Published in final edited form as:

Ment Health Phys Act. 2012 December ; 5(2): 175–182. doi:10.1016/j.mhpa.2012.08.003.

STimulant Reduction Intervention using Dosed Exercise (STRIDE) – Description of the Exercise Intervention and Behavioral Program to Ensure Adherence

Mark Stoutenberg¹, Chad Rethorst², Gabriel Fuzat³, Tracy Greer², Steven Blair^{4,5}, Timothy Church⁶, Bess Marcus⁷, and Madhukar Trivedi²

¹Department of Epidemiology & Public Health, University of Miami Miller School of Medicine, Miami, FL

²Department of Psychiatry, University of Texas Southwestern Medical Center, Dallas, TX

³Memorial Hermann Prevention and Recovery Center, Houston, TX

⁴Department of Epidemiology and Biostatistics, Arnold School of Public Health, University of South Carolina, Columbia, SC

⁵Department of Exercise Science, Arnold School of Public Health, University of South Carolina, Columbia, SC

⁶Preventive Medicine Laboratory, Pennington Biomedical Research Center, Baton Rouge, LA

⁷Department of Family and Preventive Medicine, The University of California, San Diego, La Jolla, CA

PubMed Indexing

Stoutenberg; Rethorst; Fuzat; Greer; Blair; Church; Marcus; Trivedi

INTRODUCTION

Stimulant use disorders are a major public health concern in light of the high financial and social costs associated with the cost of treatment, related health problems, worker absenteeism, and loss of productivity (Office of National Drug Control Policy, 2011). Stimulant use disorders, primarily involving the use of cocaine, amphetamines, and methamphetamines, are chronic, relapsing illnesses with few highly efficacious treatments. In 2009, the Substance Abuse and Mental Health Administration reported that more than 4.8 million Americans 12 years of age and older had abused cocaine and another 1.0 million had abused crack over the previous year (Substance Abuse and Mental Health Services Administration, 2010). Additionally, substance abuse disorders are often accompanied by other co-occurring mental health illnesses such as depression, manic episodes, schizophrenia, and obsessive compulsive disorders (Substance Abuse and Mental Health

© 2012 Elsevier Ltd. All rights reserved.

Correspondence and reprint requests should be addressed to: Madhukar H. Trivedi, M.D., University of Texas Southwestern Medical Center, Dallas, TX, Madhukar.trivedi@utsouthwestern.edu.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

Services Administration, 2010). Under normal treatment conditions for stimulant use disorders (Treatment as Usual; TAU), typically only about 13% of participants achieve abstinence (Dutra et al., 2008). Abstinence rates for treatments designed to augment TAU vary widely – ranging from 14–60% (Ball et al., 2007; Carroll et al., 2006; Rawson et al., 2006; Wetzel et al., 2004) – depending on the outcome variable and primary endpoint selected. Currently, the best treatments for cocaine and other stimulant use disorders are behavioral treatments that combine cognitive behavioral therapy with contingency management (Dutra et al., 2008; Vocci & Montoya, 2009). However, it is clear more efficacious treatments are needed for stimulant abuse and dependence.

Randomized controlled trials examining the use of exercise to improve outcomes in smoking cessation provide some of the most convincing support for investigating the use of exercise to improve outcomes in stimulant abuse (Marcus, Albrecht, Niaura, Abrams, & Thompson, 1991; Martin et al., 1997; Marcus et al., 1999; Marcus et al., 2005). Efficacious clinical trials involving exercise interventions in individuals with diabetes (Church et al., 2010a), cardiovascular disease (Church et al., 2010b), and depression (Trivedi et al., 2011) have also previously been described. Preliminary evidence provides support for the beneficial impact of exercise in drug abusing populations; however, few clinical trials have been conducted to date. In a randomized controlled trial of 187 participants evaluating the efficacy of contingency management in the treatment of substance abuse disorders (Petry, Alessi, Hanson, & Sierra, 2007), participants who completed exercise-related activities as part of their targeted behaviors, had an increased length of abstinence (Weinstock, Barry, & Petry, 2008). Furthermore, a pilot study of moderate-intensity aerobic exercise added to TAU for individuals with substance dependence demonstrated that in the exercise group percent days abstinent significantly increased from baseline and that 66.7% of the sample remained continuously abstinent at the end of the 12-week intervention (Brown et al., 2010). However, study design and rationale from randomized clinical trials involving exercise interventions involving substance abuse, other than tobacco, are not yet available.

The use of an exercise intervention for stimulant abusers may also provide additional health benefits and functional improvements beyond decreasing drug dependence. Exercise has been shown to reduce depression and anxiety during alcohol treatment (Frankel & Murphy, 1974; Palmer, Palmer, Michiels, & Thigpen, 1995), as well as during smoking cessation treatment (Bock, Marcus, King, Borrelli, & Roberts, 1999; Kawachi, Troisi, Rotnitzky, Coakley, & Colditz, 1996). Exercise is also associated with improved quality of life (Martin, Church, Thompson, Earnest, & Blair, 2009) and sleep (Youngstedt, 2005), both of which are disrupted by stimulant use even after abstinence is achieved (Borders et al., 2009; Morgan et al., 2006). In addition, concern about weight gain following cessation of abused substances may increase risk of substance use relapse (Cowan & Devine, 2008). Altogether, the use of an exercise intervention appears to present a promising new treatment option for stimulant abuse and dependence.

Given the growing body of evidence relating the beneficial impact of an active, exercising lifestyle on physical and mental health, there is a need to design and conduct clinical investigations involving exercise training in drug abusing populations, especially given that no study has systematically investigated this potentially beneficial relationship. The STimulant Reduction Intervention using Dosed Exercise (STRIDE) study presents a novel approach to investigating the efficacy of an exercise intervention on drug abuse outcomes in recovering stimulant addicts. Because of documented problems with treatment adherence and retention for patients with stimulant use disorders, the STRIDE study required a high level of staff training and re-training, monitoring, and oversight to provide the support necessary to successfully engage the study participants. Specific details regarding the overall rationale, design, and implementation of the STRIDE study can be found elsewhere (Trivedi

et al., 2011; Greer et al 2012). The specific purpose of this paper is to address the rationale and consideration that went into the design and implementation of a novel exercise intervention in a population of stimulant abusers. Unlike previous clinical trials involving exercise interventions, the design and implementation of the exercise intervention presented a novel challenge given the unique life situations, unstable living conditions, complex medical situations, and multiple co-morbidities in this population of stimulant drug abusers.

STRIDE STUDY OVERVIEW

The STRIDE study is a multi-site investigation (9 study sites) designed to investigate the efficacy of supplementing TAU with either a dosed exercise intervention (DEI) or a health education intervention (HEI) in individuals diagnosed with stimulant abuse and/or dependence. The primary aim is to compare days of abstinence, as measured by the Timeline Follow Back, between the DEI and HEI groups during a 12-week period. More detailed information regarding the study aims can be found elsewhere (Trivedi et al., 2011).

Participants

Potential participants for the STRIDE study are males or females, ages 18 to 65, with stimulant abuse or dependence, and who have had stimulant use within 30 days of admission to one of the participating substance use treatment centers. Potential participants must be admitted to the substance use residential treatment center with a 17–28 day residential stay as part of their drug treatment program. This length of stay was chosen in order to begin ingraining positive exercise habits before the participants are released from the residential treatment facility into uncontrolled, potentially high risk situations. The residential stay is also used to gradually progress the participant to their full, clinical dose of exercise. Finally, all potential participants must be capable of performing vigorous intensity exercise. Rationale for the exclusion criteria as they relate to the exercise intervention are outlined and described in Table 1. A more comprehensive description of study participants and eligibility criteria can be found elsewhere (Trivedi et al., 2011).

STRIDE Exercise Intervention Team

A National Intervention Director and the Exercise Protocol Specialist are responsible for the proper administration of the DEI across all study sites to ensure adherence and continuity to the protocol. Together, they oversee the initial and continuing training of all DEI team members and serve as the central points of contact to assist with intervention related issues that occur during the study. Each study site has an exercise team consisting of a primary Exercise Facilitator (EF), who is responsible for the organization and implementation of the DEI and serves as the primary point of contact with the DEI participants, and one study Research Assistant, who received training to serve as a Secondary EF for situations when the EF is unavailable or has a high volume of participants. The EFs have an undergraduate or master's degree in kinesiology, exercise physiology, or a related field with preference being given to candidates with additional academic or vocational [i.e., current American College of Sports Medicine (ACSM) certification] training.

The exercise teams went through an extensive training process beginning with a National Exercise Training modeled after the ACSM Health Specialist training course, specifically modified for the STRIDE study. Other training requirements included the completion of the American Heart Association's Basic Life Support for Healthcare Providers, a pedometer training assignment (wearing a pedometer for a week to understand the challenges and barriers faced by the participants), videotaping of the introductory session with mock participants, and an exercise practicum that required the completion of 3 different training sessions using volunteer participants. After these training requirements were completed, the

National Intervention Director and/or the Exercise Protocol Specialist performed site visits for final approval of the maximal exercise testing process and the exercise facility. The site visits included DEI staff certification in the assessment of physiological measurements [height, weight, waist circumference, manual measurement of resting and exercising heart rate (HR) and blood pressure (BP)], proper usage of the Polar HR monitors, application of study software programs, and a final in-person mock DEI session.

The Exercise Intervention

The DEI is divided into 2 phases: Acute and Continuation. The Acute Phase (the initial 12 weeks) is designed to determine the efficacy of DEI augmentation for the treatment of stimulant abusers who have received treatment in a residential setting. During the Acute Phase, participants are asked to complete 3 supervised sessions at the study site with the EF. During the Continuation Phase (weeks 13–36), which is designed to assess the sustained response to the DEI, one supervised session is completed at the study site along with 2 home-based, unsupervised sessions.

The Exercise Prescription - Dose

The DEI sessions are based on the expenditure of a specific, individualized number of calories (kilocalories per kilogram of bodyweight per week; KKW). While some previous studies have based their DEIs on volume of time (Marcus et al., 2003) or absolute caloric expenditure (Kraus et al., 2001), individualized caloric expenditure based on body weight was chosen in the STRIDE study to explicitly control for caloric expenditure. This approach has been used successfully in previous studies by this research team (Dunn, Trivedi, Kampert, Clark, & Chambliss, 2005; Trivedi et al., 2006; Church et al., 2010a; Church et al., 2010b). To obtain the weekly exercise dose, participants are weighed (kg) at the beginning of every study week and multiplied by the prescribed weekly dose (number of KKW). During the first week of the study, DEI participants complete a dose of 6 KKW, which then increases to 9 KKW during the second week. From weeks 3 – 36, participants complete a full dose of 12 KKW. This dose was selected for the following reasons: 1) it is consistent with U.S. 2008 Physical Activity Guidelines for Americans (www.health.gov/paguidelines), as well as prior recommendations from groups such as the American Heart Association and the ACSM (Nelson et al., 2007; Haskell et al., 2007); and 2) it has been used in previous studies involving physical activity (Trivedi et al., 2006; Church, Earnest, Skinner, & Blair, 2007; Church et al., 2010). A customized Microsoft Excel STRIDE spreadsheet, using the ACSM metabolic calculations for the estimation of energy expenditure (*ACSM's Guidelines for Exercise Testing and Prescription*, 2010), is used to calculate caloric expenditure over 5-minute blocks based on the speed, incline, and modality (walking or running) of the participant while on the treadmill (see Appendix A).

The Exercise Prescription - Intensity

The intensity of the exercise sessions is individualized for each participant based on their HR maximum (HR_{max}) obtained from the maximal exercise test during the Medical Screening. As with the dose, the exercise intensity is incrementally increased over the first 3 weeks of the study. The ramping of the exercise intensity used in this study was similar to that used in previous studies involving previously untrained, sedentary populations (Trivedi et al., 2006; Church et al., 2007; Church et al., 2010a). Furthermore, initiation of study interventions in the residential treatment setting is designed to assist with the gradual increase in intensity under supervised assistance. During the first week of the DEI, participants exercise between 50–60% of their HR_{max} , increasing to 60–70% of their HR_{max} during the second week. For weeks 3–36, participants will exercise at an intensity range of 70–85% of their HR_{max} . This intensity is both above the suggested minimum intensity of 50% of HR_{max} and within the currently recommended training intensity guidelines for

producing physiological adaptations and benefits (*ACSM's Guidelines for Exercise Testing and Prescription*, 2010). By selecting a range of 70–85% of HR_{max} , there is some flexibility to increase comfort while ensuring that all participants are exercising at a consistent relative intensity above the minimum recommended threshold. At the end of the exercise session, participants are asked to provide a global Rating of Perceived Exertion (RPE) for the exercise session.

The Exercise Prescription - Frequency

Participants are encouraged to complete their prescribed weekly exercise dose over 3 exercise sessions. However, participants are permitted an additional 2 sessions per week in order to achieve the target exercise dose and to accommodate variations in baseline fitness levels and bodyweights. Individuals who are more unfit have a relatively low caloric expenditure rate when exercising within their relative intensity range (i.e., higher observable HRs at lower treadmill settings). This requires that these participants exercise for a greater duration to achieve their weekly exercise dose than individuals who have higher baseline fitness levels and/or a more moderate HR response to exercise. This is particularly true for overweight/obese individuals who may have a difficult time completing 1/3 of their exercise dose in one session. Other participants, due to time constraints (i.e., treatment or group sessions), may also require additional sessions to complete their weekly caloric expenditure targets. The additional exercise sessions allow participants the flexibility of shorter, more manageable exercise sessions. When possible, attempts are made to evenly split the exercise dose between the number of sessions that the participant is planning to attend that week. The remaining caloric expenditure, due to missed or incomplete sessions, is not carried over to future weeks and cannot be completed after the study week has ended.

Continuation Phase

During the Continuation Phase, DEI participants complete one supervised exercise session at the study site with the remainder of the exercise dose being completed through 2 unsupervised, home-based sessions. The EFs assist in the planning of the unsupervised sessions, but each participant must independently complete their sessions, as well as recording their own data. To better facilitate the transition to the Continuation Phase, the EFs may make one trip to the participant's local neighborhoods and/or use online mapping programs to help the participants design routes for their home-based sessions. This may include using a local track and field complex, local park routes, or a path through their community streets. Measured courses, combined with total exercise time, allows for the calculation of a walking/running speed that can be used in the ACSM metabolic calculations for the estimation of energy expenditure. Participants are encouraged to exercise on flat courses so that the incline of the exercise session can be assumed to be zero. Participants are not provided with Polar HR monitors for their homebased sessions and therefore, the EFs must train the participants to take manual HR measurements for both their Exercise Readiness Screening and to self-monitor their exercise intensity. Participants are reminded to duplicate a similar RPE throughout their home-based sessions in order to replicate the intensity of their supervised exercise sessions. Participants are also asked to complete an exercise log detailing the time, distance, and location for each of their home-based exercise sessions and to bring in the logs during subsequent supervised exercise sessions. Accurate collection of self-reported data is a problem during any unsupervised exercise and, as such, our EFs work continuously with their participants in order to achieve the highest level of accuracy during the unsupervised sessions.

SAFETY CONSIDERATIONS

Participant safety is of the utmost concern in clinical research. Ensuring participant safety becomes more challenging depending on the intervention being delivered and the baseline health status of the participants. Given the inherent risks involved with exercise interventions, ranging from mild musculoskeletal injuries to major cardiac events, and the general poor state of health for stimulant addicts including medical conditions such as bone fractures, muscle injuries, pain disorders, and serious cardiovascular complications, such as stroke (Mertens, Lu, Parthasarathy, Moore, & Weisner, 2003), the STRIDE study implemented several strategies to ensure participant safety.

Medical Screening

A comprehensive medical screening was considered an essential part of the STRIDE safety protocol. All potential participants undergo a comprehensive medical screening process in order to provide clearance to exercise in the event they are randomized to the DEI arm. Prior to a physical exam with the study physician, a fasting blood sample is drawn for clinical laboratory tests that include: hematology, lipids, blood chemistry, and urine analyses. In the final part of the pre-physical exam process, participants complete the *Physical Activity Readiness Questionnaire-Revised (PAR-Q)* and *Medical History Self-Report* forms. The *PAR-Q* is a form that was adopted from the ACSM Standards and Guidelines for Fitness Facilities and is designed to identify acute or chronic conditions that may prevent the potential clients from beginning an exercise program (*ACSM's Health/Fitness Facility Standards and Guidelines*, 2007). During the physician visit, the attending medical personnel perform a standard physical exam and conduct an extensive review of the participants' medical history through the use of the *Medical History Physician Form*. This form includes questions about history and/or treatment of medical conditions, allergies, past surgeries, regular current and past tobacco and alcohol use, and family history of medical conditions. Given their recent physical inactivity, participants are likely to under-report pre-existing and/or current injuries, which reinforces the need for the comprehensive medical examination. Additionally, as part of the physical exam, participants complete the *Maximal Exercise Test Screening Questions* form to identify any other potential risks in order to maximize their safety while undergoing the maximal exercise test. This form includes questions about exercise habits, tobacco use, specific adverse physical responses to exertion, and a history of sleep difficulties, circulatory and/or respiratory issues. Based on the physical exam, participants may be excluded from the study if there is evidence of a general medical condition or abnormality that contraindicates participation in the DEI. Participants with a body mass index (BMI) greater than 40 kg/m² require specific physician approval to continue with the maximal exercise test and randomization into the study. Specific individual thresholds for these safety measures were not established; rather final medical approval is at the discretion of the study physician, who can exclude potential participants based on their judgment from available data (i.e., cholesterol levels from fasting blood samples) obtained during the Medical Screening Process.

The Maximal Exercise Test

Following the physical exam, participants perform a maximal exercise test. Originally, it was proposed that the ACSM Risk Factor Stratification system be used to determine the appropriate level of supervision during the maximal exercise test (*ACSM's Guidelines for Exercise Testing and Prescription*, 2010). However, since stimulants abuse is considered an "immediate disease" and is often accompanied by multiple co-morbidities, it was decided that all participants are to be considered "high" risk, thereby necessitating physician supervision at all maximal exercise tests.

The purpose of conducting the maximal exercise test during the Medical Screening process is to: 1) examine cardiorespiratory responses in order to rule out ischemic response to exercise (with its implication in cardiovascular diseases), 2) to identify participants for whom exercise might be hazardous, and 3) to provide data for the exercise prescription (HR_{max}). All testing takes place in facilities that comply with ACSM testing and safety guidelines (*ACSM's Health/Fitness Facility Standards and Guidelines*, 2007). Prior to beginning the maximal exercise test, a predicted HR_{max} , based on the Tanaka Formula [$(HR_{max} = 208 - (.7 * age))$] (Tanaka, Monahan, & Seals, 2001), is calculated for each participant. In order to qualify for enrollment into the study, participants must achieve an observed HR_{max} within 2 standard deviations of their age-predicted HR_{max} (20 beats per minutes). If the appropriate HR_{max} is not achieved, the maximal exercise test is considered invalid and may be repeated within 48 hours at the discretion of the participant, research team, and medical staff. It is crucial that the participant achieve a value as near to their HR_{max} as possible as the DEI prescription consists of HR zones based on a percent of their HR_{max} .

Prior to beginning the maximal exercise test, all participants are fitted with a 12-lead electrocardiogram (ECG). Throughout the maximal exercise test, the grade and speed is progressively increased during subsequent 2-minute stages, according to a modified Cornell Protocol (see appendix B), until the participant is physically unable to continue. During the test, measurements taken include: HR each minute, a rating of perceived exertion (RPE) in the last 30 seconds of each stage, and BP at the end of each stage. Licensed medical personnel are present at all maximal exercise tests and continuously review the ECG readings for safety monitoring. The attending medical technician is then asked to complete the *Maximal Exercise Test Data Form*, which records all of the participant's data from before, during, and after the maximal exercise test. Following the completion of the maximal exercise test, the attending physician or cardiologist completes the *Medical Eligibility Checklist and Clearance Forms* documenting that the maximal exercise test did not reveal any contraindications to future exercise participation.

Immediately following the maximal exercise test, the study physician conducts a final evaluation of the laboratory results, medical exam, and the maximal exercise test to provide a final determination (documented on the *Maximal Exercise Test Clinical Summary Form*) regarding whether or not the participant is medically cleared to participate in the study. Participants randomized to the study repeat the maximal exercise test at the end of the 12-week Acute Phase to provide a post-intervention assessment of cardiorespiratory fitness. If abnormal ECG responses are noted in the post-intervention maximal exercise test, DEI participants are not permitted to continue with their exercise training in the Continuation Phase.

Safety Precautions during Exercise Intervention Sessions

Medical Safety—Prior to the beginning of all supervised exercise sessions, the EFs inquire about the overall health of the participants, including recent sleep patterns, dietary habits, and hydration levels, all of which vary considerably in this study population on a daily basis. Participants then undergo an Exercise Readiness Screening process to assess for increased risk of adverse events due to recent drug and/or heavy alcohol use. A HR monitor strap and BP cuff are placed on the participants and, after a 5-minute rest period without any interaction or movement, a minimum of 2 resting HR and 2 BP measurements are conducted, each separated by 2 minutes. During the Exercise Readiness Screening, a participant with: 3 consecutive resting HR of ≥ 100 beats per minute (bpm); or a systolic BP ≥ 160 mmHg or diastolic BP >100 mmHg, is ineligible to begin the exercise session that day. These threshold values were chosen in line with recommendations for cardiac rehabilitation

in-patients that recommend thresholds of SBP >200 mmHg or a DBP >110 mmHg (*ACSM's Guidelines for Exercise Testing and Prescription*, 2010). However, since few of our study sites have an onsite physician, a more conservative threshold of 160 mmHg/100 mmHg, signifying Stage II Hypertension as defined by the American Heart Association (Chobanian et al., 2003), was selected. In order to monitor the development of chronic health concerns, participants who have a resting systolic BP $\geq$ 140 mmHg or a resting diastolic BP $\geq$ 90 mmHg over 3 consecutive exercise sessions, are not permitted to perform further exercise sessions without explicit physician clearance. Again, a conservative threshold, signifying Stage I Hypertension as defined by the American Heart Association (Chobanian et al., 2003), was selected for re-referral to a physician given the high number of co-morbidities and general poor health status found in the participant population.

After discharge from the residential setting, there is a need for increased participant safety monitoring given the heightened potential for relapse. Upon returning to the study sites for their exercise sessions, participants perform 3 urine drug screens each week as part of the study assessment protocol. Additionally, each study site has the option of using alcohol breath analysis tests if they feel it is necessary for the safety of the participants. Monthly urine pregnancy tests are performed for any woman who is able to have children, given the potential risks of vigorous intensity exercise in pregnant women (*ACSM's Guidelines for Exercise Testing and Prescription*, 2010; Artal & O'Toole, 2003). Women who are pregnant prior to randomization are excluded from the study (see Table 1), while women who become pregnant after randomization are not permitted to complete the DEI. Lastly, all sites are provided with the ability to postpone or cancel exercise sessions if they feel continuing would not be in the best interests of the participant or the research team. To increase safety during home-based exercise sessions, participants are educated on how to perform manual HR measurements and are instructed not to complete any unsupervised session in which their resting HR is above 100 bpm, a value considered abnormal and a sign of tachycardia (*American Heart Association: Tachycardia*, 2012).

During the exercise session, BP is assessed after the initial 5-minutes of exercise to monitor for acute adverse events to the exercise session. Exercise sessions are immediately terminated with extreme BP responses (systolic BP >250 mmHg). Moderate BP responses to exercise, a drop in systolic BP >10 mmHg or a rise in diastolic BP >15 mmHg from resting values, trigger the need for additional BP measurements taken every 5 minutes throughout the rest of the exercise session. These threshold values were taken from the ACSM's "Indications for Terminating Exercise Testing" (*ACSM's Guidelines for Exercise Testing and Prescription*, 2010) and have been applied as additional safety precautions. Finally, prior to exiting the study site, the EF completes a final resting HR and BP measurement to ensure a return to baseline values and that the participant has no lingering ill effects (i.e., dizziness) from the exercise session.

Injury Prevention—After the Exercise Readiness Screening process, participants are led through a brief dynamic warm-up to prepare them for the exercise session and minimize the chance for injury. The dynamic warm-up is tailored for each participant to: ensure optimal muscle function during the session, strengthen complimentary muscles used in walking/running, and to provide dynamic movements for body parts that may be overly tight (i.e., tight iliotibial band). Recent inactivity also has the potential to put participants at a higher risk of injury, therefore the warm-up and stretching activities were deemed particularly important for the prevention of exercise-related injuries. Given that the participants are physically inactive at baseline, the first 3 weeks of the intervention are used to acclimate them to regular physical activity through a ramping of the exercise dose. Additionally, increases in intensity are encouraged through elevation in the incline as opposed to increases in treadmill velocity. This results in participants briskly walking up steep inclines rather than

running on a flat surface. In rare circumstances, participants are allowed to exercise below their HR training zone if a physical limitation (i.e., recent musculoskeletal injury) prevents them from consistently maintaining the prescribed intensity. After completing the exercise session, the EFs lead the participants through a series of static stretching with special emphasis on overly fatigued, sore, or tight muscle groups to minimize potential injuries and delayed onset of muscle soreness.

INTERVENTION STANDARDIZATION AND FIDELITY

Equipment

Participants perform all supervised exercise sessions on a Life Fitness 95T-series Treadmill at the study site. Original study design included the use of a cycle ergometer, in addition to the treadmill. However, in an attempt to increase the precision of the DEI (i.e., the HR_{max} is obtained only from maximal exercise test on a treadmill, unpredictability of home-based exercise sessions using street cycling), the cycle ergometer was removed as a mode of exercise training in the DEI. Polar HR monitors (RS-400) were chosen to monitor HR training intensity during supervised sessions, as well as provide a secondary, individualized estimate of energy expenditure. In the event of a Polar HR watch malfunction, the EFs were trained to conduct manual HR measurements on an ongoing basis throughout the intervention session.

All STRIDE study participants are asked to wear Lifestyles Digi-Walker SW-200 pedometers to track physical activity levels on an on-going basis throughout the 9 months of the study. Participants are asked to wear the pedometers during all waking hours and to record daily step count totals in a *Monthly Step Count Log*. Data from the pedometers will be used to track noticeable changes in daily physical activity levels and to attempt to control for routine activity variance throughout the study. Pedometers were used to estimate daily physical activity levels, as well as the specific step counts taken during an exercise intervention session.

Exercise Adherence Monitoring

At each site, the EFs are responsible for completing a *Daily Adherence Report* that is sent to and regularly monitored by the National Intervention Director and the Exercise Protocol Specialist to allow for real time responses to problems at the study sites. Additionally, biweekly conference calls with the DEI research team are conducted to promote the discussion of current problems and challenges encountered at the study sites. On a weekly basis, the EFs send their STRIDE spreadsheets to the National Intervention Director and the Exercise Protocol Specialist for quality control review. On a monthly basis, the Secondary EFs are required to perform a minimum of one supervised exercise session and to send in all exercise session documentation for ongoing quality assurance and monitoring. Finally, the National Intervention Director or the Exercise Protocol Specialist travel to each study site semiannually to perform monitoring visits and observe DEI sessions for both the EFs and Secondary EFs, provide continuing education and training, and re-test physiological measure assessments with the entire research team.

Exercise Adherence Program

As in most clinical trials, participant retention is an ongoing challenge and adherence/compliance to the exercise intervention can be extremely difficult. The STRIDE study is augmented by a comprehensive behavioral adherence program that targets intervention adherence that has been refined in previous trials (Hughes et al., 2009; Trivedi et al., 2006). Briefly, the EFs are provided with specific training to address adherence-related issues with their participants, including barrier identification and modification, facilitating

empowerment, working collaboratively with the participants, maximizing ease of access to research visits, remaining accessible, providing appointment reminders, and setting appropriate boundaries with the participants. The most anticipated reason for non-compliance is relapse. Previous studies have suggested that the most common time point for relapse typically occurs within 90 days of leaving residential treatment and is associated with discontinuation of research and treatment activities (Paliwal, Hyman, & Sinha, 2008; Sinha, Garcia, Paliwal, Kreek, & Rounsaville, 2006). Subsequent participant disappearance is due, in part, to their relapse and part to the embarrassment associated with their relapse. Therefore, it is critical for each research team to address the issue of relapse early in the study while compliance is still high.

Additional reasons for non-compliance include unstable living conditions, employment, lack of transportation, and legal issues. These barriers present a challenge for the EFs in working with the participants to create time in their schedule for three supervised exercise sessions each week. EFs devote time at each session to identifying potential barriers and to work with participants to create and implement potential solutions. Of these, flexibility on the part of the research team is essential to ease scheduling concerns while transportation issues can be partially alleviated through the use of public transportation, taxis, or direct transportation provided by the research team.

SUMMARY

The burden associated with stimulant use and dependence, along with the relative inefficacy of current treatment strategies, indicates the need for more efficacious treatments. The STRIDE study aims to address this need by examining exercise training as a potential augmentation to TAU. The implementation of exercise interventions in clinical trials present inherent challenges related to participant safety, intervention fidelity and exercise adherence. Given the unique nature of the study population, a great deal of planning was required to ensure the safe and effective implementation of the exercise intervention in stimulant abusers. A series of safety precautions were implemented throughout the STRIDE study to ensure participant well-being and a rigorous staff training and monitoring process was developed to ensure the proper implementation of the exercise intervention. In summary, this paper has described the design and rationale of the DEI used in the STRIDE study including: the training and oversight of the research team responsible for delivering the intervention, the design and considerations taken in developing the DEI, the additional safety precautions taken to insure participant well-being, and the DEI standardization through the use of an exercise adherence and monitoring plan.

Acknowledgments

Sources of Support:

This work was supported by the National Institute on Drug Abuse through the Clinical Trials Network for the Texas Node [3U10DA020024-06S1], Madhukar H. Trivedi, M.D., Principal Investigator; and the Stimulant Reduction Intervention using Dosed Exercise (STRIDE) study [2U10DA020024-06], Madhukar H. Trivedi, M.D., Lead Investigator.

Abbreviations

ACSM	American College of Sports Medicine
BMI	Body Mass Index
BP	Blood Pressure

BPM	Beats per Minute
CTF	Certified Treatment Facility
ECG	Electrocardiogram
EF	Exercise Facilitator
HEI	Health Education Intervention
HR	Heart Rate
KKW	Kilocalories per Kilogram of Bodyweight per Week
PAR-Q	Physical Activity Readiness Questionnaire
RPE	Rating of Perceived Exertion
STRIDE	STimulant Reduction Intervention using Dosed Exercise
TAU	Treatment as Usual
DEI	Dosed Exercise Intervention

References

- Thompson, WR., editor. ACSM's Guidelines for Exercise Testing and Prescription. 8th Edition ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2010.
- Tharrett, SJ.; McInnis, KJ.; Peterson, JA., editors. ACSM's Health/Fitness Facility Standards and Guidelines. 3rd Edition ed. Champaign, IL: Human Kinetics; 2007.
- American Heart Association: Tachycardia. Retrieved June 4, 2012, from http://www.heart.org/HEARTORG/Conditions/Arrhythmia/AboutArrhythmia/Tachycardia_UCM_302018_Article.jsp
- Artal R, O'Toole M. Guidelines of the American College of Obstetricians and Gynecologists for exercise during pregnancy and the postpartum period. *British Journal of Sports Medicine*. 2003; 37(1):6–12. discussion 12. [PubMed: 12547738]
- Ball SA, Martino S, Nich C, Frankforter TL, Van Horn D, Crits-Christoph P. National Institute on Drug Abuse Clinical Trials Network. Site matters: Multisite randomized trial of motivational enhancement therapy in community drug abuse clinics. *Journal of Consulting and Clinical Psychology*. 2007; 75(4):556–567. [PubMed: 17663610]
- Bock BC, Marcus BH, King TK, Borrelli B, Roberts MR. Exercise effects on withdrawal and mood among women attempting smoking cessation. *Addictive Behaviors*. 1999; 24(3):399–410. [PubMed: 10400278]
- Borders TF, Booth BM, Falck RS, Leukefeld C, Wang J, Carlson RG. Longitudinal changes in drug use severity and physical health-related quality of life among untreated stimulant users. *Addictive Behaviors*. 2009; 34(11):959–964. [PubMed: 19560873]
- Brown RA, Abrantes AM, Read JP, Marcus BH, Jakicic J, Strong DR, Gordon AA. A pilot study of aerobic exercise as an adjunctive treatment for drug dependence. *Mental Health and Physical Activity*. 2010; 3(1):27–34. [PubMed: 20582151]
- Carroll KM, Ball SA, Nich C, Martino S, Frankforter TL, Farentinos C. National Institute on Drug Abuse Clinical Trials Network. Motivational interviewing to improve treatment engagement and outcome in individuals seeking treatment for substance abuse: A multisite effectiveness study. *Drug and Alcohol Dependence*. 2006; 81(3):301–312. [PubMed: 16169159]
- Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL Jr. National High Blood Pressure Education Program Coordinating Committee. Seventh report of the joint national committee on prevention, detection, evaluation, and treatment of high blood pressure. *Hypertension*. 2003; 42(6):1206–1252. [PubMed: 14656957]
- 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 : The Journal of the American Medical Association*. 2007; 297(19):2081–2091. [PubMed: 17507344]
- 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 : The Journal of the American Medical Association*. 2010a; 304(20):2253–2262. [PubMed: 21098771]
- Church TS, Earnest CP, Thompson AM, Priest EL, Rodarte RQ, Saunders T, Blair SN. Exercise without weight loss does not reduce C-reactive protein: The INFLAME study. *Medicine and Science in Sports and Exercise*. 2010b; 42(4):708–716. [PubMed: 19952828]
- Cowan J, Devine C. Food, eating, and weight concerns of men in recovery from substance addiction. *Appetite*. 2008; 50(1):33–42. [PubMed: 17602790]
- Dunn AL, Trivedi MH, Kampert JB, Clark CG, Chambliss HO. Exercise treatment for depression: Efficacy and dose response. *American Journal of Preventive Medicine*. 2005; 28(1):1–8. [PubMed: 15626549]
- Dutra L, Stathopoulou G, Basden SL, Leyro TM, Powers MB, Otto MW. A metaanalytic review of psychosocial interventions for substance use disorders. *The American Journal of Psychiatry*. 2008; 165(2):179–187. [PubMed: 18198270]
- Frankel A, Murphy J. Physical fitness and personality in alcoholism. Canonical analysis of measures before and after treatment. *Quarterly Journal of Studies on Alcohol*. 1974; 35(4 Pt A):1272–1278. [PubMed: 4155516]
- Greer TL, Ring KM, Warden D, Grannemann BD, Church TS, Somoza E, Trivedi MH. Rationale for using exercise in the treatment of stimulant use disorders. *Journal of Global Drug Policy and Practice*. 2012; 6(1) Epub.
- Haskell WL, Lee IM, Pate RR, Powell KE, Blair SN, Franklin BA, Bauman A. Physical activity and public health: Updated recommendation for adults from the American College of Sports Medicine and the American Heart Association. *Medicine and Science in Sports and Exercise*. 2007; 39(8): 1423–1434. [PubMed: 17762377]
- Hughes CW, Trivedi MH, Cleaver J, Greer TL, Emslie GJ, Kennard B, Barnes C. DATE: Depressed adolescents treated with exercise: Study rationale and design for a pilot study. *Mental Health and Physical Activity*. 2009; 2(2):76–85. [PubMed: 20454641]
- Kawachi I, Troisi RJ, Rotnitzky AG, Coakley EH, Colditz GA. Can physical activity minimize weight gain in women after smoking cessation? *American Journal of Public Health*. 1996; 86(7):999–1004. [PubMed: 8669525]
- Kraus WE, Torgan CE, Duscha BD, Norris J, Brown SA, Cobb FR, Slentz CA. Studies of a targeted risk reduction intervention through defined exercise (STRIDE). *Medicine and Science in Sports and Exercise*. 2001; 33(10):1774–1784. [PubMed: 11581566]
- Marcus BH, Albrecht AE, Niaura RS, Abrams DB, Thompson PD. Usefulness of physical exercise for maintaining smoking cessation in women. *The American Journal of Cardiology*. 1991; 68(4):406–407. [PubMed: 1858687]
- Marcus BH, Albrecht AE, King TK, Parisi AF, Pinto BM, Roberts M, Abrams DB. The efficacy of exercise as an aid for smoking cessation in women: a randomized controlled trial. *Archives of Internal Medicine*. 1999; 159(11):1229–1234. [PubMed: 10371231]
- Marcus BH, Lewis BA, Hogan J, King TK, Albrecht AE, Bock B, Abrams DB. The efficacy of moderate-intensity exercise as an aid for smoking cessation in women: A randomized controlled trial. *Nicotine & Tobacco Research : Official Journal of the Society for Research on Nicotine and Tobacco*. 2005; 7(6):871–880.
- Marcus BH, Lewis BA, King TK, Albrecht AE, Hogan J, Bock B, Abrams DB. Rationale, design, and baseline data for commit to quit II: An evaluation of the efficacy of moderate-intensity physical activity as an aid to smoking cessation in women. *Preventive Medicine*. 2003; 36(4):479–492. [PubMed: 12649057]
- Martin CK, Church TS, Thompson AM, Earnest CP, Blair SN. Exercise dose and quality of life: A randomized controlled trial. *Archives of Internal Medicine*. 2009; 169(3):269–278. [PubMed: 19204218]

- Martin JE, Calfas KJ, Patten CA, Polarek M, Hofstetter CR, Noto J, Beach D. Prospective evaluation of three smoking interventions in 205 recovering alcoholics: One-year results of project SCRAP-tobacco. *Journal of Consulting and Clinical Psychology*. 1997; 65(1):190–194. [PubMed: 9103749]
- Mertens JR, Lu YW, Parthasarathy S, Moore C, Weisner CM. Medical and psychiatric conditions of alcohol and drug treatment patients in an HMO: Comparison with matched controls. *Archives of Internal Medicine*. 2003; 163(20):2511–2517. [PubMed: 14609789]
- Morgan PT, Pace-Schott EF, Sahul ZH, Coric V, Stickgold R, Malison RT. Sleep, sleep-dependent procedural learning and vigilance in chronic cocaine users: Evidence for occult insomnia. *Drug and Alcohol Dependence*. 2006; 82(3):238–249. [PubMed: 16260094]
- Nelson ME, Rejeski WJ, Blair SN, Duncan PW, Judge JO, King AC, Castaneda-Sceppa C. Physical activity and public health in older adults: Recommendation from the American College of Sports Medicine and the American Heart Association. *Medicine and Science in Sports and Exercise*. 2007; 39(8):1435–1445. [PubMed: 17762378]
- Office of National Drug Control Policy. InfoFacts: Understanding drug abuse and addiction. 2011. Retrieved March 7, 2012, from <http://www.drugabuse.gov/publications/infofacts/understandingdrug-abuse-addiction#references>.
- Office of National Drug Control Policy. The economic costs of drug abuse in the united states, 1992–2002. (No. Publication No. 207303). Washington, DC: Executive Office of the President; 2004.
- Paliwal P, Hyman SM, Sinha R. Craving predicts time to cocaine relapse: Further validation of the now and brief versions of the cocaine craving questionnaire. *Drug and Alcohol Dependence*. 2008; 93(3):252–259. [PubMed: 18063320]
- Palmer JA, Palmer LK, Michiels K, Thigpen B. Effects of type of exercise on depression in recovering substance abusers. *Perceptual and Motor Skills*. 1995; 80(2):523–530. [PubMed: 7675585]
- Petry NM, Alessi SM, Hanson T, Sierra S. Randomized trial of contingent prizes versus vouchers in cocaine-using methadone patients. *Journal of Consulting and Clinical Psychology*. 2007; 75(6):983–991. [PubMed: 18085914]
- Rawson RA, McCann MJ, Flammino F, Shoptaw S, Miotto K, Reiber C, Ling W. A comparison of contingency management and cognitive-behavioral approaches for stimulant-dependent individuals. *Addiction (Abingdon, England)*. 2006; 101(2):267–274.
- Substance Abuse and Mental Health Services Administration. Results from the 2009 National Survey on Drug Use and Health: Volume I. Summary of National Findings (Office of Applied Studies, NSDUH Series H-38A, HHS Publication No. SMA 10-4856Findings). Rockville, MD: 2010.
- Sinha R, Garcia M, Paliwal P, Kreek MJ, Rounsaville BJ. Stress-induced cocaine craving and hypothalamic-pituitary-adrenal responses are predictive of cocaine relapse outcomes. *Archives of General Psychiatry*. 2006; 63(3):324–331. [PubMed: 16520439]
- Tamesis B, Stelken A, Byers S, Shaw L, Younis L, Miller DD, Chaitman BR. Comparison of the asymptomatic cardiac ischemia pilot and modified asymptomatic cardiac ischemia pilot versus bruce and cornell exercise protocols. *The American Journal of Cardiology*. 1993; 72(9):715–720. [PubMed: 8249851]
- Tanaka H, Monahan KD, Seals DR. Age-predicted maximal heart rate revisited. *Journal of the American College of Cardiology*. 2001; 37(1):153–156. [PubMed: 11153730]
- Trivedi MH, Greer TL, Church TS, Carmody TJ, Grannemann BD, Galper DI, Blair SN. Exercise as an augmentation treatment for nonremitted major depressive disorder: A randomized, parallel dose comparison. *The Journal of Clinical Psychiatry*. 2011; 72(5):677–684. [PubMed: 21658349]
- Trivedi MH, Greer TL, Grannemann BD, Church TS, Galper DI, Sunderajan P, Carmody TI. TREAD: Treatment with exercise augmentation for depression: Study rationale and design. *Clinical Trials (London, England)*. 2006; 3(3):291–305.
- 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; 12:206. [PubMed: 21929768]
- Vocci FJ, Montoya ID. Psychological treatments for stimulant misuse, comparing and contrasting those for amphetamine dependence and those for cocaine dependence. *Current Opinion in Psychiatry*. 2009; 22(3):263–268. [PubMed: 19307968]

Weinstock J, Barry D, Petry NM. Exercise-related activities are associated with positive outcome in contingency management treatment for substance use disorders. *Addictive Behaviors*. 2008; 33(8): 1072–1075. [PubMed: 18486352]

Wetzel H, Szegedi A, Scheurich A, Lorch B, Singer P, Schlafke D. NeVeR Study Group. Combination treatment with nefazodone and cognitive-behavioral therapy for relapse prevention in alcohol-dependent men: A randomized controlled study. *The Journal of Clinical Psychiatry*. 2004; 65(10): 1406–1413. [PubMed: 15491246]

Youngstedt SD. Effects of exercise on sleep. *Clinics in Sports Medicine*. 2005; 24(2):355–365. xi. [PubMed: 15892929]

Appendix A

STRIDE Intervention Worksheet				Week	Session	KKW (kcal/kg/wk)	Wt (kg)	Visits (per Wk)	Kcals (per wk)	Estimated Kcals (per sess)	Kcals (this sess)
Participant ID				3	1	12	50.0	3	600.0	200.0	
Date				Max HR Sess Min Sess Max							
				185	129.5	157.25					
Time			HR	Modality	Speed (mph)	Grade (%)	Kcal/5min	Cumulative Kcal	Total Kcals/Sess	Distance (mi)	
min	sec	min.sec									
5	0	5.00	140	1	3	3	19.9	19.9	0.0	0.25	
10	0	10.00	145	1	3	4	21.7	41.5	0.0	0.50	
15	0	15.00	145	1	3	4	21.7	63.2	0.0	0.75	
20	0	20.00	150	1	3	5	23.5	86.6	0.0	1.00	
25	0	25.00					N/A	N/A	0.0	N/A	
30	0	30.00					N/A	N/A	0.0	N/A	
35	0	35.00					N/A	N/A	0.0	N/A	
40	0	40.00					N/A	N/A	0.0	N/A	
45	0	45.00					N/A	N/A	0.0	N/A	
50	0	50.00					N/A	N/A	0.0	N/A	
55	0	55.00					N/A	N/A	0.0	N/A	
60	0	60.00					N/A	N/A	0.0	N/A	
65	0	65.00					N/A	N/A	0.0	N/A	
70	0	70.00					N/A	N/A	0.0	N/A	
75	0	75.00					N/A	N/A	0.0	N/A	
80	0	80.00					N/A	N/A	0.0	N/A	
85	0	85.00					N/A	N/A	0.0	N/A	
90	0	90.00					N/A	N/A	0.0	N/A	
Total Time to Finish (min)				20.00							
Average				145.0	3.00	4.00	1.00				
Estimated End Time				1 min 32 sec							

Appendix B

The modified Cornell Protocol (Tamesis et al., 1993) used during the Maximal Exercise test.

All stages are 2 minutes in duration:

Stage 1:	1.7 mph / 5%
Stage 2:	1.7 mph / 10%
Stage 3:	2.0 mph / 10%
Stage 4:	2.5 mph / 12%
Stage 5:	3.0 mph / 13%

Stage 6:	3.4 mph / 14%
Stage 7:	3.8 mph / 15%
Stage 8:	4.2 mph / 15%
Stage 9:	4.8 mph / 15%
Stage 10:	5.0 mph / 15%
Stage 11:	5.3 mph / 15% *
Stage 12:	5.5 mph / 15% *

* The incline in stages 11 and 12 were further modified to remain at 15% (from the 20%) due to treadmill incline limitations at one participation site.

HIGHLIGHTS

- The rationale and design of a clinical exercise intervention is described.
- Stimulant abusers with multiple co-morbidities need enhanced safety procedures.
- Details of the structure the intervention teams and medical screening process.
- Prescription of a clinical dose of exercise based on kilocalories of energy expenditure.
- Strategies for promoting intervention adherence.

Table 1

Description and rationale of exclusionary criteria used in STRIDE.

Exclusion Criteria	Rationale
1. Medical condition contraindicating exercise based on Medical Screening Visit.	All potential STRIDE participants, regardless of the intervention assignment, must be capable of safely completing vigorous intensity exercise. Contraindicated medical conditions include, but are not limited to, chronic pulmonary disease, cardiac abnormalities, and degenerative joint conditions/arthritis.
2. High suicide/psychiatric risk or psychiatric disorder.	This exclusion criteria was added to help ensure the safety of the study staff during study assessment and intervention visits.
3. Pregnancy.	Previously sedentary women, capable of childbearing, may be putting their fetus at-risk by engaging in vigorous intensity exercise.
4. Significant physical activity defined as regular physical activity >20 minutes per week, more than 3 times per week consistently over the 3 months prior to enrollment.	The STRIDE study is designed to examine the efficacy of DEI to increase percent days abstinent. The inclusion of participants who are physically active at baseline would likely reduce the interventions measured efficacy. Therefore, those participants were excluded from participation.
5. Current psychotic disorder.	Co-morbid diagnosis that, in the investigator's judgment, will pose a safety issue or make it difficult for the participant to understand or complete the intervention.
6. Concomitant treatments (beta blockers; methadone, buprenorphine or other opioid replacement therapy) that influence heart rate or rhythm.	The intensity of the exercise intervention is based on target heart rate zones. Treatments that influence HR or rhythm prevent accurate monitor of exercise intensity and may put the participant at increased risk of injury.
7. Any reason not listed herein yet, determined by the site PI, medical personnel, or designees that constitutes good clinical practice and that would in the opinion of the site PI, medical personnel, or designee make participation in the study hazardous.	All site PIs and/or study physicians have the discretion to exclude potential participants based on the overall evidence during the baseline screening process.