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Reductions in Cannabis Use Are Associated with Improvements in Anxiety, Depression, and Sleep Quality, But Not Quality of Life

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Abstract

Aims—This study examined the longitudinal association between reductions in cannabis use and changes in anxiety, depression, sleep quality, and quality of life.

Methods—Secondary analyses were conducted based on data from a cannabis use disorder medication trial in 302 adults (ages 18–50). Changes in symptoms of anxiety and depression, sleep quality, and quality of life were assessed in relation to changes in cannabis use during the 12-week trial of treatment.

Results—Based on the slope of individual cannabis use trajectory, the sample was classified into two groups (Cannabis Use Reduction, n=152 vs. Cannabis Use Increase, n=150) which was included as a binary covariate in subsequent modeling. Controlling for demographics (age, gender, race/ethnicity), treatment condition, and time-varying tobacco and alcohol use, separate latent growth curve models showed a significant association between the Cannabis Use Reduction group and improvement (i.e., lower values in slope) in anxiety ($\beta = -.09$, SE=0.04; $p<0.05$), depression ($\beta = -0.11$, SE=0.04; $p<0.01$), and sleep quality ($\beta = -0.07$, SE=0.03; $p<0.05$) over the observation period, but not in quality of life.

Conclusions—These results indicate a longitudinal relationship between reductions in cannabis use and improvements in anxiety, depression, and sleep quality. Clinicians treating patients with co-occurring cannabis use and problems with anxiety, depression, or sleep quality should attend to cannabis use reduction as a component of treatment.

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Keywords

cannabis use disorder; depression; anxiety; sleep quality; quality of life

1. INTRODUCTION

Cannabis is the most commonly used illicit substance worldwide (UNODC, 2012; WHO, 2014), and approximately 3 out of 10 users in the United States (U.S.) develop cannabis use disorder (CUD) (Hasin et al., 2015). Though acute psychoactive effects of cannabis vary widely, individuals use cannabis most commonly for its euphoric and calming effects (Rella, 2015). Use of cannabis may elevate mood and improve sleep for some individuals, at least in the short-term (Buckner et al., 2015; Whiting et al., 2015). However, as use becomes chronic or CUD develops, cannabis use may actually worsen these symptoms. Although relevant literature has been limited, existing studies have shown that chronic use of cannabis is associated with increased rates of depression, anxiety, and psychosis (Fergusson and Bowden, 2008; Volkow et al., 2014).

The proportion of individuals seeking treatment for CUD in the U.S. is on the rise (SAMHSA 2010, NCPIC 2012). Many individuals report seeking CUD treatment to address associated mental health problems and functional impairment (van der Pol et al., 2013), such as problems with interpersonal relationships, family, and financial status, in addition to poor energy and motivation (Stephens et al., 2002). However, the question of whether reduction in cannabis use is associated with improvement in mental health and overall functioning has not been adequately examined. Research is needed to address this issue because fear of worsening mood, anxiety, or health conditions may be a barrier for quitting cannabis use. If reduction in cannabis use actually improves functional domains, it has important implications for clinicians treating patients with comorbid cannabis use and other disorders.

Furthermore, evaluations of treatments for substance use disorders (SUDs) have predominantly focused on abstinence-based primary outcomes, an approach that does not encompass the functional status of patients who may reduce drug use and experience improvements in health and other functional domains. Identification of diverse, clinically relevant outcomes for use in future research may advance treatment development for SUDs. Nevertheless, reduced use is a necessary condition for these other outcomes to be considered, and therefore, our focus on the cannabis reduction. Using data from a recently completed multi-site medication trial for CUD conducted in the U.S. by the National Drug Abuse Treatment Clinical Trials Network (Gray et al., in press), we conducted secondary analyses assessing the longitudinal association between reductions in cannabis use and four functional outcomes including anxiety, depression, sleep quality, and quality of life during a 12-week trial. Findings will inform future efforts in identifying promising functional outcomes if reductions in cannabis use are associated with positive changes in health, psychosocial, and other functional outcomes in individuals with CUD.

1.1 Cannabis use and symptoms of anxiety and depression

While individuals often report reduced levels of psychological distress such as anxiety or depression as a motivation to use cannabis (Bonn-Miller et al., 2014), they also report heightened levels of anxiety or depression as a consequence of use (Hanna et al., 2017). Cross-sectional studies and the few available longitudinal studies mostly demonstrated that cannabis use increased risk for development of anxiety (Crippa et al., 2009), depression (Degenhardt, Hall, Lynskey, 2003), and overall dysfunction (Fergusson and Bowden, 2008), but limited research has examined how these functional outcomes might change relative to reductions in cannabis use. Among the few exceptions, a study by Moitra and colleagues (2015) found a longitudinal relationship between reductions in cannabis use and reductions in depression symptoms among female young adults who report at least mild depression symptoms.

1.2 Cannabis use and sleep quality

Likewise, many people report using cannabis to help them initiate sleep (Boys et al., 2001) but chronic cannabis use has been found to be associated with disrupted sleep or poorer sleep quality (Maple et al., 2016). Poor sleep quality was considered a risk factor predicting individuals' lack of success in a cannabis quit attempt (Budney et al., 2001) and sleep quality has been shown to be a feature of cannabis withdrawal in chronic users (Budney et al., 2003). However, limited longitudinal research has examined how a cessation attempt and subsequent reductions in cannabis use impacts sleep among individuals with CUD.

1.3 Cannabis use and quality of life (QoL)

Few studies have examined the relationship between cannabis use and quality of life, even though cannabis is generally used to enhance mood and thus quality of life. The few available cross-sectional studies have reported that higher frequencies of cannabis use were assoicatd with poorer quality of life (Green et al., 2004; Swain et al., 2012). One exception is a cross-sectional study by Allen & Holder (2014) which found no relationship between frequency of cannabis use and well-being among 570 undergraduate students (Allen & Holder, 2014). There has been some evidence showing that cannabis use provided symptom relief in chronic pain and thus may enhance quality of life (Hazekamp et al., 2013).

Extant longitudinal studies generally have not found significant relationships between cannabis use and quality of life (e.g., Swain et al., 2012; Bogart et al., 2007). In contrast, one longitudinal study of offspring of pregnant women in Australia revealed that those who used cannabis more frequently had a lower quality of life at a later time (Fischer et al., 2015). The mental health related quality of life has been shown to be poorer among cannabis users than the general population, particularly among female users (Lev-Ran et al., 2012). Long-term and heavy cannabis users report greater dissatisfaction with quality of life domains and a negative impact of use on their social functioning, cognition, career, physical health, and mental health than infrequent users (Gruber et al., 2003).

1.4 The present study

In the present study, we aim to investigate if reductions in cannabis use lead to improvement in functional status in anxiety, depression, sleep quality, and quality of life. We hypothesize

that there are improvements in anxiety, depression, sleep quality, and quality of life among individuals demonstrating a reduction in cannabis use over time compared to those without reduction, even after controlling for alcohol and tobacco use, as well as treatment condition of the original trial. By examining the associations between within-subjects changes in both cannabis use and functional outcomes, we will gain knowledge about the link between cannabis use reduction and changes in clinical outcomes in anxiety, depression, sleep quality, and quality of life. We focus on the examination of relationships between within-subject changes in cannabis use and changes in functional outcome over time by applying growth modeling for each of the functional measures (anxiety, depression, sleep quality, and quality of life) to test if reduction in cannabis use predicts changes in these functions over time.

2. MATERIAL AND METHODS

2.1 Study Design

We divided the sample (N=302 adults) into those who showed cannabis use reductions over time vs. those who did not, and incorporated this variable as a covariate to assess its impact in the growth curve modeling for each of the four functional outcomes. Cannabis users often use alcohol and tobacco (Pacifci et al., 2003; Richter et al., 2016), and association of health outcomes with cannabis use often disappear after controlling for alcohol and tobacco use (Rooke et al., 2013). Thus, the present study takes into consideration these potential confounds in the examination of association between cannabis use reduction and changes in anxiety, depression, sleep quality, and quality of life.

2.2 Participants

The current study used longitudinal data from a randomized, double-blind, placebo controlled medication trial for CUD (Gray et al., in press). In the parent study (Achieving Cannabis Cessation: Evaluating N-Acetylcysteine Treatment [ACCENT]), 302 adults (ages 18–50) with a diagnosis of cannabis dependence (per Diagnostic and Statistical Manual of Mental Disorders, 4th Edition, Text Revision [DSM-IV] criteria) were randomized to receive either N-acetylcysteine (NAC) 1200 mg or placebo twice daily, added to a contingency management (CM) and medication management platform. Participants were required to submit a cannabis-positive urine drug screen (UDS) during screening, could not meet criteria for dependence on substances other than tobacco, and could not endorse recent use of synthetic cannabinoids. It should be noted that other than severe psychopathology, psychiatric status and symptoms were not considered for inclusion or exclusion.

The trial was implemented at six sites across the U.S. between January 2014 and April 2015. Sites obtained local institutional review board (IRB) approval prior to study initiation, and all participants provided written informed consent. The study was registered on ClinicalTrials.gov (identifier: NCT01675661). Details of study procedures and eligibility criteria have been published elsewhere (McClure et al., 2014).

2.3 Procedures

Participants were assessed at baseline and were randomized in a 1:1 ratio to receive NAC vs. matched placebo twice daily for 12 weeks; participants were seen twice weekly for assessments during the treatment phase and again at 4 weeks post-treatment. All participants received CM twice weekly during the medication phase; escalating CM cash vouchers targeted visit attendance and cannabis abstinence as supported by UDS (diptstick) results. Participants also met with study clinicians weekly for medication management sessions. For the current study, anxiety, depression, and quality of life assessments were conducted at baseline and following 4, 8, and 12 weeks of treatment, and sleep quality had additional weekly assessments during the first month of the treatment phase.

2.4 Instruments and measures

2.4.1 Anxiety and depression—Hospital Anxiety and Depression Scale (HADS; Zigmond and Snaith, 1983) is a brief (7 items each), validated instrument that screens for both anxiety and depression (Bjelland et al. 2002). Each item was rated on a four point (0–3) response category with scores ranged from 0 to 21 for both anxiety and depression. A score of greater than or equal to 8 on the two subscales is indicative of clinically significant depression and anxiety. Cronbach alpha was 0.81 for anxiety and 0.77 for depression.

2.4.2 Sleep quality—The Pittsburgh Sleep Quality Index (PSQI; Buysse et al., 1989) was used to assess sleep quality. The standard (past month) version was used at the screening visit, and a modified (past week) version was used at all subsequent administrations. The scores ranged from 0 to 21 with a higher value indicates poorer sleep quality. A score greater than 5 indicates poor sleep quality. Cronbach alpha was 0.67 for sleep quality.

2.4.3—*Quality of life* was the sum of two measures from the Phenx Toolkit which asked number of days having problems in physical and mental health in the past 30 days, and thus has the range of 0 to 60 (https://www.phenxtoolkit.org/index.php?pageLink=browse.protocoldetails&id=180301). A higher value indicates poorer quality of life; with 14 or more unhealthy days considered poor quality of life (CDC, 2000). Correlation between the 2 items was 0.44.

2.4.4 Cannabis, alcohol, and tobacco use—Timeline Follow-Back (TLFB; Sobell & Sobell, 1992; Levy, et al., 2004; Robinson et al., 2014) methods were used to self-report days of cannabis, number of standard alcohol drinks, and number of tobacco smoked in the past 7 days.

2.5 Statistical analyses

We report descriptive statistics to summarize baseline characteristics of participants. Based on a growth curve model (using SAS PROC MIXED procedures; SAS, 2013), the slope of the cannabis use trajectory (number of days using cannabis in the past week, weekly measured at baseline and over the 12 weeks of the trial) was estimated for each individual. We used this model-based approach to estimate individual slopes to accommodate fluctuation of repeated measures as well as missing observations. The sample was classified into the Cannabis Use Reduction group (n=152) for those with negative slope versus the

Cannabis Use Increase (n=150) for those with positive slope values. This binary indicator was then included in the subsequent analysis as a covariate for investigating its association with each of the four functional outcomes.

To examine associations of cannabis use reduction with changes in anxiety, depression, quality of life, and quality of sleep, a separate latent growth model was developed and tested (Model Is). Trend of each outcome was estimated as a linear growth curve with a random intercept and a random slope. Final models (Model IIs) then include demographics (i.e., age, gender and race/ethnicity) and treatment condition, in addition to the Reduction Group, as time-invariant covariates and alcohol and tobacco use as time-varying covariates. We considered the following three indicators to determine model fit: Chomparative Fit Index (CFI), the Tucker-Lewis Index (TLI) (Bentler & Bonett 1980) and the Root Mean Squared Estimate of Approximation (RMSEA) (Browne & Cudeck 1993). A value of CFI greater than 0.97 and TLI greater than 0.95 are interpreated as acceptable fit, and a RMSEA value between 0.05 and 0.08 indicates a fit close to good (Cangur & Ercan, 2015). These models were tested using Mplus (Muthén & Muthén, 2007).

3. RESULTS

3.1 Demographics and baseline characteristics

Demographics of the study sample are provided in Table 1. The Cannabis Use Reduction Group and the Increase Group did not differ in age (mean of 30.8 vs. 29.9 years), gender (32.2% vs. 24.7% female), educational achievement (64.5% vs. 58% college or higher degree), or employment (61.8% vs. 64% employed). The two groups differed significantly in race/ethnicity with relatively more Black (35.5% vs. 19.3%, $p < .01$) and fewer other (4.0% vs. 11.3%, $p < .05$) in the Reduction group compared to the Increase group.

Frequency of cannabis, alcohol, and tobacco use at baseline did not differ between the groups (see Table 2). The two groups were also similarly distributed across randomized study conditions (medication vs. control) in the parent trial, as well as in primary outcomes at baseline in terms of anxiety, depression, sleep quality, and quality of life. Although there were no group differences, 35.8% of the total sample indicated clinically significant anxiety, and 15.5% depression at the baseline. A high percentage (68.9%) of the study sample reported poor sleep quality. For the quality of life measure, the mean value was 8.0 (SD=10.9) with 21.2% of the sample reported 14 or more unhealthy days in the past 30 days.

3.2 Latent growth curve models

Results of the latent growth curve models are provided in Table 3. Model fit was generally acceptable for anxiety, depression, and sleep quality, but less so for quality of life. All intercepts were significant but none of the mean slopes were except for Model II for anxiety, which indicate that overall mean levels of anxiety, depression, sleep quality, and quality of life did not significantly change over time. The most important finding is reflected in the link between Cannabis Use Reduction and the slope of each outcome measure. Similar relationships were found in the association of Cannabis Use Reduction with each of the four primary outcome measures with (Model IIs) or without (Model Is) controlling for cigarette

and alcohol use at each observation point. Specifically, Cannabis Use Reduction was negatively associated with the slope of anxiety, depression, sleep quality, but not with quality of life. Thus, compared to those without reductions in cannabis use, individuals who reduced use of cannabis over the trial demonstrated significantly greater reduction of anxiety, depression, and improvements of sleep quality over time.

4. DISCUSSION

The present study demonstrated that reduction in cannabis use among individuals treated for CUD is associated with improvement in anxiety, depression, and sleep quality, but not quality of life. These findings are consistent with those studies demonstrating positive association between cannabis use and adverse health outcomes. By examining the association between reductions in cannabis use and changes in functional outcomes, the present study directly demonstrates that reductions in cannabis use are associated with improvement in anxiety, depression, and sleep quality over time. We did not find a similar relationship in quality of life—which may be less sensitive to change, particularly because the values in this measure appeared to be low in our sample, which may result in floor effects. Alternatively, it may be that improvement in anxiety, depression, and sleep symptoms are evident prior to changes in quality of life, which may be slow to change. Nevertheless, our findings have several important clinical implications. Often, individuals with CUD may not be motivated or ready to completely abstain from cannabis use. Many regular cannabis users endorse using cannabis to cope with distress or to improve sleep and these individuals are more susceptible to cannabis-related problems (Lee et al., 2009). Thus, individuals may be hesistant to reduce their cannabis use for fear of elevated negative mood or sleep problems, which can lead to compromised treatment compliance and outcomes. In contrast, these data suggest that reduction in cannabis use is associated with reduction in anxiety and depression and improvement in sleep, on average, and may be used to modify individuals' expectancies. The present study provides empirical evidence to suggest clinicians treating patients with co-occurring cannabis use and anxiety, depression, or sleep problems focus on use reduction or abstinence goals, as reduction in cannabis use is likely to beneficially impact anxiety, depression, and sleep quality.

Also consistent with previous studies, the association between intercept and slope was significantly negative for anxiety, depression, sleep quality, and quality of life, indicating that individuals with greater severity in these areas exhibited more rapid subsequent improvements. However, we did not find significant associations in cigarette smoking or alcohol use with the functional outcomes except that higher level of alcohol use was associated with lower levels of anxiety and depression, and better quality of life at baseline. This may be related to individuals' perception of shortened sleep latency after acute ingestion of alcohol and difficulty interpreting overall sleep quality, which is known to worsen with chronic or heavy alcohol use.

A significant ethnicity/race difference in Reduction vs. Increase groups was found, with more Black participants showing reduction in cannabis use over the trial. Nevertheless, fewer other minority groups (Hispanic, individuals identified themselves multiracial, and other ethnic/racial groups) were in the Reduction groups. While the reasons for the lack of

cannabis use reduction require further research, intervention efforts may need to pay special attention to help these groups reduce their cannabis use.

The present study findings should be interpreted in the context of several study limitations. First, although our findings were based on longitudinal data, the observation period of 12 weeks is relatively short to allow functional outcomes that may require longer time to develop. For example, quality of life may take much longer to change. On the other hand, the value of this measure in our sample was comparable to those reported among the general population (Brown et al., 2003, CDC, 2000, Cook & Harman, 2008); this low value may leave little room to improve. Future studies using alternative measures should be conducted to see if these findings can be replicated. Second, assessment of cannabis use is based on self-reported number of days using; therefore we were not able to control for variation in concentration or potency. Future studies should also take into consideration genetic vulnerability. Otten and colleagues reported a series of studies demonstrating the genetic factors that influenced relationships between cannabis use and symptoms of depression (Otten et al., 2013) and anxiety (Otten et al., 2016). Specifically, they found that cannabis use is associated with an increase in depression and anxiety among carriers of the short allele of the 5-HTTLPR genotype, but not among non-carriers. Efforts to incorporate these factors may contribute to a better understanding of the diverse responses to cannabis use in order to develop more effective individualized interventions.

The study extends the literature on clinical outcomes in cannabis users in several ways. First, although there is a large body of research examining the relationship between cannabis use and a variety of psychiatric symptoms, few studies have focused on multiple domains such as anxiety, depression, sleep and quality of life. Second, the modeling approach we applied testing relationships between within-subjects changes in cannabis use and changes in functional outcomes is in contrast to most previous studies based on between-subjects relationships, and provides further support of the benefit in reduction of cannabis use. To maximize available data, we have included all study participants in the analysis—future studies with larger sample size should examine if greater reductions are associated with stronger functional improvements. Most importantly, given preliminary evidence for significant improvement in these domains after heavy cannabis users successfully reduced their use, functional outcomes in anxiety, depression, and sleep quality may be considered in future development of endpoints for assessing clinical trial for cannabis use disorder. Consitent with studies demonstrating improvement in health and psychological outcomes in alcohol users who reduce or moderate their use (Rehm et al., 2003), use reduction in cannabis users may be a viable treatment goal with associated clinical benefits. Future studies with larger sample sizes should be conducted to quantify the amount of reduction in cannabis use needed for functional improvements that is clinically meaningful.

5. CONCLUSION

Our results indicate that cannabis use reduction is likely to be associated with concurrent reduction in symptoms of anxiety and depression, and improve sleep quality. Further research in clinically meaningful targets of treatment intervention trials for CUD is warranted.

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Highlights

1. Reduction in cannabis use is associated with reduced anxiety and depression
2. Reduction in cannabis use is associated with improvement in sleep quality
3. Cannabis use reduction should be part of the treatment for co-morbid patients

Table 1

Demographics

	Cannabis Reduction Group N=152	Cannabis Increase Group N=150	Total N=302
Age (mean/SD)	30.8/9.3	29.9/8.8	30.3/9.0
Age (%)			
18–25	40.1	39.3	39.7
26–35	30.3	32.7	31.5
36–50	29.6	28.0	28.8
Female (%)	32.2	24.7	28.5
Ethnicity/race (%) **			
White	41.5	45.3	43.4
Black **	35.5	19.3	27.5
Hispanic	19.1	24.0	21.5
Other *	4.0	11.3	7.6
Education (%)			
No high school graduate	9.2	9.3	9.3
High school graduate or GED	26.3	32.7	29.5
College or higher degree	64.5	58.0	61.3
Employed (%)	61.8	64.0	62.9

* p< .05,

** p<.01

Table 2

Clinical profile at baseline

	Cannabis use Reduction Group N=152	Cannabis Increase Group N=150	Total N=302
Cannabis use in past 30 days (mean/SD)	27.2/4.8	24.8/7.2	26.0/6.2
Number of standard alcohol drinks per week (mean/SD)	4.0/7.2	4.9/6.8	4.5/7.0
Number of Cigarettes per week (mean/SD)	22.4/41.3	21.1/43.8	21.8/42.5
N-acetylcysteine/Placebo (%)	45.4/54.6	56.0/44.0	50.7/49.3
Anxiety (Mean/SD)	6.3/3.8	6.5/4.0	6.4/3.9
Above the normal range (N/%)	57/37.5	51/34.0	108/35.8
Depression (Mean/SD)	3.9/3.2	4.0/3.4	4.0/3.3
Above the normal range (N/%)	31/13.8	26/17.4	47/15.5
Quality of Life (Mean/SD)	7.4/10.8	8.5/11.0	8.0/10.9
>=14 days (N/%)	28/18.4	36/24.0	64/21.2
Sleep Quality (Mean/SD)	6.5/3.3	6.3/3.3	6.4/3.3
Poor sleep quality (N/%)	105/69.1	103/68.7	208/68.9

There were no significant differences between two groups for any characteristic except for cannabis use in 30 days prior to informed consent. (p<0.01 by chi-square test and T-test)

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Table 3

Coefficient estimates (standard errors) of latent growth modeling for anxiety, depression, sleep quality, and quality of life

Parameter	Anxiety		Depression		Quality of Life		Sleep Quality	
	Model I	**Model II**	**Model I**	**Model II**	**Model I**	**Model II**	**Model I**	**Model II**
Intercept	5.91(0.94)**	6.75(1.14)**	2.49(0.76)**	2.98(0.89)**	9.36(2.64)**	9.44(3.12)**	5.30(0.70)**	5.39(0.82)**
Age	0.03(0.02)	0.02(0.03)	0.04(0.02)	0.03(0.02)	0.04(0.07)	0.03(0.08)	0.03(0.02)	0.02(0.02)
Gender	−1.37(0.49)**	−1.33(0.58)*	0.23(0.40)	0.18(0.45)	−3.90(1.38)**	−2.74(1.59)	−0.76(0.36)*	−0.69(0.42)
White	0.81(0.53)	1.20(0.63)	−0.51(0.43)	0.13(0.49)	1.93(1.48)	2.98(1.72)	0.17(0.39)	0.40(0.46)
Black	−1.09(0.59)	−0.25(0.70)	−0.08(0.48)	0.53(0.55)	−0.40(1.66)	0.67(1.93)	−0.24(0.44)	−0.06(0.51)
Treatment arm	0.56(0.44)	0.02(0.52)	0.57(0.36)	0.17(0.41)	0.73(1.24)	−0.21(1.43)	−0.09(0.33)	−0.18(0.38)
Cannabis Use Reduction	0.03(0.44)	−0.63(0.54)	−0.04(0.36)	−0.31(0.42)	−1.15(1.25)	−1.69(1.49)	0.30(0.33)	0.09(0.40)
Slope	−0.14(0.08)	−0.18(0.08)*	0.003(0.07)	−0.007(0.08)	−0.35(0.28)	−0.31(0.29)	−0.07(0.07)	−0.03(0.07)
Age	0.002(0.002)	0.003(0.002)	−0.001(0.002)	−0.001(0.002)	0.01(0.01)	0.01(0.007)	0.00(0.002)	0.00(0.002)
Gender	0.04(0.04)	0.01(0.04)	0.01(0.04)	−0.007(0.04)	0.11 (0.14)	−0.03(0.15)	0.01(0.03)	−0.01(0.03)
White	0.01(0.04)	−0.02(0.05)	0.005(0.04)	−0.04(0.04)	−0.07(0.15)	−0.17(0.16)	−0.02(0.04)	−0.03(0.04)
Black	0.03(0.05)	0.005(0.05)	−0.04(0.05)	−0.06(0.05)	0.05(0.17)	0.03(0.18)	−0.06(0.04)	−0.06(0.04)
Treatment arm	−0.01(0.04)	−0.006(0.04)	−0.005(0.03)	0.001(0.04)	−0.14(0.13)	−0.14(0.13)	0.05(0.03)	0.04(0.03)
Cannabis Use Reduction	−0.10(0.04)**	−0.09(0.04)*	−0.10(0.04)**	−0.11(0.04)**	−0.06(0.13)	−0.12(0.14)	−0.06(0.03)	−0.07(0.03)*
Covariance Slope and Intercept	−0.16(0.09)	−0.18(0.09)*	−0.15(0.07)*	−0.13(0.07)	−2.48(1.07)*	−2.13(1.06)*	−0.12(0.05)**	−0.12(0.05)*
Time varying covariates								
Cigarettes baseline		0.005(0.006)		0.004(0.005)		0.03(0.02)		0.003(0.005)
Week 1								−0.002(0.005)
Week 2								−0.004(0.005)
Week 3								−0.005(0.005)
Week 4								−0.007(0.005)
Week 5		−0.004(0.006)		0.003(0.005)		0.02(0.02)		0.001(0.005)
Week 9		−0.005(0.007)		0.01 (0.006)		0.03(0.02)		−0.003(0.006)
Week 12		0.007(0.007)		0.02(0.006)**		0.02(0.02)		0.00(0.006)
Alcohol Baseline		−0.07(0.03)*		−0.05(0.03)*		−0.24(0.09)*		0.03(0.03)
Week 1								−0.004(0.02)

Parameter	Anxiety		Depression		Quality of Life		Sleep Quality	
	Model I	**Model II**	**Model I**	**Model II**	**Model I**	**Model II**	**Model I**	**Model II**
Week 2								0.02(0.02)
Week 3								0.001(0.02)
Week 4								−0.02(0.02)
Week 5		−0.05(0.02) *		−0.04(0.02)		−0.02(0.09)		−0.02(0.02)
Week 9		0.05(0.03)		−0.004(0.02)		−0.04(0.08)		−0.004(0.02)
Week 12		0.03(0.03)		0.007(0.03)		0.14(0.13)		−0.02(0.03)
Goodness of fit								
N	302	219	302	219	302	219	302	219
χ^2	29.73 *	47.54	29.73 *	58.97 *	28.21 *	71.53 **	156.89 **	257.34 **
Df	17	41	17	41	17	41	67	179
RMSEA	0.05	0.03	0.05	0.05	0.05	0.06	0.07	0.05
CFI	0.98	0.99	0.97	0.95	0.96	0.88	0.93	0.93
TLI	0.96	0.98	0.94	0.93	0.92	0.82	0.91	0.92

* p< .05,

** p<.01