FEASIBILITY OF AN EXERCISE INTERVENTION FOR HOMELESS COCAINE-USING MEN

BY

STACY O. TOLLIE

A Thesis Submitted to the Graduate Faculty of

WAKE FOREST UNIVERSITY GRADUATE SCHOOL OF ARTS AND SCIENCES

in Partial Fulfillment of the Requirements

for the Degree of

MASTER OF SCIENCE

Health and Exercise Science

December 2017

Winston-Salem, North Carolina

Approved By:

Peter H. Brubaker, Ph.D., Advisor

Jeffrey H. Katula, Ph.D., Chair

Michael A. Nader, Ph.D.

TABLE OF CONTENTS

LIST OF TABLES AND FIGURES

LIST OF ABBREVIATIONS

6MW…….. 6 Minute Walk Test

ACSM……. American College of Sports Medicine

ASI…….. Addiction Severity Index

BP……... Blood Pressure

CBT…… Cognitive Behavioral Therapy

CRC…… Clinical Research Center

DSM…… Diagnostic Statistical Manual of Mental Disorders

ECG…… Electrocardiogram

FDA…… Food and Drug Administration

GXT…… Graded Exercise "Stress" Test

HR…….. Heart Rate

MET…… Metabolic Equivalent

NRT…… Nicotine Replacement Therapy

OTC…… Over-the-Counter

RCT…… Randomized Controlled Trial

TLFB…….. Timeline Follow Back

UDS…… Urine Drug Screen

WFU…… Wake Forest University

ABSTRACT

Substance abuse/addiction rates are higher in the homeless than the general population, and cocaine is especially problematic, with high rates of use and poor treatment outcomes. PURPOSE: The objective was to determine feasibility of homeless cocaine-using men participating in a 6-week standardized exercise regimen. METHODS: Twenty-five homeless men were screened and five who had used cocaine within the past year were enrolled. All participants completed an initial graded exercise "stress" test. Standardized, vigorous-intensity exercise intervention sessions were held 3 times per week for 6 weeks at a homeless shelter. Heart rate/blood pressure were assessed before/after each exercise session. Urine drug screens were administered twice weekly. Logs were kept of attendance, minutes exercised per session, urine drug screen results, and heart rates/blood pressures. RESULTS: Two participants completed follow-up, yielding a 40% retention rate. Mean number of exercise sessions attended was 5 (SD= 5.73) out of 17. Mean number of minutes exercised per session was 49.28 out of 60. Where 1 is Poor and 10 is Excellent, mean rating by participants of the overall exercise class experience was 9. CONCLUSION: Although recruiting was difficult and retention was low, exercise intervention sessions were well-tolerated. Further study of the homeless population is warranted in order to increase recruitment and retention.

INTRODUCTION

Abuse of and addiction to substances including alcohol, tobacco, prescription and illicit drugs contribute to the deaths of 570,000 Americans annually[4]. Financial costs total $700 billion annually and include increased health-care costs, lost productivity, and crime[4]. Cocaine is the second-most-commonly used illicit drug after cannabis, and in 2015 900,000 people over age 12 had had a cocaine-use disorder within the past year[5].

The "crack" form of cocaine accounts for a large proportion of use, and users of this form of cocaine tend to be among the most socioeconomically marginalized drug users and to have high rates of mortality and comorbid problems[6, 7]. Substance abuse and addiction is particularly a problem in the homeless population, with approximately one in five homeless individuals having a chronic substance abuse problem in January 2016[76, 78]. Cocaine use is especially problematic in the homeless population, with high rates of use and poor treatment outcomes[80, 81, 82, 83].

Although there are pharmacologic options for treating addiction to some substances, there are currently not any pharmacologic options for treating cocaine addiction[9]. Current non-pharmacologic treatments include behavioral therapy, therapeutic communities, 12-Step programs, and alternative therapies such as yoga, mindfulness meditation, nutritional supplements, acupuncture and qigong.

Exercise is a promising addition to the list of non-pharmacologic options. There is a body of preclinical animal research in which investigators have taught animals to self-administer cocaine and then manipulated various factors to mimic the stages of drug use through which humans proceed[28]. Exercise is introduced and the findings regarding the effects of exercise on the various stages of drug use has been mostly positive. There

has been minimal human research regarding the effects of exercise on substance abuse and addiction, and none at all specifically investigating the effects of exercise on cocaine use or utilizing a sample of homeless individuals. Thus, the purpose of the present study was to assess the feasibility of homeless cocaine-using men, who are not in or seeking treatment for their cocaine use, participating in a standardized exercise regimen for six weeks.

REVIEW OF LITERATURE

Addiction

Addiction is a chronic condition involving a repeated powerful motivation to engage in a rewarding behavior, acquired as a result of engaging in that behavior, that has significant potential for unintended harm[1]. Someone is addicted to something to the extent that they experience this repeated powerful motivation[1]. The American Psychiatric Association's Diagnostic Statistical Manual of Mental Disorders, 5th edition (DSM-5) defines substance dependence as the maladaptive pattern of substance abuse leading to clinically significant impairment or distress[2]. Diagnosis of substance use disorder is based on evidence of impaired control, social impairment, risky use and pharmacological criteria[2] including tolerance, dependence, and physical withdrawal symptoms. Substances to which individuals can become addicted include tobacco, alcohol, inhalants, and both prescription and illicit drugs[3].

Substance abuse and addiction is a major public health problem. Alcohol and prescription and illicit drugs contribute to the deaths of 90,000 Americans annually, while tobacco use is linked to 480,000 more annual deaths[4]. Along with the mortality linked to substance abuse and addiction, there are financial costs as well, with an average $700 billion per year in increased health-care costs, crime and lost productivity[4]. In 2015 20.8 million people in the U.S. over age 12 had had a substance abuse disorder within the past year; 900,000 of those were cocaine use disorders[5]. Cocaine is the second most commonly used illicit drug, after cannabis[5]. Although exact numbers are not known, a large proportion of cocaine use is in the "crack" cocaine form, users of which tend to be

the most socio-economically marginalized of all groups of drug users and to have high rates of mortality and comorbid problems[6, 7].

Substance Abuse and Homelessness

Substance abuse and addiction in the homeless population is higher than in the general population[76] and accordingly takes a higher toll. Though numbers vary, on a given night in January 2016 549,928 people were experiencing homelessness in the United States[77]. At that same time, approximately one in five of those people had a chronic substance abuse disorder[78] and drug overdose is a rising cause of death among the homeless[79]. Substance abuse is often a cause of homelessness[76] in that substance addiction often causes loss of employment and from there, without income, housing as well[76]. Substance addiction may also be a result of homelessness, with substance use beginning after someone loses their housing[76]. Use of cocaine is especially problematic among the homeless population, with high rates of use and poor treatment outcomes[80, 81, 82, 83].

Current Treatments for Substance Addiction

Current methods of treating substance addiction mainly fall into the categories of pharmacologic, behavioral, or alternative treatments. Often combinations of treatments are used to create the most efficacy.

Pharmacologic Treatments

The United States' Food and Drug Administration (FDA) has approved pharmacologic treatments for addiction to some substances. There is not a standard medication for use with all substance addictions. Pharmacologic options differ with

reference to which substance is being used, and some substances have no FDA-approved pharmacologic treatment options.

For tobacco users, there are nicotine replacement therapy (NRT) products, which have been available on the market for approximately 30 years, and also medications which do not contain nicotine[8]. NRT products are used when someone first stops smoking to help manage withdrawal symptoms. There are three types of FDA-approved NRT available over the counter (OTC): nicotine gum, transdermal nicotine patch, and nicotine lozenge[8]. There are also prescription-only NRT nasal spray and oral inhalers and the FDA has approved two prescription-only medications that do not contain nicotine- Chantix and Zyban[8]. However, both the prescription and non-prescription smoking-cessation medications do have side effects and come with warnings for individuals who have certain medical conditions.

For alcohol addiction there are currently three FDA-approved medications, all of which require a prescription: naltrexone, acamprosate, and disulfiram. Naltrexone blocks receptors which are responsible for alcohol cravings and the rewarding effects of consuming alcohol. Disulfiram produces an unpleasant reaction including flushing, nausea, and palpitations upon an individual's drinking alcohol. Acamprosate reduces symptoms of alcohol withdrawal such as anxiety, insomnia and restlessness[9].

Addiction to opioids such as heroin, morphine, and codeine, as well as semi-synthetic opioids such as oxycodone and hydrocodone, is treated with the FDA-approved medications methadone, buprenorphine, or naltrexone[10]. Methadone and buprenorphine suppress and reduce cravings for the opioid that has been abused. Naltrexone works

differently, blocking the desired effects of the opioid if an individual who has achieved abstinence has a relapse and uses the drug to which they had been addicted[10].

There are currently no FDA-approved medications to treat addiction to cocaine, cannabis, or methamphetamines[9], though research is in progress investigating potential pharmacologic treatments for all three [12, 13]. Specifically regarding cocaine, beta blockers propranolol and carvedilol, the GABAergic medications baclofen, tiagabine, and topiramate, and modafinil, which is currently approved for the treatment of narcolepsy, are showing promise[12, 14]. Another possibility is disulfuram, currently used for treating alcohol addiction. For cocaine users, disulfuram makes the cocaine high less pleasant by increasing the anxiety associated with it. Also under investigation is a vaccine, TA-CD, which produces cocaine-specific antibodies that lower the euphoric effect of cocaine[14,15]. However, it is unknown when any pharmacologic treatment for cocaine addiction might be approved by the FDA and in the meantime costs of cocaine addiction continue to mount.

Non-Pharmacologic Treatments

Behavioral Therapy

Current treatments for substance addiction also include behavioral therapies, which may in some cases be combined with pharmacologic treatment. Cognitive behavioral therapy (CBT) for addiction generally includes strategies to increase self-control[16]. A central element of this therapy is anticipating problems likely to arise when attempting to maintain sobriety and helping the patient to develop effective strategies to cope with these problems[16]. Another type of intervention, contingency management, gives patients the opportunity to earn incentives/prizes for drug-free urine screens[17].

Motivational enhancement therapy is a counseling approach that works towards behavior change for individuals who may have ambivalence about stopping substance use and seeking treatment[18]. This approach is most effective in getting individuals in the door to begin treatment, and may then be combined with CBT during active treatment.

Therapeutic Communities

Another treatment option for addiction is therapeutic communities. These sprang out of self-help recovery models in the late 1950s and began as long-term residential treatment programs run by peers in recovery[19]. Now many of these communities have begun incorporating professional staff including some who may be in recovery themselves, and offer shorter-term residential programs as well as outpatient day programs[19]. Therapeutic communities focus on mutual self-help and on the whole person, attempting to bring about numerous lifestyle changes, rather than just abstinence from substance use[19].

12-Step Facilitation

12-Step facilitation programs are a model of peer support and self-help that began with Alcoholics Anonymous in the 1930s[20]. The three main tenets of this model of behavioral therapy are acceptance of the problem, surrender to a higher power, and active involvement in 12-Step meetings and activities[21]. Along with the original 12-Step program for alcohol, offshoots now exist for addictions to other substances, including Narcotics Anonymous (stimulants) and Heroin Anonymous (opiates)[20].

Alternative Therapies

While not as common as mainstream pharmacologic or behavioral treatments for addiction, there are other therapies available, often as adjuncts to mainstream therapy.

Current findings have supported the use of yoga and mindfulness meditation as adjunctive therapies for addiction, as they deal with stress-related aspects of addiction and recovery such as emotions and behavioral urges such as cravings[22]. Nutritional supplements including high-potency multi-vitamins and amino acids as well as natural supplements and herbs are thought to help correct and restore neurotransmitter imbalances in the body that occur as a result of drug use[23, 24]. Although current evidence shows that acupuncture is not effective as the sole treatment for cocaine addiction, over 300 clinics in the U.S. utilize acupuncture as a component of treatment[25]. The ancient traditional Chinese practice of qigong has also been also been investigated for use in treatment, specifically for heroin addiction[26].

Exercise Interventions

With the high societal costs of substance addiction, other alternative treatment methods are being explored as well, including exercise. There is the potential that exercise may be an effective option, either as main treatment or adjunct to other treatment for substance addiction. Whether main treatment or adjunct, exercise in comparison to pharmacologic options is relatively inexpensive and without the potential side effects of some of the treatment medications. In fact, utilization of exercise as treatment may bring about secondary improvements in health as well. Many addiction treatment centers already do include exercise- voluntary or mandatory- in their courses of treatment, even without firm evidence of its effectiveness[27].

Not everyone who uses drugs becomes addicted, just as not everyone is equally susceptible to other chronic diseases[92]. Under the concept of addiction as a brain disease, exercise may be effective as part of treatment for substance abuse because of effects that

both exercise and drugs have on the brain[92]. Neurobiological investigators indicate that most drugs have dopamine-enhancing effects on the brain[92]. Reward regions of the brain are activated by addictive drugs, which cause increases in the release of dopamine, triggering further craving for the drug[92]. Exercise can increase measures of euphoria and well-being in humans in a way similar to that of abused drugs[93, 28]. It has been shown that bouts of exercise increase the brain's concentration of dopamine[94, 28] and that exercise influences many of the brain's molecules and structures that mediate the positive reinforcing effects of drugs[28]. Research has shown that exercise may produce neurologic adaptations that decrease an individual's susceptibility to developing a substance abuse disorder[28].

Investigators in Volkow et al. (2016) have suggested that there may be brain changes accompanying exercise that decrease the ability of drugs to produce reinforcement or craving[92]. Based on their findings, investigators posit that adding exercise to abstinence and behavioral treatment may be an alternative, non-pharmaceutical reinforcer and way to increase dopamine receptor availability[95, 28]. Under the brain disease model of addiction, it is suggested that development of behavioral interventions involving exercise can help restore balance in brain circuitry negatively affected by drugs[92].

Animal Research

There is a body of preclinical research investigating the effects of exercise on self-administration of drugs in lab animals. Self-administration of a drug is the main way in which the reinforcing effects of that drug are studied in the laboratory setting[28]. For self-administration the animal has a catheter implanted and during experimentation

sessions that catheter is connected to a supply of the drug being studied. The animals are trained to self-administer the drug, e.g. by pressing a lever. By using self-administration along with manipulation of various factors, investigators are able to mimic the different stages of drug use that humans typically progress through: acquisition, maintenance of regular use, escalation of use, binges, and relapse/reinstatement after cessation of use[28].

Studies involving animals have examined exercise in relation to a number of illicit drugs, though most frequently cocaine and methamphetamine. This review will focus on cocaine, as that form of addiction is the focus of this thesis. Preclinical work in this area has mainly been done utilizing rats and aerobic exercise (wheel running), and has shown promising results in all stages of drug use.

The acquisition stage is where an individual goes from initial contact or experimentation with a drug to establishing patterns of its use[28]. It has been shown by Smith & Pitts (2011) that exercising rats with access to a running wheel acquired (learned) self-administration more slowly than sedentary rats that had no such access and did fewer lever presses overall[29]. Male rats were obtained at weaning and raised for six weeks with exercise (had access to a running wheel) or sedentary behavior (no wheel access). The rats were then taught self-administration, with responding (lever presses) reinforced by infusions of cocaine. Acquisition was considered to be reached when a rat obtained 12 infusions of cocaine on at least two consecutive days; the first day was then considered the date of acquisition. Sedentary rats reached acquisition on average three days sooner than exercising rats, and over a 15-day period the number of lever presses by sedentary animals was twice that of the exercising rats[29]. This suggests that exercise inhibits the acquisition of cocaine self-administration and may prevent regular patterns of

substance use from being established[28]. In humans this could mean that exercise potentially could have a "preventive" effect, so that an individual would be less likely to progress from experimenting with cocaine to becoming a regular user.

The maintenance phase of drug use is entered when stable patterns of usage have been established. When both male and female rats had access to a running wheel at the same time as having access to the ability to self-administer cocaine, access to and use of the wheel has been found to decrease self-administration. It is worth noting that the finding was only statistically significant in the female rats[30]. Investigators first gave male and female rats access to a running wheel, then taught them self-administration and gave them access to cocaine only, without the wheel. The cocaine and wheel access were then concurrently available, followed by a period when only the cocaine was available. When the rats had wheel access, cocaine infusions decreased by 21.9% in males and 70.6% in females compared to when rats had access to cocaine only[30]. Investigators also found that the exercise/self-administration relationship was reciprocal, as concurrent access to cocaine decreased wheel-running in both male and female rats[30].

Another study examining the maintenance phase used female rats raised for six weeks from weaning either as exercisers (had running wheel access) or sedentary (no access) before implantation of catheters and self-administration training. The number of responses (lever presses) required to obtain an infusion of cocaine increased during a session until responding (lever presses) ceased, i.e. the breakpoint[31]. Breakpoints were found to be lower in exercising compared to sedentary rats, leading to fewer infusions and a lower amount of total cocaine intake per session in the exercising rats[31]. The main finding was that long-term voluntary exercise decreases sensitivity to the positive-

reinforcing effects of cocaine in female rats, suggesting that exercise may have "protective effects."[31]

Substance-abusing humans tend to progressively escalate their drug use over time[32, 28,] and the same pattern is seen in rats if access to a drug is extended by lengthening daily self-administration sessions[33]. Smith et al. (2011) obtained male and female rats at weaning, then raised them for six weeks as either exercising (had running wheel access) or sedentary (no access) before catheter implantation and training in self-administration. For 14 days the self-administration sessions were extended to 6 hours each, allowing unlimited lever presses during that time and access to running wheels for the exercisers. Both groups escalated their cocaine use, but exercising rats did so significantly less than the sedentary rats. Female rats escalated cocaine use more than males, but exercise attenuated escalation in both[34].

Another arm of the aforementioned study[34] gave a group of rats, raised and trained the same as was previously described, the ability to "binge" on cocaine. All rats were given 23-hour access to unrestricted cocaine self-administration with 72 hours between each self-administration session. The exercising rats self-administered significantly less cocaine than the sedentary rats during those 23-hour periods, and ended their "binges" 2.3 hours sooner. This was observed in both the male and female rats[34]. These findings suggest that exercise could protect against binges of excessive drug intake, and may be an effective treatment intervention in populations with high rates of compulsive substance abuse[28].

The final stage of drug use is relapse/reinstatement after cessation, and investigators have been able to mimic this stage in animals as well. Smith et al. (2012)

obtained rats at weaning and raised for six weeks as either exercisers (had access to running wheel) or sedentary (no wheel access). They were then trained to self-administer cocaine and allowed to do so for 14 days. Extinction of drug use was brought about by replacing the cocaine supply with saline for seven days. The exercising and sedentary rats had similar levels of self-administration with the cocaine, but the sedentary rats responded more than the exercisers in extinction, i.e. they pressed the lever even though they only received saline[35]. The researchers brought about extinction again, then looked at cue-induced reinstatement, which was relapse to drug-seeking behavior after exposure to environmental stimuli associated with drug use. They also looked at drug-primed reinstatement, which was relapse to drug-seeking behavior after an injection of cocaine. In both instances, sedentary rats responded (pressed the lever to obtain cocaine) significantly more frequently than did the exercisers, and the same was true for both males and females[35].

Incubation of drug-seeking is important in drug research. Incubation is defined as where drug cravings are low during the initial period of cessation of use, but then after a period of abstinence (as long as 28 weeks in humans) there is a return of intense craving brought about by drug-paired cues[36]. In a study by Zlebnick and Carroll (2015), female rats were trained for 10 days to self-administer cocaine, then went through either a three or 30-day withdrawal period when they did not have access to cocaine or cocaine-paired cues. During withdrawal each group also had access to either a locked or unlocked running wheel. After the withdrawal period the rats were returned to the cocaine self-administration chamber, where they were exposed to cocaine-paired cues but their responding (lever presses) did not yield cocaine. There was a notable increase in drug-

seeking behavior in the locked versus unlocked 30-day group when the behavior was measured in response to cocaine-paired cues[36]. There were no differences between the locked versus unlocked 3-day groups. The locked 30-day group had a greater level of responding than the locked 3 day group, demonstrating incubation of drug-seeking behavior during abstinence. A greater level of responding (lever presses) was not seen in the unlocked 30 versus three-day groups, indicating that exposure to exercise may prevent the incubation of drug-seeking behavior[36].

The timing of exercise in relation to relapse has also been investigated. In a study by Beiter et al. (2016) male rats were trained to self-administer cocaine, with 10 days of 24-hr-per-day access followed by a 14-day period of abstinence. During abstinence the rats were either sedentary or given access to a running wheel on days 1-7, 8-14, or 1-14; then access to self-administration was returned. The early (1-7) and throughout (1-14) exercisers had lower levels of responding (although not significantly different between the two groups) than did the sedentary and late (exercise on days 8-14) exercisers. The late exercisers also had a higher level of responding than the sedentary group, but the difference between the groups was not statistically significant. The results showed that exercise during early abstinence, even though there was no exercise on days 8 through 14, was as effective as exercising throughout abstinence at decreasing lever presses when cocaine was again available[37]. These findings suggest there is a persistent beneficial effect of exercise and that timing of exercise initiation, in relation to beginning of abstinence, is more important than length of exposure to exercise[37].

Recent research has also examined the effects of single, short bouts of acute exercise and of resistance exercise on cocaine self-administration. In a study by Smith et

al. (2016) male rats were exposed to acute bouts of exercise, running for 0 (sedentary), 30 or 60 minutes, and then given immediate access to a self-administration session or to a self-administration session that began 12 hours after exercise[38]. When the self-administration session was immediately after running, there was a significant decrease in self-administration in an output-dependent manner. The greatest reduction in cocaine intake was seen in the 60-minutes run group and the smallest reduction in cocaine intake was seen in the sedentary (0 minutes of running) group. However, there was no significant decrease in self-administration when the wheel-running was 12 hours prior to the self-administration session[38]. Virtually all other studies have involved a longer history of exercise, but Smith et al. (2016) indicate that history of exercise might not be necessary for exercise training to produce a rapid and significant reduction in cocaine intake[38].

In contrast to all the studies that have used aerobic exercise, Strickland et al. (2016) investigated the effects of resistance training on cocaine use. Strickland et al. (2016) used female rats that were either sedentary or participated in simulated resistance/strength training by climbing a ladder wearing a weighted vest[39]. Rats were trained in three-set pyramids, where they did eight ladder climbs carrying 70% of their body weight (BW), six climbs carrying 85% of their BW, and four climbs carrying 100% of their BW. These rats were also taught self-acquisition of cocaine. Strickland et al. found that exercising rats responded (pressed the lever for cocaine access) significantly fewer times than sedentary rats[39]. Further, this experiment was repeated three months later with a different cohort of rats but had the same results[39]. These findings suggest that resistance training may be a potential therapy to decrease cocaine use in humans.

The literature investigating exercise as a treatment for cocaine use in rats has found that exercise holds great promise for all the stages of drug use through which humans progress. However, while studies in rats may be important, they are very different from humans. Consequently, non-human primate models may be more valuable. It has been shown in monkeys that environmental enrichers can decrease cocaine reinforcement[73, 74]. Nader & Wolverton (1991) trained rhesus monkeys to self-administer cocaine after being implanted with catheters, and also to choose between cocaine and food. When the amount of food was held constant and the cocaine dosage was varied, the preference of cocaine over food increased as dosage increased[73]. But when cocaine dosage was held constant and the amount of food was varied, the monkeys decreased the choice of cocaine as the amount of food increased. These findings suggest that increasing the magnitude of a non-drug enforcer decreased the frequency of cocaine choice and total cocaine intake[73].

In another study, monkeys that had been taught to self-administer cocaine were exposed to environmental stimuli hypothesized by investigators to be either enriching (treats and having enlarged cage space) or stressful (a rubber snake). Although not all monkeys were affected and the effects were temporary, brief exposure to either environmental stressors or enrichment altered cocaine choice and suggest that positive changes in environment produce desirable effects in cocaine self-administration[74]. Although speculative, these findings suggest that the addition of exercise into daily activity may produce a positive environmental change which could lead to a reduction in cocaine use.

Human Research on Exercise and Addiction

Based on preclinical work with animals, exercise would seem to hold promise for treatment of addiction in humans. However, there is a paucity of human research into this topic and existing research has mainly been limited to small pilot studies. The largest amount of research on exercise and addiction has been done on nicotine/tobacco use, followed by alcohol, and then illicit drugs. There has been little research on exercise, specifically for cocaine abuse/addiction.

In 2012 a review was performed regarding studies of exercise and physical activity for the treatment of substance abuse disorders. The review searched studies published in English or German between 1970 and 2011[40]. Seventeen randomized controlled trials (RCTs) were found on exercise for nicotine use and dependence[40]. The review authors noted that RCTs regarding exercise for alcohol use and dependence are extremely rare, finding only nine studies[40]. No studies that met RCT criteria for illicit drug use were found, although eight non-RCT studies were identified that examined the therapeutic effects of exercise in drug-dependent individuals[40]. However, one of those studies involved a non-traditional Chinese practice called qigong, which includes meditation, relaxation, guided imagery, deep tranquility, mind-body integration, and breathing exercises[26].

A 2015 review by Linke and Ussher[75] failed to identify any new studies of exercise and illicit drug use since the 2012 review.

Nicotine/Tobacco

Regarding nicotine/tobacco use, in five of the studies that Zschucke et al. (2012) reviewed there was no difference in abstinence between regular exercisers and non-

exercising controls[41, 42, 43, 44, 45]. One study did find higher abstinence from nicotine/tobacco after one and two weeks of exercise, but this behavior was not maintained at six weeks of follow-up[46]. Eight studies found a trend toward abstinence and reduced cravings in exercisers[47,48, 49, 50, 51, 52, 53, 54]. One study found a higher rate of abstinence among exercisers, but that was not maintained at six and 12 month follow-ups[55]. Another study showed that there was no improvement in abstinence among exercisers, but fewer exercisers smoked cigarettes 26 weeks after the intervention ended[56].

Alcohol

Of the 9 studies involving alcohol dependence reviewed by Zschucke et al. (2012), one study examined subjects in outpatient treatment[57], one study examined subjects in both inpatient and outpatient treatment[58], and one study examined subjects who were heavy drinkers but without clinical diagnosis of alcohol abuse or dependence[60]. Subjects in the other six studies were in inpatient treatment. Two studies reported significantly higher abstinence rates at 3-month follow-up among the exercisers[57, 59]. Murphy et al. (1986) found a significant reduction in alcohol consumption during the treatment and trend for reduction during the follow-up among the exercisers[60]. One study reported no significant difference in abstinence rates, but did observe fitness gains and improvement in mental health aspects such as anxiety and depression among the exercisers[58]. Another study found significant reductions in alcohol cravings, though the exercise intervention also had other components making it unclear which behavior was related to the changes in craving[61]. Three of the studies had no alcohol-related outcomes reported, but did report fitness gains and improvements in mental health items such as

anxiety, depression, stress, and paranoia[62, 63, 64]. One study reported only that there were no differences regarding drinking episodes between groups, as observed by staff, but fitness gains and improvements in mental health were seen among exercisers[65].

Illicit Drugs

Of the eight studies that used exercise interventions for illicit drug users, five reported drug-use-related results. All five found significant improvements in abstinence or decreased drug usage with exercise[66, 67, 68, 69, 70]. Of those five studies, three used subjects who were in treatment for drug use[67, 68, 70], one study examined participants who were not seeking treatment[66], and one study used a mix of treatment and prevention programs[69].

In one of the five studies the substance(s) being abused was not specified[70]. In one study the substance being abused was cannabis (marijuana)[66], and in three studies subjects were addicted to mixtures of substances without separating: cigarettes, alcohol and marijuana[70]; alcohol, cocaine, marijuana, opiates and sedatives[67]; and cannabis, opiates, cocaine, heroin, amphetamines, medicine (type not specified) and alcohol[68]. None of the studies looked at cocaine use specifically.

The types of exercise used in the interventions were also varied. One utilized aerobic treadmill exercise[66], while another used the aerobic exercise modes of treadmill, recumbent bike, or elliptical[67]. A Danish study used both aerobic (type not specified) and resistance exercise[68]; a study involving adolescents did not specify exercise type[69], and one with subjects who were homeless veterans utilized membership on a softball team with a weekly game and twice-weekly practices for six months/three "seasons" of a city league[70].

All five studies had positive outcomes, though outcome definitions were not standardized. Burling et al. (1992) did not specify substances being abused but found that softball team members were more likely to complete treatment than those not on a team. Further, team members also had significantly higher drug/alcohol abstinence at three-month follow-up after treatment[70]. Roessler et al.'s (2010) subjects used a mix of cannabis, opiates, cocaine, heroin, amphetamines, medicine (type not specified) and alcohol and completed a two-month intervention using unspecified aerobic exercise and weight training. The results suggest that substance intake and urges had decreased at the end of the intervention, but this study was limited because there was no control group[68]. Collingwood et al.'s (1991) cohort of adolescents were either in treatment for use of cigarettes, alcohol, or marijuana or in a substance abuse prevention program. At the end of nine weeks those who improved their time on a one-mile run the most had a lower percentage of multi-drug use and a more significant gain in percentage of abstainers than those who didn't[69]. Buchowski et al. (2011) used participants who were non-treatment-seeking cannabis (marijuana) users and who participated in a two-week intervention utilizing aerobic treadmill exercise. This study demonstrated a statistically significant decrease in cannabis usage per day during exercise treatment, but also a statistically significant increase in cannabis usage per day during follow-up. However, the craving for cannabis was found to be significantly reduced by exercise[66].

A study by Brown et al. (2010) may offer the most promising results related to exercise and substance abuse. Subjects in this study were a mix of alcohol, cocaine, marijuana, opiate and sedative users in treatment who participated in a 12-week aerobic exercise intervention. The results demonstrated a statistically significant increase in

percentage of days abstinent during the intervention and at follow-up. Those who attended ≥75% of the sessions (attenders) had more abstinence than those who attended <75% of the exercise sessions (non-attenders). Non-attenders were 80% likely to relapse, while attenders were only 20% likely to relapse[67].

Two studies which used exercise interventions for subjects with abuse/dependence of illicit drugs have been published since the 2015 review by Linke and Ussher. One study utilized an eight-week program of aerobic and resistance exercise for methamphetamine users versus sedentary control for methamphetamine users[71]. Though not statistically significant, fewer exercisers returned to methamphetamine use after one, three and six months compared to sedentary subjects. The results appear to be better for those who were lower-severity users (≤18 days/month) at baseline than for those who were higher-severity users (>19 days/month) at baseline[71]. The other study utilized a four-week treadmill exercise program of either walking or running versus a non-exercise control group for concurrent cocaine and tobacco users who were seeking treatment but not in treatment. Both the exercisers and the controls received computerized cognitive behavioral therapy[72]. Although not statistically significant, results indicated that regular exercise improved abstinence from cocaine, verified by urine drug screen, and self-report within the last 24 hours. There was no significant difference in cocaine cravings but there were non-significant reductions in number of cigarettes smoked and smoking urges[72]. This was the first published study that examined the potential of exercise as treatment specifically for cocaine addiction.

Fischer et al.'s 2015 review of English-language studies investigating the effectiveness of secondary prevention and treatment interventions for crack cocaine abuse

divides its treatment intervention discussion into three sections: psycho-social treatment, adjunct/ancillary treatments, and pharmaco-therapeutic interventions[90]. There are no exercise interventions in the adjunct/ancillary treatment section.

Although results have not yet been reported, a multisite randomized controlled trial has been done which compared exercise (EX) to health education (HE) as treatment for abuse of stimulants including cocaine, as well as methamphetamine, amphetamines or other stimulants except nicotine or caffeine[98]. This is the STRIDE study (Stimulant Reduction Intervention using Dosed Exercise)[98], results of which have not yet been published. All participants in the study were receiving treatment as usual throughout, which included inpatient substance abuse treatment at the start of the intervention and transitioning to outpatient treatment or community care[98]. Participants underwent a medical history and exam as well as maximum exercise test prior to beginning exercise, for safety and exercise prescription[98]. Both study arms included supervised sessions three times per week during the initial 12-week acute phase of the study, then had supervised sessions once per week for six months following[96]. The exercisers engaged in vigorous intensity aerobic exercise on a treadmill, either walking with a grade or running with a ramp-up of intensity over the first three weeks[98]. The health education group viewed educational items presented to them during sessions, so that they were receiving equivalent attention[96].

STRIDE investigators cited the lack of a gold standard endpoint for studies in this field, and indicated that a standardized endpoint is needed for comparison across studies[97]. It was noted that long-term continuous abstinence is the clinical goal for stimulant use disorders but may be unrealistic[97]. Therefore, STRIDE utilized the primary

endpoint of percentage of days abstinent as measured by Timeline Follow Back, aided by using a take-home Substance Use Diary to assist recall, and confirmed by urine drug screen thrice weekly during 12-week acute phase of the study[97]. Investigators noted the challenge of designing and implements an exercise intervention because of the unique life situations, unstable living conditions, complex medical situations, and multiple co-morbidities in this population[98]. The results of this study, when published, are certain to be enlightening.

The aforementioned De La Garza et al. (2016) study did not indicate what form of cocaine its participants used and was also published after the Fischer et al. review. At this time the De La Garza et al. (2016) study stands alone as an investigation of the effects of exercise on cocaine use in humans. However, this study did look at exercise for concurrent cocaine and tobacco use, and its participants were all in or seeking treatment at the time of recruitment[72]. The study's participants did earn $700.00 if they completed all study visits and were provided with running shoes and socks, running shorts, and a T-shirt, which they were allowed to keep if they completed the protocol. The study had a > 90% retention rate. There has yet to be a study published seeking evidence regarding the effects of exercise solely on cocaine use rather than concurrent substances, one that does not utilize subjects currently seeking treatment for substance use, one investigating exercise as sole therapy for cocaine addiction, or one looking at exercise as potential treatment for substance abuse in the subpopulation of the homeless.

Purpose

Promising preclinical findings in animal research report the positive effects of exercise on cocaine use, suggesting that exercise may also have positive effects on

humans. Current research also supports the utilization of exercise in treatment for use of the substances nicotine and alcohol and therefore suggests that it might be useful in treatment for the use of other substances as well. However, there is a dearth of human research into the area of exercise as treatment for cocaine usage and addiction, particularly in the homeless population.

Thus, the purpose of this study is to determine the feasibility of homeless cocaine-using men, who are not currently in or seeking treatment for their cocaine use, participating in a standardized exercise regimen for six weeks. The specific aims of this study are the assessment of the feasibility and acceptability of recruiting homeless cocaine-addicted men from a local homeless shelter for an exercise intervention, examining adherence and retention rates of homeless cocaine-addicted men participating in a standardized exercise intervention, and assessing the feasibility and acceptability of the physical assessment and other outcome measures utilized.

METHODS

The purpose of this study was to determine the feasibility of homeless cocaine-using men, who were not in or seeking treatment for their cocaine use, participating in an exercise intervention for up to six weeks in order to determine the effect(s) of exercise on their cocaine use.

Participants

Ten homeless adults were sought for a six-week exercise program. It was anticipated that fifteen individuals would be consented in order to obtain a sample of ten individuals approved to take part in the program. Participants were originally recruited from a homeless shelter for men in Winston-Salem called Samaritan Ministries. Recruitment was conducted via announcement by a study team member at a monthly meeting at which all shelter guests were present as well as by flyers posted at the shelter and by word of mouth. Recruitment was later expanded by posting the flyers at other area homeless shelters and at other community locations such as libraries and health centers.

Inclusion

Interested individuals met with one of the study team members to determine whether they met the screening criteria. Initial inclusion criteria were as follows: male, age 18-64, having self-reported use of cocaine within the past 30 days, currently homeless and living at Samaritan Ministries men's shelter, willing to participate in a six-week exercise intervention to be held at the Samaritan Ministries facility, and willing to participate in a physical exam, physical activity testing to include a graded exercise

"stress" test (GXT), and follow-up visit and testing at the Clinical Research Center (CRC) of Wake Forest University (WFU) with transportation provided to this location.

Participants were limited to males for two reasons. First, the shelter where the recruitment and intervention were to be held only serves males and the study was investigating whether this type of intervention could be added into existing services. If successful, the study team planned to assess the feasibility of an exercise intervention with women later at a different setting. Secondly, based on the Principal Investigator's extensive clinical experience, it was felt homeless women do not want to participate in group activities with men.

Due to difficulties with initial recruiting efforts, the inclusion criteria were expanded in two ways. The requirement that an individual had used cocaine within the past 30 days was expanded to require that an individual had used cocaine within the past year. Further, the requirement that an individual reside at Samaritan Ministries shelter was expanded to include individuals who were homeless and resided at any homeless shelter in Forsyth County. At that time, recruitment flyers were posted in two other homeless shelters, as well as at local libraries and the Samaritan Inn soup kitchen.

Exclusion

Individuals were excluded if they were impaired by any substance or actively psychotic at the time of enrollment or had any type of cognitive impairment that would preclude them from giving informed consent at the time of enrollment. Determination of these exclusion conditions was based on observation by a trained study team member. Other exclusion criteria were as follows: having a legal guardian, regular exercise ($\geq$ 30 minutes three times per week), a physical impairment or condition that would prevent

them from doing physical exercise, having been told by a physician within the past year that they should not exercise, or answering "Yes" to the following question: "Have you been told that you had a heart attack or stroke, or have you had eye, chest, or abdominal surgery within the past three months?" Any individual that met the screening criteria was offered the opportunity to review the informed consent, ask any questions regarding the informed consent, and enroll.

Table I: Final Inclusion/Exclusion Criteria

Inclusion Criteria:	**Exclusion Criteria:**
- Male	- Impaired by substance, psychotic, or cognitive impairment
- Age 18-64	- Has legal guardian
- Homeless	- Regular exerciser
- Staying at any Forsyth County shelter	- Told by physician within past year not to exercise
- Willing to participate in 6-week exercise intervention	- Heart attack, stroke, or eye, chest, or abdominal surgery within last 3 mos.
- Willing to undergo initial and follow-up physical assessments	-Physical impairment precluding Exercise
- Cocaine use within past year	

Assessments

Once a subject was enrolled a physical and behavioral assessment was conducted at the WFU CRC. The purpose of the physical assessment was to ensure that participants were evaluated by a physician and were determined to be safe to participate in a vigorous intensity exercise intervention. The behavioral assessment included a brief survey about the subject's life and behaviors, as well as an interview by a study team member. The

behavioral assessment was repeated at three weeks after the intervention started, the end of the intervention, and three weeks after the end of the intervention. The physical assessments included the 6 Minute Walk Test (6MW), anthropometric measurements, and a urine drug screen (UDS) and were repeated at the end of the six-week intervention. Participants also completed an exit interview survey at the final nine-week assessment.

Physical Assessment

The physical assessment included a brief exam by a physician as well as a graded exercise "stress" test (GXT), the 6MW and anthropometric measurements. American College of Sports Medicine (ACSM) Guidelines for Exercise Testing (9^{th} edition) were adhered to for all exercise tests.

Participants underwent a GXT in order to screen for any abnormal cardiovascular responses or other potential contraindications to the exercise program. Medical history and current medications were obtained prior to conducting the GXT, including any acute illness or injury that might affect the validity of the test. Baseline resting information on heart rate (HR), blood pressure (BP), and electrocardiograms (ECGs) was obtained and then the participant began to walk on a motor-driven treadmill at a very low level that gradually progressed to a higher speed and grade every two minutes. During the GXT a 12-lead ECG was continuously monitored and printed at the end of every two-minute stage. Any arrhythmia or ST-segment change was documented and BP was taken during the last minute of every stage. The test was terminated when the participant wished to stop due to fatigue, shortness of breath, pain, etc. or when the attending physician decided to terminate the test in accordance with established test termination criteria. Once the test was terminated, the participant was placed in the supine position while still connected to

the ECG and BP cuff to continue recovery. Recovery continued for a minimum of six minutes until HR and/or BP had returned to resting values and the participant was stable. An estimated MET level was determined based on the ACSM equation, which is based on maximum speed and grade obtained during the GXT. The medical doctor supervising the test made the decision whether the participant was allowed to proceed to take part in the exercise intervention. The GXT was only performed at baseline, primarily for screening, and not at follow-up.

The 6MW for assessing submaximal exercise capacity was administered by trained study personnel on the 120-meter track of the WFU CRC. Participants were instructed to walk at their own pace while trying to cover as much ground as possible in six minutes. The same course and procedures were used at baseline and follow-up testing. Anthropometric measurements including body weight and percent body fat were also measured using a calibrated scale, skinfold calipers and the standard three-site skinfold techniques for men.

At both the baseline and follow-up fitness assessments participants were tested for the presence of cocaine and other drugs of abuse using the iCup Drug Screening Device (Redwood Toxicology Laboratory), which was provided to each participant to collect his own urine specimen. The test kits generated a result on the outside of the test unit which was logged by a study team member. The participant then disposed of his own urine in the restroom.

Behavioral Assessments

Basic demographic data was collected from each participant, along with information about participants' history of homelessness, current and past substance abuse

treatment if any, attendance at 12-Step or other self-help meetings, health and mental health problems, current medications, and employment status. Assessments regarding substance abuse, social support and psychiatric symptoms- all factors that might be directly or indirectly impacted by the intervention- were conducted to see if these measures are appropriate for use in this population. The following assessments were used at baseline and follow-up.

The Addiction Severity Index (ASI) was used to assess substance use severity. The ASI is a semi-structured interview tool that assesses problems in a variety of life domains: medical, employment/support, drug and alcohol use, legal, family/social and psychiatric[91]. The questions assess lifetime and past-30-days behavior[91]. The Timeline Follow Back (TLFB) was used to assess the frequency of use of cocaine and other substances in the six months prior to study enrollment and during the entire time of the study period. The TLFB is a calendar-based method of obtaining retrospective reports of behaviors. It has been previously used in research with persons who are homeless and has established reliability as a means of assessing cocaine use and other substances[84].

Social support was assessed using the Multidimensional Scale of Perceived Social Support. This is a 12-item measure with three subscales that uses a seven-point Likert scale. It has established psychometric properties[85] and has been used in other research on substance abuse[86, 87]. To assess severity of psychiatric symptoms the Modified Colorado Symptom Index was used. This 14-item measure was developed for use in treatment-outcome studies and has established psychometric properties for use with homeless adults[88].

Exercise Intervention

The exercise intervention for this study originally consisted of eighteen sessions of an aerobic exercise class over six weeks. However, one session was canceled when it became known that the sole individual who was participating in the exercise intervention sessions at that time would be unable to attend the session due to a doctor's appointment. Therefore, total number of exercise intervention sessions offered was seventeen. The sessions were held three times per week on Monday, Tuesday and Thursday evenings in the lobby area of the Samaritan Ministries homeless shelter at 5:00pm, 1.5 hours before the shelter was open to other shelter guests. Having the intervention at this time allowed participants to check into the shelter early, which was anticipated to be a way to attract participants. Only study participants were allowed to take part in the exercise sessions at the shelter. Each session was a one-hour standardized, pre-choreographed Body Attack or Body Combat cardio class developed by the Les Mills fitness corporation (Les Mills International). Each session was led by two instructors from the YMCA of Northwest North Carolina who are certified to use the exercise routines and music developed as part of the Les Mills group exercise system. These routines include a five-minute warmup and five-minute cooldown.

Prior to the start of each session, participants checked in with a study team member and had resting heart rate and blood pressure measured and recorded. Twice per week, just prior to participating in an exercise session, participants provided a urine sample that was used to test for the presence of cocaine and other drugs of abuse. This UDS was performed following the same procedures as at the time of initial physical

assessment. Heart rate and blood pressure was measured and recorded again at the end of each exercise session.

A study team member was present for the duration of all exercise sessions and a log was kept of each participant's attendance, heart rate and blood pressure prior to and following each exercise session, and total minutes (out of 60) that each participant exercised at each session.

Compensation

Each participant was given two shirts and two pair of shorts to wear during the exercise sessions and to keep after completion of the study. Participants were also given a pair of sneakers to wear for each exercise session. If the participant completed the study he was able to keep the sneakers. However, until then he turned in the shoes at the end of each session for study staff to keep until the next session. For study assessments, the participant was paid in the form of gift cards; $15.00 for the first assessment visit at the CRC, $20.00 for the week three assessment, $20.00 for the week six assessment, which included follow-up assessment at the CRC, and $20.00 for the final assessment at the end of the study.

Exit Interview Survey

At nine-week follow-up an Exit Interview survey was administered to participants. The survey consisted of six questions where the participants were to choose an answer number between one and ten, with one being poor and ten being excellent. These six questions asked about overall class experience, intensity level, length (in minutes), location and time of day of the class as well as the class instructors. The survey also contained one question asking how likely it was that the participant will continue to

exercise. For this question the participant was to choose a number between one and ten, with one being very unlikely and ten being very likely to continue to exercise.

The Exit Interview survey also asked which class format the participant liked best, whether the participant noticed a decreased interest in using cocaine when exercising and the day after exercising, whether the participant did any other exercise while in the study, and what the participant liked best and least about the study.

Instructor Debriefing

After all exercise intervention sessions were completed, the study team held a meeting with the Les Mills instructors. The instructors were asked for feedback, and offered suggestions about what might have been done to improve the exercise intervention sessions. The first suggestion was that "exercise class" may have been the wrong wording to use to attract potential participants. It was suggested "fitness session" or "training workout" be used instead. At this meeting the study team learned that the two Les Mills classes utilized had a "Smart Start" option, which would be a shortened version of the classes using the first five music/exercise tracks. Each session using this option would be approximately 30 minutes long rather than 60 minutes. The instructors suggested that using this Smart Start option for the first few classes could assist the participants in feeling more in control and more successful before progressing to the full 60-minute class. The instructors also pointed out that free weights are a big draw for males and that the Les Mills Bodypump class utilizes weights. It was suggested by the instructors that the Bodypump class be used in any future interventions with this population.

Analytical Plan

Descriptive statistics were utilized to analyze sample characteristics. Feasibility was defined as recruitment rate, retention, acceptability of treatment, and limited efficacy testing. Recruitment rate was determined by the percentage of subjects screened who were enrolled in the study. Retention was defined as the percentage of enrolled participants who completed nine week follow-up.

Acceptability of treatment was based on session attendance, minutes exercised, and participant satisfaction. Session attendance was calculated by totaling the number of sessions attended, then dividing that number by the total number of sessions multiplied by the number of participants. Mean minutes exercised per session was calculated by totaling number of minutes exercised by all participants at all sessions attended and dividing that by the total number of sessions attended. Percentage of minutes exercised was calculated by totaling the number of minutes exercised during all sessions attended and dividing that number by the total number of sessions attended multiplied by the total minutes in each session (60). Participant satisfaction was based on the mean of the responses in each category of the exit survey, with 1 being Poor and 10 being Excellent, as well as on the answers to the survey questions "What did you like best about the study?" and "What did you like least about the study?"

Limited efficacy testing was determined by: change in the results of urine drug screens (UDS) testing for presence of cocaine from the beginning of the exercise intervention to follow-up, reporting of cocaine usage after the start of the exercise intervention on the Timeline Follow Back questionnaire, change in 6 Minute Walk (6MW) distance, and change in body weight.

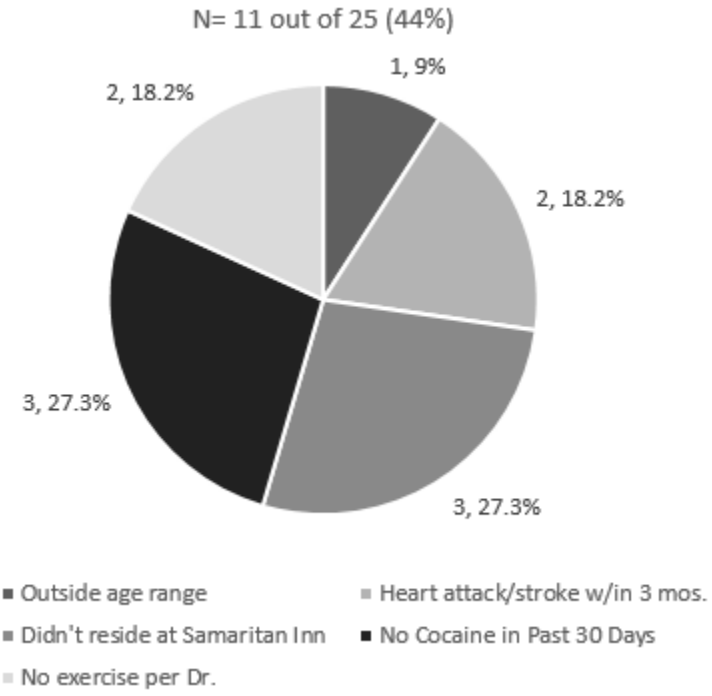
RESULTS

This study investigated the feasibility of conducting an exercise intervention utilizing homeless cocaine-using men as participants. The components of feasibility were defined as recruitment, retention, acceptability of treatment, and limited efficacy.

Recruitment and Retention

A total of 25 potential subjects were screened, and of those, eleven subjects (44%) did not qualify to participate under the initial inclusion/exclusion criteria, prior to GXT assessment. The most common exclusions (Figure 1) were a history of stroke or heart attack within the last 3 months (18.2%=2), being told by a physician within the past year not to exercise (18.2%=2), not being within the required age range (9.0%=1), not living at the Samaritan Inn homeless shelter (27.3%=3) and not having used cocaine within the past 30 days (27.3%=3).

Figure 1: Initial Exclusions

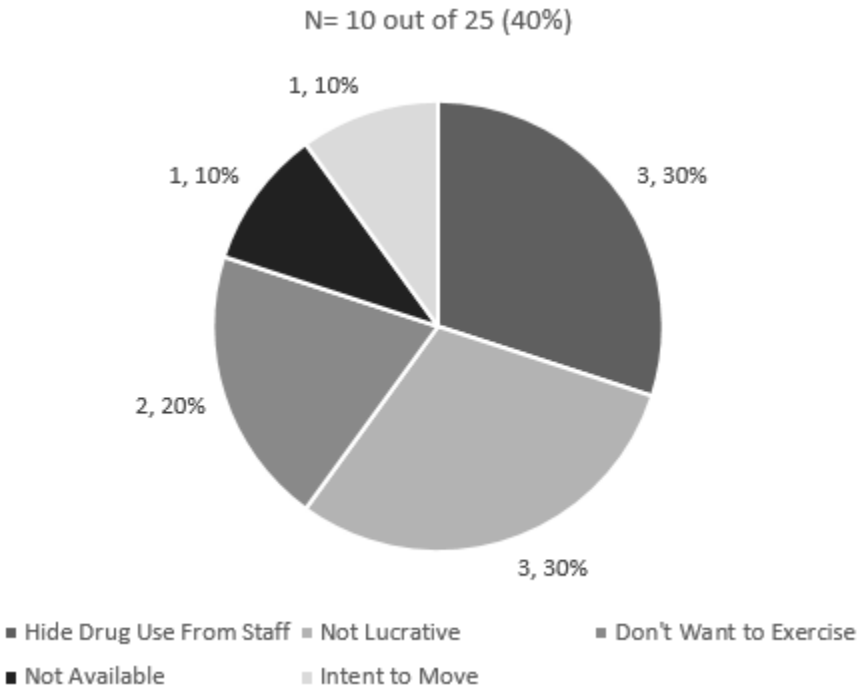


Once the inclusion criteria were amended to cocaine use within the past year, all three subjects who had been ineligible due to no cocaine use within the past 30 days became eligible. Two of those subjects did enroll in the study, and one attempted to enroll but was screened out as a result of his abnormal GXT. The subjects who were not living at the Samaritan Inn homeless shelter at initial screening would have become eligible for the study when inclusion criteria were amended to allow residence at any homeless shelter in Forsyth County. However, a study team member tried to locate or contact those subjects via contact information they had provided but was unable to do so.

Ten of the screened subjects (40%) who were eligible to participate in the study declined to do so (Figure 2). Thirty percent (30%= 3) of these subjects declined to participate because they did not want shelter staff to know that they had used or were using cocaine. These subjects stated that they were afraid of losing their residence at the Samaritan Inn homeless shelter since drug use is not permitted. These subjects also stated that they were afraid that the shelter staff would treat them differently and would be judgmental if staff knew that they were using or had used cocaine. Each of these subjects indicated having a history of denied drug use to shelter counselors when asked because of fear of losing shelter services and that shelter staff would be aware of their drug use if they enrolled in the study.

Another 30% (30%= 3) of subjects declined to participate because participation in this study was not lucrative and they could "make more money by panhandling." Other common reasons for declining participation were lack of interest in exercising (20%= 2), inability to be available during intervention hours due to work (10%= 1), and intent to move out of the Winston-Salem area in the near future (10%= 1).

Figure 2: Reasons for Declining Participation



Of the 25 potential subjects screened, seven subjects (28%) were eligible under the final inclusion/exclusion criteria. Of those seven subjects, two became ineligible based on their abnormal graded exercise "stress" test (GXT) results obtained at initial assessment. The remaining five subjects enrolled in the study, for a recruitment rate of 20%.

It should be noted that all seven of the individuals that were recruited did successfully meet the taxicabs at the shelter and arrived at the CRC at the appointed times for assessments. None of the seven displayed signs of intoxication, as determined by the medical doctors supervising the graded exercise "stress" tests, upon arrival at the CRC. Furthermore, none of the five enrolled participants exhibited signs of intoxication at the beginning of any exercise intervention session. During the exercise intervention sessions

there were no medical issues observed while engaging in the vigorous exercise or afterwards.

Retention in the exercise program was very low, with only two of the five participants (40%) completing nine-week follow-up assessments and the exit interview survey. One of the three drop-outs never attended any of the exercise intervention sessions after completing the initial assessments and was no longer residing at Samaritan Inn at the time exercise intervention sessions began. His location during the study was unknown. Another drop-out attended four sessions and then moved to Greensboro to reside there. He did not have his own transportation and therefore did not return for exercise sessions or follow-up testing. The third individual, who dropped out after the first exercise intervention session, obtained permanent housing and did not have transportation to return to Samaritan Inn to continue the intervention.

Sample Characteristics of Participants

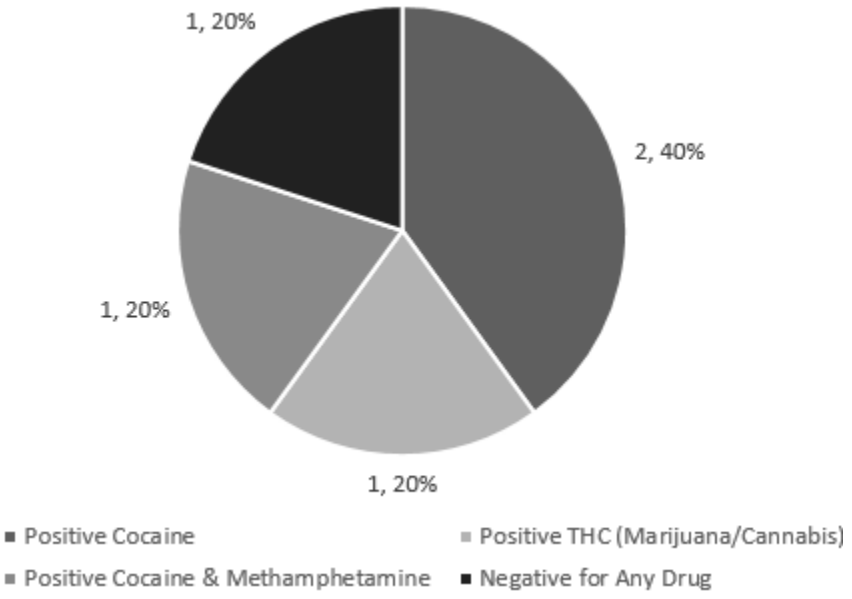
Enrolled participant demographics are displayed in Table I. The baseline sample included five men who were homeless and had used cocaine within the past year. The mean age of the sample was 53.4 (SD=3.2) years, with participants ranging from 50 to 58 years old, and the entire sample was African American. Mean years of education completed was 12.2 (SD=.9), with 60% having some college education. Sixty percent (3) of the sample was divorced, while 40% (2) had never been married. Mean BMI of the sample was 34.0 (SD=2.2). One hundred percent of the sample stated that they did not exercise $\geq$ 30 minutes three times per week, but 100% of the sample used walking as their main method of transportation. Sixty percent (3) of the sample had used cocaine within the past 30 days, while 40% (2) of the sample had used cocaine within the past

year but not within the past 30 days. Number of times homeless, including the present time, ranged from one to eight, with 40% (2) of the sample homeless for the first time, 40% (2) of the sample homeless for the 2nd to 5th time, and 20% of the sample (1) homeless for > five times. Eighty percent (4) of the sample had a diagnosed mental health disorder. Results of the urine drug screen at the initial assessment are presented in Figure 3.

Table II: Sample Characteristics of Enrolled Participants

DESCRIPTION	N (%) or Mean (SD)
N=5	
Age	53.4 (± 3.2)
Race	
Black/African American	5 (100)
Marital Status	
Divorced	3 (60)
Never Married	2 (40)
Years of Education Completed	12.2 (± .9)
BMI	34.0 (± 2.2)
Exercise	
Regular Structured Exercise	0 (0)
Walking as Transportation	5 (100)
Cocaine Use	
Within Past 30 Days	3 (60)
Within Past Year But Not Past 30 Days	2 (40)
# Times Homeless Including Present	
1	2 (40)
2-5	2 (40)
> 5	1 (20)
Diagnosed Mental Health Disorder Other Than Addiction	
Yes	4 (80)
No	1 (20)

Figure 3: Initial Assessment Urine Drug Screen Results (N= 5)



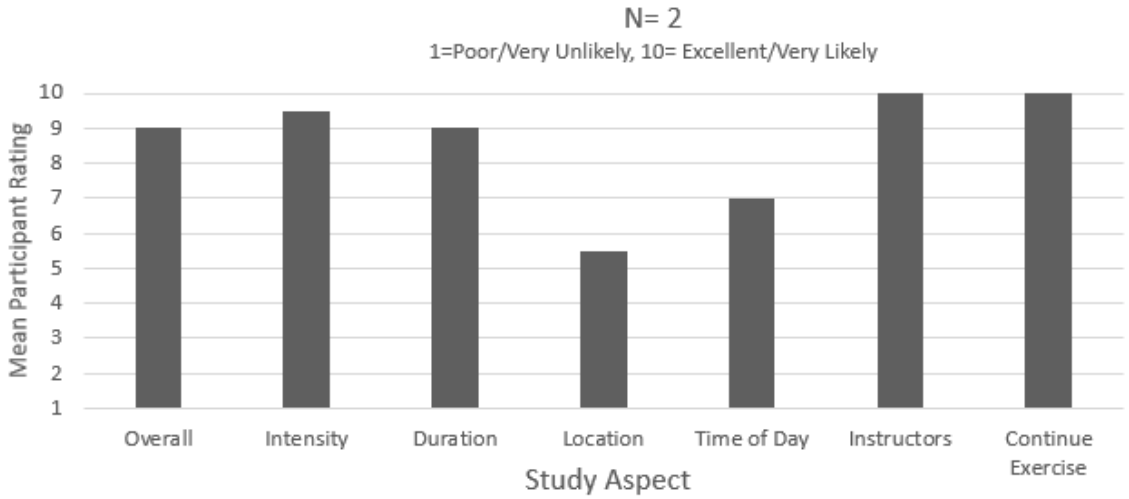
Acceptability of Treatment

Acceptability of treatment was based on exercise session attendance, minutes exercised, and participant satisfaction as indicated on an Exit Interview survey at nine-week follow-up. Of 17 total exercise intervention sessions offered over six weeks, the mean number attended was five (SD=5.73). Based on the total number of sessions attended, an attendance rate of 29.41% was calculated. The mean number of minutes exercised per session attended was 49.28. Based on a total number of minutes of exercise performed per session, out of a total number of possible minutes exercised per session, it was calculated that participants exercised for 82.13% of possible minutes during the intervention.

Two participants completed nine-week follow-up assessments and both completed the Exit Interview survey as part of that follow-up. Mean results of the survey are presented in Figure 4. Where 1 is Poor and 10 is Excellent, one participant rated the

overall exercise class experience as an 8 and the other rated overall exercise class experience as a 10. Where 1 is Very Unlikely and 10 is Very Likely, the answers of both participants to the question "How likely is it that you will continue to exercise?" were 10. One participant indicated that he noticed a decreased interest in using cocaine when exercising and the day after exercising. The other participant answered that those questions were "* Not Applicable."

Figure 4: Exit Survey Ratings at 9 Weeks



In answer to the question "What did you like best about the study?" one participant answered "Getting to know individuals, getting to relate, getting to talk to someone who can relate, intellectual conversation." The other participant responded "The Girls" (referencing the YMCA instructors). In answer to the question "What did you like least about the study?" one participant answered "Nothing" and the other participant responded "Location; rather go to the YMCA or a place less "spotlighted.""

One of the participants (#5) who participated all the way through to the nine-week follow-up stated to a study team member before one of the exercise intervention sessions

"This is tough when you're doing it but you sure feel good afterwards. It's kind of like a high. Actually, it's better than the high you get from drugs."

Limited Efficacy Testing

Investigators were not expecting to see any statistically significant changes as this study was a very small feasibility study. However, several potential outcomes for a larger study were explored.

Cocaine usage, as measured by urine drug screens at baseline and nine-week follow-up, was negative at both time points for the two participants who completed the study (#5 & #7). Cocaine usage as measured by self-report on the Timeline Follow Back questionnaire indicated that at baseline one participant hadn't used cocaine since June 2016 and at 9-week follow-up had not used it at any time after beginning the exercise intervention. At initial assessment the other participant reported his most recent use of cocaine as nine days before completing the Timeline Follow Back and at 9 week follow-up reported that he hadn't used cocaine at any time since beginning the exercise intervention.

The participant who attended the most exercise sessions (15 of 17) lost one pound over the six weeks but had a decrease of 56.5 meters (10%) on the 6MW. The other participant that completed the six-week physical assessment, but was much less compliant to the exercise program (4 of 17 sessions), lost three pounds and had a 82 meter (13%) decrease in 6MW from baseline to follow-up.

DISCUSSION

The purpose of this study was to determine the feasibility of homeless cocaine-using men, not in or seeking treatment for their cocaine use, participating in a standardized exercise regimen for six weeks. The long-term goal is to utilize the findings of this feasibility study to inform the design of a pilot study and to eventually progress to a randomized controlled trial investigating exercise as a substance abuse treatment for homeless men who use cocaine.

The conceptual model of feasibility utilized for this study was derived from Bowen et al.[89] and the components of feasibility chosen as measures for this study were recruitment, retention, acceptability of treatment, and limited efficacy testing. An overall review of the results suggests that significant changes to study design and methods would be required in order to reproduce this study as a larger scale pilot study. However, this study certainly helped inform the study team and guide them towards potential amendments that could be implemented in order to increase the overall feasibility of a pilot study.

Recruitment

Investigators knew from the onset that the study would involve a very unique population, but found recruitment to be even more challenging than expected. Fewer individuals were screened than anticipated, leading to a small potential sample size. Since there is a fairly significant proportion of the homeless population using or abusing illicit drugs[76, 78] it was not anticipated that potential participants would be resistant to having their peers in the homeless community know that they are or were drug users if they are not currently in treatment for such use. Buchowski et al. (2011)[66] was the only

study reviewed that examined exercise and illicit drug use in participants who were not in or seeking treatment. However, those participants were not homeless and as such did not have shelter services to lose if their drug use became known. One alternative for the current study would be to amend recruitment flyers to seek participants who are homeless and would be willing to engage in an exercise or fitness regimen. The screening questionnaire could then inquire about drug use. This approach would likely require that more individuals be screened in order to obtain the desired number of drug-addicted participants. However, it would keep cocaine use history from being open knowledge and would preclude shelter staff from knowing that the study specifically sought cocaine users. As it would cast a wider net, this approach would also be likely to produce a larger initial pool from which a larger sample would be likely to be produced. Another alternative would be to alter the focus of the study to specifically utilize participants who were in substance abuse treatment programs provided as part of shelter services, thus removing the drug use stigma entirely while still investigating the possibility of incorporating exercise into existing shelter services. It should be noted that three of the studies reviewed[67, 68, 70] used exercise as part of substance-abuse treatment, a practice not uncommon in substance abuse treatment programs[27].

Another barrier to recruitment was that the $75.00 that participants would receive for completing all study visits including six weeks of thrice-weekly exercise sessions was not sufficient to induce participation. Potential participants perceived that they could acquire more than that amount in ways that would not require them to exercise-specifically, by panhandling. De La Garza et al. (2016)[72] is, to date, the only published study which specifically investigated exercise and cocaine use. In their intervention,

participants who completed all study visits earned $700. The visits included only four weeks of thrice-weekly exercise sessions. It was learned through the current study that in the homeless population potential participants will consider the amount of compensation they might receive and weigh that against alternative methods of obtaining that amount of money when deciding whether to participate.

In designing an exercise intervention for the homeless population, investigators must take the general health of this population into account. Of the 25 individuals screened, six (24%) were excluded due to health issues. Two potential participants were excluded due to history of heart attack or stroke within the past three months, two were excluded due to having been told by their physician not to exercise, and two were excluded because their graded exercise "stress" tests indicated that they were not capable of safely performing the moderate to vigorous intensity exercise in this intervention. These results indicate that investigators must contend with the fact that health issues are likely to be seen in this population. Therefore, attempts to screen a larger number of people must occur and a light to moderate intensity exercise intervention, rather than a vigorous intensity intervention, should be considered.

Retention

Investigators strive for the highest retention rate possible, in order to acquire enough data to determine whether in fact an effect was seen. In the current study, it appears that retention rate was affected by the "transience" of this particular population. The two participants who completed all assessment visits (baseline and follow-up) resided continuously at the Samaritan Inn homeless shelter, and transportation was provided by the study to the CRC. All three drop-outs were related to the fact that each

participant ceased residing at Samaritan Inn homeless shelter at some point after study enrollment. It is very common for members of this population to transition in and out of shelters. It is known that at least two of the drop-outs did not have their own transportation. Although there may be public transportation available for participants not living at the shelter to have attended the exercise intervention sessions, the transportation issue may also be tied to the previously-mentioned issue of financial incentives. Financial reimbursement was not offered to participants, not living at the shelter, who required transportation to exercise intervention sessions.

It should be noted that Burling et al. (1992)[70] was the only study to use exercise for substance abuse treatment in homeless participants. That study had a much higher rate of retention (67.60%) for exercisers than the current study. However, all participants in that study were at an inpatient residential treatment center for homelessness and substance abuse, whereas participants in the current study were not in a treatment program.

Acceptability of Treatment

A review of the acceptability of treatment of a particular intervention involves determining whether an intervention is suitable and attractive to the targeted individual recipients[89]. If it is found that acceptability is low, investigators can determine future amendments needed in order to increase participant satisfaction.

Acceptability of treatment, as measured by exercise intervention session attendance, was extremely low, with an attendance rate of 29.41% and a mean session attendance of five out of a possible 17 sessions. However, these numbers are deceiving because the calculations include the three drop-outs; one attended no sessions, one

attended one session, and a third attended four sessions. For one subject the attendance rate was 94% (16 of 17 sessions).

A questionnaire was also used at the nine-week follow-up to assess Acceptability. On a scale of 1 to 10, with 1 being Poor and 10 being Excellent, the mean rating of the study overall was a 9, indicating very good acceptability of treatment. The lowest mean score of 5.5 was for "Location." One participant had listed "Location" as what he liked least about the study, indicating that he would prefer to go to the YMCA or somewhere else that wouldn't be watched by others. However, in light of the previously mentioned transportation issues, moving the exercise intervention off-site from the homeless shelter would likely worsen the retention issues unless transportation was provided to the off-site location. Also, moving the exercise intervention off-site would negate the study's attempt to integrate exercise as a treatment for cocaine use/abuse into a homeless shelter's existing programs.

Although "Intensity of Exercise" received a mean score of 9.5 on the exit interview survey, a slight change to the exercise intervention should be considered. The study team expected to attract participants in the age range of 20 to 30 years old, but in fact all participants were 50 years of age or greater and none exercised regularly. Since the Les Mills Body Attack and Body Combat programs utilize vigorous intensity exercise, to increase acceptability of treatment it is suggested that Les Mills' Smart Start option, which reduces exercise time to approximately 30 minutes, be utilized for the initial exercise intervention sessions. This would allow previously non-exercising participants to adjust to the vigorous intensity exercise while maintaining standardization of program and potentially increase the acceptability in a larger sample.

Another method of increasing acceptability of treatment would be to alter the payment of incentives. In the current study, payment of incentives was tied to completion of assessments only, with incentives distributed at the first, three-week, six-week, and final nine-week assessments. No incentives were distributed at each exercise intervention session for attendance. In contrast, Brown et al. (2010) provided an incentive of $5.00 for attending each exercise session[67]. Although overall attendance rate was not provided in the report, the lowest attendance rate at any session was 50%[67]. Tying incentive compensation to exercise session attendance as well as completion of assessments, and offering immediate reward for attendance, may increase acceptability of treatment and increase session attendance.

Limited Efficacy Testing

It was not expected that change would be seen in potential outcome measures since this was a feasibility study. The negative urine drug screen results at both initial and six-week assessments indicate no change in this behavior during the study. However, a urine drug screen (UDS) simply indicates positive or negative and if positive does not indicate level of cocaine usage. Utilizing the Timeline Follow Back (TLFB) questionnaire adds refinement to the urine drug screens in that if a participant reports substance use on the TLFB, he is also asked to indicate the amount. Therefore the TLFB can provide a measure of usage level so that investigators may observe any change from beginning to the end of an intervention. The combination of the UDS and TLFB measures allows the most accurate observance of any changes in cocaine usage.

The decrease in 6MW distance for one participant (#7) was not surprising since he only participated in four of seventeen exercise sessions. The other participant (#5)

participated in 15 out of 17 exercise intervention sessions, (exercising for an average of 58.33 minutes out of 60 per session) which made his decrease in his 6MW distance unexpected. However, the high intensity Les Mills Body Combat and Body Attack classes done in the intervention may not translate into increased performance when testing is done with a different modality such as moderate intensity walking.

The weight changes of both individuals were minor enough to indicate no change in this outcome. This was not an unexpected result since diet was not restricted and the participants ate the food served at the shelter, without any control over the contents of the meals. Moreover, six weeks is a very short time frame to expect weight loss.

Strengths and Weaknesses

Strengths of this study included utilization of a standardized exercise regimen that is available worldwide, which allows for replication and comparison. Also, all exercise sessions occurred in the presence of at least one study team member so that exercise adherence, as indicated by minutes exercised, was directly observed. Further, reasons for subjects' declining to participate were recorded, which could assist in amending the design of future studies to increase recruitment. Use of a graded exercise "stress" test as a screening tool ensured safety of participants and increased probability of adherence by ensuring study enrollment only of those for whom a prescription of vigorous intensity exercise was appropriate. Consequently, there were no medical issues during the exercise sessions. Use of a community-based intervention conducted at the Samaritan Inn shelter allowed for evaluation of the possibility of integrating exercise as treatment for cocaine abuse into current services provided by a homeless shelter. Utilizing a conceptual model

to guide the examination of feasibility allowed specific measures to be chosen that would best reflect whether various aspects of the study were in fact feasible.

This study is not without its limitations, some which have been previously discussed. This was a feasibility study with a very small sample size so its power to detect statistically significant effects on cocaine use was limited. Another limitation is that all participants were male, so the effects of gender could not be evaluated. Lack of a control group precluded evaluation of the effects of an exercise intervention.

Future Directions

Research focused on obtaining a better understanding of this particular population would be informative in improving recruitment for future exercise interventions utilizing substance-abusing members of the homeless population within the confines of existing services. The recruiting challenges experienced also point to the potential need for a multisite trial to increase the sample size. Conducting interventions with women and a mix of men and women utilizing similar methods would provide insight into how the different sexes would respond, including whether homeless women might be a less transient population.

In summary, the results of this study indicate that the current study design is not feasible and that alterations would need to be made in order to proceed to a pilot study that would investigate the effects of an exercise intervention on cocaine usage in homeless men. However, this feasibility study did produce valuable knowledge that would assist in creating better methods for investigating this topic. Further, despite the size and limitations, this feasibility study will add to the body of knowledge about the potential use of exercise as a treatment for substance abuse.

REFERENCES

1. Brown, J., & West, R. (2013). *Addiction press: Theory of addiction* (2) Wiley.

2. American Psychiatric Association (2013). *Diagnostic and statistical manual of mental disorders: DSM-5* (5th Ed.). Washington, DC: American Psychiatric Association.

3. American Psychiatric Association. What is addiction? (2017). Retrieved June 1, 2017 from https://www.psychiatry.org/patients-families/addiction/what-is-addiction

4. National Institute of Drug Abuse (2016). The science of drug abuse and addiction: the basics. Retrieved May 30, 2017 from htttps://www.drugabuse.gov/publications/media-guide/science-drug-abuse-addiction-basics.

5. Substance Abuse and Mental Health Services Administration. *Key substance use and mental health indicators in the United States: Results from the 2015 National Survey on Drug Use and health.* Substance Abuse and Mental Health Services Administration, U.S. Dept. of Health and Human Services, Rockville, MD, 2016.

6. Fischer, B., Cruz, M.S., Bastos, F.I., Tyndall, M. (2013). Crack across the Americas-a massive problem in continued search of viable answers: exemplary views from the north (Canada) and the south (Brazil). *Int J Drug Policy* 24:631-633.

7. Fischer, B., Blanken, P., Da Silveira, D., Gallassi, A., Goldner, E.M., Rehm, J., Tyndall, M., Wood, E. (2015). Effectiveness of secondary prevention and treatment interventions for crack-cocaine abuse: a comprehensive narrative overview of English-language studies. *Int J Drug Policy* 26:352-363.

8. U.S. Food & Drug Administration. FDA 101: smoking cessation products (2016). Retrieved May 11, 2017 from https://www.fda.gov/ForConsumers/ConsumerUpdates/ucm198176.htm

9. National Institute on Drug Abuse (2012). Principles of Drug Addiction Treatment: A Research-Based Guide (Third edition); Alcohol addiction. Retrieved May 11, 2017 from https://drugabuse.gov/publications/principles-drug-addiction-treatment-research-guide-third-edition/evidence-based approaches-to-drug-addiction-treatment/pharmacotherapi-1.

10. Substance Abuse and Mental Health Services Administration. Medication and counseling treatment (2015). Retrieved May 10, 2017 from https://www.samhsa.gov/medication-assisted-treatment/treatment

11. Substance Abuse and Mental Health Services Administration, Principles of Adolescent Substance Use Disorder Treatment: A Research-Based Guide (2014). Addiction Medications. Retrieved May 12, 2017 from https://www.drugabuse/gov/publications/principles-adolescent-substance-use-disorder-treatment-research-based-guide/evidence-based-approaches-to-treating-adolescent-substance-use-disorders/addiction.

12. Johnson, B.A., Ait-Daoud, Wang, X., Penberthy, J.K., Javors, M.A., Seneviratne, C., Liu, L. (2013). Topiramate for the treatment of cocaine addiction. *JAMA Psychiatry*, 70(12): 1338-1346.

13. National Institute on Drug Abuse (2016). How is cocaine addiction treated? Retrieved May 12, 2017 from https://www.drugabuse.gov/publications/research- reports/cocaine/what-treatments-are-effective-cocaine-abusers.

14. Kampman, K.M. (2005). New medications for the treatment of cocaine dependence. *Psychiatry*, 2(12):44.

15. Martell, B.A., Mitchell, E., Poling, J., Gonsai, K., Kosten, T.R. (2005). Vaccine pharmacotherapy for the treatment of cocaine dependence. *Biological Psychiatry* 58(2): 158-164.

16. National Institute on Drug Abuse (2012). Principles of Drug Addiction Treatment: A Research-Based Guide (Third edition). Cognitive behavioral therapy. Retrieved May 13, 2017 from https://www.drugabuse.gov/publications/principles-drug-addiction-treatment-research-based-guide-third-edition/evidence-based-approaches-to-drug-addiction-treatment/behavioral.

17. National Institute on Drug Abuse (2012). Principles of Drug Addiction Treatment: A Research-Based Guide (Third edition). Cognitive behavioral therapy. Retrieved May 13, 2017 from https://www.drugabuse.gov/publications/principles-drug-addiction-treatment-research-based-guide-third-edition/evidence-based-approaches-to-drug-addiction-treatment/behavioral-0.

18. National Institute on Drug Abuse (2012). Principles of Drug Addiction Treatment: A Research-Based Guide (Third edition). Cognitive behavioral therapy. Retrieved May 13, 2017 from https://www.drugabuse.gov/publications/principles-addiction-treatment-research-based-guide-third-edition/evidence-based-approaches-to-drug-addiction-treatment/behavioral-2.

19. National Institute on Drug Abuse (2015). What are therapeutic communities? Retrieved May 13, 2017 from https://www.drugabuse.gov/publications/research-reports/therapeutic-communities/what-are-therapeutic-communities.

20. American Addiction Centers. What to know about 12-Step rehabs. Retrieved May 14, 2017 from americanaddictioncenters.org/rehab-guide/12-step/

21. National Institute on Drug Abuse (2012). Principles of Drug Addiction Treatment: A Research-Based Guide (Third edition). Cognitive behavioral therapy. Retrieved May 13, 2017 from https://www.drugabuse.gov/publications/principles-drug-addiction-treatment-research-based-guide-third-edition/evidence-based-approaches-to-drug-addiction-treatment/behavioral-4.

22. Khanna, S. and Greeson, J.M. (2013). A narrative review of yoga and mindfulness as complementary therapies for addiction. *Complement Ther Med,* 21(3): 244-252.

23. Drake, M.E. (2014). Natural treatments for alcoholism & addiction. *Nutraceuticals World* 7/29/14. Retrieved 5/16/17 from www.nutraceuticalsworld.com/contents/view_experts-opinion/2014-07-29/natural-treatments-for-alcoholism-addiction/.

24. The Addiction Recovery Guide; Nutrition. Retrieved 5/16/17 from www.addictionrecoveryguide.org/holistic/nutrition

25. Kim, Y., Schiff, E., Waalen, J., Hovell, M. (2006). Efficacy of acupuncture for treating cocaine addiction. *Journal of Addictive Diseases,* 24(4): 115-132.

26. Li, M., Chen, K., Mo, Z. (2002). Use of Qigong therapy in the detoxification of heroin addicts. *Alternative Therapies in Health and Medicine; Aliso Viejo*, 8(1): 50-54, 56-59.

27. Daniloff, C. (2017). The runner's high. *Runner's World,* April 2017: 68-75.

28. Smith, M.A. and Lynch, W.J. (2012). Exercise as a potential treatment for drug abuse: evidence from preclinical studies. *Frontiers in Psychiatry*, 2(82): 1-10.

29. Smith, M.A. and Pitts, E.G., (2011). Access to a running wheel inhibits the acquisition of cocaine self-administration. *Pharmacol Biochem Behav*, 100:237-243.

30. Cosgrove, K.P., Hunter, R.G., Carroll, M.E. (2002). Wheel-running attenuates intravenous cocaine self-administration in rats: sex differences. *Pharmacol Biochem Behav* 73:663-671.

31. Smith, M.A., Schmidt, K.T., Iordanou, J.C., Mustroph, M.L. (2008). Aerobic exercise decreases the positive-reinforcing effects of cocaine. *Drug Alcohol Depend* 98: 129-135.

32. Gawin, F.H. (1991). Cocaine addiction: psychology and neurophysiology. *Science* 251:1580-1586.

33. Ahmed, S.H. and Koob, G.F. (1998). Transition from moderate to excessive drug intake: change in hedonic set point. *Science* 282:298-300.

34. Smith, M.A., Walker, K.L., Cole, K.T., Lang, K.C. (2011). The effects of aerobic exercise on cocaine self-administration in male and female rats. *Psychopharmacology,* 218: 357-369.

35. Smith, M.A., Pennock, M.M, Walker, K.L., Lang, K.C. (2012). Access to a running wheel decreases cocaine-primed and cue-induced reinstatement in male and female rats. *Drug and Alcohol Dependence,* 121(1-2): 54-61.

36. Zlebnik, N.E., and Carroll, M.E. (2015). Prevention of the incubation of cocaine seeking by aerobic exercise in female rats. *Psychopharmacology,* 232(19): 3507-3513.

37. Beiter, R.M., Peterson, A.B., Abel, J., Lynch, W.J. (2016). Exercise during early, but not late abstinence attenuates subsequent relapse vulnerability in a rat model. *Transl Psychiatry,* 6(4): e792.

38. Smith, M.A., Fronk, G.E., Zhang, H., Magee, C.P., Robinson, A.M. (2016). Acute bouts of wheel running decrease cocaine self-administration: Influence of exercise output. *Pharmacology Biochemistry and Behavior,* 150-151:94-99.

39. Strickland, J.C., Abel, J.M., Lacy, R.T., Beckmann, J.S., Witte, M.A., Lynch, W.J., Smith, M.A. (2016). The effects of resistance exercise on cocaine self-administration, muscle hyper-trophy and BDNF expression in the nucleus accumbens. *Drug and Alcohol Dependence,* 163: 186-194.

40. Zschucke, E., Heinz, A., Strohle, A. (2012). Exercise and physical activity in the therapy of substance use disorders. *The Sci World J,* 2012: 901741, 1-19.

41. Kinnunen, T., Leeman, R.F., Korhonen, T. (2008). Exercise as an adjunct to nicotine gum in treating tobacco dependence among women. *Nicotine and Tobacco Research,* 10(4): 689-703.

42. Prapavessis, H., Cameron, L., Baldi, J.C. (2007). The effects of exercise and nicotine replacement therapy on smoking rates in women. *Addictive Behaviors,* 32(7): 1416-1432.

43. Marcus, B.H., Lewis, B.A., Hogan, J. (2005). The efficacy of moderate intensity exercise as an aid for smoking cessation in women: a randomized controlled trial. *Nicotine and Tobacco Research,* 7(6): 871-880.

44. Vickers, K.S., Patten, C.A., Lewis, B.A. (2009). Feasibility of an exercise counseling intervention for depressed women smokers. *Nicotine and Tobacco Research,* 11(8): 985-995.

45. Russell, P.O., Epstein, L.H., Johnston, J.J., Block, D.R., Blair, E. (1988). The effects of physical activity as maintenance for smoking cessation. *Addictive Behaviors,* 13(2): 215-218.

46. Ussher, M., West, R., McEwen, A., Taylor, A., Steptoe, A. (2003). Efficacy of exercise counselling as an aid for smoking cessation: a randomized controlled trial. *Addiction,* 98(4): 523-532.

47. Williams, D.M., Whiteley, J.A., Dunsiger, S. (2010). Moderate intensity exercise as an adjunct to standard smoking cessation treatment for women: a pilot study. *Psychology of Addictive Behaviors,* 24(2): 349-354.

48. Chaney, S.E. and Sheriff, S. (2008). Weight gain among women during smoking cessation: testing the effects of a multifaceted program. *AAOHN Journal,* 56(3): 99-105.

49. Bock, B.C., Marcus, B.H., King, T.K., Borelli, B., Roberts, M.R. (1999). Exercise effects on withdrawal and mood among women attempting smoking cessation. *Addictive Behaviors,* 24(3): 399-410.

50. Marcus, B.H., Albrecht, A.E., King, T.K. (1999). The efficacy of exercise as an aid for smoking cessation in women: a randomized controlled trial. *Archives of Internal Medicine,* 159(11): 1223-1234.

51. Marcus, B.H., Albrecht, A.E., Niaura, R.S. (1995). Exercise enhances the maintenance of smoking cessation in women. *Addictive Behaviors,* 20(1): 87-92.

52. Hill, R.D., Rigdon, M., Johnson, S. (1993). Behavioral smoking cessation treatment for older chronic smokers. *Behavior Therapy,* 24(2):321-329.

53. Marcus, B.H., Albrecht, A.E., Niaura, R.S., Abrams, D.B., Thompson, P.D. (1991). Usefulness of physical exercise for maintaining smoking cessation in women. *American Journal of Cardiology,* 68(4): 406-407.

54. Hill, J.S. (1985). Effect of a program of aerobic exercise on the smoking behaviour on a group of adult volunteers. *Canadian Journal of Public Health,* 76(3): 183-186.

55. Martin, J.E., Calfas, K.J., Patten, C.A., (1997). Prospective evaluation of three smoking interventions in 205 recovering alcoholics: one-year results of project SCRAP-tobacco. *Journal of Consulting and Clinical Psychology,* 65(1): 190-194.

56. Taylor, C.B., Houston-Miller, N., Haskell, W.L., Debusk, R.F. (1988). Smoking cessation after acute myocardial infarction: the effects of exercise training. *Addictive Behaviors,* 13(4): 331-335.

57. Brown, R.A., Abrantes, A.M., Read, J.P. (2009). Aerobic exercise for alcohol recovery: rationale, program description, and preliminary findings. *Behavior Modification,* 33(2): 220-249.

58. Donaghy, M.E. (1977). The investigation of exercise as an adjunct to the treatment and rehabilitation of the problem drinker. *University of Glasgow,* Glasgow, UK.

59. Sinyor, D., Brown, T., Rostant, L., Seraganian, P. (1982). The role of a physical fitness program in the treatment of alcoholism. *Journal of Studies on Alcohol,* 43(3): 380-386.

60. Murphy, T.J., Pagano, R.R., Marlatt, G.A. (1986). Lifestyle modification with heavy alcohol drinkers: effects of aerobic exercise and meditation. *Addictive Behaviors,* 11(2): 175-186.

61. Ermalinski, R., Hanson, P.G., Lubin, B., Thornby, J.I., Nahormek, P.A., (1997). Impact of a body-mind treatment component on alcoholic inpatients. *Journal of Psychosocial Nursing and Mental Health Services,* 35(7): 39-45.

62. Palmer, J., Vacc, N., Epstein, J. (1988). Adult inpatient alcoholics: physical exercise as a treatment intervention. *Journal of Studies on Alcohol,* 49(5): 418-421.

63. Weber, A. (1984). Running as treatment for hospitalized alcoholics. *Suchtgefahren,* 30(3): 160-167.

64. Frankel, A., Murphy, J. (1974). Physical fitness and personality in alcoholism. Canonical analysis of measures before and after treatment. *Quarterly Journal of Studies on Alcohol,* 35(4A): 1272-1278.

65. Gary, V., Guthrie, D. (1972). The effect of jogging on physical fitness and self-concept in hospitalized alcoholics. *Quarterly Journal of Studies on Alcohol,* 33(4): 1073-1078.

66. Buchowski, M.S., Charboneau, E., Park, S., Dietrich, M.S., Cowan, R.L., Martin, P.R. (2011). Aerobic exercise training reduces cannabis craving and use in non-treatment seeking cannabis-dependent adults. *PLoS One,* 6(3): e17465.

67. Brown, R.A., Abrantes, A.M., Marcus, B.H., Jakicic, J., Strong, D.R., Oakley, J.R., Ramsey, S.E., Kahler, C.W., Stuart, G.L., Dubreuil, M.E., Gordon, A.A. (2010). A pilot study of aerobic exercise as an adjunctive treatment for drug dependence. *Mental Health and Physical Activity,* 3(1): 27-34.

68. Roessler, K.K. (2010). Exercise treatment for drug abuse- a Danish pilot study. *Scandinavian Journal of Public Health,* 38(6): 664-669.

69. Collingwood, T.R., Reynolds, R., Kohl, H.W., Smith, W., Sloan, S. (1991). Physical fitness effects on substance abuse risk factors and use patterns. *J Drug Education,* (2191): 73-84.

70. Burling, T.A., Seidner, A.L., Robbins-Sisco, D., Krinsky, A., Hanser, S.B. (1992). Batter up! Relapse prevention for homeless veteran substance abusers via softball team participation. *Journal of Substance Abuse,* 4: 407-413.

71. Rawson, R.A., Chudzynski, J., Mooney, L., Gonzales, R., Ang, A., Dickerson, D., Penate, J., Salem, B.A., Dolezal, B., Cooper, C.B. (2015). Impact of an exercise intervention on methamphetamine use outcomes post-residential treatment care. *Drug Alcohol Depend,* 156: 21-28.

72. De La Garza II, R., Yoon, J.H., Thompson-Lake, D.G.Y., Haile, C.N., Eisenhofer, J.D., Newton, T.F., Mahoney III, J.J. (2016). Treadmill exercise improves fitness and reduces craving and use of cocaine in individuals with concurrent cocaine and tobacco-use disorder. *Psychiatric Research,* 245: 133-140.

73. Nader, M.A., Wolverton, W.L. (1991). Effects of increasing the magnitude of an alternative reinforcer on drug choice in a discrete-trials choice procedure. *Psychopharmacology,* 105: 169-174.

74. Czotny, P.W., Nader, M.A. (2012). Individual differences in the effects of environmental stimuli on cocaine choice in socially housed male cynomolgus monkeys. *Psychopharmacology,* 224:69-79.

75. Linke, S.E. and Ussher, M. (2015). Exercise-based treatments for substance abuse disorders: evidence, theory, and practicality. *Am J Drug Alcohol Abuse,* 41(1): 7-15.

76. National Coalition for the Homeless, July 2009. Substance abuse and homelessness.

77. The U.S. Department of Housing and Urban Development, Office of Community Planning and Development, November 2016. The 2016 Annual Homeless Assessment Report (AHAR) to Congress.

78. Substance Abuse and Mental Health Administration, 6/29/17. Homelessness and housing. Retrieved July 14, 2017 from https://www.samhsa.gov/homelessness-housing.

79. National Institute on Drug Abuse, January 2013. Overdose deaths among homeless persons. Retrieved July 14, 2017 from https://www.drugabuse.gov/about-nida/directors- page/messages-director/2013/01/overdose-deaths-among-homeless-persons.

80. O'Toole, T.P., Conde-Martel, A., Gibbon, J.L., Hanusa, B.H., Freyder, P.J., Fine, M.J. (2004). Substance-abusing urban homeless in the late 1990s: how do they differ from non-substance-abusing homeless persons? *J Urban Health,* 81:606-617.

81. Grinman, M.N., Chiu, S., Redelmeier, D.A., Levinson, W., Kiss, A., Tolomiczenko, G., Cowan, L., Hwang, S.W., (2010). Drug problems among homeless individuals in Toronto, Canada: prevalence, drugs of choice, and relation to health status. *BMC Public Health,* 10:94.

82. Rhoades, H., Wenzel, S.L., Golinelli, D., Tucker, J.S., Kennedy, D.P., Green, H.D., Zhou A. (2011). The social context of homeless men's substance use. *Drug Alcohol Depend,* 118: 320-325.

83. Maremmani, A.G., Bacciardi, S., Gehring, N.D., Cambioli, L., Schultz, C., Jang, K., Krausz, M. (2017). Substance abuse among homeless individuals with schizophrenia and bipolar disorder. *Journal of Nervous and Mental Disease,* 205(3): 175-177.

84. Robinson, S.M., Sobell, L.C., Sobell, M.B., Leo, G.I. (2014). Reliability of the Timeline Followback for cocaine, cannabis, and cigarette use. *Psychology of Addictive Behaviors,* 29: 154-162.

85. Zimet, G.D., Powell, S.S., Farley, G.K., Werkman, S., Berkoff, K.A. (1990). Psychometric characteristics of the Multidimensional Scale of Perceived Social Support. *J Personal Assess,* 55:610-617.

86. Minnes, W., Singer, L.T., Humphrey-Wall, R., Satayathum, S. (2008). Psychosocial and behavioral factors related to the post-partum placement of infants born to cocaine-using women. *Child Abuse Neglect,* 32: 353-366.

87. Dragic, N.B., Dickov, A.S., Nilolic, E.F., Vuckovi, N.S. (2013). Social functioning and support of addicts on methadone. *Cent Eur J Med,* 8: 455-462.

88. Conrad, K.J., Yagelka, J.R., Matters, M.D., Rich, A.R., Williams, V., Buchanan, M. (2001). Reliability and validity of a modified Colorado Symptom Index in a national homeless sample. *Mental Health Services Research,* 3: 141-153.

89. Bowen, D.J., Kreuter, M., Spring, B., Cofta-Woerpel, L., Linnan, L., Weiner, D., Bakken, S., Kapalan, C.P., Squiers, L., Fabrizio, C., Fernandez, M. (2009). How we design feasibility studies. *Am J Prev Med,* 36(5): 452-457.

90. Fischer, B., Blanken, P., Da Silveira, D., Gallassi, A., Goldner, E.M., Rehm, J., Tyndall, M., Wood, E. (2015). Effectiveness of secondary prevention and treatment interventions for crack-cocaine abuse: A comprehensive narrative of overview of English-language studies. *International Journal of Drug Policy,* 26:352-363

91. McLellan, A.T., Luborsky, L., O'Brien, C.P., Woody, G.E. (1980). An improved diagnostic instrument for substance abuse patients: The Addiction Severity Index. *J Nerv Mental Dis,* 168:26-33.

92. Volkow, N., Koob,. G & McLellan, A. (2016). Neurobiologic advances from the brain disease model of addiction. *New England Journal of Medicine,* 374(4): 363-371.

93. Janal, M.N., Colt, E.W., Clark, W.C. and Glusman, M. (1984). Pain sensitivity, mood and plasma endocrine levels in man following long-distance running: effects of naloxone. *Pain* 19: 13-25.

94. Meeusen, R., and De Meirleir, K. (1995). Exercise and brain neurotransmission. *Sports Med.* 20, 160-188.

95. Robertson, C., Ishibashi, K., Chudzynski, J., Mooney, L., Rawson, R., Dolenzal, B. …London, E. (2016). Effect of exercise training on striatal dopamine D2/D3 receptors in methamphetamine users during behavioral treatment. *Neuropsychopharmacology,* 41(6): 1629-1636.

96. Trivedi, M.H., Greer, T.L., Grannemann, B.D., Church, T.S., Somoza, E., Blair, S.N., Szapocznik, J., Stoutenberg, M., Rethorst, C., Warden, D., Ring, K.M., Walker, R., Morris, D.W., Kosinski, A., Kyle, T., Marcus, B., Crowell, B., Oden, N., Nunes, E. (2011). Stimulant Reduction Intervention using Dosed Exercise (STRIDE)- CTN 0037: Study protocol for a randomized controlled trial. *Trials,* 12: 206.

97. Trivedi, M.H., Greer, T.L., Potter, J.S., Grannemann, B.D., Nunes, E.V., Rethorst, C., Warden, D., Ring, K.M., Somoza, E. (2011). Determining the primary endpoint for a stimulant abuse trial: lessons learned from STRIDE (CTN 0037). *Am J Drug Alcohol Abuse,* 2011 September; 37(5): 339-349.

98. Stoutenberg, M., Rethorst, C., Fuzat, G., Greer, T., Blair, S., Church, T., Marcus, B., Trivedi, M. (2012). Stimulant Reduction Intervention using Dosed Exercise (STRIDE)- description of the exercise intervention and behavioral program to ensure Adherence. *Ment Health Phys Act,* 2012 December; 5(2): 175-182

CURRICULUM VITAE

STACY ONDERS TOLLIE

Education:

M.S. in Health & Exercise Science, anticipated December 2017
Wake Forest University, Winston-Salem, NC

Relevant Experience:

Teaching Assistant, *Food Politics & Policy*
Wake Forest University, August 2017- Present
-Assist undergraduate students with writing assignments
-Grade student writing assignments
-Coordinate student projects at community agencies
-Review and edit student presentations

Graduate Assistant, Employee Weight Management Program
Wake Forest University, January 2017- Present
-Assist with fitness/stress testing
-Perform DXA body composition scans on participants
-Assist with weekly group educational sessions
-Review weekly participant food logs
-Record and track participant compliance
-Participate in program staff progress meetings

Graduate Research, Multidisciplinary Exercise Intervention Study
Feasibility of an Exercise Intervention for Homeless Cocaine-Using Men
Wake Forest University, March 2017- May 2017
-Assisted with physical assessments
-Monitored exercise sessions at homeless shelter
-Recorded participants' vital signs, urine drug screen results & compliance
-Participated in study team meetings & debriefings.

Graduate Assistant, Therapeutic Lifestyle Changes (TLC) Program
Wake Forest University, September 2016- Present
-Perform fitness assessments
-Record & track participant exercise/physical activity
-Review weekly participant food logs

Program Staff, Healthy Exercise & Lifestyle Programs (HELPS)
Wake Forest University, August 2016- Present
-Monitor participants' blood pressure and heart rate/rhythm (ECG)
-Lead Silver Sneakers Classic classes
-Lead small group weight training and stretching circles
-Create and maintain participant attendance &exercise logs

	-Track participant attendance
Other Relevant Experience:	Volunteer, Healthy Exercise & Lifestyle Programs (HELPS) Wake Forest University, August 2015- August 2016 Volunteer, Cardiopulmonary Rehabilitation Wake Forest Baptist Health, June 2015- July 2016
Additional Degrees:	J.D. 1993 Albany Law School, Albany, NY B.A. 1988 Bucknell University, Lewisburg, PA
Prior Employment:	Magistrate, State of North Carolina 1996-2016 -presided over civil & criminal hearings -researched & applied law to facts of individual cases -assisted in training new magistrates -wrote portions of office procedure manual -managed courtrooms/court sessions -communicated findings of fact & law to citizen parties
Current Certifications:	Certified Exercise Physiologist, ACSM CPR/AED, American Heart Association CITI certification First Aid for Coaches, Red Cross Level I Running Coach, Road Runners Clubs of America Healthways Silver Sneakers Classic Instructor Bar License, State of NC Bar License, State of NY