Virtual Strategies for the Broad Delivery of High Intensity Exercise in Persons With Spinal Cord Injury: Ongoing Studies and Considerations for Implementation

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Spinal cord injury (SCI) results in a multitude of metabolic co-morbidities that can be managed by exercise. As in the non-injured population, manipulation of exercise intensity likely allows for fruitful optimization of exercise interventions targeting metabolic health in persons with SCI. In this population, interventions employing circuit resistance training (CRT) exhibit significant improvements in outcomes including cardiorespiratory fitness, muscular strength, and blood lipids, and recent exploration of high intensity interval training (HIIT) suggests the potential of this strategy to enhance health and fitness. However, the neurological consequences of SCI result in safety considerations and constrain exercise approaches, resulting in the need for specialized exercise practitioners. Furthermore, transportation challenges, inaccessibility of exercise facilities, and other barriers limit the translation of high intensity "real world" exercise strategies. Delivering exercise via online ("virtual") platforms overcomes certain access barriers while allowing for broad distribution of high intensity exercise despite the limited number of population-specific exercise specialists. In this review, we initially discuss the need for "real world" high intensity exercise strategies in persons with SCI. We then consider the advantages and logistics of using virtual platforms to broadly deliver high intensity exercise in this population. Safety and risk mitigation are considered first followed by identifying strategies and technologies for delivery and monitoring of virtual high intensity exercise. Throughout the review, we discuss approaches from previous and ongoing trials and conclude by giving considerations for future efforts in this area.

Keywords: virtual fitness, home-based exercise, high intensity exercise, paralysis, disability
INTRODUCTION

Spinal cord injury (SCI) is an insult to the nervous systems that leads to a host of co-morbidities. For example, metabolic complications post-injury begin with a rapid and precipitous loss of lean muscle (Grimby et al., 1976; Castro et al., 1999; Gorgey and Dudley, 2007; Moore et al., 2015) and bone mass (Zieik et al., 2019; McMillan et al., 2021c) and increase in fat mass (Groah et al., 2011; Farkas et al., 2019; McCauley et al., 2020; Gater et al., 2021). The profound post-injury changes in body composition occur in parallel with disordered lipid (Breces et al., 1986; Zlotolow et al., 1992; Karlsson et al., 1995; Maki et al., 1995; McGlincey-Berroth et al., 1995; Nash et al., 2005; Emmons et al., 2010; Ellenbroek et al., 2014; La Fountaine et al., 2017, 2018) and glucose metabolism (Palmer et al., 1976; Duckworth et al., 1980, 1983; Karlsson et al., 1995; Aksnes et al., 1996; Bauman et al., 1999; Chilibeck et al., 1999; Jeon et al., 2002; Elder et al., 2004; Batttram et al., 2007; Segal et al., 2007; Wang et al., 2009; Lewis et al., 2010; Gorgey and Gater, 2011; Yarar-Fisher et al., 2013). The coalition of these component risk factors is defined as cardiometabolic disease (CMD), and the Consortium for Spinal Cord Medicine has released Clinical Practice Guidelines for CMD in SCI (Nash et al., 2019). Importantly, these guidelines identify obesity as the most common CMD component risk factor in SCI, and other dyslipidemic CMD risk factors cluster in a manner favoring disordered fat metabolism after SCI (Libin et al., 2013). Mitigation strategies are warranted since this disordered fat metabolism in SCI is both a cause and the effect of the aberrant accumulation of whole-body fat mass, as well as regionally specific infiltration of fat deposits into various tissues such as skeletal muscle (Moore et al., 2015) and bone marrow (McMillan et al., 2021c). In persons without SCI, physical activity is an important management strategy for obesity (Piercy et al., 2018). Furthermore, regular physical activity is important for promoting health in SCI as well (Martin Ginis et al., 2018; Nash et al., 2019), but in this population there are considerations for tailoring exercise interventions to target specific outcomes such as obesity (McMillan et al., 2021b). Developed by experts in nutrition, exercise, rehabilitation, cardiology, endocrinology, and internal medicine, the Consortium’s clinical practice guidelines (Nash et al., 2019) recommend exercise as a primary treatment for the management of CMD in SCI. These guidelines recommend “at least 150 min per week […] satisfied by sessions of 30–60 min performed three to five days per week, or by completing at least three 10-min sessions per day” (Nash et al., 2019). Furthermore, recent systematically developed (Appraisal of Guidelines, for Research, and Evaluation second edition; AGREE II) evidence-based activity guidelines developed by an international team of scientists endorse with moderate to high confidence the beneficial effects of exercise on CMD in persons with SCI (Martin Ginis et al., 2018). or These guidelines recommend “at least 30 min of moderate to vigorous intensity aerobic exercise three times per week” (Martin Ginis et al., 2018). Thus, current SCI CMD exercise guidelines are designed primarily around volume and frequency. However, experts are calling into question the importance of intensity in exercise prescription for persons with SCI (Nightingale et al., 2017a), especially in the context of addressing the metabolic co-morbidities of this condition.

In the general population, exercise intensity is an important parameter to consider for prescribing exercise to target CMD-related health outcomes (Weston et al., 2014; Batacan et al., 2017; Campbell et al., 2019; Taylor et al., 2019), with higher intensity exercise generally showing more favorable outcomes compared to moderate-intensity continuous training (MICT). Despite challenges related to proper implementation, there is a growing body of emerging evidence in SCI showing that higher exercise intensities promote greater physiological and potentially greater clinical benefits (Harnish C. et al., 2017; Nightingale et al., 2017a; Graham et al., 2019; McLeod et al., 2020), though not all results are universal (Solinsky et al., 2020). For example, multiple findings show the feasibility of high-intensity interval training (HIIT) arm cycling in SCI (de Groot et al., 2003; Harnish C. et al., 2017; Harnish C. R. et al., 2017; Nightingale et al., 2017a; Astorino and Thum, 2018b; Astorino, 2019; Graham et al., 2019; McLeod et al., 2020; McMillan et al., 2020; Solinsky et al., 2020), and one study demonstrates that HIIT performed on an arm ergometer allows a reduced time commitment to achieve a fixed calorie target vs. MICT (McMillan et al., 2020). However, all of these data stem from trials performed in laboratory settings in which the experimenter implements the exercise regimen and the only requirement of the patient is to follow his/her instructions. Moreover, one challenge of employing HIIT in a “real-world” setting is the staggering number of permutations of parameters including work and recovery durations and intensities. Real-time manipulation of these variables, especially while also exercising, can require substantial cognitive processing and experience with this modality that may be inappropriate for a novice exerciser to perform on their own. Other forms of intermittent exercise such as circuit resistance training (CRT) combining brief bouts of arm ergometry with dynamic whole-body resistance training have been employed in this population and show substantial metabolic effects (Jacobs et al., 2001, 2002; Nash et al., 2001, 2002, 2007; Kressler et al., 2014; McMillan et al., 2021a). Accordingly, a recent systematic review concluded that CRT elicits more favorable changes in the clinical lipid profile compared to aerobic exercise alone (Farrow et al., 2020). However, despite the emerging evidence supporting the role of exercise intensity in targeting CMD-related outcomes, there are many considerations for implementing “real world” high intensity exercise in this population.

Persons with SCI face multiple barriers to exercise participation and adherence, helping explain why this population spends such a high proportion (~87%) of the day in a sedentary state (Nightingale et al., 2017b). Internal barriers include lack of energy and motivation (Cowan et al., 2013). In addition, external barriers include factors such as transportation, the cost of exercise programs, the inaccessibility of fitness centers (Rimmer et al., 2000; Kehn and Kroll, 2009), and low trust in a non-specialized exercise instructor’s ability to meet the unique needs of an individual with SCI (Rimmer et al., 2000; Sceleza et al., 2005; Kehn and Kroll, 2009; Cowan et al., 2013). These barriers exceed the agency of the individual and are superimposed upon demographic variables such as socioeconomic, minority status,
sex, age, and location of residence (Rimmer et al., 2000; Kehn and Kroll, 2009; Cowan et al., 2012). To address these population-specific barriers, recent studies have delivered exercise via online (“virtual”) platforms (Wilroy et al., 2017, 2020; Lai et al., 2019). Virtual strategies for delivering exercise to persons with SCI overcomes certain structural barriers while allowing for a limited number of specialists to broadly distribute population-specific exercise services to many exercisers regardless of geographic location. Although technological requirements for accessing virtual exercise platforms exclude certain people such as those without internet access, computer or smartphone, or lack of adequate hand function, the COVID-19 pandemic has caused a shift in internet usage in general (Lemenager et al., 2021) and toward virtual exercise participation in particular (Parker et al., 2021). This online transition presents an opportunity to broadly deliver high intensity exercise to persons with SCI, by using virtual platforms to deliver population-specific exercise safely and effectively to the people where they live.

**Explanation of Virtual Exercise**

Virtual exercise (VEX) is any form of exercise that involves real-time exchange of information via the internet. As such, this practice mandatorily excludes a portion of the population that cannot or does not have online access. Researchers and practitioners must remain cognizant of the limitations to internet access. However, despite limitations in this domain of access, VEX overcomes barriers in other domains such as transportation and infrastructure by allowing exercise to be remotely delivered to participant’s homes by professionals who have specific expertise regarding a given population’s unique safety and implementation needs. While solutions to internet access may seem more feasible than upgrades to transportation and infrastructure, the former solution risks a greater potential for allowing the burden of responsibility to be shifted onto the individual whereas the latter requires public resources. To mitigate this risk, we support a multifaceted approach including but extending beyond online services, and urge researchers and practitioners to share and mitigate the resource responsibility wherever possible.

There are various VEX delivery strategies available to SCI exercise providers. Simple unidirectional guidance can be provided via graphics on a web page or mobile app depicting exercises for participants to complete. More advanced unidirectional guidance can occur via pre-recorded "on demand" video of an exercise instructor conducting a follow-along exercise session for streaming at the participant’s convenience. However, for neither of these options is real-time feedback or monitoring provided to the participant. Therefore, if desired and possible, multidirectional connection via video conferencing allows for instructor(s) and participant(s) to engage during the exercise session. This live streaming of VEX gives exercise professionals the potential to actively monitor participants during the session, allowing for remote delivery of exercise to specialty populations (Chen et al., 2018). The availability of virtual platforms has increased recently, especially since the online transition in response to the COVID-19 pandemic.

In April of 2021 we conducted an informal search of ClinicalTrials.gov to locate ongoing and current studies employing VEX in persons with SCI using the search terms: “spinal cord injury” AND (exercise OR “physical activity” OR workout) AND (online OR virtual OR “home based”). As of the search date, the search revealed five ongoing trials registered in the ClinicalTrials.gov system (NCT03024320, NCT04408287, NCT04564495, NCT03495986, and NCT04397250). Utilizing virtual platforms to deliver on-demand exercise instructions, in the form of graphics and/or pre-recorded videos, has been successfully implemented in adults with a mobility limitation including those with SCI as part of the “Scale Up Project Evaluating Responsiveness to Home Exercise and Lifestyle Tele-Health” (SUPER-HEALTH; NCT03024320) study (Wilroy et al., 2017, 2020; Lai et al., 2019; Rimmer et al., 2019). Further utilization of video conferencing technologies can be used to deliver an even more interactive service to exercise participants, similarly to the implementation of VEX for other populations (Hong et al., 2017; Chen et al., 2018). Currently, there are three ongoing registered trials involving real-time participant monitoring during home-based VEX individualized for persons with SCI. In the “Spinal Cord Injury Exercise and Nutrition Conceptual Engagement” (SCIENCE; NCT03495986) trial, a single participant conducting functional electrical stimulation (FES)-cycling exercise is monitored by the study team, with the study team having remote access to the FES ergometer. This trial requires months of FES exercise training and will determine its effects on body composition and other cardiometabolic health outcomes. In the “Improving Activity Engagement Among Persons with SCI During COVID-19” (NCT04408287) trial, a fitness instructor conducts real-time follow-along VEX sessions for a group of participants with SCI. In the “Home Based Tele-exercise for People with Chronic Neurological Impairments” (Telex; NCT04564495) trial, the effects of sessions of VEX delivered in real-time compared to pre-recorded sessions will be compared in adults with chronic neurological impairments including multiple sclerosis and SCI. The results of this trial will be pivotal in comparing the added benefit of having multidirectional exchange of information during VEX. The logistical cost of pre-recorded sessions is substantially less, greatly reducing the time requirements of the instructor. However, the added benefit of the real-time feedback from the instructor, as well as the interaction between and within the participants themselves, likely confers an added benefit not possible with pre-recorded sessions.

**Safety Considerations and Screening**

The pathophysiology of SCI warrants unique considerations for VEX beyond the necessary adaptation of exercise mode to accommodate the altered volitional motor function of the participants. The participants and instructors need to be aware of, and actively mitigate, the increased risk for autonomic dysreflexia (AD), hypotension due to circulatory hypokinesis (Hjeltnes, 1984), thermal dysregulation, skin injury, fracture (Jacobs and Nash, 2004), and musculoskeletal overuse injury (Vives Alvarado et al., 2021) consequent with SCI. Of greatest concern among exercising paraplegics and tetraplegics with
SCI above the 5th thoracic vertebrae is AD (Karlsson, 1999) classified as an increase in systolic or diastolic blood pressure of >20 mmHg from baseline (Krassioukov et al., 2009). These transient episodes of uncoordinated sympathetic outflow occur 10 (Popok et al., 2017) to 40 (Hubli et al., 2015; West et al., 2015) times per day in response to peripheral stimuli. These episodes cause a rapid rise in blood pressure combined with either bradycardia or tachycardia and further symptoms such as sweating, goosebumps, headache, nausea, anxiety, and blurry vision (Karlsson, 1999; Krassioukov et al., 2009). It should be noted that due to a reduced blood pressure in higher levels of SCI (discussed below), AD-induced increases in blood pressure can be exploited during exercise known as “boosting” in athletes (Gee et al., 2015). However, boosting is not always intentional (Nightingale et al., 2021), influences exercise performance, and is considered dangerous and therefore is discouraged (Gee et al., 2015). Circulatory hypokinesis (H jeltnes, 1984; Davis, 1993; Faghri et al., 2001; Dela et al., 2003) is a phenomenon of reduced cardiac output for any given oxygen uptake due to venous pooling in the paralyzed lower extremities during exercise. The outcome is possible hypokinetic hypotension during upper extremity volitional exercise (H jeltnes, 1984; Davis, 1993) but not lower extremity electrically-stimulated exercise (Faghri et al., 2001; Dela et al., 2003) likely because active contraction transiently increases venous pressures (i.e., “skeletal muscle pump”). Along with skeletal muscle flaccidity, decentralization of the sympathetic efferent signals to blood vessels also contributes to the risk of hypokinetic hypotension because autonomic signals usually actively oppose vasodilation from local metabolites produced by skeletal muscle contraction (Dela et al., 2003). Autonomic decentralization of blood vessels and associated pseudomotor cholinergic efferents innervating sweat glands further results in an impaired ability to regulate body temperature during exercise (West et al., 2013), increasing risk for hyperthermia especially when environmental temperatures are high. The high intensity nature of HIIE requires a greater metabolic rate than MICE, possibly serving as a greater thermoregulatory challenge. Below the level of injury, risk of skin injury is significantly increased in response to abrasion and pressure changes that might occur due to excessive/enhanced movement required during more dynamic exercise such as HIIE or CRT. Bone loss begins very early post-injury (Edwards et al., 2014) with periarticular hip and knee bone mineral density decreasing 2 to 4% per month (Bieringsorensen et al., 1990; Edwards et al., 2014) and declining up to ~20% (Bauman et al., 2015; Goenka et al., 2018) within the first year of SCI, resulting in increased risk of fracture (Carbone et al., 2014; Gifre et al., 2014). These pathophysiological considerations are superimposed on the increased risk for musculoskeletal injury in SCI due to overuse (Bayley et al., 1987; Burnham et al., 1993; Curtis et al., 1999; Ballinger et al., 2000; Vives Alvarado et al., 2021) and possibly also spasticity (Hartkopp et al., 1998).

Delivering Real World High Intensity Virtual Exercise

The Consortium’s consensus-based clinical practice guidelines in the United States denote “at least 150 min per week […] satisfied by performing sessions of 30–60 min three to five days per week, or at least three 10-min sessions per day (Nash et al., 2019).” Other evidence-based physical activity guidelines for metabolic health persons with SCI have been updated to recommend “at least 30 min of moderate to vigorous intensity aerobic exercise three times per week (Martin Ginis et al., 2018).” These SCI activity guidelines are designed primarily around volume and frequency of activity with less clear recommendations for exercise intensity expressed according to %HR/VO2max or mode. The Exercise and Sport Science Australia (ESSA) position statement on exercise and SCI recommends “150 min/wk of moderate-intensity or 60 min/wk of vigorous-intensity” and allows for a range of intensities similar to recommendations for persons without SCI from governmental health authorities [e.g., CDC (Piercy et al., 2018) and WHO (Bull et al., 2020)]. It is important
to understand that these intensity levels are relative, with average maximal rate of whole-body oxygen consumption in persons with tetraplegia (7.9–9.5 ml/kg/min) (Simmons et al., 2014) being below the values that qualify as “moderate” intensity (10.5–21.0 ml/kg/min) in persons without SCI (Pieryc et al., 2018). The low rates of oxygen consumption and thus calorie expenditure that can be achieved and sustained during exercise by persons with SCI have important considerations for the tailoring of exercise to address various CMD-related outcomes (McMillan et al., 2021b), calling for novel approaches such as HIIT (Nightingale et al., 2017a) and CRT. These high intensity approaches have been shown in persons with SCI to increase post-exercise energy expenditure and fat utilization (McMillan et al., 2021a,b), thereby conferring benefits by influencing metabolism beyond the transient increases seen during exercise.

Despite the lack of emphasis in current SCI guidelines, experts have called for a recognition of the importance of exercise intensity in this population (Nightingale et al., 2017a). This call to “raise the intensity” originates from the important role that exercise intensity plays in the physiological responses and adaptations to exercise in persons without SCI. In adults without SCI, HIIT has classically been prescribed to enhance athletic performance (Billat, 2001) and more recently has been realized in the context of enhancing indices related to health status (Weston et al., 2014; Batacan et al., 2017; Campbell et al., 2019; Taylor et al., 2019). Notably, when using HIIT, a dramatically lower exercise volume is required to achieve increases in cardiorespiratory fitness and oxidative capacity compared to steady-state exercise (Burgomaster et al., 2008).

Furthermore, HIIT enhances metabolic function thus more specifically addresses cardiometabolic disease component risks (Weston et al., 2014; Batacan et al., 2017; Campbell et al., 2019). Unfortunately, there is a paucity of research investigating efficacy of HIIT in persons with SCI, and the few HIIT interventions in SCI are limited by small sample size (de Groot et al., 2003; Harnish C. R. et al., 2017), subject heterogeneity, short training duration (Harnish C. R. et al., 2017), and complicated exercise modes (Solinsky et al., 2020). Studies examining the acute physiological response to HIIT (Astorino and Thum, 2018b; Astorino, 2019; Graham et al., 2019; McLeod et al., 2020; McMillan et al., 2020) in persons with SCI have established its safety and feasibility in persons with paraplegia, with preliminary safety and feasibility evidence indirectly available for tetraplegia (Solinsky et al., 2020). Importantly, the cardiovascular and metabolic response to exercise undulates with changing exercise intensity during a HIIT session in persons with SCI (McMillan et al., 2020), showing that SCI does not ablate the acute physiological responses that chronic adaptations are dependent upon. Furthermore, one study (McMillan et al., 2020) in persons with paraplegia demonstrated a reduced time commitment with HIIT vs. steady-state arm cycling to achieve a fixed energy expenditure equal to 120 kcal, providing indirect evidence for the time-efficiency of HIIT in SCI. In addition, results from one study in men and women with SCI (Astorino and Thum, 2018a) exhibited significantly higher enjoyment in response to submaximal or supramaximal interval exercise vs. continuous exercise, and no participants preferred the bout of continuous exercise. Gauthier et al. (2018) examined the feasibility and efficacy of six wk of home-based HIIT performed using their own wheelchair. Participants did not report any serious adverse events, deemed training to be feasible, and reported significant subjective improvements in health.

Despite this burgeoning evidence supporting HIIT in SCI, the broad delivery of high intensity exercise in this population has yet to be achieved. The use of VEX could allow for the widespread adoption of high intensity exercise by persons with SCI in a “real world” context. Accordingly, there are multiple on-going registered clinical trials deploying home-based high intensity exercise in persons with SCI. In the “High-intensity Interval Training for Cardiometabolic Health in Persons with Spinal Cord Injury” (NCT04397250) trial, high-intensity exercise sessions are completed at home with remote monitoring of cardiovascular responses (Farrow et al., 2021). In this study, practitioners administer arm cycles for home use, and prescribe a HIIT paradigm to determine the effect of a home-based HIIT intervention on cardiometabolic health outcomes. The “Telehealth High Intensity Interval Exercise and Cardiometabolic Health in Spinal Cord Injury” (Award Number R21NR019309) trial was recently funded, and while details about the trial have yet to be released, the purpose is to evaluate the effect of a “home-based telehealth HIIT arm crank exercise training program” on cardiometabolic health outcomes. These trials will be the first to scientifically test the use of VEX to deliver high intensity exercise to persons with SCI. However, it should be noted that at least two previous studies have demonstrated the feasibility of delivering non-virtual home-based high intensity exercise in persons with SCI (Nash et al., 2002; Solinsky et al., 2020). One of these studies used FES-assisted rowing (Solinsky et al., 2020), a complicated mode of exercise that is not readily accessible in a “real world” context. The other study (Nash et al., 2002); however, employed a modified version of a well-established CRT paradigm (Jacobs et al., 2001, 2002; Nash et al., 2001, 2002, 2007; Kressler et al., 2014; McMillan et al., 2021a) that has been shown to benefit multiple components of fitness and health in persons with SCI (Jacobs et al., 2001, 2002; Nash et al., 2001, 2007; Kressler et al., 2014). In this study, simple and inexpensive adaptations—such as using resistance bands attached to a home door—were used to reproduce the CRT in a home environment, and similar cardiovascular and metabolic responses were shown with the home-based vs gym-based CRT variants (Nash et al., 2001). Resourceful approaches such as this can now be combined with increases in internet access to broadly deliver VEX in a “real world” context to persons with SCI. This combination will possibly influence the viability of high intensity VEX in persons with SCI (Astorino et al., 2021), especially given the known (e.g., Astorino and Thum, 2018a) and anticipated psychological and social impacts of HIIT in SCI. For example, it has been demonstrated that HIIT is more enjoyable than MICT in persons with SCI (Astorino and Thum, 2018a). This increased enjoyment could yield a benefit to both recruitment and retention. Additionally, intrapersonal as well as interpersonal incentives should be considered. For example, exercise professionals can capitalize on the social exchange that can occur during VEX. Recent qualitative evidence showed that
persons with SCI desire to belong to a collective of SCI peers when participating in VEX (Lai et al., 2021). As suggested by research demonstrating associations between exercise and social belonging (Ginis et al., 2010; Richardson et al., 2017), integrating prosocial components into VEX could prove beneficial to uptake, adherence, and impact.

Conclusions
Exercise’s health benefits have been recognized since ancient times (Booth et al., 2002), but advances in technology allow us to reconceptualize the means by which we deliver this potent biological stimulus. The rising tide of digital platforms, allowing for the flexibility of on-demand content and the granularity and interactivity of real-time sessions. After accounting for population-specific safety considerations, this VEX will allow for persons with SCI to connect with specialized exercise practitioners without specific transportation and infrastructure requirements. Overcoming these barriers via VEX allows for increased access to specialized exercise required to optimize function and health in persons with SCI. Emerging evidence supports a call to “raise the intensity” in SCI, while the COVID-19 pandemic has increased internet usage and our familiarity with virtual platforms facilitating social exchange. When taken together, now is the time to employ VEX for the broad delivery of “real world” high intensity exercise in persons with SCI.

AUTHOR CONTRIBUTIONS
TA and DM conceptualized the topic of this manuscript. DM and MC developed the outline and first draft for the manuscript. All authors contributed edits that yielded the final form of the manuscript.

ACKNOWLEDGMENTS
The Authors appreciate the dedication of the men and women who serve as participants in research studies.

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