adverse effects were monitored at each appointment using a version of the Systematic Assessment for Treatment Emergent Effects (SAFTEE) interview (Johnson, Ait-Daoud, Roache, 2005; Levine & Schooler, 1986) adapted for this study. The SAFTEE includes 1) open-ended questions about any changes in physical or health problems, appearance, or activity level, and 2) questions regarding a specific list of symptoms, which correspond to anticipated adverse events associated with naltrexone for the time period since the last appointment.

Alcohol-related consequences were assessed for the prior 3-month period at baseline and at 12 weeks using the Rutgers Alcohol Problem Index (RAPI; White & Labouvie, 1989). The RAPI is a unidirectional scale comprised of 23 adverse alcohol-related events. Each event that has occurred at least once or twice during the past three months as a result of alcohol use was scored as a "1" and these were totaled to yield an overall score out of a possible 23. The authors reported an internal consistency estimate of .92 for the scale. In the baseline administration in the present study, internal consistency reliability was .89.

At the end of treatment, participants were asked to rate "How effective do you believe naltrexone has been in helping to reduce your drinking?" on a 5-point scale from "not effective at all" to "very effective." They were also asked "How likely are you to continue with naltrexone treatment in the future?" on a 5-point scale from "highly unlikely" to "highly likely."

2.4 Analyses

In addition to our ability to recruit for the study, evidence of adherence was also considered relevant to the issue of feasibility. Adherence was calculated in two ways: 1) based on medication taken and appointments attended while participants were actively enrolled and 2) for the entire treatment period, in which case appointments and medication doses following treatment discontinuation were coded as missed. Given that participants were instructed to take the targeted dose in anticipation of drinking situations, the number of days on which any drinking occurred during treatment was considered to be the number of possible targeted doses. While this metric did not take into account possible days on which drinking was anticipated but did not occur, we did not have a means to identify these situations.

Tolerability was assessed through a count of adverse effects and ratings of the severity of these effects as reported on the SAFTEE. Preliminary efficacy was assessed by comparing self-reported drinking levels at baseline (i.e., 30 days prior to beginning treatment) with reports during the first-half of treatment, the second half of treatment (each four weeks in duration) and the four-week follow-up period using repeated measures ANOVA with post-hoc, Bonferroni-corrected comparisons. The treatment period was divided in this way for the purposes of analysis due to the dose changes that were implemented during the second half of treatment with the first cohort of participants. Because of the small number of participants who were prescribed different doses, we collapsed across dose conditions in our preliminary analyses. However, we also made descriptive comparisons of outcome means and standard deviations by dose because of the concern that different doses may have been associated with better or worse outcomes.

Three drinking outcomes were evaluated: drinks per drinking day, percent drinking days and percent heavy drinking days. A paired samples *t*-test was used to assess changes in alcohol-related consequences from baseline to 12 week follow-up. Effect size estimates were computed using partial eta squared ($\eta^2 p$) for *ANOVA*s and Cohen's *d* for the *t*-test (Cohen, 1988). Distributions of all variables were examined prior to analysis. Missing data was imputed with the last value carried forward if a participant was lost to follow-up. Sample demographics, alcohol use disorder diagnoses, family history of alcohol problems and motivation to reduce drinking at baseline were also examined descriptively.

3. Results

3.1 Sample characteristics

Twenty-one young adults attended an intake appointment between January 2006 and May 2007. Four were deemed ineligible at intake. Two were ineligible due to low levels of alcohol

use, one due to schizophrenia and another due to a history of severe anxiety. Of the remaining 17 eligible individuals, 2 chose not to enroll.

Of the 15 who enrolled, 14 provided further information about their drinking following the initial receipt of medication and BASICS and are the focus of this report. Twelve of the 14 (12 male) completed treatment and 13 provided data at Week 12. The average age was 22 (*SD* = 1.57). The majority were White, non-Hispanic (*n* = 11) and the remainder were White Hispanic, African-American and Asian-American (*n* = 1 each). Overall, the sample reported frequent heavy drinking and repeated adverse consequences (See Table 1). Eight participants were diagnosed with lifetime alcohol dependence, 7 of these diagnoses were current. Two other participants met criteria for lifetime abuse, 1 of which was current. The remaining 4 had no lifetime alcohol use disorder diagnosis. Regarding family history, 6 participants reported having at least one biological parent with a possible or definite problem with alcohol. Levels of interest in reducing drinking varied widely. Eight reported scores between "1" and "5," indicating a lack of readiness to reduce their drinking while the remaining 6 reported some inclination to reduce their alcohol use. Only 1 responded with a "10," which indicates one is currently taking action.

3.2 Feasibility

While the sample was small, it was recruited almost entirely through free methods (i.e., flyers posted in and around local colleges). We believe that our ability to recruit the sample for this study in this manner indicates that recruitment of a larger sample would be feasible with additional funding.

Based on medication taken and appointments attended only while participants were actively enrolled, adherence during the first half was as follows: daily doses—83.3%, targeted doses—75.4% , all doses—78.3%, session attendance—97.5%. During the second half of treatment, adherence while actively enrolled was as follows: daily—99.5%, targeted—82.3%, all doses—91.8%, session attendance—95.8%. When adherence was calculated using the entire treatment period regardless of dropout, adherence during the first four weeks was as follows: daily—64.7%, targeted—68.6%, all doses—67%, attendance—92.9%. During the second half of treatment, adherence according to this definition was as follows: daily—77.8%, targeted—71.1%, all doses—74.9%, attendance—82.1%.

3.3 Tolerability

All adverse effects were rated as mild to moderate. The most common events were gastro-intestinal. Adverse effects led to a recommendation for a dose reduction for two participants. In one case the dose reduction resolved the issue, while in the other case, the participant discontinued medication when the reported effects persisted despite a dose reduction.

3.4 Preliminary efficacy findings

Drinking-related outcomes and baseline values are presented in Table 1. The assumption of sphericity was met in all *ANOVA*s. Drinks per drinking day, $F(3, 39) = 10.72$, $p < .001$, $\eta^2 p = 0.45$, and percent heavy drinking days, $F(3, 39) = 17.25$, $p < .001$, $\eta^2 p = 0.57$, both decreased significantly. According to post-hoc analyses, the drinks per drinking day finding was due to significant declines from baseline observed during the second half of treatment and during the follow-up period. The significant percent heavy drinking days finding was due to significant declines compared with baseline observed during the first and second half of treatment, as well as during the follow-up period. In addition, there was a significant reduction observed during the follow-up period, compared with the first half of treatment (Table 1). Reductions observed in percent drinking days were not significant, $F(3, 39) = 2.62$, $p = .064$, $\eta^2 p = 0.17$.

A significant decrease from baseline in number of alcohol-related consequences was observed at Week 12, $t(12) = 3.77$, $p = .003$, Cohen's $d = 0.46$. This analysis included all participants except for 1 treatment completer who failed to complete the RAPI at baseline.

Given improvements noted on drinking outcomes and consequences at post-treatment follow-up, we examined the extent to which participants reported using protective strategies taught as part of BASICS. A comparison of baseline with Week 12 total PSQ scores revealed a significant increase in the use of protective strategies ($M = 52$, $SD = 11.39$), compared with baseline ($M = 43.57$, $SD = 10.14$), $t(13) = -3.89$, $p = .002$, Cohen's $d = 0.78$. Participants reported using the following strategies more often at Week 12 than at baseline: counting drinks, drinking slowly in a safe environment, avoiding drinking games, watching out for male and female friends and having a plan with a friend to watch out for each other.

The first 9 participants were prescribed only 25mg targeted naltrexone during the first half of treatment. During the second half, 2 of these participants continued on 25 mg targeted based on adequate improvement. Those who did not meet the improvement criterion received either 50 mg targeted ($n = 3$) or 25 targeted + 25 daily ($n = 4$) for the second half of treatment. The final 5 participants received 25 mg targeted and 25 mg daily throughout treatment. The small numbers of participants who were prescribed each dose did not permit statistical comparisons, however a descriptive examination of outcomes by dose showed a high degree of similarity with one exception, which is detailed in Table 2. During the second half of treatment, those taking 25mg targeted + 25mg daily ($n = 7$) seemed to report lower percent heavy drinking days than those taking 50mg targeted ($n = 3$).

3.5 Attitudes about Treatment

The 12 participants who completed treatment rated the effectiveness of naltrexone in helping them to reduce their drinking a "4" out of "5" on average ($SD = 0.85$). No participant gave a rating of less than "3." Participants' mean rating of 2.27 out of 5 ($SD = 1.35$) did not indicate a strong interest in future naltrexone use, although 3 participants gave a rating of "4."

4. Discussion

To our knowledge, this is the first study of pharmacotherapy as a component of treatment to reduce heavy drinking in young adults. In addition to traditional BASICS, the counseling provided specific strategies to moderate drinking that were designed to capitalize on the pharmacological effects of naltrexone. Findings from this pilot study suggest that this line of research is feasible given our ability to recruit this sample and the adherence findings. While our sample was small, it was recruited mainly using flyers, suggesting that it would be possible to recruit a much larger sample with additional funding. Treatment attendance and medication adherence were good, and almost all participants completed the eight weeks of treatment and provided follow-up data. While participants were paid for attending appointments and for completing daily surveys, compensation was not tied to medication adherence.

A prior survey of undergraduate drinkers found that those who expressed interest in pharmacotherapy for drinking reduction tended to favor targeted dosing (Epler et al., in press). Rates of adherence to targeted medication, while lower than adherence to daily doses, were nonetheless respectable, particularly considering the relatively low motivation reported by the majority of the sample. The survey findings and our adherence findings suggest that targeted dosing is a strategy that is well suited to heavy drinking young adults. At the same time, daily dosing, which was associated with particularly good adherence in the present study, could provide coverage for missed targeted doses. Consistent with prior studies, naltrexone was well tolerated and the adverse effects experienced were similar to those reported by older samples (e.g., Anton et al., 2006).

In their meta analysis of individual-level interventions to reduce college student drinking, Carey et al. (2007) reported that Cohen's *d* for decreases in quantity of drinking, frequency of heavy drinking and alcohol-related consequences at immediate follow-up were 0.13, 0.18 and 0.15, respectively, which approximate the 0.20 convention for a small effect using the *d* statistic (Cohen, 1988). Again, while preliminary, significant decreases reported in drinks per drinking day and percent heavy drinking days in the present study had η^2p's of 0.45 and 0.57, respectively, far above the convention of 0.14 for a large effect using the η^2p statistic (Cohen). Cohen's *d* for the significant decrease in alcohol-related consequences in the present study was 0.46, which approximates the 0.50 convention for a medium effect using the *d* statistic (Cohen). The Carey et al. findings suggest the need for novel treatment approaches in young adults and while far from definitive, the present findings suggest that naltrexone represents a promising addition to brief counseling for the reduction of young adult heavy drinking.

Despite the promise of the current findings, considerable caution should be used in interpreting these results because the study was not placebo controlled and the sample was small and almost entirely male. Further, we did not test a single dosing strategy, but rather several approaches were piloted. These limitations make it impossible to attribute improvements definitively to naltrexone. A range of factors such as observer bias, placebo effects, the benefit of BASICS and the medication-related counseling could have been responsible for the significant behavior changes that participants reported.

Heavy drinking in young adults is a serious public health concern. At present, brief counseling, similar to the BASICS approach we implemented in this study, is the standard of care in this population. While often associated with significant reductions in drinking, the effect sizes of these changes tend to be very small. The present findings suggest that the naltrexone + BASICS treatment approach is worth exploring in a larger scale, double-blind, placebo controlled trial. By intervening during young adulthood, a period in which environmental circumstances permit and promote heavy drinking, the goal of this intervention is to help to prevent the development of long-term patterns of problematic alcohol use.

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Table 1

Baseline drinking and consequences, drinking during treatment, drinking and consequences at post-treatment follow-up (N = 14)

Variable	Baseline[1]		Treatment Weeks 1–4[2]		Treatment Weeks 5–8[2]		Post-treatment follow-up[3]	
	Mean (*SD*)	Range	Mean (*SD*)	Range	Mean (*SD*)	Range	Mean (*SD*)	Range
Drinks per drinking day	7.69 (3.57)	4.50–15.18	5.42 (2.71)	2.50–11.90	4.62* (2.41)	1.75–12	3.98** (1.72)	2–7.20
% drinking days	57.6% (18.6%)	33.3%–93.3%	53.4% (16.8%)	35.7%–96.3%	49.1% (17.2%)	25.8%–86.2%	44% (28.1%)	7.1%–100%
% heavy drinking days	39.1% (13.7%)	20%–63.3%	25.1%*a (14.4%)	0%–46.7%	18.6%** (13.4%)	0%–42.9%	13.6***b (12%)	0%–32.1%
RAPI (consequences)	11.54 (5.81)	4–23	n/a		n/a		8.69** (6.51)	1–23

Note: All significant comparisons indicated with asterisks were with baseline level:

* $p \leq .05$

** $p \leq .01$

*** $p \leq .001$

a > b at $p \leq .05$

[1] The baseline period covers the prior 30 days for drinking variables and the prior 3 months for consequences

[2] Treatment drinking outcomes were carried forward for 1 participant who dropped out and did not provide further information.

[3] For drinking outcomes, only the post-treatment period (Weeks 9–12) is covered, but for consequences, the entire period from Week 1–12 is covered. Baseline values were carried forward where there was missing data (drinking outcomes: 1 missing, RAPI: 3 missing). One treatment completer who failed to complete the baseline RAPI was omitted from that analysis.

Table 2

Percent heavy drinking days during the first and second half of treatment by dose (N = 14)

FIRST COHORT OF PARTICIPANTS					
Treatment Weeks 1–4 (N = 14)			**Treatment Weeks 5–8[1] (N = 12)**		
Dose	**Baseline Mean (*SD*)**	**Treatment Mean (*SD*)**	**Dose**	**Baseline Mean (*SD*)**	**Treatment Mean (*SD*)**
			25mg targeted (n = 2)	45% (16.5%)	1.8% (2.5%)
25mg targeted			50mg targeted (n = 3)	36.7% (23.3%)	27.3% (6.1%)
(n = 9)	42.6% (14%)	24.7% (15.8%)	25mg targeted + 25mg daily[2] (n = 4)	45.8% (4.2%)	21% (10.7%)
SECOND COHORT OF PARTICIPANTS					
Treatment Weeks 1–4 (N = 14)			Treatment Weeks 5–8[1] (N = 12)		
Dose	Baseline Mean (*SD*)	Treatment Mean (*SD*)	Dose	Baseline Mean (*SD*)	Treatment Mean (*SD*)
25mg targeted + 25mg daily (n = 5)	32.7% (11.9%)	25.7% (13.2%)	25mg targeted + 25mg daily[2] (n = 3)	34.4% (16.4%)	13.6% (17.5%)

[1] Excludes two participants who dropped out before the second half of treatment

[2] When the participants prescribed 25mg targeted + 25mg daily in the second half of the study were combined (n = 7), the mean and standard deviation were 17.8% (13.2%).