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Racial and Ethnic Differences in Treatment Outcomes among Adults with Stimulant Use Disorders after a Dosed Exercise Intervention

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Abstract

The current study examined differences in substance abuse treatment outcomes among racial and ethnic groups enrolled in the Stimulant Reduction Intervention using Dosed Exercise (STRIDE) trial, a multisite randomized clinical trial implemented through the National Institute on Drug Abuse's (NIDA's) Clinical Trials Network (CTN). STRIDE aimed to test vigorous exercise as a novel approach to the treatment of stimulant abuse compared to a health education intervention. A hurdle model with a complier average causal effects (CACE) adjustment was used to provide an unbiased estimate of the exercise effect had all participants been adherent to exercise. Among 214 exercise adherent participants, we found significantly lower probability of use for Blacks ($z = -2.45$, $p = .014$) and significantly lower number of days of use for Whites compared to Hispanics ($z = -54.87$, $p < .001$) and for Whites compared to Blacks ($z = -28.54$, $p < .001$), which suggests that vigorous, regular exercise might improve treatment outcomes given adequate levels of adherence.

Keywords

Stimulant Use Disorder; stimulants; exercise; race; ethnicity

INTRODUCTION

There is a need for innovation in the treatment of substance use disorders, especially for racial and ethnic minority populations. Forty percent of patients admitted to publicly funded treatment programs are minorities (National Institute on Drug Abuse, 2011). Blacks and Hispanics are at greater risk for poor treatment outcomes and are less likely to complete substance abuse treatment, primarily as the result of greater unemployment and housing instability (Saloner & Le Cook, 2013). Because of its success in recruitment and retention of minority populations in substance abuse treatment trials, the NIDA Clinical Trials Network

(CTN) offers a unique opportunity to examine differences in outcomes and other important treatment issues such as mechanisms of change, correlates of drug use and the presence of comorbid disorders which may vary for specific subgroups (Burlew, Feaster, Brecht, & Hubbard, 2009; Carroll et al., 2007; Sanchez et al., 2015).

Stimulant Use Disorder is characterized by a range of relationship, financial and work problems associated with the problematic use of stimulant drugs, including cocaine, methamphetamines, and amphetamines (American Psychiatric Association, 2013). Among racial and ethnic minorities diagnosed with Stimulant Use Disorder, differences in patterns of use and subtypes have been identified, for example, Blacks primarily use cocaine, while Whites and Hispanics are more likely to use amphetamine (Wu et al., 2009). Galea and Rudenstine (2005) have identified key challenges in addressing disparities in drug treatment, which include understanding the complexity of patterns of use and differences in adherence to treatment.

The current study examined differences in substance abuse treatment outcomes among racial and ethnic groups enrolled in the Stimulant Reduction Intervention using Dosed Exercise (STRIDE) trial, a multisite randomized clinical trial implemented through the National Institute on Drug Abuse's (NIDA's) Clinical Trials Network (CTN). STRIDE aimed to test vigorous exercise as a novel approach to the treatment of stimulant abuse compared to a health education intervention (Trivedi, Greer, et al., 2011). In the primary analysis of STRIDE outcomes (Trivedi et al., in press), a marginally significant interaction between treatment and ethnicity (Hispanic and non-Hispanic) ($p=0.051$) was found, such that Hispanic participants in the Exercise intervention had 87% abstinent days compared 71% in Health Education, whereas non-Hispanic participants in the Exercise group had 73% abstinent days, compared to 77% in Health Education. Importantly, we also found a large between-group difference in adherence, defined as number of intervention sessions attended / number of sessions required. For the current secondary analysis of STRIDE, we specifically sought to examine differences in treatment outcomes for various racial and ethnic groups, with specific emphasis on adherence to the intervention. Because adherence rates could differ among racial and ethnic groups and confound differences in exercise outcomes among these groups we used an adjustment for adherence which produces estimates of treatment outcomes as if all groups were adherent to exercise. Use of this adjustment revealed significant treatment effects in a secondary analysis of STRIDE data after the primary intent-to-treat analysis showed no treatment effects.

METHOD

Participants were enrolled in the multi-site STRIDE (CTN-0037) Stimulant Reduction Intervention using Dosed Exercise trial within the NIDA National Drug Abuse Treatment Clinical Trials Network (CTN). Details of the study rationale and design have been previously published (Trivedi et al., 2011). The study was reviewed and approved by the Institutional Review Board (IRB) at University of Texas Southwestern Medical Center, as well as the IRBs of each of the participating treatment programs. All participants provided written informed consent.

Study Sample and Procedures

Participants were adult stimulant users (e.g., cocaine, methamphetamine, or amphetamine), aged 18–65, recruited from 9 geographically diverse, residential substance abuse treatment programs across the United States. In order to be enrolled in STRIDE, participants met DSM-IV criteria for stimulant abuse or dependence within the last 12 months, reported illicit stimulant drug use within the 30 days prior to admission and were medically cleared to exercise via a protocol-defined stress test. Participants with opioid dependence, general medical conditions or medications that contraindicated exercise, pregnancy, and those with psychosis or other psychiatric conditions that posed a safety risk were excluded (Trivedi et al., 2011). Participants were classified as White (non-Hispanic), Black (non-Hispanic), or Hispanic. Five participants classified as other than White, Black, or Hispanic were excluded from the analysis, resulting in a total sample of 297.

Eligible participants were randomized to one of two treatment arms in addition to usual care in a residential treatment program: 1) dosed exercised intervention (DEI) or 2) health education intervention (HEI). Both treatment arms consisted of a 3-month acute phase which included intervention and assessment visits three times per week. Randomization to the two treatment groups was stratified based on the presence of depressive symptoms and severity of stimulant use.

Measures

Stimulant use disorders were assessed using the substance use modules from the World Health Organization (WHO) Composite International Diagnostic Interview (CIDI) (Version 2.1) (Robins et al., 1988; WHO, 1997). Several participants received more than one stimulant diagnosis, therefore the sample was grouped into the following categories to better reflect the substance(s) used, as follows: 1) cocaine use disorder only; 2) cocaine plus other stimulant use disorder (e.g., methamphetamine); and 3) other stimulant use disorder only.

Participants completed the Self-Administered Comorbidity Questionnaire (SCQ) (Sangha, Stucki, Liang, Fossel, & Katz, 2003), which assesses the presence of medical problems, their severity, and whether or not the condition limits functioning. Participants received a maximum of 3 points for each medical condition (1 point for its presence, 1 point if the condition was treated, and 1 point if the condition limited activities). There were 15 conditions and the option to add 3 additional conditions. The possible score range was 0–54.

The MGH Cognitive and Physical Functioning Questionnaire (CPFQ) (Fava et al., 2006) is a 7-item measure of physical well-being and cognitive and executive dysfunction. Each item uses a 6-point scale ranging from 1 (greater than normal) to 6 (totally absent). The total score is the sum of items a-g, with a range of 7 – 42. Higher scores indicate poorer functioning.

The Addiction Severity Index-Lite (ASI-Lite) assessed multiple domains commonly affected by substance use, including medical, employment/self-support, alcohol use, drug use, legal status, family/social, and psychiatric status (McLellan, Luborsky, Woody, & O'Brien, 1980). The Stimulant Selective Severity Assessment (SSSA) measured stimulant abstinence symptom severity for the past 24 hours and was adapted from the Cocaine Selective Severity

Assessment (CSSA) (Kampman et al., 1998). Domains measured included carbohydrate craving, mood, appetite, sleep, energy, and pulse rate.

Drug, alcohol, and nicotine quantity and frequency were assessed for the 30 days prior to residential treatment admission and at each assessment visit using the Timeline Followback (TLFB) method (Sobell & Sobell, 1992). Urine drug screens (UDS) measured stimulant use (cocaine, amphetamine, methamphetamine), as well as opiates, marijuana, benzodiazepines, barbiturates, methadone, methylenedioxymethamphetamine (MDMA, ecstasy), and oxycodone. Stimulant use was assessed three times per week during the acute intervention phase.

Study Interventions

Both treatment groups received substance use disorder usual care in a residential treatment program (RTP) with a length of stay generally between 21 and 30 days, and then continued in an outpatient treatment program at or near the residential setting. The two treatment arms were structured such that the number of visits was similar to allow for equivalent contact with professionals between groups, which began with 12 weeks of acute phase intervention (primary outcome period) followed by an additional 24 weeks of intervention with supervision once per week.

Dosed Exercise Intervention (DEI)—Participants randomized to DEI (Stoutenberg et al., 2012; Trivedi et al., 2011) completed supervised, one-on-one exercise sessions 3 times per week during the 12-week acute phase. DEI was prescribed at a dose of 12 kcal/kg/week (KKW), with intensity ranging from 70–85% of maximal heart rate (HRmax). This dose is similar to those used in several studies of exercise interventions (Church et al., 2010; Church, Earnest, Skinner, & Blair, 2007). Exercise dose and intensity were gradually increased during the first 3 weeks to increase tolerability for participants (Week 1: 4KKW @ 50–60% HRmax; Week 2: 8 KKW @ 60–70% HRmax; Week 3–12: 12 KKW @ 70–85% HRmax). For the majority of participants, the maximum intensity was equivalent to walking at a moderate speed (3.0 mph) and moderate incline (5%) for approximately 150 minutes per week.

Health Education Intervention (HEI)—Participants randomized to the HEI (Rethorst et al., 2014) also completed 3 visits per week during the 12-week acute phase. HEI consisted of one-on-one sessions in which information on health-related topics (e.g., cancer, heart disease, mental health) was distributed via didactics, websites, audio, video, and written materials.

Data Analysis

Baseline demographic and drug use characteristics were compared between race/ethnicity groups by analysis of variance for continuous outcomes and chi-square tests for categorical outcomes using the sample of 297 participants classified as either White, Black, or Hispanic, and have been reported previously (Sanchez et al., 2015). Five participants with other classifications were excluded. Significant effects were followed by comparisons between

each pair of race/ethnicity groups using the Bonferroni correction to adjust the significance level for multiple comparisons ($.05/3=0.0167$).

The outcome measure (days of post-RTP stimulant use) was analyzed using a hurdle model because the number of participants with zero days of use was larger than would be expected from the assumed Poisson distribution of count data (Carmody, Greer, Walker, Rethorst, & Trivedi, revise and resubmit). A hurdle model is based on the assumption that, although any participant may use drugs, there is “resistance” to drug use (a hurdle) which must be overcome before drugs are used. The existence of the hurdle results in an excess of participants with zero days of use (Agresti & Min, 2005). The STRIDE study fits the assumptions of the hurdle model in that all participants have the potential to resume using stimulants, but resistance to use is present due to the fact that participants chose to enter treatment and we expect a beneficial effect of treatment as usual (Carmody et al., revise and resubmit).

The hurdle model provides estimates for the probability of stimulant use and the number of days of stimulant use among those who used stimulants. The actual post-RTP days of use were standardized to reflect the days of use that would have been observed in a 63 day post-RTP period (i.e., it is assumed the participant spent 21 days in RTP). The hurdle model contained random site effects and fixed effects for treatment group, race/ethnicity, treatment group by race/ethnicity interaction, and covariates. Mplus software Version 7.3 was used to implement the hurdle model based on the Negative Binomial Distribution, which is a more flexible variant of the Poisson distribution (Muthén & Muthén, 2012). Some sites had no Hispanics participants and reliable estimates could not be obtained using all 9 sites, therefore, the sites were collapsed into 2 sites based on presence of Hispanic participants, baseline days of stimulant use, and days in RTP. Pre-specified covariates (days of stimulant use in the 30 days prior to RTP, age, and gender) were included as well as two additional covariates specifically for the race/ethnicity moderator analysis: number of medical comorbidities (SCQ total score) and type of drug (cocaine use disorder, cocaine plus other stimulant use disorder and other stimulant use disorder).

In addition to the unadjusted hurdle model, a hurdle model with a complier average causal effects (CACE) adjustment was used to provide an unbiased estimate of the exercise effect had all participants been adherent to exercise (Carmody et al., revise and resubmit). This type of analysis has been used in trials of behavioral interventions (Knox, Lall, Hansen, & Lamb, 2014; Liang, Ehler, Hollenbeak, & Turner, 2015), including substance abuse research (Connell, 2009; Huang et al., 2014). Details of the CACE adjustment are found in Stuart & Jo (2015).

Briefly, to implement the CACE method, a model of pre-randomization variables was created to predict adherence among DEI participants. In order for the CACE method to produce unbiased estimates, it is necessary to identify all important predictors of adherence in the model. The median split in average KKW expended per week was used to define adherence (8.3 KKW) as this choice will maximize the power to detect predictors of adherence. Due to randomization, this adherence model can be applied to health education participants to produce propensity score weights which make the weighted health education

group comparable to exercise adherent participants. Therefore, the stimulant use outcome of the weighted health education group is an estimate of what the outcome of the health education group would have been if the health education group were composed of participants who would have been adherent to exercise if they had been assigned to exercise. A comparison between exercise adherent participants in the DEI group and the weighted HEI group is an unbiased estimate of treatment effect among adherent participants as long as the adherence model does not omit any important predictors of adherence, as described in Carmody, et al. (revise and resubmit). Eleven additional covariates were added to the adjusted hurdle model due to the requirement of the CACE analysis to balance DEI and HEI groups with respect to all covariates related to adherence: ASI drug use subscale score, percent attendance of TAU sessions in the 30 days prior to RTP, SSSA hyperphagia item, days of cocaine use in the 30 days prior to baseline assessment based on the ASI, study conducted at site 2 (yes/no), CPFQ total score, CAST sleep item, days of cocaine use in the 30 days prior to RTP based on TLFB, study conducted at site 1 (yes/no), days of illegal activity in the 30 days prior to baseline assessment, and days incarcerated in the 30 days prior to baseline assessment.

Three unadjusted and adjusted hurdle models were fit: one for White and Black subjects only, one for White and Hispanic subjects only, and one for Black and Hispanic subjects only. A Bonferroni corrected p -value of $0.5/3 = 0.0167$ was used for the pairwise comparisons.

RESULTS

Demographic and Drug Use Characteristics

The demographic and drug use characteristics of the sample ($N=297$) have been reported previously (Sanchez et al., 2015) and are presented in Table 1, stratified by race and ethnicity: White ($n=136$), Black ($n=130$), and Hispanic ($n=31$). Black participants were significantly older than Whites or Hispanics ($M=44.1$ years, $SD=10.0$, $p<.001$). Gender also varied significantly across race and ethnicity ($p<.001$) as did level of education ($p=.011$).

Significant differences between race/ethnicity groups were found on drug use characteristics. Black participants were more likely to use alcohol (78.5%) than White participants (66.3%), $p<.001$. Blacks had higher rates of cocaine use (97.7%) versus Whites (63.2%) or Hispanics (67.7%), $p<.001$, but much lower rates of methamphetamine use (3.8%) than Hispanics (35.5%) and Whites (47.8%), $p<.001$. Whites used other stimulants (5.1%) at higher rates than Blacks (0.0%), $p=.009$ and combinations of drugs (31.6%) at higher rates than Blacks (4.6%) and Hispanics (9.7%), $p<.014$.

There were significant differences in stimulant use disorder diagnoses by race and ethnicity, $p<.001$. Black participants (90.8%) were more likely to be diagnosed with abuse or dependence of cocaine only than Hispanics (51.6%), $p<.001$, and Hispanics were more likely to have this diagnosis than Whites (28.9%), $p=.0153$. Whites (52.6%) and Hispanics (38.7%) were more likely than Blacks (6.2%) to be diagnosed with a combined cocaine and other stimulant use disorder ($p<.001$) and Whites (18.5%) were more likely than Blacks

(3.1%) to be diagnosed with other stimulant (not cocaine) use disorder only ($p < .001$). Regarding route of drug use, Blacks were significantly more likely to report smoking cocaine (75.2%) than Whites (45.5%), $p < .001$, while Whites (39.3%) were more likely to use cocaine via nasal route than Blacks (22.5%), $p = .005$ and also more likely to use the injection route (Whites 15.2% vs Blacks 1.6%, $p < .001$).

Unadjusted Hurdle Model of Stimulant Use

Altogether, 288 participants were used in this analysis because 7 participants had no post-baseline data and two participants had missing values on some covariates. A median split was used to define adherence, therefore, by definition the adherence rate was 50% in the entire sample. Adherence rates by race/ethnicity were 47% for Whites, 55% for Blacks, and 47% for Hispanics. The CACE analysis, where results are adjusted to reflect what would be expected if 100% of participants were adherent in each race/ethnic group, presents a perspective in which differences in adherence by race/ethnic group do not influence the results, therefore, an unadjusted analysis is also presented to allow for differences in adherence across race/ethnic groups to influence the results.

The unadjusted results for the probability of use among Whites, Blacks, and Hispanics with all other covariates set to mean levels are depicted in Figure 1. Pairwise comparisons of the main effect of race/ethnicity on probability of use showed that the probability of use when averaged across treatment groups did not differ between Whites and Blacks ($z = -0.49$, $p = .672$), between Whites and Hispanics ($z = 0.60$, $p = .550$), or between Blacks and Hispanics ($z = -1.86$, $p = .063$). Pairwise comparisons of the interaction between race/ethnicity and treatment effect showed that the difference between treatment groups was not significantly different for Whites compared to Blacks ($z = -.97$, $p = .333$) or Blacks compared to Hispanics ($z = 1.55$, $p = .121$). However, the treatment effect was significantly larger for Hispanics compared to Whites ($z = 6.29$, $p < .001$) with the probability of use found to be 3.9 percentage points higher in the DEI group than the HEI group among Hispanics but only 0.8 percentage point higher among Whites (Figure 1).

The unadjusted results for days of stimulant use among White, Black, and Hispanic users with all other covariates set to mean levels are depicted in Figure 2. Pairwise comparisons for the main effect of days of use showed that days of use when averaged across treatment groups did not significantly differ between Whites and Hispanics ($z = 1.34$, $p = .181$) or between Blacks and Hispanics ($z = 0.39$, $p = .695$) but did differ between Whites and Blacks ($z = -3.90$, $p < .001$) where Whites averaged 8.5 days of use and Blacks averaged 11.6 days of use. Pairwise comparisons of the interaction of treatment group with a race/ethnicity group showed that the difference between treatment groups did not differ significantly for Whites compared to Hispanics ($z = -1.47$, $p = .141$), Whites compared to Blacks ($z = -0.52$, $p = .602$) or for Blacks compared to Hispanics ($z = 0.98$, $p = .329$).

CACE Adjusted Hurdle Model of Stimulant Use

Altogether, 214 of the 297 participants were used in this analysis because 7 had no post-baseline data, 72 were non-adherent participants in the DEI group and are not used in a CACE analysis (Stuart & Jo, 2015), and 4 subjects had missing values on some of the

covariates. The CACE adjusted results for the probability of use among Whites, Blacks, and Hispanics with all other covariates set to mean levels are depicted in Figure 3. Pairwise comparisons of the main effect of race/ethnicity on probability of use showed that the probability of use when averaged across treatment groups did not differ between Whites and Blacks ($z=0.75$, $p=.451$), between Whites and Hispanics ($z=0.91$, $p=.361$), or between Blacks and Hispanics ($z=-0.11$, $p=.911$). Pairwise comparisons of the interaction between race/ethnicity and treatment effect showed that the difference between treatment groups was not significantly larger for Whites compared to Hispanics after Bonferroni correction ($z=-2.19$, $p=.028$) nor for Whites compared to Blacks ($z=-0.05$, $p=.963$). However, the difference between treatment groups was significantly larger for Blacks compared to Hispanics ($z=-2.45$, $p=.014$), with a reduction of DEI compared to HEI of 15.3 percentage points for Blacks versus an increase of 0.9 percentage points for Hispanics (Figure 3).

The CACE adjusted results for days of stimulant use among White, Black, and Hispanic users with all other covariates set to mean levels are depicted in Figure 4. Pairwise comparisons for the main effect of days of use showed that days of use when averaged across treatment groups did not differ between Whites and Hispanics ($z=1.24$, $p=.216$), between Whites and Blacks ($z=0.18$, $p=.855$), or between Blacks and Hispanics ($z=0.30$, $p=.760$). Pairwise comparisons of the interaction of treatment group with a race/ethnicity group showed that the difference between treatment groups differed significantly for Whites compared to Hispanics ($z=-54.87$, $p<.001$) and for Whites compared to Blacks ($z=-28.54$, $p<.001$). Days of use did not differ for Blacks compared to Hispanics after Bonferroni correction ($z=-2.33$, $p=.020$). The reduction in days of use was estimated to be 5.8 days for Whites, 2.6 days for Blacks, and 9.9 days for Hispanics (Figure 4).

DISCUSSION

In this large-scale study of a unique exercise intervention for the treatment of stimulant abuse in a community-based, treatment-seeking sample, the significant finding of lower probability of use for Blacks in the exercise intervention using the CACE adjustment for adherence suggests that vigorous, regular exercise might improve treatment outcomes given adequate levels of adherence. In light of recent research which suggests Blacks may be at particular risk for poor treatment outcomes, largely due to early drop out, novel strategies to increase patient engagement are necessary (Saloner & Le Cook, 2013). Such strategies may help reduce barriers to treatment, which include socioeconomic stressors, a general mistrust of medical providers and mistreatment based on race (Sanchez, Ybarra, Chapa, & Martinez, 2016). Findings of lower probability of use in the exercise group were similar for Whites, though not significant.

Additionally, at the end of treatment, the number of days of use for Whites in the exercise intervention was significantly lower than the health education intervention. Since production and acquisition of methamphetamine occurs largely through White social networks, and rates of use among young White males are growing at an alarming rate (Borders et al., 2008; Herbeck, Brecht, & Pham, 2013), exercise shows promise as an effective intervention for stimulant use and dependence. Though previous studies of exercise as treatment for substance use have reported improved outcomes, a comprehensive review found the

evidence is weak with poor methodology (Zschucke, Heinz, & Strohle, 2012). The current study was a randomized control trial whose participants were recruited from a geographically diverse set of community treatment programs, thus yielding stronger evidence and more generalizable results.

Hispanics appeared to benefit from the exercise intervention, as demonstrated by the greatest difference in number of days of use between treatment groups, though findings were not significant. This is likely due to the small sample size of and large variance within the Hispanic group. And while previous research has found Hispanics to be less likely to seek treatment, less likely to stay in treatment and less satisfied with treatment, nonetheless, they tend to achieve greatest outcomes in the shortest period of time (Guerrero, Marsh, Khachikian, Amaro, & Vega, 2013). There remains a lack of studies with adequate Hispanic sample size to have sufficient statistical power to describe precise effects of the intervention (Miranda, Nakamura, & Bernal, 2003) and our study was challenged with similar barriers.

Patterns of stimulant use in the United States vary by geographic region, type of stimulant used, route of administration and demographic characteristics of the users. Findings from the current study support previous research and clinical anecdote which suggest cocaine and amphetamine users represent two discrete groups of stimulant users with distinct age and racial background and little overlap in profile (Maxwell & Rutkowski, 2008). Blacks in the current study were older, which suggests prolonged addiction and corresponds with previous research that found Blacks were least likely to initiate substance abuse treatment (Acevedo et al., 2012). Additionally, Blacks report higher rates of cocaine use, by routes with faster absorption (i.e., smoking or injection), which are associated with higher rates of dependence (Chen & Kandel, 2002).

There are limitations to this study that should be noted. Namely, persons with physical issues or illness that would preclude exercise, or with psychiatric safety concerns, were not eligible for inclusion in STRIDE, thus limiting the scope of recruitment. Participants also had to be interested and willing to exercise, which may reduce generalizability to the larger treatment-seeking population. The limits of the CACE adjustment analysis should also be noted as the study findings reflect the effect of exercise among adherent participants. Additionally, the days of use data are self-report, which may be subject to recall bias, although the time periods assessed for most measures were relatively short (30 days).

CONCLUSION

The STRIDE study demonstrated intensive exercise interventions for people with stimulant use disorders, in community-based addiction treatment, are feasible. Examining race/ethnicity differences in treatment outcomes using novel approaches is important to understanding disparities and what contributes to success. There is a need for engagement strategies for sustaining Blacks in treatment and recruiting them into treatment earlier in life (Burlew et al., 2009). Vigorous exercise may benefit racial and ethnic minority populations with stimulant use disorder. Future research should focus on intentional inclusion of race/ethnic groups, early in the study design, to test interventions targeted with a specific focus on what works for certain populations.

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References

- Acevedo A, Garnick DW, Lee MT, Horgan CM, Ritter G, Panas L, ... Reynolds M. Racial and ethnic differences in substance abuse treatment initiation and engagement. *Journal of ethnicity in substance abuse*. 2012; 11(1):1–21. DOI: 10.1080/15332640.2012.652516 [PubMed: 22381120]
- Agresti A, Min Y. Simple improved confidence intervals for comparing matched proportions. *Stat Med*. 2005; 24(5):729–740. DOI: 10.1002/sim.1781 [PubMed: 15696504]
- American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders DSM-5*. 5. Washington. D.C: American Psychiatric Association; 2013.
- Borders TF, Booth BM, Han X, Wright P, Leukefeld C, Falck RS, Carlson RG. Longitudinal changes in methamphetamine and cocaine use in untreated rural stimulant users: racial differences and the impact of methamphetamine legislation. *Addiction*. 2008; 103(5):800–808. DOI: 10.1111/j.1360-0443.2008.02159.x [PubMed: 18412758]
- Burlew AK, Feaster D, Brecht ML, Hubbard R. Measurement and data analysis in research addressing health disparities in substance abuse. *Journal of Substance Abuse Treatment*. 2009; 36(1):25–43. DOI: 10.1016/j.jsat.2008.04.003 [PubMed: 18550320]
- Carmody T, Greer TL, Walker R, Rethorst C, Trivedi MH. A complier average causal effect analysis of the Stimulant Reduction Intervention using Dosed Exercise study. *Journal of Consulting and Clinical Psychiatry*. revise and resubmit.
- Carroll KM, Rosa CL, Brown LS, Daw R, Magruder KM, Beatty LB. Addressing Ethnic Disparities in Drug Abuse Treatment in the Clinical Trials Network. *Drug and Alcohol Dependence*. 2007; 90(1):101–106.
- Chen K, Kandel D. Relationship between extent of cocaine use and dependence among adolescents and adults in the United States. *Drug and Alcohol Dependence*. 2002; 68(1):65–85. DOI: 10.1016/S0376-8716(02)00086-8 [PubMed: 12167553]
- Church TS, Blair SN, Cocroham S, Johannsen N, Johnson W, Kramer K, ... Earnest CP. Effects of aerobic and resistance training on hemoglobin A1c levels in patients with type 2 diabetes: a randomized controlled trial. *JAMA*. 2010; 304(20):2253–2262. DOI: 10.1001/jama.2010.1710 [PubMed: 21098771]
- Church TS, Earnest CP, Skinner JS, Blair SN. Effects of different doses of physical activity on cardiorespiratory fitness among sedentary, overweight or obese postmenopausal women with elevated blood pressure: a randomized controlled trial. *JAMA*. 2007; 297(19):2081–2091. DOI: 10.1001/jama.297.19.2081 [PubMed: 17507344]
- Connell AM. Employing complier average causal effect analytic methods to examine effects of randomized encouragement trials. *Am J Drug Alcohol Abuse*. 2009; 35(4):253–259. DOI: 10.1080/00952990903005882 [PubMed: 20180678]
- Fava M, Graves LM, Benazzi F, Scalia MJ, Iosifescu DV, Alpert JE, Papakostas GI. A cross-sectional study of the prevalence of cognitive and physical symptoms during long-term antidepressant treatment. *J Clin Psychiatry*. 2006; 67(11):1754–1759. [PubMed: 17196056]
- Galea S, Rudenstine S. Challenges in understanding disparities in drug use and its consequences. *Journal of Urban Health-Bulletin of the New York Academy of Medicine*. 2005; 82(2):III5–III12. DOI: 10.1093/jurban/jti059 [PubMed: 15933331]
- Guerrero EG, Marsh JC, Khachikian T, Amaro H, Vega WA. Disparities in Latino substance use, service use, and treatment: Implications for culturally and evidence-based interventions under health care reform. *Drug and Alcohol Dependence*. 2013; 133(3):805–813. DOI: 10.1016/j.drugalcdep.2013.07.027 [PubMed: 23953657]

- Herbeck DM, Brecht ML, Pham AZ. Racial/ethnic differences in health status and morbidity among adults who use methamphetamine. *Psychology Health & Medicine*. 2013; 18(3):262–274. DOI: 10.1080/13548506.2012.701754
- Huang S, Cordova D, Estrada Y, Brincks AM, Asfour LS, Prado G. An application of the Complier Average Causal Effect analysis to examine the effects of a family intervention in reducing illicit drug use among high-risk Hispanic adolescents. *Fam Process*. 2014; 53(2):336–347. DOI: 10.1111/famp.12068 [PubMed: 24611528]
- Kampman KM, Volpicelli JR, McGinnis DE, Alterman AI, Weinrieb RM, D'Angelo L, Epperson LE. Reliability and validity of the Cocaine Selective Severity Assessment. *Addict Behav*. 1998; 23(4): 449–461. [PubMed: 9698974]
- Knox CR, Lall R, Hansen Z, Lamb SE. Treatment compliance and effectiveness of a cognitive behavioural intervention for low back pain: a complier average causal effect approach to the BeST data set. *BMC Musculoskelet Disord*. 2014; 15:17.doi: 10.1186/1471-2474-15-17 [PubMed: 24423146]
- Liang Y, Ehler BR, Hollenbeak CS, Turner BJ. Behavioral support intervention for uncontrolled hypertension: a complier average causal effect (CACE) analysis. *Med Care*. 2015; 53(2):e9–e15. DOI: 10.1097/MLR.0b013e31827da928 [PubMed: 23269112]
- Maxwell JC, Rutkowski BA. The prevalence of methamphetamine and amphetamine abuse in North America: a review of the indicators, 1992–2007. *Drug and Alcohol Review*. 2008; 27(3):229–235. DOI: 10.1080/09595230801919460 [PubMed: 18368603]
- McLellan AT, Luborsky L, Woody GE, O'Brien CP. An improved diagnostic evaluation instrument for substance abuse patients. The Addiction Severity Index. *J Nerv Ment Dis*. 1980; 168(1):26–33. [PubMed: 7351540]
- Miranda J, Nakamura R, Bernal G. Including ethnic minorities in mental health intervention research: A practical approach to a long-standing problem. *Culture, Medicine and Psychiatry*. 2003; 27(4): 467–486.
- Muthén, LK., Muthén, BO. *Statistical Analysis with Latent Variables Using Mplus*. 7. Los Angeles: Muthén & Muthén; 2012.
- National Institute on Drug Abuse. *DrugFacts: Treatment statistics*. Rockville, MD: NIDA; 2011. Retrieved from <http://www.drugabuse.gov/publications/drugfacts/treatment-statistics>
- Rethorst CD, Greer TL, Grannemann B, Ring KM, Marcus BH, Trivedi MH. A Health Education Intervention as the Control Condition in the CTN-0037 STRIDE multi-site exercise trial: Rationale and Description. *Ment Health Phys Act*. 2014; 7(1):37–41. DOI: 10.1016/j.mhpa.2013.12.001 [PubMed: 24729793]
- Robins LN, Wing J, Wittchen HU, Helzer JE, Babor TF, ... Burke J, et al. The Composite International Diagnostic Interview. An epidemiologic instrument suitable for use in conjunction with different diagnostic systems and in different cultures. *Arch Gen Psychiatry*. 1988; 45(12):1069–1077. [PubMed: 2848472]
- Saloner B, Le Cook B. Blacks And Hispanics Are Less Likely Than Whites To Complete Addiction Treatment, Largely Due To Socioeconomic Factors. *Health Affairs*. 2013; 32(1):135–145. DOI: 10.1377/hlthaff.2011.0983 [PubMed: 23297281]
- Sanchez K, Chartier K, Greer TL, Walker R, Carmody T, Rethorst CD, ... MHT. Comorbidities and Race/Ethnicity among Adults with Stimulant Use Disorders in Residential Treatment Setting: A Baseline Analysis of the STRIDE Cohort. *Journal of Ethnicity and Substance Abuse*. 2015
- Sanchez K, Ybarra R, Chapa T, Martinez ON. Eliminating Behavioral Health Disparities and Improving Outcomes for Racial and Ethnic Minority Populations. *Psychiatric services (Washington, DC)*. 2016; 67(1):13–15. DOI: 10.1176/appi.ps.201400581
- Sangha O, Stucki G, Liang MH, Fossel AH, Katz JN. The Self-Administered Comorbidity Questionnaire: A new method to assess comorbidity for clinical and health services research. *Arthritis & Rheumatism*. 2003; 49:156–163. [PubMed: 12687505]
- Sobell, LC., Sobell, MB. Timeline Follow-back: A technique for assessing self-reported ethanol consumption. In: Allen, J., Litten, RZ., editors. *Measuring Alcohol Consumption: Psychosocial and Biological Methods*. Totowa, NJ: Humana Press; 1992. p. 41-72.

- Stoutenberg M, Rethorst C, Fuzat G, Greer T, Blair S, Church T, ... Trivedi M. STimulant Reduction Intervention using Dosed Exercise (STRIDE) - Description of the Exercise Intervention and Behavioral Program to Ensure Adherence. *Ment Health Phys Act*. 2012; 5(2):175–182. DOI: 10.1016/j.mhpa.2012.08.003 [PubMed: 23667387]
- Stuart EA, Jo B. Assessing the sensitivity of methods for estimating principal causal effects. *Statistical Methods in Medical Research*. 2015; 24(6):657–674. DOI: 10.1177/0962280211421840 [PubMed: 21971481]
- Trivedi MH, Greer TL, Grannemann BD, Church TS, Somoza E, Blair SN, ... Nunes E. Stimulant Reduction Intervention using Dosed Exercise (STRIDE) - CTN 0037: Study protocol for a randomized controlled trial. *Trials*. 2011; 12:15.doi: 10.1186/1745-6215-12-206 [PubMed: 21244698]
- Trivedi MH, Greer TL, Rethorst C, Carmody T, Grannemann B, Walker R, ... Nunes E. Randomized trial comparing exercise to health education for stimulant use disorder: Results from STimulant Reduction Intervention using Dosed Exercise (CTN-0037; STRIDE). *Journal of Clinical Psychiatry*. in press.
- WHO. Composite International Diagnostic Interview, version 2.1. Geneva: World Health Organization; 1997.
- Wu LT, Blazer DG, Patkar AA, Stitzer ML, Wakim PG, Brooner RK. Heterogeneity of Stimulant Dependence: A National Drug Abuse Treatment Clinical Trials Network Study. *American Journal on Addictions*. 2009; 18(3):206–218. DOI: 10.1080/10550490902787031 [PubMed: 19340639]
- Zschucke E, Heinz A, Strohle A. Exercise and Physical Activity in the Therapy of Substance Use Disorders. *Scientific World Journal*. 2012; 19doi: 10.1100/2012/901741

Figure 1. Unadjusted model estimated probability of stimulant use by race/ethnicity

*** $p < .001$, using Whites as reference group

#Estimated probability of post-RTP stimulant use

Figure 2. Unadjusted model estimated days of stimulant use by race/ethnicity
 #Estimated post-RTP days of use for those who relapse

Figure 3. CACE adjusted model estimated probability of stimulant use by race/ethnicity

* $p < .05$, after Bonferroni correction, using Hispanics as reference group

Estimated probability of post-RTP stimulant use

Figure 4. CACE adjusted model estimated days of stimulant use by race/ethnicity

*** $p < .001$, after Bonferroni correction

¹using Hispanics as reference group

²using Blacks as reference group

#Estimated post-RTP days of use for those who relapse

Table 1

Demographic and Drug Use Characteristics by Race/Ethnic Groups

Demographic Characteristic	All N = 297	White n = 136 (46%)	Black n = 130 (44%)	Hispanic n = 31 (10%)	χ^2/F stat	p-value	Effect Size
	M (SD)	M (SD)	M (SD)	M (SD)			
Age (yrs)	39.0 (10.8)	35.3 (9.8)	44.1 (10.0)	33.7 (9.2)	31.8	<0.001	0.17
	n (%)	n (%)	n (%)	n (%)			
Female	119 (40.1)	62 (45.6)	36 (27.7)	21 (67.7)	19.9	<0.001	0.26
Education Level					12.9	0.011	0.15
Less Than High School	55 (18.5)	16 (11.8)	29 (22.3)	10 (32.3)			
High School Grad	153 (51.5)	70 (51.5)	71 (54.6)	12 (38.7)			
Post High School	89 (30.0)	50 (36.8)	30 (23.1)	9 (29.0)			
Substance Use (Past 30 days)							
Cigarettes	231 (77.8)	111 (81.6)	94 (72.3)	26 (83.9)	4.1	0.130	0.12
Other Tobacco	10 (3.4)	4 (2.9)	5 (3.8)	1 (3.2)	0.2	0.919	0.02
Alcohol	197 (66.3)	73 (53.7)	102 (78.5)	22 (71.0)	18.6	<0.001	0.25
Cocaine	234 (78.8)	86 (63.2)	127 (97.7)	21 (67.7)	49.7	<0.001	0.41
Amphetamine	4 (1.3)	4 (2.9)	0 (0.0)	0 (0.0)	4.8	0.091	0.13
Methamphetamine	81 (27.3)	65 (47.8)	5 (3.8)	11 (35.5)	65.9	<0.001	0.47
Other Stimulants	7 (2.4)	7 (5.1)	0 (0.0)	0 (0.0)	8.5	0.014	0.17
Marijuana	129 (43.4)	62 (45.6)	53 (40.8)	14 (45.2)	0.7	0.715	0.05
Several Drugs Combined	52 (17.5)	43 (31.6)	6 (4.6)	3 (9.7)	35.0	<0.001	0.34
Substance Use Disorders		105.5	<0.001	0.42			
Cocaine (not stimulant) abuse or dependence	173 (58.4)	39 (28.9)	118 (90.8)	16 (51.6)			
Cocaine and stimulant abuse or dependence	91 (30.7)	71 (52.6)	8 (6.2)	12 (38.7)			
Stimulant (not cocaine) abuse or dependence	32 (10.8)	25 (18.5)	4 (3.1)	3 (9.7)			
Cocaine Route of Use		29.5	<0.001	0.23			
Oral	1 (0.4)	0 (0.0)	1 (0.8)	0 (0.0)			
Nasal	82 (30.6)	44 (39.3)	29 (22.5)	9 (33.3)			
Smoking	164 (61.2)	51 (45.5)	97 (75.2)	16 (59.3)			

Demographic Characteristic	All <i>N</i> = 297	White <i>n</i> = 136 (46%)	Black <i>n</i> = 130 (44%)	Hispanic <i>n</i> = 31 (10%)	χ^2/F stat	<i>p</i> -value	Effect Size
	<i>M</i> (<i>SD</i>)	<i>M</i> (<i>SD</i>)	<i>M</i> (<i>SD</i>)	<i>M</i> (<i>SD</i>)			
Injection	21 (7.8)	17 (15.2)	2 (1.6)	2 (7.4)			

Note: Data for variable age are mean (standard deviation) or all other variables are *n* (percentage); statistics were χ^2 and *F* tests for categorical and continuous variables, respectively. Bolded information indicates group differences that were significant at *p* < 0.05.