Annals of Case Reports
Bigford GE, et al. Ann Case Rep: 9: 101755
www.doi.org/10.29011/2574-7754.101755
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# The Impact of Caregiver/Care-Receiver Co-Treatment in a Therapeutic Lifestyle Intervention for Chronic Spinal Cord Injury: A Comparative Case Series

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**Citation**: Bigford GE, Lehmann DA, Mendez AJ, Nash MS (2024) The Impact of Caregiver/Care-Receiver Co-Treatment in a Therapeutic Lifestyle Intervention for Chronic Spinal Cord Injury: A Comparative Case Series. Ann Case Report. 9: 1755. DOI:10.29011/2574-7754.101755

**Received:** 05 April 2024, **Accepted:** 09 April 2024, **Published:** 12 April 2024

## Abstract

**Introduction:** This study is a prospective comparative case series analysing the differential impacts of a therapeutic lifestyle intervention (TLI) on individuals with spinal cord injury (SCI) and their caregivers. The primary objective was to assess changes across several health metrics predictive of cardio metabolic disease (CMD), fitness, and quality of life, in dyadic partners and between 2 separate cases. **Case Presentation:** SCI participants and their respective caregivers, forming 10 dyads, were included in the study. Dyads were randomly assigned to two distinct case scenarios: Case 1, where both dyadic partners received TLI; and Case 2, where only the SCI partner received the intervention. Each case series comprised five dyads. TLI constituted a rigorous 6-month program consisting of exercise, adherence to a Mediterranean diet, and behavioural support. Across cases, notable improvements were observed in body mass, and strength among SCI partners; and reductions in body mass and fasting glucose, and improved mental well-being was observed in caregiver partners. Dyadic interaction analysis found that insulin, HOMA, HDL, and mental health improvements in SCI were strongly linked to improvements in caregiver when both dyadic partners received TLI. **Conclusion:** We conclude that TLI co-treatment for dyadic partners, including exercise, nutrition, and behaviour modification, improves health outcomes related to CMD risks and quality of life in both populations.

**Trial Registration:** ClinicalTrials.gov, ID: NCT02853149 Registered August 2, 2016.

## Introduction

Advancement in medicine and science has resulted in the increased survivability of individuals who sustain a traumatic spinal cord injury (SCI), and a notable shift in healthcare focus towards managing chronically acquired diseases, particularly cardio-metabolic disease (CMD). A significant contributing factor to CMD in chronic SCI is the complex interplay of physical inactivity [1,2] altered body composition [3-6], and metabolic dysfunction [7,8] due to the neurological impairment. The resultant prevalence of conditions such as obesity [9-11], dyslipidemia [12-15], and insulin resistance [16-18], which often cluster into so-called cardio metabolic syndrome, constitute leading causes of mortality and morbidity in the population. Consequently, interventions for chronic SCI have also significantly evolved over time, where rehabilitation strategies initially focused on maximizing functional recovery through task-specific training [19], current approaches prioritize a multidisciplinary strategy [20]. Lifestyle modification such as exercise [21,22] and nutrition [21,23] have resulted in marginal improvements in CMD risks including obesity [24,25], dyslipidemia [24], and insulin resistance [26-28], and recent reviews have also emphasized the effectiveness of behavioral therapies in addressing psychosocial issues in patients with SCI [29]. In this way, comprehensive therapeutic lifestyle intervention (TLI), that combines regular physical activity, healthy nutrition, behavioral interventions and stress management, is cited as a key strategy for weight management and overall health in the SCI population [30]. The health state of individuals with SCI also has an impact on their caregivers, where they may experience functional and health decline accompanying their own aging [31]. In general, caregivers play a crucial role in offering both physical and emotional support to care-receivers throughout their rehabilitation journey and lifespan. It has been reported that caregivers of individuals with SCI experience high levels of pain, anxiety, and depression [32]. Studies have underscored the significance of considering social factors and the mental health of caregivers in the rehabilitation process [33], and highlighted how caregiver support can enhance patient outcomes and quality of life [34]. Importantly, early evidence also indicates benefits to the care-receiver when a caregiver participates in a coordinated and linked behavioural intervention program [30]. Our team previously adapted the TLI originally based on the Diabetes Prevention Program (DPP) framework, to address the increased risk of developing CMD in individuals with SCI. Based on prior research linking diabetes risk to higher body weight and BMI levels [35,36], and the success of the DPP [37,38], our intervention aimed to achieve and maintain at least a 7% weight loss. Exploratory results showed that the TLI significantly reduced body mass, surpassing the target, and effectively lowered CMD risks [39]. In addition, we recently published a comprehensive follow-up study that confirmed the initial results, demonstrating significant and clinically relevant improvements across a wide range of health markers, including body composition, glucose metabolism, cardiovascular risk factors, aerobic capacity, and health-related quality of life [40]. Notably, the study included a refined TLI, which incorporated a linked caregiver intervention, and the expanded protocol was also published separately [41]. The primary objective of the current comparative case series aims to extend the co-treatment protocol and investigate its impact on health outcomes for both partners in the dyad.

## Methodology

The methods outlined here are a brief summary of each intervention and testing. For a comprehensive and detailed methodology, please refer to the original protocol publication [40].

### Statement of Ethics

Following presentation of study privacy practices and the Health Insurance Portability and Accountability Act (HIPAA) protections, written and verbal informed consent was obtained from all participants. The protocol was approved by the Human Subjects Research Office, Miller School of Medicine, and University of Miami.

### Intervention

#### SCI Participants

#### 6-Month Supervised Exercise Intervention

- Circuit Resistance Training (CRT) consisted of thrice-weekly sessions lasting 40–45 minutes.
- Each session included resistance and endurance activities with alternating periods of incomplete recovery.
- Resistive loads were gradually increased over four-week cycles, with adaptations made for individuals with tetraplegia.
- The endurance exercise component utilized the Vita-glide® arm ergometer or a similar alternative.
- Exercise intensity was monitored using heart rate reserve (HRR) and the Borg Rating of Perceived Exertion (RPE) scale.

#### 6-Month Nutritional Intervention

- The Mediterranean-style diet aimed for a 500–1000 kcal/d deficit to achieve a 7% weight loss over 24 weeks.
- Daily energy intake emphasizes fruits, vegetables, whole grains, olive oil, poultry, and fish.
- Macronutrient composition included 45–50% carbohydrate, 15% protein, and 35–40% fat, with a focus on monounsaturated fats.
- Dietary education and assessment included self-monitoring skills and nutrition booklets.

#### 6-Month Behavioral Intervention

- A 16-session protocol targeted behavior change through education, problem-solving skills training, and cognitive restructuring.
- The intervention covered various aspects, including education, nutrition, exercise, goal setting, and self-monitoring.
- Sessions were delivered primarily in a one-on-one format, tailored to individual needs.
- Participants received a personalized lifestyle intervention manual to support their progress and lifestyle change goals.

#### Complimentary Caregiver Curriculum (CCC) Participants

#### 6-Month Supervised Exercise Intervention

- The caregiver intervention group underwent a 6-month supervised exercise program at the Medical Wellness Center three times weekly, lasting 40–45 min.
- Activities included resistance training (weightlifting) and endurance training (treadmill and bicycles), overseen by study personnel.

- The resistance training protocol consisted of seven exercises performed on selectorized resistance training equipment, progressing from one set of 12–15 repetitions to two sets of 8–12 repetitions over 72 weeks.
- Cardiovascular exercise prescription ranged from 50 to 70% of estimated VO2 max for 20–40 min, gradually progressing over three months.

**6-Month Nutritional Intervention**

- The nutritional intervention for CCC participants followed the same protocol as for SCI participants.

**6-Month Behavioral Intervention**

- The behavioral intervention for CCC participants followed the same protocol as for SCI participants.

**Caregiver Control**

The control caregiver participants received generic (“unstructured’) information about healthy eating and exercising without specific education on food types, exercise guidelines, caloric expenditure, or nutritional composition. The content sources included online websites, such as WebMD Living Healthy (www.webmd.com/living-healthy, (accessed on 2 August 2016)), which typically provide generic information describing the need to exercise (but not providing an exercise prescription), eat well (but not providing a defined diet), and broad lifestyle recommendations.

**Participant Testing**

**SCI Participants**

**Anthropometry**

- Body Mass (BM) was measured using a calibrated wheelchair scale, averaging measurements in and out of wheelchairs.
- Height was measured with a wall-mounted scale to the nearest 0.5 cm.
- Waist circumference was measured with a Gulick tape measure at the umbilicus level to the nearest 0.5 cm.
- BMI was calculated from height and weight (kg/m$^2$).

Cardiorespiratory Endurance

- Peak oxygen consumption (VO2 peak) was measured on an arm crank ergometer using spirometry.
- Participants underwent a graded exercise test to determine VO2 sub-peak/peak, HR sub-peak/peak, and ratings of perceived exertion (RPE).
- The test was conducted using calibrated equipment, with adjustments for individuals with tetraplegia.

Strength

- Upper-extremity dynamic strength was measured using Helms Equalizer 7000 or equivalent equipment.
- Subjects performed maneuvers with incremental increases in weight until volitional fatigue, with 1-RM calculated accordingly.

Insulin Resistance, CVD Risk, and Inflammatory State

- Basal glucose and insulin or C-peptide concentrations were used to calculate HOMA2.
- Blood samples were analyzed for hemoglobin A1C and lipid profiles.

Health Related Quality of Life (HRQoL)

- HRQoL was assessed using the Shortform-36 (SF-36) Health Questionnaire, measuring eight dimensions of health and generating Physical Component Score (PCS) and Mental Component Score (MCS).

**CCC participants**

1. Anthropometry:

- Body mass was measured using a digital platform scale to the nearest 0.1 kg.
- Height was measured with a wall-mounted scale to the nearest 0.5 cm.
- Waist circumference was measured with a Gulick tape measure at the umbilicus level to the nearest 0.5 cm.
- BMI was calculated from height and weight (kg/m2).

2. Cardiovascular Fitness:

- Bruce treadmill protocol was utilized, with heart rate monitored throughout.
- Treadmill speed and incline was systematically increased after a 3 min warmup.
- Cardiorespiratory Endurance was estimated by extrapolating VO2 estimates achieved during submaximal steady-state heart rates to predict maximum heart rate.

3. Strength:

- 1-RM strength for chest press and leg press was estimated using the 7–10 repetition method and regression equation.
- Resistance increased by 10 pounds when the upper end of the repetition range can be completed before fatigue.

4. Insulin Resistance, CVD Risk, and Inflammatory State:

- Measured as described for SCI participants.

5. HRQoL:

- Assessed as described previously.

**Analysis**

Data were analyzed using GraphPad, Prism (v9.3.1) and R Studio (v1.4.1106). Descriptive statistics were calculated to identify measures of central tendency and variability for continuous outcome variables. The Wilcoxon-Rank Sum (Mann-Whitney U) nonparametric test for non-normal distributions and ordinal data, was performed to evaluate the median change in values in SCI participants between cases, and in caregivers between cases. The Kendall's Tau Coefficient nonparametric test was performed to assess the strength and direction of association between variable for dyads in case 1 compared to those in case 2.

A p-value of <.05 was used as the criterion for significance. All p-values <.05 are denoted in the figure legends, where number of asterisks indicate level of significance.

**Case Presentation**

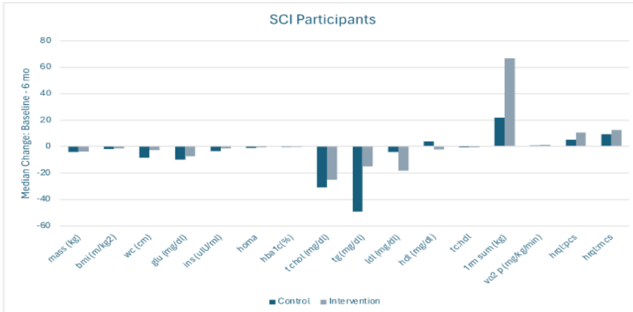
Case participants were 10 SCI and 10 neurologically intact (non-injured) caregivers, where SCI participant and their caregiver constituted 1 dyad. Dyads were randomized to two distinct case scenarios: Case 1 (Intervention Group): where both SCI participants and their caregivers (CCC) received TLI, and Case 2 (Control Group): where SCI participants received TLI, but their caregivers received no intervention (n=5 dyads/case series). Health metrics, including body mass, BMI, waist circumference, glucose and lipid metabolism markers, physical strength, aerobic capacity, and health-related quality of life measures, were analysed. Participant characteristics and descriptive statistics are summarized in Table 1, and case comparison results are summarized in Figures 1 and 2.

**Table 1.** Demographic Characteristics and Descriptive Statistics from Dyads in Control and Intervention Groups at Baseline and After 6-month Intervention.

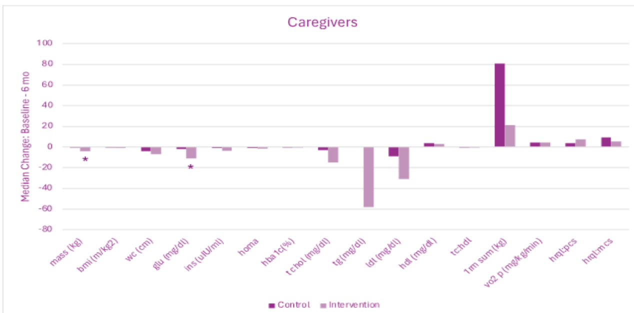
| Variable | | SCI (n=10) | | Caregiver (n=10) | |
|---|---|---|---|---|---|
| | | Control | Intervention | Control | Intervention |
| Gender (m\|f) | | 3\|2 | 4\|1 | 1\|4 | 2\|3 |
| Ethnicity (c\|h\|b) | | 0\|4\|1 | 0\|4\|1 | 0\|5\|0 | 0\|4\|1 |
| LOI (p\|t) | | 3\|2 | 2\|3 | N/A | |
| AIS (A-D) | | 2; 1; 1; 1 | 3 ;0; 1; 1 | N/A | |
| Age (y), mean +/- SD | | 44 +/- 14.14 | 48.8 +/- 7.92 | 36.4 +/- 18.68 | 49 +/- 18.48 |
| Body Mass (kg) | | | | | |
| | b | 89.4 +/- 26 | 91.7 +/- 18.2 | 66.7 +/- 11.2 | 99.2 +/- 24.2 |
| | 6 mo | 84.7 +/- 26.7 | 88.1 +/- 17.9 | 66.1 +/- 10.6 | 94/4 +/- 25.9 |
| BMI (kg/m2) | | | | | |
| | b | 32.4 +/- 11.3 | 29.1 +/- 5.9 | 25.7 +/- 3.9 | 36.3 +/- 7.2 |
| | 6 mo | 30.5 +/- 11.6 | 27.5 +/- 5.4 | 25.4 +/- 3.6 | 34.9 +/- 8.1 |
| WC (cm) | | | | | |
| | b | 120 +/- 18.7 | 113.7 +/- 18.5 | 77.3 +/- 12.1 | 101.6 +/- 13.2 |
| | 6 mo | 114.8 +/- 22.1 | 110.9 +/- 19.6 | 73.7 +/- 7.7 | 94.2 +/- 14.5 |
| Fasting GLU (mg_dl) | | | | | |
| | b | 104.6 +/- 24.2 | 89.4 +/- 6.1 | 102.6 +/- 17.6 | 103.4 +/- 10.4 |
| | 6 mo | 91.6 +/- 18.7 | 83.4 +/- 5.1 | 102.8 +/- 16.5 | 90.6 +/- 9.9 |
| Insulin (uIU_ml) | | | | | |
| | b | 22.8 +/- 24.9 | 14.3 +/- 13.4 | 15.7 +/- 6.1 | 19.5 +/- 15 |
| | 6 mo | 10.2 +/- 8.9 | 8.7 +/- 4 | 14.7 +/- 7.8 | 16.5 +/- 15 |
| HbA1C% | | | | | |
| | b | 5.4 +/- 0.4 | 5.2 +/- 0.4 | 5.3 +/- 0.4 | 5.8 +/- 0.5 |
| | 6 mo | 5 +/- 0.7 | 5 +/- 0.4 | 5.2 +/- 0.2 | 5.4 +/- 0.4 |
| HOMA | | | | | |
| | b | 3.9 +/- 2.6 | 3.2 +/- 2.9 | 3.7 +/- 1 | 7.6 +/- 9.8 |
| | 6 mo | 2.6 +/- 2.4 | 1.8 +/- 0.8 | 3.3 +/- 1.8 | 3.8 +/- 3.8 |
| Total Cholesterol (mg_dl) | | | | | |
| | b | 199.2 +/- 34.4 | 185.4 +/- 28.1 | 190.6 +/- 41.7 | 231.4 +/- 56 |
| | 6 mo | 179.4 +/- 63.1 | 158.2 +/- 28.9 | 189.4 +/- 41.1 | 205.8 +/- 38.4 |
| Triglyceride (mg_dl) | | | | | |
| | b | 190.2 +/- 89.3 | 181.6 +/- 145.4 | 133 +/- 46.1 | 168.6 +/- 124 |
| | 6 mo | 158.2 +/- 132.3 | 150.6 +/- 81.6 | 148.4 +/- 105.7 | 123 +/- 90.5 |
| HDL (mg_dl) | | | | | |
| | b | 40.8 +/- 15.6 | 41.2 +/- 15.2 | 42 +/- 9.2 | 57.4 +/- 26.4 |
| | 6 mo | 44.2 +/- 17.6 | 40 +/- 11.3 | 53.6 +/- 20.1 | 60.2 +/- 23.2 |
| LDL (mg_dl) | | | | | |
| | b | 112.2 +/- 30.7 | 108 +/- 18.3 | 115.6 +/- 34.3 | 140.6 +/- 43 |
| | 6 mo | 104.6 +/- 44.5 | 88 +/- 21.9 | 107 +/- 32.4 | 114.6 +/- 43 |
| TC:HDL | | | | | |
| | b | 5.3 +/- 1.4 | 4.8 +/- 1.3 | 4.8 +/- 1.6 | 4.7 +/- 1.9 |
| | 6 mo | 4.3 +/- 1.7 | 4.2 +/- 1.2 | 4 +/- 2 | 3.8 +/- 1.4 |
| 1RM (kg) | | | | | |
| | b | 137.7 +/- 113.3 | 154.9 +/- 53.2 | 368.3 +/- 109.2 | 338.6 +/- 100.4 |
| | 6 mo | 173.5 +/- 133.4 | 237 +/- 97.4 | 432.9 +/- 114.4 | 399.5 +/- 145.7 |
| VO2 Peak (mg/kg/min) | | | | | |
| | b | 6.6 +/- 4.4 | 8.6 +/- 4.8 | 39.3 +/- 7.6 | 35.6 +/- 7.3 |
| | 6 mo | 7.5 +/- 4.9 | 11.2 +/- 6.1 | 44.4 +/- 8.2 | 47.8 +/- 19.7 |
| HRQoL PCS | | | | | |
| | b | 36.8 +/- 4.4 | 39 +/- 6.7 | 73.9 +/- 12.3 | 77.8 +/- 7.4 |
| | 6 mo | 43.8 +/- 4.6 | 49.3 +/- 2.5 | 79.3 +/- 14.7 | 87 +/- 5.8 |
| HRQoL MCS | | | | | |
| | b | 43.9 +/- 8.3 | 40.3 +/- 11 | 48 +/- 3.9 | 47.3 +/- 2.6 |
| | 6 mo | 57.3 +/- 4.8 | 53.8 +/- 5.5 | 56.4 +/- 2.3 | 54.5 +/- 1.3 |

Abbreviations: SCI, spinal cord injury; m, male; f, female; c, caucasian; h, hispanic; b, black; p, paraplegic; t, tetraplegic; LOI, level of injury; AIS, ASIA Impairment Scale; y, years; SD, standard deviation; kg, kilogram; BMI, body mass index; WC, waist circumference; cm, centimeter; GLU, glucose; mg_dl; milligram per deciliter; uIU_ml, microunits per milliliter; HbA1C, glycated hemoglobin; HOMA, homeostatic model assessment for insulin; RM, repetition maximum; VO2, volume of oxygen; min, minute; HRQoL, health related quality of life; PCS, physical component score; MCS, mental component score.

**Table 1:** Demographic Characteristics and Descriptive Statistics from Dyads in Control and Intervention Groups at Baseline and after 6-month Intervention.

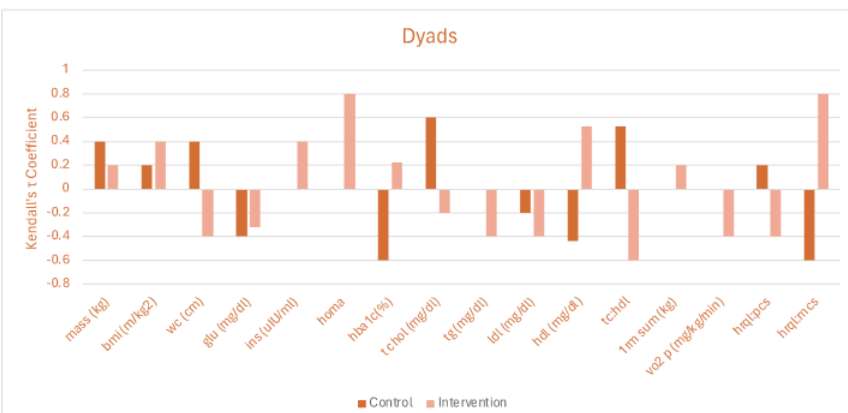



| SCI Participants | Control | Intervention | p |
|---|---|---|---|
| mass (kg) | -3.98 | -3.87 | 0.69 |
| bmi (m/kg$^2$) | -1.6 | -1.4 | 0.84 |
| wc (cm) | -8.4 | -2.41 | 0.31 |
| glu (mg/dl) | -10 | -7 | 0.68 |
| ins (uIU/ml) | -3.42 | -1.23 | 0.42 |
| homa | -0.9 | -0.43 | 0.55 |
| hba1c(%) | -0.2 | -0.2 | 1 |
| t chol (mg/dl) | -31 | -25 | 1 |
| tg (mg/dl) | -49 | -15 | 1 |
| ldl (mg/dl) | -4 | -18 | 0.42 |
| hdl (mg/dl) | 4 | -2 | 0.24 |
| tc:hdl | -0.66 | -0.47 | 0.53 |
| 1rm sum (kg) | 21.78 | 66.84 | 0.06 |
| vo$_2$ p (mg/kg/min) | 0.97 | 1.54 | 0.31 |
| hrql:pcs | 5.27 | 10.82 | 0.84 |
| hrql:mcs | 9.4 | 12.7 | 1 |




| Caregivers | Control | Intervention | p |
|---|---|---|---|
| mass (kg) | -0.59 | -3.8 | 0.02* |
| bmi (m/kg$^2$) | -0.26 | -1.11 | 0.22 |
| wc (cm) | -3.82 | -7.19 | 0.55 |
| glu (mg/dl) | -2 | -11 | 0.02* |
| ins (uIU/ml) | -1.15 | -3.64 | 0.55 |
| homa | -1.18 | -1.48 | 0.42 |
| hba1c(%) | -0.1 | -0.5 | 0.12 |
| t chol (mg/dl) | -3 | -15 | 0.08 |
| tg (mg/dl) | 0 | -58 | 0.55 |
| ldl (mg/dl) | -9 | -31 | 0.42 |
| hdl (mg/dl) | 4 | 3 | 0.92 |
| tc:hdl | -0.34 | -0.68 | 0.42 |
| 1rm sum (kg) | 80.68 | 21.2 | 0.31 |
| vo$_2$ p (mg/kg/min) | 4.45 | 4.34 | 1 |
| hrql:pcs | 3.83 | 7.59 | 0.42 |
| hrql:mcs | 9.11 | 5.56 | 0.55 |

**Figure 1: Wilcoxon-Rank Sum test results for SCI participants and caregiver participants between cases after 6-month TLI.** The Wilcoxon-Rank Sum test compares the health metrics of SCI participants and caregiver participants between case 1 (Intervention Group) and case 2 (Control Group) after 6-month TLI. The health metrics analyzed include body mass, BMI, waist circumference, glucose and lipid metabolism markers, physical strength, aerobic capacity, and health-related quality of life measures. Each bar plot represents the mean change value for a specific metric after 6 months for both case 1 and case 2. The p-values obtained from the Wilcoxon-Rank Sum tests are displayed to indicate the significance of differences between the two cases for each health metric. *$p < .05$.




| Dyads τ Coefficient | Control | Intervention |
|---|---|---|
| mass (kg) | 0.4 | 0.2 |
| bmi (m/kg$^2$) | 0.2 | 0.4 |
| wc (cm) | 0.4 | -0.4 |
| glu (mg/dl) | -0.4 | -0.32 |
| ins (uIU/ml) | 0 | 0.4 |
| homa | 0 | 0.8 |
| hba1c(%) | -0.6 | 0.22 |
| t chol (mg/dl) | 0.6 | -0.2 |
| tg (mg/dl) | 0 | -0.4 |
| ldl (mg/dl) | -0.2 | -0.4 |
| hdl (mg/dl) | -0.44 | 0.53 |
| tc:hdl | 0.53 | -0.6 |
| 1rm sum (kg) | 0 | 0.2 |
| vo$_2$ p (mg/kg/min) | 0 | -0.4 |
| hrql:pcs | 0.2 | -0.4 |
| hrql:mcs | -0.6 | 0.8 |

**Figure 2: Kendall's Tau Coefficient results for SCI and caregiver dyads between cases after 6-month TLI.** The Kendall's Tau Coefficient results compares the correlation between the health metrics of SCI and caregiver dyads between case 1 (Intervention Group) and case 2 (Control Group) after 6-month TLI. The health metrics analyzed include body mass, BMI, waist circumference, glucose and lipid metabolism markers, physical strength, aerobic capacity, and health-related quality of life measures. Each bar plot represents the strength and direction of correlation between a specific health metric for dyadic partners after 6-month TLI for both case 1 and case 2.

**Summary statistics**

Case 1 and case 2 exhibited favourable changes across multiple health markers. Dyadic partners from both groups experienced a slight decrease in body mass and BMI, accompanied by reductions in Waist Circumference WC, suggesting improvements in weight management and body composition. Additionally, reductions were observed in fasting glucose levels and insulin levels, indicating enhanced glucose metabolism. HbA1c levels remained relatively stable in both groups, suggesting no significant changes in long-term glucose control, however, decreases in HOMA values signify improvements in insulin sensitivity following the intervention. Lipid profiles showed positive changes, with decreases in total cholesterol and triglyceride levels, along with an increase in HDL levels, indicative of improved cardiovascular health. Notably, LDL levels decreased in both groups, leading to a favourable shift in the lipid profile. The TC: HDL ratio, a marker of cardiovascular risk, demonstrated a decrease, further supporting improved lipid profiles. Furthermore, both dyadic partners in case 1 and case 2 groups exhibited improvements in strength and aerobic capacity, as evidenced by increases in 1RM values and VO2 peak values, respectively. These findings suggest enhanced physical fitness following the intervention. Lastly, Health-Related Quality of Life (HRQoL) scores, including both physical composite score (PCS) and mental composite (MCS), demonstrated an increase in both groups, reflecting improvements in overall well-being. Collectively, these results highlight the comprehensive benefits of the intervention program, encompassing improvements in body composition, glucose metabolism, lipid profiles, physical fitness, and quality of life for individuals with SCI and their caregivers.

Wilcoxon-Rank Sum results for **SCI** participants between cases from baseline to 6 months:

SCI participants in both cases exhibited decreases in body mass and BMI over the study period, with no statistically significant difference observed between them ($p = 0.69$ and $p = 0.84$, respectively). Similarly, reductions in WC were observed in both groups, yet the differences were not statistically significant ($p = 0.31$). Glucose levels were reduced in both groups, with no statistical significance ($p = 0.68$), and although case 2 demonstrated a larger decrease in insulin levels compared to case 1, this disparity also did not reach statistical significance ($p = 0.42$). Both cases exhibited marginal decreases in HOMA and HbA1c without significant between-group differences (both $p > 0.05$). Notably, HDL levels increased in case 2 while decreasing in case 1, while total cholesterol, triglyceride, and LDL levels decreased across both cases, with no significant differences observed between the groups (all $p > 0.05$). Case 1 demonstrated a substantially larger increase in 1RM sum compared to case 2, with a marginally significant difference ($p = 0.06$). VO2 peak increased in both cases, with no significant difference between the groups ($p = 0.31$). Case 1 exhibited higher improvements in both PCS and MCS compared to case 2, although these differences did not reach statistical significance (both $p > 0.05$).

Wilcoxon-Rank Sum results for **caregivers** between cases from baseline to 6 months:

Case 1 caregivers exhibited a statistically significant greater decrease in mass compared to case 2 caregivers (-3.8 kg vs. -0.59 kg; $p = 0.02$), indicating a more pronounced reduction in body mass among caregivers receiving the full TLI. While both cases showed decreases in BMI, the difference between the groups was not statistically significant ($p = 0.22$). Similarly, reductions in WC were observed in both cases, with case 1 showing a larger decrease compared to case 2, although the difference was not statistically significant ($p = 0.55$). Notably, case 1 caregivers demonstrated a statistically significant greater decrease in glucose levels compared to case 2 caregivers (-11 mg/dl vs. -2 mg/dl; $p = 0.02$), indicating a more significant improvement in glycemic control among caregivers receiving the full TLI. While insulin levels were decreased in both cases, there was no statistically significant difference between cases ($p = 0.55$). Additionally, both cases showed decreases in markers HOMA and HbA1c, although there were no statistically significant differences between the cases (both $p > 0.05$). HDL levels increased in both cases, while all other cholesterol markers decreased across cases, with no statistically significant differences between the groups in cholesterol levels or ratios ($p > 0.05$). Additionally, although case 2 showed a larger increase in 1RM Sum compared to case 1, this difference was not statistically significant ($p = 0.31$). VO2 peak exhibited similar increases between cases, with no statistically significant difference in changes between the groups ($p = 1$). Moreover, there was a notable increase in physical and mental component summaries of HRQL in both cases, although there were no statistically significant differences between the cases (both $p > 0.05$).

Kendall's Tau coefficient measures for **dyads** between cases from baseline to 6 months:

For changes in body mass, case 1 showed a weak positive association (0.2), while case 2 exhibited a moderate positive association (0.4), indicating a tendency for changes in SCI participant mass to be positively associated with changes in caregivers' mass across cases. Changes in BMI showed a moderate positive association (0.4) in case 1, and weak positive association (0.2) in case 2, also suggesting a modest positive association between changes in BMI for SCI participants and caregivers. Conversely, in case 2, changes in WC exhibited a moderate negative association (-0.4), contrasting with case 1 having a moderate positive association (0.4). Changes in glucose levels showed a slightly stronger negative association in case 2 (-0.4) compared to case 1 (-0.32), and changes in insulin levels demonstrated a moderate positive association (0.4) in case 1, while no association (0) was observed in case 2. Notably, changes in HOMA exhibited a strong positive association (0.8) in case 1, indicating a robust correlation between changes in insulin resistance for SCI participants and caregivers. Oppositive changes were seen for HbA1c, where case 1 showed a weak positive association (0.2), while case 2 exhibited a moderate negative association (-0.6). The associations between changes in cholesterol levels and ratios differed between cases. Total cholesterol showed a weak negative association (-0.2), and both triglyceride and LDL showed a moderate negative association (-0.4) in case 1, whereas a strong positive association (0.6) for total cholesterol, no association for triglyceride (0), and a weak negative association for LDL (-0.2) was observed in case 2. HDL exhibited a strong positive association (0.53) for case 1, contrasting with a moderate negative association (-0.44) in case 2. Changes in the TC:HDL ratio also demonstrated contrasting associations between the cases, with a moderate negative association (-0.6) in case 1 and a moderate positive association (0.53) observed in case 2. Changes in PCS exhibited a moderate negative association (-0.4) in case 1 and a weak positive association (0.2) in case 2, and changes in MCS showed a strong positive association (0.8) in case 1, contrasting with a moderate negative association (-0.6) in case 2.

## Discussion

This comparative case series demonstrated the effectiveness of tailored intervention in improving health outcomes for individuals with SCI and their caregivers. Notable improvements were observed in body mass, cardiovascular fitness, and strength among SCI participants, and reductions in body mass, fasting glucose, and improvements in mental well-being, were observed in caregiver participants, highlighting the indirect benefits of caregiver-focused interventions on mental health outcomes. SCI individuals face significant health challenges, including increased risks of CMDs and decreased quality of life. Caregivers, often family members, also experience health effects due to the demands of caregiving. Thus, understanding the efficacy of interventions for both groups is crucial for optimizing healthcare strategies. This study reinforces and extends our understanding of the TLI efficacy within the SCI population, corroborating our prior report demonstrating significant, and clinically meaningful health improvements. Such enhancements span critical health domains including body composition, glucose metabolism, cardiovascular risk factors, aerobic capacity, and health-related quality of life [REF]. The supervised exercise intervention, incorporating CRT, has been shown to enhance muscular strength and cardiorespiratory endurance in SCI, [41,42] and the nutritional intervention based on the Mediterranean-style diet aligns with previous research highlighting the benefits of such dietary patterns in CMD risk prevention [43] While improvements were anticipated across all SCI participants due to the standardized nature of the TLI, a novel aspect of this research anticipated more pronounced benefits among caregivers in the intervention group (CCC), in comparison to those in the control group. Notably, significant alterations were observed in the CCC group's body mass and glucose levels relative to the control group, with CCC participants experiencing an approximate 5% reduction in body mass – nearing the 7% target criterion set by prior Diabetes Prevention Programs [37,38,44,45], and fasting glucose levels transitioning from prediabetic to within normal ranges as defined by the American Diabetes Association. Additional findings, however, were not uniformly significant, potentially due to limited study power, thus highlighting the need for larger cohort sizes. Despite this, the results underscore the intervention's potential benefits for caregivers, especially in terms of weight management and glucose regulation. Moreover, the smaller p-values observed when comparing mean differences between caregiver groups, as opposed to those between SCI groups, indicate a suggestive trend towards the beneficial impact of the caregiver-focused intervention. The study's dyad design, with both partners receiving the intervention or one partner acting as a control, allows for an investigation of potential interaction effects between the intervention and caregiver involvement. This design accounts for the interdependence between SCI participants and their caregivers and enables the assessment of how the intervention affects both parties. Several previous studies have investigated the impact of dyadic support mechanisms on exercise and diet adherence, and on patient well-being and rehabilitation outcomes. For example, a recent systematic review highlighted the important role of dyadic influences in promoting and supporting healthy physical activity and diet behaviours [46], and a report on interventions that target dyads suggest that adoption of exercise or diet modifications in one individual has a large impact on proximate others [47]. Similarly, Barone & Waters demonstrate the importance of social support on coping and adaptation in adults living with SCI [48], With respect to the relationships between changes observed in SCI partners and their dyadic caregiver, the strength and direction of these associations varied across different metrics and between cases, reflecting the complex dynamics of dyadic relationships. In case 1, or the full TLI group, moderate to strong interdependence and synchronization were observed between SCI and caregivers within dyads for several variables. Increases in insulin levels, HOMA, and HDL in SCI partners were strongly associated with corresponding increases in CCC partners, suggesting synchronized metabolic changes. Similarly, improvements in MCS in SCI partners were strongly linked to corresponding improvements in CCC partner, altogether suggesting an impact of TLI on both physiological and mental well-being within dyadic relationships. Interestingly, a few results were not an anticipated outcome of TLI. For example, though waist circumference and TC:HDL went down in both groups, in the full TLI group, the more the SCI partners decreased, the less the CCC partners decreased for these variable. While it indicates a negative association between the variables, it doesn't inherently imply a reciprocal relationship, and likely reflects one or two outliers for this particular case.To this point, the variability in responses observed across groups may reflect the complexity of the dyadic relationship and the diverse needs and characteristics of individuals within each group. In this way, alternative analyses may be needed to adequately evaluate the effects of the intervention on various health outcomes. For example, the split between paraplegic and quadriplegic individuals within the SCI group may introduce variability in physiological and functional characteristics, and responses to the intervention, and warrant a stratified analytical approach. However, overall, these findings between SCI and CCC partners undergoing full TLI, represent first steps toward understanding the significance of comprehensive strategies for enhancing health and quality of life for both dyadic partners. Our findings have significant implications for healthcare practice for care-receivers and caregivers, where emphasizing multidisciplinary approaches incorporating exercise, nutrition, and behavioural modifications hold promise for improving health outcomes and enhancing quality of life in both populations. Future research endeavours should focus on longitudinal studies to assess the long-term efficacy and sustainability of interventions, as well as explore novel strategies to optimize healthcare delivery and promote holistic well-being in SCI and CCC populations.

## Declarations

**Author Contributions:**

Conceptualization, MSN and GEB; methodology, MSN and GEB; formal analysis, GEB, and DAL; investigation, GEB and AJM; writing—original draft preparation, GEB; writing—review and editing, GEB, DAL, and MSN; supervision, MSN, project administration, GEB, and AJM; funding acquisition, MSN. All authors have read and agreed to the published version of the manuscript.

**Funding:**

This research was funded by Disability Rehabilitation Research Program (DRRP) from the Department of Health and Human Services National Institute for Disability, Independent Living, and Rehabilitation Research (NIDILRR #90DP0074).

**Institutional Review Board Statement:**

The study was conducted in accordance with the Declaration of Helsinki, and approved by the Human Subjects Research Office, Miller School of Medicine, University of Miami (Institutional Review Board No. 20151065, dated 2 August 2016).

**Informed Consent Statement:**

Informed consent was obtained from all subjects involved in the study.

## References

1. Itodo, O.A, Flueck JL, Raguindin PF, Stojic S, Brach M, et al, (2022) Physical activity and cardiometabolic risk factors in individuals with spinal cord injury: a systematic review and meta-analysis. Eur J Epidemiol, 37: 335-365.
2. Soriano, J.E, Squair IW, Cragg JJ, Thompson J, Sanguinetti R, Vaseghi B, et al, (2022) A national survey of physical activity after spinal cord injury. Sci Rep, 12: 4405.
3. Castro, M.J, Apple Jr DF, Staron RS, Campos GE, Dudley GA (1999) Influence of complete spinal cord injury on skeletal muscle cross-sectional area within the first 6 months of injury. Eur J Appl Physiol Occup Physiol, 80: 373-8.
4. Modlesky, C.M, Bickel CS, Slade JM, Meyer A, Cureton KJ, et al, (2004) Assessment of skeletal muscle mass in men with spinal cord injury using dual-energy X-ray absorptiometry and magnetic resonance imaging. J Appl Physiol 96: 561-5.
5. Giangregorio, L. and N. McCartney, (2006) Bone loss and muscle atrophy in spinal cord injury: epidemiology, fracture prediction, and rehabilitation strategies. J Spinal Cord Med, 29: 489-500.
6. Maimoun, L, Peruchon E, Rabischong P (2006) Bone loss in spinal cord-injured patients: from physiopathology to therapy. Spinal Cord, 44: 203-10.
7. Bauman, W.A. and A.M. Spungen, (1994) Disorders of carbohydrate and lipid metabolism in veterans with paraplegia or quadriplegia: a model of premature aging. Metabolism, 43: 749-56.
8. Bauman, W.A. and A.M. Spungen, (2001) Carbohydrate and lipid metabolism in chronic spinal cord injury. J Spinal Cord Med, 24: 266-77.
9. Gater, D.R, Jr, (2007) Obesity after spinal cord injury. Phys Med Rehabil Clin N Am, 18: 333-51, vii.
10. Gorgey, A.S. and D.R. Gater, Jr, (2007) Prevalence of Obesity After Spinal Cord Injury. Top Spinal Cord Inj Rehabil, 12: p. 1-7.
11. McMillan, D.W, G.E. Bigford, and G.J. Farkas, (2023) The Physiology of Neurogenic Obesity: Lessons from Spinal Cord Injury Research. Obes Facts, 16: 313-325.
12. Brenes, G, Dearwater S, Shapera R, Laporte RE, Collins E (1986) High density lipoprotein cholesterol concentrations in physically active and sedentary spinal cord injured patients. Arch Phys Med Rehabil, 67: 445-50.
13. Bauman, W.A, Spungen AM, Zhong YG, Rothstein L, Petry C, et al, (1992) Depressed serum high density lipoprotein cholesterol levels in veterans with spinal cord injury. Paraplegia, 30: 697-703.
14. Zlotolow, S.P, E. Levy, and W.A. Bauman, (1992) The serum lipoprotein profile in veterans with paraplegia: the relationship to nutritional factors and body mass index. J Am Paraplegia Soc, 15: 158-62.
15. Bauman, W.A, Kahn NN, Grimm DR, Spungen AM (1999) Risk factors for atherogenesis and cardiovascular autonomic function in persons with spinal cord injury. Spinal Cord, 37: 601-16.
16. Duckworth, W.C, Soloman SS, Jallepalli P, Heckmeyer C, Powers A (1980) Glucose intolerance due to insulin resistance in patients with spinal cord injuries. Diabetes, 29: 906-10.
17. Karlsson, A.K,(1999) Insulin resistance and sympathetic function in high spinal cord injury. Spinal Cord, 37: 494-500.
18. Gordon, P.S, G.J. Farkas, and D.R. Gater, Jr, (2021) Neurogenic Obesity-Induced Insulin Resistance and Type 2 Diabetes Mellitus in Chronic Spinal Cord Injury. Top Spinal Cord Inj Rehabil, 27: 36-56.
19. Powell, E.S, et al, (2022) Effects of Dynamic Overground Body Weight

Support Training During Inpatient Rehabilitation After Traumatic Spinal Cord Injury: A Retrospective Case Series. Am J Phys Med Rehabil, 101: 196-200.

20. Afshari, F.T, D. Choi, and A. Russo, (2020) Controversies regarding mobilisation and rehabilitation following acute spinal cord injury. Br J Neurosurg, 34: 123-126.
21. Kressler, J, (2014) Reducing cardiometabolic disease in spinal cord injury. Phys Med Rehabil Clin N Am,. 25: 573-604.
22. Nash, M.S, Farkas GJ, Tiozzo E, Gater DR (2022) Exercise to mitigate cardiometabolic disorders after spinal cord injury. Curr Opin Pharmacol, 62: 4-11.
23. Farkas, G.J, et al, (2022) Energy expenditure and nutrient intake after spinal cord injury: a comprehensive review and practical recommendations. Br J Nutr, 128: 863-887.
24. Bakkum, A.J, Paulson TAW, Bishop NC, Goosey-Tolfrey VL, Swuste JMS, et al, (2015) Effects of hybrid cycle and handcycle exercise on cardiovascular disease risk factors in people with spinal cord injury: A randomized controlled trial. J Rehabil Med, 47: 523-30.
25. Farkas, G.J, (2021) Energy Expenditure, Cardiorespiratory Fitness, and Body Composition Following Arm Cycling or Functional Electrical Stimulation Exercises in Spinal Cord Injury: A 16-Week Randomized Controlled Trial. Top Spinal Cord Inj Rehabil, 27: 121-134.
26. Nightingale, T.E, (2017) Impact of Exercise on Cardiometabolic Component Risks in Spinal Cord-injured Humans. Med Sci Sports Exerc, 49: 2469-2477.
27. Bresnahan, J.J (2019) Arm crank ergometry improves cardiovascular disease risk factors and community mobility independent of body composition in high motor complete spinal cord injury. J Spinal Cord Med, 42: 272-280.
28. Graham, K, Fisher CY, Li J, McCully KM, Rimmer JH (2019) Effects of High-Intensity Interval Training Versus Moderate-Intensity Training on Cardiometabolic Health Markers in Individuals With Spinal Cord Injury: A Pilot Study. Top Spinal Cord Inj Rehabil, 25: 248-259.
29. Post, M.W. and C.M. (2012) van Leeuwen, Psychosocial issues in spinal cord injury: a review. Spinal Cord, 50: 382-9.
30. Nash, M.S, Groah SL, Gater DR, Hudson TA, Lieberman JA, et al, (2018) Identification and Management of Cardiometabolic Risk after Spinal Cord Injury: Clinical Practice Guideline for Health Care Providers. Top Spinal Cord Inj Rehabil, 24: 379-423.
31. Dreer, L.E (2007) Family Caregivers of Persons With Spinal Cord Injury: Predicting Caregivers at Risk for Probable Depression. Rehabil Psychol, 52: 351-357.
32. Schulz, R, Czaja SJ, Lustig A, Zdaniuk B, Martire LM, et al, (2009) Improving the quality of life of caregivers of persons with spinal cord injury: a randomized controlled trial. Rehabil Psychol, 54: 1-15.
33. Rao M, L.Y, Liu H, Wang I, Ren Y, (2022) Influencing Factors Analysis of Rehabilitation for Patients with Spinal Cord Injury. Intelligent Automation & Soft Computing, 34: 455–466.
34. Abdul-Sattar, A.B, (2014) Predictors of functional outcome in patients with traumatic spinal cord injury after inpatient rehabilitation: in Saudi Arabia. NeuroRehabilitation, 35: 341-7.
35. Ford, E.S, (1999) Body mass index, diabetes, and C-reactive protein among U.S. adults. Diabetes Care, 22: 1971-7.
36. Seidell, J.C, (2000) Obesity, insulin resistance and diabetes--a worldwide epidemic. Br J Nutr, 83 Suppl 1: S5-8.
37. Diabetes Prevention Program Research, G (2009) 10-year follow-up of diabetes incidence and weight loss in the Diabetes Prevention Program Outcomes Study. Lancet, 374: p 1677-86.
38. Ratner, R.E. and R. (2006) Diabetes Prevention Program, An update on the Diabetes Prevention Program. Endocr Pract, 12 Suppl 1: 20-4.
39. Bigford, G.E, mendez AJ, Betancourt LF, Drecq PB, Backus D, et al (2017) A lifestyle intervention program for successfully addressing major cardiometabolic risks in persons with SCI: a three-subject case series. Spinal Cord Ser Cases, 3: 17007.
40. Bigford, G.E., Lehmann, D.A., Betancourt, L.F., Maher, J.L., Mendez, A.J., Nash, M.S., Modification of the Diabetes Prevention Program Lifestyle Intervention in Persons with Spinal Cord Injury: Efficacy for Reducing Major Cardiometabolic Risks, Increased Fitness, and Improved Health-Related Quality of Life. Journal of Spine Research and Surgery., 2024. 6: p. 6-25.
41. Bigford, G.E, Betancourt LF, Charlifue S, Nash MS (2023) Therapeutic Lifestyle Intervention Targeting Enhanced Cardiometabolic Health and Function for Persons with Chronic Spinal Cord Injury in Caregiver/Care-Receiver Co-Treatment: A Study Protocol of a Multisite Randomized Controlled Trial. Int J Environ Res Public Health, 20.
42. Jacobs, P.L, M.S. Nash, and J.W. Rusinowski, (2001) Circuit training provides cardiorespiratory and strength benefits in persons with paraplegia. Med Sci Sports Exerc, 33: 711-7.
43. Nash, M.S (2007) Effects of circuit resistance training on fitness attributes and upper-extremity pain in middle-aged men with paraplegia. Arch Phys Med Rehabil, 88: 70-5.
44. Sleiman, D, M.R. Al-Badri, and S.T. Azar, (2015) Effect of mediterranean diet in diabetes control and cardiovascular risk modification: a systematic review. Front Public Health, 3: 69.
45. Diabetes Prevention Program Research, G, (2002) The Diabetes Prevention Program (DPP): description of lifestyle intervention. Diabetes Care, 25: 2165-71.
46. Ratner, R, (2005) Impact of intensive lifestyle and metformin therapy on cardiovascular disease risk factors in the diabetes prevention program. Diabetes Care, 28: 888-94.
47. John, J.C, (2003) Dyad and group-based interventions in physical activity, diet, and weight loss: a systematic review of the evidence. J Behav Med, 2023.
48. Perry, B, (2016) Partner Influence in Diet and Exercise Behaviors: Testing Behavior Modeling, Social Control, and Normative Body Size. PLoS One, 11: e0169193.
49. Barone, S.H. and K. Waters, (2012) Coping and adaptation in adults living with spinal cord injury. J Neurosci Nurs, 44: 271-83.