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RESEARCH ARTICLE

Opiate Use Disorder and Exercise: A Systematic Review

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ABSTRACT

Background: The opiate epidemic continues to cause hardship to American communities, including in all counties in Ohio, and resulted in 100 000 drug overdoses in 2021. Medications such as buprenorphine have helped people affected by opiate use disorder (OUD) to continue through recovery, although medication assisted therapy (MAT) has shown limited retention rates, calling for complimentary interventions to be implemented. Exercise has potential to reduce cardiovascular risk, lower obesity, and improve mental health. The aim of this study is to systematically review the literature on OUD and exercise as an adjunct to MAT. The authors hypothesize that there is a gap in the knowledge as to whether this modality has been thoroughly researched to aid in OUD recovery.

Methods: A database literature search of PubMed, CINHAL, and PsychInfo returned a total of 458 abstracts. Four sets of exclusion criteria were implemented resulting in a total of 26 articles. After further review, 8 more articles were excluded by the authors.

Results: Eighteen articles including participants with OUD were systematically reviewed. Only 1 article solely focused on participants with OUD and exercise as an adjunct to treatment.

Conclusion: Exercise as an adjunct to treatment for OUD is an area of addiction treatment that warrants further investigation. Incorporating exercise into a recovery program for people with substance use disorders (SUD) specifically has been touted as a promising modality, however, limitations in OUD only studies and lack of control groups make it difficult to draw a conclusion to support our hypothesis.

Keywords: Substance use disorder; Opioids; Exercise; Physical activity; Systematic review

INTRODUCTION

The opiate epidemic continues to cause hardship to American communities and, too often, takes the lives of family members, friends, and neighbors. Due to this rising trend coupled with the COVID-19 pandemic, more than 100 000 Americans died from drug overdoses in 2021, which was the highest rate of overdose deaths on record.[1] Individuals with opiate use disorder (OUD) have difficulty being able to complete everyday tasks, struggle with malnutrition, and often battle with other physical and mental illnesses.

Ohio is considered by some as an epicenter of the opiate epidemic. In 2020, Ohio had more than 500 deaths, which translates into 45.6 deaths per 100 000 people. At the county level, Cuyahoga County, one of the largest Ohio counties, had more than 489 deaths in 2020, equating to 37.8 deaths per 100 000 people. In contrast, Vinton County, the smallest county in Ohio, recorded 12 overdose deaths in 2020, which equates to the highest per capita death rate in Ohio of 80 deaths per 100 000 people.[2]

To combat the opioid epidemic at the national, state, and local level, OUD rehabilitation is warranted. Opioid use disorder rehabilitation can be viewed as a multifactorial long-term process that

involves numerous modalities to reduce the likelihood of relapse. Of these modalities, medication assisted treatment (MAT) is among the most studied interventions for treatment of OUD. Clinical trials have demonstrated that long-term opioid agonist therapy with methadone or buprenorphine has great efficacy for OUD treatment.[3] Although MAT is commonly used to reduce relapse, studies have shown that the retention rate is 50% or less at 6 months after initiating treatment.[4] This suggests the need for complementary or adjunctive interventions.

Research has suggested that drug-dependent patients commonly show deterioration in their physical health, either due to direct drug consumption, loss of healthy habits, or these things in combination.[5] Of particular concern are negative effects on the cardiovascular system in individuals who have achieved recovery, as studies have shown participants in recovery have higher rates of overweight and obesity.[6] It has also been observed that participants with substance use disorders (SUD) develop dysfunctional eating patterns, also contributing to excessive weight gain and increasing risk for cardiovascular disease.[7]

Between 2008 and 2018, a total of 67 137 individuals with OUD were diagnosed with heart failure out of the 11 692 995 heart failure admissions identified in the general population.[8] A study on OUD and myocardial infarction (MI) showed that the prevalence of individuals with OUD experiencing MI doubled from 2006 to 2015, increasing from 163 to 326 cases per 100 000.[9] In terms of general cardiovascular mortality, research with participants aged 40 to 75 years found long-term opiate use was associated with increased cardiovascular mortality, independent of the traditional risk factors.[10] The American Heart Association (AHA) presidential advisory has concluded that there is a lack of knowledge provided in the existing research with respect to opiates and cardiovascular disease and has called for nonopioid therapies, including multifaceted and community-based interventions to treat OUD, further emphasizing the need for research on other modalities outside of MAT.[11]

Prior researchers have found brief bouts of exercise to be effective for short term relief from alcohol cravings.[12] Additionally, literature on participants in methamphetamine recovery concluded aerobic exercise in combination with a strength training program increased dopamine levels in the subjects, which potentially improves the mental health of participants and reduces their drug cravings.[13] Although these research results suggest exercise has potential to be effective as an adjunct treatment for SUDs, there is insufficient evidence to suggest that exercise is a benefit for people with OUD specifically.

Our interest is specific to the role of exercise as adjunctive treatment for OUD. Opioid use disorder differs from other SUDs in terms of its heightened morbidity and mortality. Although there is abundant evidence that current pharmacological interventions are safe and effective, rates of opiate overdose have continued to increase, stressing the need for additional evidence-based research to augment current OUD therapy. Hence, nonpharmacological modalities warrant further investigation. To this end, it is of the utmost importance to systematically analyze the current literature on the topic of exercise in the context of OUD.

METHODS

A literature search was conducted with the assistance of a research librarian on exercise in the context of SUD. Databases searched included PubMed, CINHAL, and PsychInfo which returned a total of 458 abstracts. The first set of exclusion criteria removed articles unrelated to exercise and SUD. The second set of exclusion criteria removed systematic reviews and meta-analysis, animal studies, studies not in English, studies with the protocol only, duplicate studies from the 3 databases, professional trainings articles, outdated studies (1995 or earlier), studies involving adolescents, and studies that were inaccessible either by the librarian or the study team. The third set of exclusion criteria focused on yoga being the sole exercise, as mind body exercise is a separate topic for investigation. A subtotal of 163 articles remained. The last exclusion set criteria focused on the types of substances being used by participants. The studies had a mix of various substances being used by their participants: alcohol, methamphetamine, cannabis, and tobacco. With all the exclusion criteria, 26 articles remained to systematically review.

These 26 articles were sorted by either “mixed substances with opiates'' or “opiate only.” The authors reviewed the papers. Author 1 was the primary reviewer and reviewed all 26 articles. After review by author 1, authors 2 and 3 split the articles for second review. Author 2 reviewed 14 articles while author 3 reviewed 12 articles. The following criteria were used to systematically review all 26 articles: (1) author, journal, title, (2) alcohol, tobacco, cocaine, amphetamine, cannabis, opiates, other substance, (3) review paper (yes/no), retrospective (yes/no), (4) (cardio, strength, both) exercise type, exercise duration (5) control type, number of control, number of subjects, number of men, number of women, (6) recovery outcomes, included recovery endpoints (yes/no), (7) study limitations, (8) comments. The results were then compared to reviewer 1 comments. Discrepancies were resolved by consensus of the 3 authors. After review, 6 papers were excluded due to systematic reviews and/or meta-analysis in the study design. Two other additional articles were excluded due to discrepancies within the study designs, leaving 18 articles (Figure 1) for full review.[14-31]

RESULTS

Results of the exclusion criteria are as follows: 125 unrelated to SUD in clinical practice, 54 nonrelated exercise/sport modality, 6 duplicates, 26 outdated (earlier than 1995), 10 adolescents, 15 unrelated nonhuman trials, 6 professional trainings/review, 7 inaccessible, 6 non-English, 3 study protocol only, 38 yoga exclusion, 47 methamphetamine only, 63 alcohol only, 22 tobacco only, 4 other substances, and 6 systematic reviews/meta-analysis. Two additional articles were removed after author review (Figure 1).

Those 18 articles were systematically reviewed (Appendix) and all included individuals with OUD. Nine articles were published in the United States, 3 published in China, and 1 published each in Taiwan, Australia, India, Spain, Norway, and Ireland. Of the 18 articles, 17 of the studies focused on participants with various SUDs, 9 included alcohol use disorder, 2 included tobacco use disorder, 13 included cocaine use disorder, 7 included amphetamines, and 9 included cannabis. Other substances were also included in these research designs, including ecstasy, sedatives, inhalants, tranquilizers, and benzodiazepines. Only 2 articles exclusively focused on participants with OUD.

Of the 18 articles, 6 included cardiovascular exercise only, 1 included strength exercise, and 10 included both cardiovascular

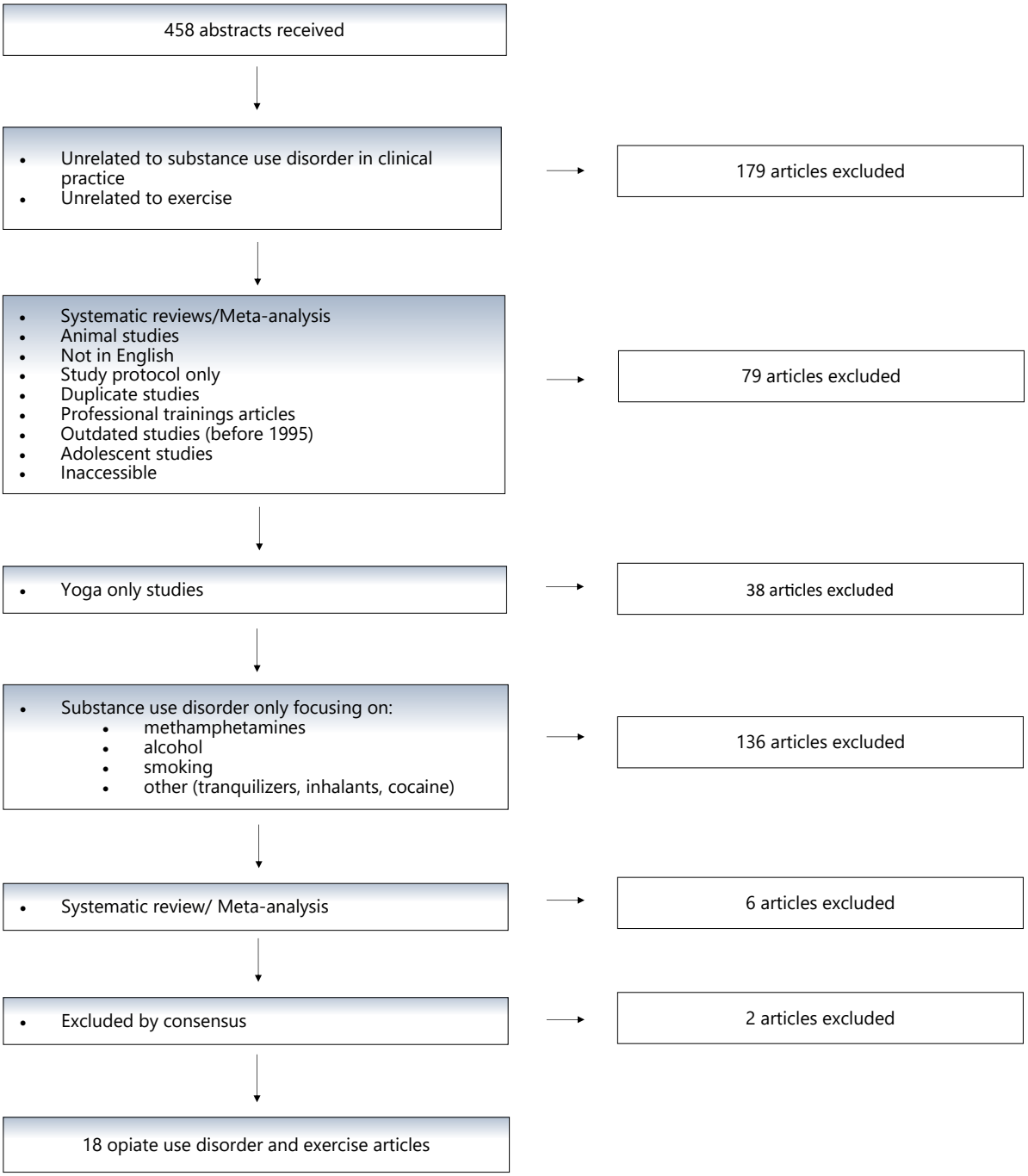

Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) Methodology

exercise and strength exercise. Nine of the studies were retrospective in nature. Of the studies that were prospective, exercise duration ranged from 5 days to 14 weeks, with 12 weeks being the mean duration for protocol design. The studies that included control groups varied and included OUD versus no OUD, exercise versus no exercise, and stimulants versus depressants. Eleven articles did not include either a control group for an intervention or a comparison group for a retrospective or recall study. In all, there were 2326 participants; 1154 male and 1172 female. Fourteen of the studies included recovery endpoints. The full table is shown in the Appendix.

DISCUSSION

Regular physical activity is beneficial for many physical and mental health conditions. The reviewed articles illustrate continuing interest in the role exercise plays in recovery from addiction in general. Our specific interest is in the specific effect exercise has in the recovery for OUD. While studies have been conducted that include OUD patients, most studies in our review were conducted with subjects recovering from various SUDs. Only 2 studies[18,24] solely examined the role of exercise in an OUD recovery group. Cocaine was the most common substance included in the studies, identified in 13 of 18 articles, with alcohol use next most common, identified in 9 of 18 articles. This suggests a lack of research with OUD participants at the focus of the study.

Among reviewed studies there was great variation in the type of exercise, intensity, and duration. Studies ranged in duration from days to months. The lack of consistent exercise durations used by different researchers demonstrates a lack of protocol standardization oriented with respect to exercise and SUD. There was also no standard type of exercise used across these studies. The exercise heterogeneity among the studies regarding type and duration makes it difficult to conclude what mode or modes of physical activity is most beneficial for OUD participants.

The lack of control groups is important to note. Only 7 articles were of an experimental design that had control groups. Without a control or comparison group, it is difficult to know to what extent results are similar to or different from non-substance users, and this weakens credibility of results. Of the studies that had a control group, exercise versus no exercise was the most common, with other types of controls also being utilized. The studies with the controls generally generated more concrete results. As an example, a study with 142 control subjects showed that those who completed an exercise-related activity had significantly longer durations of abstinence compared to participants who did not complete an exercise.[14] Another study with a control population of 42 participants showed that a 12-week yoga intervention did not appear to be significantly more effective than the 12-week physical exercise program.[15] The most supporting study with a control group for OUD and exercise came from Giménez-Meseguer et al, which demonstrated improved fitness, reduced injuries, increased vitality, improved mood, increased self-esteem, and reduced cravings.[16] The variety of findings with the small population of control groups supports the need for experimental studies when researching exercise and OUD.

To evaluate the effectiveness of exercise as an adjunct to treatment for OUD, randomized control trials are needed to accurately assess this potential treatment. The review papers mostly consisted of meta-analysis, focusing on numerous papers. It is important to note that these reviews did not solely focus on opiates, and opiates were only a small subsection of the included studies. It seems that there is a greater focus on studying exercise as an adjunct to treatment for alcohol and methamphetamine use disorders. For example, according to the authors of 1 study, their results were encouraging with respect to exercise as an adjunct for individuals diagnosed with various drug and alcohol dependencies,[23] but this study did not provide explicit evidence to support exercise among opiate dependent individuals specifically.

Of the 18 articles, only 2 studies included participants solely with OUD. Opiate use disorder should be studied independently to ensure that the benefits of exercises are applicable to this specific patient population undergoing MAT. Furthermore, within the mixed substance use studies, participants with OUD made up a small fraction of the total study population. Generally speaking, there is a greater proportion of literature to support exercise for other SUDs such as alcohol, tobacco, and methamphetamine, but little to no evidence to support using exercise as an adjunctive treatment specifically for OUD.

Limitations to this research associated with the reviewed sources include limited ability to draw conclusions due to lack of standardization of design and lack of consistency in participants. Variations in interventions and design were described previously. Additionally, 3 studies only involved men while 1 study included only women participants. Participant eligibility with respect to substances varied with alcohol, tobacco, cocaine, amphetamines, cannabis, and others being included as well as opioids. These variabilities limit our ability to draw conclusions regarding the nature of exercise specifically to OUD treatment.

Other potential limitations include that, despite a persistent search, the authors might have overlooked 1 or more eligible articles. Additionally, our sources only included published articles available in English. Other studies may exist which would strengthen this evidence or offer contradictory findings.

Incorporating exercise into a recovery program for people with addiction in general and opiate addiction specifically has been promoted as a promising modality. Based on the findings from this review, participants in the studies generally derived benefit from physical activity participation with respect to physical and mental health. However, because of the limitations of the literature, including the fact that two-thirds of the studies lacked a control group, it is difficult to draw any conclusions regarding benefits to individuals with OUD. Aside from the benefits that ex-

ercise has for general cardiovascular health, it is unclear from the literature if physical activity improves OUD recovery outcomes.

PUBLIC HEALTH IMPLICATIONS

Exercise as an adjunct to treatment for OUD is an area of addiction treatment that warrants further investigation. Specific future areas of focus include use of standardized exercise protocols of long enough duration to demonstrate benefit. Preferably, studies should be designed to compare different modalities of physical activity. Excess cardiovascular morbidity and mortality in this population should also be a research priority. Furthermore, future studies should focus on exercise in respect to recovery outcomes and endpoints. Finally, there needs to be more investigation in a prospective manner to fill the voids that exist in the current literature on exercise as an adjunct to treatment for OUD.

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Other Information

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APPENDIX Articles Fully Reviewed

First author	Publish date	Country	Substance*	Exercise category	Activity type	Duration of intervention	# men/ women participants	# in control/ comparison	Reported outcomes	Recovery endpoints included
Lee	2004	Taiwan	C,AM,O	Cardio	Hiking	25 days	26/0	17	Decreased BMI, decreased hyperinsulemia	N
Zhu	2020	China	C, AM, O, OT	Strength	Mind-body exercise	12 weeks	100/0	50	Showed better effects on BMI, SBP, pulse, and PACER test	N
Wang	2019	China	C,AM,O,OT	Cardio, strength	General physical activity	N/A (single measure of VO 2 max)	0/465	0	Physical activity negatively correlated with drug craving, positive for internal inhibition	Y
Dai	2020	US	A,C,O,OT	Cardio	Walking/ running	14 weeks	50/59	0	Study evidenced the influence of utilizing exercise as an adjunct treatment on SUD recovery via participants' perceptions and provided implications for SUD treatment services	Y
Alessi	2020	US	C, M,O	Cardio, strength	Aerobic, strength	Varied	91/29	58	Study did not find benefits of exercise on substance use outcomes	Y
Tremain	2017	Australia	A,C,O	Cardio	Moderate intensity physical activity	N/A (30 day recall)	253/133	0	More than 50% of substance use clients reported that they were seriously considering quitting smoking, increasing physical activity levels and consuming more fruit and vegetables, higher levels of exercise reported than general population	Y
Brown	2010	US	A,C,M,O,OT	Cardio	Walking/ running	12 weeks	11/5	0	Significant increases in percent days abstinence of alcohol and drug use at follow-up timepoints and participants who attended at least 75% of the exercise sessions had significantly better substance use outcomes than those who did not	Y
Rutherford	2021	Ireland	A,C,AM,M, O,OT	Cardio, strength	Aerobic, resistance	6 weeks	5/1	0	Clinically important reductions in depression and anxiety symptoms after the intervention; positive qualitative feedback was provided by participants	Y
Cutter	2014	China	C,O	Cardio, strength	Wii Fit videogame	8 weeks	12/17	14	Results showed a significant reduction in self-reported levels of illicit opioid or cocaine use over time	Y
Wang	2021	US	AM,M,O,OT	Cardio, strength	Power bike, walking, strength assessment	5 days	30/0	15	VO2 max of chemically synthesized drug addicts was significantly higher than that of natural plant-derived drug addicts (heroin), heroin was more damaging than other types of drugs to immune/ organ systems	N
Abrantes	2019	US	O	Cardio	General physical activity	12 weeks	26/7	0	Participants reported high levels of satisfaction; tracking showed low adherence and low compliance with fitbit use	Y
Powers	1999	US	A,C,M,O	Cardio, strength	Sports	N/A (non-specific recall)	32/13	0	Sports provides an escape for people using intravenous drugs, reduce stress Participants observed that sports participation and substance use are incompatible behaviors	Y
Caviness	2013	US	T,O	Cardio, strength	General physical activity	7 days	79/108	0	Findings highlight that methadone programs are treating persons who are at very high risk for cardiovascular disease and other chronic health concerns and may benefit from increased physical activity, participants expressed desire for benefits of exercise	Y
Weinstock	2008	US	A,C,O	Cardio, strength	Sports, aerobic exercises	12 weeks	265/304	0	Those who completed an exercise-related activity had significantly longer durations of abstinence compared to participants who did not complete an exercise-related activity	Y
Pieper	2010	US	O	Cardio	Occupational, sports, walking	N/A (5 year recall)	96/0	0	Chronic venous disease was identified in 92.4% of participants and PAD in 18.5%. Advanced chronic venous disease was highly correlated with injecting in the legs. The high occurrences of chronic venous disease and PAD observed in this study were associated with low level of physical activity	Y
Gaihre	2021	India	A,C,AM,M, O,OT	Cardio, strength	Yoga, aerobic, body-weight	12 weeks	26/11	48	The 12-week yoga intervention did not appear to be significantly more effective than the 12-week physical exercise program on psychological well-being in male participants with substance use disorder, although the 12-week physical exercise program had a positive impact on anxiety, depression, and sleep	Y
Gimenez-Meseguer	2015	Spain	A,C,M,O	Cardio, strength	Aerobic, muscular endurance	12 weeks	26/11	22	Improved fitness, reduced injuries and muscle pain, increased vitality, improved mood, increased self esteem, reduced cravings	Y
Muller	2015	Norway	A,C,AM,M, O, OT	Cardio, strength	Group exercise	10 weeks	26/9	0	Increased peer support for fitness, decrease in anxiety, decrease in use (from 63% to 26%)	N
TOTAL:							1154/1172	224		

*A = alcohol, T = tobacco, C = cocaine, AM = amphetamine, M = cannabis, O = opioids, OT = others (MDMA; inhalants, etc.)