COMPARISON OF ONE YEAR POST-INJURY OUTCOMES BETWEEN INTENSIVE LOCOMOTOR TRAINING AND CONVENTIONAL THERAPY AFTER MOTOR INCOMPLETE SPINAL CORD INJURY

by

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A Comparison of One Year Post-Injury Outcomes Between Intensive Locomotor Training and Conventional Therapy After Motor Incomplete Spinal Cord Injury

Thesis directed by Associate Professor Matthew Taylor.

ABSTRACT

Background: Spinal cord injury (SCI) is often a devastating condition that negatively affects an individual’s physical, psychological, and social well-being requiring extensive rehabilitation. The majority of all SCIs are incomplete with at least some sensory and/or motor activity remaining intact below the level of the injury, sparing some function. The NeuroRecovery Network (NRN) is a collaboration of six centers implementing a locomotor training (LT) protocol focused on recovery after SCI. These centers are also SCI Model Systems (SCIMS) Centers which capture longitudinal outcomes after injury. The purpose of this study was to evaluate one year outcomes between individuals who participated in the NRN LT program and those who did not.

Methods: A retrospective (nested case/control) analysis was completed comparing one year post-injury outcomes between individuals who participated in NRN LT (cases) and controls matched on age, gender, injury year, mode of mobility, and NRN site. Outcomes evaluated include the following: Functional Independence Measure (FIM™) total motor score, FIM Transfer Index, FIM Locomotion and Stairs, household and community mobility, Satisfaction with Life Scale (SWLS™), Craig Handicap Assessment and Reporting Technique (CHART™), re-hospitalizations, and days re-hospitalized.
**Results:** Statistically significant improvements for cases were found in the following outcomes: FIM Total Motor Score ($p=0.002$); FIM Transfer Index ($p=0.007$); SWLS ($p=0.019$); household mobility ($p=0.047$); and CHART subscales [mobility ($p=<0.001$); occupation ($p=0.025$); social integration ($p=0.038$)] with medium to large effects sizes.

**Conclusions and Significance:** Individuals who completed the NRN protocol reported greater improvements in mobility, satisfaction with life, community participation, and fewer re-hospitalizations at one year post-injury, but also spent significantly more days re-hospitalized. Evaluating interventions that improve outcomes while decreasing health complications serve to benefit individuals who sustain SCIs and the entire health care system by decreasing the societal and economic burden associated with SCIs. Larger prospective studies are warranted to develop a more comprehensive understanding of intensive LT after SCI.

The form and content of this abstract are approved. I recommend its publication.

Approved: Matthew Taylor
DEDICATION

This dissertation would not have been possible without tireless support from my friends and family. This work is dedicated to all of them.
TABLE OF CONTENTS

CHAPTER

I. INTRODUCTION ..................................................................................................................... 1

  Purpose of the Study ........................................................................................................... 10

  Specific Aims and Hypotheses ............................................................................................. 11

  Significance .......................................................................................................................... 14

  Summary ............................................................................................................................. 19

II. REVIEW OF RELATED LITERATURE ...................................................................................... 21

  Overview .............................................................................................................................. 21

  Literature Search Methods ................................................................................................. 24

  Literature Search Results .................................................................................................... 28

  Review of Literature ............................................................................................................ 28

    Case Studies/Case Series ................................................................................................... 28

    Prospective Cohort ........................................................................................................... 37

    Randomized Controlled Trials ........................................................................................ 43

    Systematic Reviews ........................................................................................................ 59

  Summary of Gaps in the Literature ..................................................................................... 60

III. METHODS .......................................................................................................................... 73

  Research Design and Data Collection .................................................................................. 73

  Sample Size and Power Analysis ........................................................................................ 78

  Analysis Plan ........................................................................................................................ 78

    Analysis Plan for Research Aim 1 and Hypothesis ............................................................. 79
Analysis Plan for Research Aim 2 and Hypothesis ............................................................... 83
Revised Methods .................................................................................................................. 86

IV. RESULTS OF ANALYSIS ........................................................................................................ 88

Variables at Discharge from Inpatient Rehabilitation ................................................................. 90
Unadjusted Outcomes ............................................................................................................. 91

Research Aim 1 ..................................................................................................................... 93

FIM Transfer Index ............................................................................................................. 98
FIM Locomotion and Stairs ................................................................................................. 100
Ability to walk >150 ft. with or without a mobility aide within the home ....................... 104
Ability to walk with or without a mobility aide one street block outside the home ... 107
Ability to walk with or without mobility aide up one flight of steps ............................ 108

Research Aim 2 .................................................................................................................. 111

Life Satisfaction ................................................................................................................. 111
Community Participation .................................................................................................. 113
Re-Hospitalization ............................................................................................................. 121

V. DISCUSSION ..................................................................................................................... 125

Baseline Comparison ......................................................................................................... 125
Primary Results .................................................................................................................. 127

Research Aim 1 (H1): FIM Total Motor Score, Transfer Index, Locomotion and Stairs... 128

FIM Total Motor Score ....................................................................................................... 128
FIM Locomotion and Stairs ............................................................................................... 132
FIM Transfer Index ........................................................................................................... 136
<table>
<thead>
<tr>
<th>Table</th>
<th>Description</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.1</td>
<td>Inclusion/Exclusion Criteria</td>
<td>74</td>
</tr>
<tr>
<td>3.2</td>
<td>Variable Matching</td>
<td>77</td>
</tr>
<tr>
<td>3.3</td>
<td>One Year Outcome Data Variables</td>
<td>80</td>
</tr>
<tr>
<td>4.1</td>
<td>Demographics for Cases and Controls</td>
<td>92</td>
</tr>
<tr>
<td>4.2</td>
<td>Variables at Discharge from Inpatient Rehabilitation</td>
<td>94</td>
</tr>
<tr>
<td>4.3</td>
<td>Unadjusted Comparisons of Continuous Outcomes at One year Follow-Up</td>
<td>95</td>
</tr>
<tr>
<td>4.4</td>
<td>Unadjusted Comparison of Dichotomous Outcomes at One Year Follow-Up</td>
<td>96</td>
</tr>
<tr>
<td>4.5</td>
<td>Unadjusted Comparison of Non-Parametric Data at One Year Follow-Up</td>
<td>97</td>
</tr>
<tr>
<td>4.6</td>
<td>Adjusted FIM Total Motor Score at One Year Follow-Up</td>
<td>99</td>
</tr>
<tr>
<td>4.7</td>
<td>Adjusted FIM Transfer Index at One Year Follow-Up</td>
<td>101</td>
</tr>
<tr>
<td>4.8</td>
<td>Adjusted FIM Locomotion and Stairs at One Year Follow-Up</td>
<td>102</td>
</tr>
<tr>
<td>4.9</td>
<td>Adjusted Odds Ratio of FIM Locomotion at One Year Follow-Up</td>
<td>105</td>
</tr>
<tr>
<td>4.10</td>
<td>Adjusted Odds Ratio of FIM Stairs at One Year Follow-Up</td>
<td>106</td>
</tr>
<tr>
<td>4.11</td>
<td>Adjusted Odds Ratio Walking 150ft in the Home at One Year Follow-Up</td>
<td>109</td>
</tr>
<tr>
<td>4.12</td>
<td>Adjusted Odds Ratio Walking 1 Block Outside at One Year Follow-Up</td>
<td>110</td>
</tr>
<tr>
<td>4.13</td>
<td>Adjusted Odds Ratio Walking One Flight of Stairs at One Year Follow-Up</td>
<td>112</td>
</tr>
<tr>
<td>4.14</td>
<td>Adjusted Life Satisfaction Scores at One Year Follow-Up</td>
<td>114</td>
</tr>
<tr>
<td>4.15</td>
<td>Adjusted CHART-SF Physical Independence Subscale at One Year Follow-Up</td>
<td>117</td>
</tr>
<tr>
<td>4.16</td>
<td>Adjusted CHART-SF Mobility Subscale at One Year Follow-Up</td>
<td>118</td>
</tr>
<tr>
<td>4.17</td>
<td>Adjusted CHART-SF Occupational Subscale at One Year Follow-Up</td>
<td>119</td>
</tr>
<tr>
<td>4.18</td>
<td>Adjusted CHART-SF Social Integration Subscale at One Year Follow-Up</td>
<td>120</td>
</tr>
</tbody>
</table>
Table 4.19 Adjusted Re-Hospitalization Numbers at One year Follow-Up......................... 123

Table 4.20 Adjusted Re-Hospitalization Days at One Year Follow-Up............................ 124
LIST OF FIGURES

Figure 1.1 Treadmill Training with Body Weight Support ...................................................... 10
Figure 1.2 Over Ground Walking Training ................................................................. 10
Figure 3.1 Data Retrieval Process .................................................................................... 75
Figure 4.1 Subject Allocation and Matching ................................................................. 89
ABBREVIATIONS

ADLs: Activities of Daily Living
AIS: ASIA Impairment Scale
ASIA: American Spinal Cord Injury Association
BBS: Berg Balance Scale
BWS: Body Weight Support
COPM: Canadian Occupational Performance Measure
CPG: Central Pattern Generator
CHART-SF: Craig Handicap Assessment and Reporting Technique - Short Form
CI: Confidence Interval
ft: Feet
FES: Functional Electrical Stimulation
FIM: Functional Independence Measure
ISNCSCI: International Standards for the Neurological Classification of Spinal Cord Injury
IQR: Interquartile Range
LEMS: Lower Extremity Motor Score
LOI: Level of Injury
LOS: Length of Stay
LR: Robotic Locomotor Training
LT: Locomotor Training
mEFAP: Modified Emory Functional Ambulation Profile

MID: Minimal Important Difference

m/s: meters per second

NRN: NeuroRecovery Network

NIDILRR: National Institute on Disability, Independent Living, and Rehabilitation Research

NSCISC: NIDILRR-funded National Spinal Cord Injury Statistical Center

OG: Over ground

QOL: Quality of Life

PD: Parkinson’s Disease

PT: Physical Therapy

RCT: Randomized Controlled Trial

SAWS: Satisfaction with Abilities and Well-Being Scale

SCI: Spinal Cord Injury

SCIM: Spinal Cord Independence Measure

SCIMS: Spinal Cord Injury Model Systems

SEIQoL: Schedule for the Evaluation of Individual Quality of Life

SF-36: Medical Outcomes Study 36-Item Short Form Health Survey

SE: Standard Error

SD: Standard Deviation

SWLS: Satisfaction With Life Scale

TBI: Traumatic Brain Injury

TM: Treadmill
TS: Treadmill Training with Electrical Stimulation

TRK: Overhead Track

US: United States

WCS: Walking Capacity Scale

WISCI: Walking Index for Spinal Cord Injury

10MWT: 10 Meter Walk Test

6minWT: 6 minute Walk Test

2minWT: 2 minute Walk Test
INTRODUCTION

Traumatic spinal cord injury (SCI) is a devastating condition that affects an individual’s physical, psychological, and social well-being. The annual incidence of SCI is 17,000 new cases per year, with an estimated 300,000 people living in the United States (US) with a SCI. The primary etiology for SCI is due to motor vehicle crashes (38%), followed by falls (30%), violence (14%), and recreational activities (9%). The mean age for individuals who sustain a SCI is 42 years old, and men incur approximately 80% of all injuries. In terms of level of injury and severity of injury, individuals diagnosed with incomplete tetraplegia (partial damage to the cervical spinal cord) make up the largest subgroup of this population at 45%, followed by incomplete paraplegia (partial damage to the thoracic and/or lumbar spinal cord) at 21%. Twenty percent of individuals with SCI are diagnosed with complete paraplegia (damage to the thoracic and/or lumbar spinal cord resulting in complete loss of sensory and motor activity below the lesion), while 14% are diagnosed with complete tetraplegia (damage to the cervical spinal cord resulting in complete loss of sensory and motor activity below the lesion).\(^1\)

Completeness and location of injury have a significant impact on the magnitude of limitations associated with activities of daily living in SCI. In general, when there is complete loss of sensory and motor activity transmitting through the injury site, individuals with higher levels of SCI (cervical region) will require more assistance for activities of daily living than those with lower levels of injury. Although there are many exceptions due to associated factors such as age, body morphology, and premorbid conditions, individuals
with complete SCIs are usually able to regain independence with self-care activities when their injuries occur in the thoracic and lumbar regions. Unfortunately, this is not the expectation for individuals with low cervical injury (C6-C8) as they may require assistance for bowel and bladder care as well as bathing. The outlook is even less optimistic for those with higher cervical injuries (C1-C5) who exhibit additional dependency in the areas of respiratory functioning, hygiene, writing, self-feeding, typing and operating a power wheelchair.²

Predicting who will achieve independence with mobility and activities of daily living after motor incomplete SCI (at least some motor and sensory information cross the injury site) is more difficult and is also impacted by severity of injury and location as well as gender, age, and premorbid health.³⁻⁵ Timing of recovery has also been shown to be impactful for long term walking ability as Fawcett et al⁶ reported 77% of significant improvement in neurologic functioning occurs within the first three months after SCI. Hicks et al⁴ recently introduced a simplified clinical prediction equation that uses three clinical variables assessed at hospital admission to predict independent ambulation after SCI which include the following: age (greater or less than 65 years old), strength in the quadriceps muscles, and light touch sensation over the calf area. This model demonstrated 85% accuracy with determining who would be walking independently at one year after injury with those who were less than 65 years old, exhibited greater strength in their quadriceps, and less sensory impairment over the calf area being more likely to be independent with walking at one year. Other studies have shown that individuals who recover the ability to accurately detect pain (using pin prick sensation) also have a better prognosis to recover
independent ambulation. Recovery of lower extremity motor function at one month post-injury has also been reported as a significant predictor of walking recovery. Waters et al. reported that the majority of individuals with SCI who achieve a score of at least 10 points on a lower extremity strength test by one month post-injury will be community walkers at one year post-injury. Zorner et al. reported that individuals who achieve 25 points on a lower extremity strength test by one month are able to walk at limited community speeds (0.6 m/s) by six months post-injury and that initial lower extremity strength score is the most significant predictor of independent walking.

The total cost attributed to SCI in the United States annually is over 45 billion dollars. The degree of disability, heavily influenced by severity and location of injury, is strongly associated with cost after SCI. The financial burden for individuals with high tetraplegia (C1-C4) who have non-functional strength in their lower extremities is expected to be over 1.1 million dollars the first year of injury with an estimated cost of $191,000 for each subsequent year. Individuals diagnosed with paraplegia (thoracic and lumbar injuries) who also have non-functional strength in their lower extremities are expected to incur a cost of $535,000 the first year estimating an additional $71,000 each year after. In comparison, the financial burden for individuals who are able to achieve functional strength in their lower extremities at any level of injury (cervical, thoracic or lumbar) is expected to be $359,000 during the first year of injury with an additional $43,000 each additional year. Therefore, research associated with helping individuals recover functional strength and independence will assist with reducing the overall cost of SCI for individuals and our health care system.
Sixty-six percent of all individuals who sustain a SCI annually are reported to have an incomplete lesion, signifying some sparing of the spinal neural connections throughout the nervous system.\textsuperscript{14} Individuals diagnosed with motor incomplete SCI are a specific subset of this population as they are known to have some existing descending neural pathways that can activate muscles below the neurologic level of injury.\textsuperscript{15} The International Standards for the Neurological Classification of SCI (ISNCSCI) is the standard tool utilized to classify severity and location of SCI and has excellent validity and reliability in this population.\textsuperscript{16} Individuals who sustain a motor incomplete SCI are categorized using the ISNCSCI as ASIA (American Spinal Cord Injury Association) impairment scale (AIS) C (less than half of the muscles below the level of injury are less than functional strength) or AIS D (half or more of the muscles below the level of injury have functional muscle strength). In terms of physical function, regaining walking ability is a primary goal for individuals diagnosed with an incomplete SCI.\textsuperscript{17,18}

Historically, walking recovery after SCI was considered limited for individuals with motor incomplete SCI if not achieved prior to leaving inpatient rehabilitation.\textsuperscript{19} Animal research published in the 1980s began to challenge this philosophy as evidence demonstrated that animals that underwent spinal cord transection were able to achieve recovery of standing and stepping activity in response to training on a treadmill in a supported therapeutic environment.\textsuperscript{20-24} Translation of the knowledge gained from animal studies to humans began in the early 1990s.\textsuperscript{25} Currently, there is a growing body of evidence published over the last 10-15 years suggesting the central nervous system is capable of synaptic plasticity and anatomical reorganization at both cortical and subcortical
levels after motor incomplete SCI in response to appropriate training that incorporated the concepts of motor learning theory into their interventions.\textsuperscript{26-30} The principles of motor learning include repetition, intensity, feedback, and task specific training. These are considered important components of intervention strategies designed to facilitate walking recovery after neurologic injury.\textsuperscript{31-33} These principles serve as the foundation for a more recent shift in the philosophical approach to SCI rehabilitation called activity-based therapy.

Activity-based therapy is focused on implementing interventions designed to minimize compensation and maximize recovery after neurologic insult by activating the neuromuscular system both above and below the injury level.\textsuperscript{34} A significant number of activity-based therapy interventions in SCI rehabilitation have been developed that concentrate on walking recovery. Locomotor training (LT) — the repetition of stepping-like patterning to promote walking recovery in either a body-weight supported (BWS) or a non-body-weight supported condition — has been a focus of activity-based therapy research to date. There is a growing evidence-base to support that various forms of LT may be effective in promoting walking recovery in individuals with motor incomplete SCI.\textsuperscript{26,28,35-41} Published literature supports that participation in intensive walking programs for this patient population may result in improved walking function including but not limited to speed, endurance, and independence.\textsuperscript{26,40-44}

Despite these successful outcomes, the integration of intensive LT largely remains outside the continuum of typical incomplete SCI rehabilitation in the outpatient setting. A significant shortcoming of the existing evidence is the lack of durability or the long-term benefit of intensive LT as studies have focused on short term gains (three months). In
addition, comparative studies between LT to usual care are lacking, leaving a significant gap in the literature. Therefore, these types of intensive LT protocols (up to 5 times per week for at least 60 sessions) are not yet considered usual care after motor incomplete SCI and are only offered at a limited number of rehabilitation centers across the US, as these intensive programs are also more costly in comparison to other more traditional therapy approaches.

Usual care after motor incomplete SCI is difficult to define and often encompasses a variety of interventions and strategies that are dictated by therapist experience and resource availability. Individuals with SCI receiving usual care are often taught how to compensate for their loss of function rather than focusing on maximizing recovery by activating neural pathways that survived the initial SCI lesion. For example, these individuals are often taught how to use a wheelchair for household and community mobility during rehabilitation rather than re-training the skill of walking even though they have remaining intact neural pathways to activate muscles below the level of their injury. This compensatory philosophy is very common when individuals are dependent for upright mobility and have limited capacity to step on their own, as a single physical therapist with limited technology may not be able to provide intensive LT practice in a safe manner. This lack of resource and technology may prevent optimization of physical recovery after SCI as it can be very difficult and labor intensive to provide individuals who are not yet walking or standing on their own with intensive walking practice. Physical therapy (PT) is reimbursed based on current procedural terminology codes which describe a procedure provided to the patient. The amount of reimbursement provided by these codes is not based on the expense associated with providing the intervention. Therefore, a facility or clinic providing
outpatient PT will receive the same reimbursement for providing care with one physical therapist not utilizing technology as they will for interventions that require multiple staff and expensive technology. The end result of usual care is potentially minimizing walking recovery which may have implications beyond mere physical limitation.46

In terms of dosing, usual care may also be defined by each individual’s insurance policy. For example, many policies have a maximum therapy cap of 20 outpatient therapy visits per year. Therefore, during the first year after injury patients receiving usual care may participate in therapy two to three times per week for eight to 10 weeks in an outpatient therapy program and then not receive therapy for the remainder of the year. Individuals receiving usual care often do not receive ongoing therapy after the first year of their injury, but instead only access therapy services when they experience a decline in health or need new equipment such as a wheelchair for mobility. Research has shown that limiting therapy visits especially in the first year after incomplete SCI may place an artificial ceiling on an individual’s long term ability for recovery.47

Community participation and social interaction are also negatively impacted by SCI and have been shown to contribute to negative consequences associated with overall well-being and depression.48 Functional impairment and activity limitations, such as walking ability after SCI, have been linked to lower community participation and serve as predictors for decreased quality of life (QOL).49,50 Re-hospitalization rates are high after SCI with more than 1/3 of individuals reporting being hospitalized one or more times annually due to SCI complications.18,51 Life expectancy for individuals with SCI is lower in comparison to those in the general population of similar age, gender, and race. In a recent study of individuals with
motor incomplete SCI who had functional strength (AIS D) below their level of injury (LOI), individuals who walked unaided had an average 10% life expectancy reduction, while those who required a wheelchair for locomotion had an average 25% life expectancy reduction compared to the general population.\textsuperscript{52} Therefore, developing intervention strategies that positively impact mobility, psychosocial, and health outcomes after SCI continues to be an important focus of rehabilitation program development and research.

The SCI Model Systems (SCIMS) Program was established by the National Institute on Disability, Independent Living, and Rehabilitation Research (NIDILRR, formally NIDRR) in 1970 to study the course and recovery of outcomes following a comprehensive multi-disciplinary approach to the care of individuals following SCI.\textsuperscript{53} Data obtained from specialized SCI rehabilitation centers in the Model Systems has been collected and maintained by the NIDILRR-funded National SCI Statistical Center (NSCISC) since 1974. Currently, there are 14 centers across the US who submit data to the NSCISC and who collaborate in research efforts designed to improve rehabilitation interventions as well as the overall QOL for individuals with SCI. Data for all centers is obtained at admission and discharge from inpatient rehabilitation as well as at one year (+/- 6 months) 1 and 5 years post-injury and then every 5 years thereafter. All sites then submit this data to the NSCISC centralized database in Birmingham, Alabama. The following outcomes are tracked longitudinally at all SCIMS centers: work and income; QOL; perception of health; pain; medical history; re-hospitalizations; and mobility.\textsuperscript{53} Model systems data provides a subjective overview of an individual’s mobility, level of independence, health, and psychosocial well-being after sustaining a SCI.
The NeuroRecovery Network (NRN) is a collaboration of centers established by the Christopher and Dana Reeve Foundation in 2004. The focus of this network is to implement systematic and standardized intervention protocols designed to maximize recovery after SCI across multiple centers in the United States who specialize in SCI rehabilitation. The overarching goal of this network is to improve functional outcomes and QOL after SCI. The NRN LT protocol has been implemented in a standardized manner at six centers across the United States and includes 55 minutes of repetitive stepping on a treadmill with BWS (Figure 1.1) followed immediately by 30 minutes of over ground (OG) walking training (Figure 1.2) at a frequency of 5 days/week in an outpatient rehabilitation program. This program is reimbursed by insurance so the number of total visits/weeks of therapy is dependent on the parameters of the individual’s policy as well as their ability to make functional progress to justify a continuation of therapy. Only individuals who have a traumatic SCI and have completed inpatient rehabilitation are considered for enrollment in this program. Standardization of this protocol includes assessment, treatment progression, discharge considerations, and program evaluation based on neurologic function and QOL indicators.

Multiple studies have been published describing and providing evidence for the standardization of the NRN LT protocol as well as reporting improved walking outcomes from participation in this protocol. The NRN protocol represents a well-controlled model incorporating the principles of motor learning into an intensive LT program within the first year after SCI. The six NRN centers are also SCIMS Centers and have contributed data to both databases since 2005.
Purpose of the Study

The primary purpose of this study is to compare one year post-injury outcomes data between individuals who completed the NRN LT protocol to that of matched controls who received usual care. The central hypothesis for this study is that individuals with motor
incomplete SCI who participated in the NRN LT protocol during post-acute rehabilitation will demonstrate superior long term (one year post-injury) mobility outcomes, QOL, community participation, and decreased re-hospitalization rates in comparison to those who received usual care. Mobility will be evaluated using the Functional Independence Measures (FIM). QOL will be evaluated using the Satisfaction with Life Scale (SWLS) and the Craig Handicap Assessment and Reporting Technique (CHART) - Short Form (SF) will be utilized to evaluate community participation after SCI. The number of times each individual required re-hospitalization and the number of days associated with each re-hospitalization will be compared between individuals who received intensive LT in the NRN and those who did not to gain a better understanding of overall health and mobility between the two groups.

Patient factors that will be considered in the analysis will include employment status, family income, and type of health insurance. Clinical characteristics that will be considered in the analysis will include independence at discharge from inpatient rehabilitation and prior health care status. The specific aims and hypothesis addressed in this study are listed below.

**Specific Aims and Hypotheses**

Research Aim 1: To evaluate and compare one year post-injury mobility outcomes from the SCIMS database for individuals with motor incomplete SCI who received the NRN LT protocol (cases) in post-acute rehabilitation and individuals who received usual care (controls) matched on age, gender, injury year, NRN center, motor function (AIS C or D), and mode of mobility at discharge from inpatient rehabilitation.
**H₁**: Individuals with motor incomplete SCI who received the NRN LT protocol will demonstrate higher FIM$_{57}$ motor scores (total motor score, locomotion, transfer index and stairs) in comparison to individuals with motor incomplete SCI who received usual care matched on age, gender, injury year, NRN center, motor function (AIS C or D), and mode of mobility at discharge from inpatient rehabilitation and adjusting for additional important patient and clinical characteristics.

**H₂**: At one year post-injury individuals with motor incomplete SCI who received the NRN LT protocol will demonstrate greater odds of being able to walk in the home, community, and up a flight of steps in comparison to individuals with motor incomplete SCI who received usual care matched on age, gender, injury year, NRN center, motor function (AIS C or D), and mode of mobility at discharge from inpatient rehabilitation adjusting for additional important patient and clinical characteristics.

1. Ability to walk >150 feet (ft) with or without a mobility aide within the home;
2. Ability to walk with or without a mobility aide one street block outside the home; and
3. Ability to walk with or without mobility aide up one flight of steps.

Research Aim 2: To evaluate and compare one year post-injury re-hospitalizations, QOL, and community participation outcomes between individuals with motor incomplete SCI who received the NRN LT protocol (cases) in post-acute rehabilitation and individuals who
received usual care (controls) matched on age, gender, injury year, NRN center, motor function (AIS C or D), and mode of mobility at discharge from inpatient rehabilitation adjusting for additional important patient and clinical characteristics.

**H$_2$1**: Individuals with motor incomplete SCI, who received the NRN LT protocol will report better QOL as measured by the SWLS$^{60}$ in comparison to individuals with motor incomplete SCI who received usual care matched on age, gender, injury year, NRN center, motor function (AIS C or D), and mode of mobility at discharge from inpatient rehabilitation adjusting for additional important patient and clinical characteristics.

**H$_2$2**: Individuals with motor incomplete SCI, who received the NRN LT protocol will report better community participation as measured by the CHART-SF$^{61}$ in comparison to individuals with motor incomplete SCI who received usual care matched on age, gender, injury year, NRN center, motor function (AIS C or D), and mode of mobility at discharge from inpatient rehabilitation adjusting for additional important patient and clinical characteristics.

**H$_2$3**: Individuals with motor incomplete SCI, who received the NRN LT protocol will report decreased number of re-hospitalizations and decreased numbers of days re-hospitalized during the first year after SCI in comparison to individuals with motor incomplete SCI who received usual care matched on age, gender, injury year, NRN center, motor function (AIS C or D), and mode of mobility at discharge from inpatient rehabilitation adjusting for additional important patient and clinical characteristics.
Significance

SCI is a devastating condition with permanent consequences that affects not only the person who sustains the injury, but also their family. Patients and families are often willing to endure significant financial and emotional burden if they believe a specific intervention or rehabilitation strategy will improve their long term physical outcome and QOL while also incurring the many other healthcare costs they’re facing (durable medical equipment, home modifications, caregiver assistance and more). As resources are constrained and often limited in the traditional rehabilitation delivery system the problem is compounded. Intensive LT provided through the NRN protocol is thought by many to provide the most optimal opportunity to regain walking function after motor incomplete SCI. Currently, there are only six centers across the US who provide the NRN LT protocol to individuals in post-acute rehabilitation for SCI and it is done outside the context of usual care. These clinical programs are offered in outpatient rehabilitation and are reimbursed by private insurance. However, because insurance reimbursement does not adequately cover the labor and technology expense associated with these programs, the centers that belong to the NRN are also provided with a stipend to reimburse for the data they submit to the network which helps to offset some of these costs. Because this program is only offered at six centers in the US, many newly injured patients and their families each year are challenged with the additional cost and impact of relocating to one of the six cities in the US who provide this care or living with the concern they were not provided with the best opportunity to maximize recovery after SCI.
Financial burden, due to lack of adequate insurance payer coverage, technology prices, and high labor utilization are likely the primary barriers preventing widespread adoption of the NRN LT program by rehabilitation facilities and hospitals. Even though LT studies have demonstrated short term mobility improvements that exceeded historically reported outcomes and expectations in both acute and chronic SCI,6,47,63,64 the financial challenge associated with implementing these programs is significant due to labor and technology utilization. This intervention requires four paid staff members to provide each training session along with a treadmill system which has a built in weight support mechanism that costs approximately $100,000. While the intervention costs significantly more to provide to each patient, insurance reimbursement rates remain the same for this intervention as they are for conventional therapy conducted by one therapist. Many rehabilitation facilities do not have the resources to staff this type of program or purchase the required capital equipment especially given that reimbursement rates remain the same for those facilities who provide usual care and those who implement the NRN LT protocol. Morrison et al62 reported that on average facilities providing the NRN LT protocol should expect a 19% profit margin when reimbursed by private insurance while also expecting a 58% profit loss, and a 65% profit loss when delivering this intervention to Medicare and Medicaid recipients, respectively. This is evidence that the staffing and technology required to provide LT to individuals with Medicare and Medicaid is greater than the insurance reimbursement received for these services as they provide lower reimbursement amounts than private insurance does for the same services.
Clearly there is misalignment in what is being delivered to patients and the evidence-base in terms of maximizing recovery. This is largely driven by the financial viability of implementing an intensive LT program under the current reimbursement system. The payers are driving for lasting benefit for their patients that are also fiscally acceptable (reasonable and necessary). The patients are caught in the middle as their primary interest for maximized recovery is limited by the cost and accessibility to these programs. Morrison et al\textsuperscript{65} published a case series on two individuals with incomplete SCI projecting lifetime care costs associated with their injury prior to initiating the NRN LT protocol and then again immediately after completing the NRN LT protocol. They reported significant life time care cost reductions (projected minus actual) in both individuals with SCI after receiving the NRN LT protocol.\textsuperscript{65} This report shows promise that there may be return for the payers for this investment as the upfront cost associated with this rehabilitation approach may be more than ameliorated by improving functional mobility and independence soon after SCI. However, to date, there have been no published reports of the long term (one year post-injury) differences between those who received intensive LT and those who received usual care representing a critical gap for durability of outcome. With consideration for the patients, the payers, and the providers quantifying the durability of gains long term and potential cost savings e.g. re-hospitalization rates for intensive LT outcomes (mobility, psychosocial, and health outcomes) in comparison to usual care could significantly impact the following:

1) Clinical decision making in post-acute SCI rehabilitation;
2) Payer policy relative to intensive LT after SCI;
3) Quantifying the benefit of intensive LT post SCI for patients/families; and

4) Provide a rationale for conducting a prospective investigation on delivering intensive LT post-SCI with long-term follow-up on outcomes.

Ultimately the future of programs like the NRN will depend on the affordability (provider and patient) and in turn the accessibility. The key drivers to grow these programs is to demonstrate their value in the rehabilitation process. It is also important to determine if there is reasonable cause and rationale to conduct an expensive prospective RCT directly comparing outcomes between the NRN LT protocol and usual care.

The findings from this study may have an important impact on the many stakeholders associated with SCI rehabilitation including patients, families, clinicians, and insurance companies. First, these results may be helpful in improving access to this type of rehabilitation for patients who are not able to receive rehabilitation at the six centers currently offering the NRN protocol in the US. Other rehabilitation centers who market to individuals and families who have sustained a SCI may be compelled to start providing these programs to maintain their referral base in the event that these findings are favorable for those patients who received the NRN LT protocol. This may positively affect patients and families as they may be able to receive these services closer to home rather than managing the emotional and financial burden of living away from home and family for an extended period of time while participating in this program. Although most clinicians who treat individuals with motor incomplete SCI are supportive of LT, finding a difference in outcomes between these two groups at one year post-injury may increase clinician advocacy for their patients to have the opportunity to participate in this program at their own facility.
Demonstrating favorable differences in mobility, QOL, community participation, and/or re-hospitalization for those who received the NRN LT protocol may also convince insurance companies that reimbursing for these services immediately after inpatient rehabilitation may save them money in the future due to improved long term health and mobility for these patients. Favorable differences may also persuade the Centers for Medicare & Medicaid Services to increase their reimbursement rates for LT so that more rehabilitation facilities are able to provide these services without enduring a financial deficit. Finally, the questions guiding this dissertation have evolved from countless discussions I have had with patients and families who have been impacted by SCI. Over 50% of the patients who receive care at Craig Hospital are from outside the state of Colorado, so, even though Craig is one of the few centers that offers the NRN LT program, many patients and families at Craig are often faced with the same challenges of living away from home in order to participate in this program. They seek my counsel regarding the importance of problem-solving the short term burden of living away from home in exchange for maximizing their long-term outcomes. The results of this study may provide objective data for future patients and families to consider when they are making these decisions.

Currently, I rely on sharing information that has been obtained from observing individuals who have participated in the NRN program at Craig to help educate patients and families about these decisions. One of the first patients who completed the NRN program at Craig was a 32 year-old father of two small children who sustained a C4 motor incomplete SCI (AIS C). At the time of discharge from inpatient rehabilitation, he was completely dependent for transfers, bed mobility and self-care (bowel and bladder management). He
was unable to walk and required the use of a power wheelchair for household and community mobility. He was unable to watch his children independently and was not able to return to work as a software engineer. At the beginning of the NRN program he reported the following goals: 1) Walk independently; 2) Independent bowel and bladder management; 3) Able to manage the physical demands of watching his two small children; and 4) Return to work. After completing the NRN LT program, he met all four of these goals which is not commonly observed in individuals with high cervical SCIs. There have been other patients who have also demonstrated very positive outcomes in the NRN program and these case studies guide prospective patient/family conversations. The results from this study will go beyond anecdotal evidence to help guide these conversations in the future.

**Summary**

Individuals who sustain a SCI often experience a variety of negative consequences including but not limited to loss of upright mobility and independence as well as decreased QOL, limited community participation, and higher re-hospitalization rates than their able-bodied counterparts. The primary goal of activity-based therapy approaches is to maximize recovery after neurologic insult including SCI. Intensive LT utilizing a treadmill and BWS followed immediately by OG walking training (NRN protocol) is an activity-based therapy approach that has been shown to improve walking speed, independence and endurance on the shorter term in individuals with motor incomplete SCI. This protocol is only provided at six centers across the US so many individuals who sustain SCIs either do not have access to this intensive LT protocol or they may choose to relocate to a city that provides this option potentially incurring significant financial and emotional burden for them and their family.
This intervention is significantly more expensive for rehabilitation centers to provide due to resource requirements and technology utilization along with limited reimbursement. This has likely prevented widespread adoption of this rehabilitation approach. Even though short term walking benefits have been reported from this intervention, there has been no long term (one year) assessment of these gains and there has been no direct comparison to usual care. There has also been inadequate evaluation of the effects of LT on psychosocial factors, community involvement, and medical complications requiring re-hospitalization. These are the primary gaps in the literature this research will focus on.
CHAPTER II
REVIEW OF RELATED LITERATURE

Overview

This chapter presents existing research related to the two research aims previously outlined and includes a comprehensive review of the literature. An initial literature search was completed to obtain a broad understanding of the types of interventions being offered to individuals after SCI with a primary goal of also defining usual care. A goal within this search was to better understand the long-term impact on health, mobility and QOL that sustaining a SCI may have and to appreciate how these factors may influence life expectancy. The search was then narrowed to concentrate more specifically on recovery-focused interventions implemented after SCI and especially those that have been shown to reinforce motor learning principles after SCI. Finally, the search was restricted to what has been published regarding the impact of LT after motor incomplete SCI and included a parallel investigation into the financial cost associated with LT as well as the potential financial gain from participating in LT interventions. Therefore, the majority of this review will emphasize studies evaluating various forms of LT utilized in SCI rehabilitation and their impact on mobility, psychosocial outcomes, and medical complications. A literature review was conducted to understand the following:

- PT interventions offered after SCI
- Rehabilitation practices after SCI
- Usual care after SCI
- The history and development of LT interventions being offered after SCI
The impact LT interventions have on mobility outcomes after SCI
The impact LT interventions have on QOL after SCI
The impact LT interventions have on community participation after SCI
The impact LT interventions have on health after SCI

The literature referenced in the first chapter was obtained primarily from completing a broad search on the current state of SCI rehabilitation and research as well as data on long term health complications and life expectancy associated with SCI. It also included known data on the financial impact associated with recovery-based interventions after SCI. Finally, a search was also conducted to examine LT utilization in other neurologic populations. Although there are small LT studies in traumatic brain injury (TBI)\textsuperscript{66-72} and Parkinson’s Disease (PD),\textsuperscript{73-77} two large RCTs\textsuperscript{78,79} and a secondary analysis\textsuperscript{80} in stroke were found and included in this review to provide context for this intervention in another neurologic condition.

Sullivan et al\textsuperscript{79} completed a randomized controlled trial (RCT) in 2007 with 80 adult stroke survivors comparing the effects of treadmill training with BWS in combination with a variety of aerobic and extremity strengthening exercises (upper extremity strengthening, lower extremity strengthening, lower extremity cycling). They reported that all individuals in the trial receiving treadmill training with BWS demonstrated significant improvements in walking function regardless of the training approach that was delivered in combination. Duncan et al\textsuperscript{78} published a RCT in 2011 which evaluated three forms of LT in 408 individuals who had sustained a stroke. Individuals in this trial were randomized into one of the
following three training groups and all groups completed 36 total sessions of training over a
12-16 week period: treadmill training with BWS two months after stroke; treadmill training
with BWS six months after stroke; physical therapy (PT) in the home two months after
stroke. These authors reported that at one year follow-up, 52% of all individuals had
significantly improved their walking ability regardless of which type of training they received
suggesting the gains made during the training paradigms were durable in the majority of
subjects who completed the trial at one year.

Nadeau et al\(^8\) completed a follow-up analysis from this study comparing the LT
group and the home-based PT group in the previous trial to usual care. They reported that
subjects receiving LT were 18% more likely to transition to a higher functional walking level
than subjects receiving usual care, and home-based PT subjects were 17% more likely to
transition to a higher level of walking than subjects receiving usual care. They also reported
mean gain in walking speed in the LT subjects was 0.13 meters per second (m/s) greater
that those receiving usual care and it was 0.10m/s greater for those receiving home-based
PT than those who received usual care. These authors concluded that intensive PT, utilizing
treadmill training with BWS or home-based PT focused on walking, strength, and balance
exercises was superior to usual care in improving walking, regardless of severity of initial
impairment. Although these results were achieved in the stroke population, they support
that intensive training after neurologic injury demonstrated durability of gains at one year
in the majority of this large population of stroke survivors and that usual care was not
enough to maximize walking recovery in comparison to intensive therapy approaches.
This section “Review of Literature” presents existing literature relevant to this dissertation specific to SCI, separated by research design. The chapter concludes with a summary of what is already known and identifies the gaps in the literature filled by this research.

**Literature Search Methods**

This literature review was conducted to identify relevant peer-reviewed publications from multiple domains including, but not limited to: rehabilitation, neuro-trauma, and PT. A narrative review of the literature was conducted using a variety of search terms to ensure that all relevant information could be identified. Searches were conducted on PubMed, Cochrane Library, and PEDro databases to identify pertinent studies. Search terms included words or phrases related to SCI or treadmill training with BWS including but not limited to the following:

- ‘activity-based therapy’ and ‘spinal cord injury’
- ‘locomotor training’ and ‘spinal cord injury’
- ‘treadmill training with body weight support’ and ‘spinal cord injury’
- ‘treadmill training with body weight support’ and ‘stroke’
- ‘walking’ and ‘spinal cord injury’
- ‘ambulation’ and ‘spinal cord injury’
- ‘mobility’ and ‘spinal cord injury’
- ‘activities of daily living’ and ‘spinal cord injury’
- ‘recovery of function’ and ‘spinal cord injury’
Article titles and abstracts were first screened to identify relevant studies. Full article copies of peer-reviewed relevant studies were obtained and reference lists were screened to identify other significant studies that met criteria for inclusion into the review. The following criteria was utilized for inclusion into this review:

**Design:** All study types

**Timeframe:** Studies included in this review were published during or after 2000 through 2018.

**Participants:**
- Adults (>18 yo)
- Diagnosed with traumatic SCI
- Paraplegia or tetraplegia
- AIS grades C or D or a sample where > 50% of the sample were grades C or D (motor incomplete)
**Intervention:**
- Interventions included forms of locomotor training with manual assistance
  - Treadmill training with body weight support and manual assistance
  - Treadmill training without body weight support and manual assistance
  - Over ground training with body weight support and manual assistance
  - Over ground training without body weight support and manual assistance
  - Treadmill training and/or over ground training augmented with electrical stimulation
  - Locomotor training with robotic assistance only included when studies were comparing various forms of locomotor training which included manual and/or over ground training
  - Studies only implementing locomotor training with robotic assistance were not included in this review as they are not relevant to the current topic
Outcome Measures:

- Mobility outcomes
  - Walking independence: Spinal Cord Independence Measure (SCIM); Functional Independence Measure (FIM); Modified Emory Functional Ambulation Profile (mEFAP); Walking Index for Spinal Cord Injury (WISCI)
  - Balance: Berg Balance Scale (BBS); Tinetti Scale
  - Walking speed: 10 meter walk test (10MWT)
  - Walking endurance: 6 minute walk test (6minWT); 2 minute walk test (2minWT)

- Strength outcomes: lower extremity motor score (LEMS)

- Psychosocial outcomes:
  - Community participation: Craig Handicap Assessment and Reporting Technique (CHART)
  - Quality of Life: Satisfaction with physical functioning; Satisfaction with Life Scale (SWLS); Satisfaction with Abilities and Well-being Scale (SAWS); Quality of Life Spinal Cord Injury Version III; Medical Outcomes Study 36-Item Short Form Health Survey (SF-36)
  - Health outcomes: re-hospitalization rates

Articles evaluating LT with robotic assistance were not included in this review as this intervention is not considered usual care after SCI rehabilitation and it is not included in the NRN LT protocol.
Literature Search Results

Over 75 peer-reviewed publications were identified and screened for relevance. Approximately 32 publications were reviewed in full and almost all met inclusion criteria to include in this work. Throughout the development of this research, the literature review was refreshed as publications became available that introduced concepts or opinions not already present.

Review of Literature

Studies will be discussed and reviewed based on hierarchy of research design: Case studies/Case Series; Prospective longitudinal cohort studies; RCTs; and Systematic Reviews.

Case Studies/Case Series

Behrman and Harkema\textsuperscript{39} published a case series describing LT using a treadmill with BWS followed by OG walking training for individuals with SCI in 2000. They reported on four individuals averaging six months post SCI who completed LT on a treadmill with BWS and assistance provided by manual trainers. Their protocol also included OG training immediately following treadmill training once subjects were able to achieve the ability to maintain standing on the treadmill supporting 80\% of their own body weight. The first subject was diagnosed with an injury to the 5\textsuperscript{th} thoracic vertebra and AIS A SCI (motor and sensory complete injury) with a LEMS of 0/50 meaning she had no voluntary motor activity in her lower extremities.\textsuperscript{81} She completed 85 sessions of treadmill training with BWS and her LEMS remained a 0/50 at completion of the training. She did not participate in OG walking training as she was not able to support her weight on the treadmill without BWS;
scores evaluating independence with walking did not demonstrate change in response to this training.

The second subject sustained an injury at the 5th thoracic vertebra AIS C injury approximately one month earlier and presented with a LEMS of 2/50 meaning that the individual only had the ability to activate two lower extremity muscles prior to training and those muscles were not strong enough to move against gravity. He completed 64 sessions of treadmill training with BWS followed immediately by OG training and he demonstrated a variety of improvements including the following: transitioned from AIS C to AIS D; LEMS improved from 2/50 to 38/50 demonstrating a large improvement in lower extremity muscle strength; and he achieved the ability to walk OG with a single point cane leading to an improvement in walking independence (improved FIM score from 2 to 6 meaning that he required two people to safely assist him with walking prior to training and he was able to walk independently using a cane after training). This allowed to him to walk in the community on his own with the cane and to climb stairs without assistance. He also achieved the ability to walk ~0.75 meters per second (m/s) which is considered appropriate speed for full-time community ambulation, but is still not considered normal walking speed of walking of 1.2m/s.

The third subject was diagnosed with a SCI at the 6th cervical vertebra AIS D eight months earlier with a LEMS of 32/50 meaning that he could activate the majority of his lower extremity muscles at the start of training, but most of these muscles were limited in strength which can make walking challenging and slow. He walked at 0.09m/s prior to starting the trial which placed him in the category of household ambulation only and he
scored a 30/56 on the BBS which placed him below the mean score published for individuals walking independently in the community demonstrating more impaired balance.\textsuperscript{84} He completed 27 sessions of treadmill training with BWS and manual assistance followed immediately by OG walking training and his LEMS improved to a 34/50 post training meaning that two of his lower extremity muscles demonstrated improved strength in response to training, but the majority of muscles did not show a strength improvement in response to training. He was able to achieve the ability to walk full-time with forearm crutches and his walking independence score (FIM) improved from a 3 to a 6 meaning that he required moderate (>50\%) assistance of one person to ambulate prior to training and was able to ambulate independently using forearm crutches after training. His final OG walking speed was 0.50m/s placing him in the category of limited community ambulation.\textsuperscript{82} He also demonstrated balance improvements increasing his BBS score to 43/56 which is above the mean score for individuals with SCI walking independently in the community.\textsuperscript{84} Finally, in terms of health-status benefits, his SF-36 physical function score improved from 10\% at the start of the trial to 20\% after completing the trial demonstrating that his health status after training did not limit his activities as much as it did prior to training.\textsuperscript{85} In terms of community participation, his CHART-SF Mobility Subscale score improved from 76 at the start of the trial to 89 after training illustrating an increase in self-rated community participation.\textsuperscript{61}

Finally, the fourth subject was diagnosed with a SCI at the 9\textsuperscript{th} thoracic vertebra AIS D nine months prior to starting LT. He started the training with a LEMS of 46/50 meaning that most of the muscles in his lower extremities demonstrated full strength\textsuperscript{81} and finished the
training with the same score suggesting that this training had no effect on his lower extremity muscle strength given that he started the trial with close to normal muscle strength. He was able to improve his walking independence score from a 6 pre-training to a 7 post-training representing that he was able to walk independently pre-training, but required more than a reasonable amount of time to do this and was able to progress to walking at normal speeds by the end of the trial. His walking speed improved from 0.6m/s pre-training to 1.2m/s post-training which progressed him from the walking category of limited household ambulation to the category of full-time community ambulation. There was only one subject in this study who received follow-up testing at four months which demonstrated this subject was able to maintain and build on these gains in walking speed as he was ambulating at 1.3m/s at his follow-up evaluation. Psychosocial and balance outcomes were not reported for this subject.

This was one of the first case series published on LT and demonstrated feasibility with this new intervention and also presented innovative perspectives about facilitating walking recovery after SCI. The first being that if someone sustains a motor incomplete SCI (AIS C or D), a combined approach of intensive repetition of walking (treadmill training with BWS) along with task specific training (OG walking) may result in improved walking function (independence, speed and balance). This type of training may also have a positive impact on psychosocial outcomes such as perceived physical disability and community participation. Conversely, the authors also bring forward the thought that severity of injury may be the primary factor predicting outcome and individuals with the most severe SCIs (motor and sensory complete) may not be able to improve walking function in response to
The third and most novel idea proposed in this case series was that traditional therapy or usual care may not be enough to promote maximal walking recovery after SCI. All three of these subjects who demonstrated improvements in their ability to walk OG had already completed traditional inpatient and outpatient therapy prior to this study, yet still demonstrated additional walking improvements in response to this intensive training protocol.

A larger case series (n=19) focused on treadmill training with BWS was then published in 2001 by Field-Fote. She reported a similar protocol as the previous authors utilizing treadmill training with BWS while also adding functional electrical stimulation (FES) to the peroneal nerve to assist with swing phase initiation when subjects were stepping on the treadmill. Another difference from the previous publication was that treadmill training was not followed by OG training in this protocol. Therefore, this training was focused on the repetition of stepping augmented with FES but did not incorporate task specific (OG) training. Subjects trained for 1.5 hours per day at a frequency of three days per week for a period of 12 weeks. All subjects enrolled in this study were AIS C (more than ½ of key muscles below the LOI have less than functional muscle strength) and were chronic injuries with a mean time since injury of 56 months (12-171 months). A pre- and post-training comparison was completed on the main outcome measures which included walking speed and LEMS. A significant change in mean walking speed was reported for the group (0.12 +/- 0.8m/s to 0.21 +/- 0.15m/s p=0.0008). Even though significant changes in walking speed were achieved in this study, the final mean walking speed of 0.21m/s is very slow and
individuals who walk at that speed are considered limited household ambulators without the ability to walk in the community. A significant change in LEMS was also noted in this cohort, but there was little to no correlation between the change in OG walking speed and the change in LEMS ($r=-0.16$) demonstrating that the change in strength may not be responsible for the improvement in OG walking speed. These findings strengthened one of the first discussion points made by Behrman and Harkema in the previously discussed study which was that severity of injury may be the most significant predictor of walking recovery. The subjects in this study were all diagnosed with AIS C injuries at the beginning of the study meaning they had more severe injuries than the three individuals with AIS D SCIs from the previous study who all gained independent community ambulatory status (walking $>0.8\text{m/s}$). Another important discussion point that emerged from this study was that individuals who have chronic SCIs (greater than one year post-injury) may also have less potential for recovery of walking than individuals who are still in the acute and subacute stages of recovery (less than one year post-injury). In terms of follow-up, this study also brought four subjects (the only subjects who lived locally) back in for follow-up walking assessments from two months to one year after completing the study and reported that three out of the four subjects met or exceeded the gains achieved during the study. The fourth individual who had not maintained gains from the study had also undergone further surgery since participating in the study which had resulted in a prolonged period of time that he was unable to ambulate. The findings from the small number of subjects who returned for follow-up suggest that
durability of these gains may depend on an individual’s ability to continue walking on their own after study completion.

Effing et al\textsuperscript{87} published a case series in 2006 evaluating treadmill training with BWS in three individuals with chronic motor incomplete SCI (AIS C n=2; AIS D n=1). All subjects were greater than 48 months post-injury and completed 12 weeks of LT with BWS five times per week for 30 minutes per day. Follow-up assessments were also completed at six months post study. The following mobility and QOL outcomes were assessed in this trial: Schedule for the Evaluation of Individual QOL (SEIQoL); Canadian Occupational Performance Measure (COPM) rating perceived difficulty with performing self-care, productivity and leisure; Walking Capability Scale (WCS) evaluating support needed for walking; BBS assessing balance; walking speed (7 meter walking test); and Get up and Go test (measuring balance and mobility). Throughout the 12 weeks of training, the goal was to reduce BWS and to increase the speed of walking on the treadmill while utilizing the assistance of three trainers. Subject one reported a statistically significant improvement in QOL after the intervention ($p<0.05$) and these gains were maintain at the six month follow-up assessment. Walking speed, balance and mobility also demonstrated significant improvements after the intervention phase and were maintained at the six month follow-up assessment. Walking support as measured by the WCS did not change after the intervention phase and remained stable at the follow-up assessment.

QOL for the second subject remained unchanged from pre-training to the follow-up assessment. However, his perceived performance on activities of self-care (COPM) improved significantly after the intervention, but these gains were not maintained at six
month follow-up. The subject’s walking performance (WCS) and balance (BBS) demonstrated significant improvement that was maintained through the follow-up period. Subject three reported no difference in QOL immediately after training, but then reported improvement during the follow-up assessment. He reported an improvement in COPM which was maintained through the follow-up period and demonstrated an improvement in the WCS, walking speed and BBS, but these did not persist through the follow-up period and he returned to baseline performance.

Overall, these authors report seeing positive trends in QOL in response to LT with BWS, but there was no consistency among the subjects and they suggest that a RCT needs to be completed before conclusions can be made. They also reported a concern that their QOL measure (SEIQoL) may not have been sensitive enough to pick up changes in their subjects. They suggest that including an OG walking component in their training strategy may have resulted in more consistent reports of improved QOL as subjects may have been able to more directly connect the training to improved functioning and QOL. Finally, they conclude that understanding the comprehensive effects of LT in SCI must also include an appreciation of psychosocial health as well as physical mobility.

Musselman et al,\textsuperscript{88} published a case series in 2009 evaluating treadmill training with BWS versus OG skill training in four individuals with chronic (median 2.7 years post-injury) motor incomplete SCI. In phase one, all four individuals started with three months of treadmill training with BWS. In phase two, subjects one and two then received three months of OG skill-based training (obstacle management, task specificity, community mobility) while subjects three and four received another three months of treadmill training
with BWS. In the final phase of treatment subjects switched to the opposite intervention from phase two and completed a final three months of training. All subjects received at least nine months of total training and the frequency of training was five days per week. Evaluations were completed pre-training, monthly, post-training (after each phase) and at three months after study completion.

At the end of nine months of training, all subjects met or exceeded the minimal clinically important difference in walking speed of 0.05m/s\textsuperscript{89} which when analyzed as a group appeared to be greater during skill-based training (0.09m/s) than during treadmill training with BWS (0.01m/s). Two subjects demonstrated consistent improvements during both skill-based training and treadmill training with BWS phases, while two subjects demonstrated greater gains during skill-based training phase only. All four subjects also demonstrated modest gains in the mEAFP (skilled walking), 6minWT (walking endurance) and modest gains in balance (BBS). An interesting finding from this study was that all four subjects continued to demonstrate improvements throughout the nine months of active intervention. Specifically, two of these subjects didn’t begin showing changes until after completing the initial three months of training so these authors suggest that standard of care should provide continued therapy beyond three months of outpatient therapy which is not typically offered. These findings support earlier findings by Hicks et al\textsuperscript{90} in which about half of their cohort of subjects with SCI continued to demonstrate walking-related improvements throughout 12 months of treadmill training with BWS. Another significant finding from this study was that three out of the four subjects demonstrated retention of walking gains at three months post study completion. The three subjects who
demonstrated durability of gains reported they had continued to walk consistently at home after study completion. The subject who did not demonstrate good retention of gains at three months had the slowest walking speed at study completion (0.15m/s) which is considered a very limited household ambulation speed. This subject also reported no walking at home after study completion and suggests there may be a minimum walking speed that needs to be obtained before it is realistic for individuals to carryover walking practice to the home environment. This follow-up data supports the motor learning principle of “use it or lose it” demonstrating that if individuals do not use the motor ability they achieve, they will likely lose this ability as a dormant central nervous system (CNS) leads to further loss in function.

Prospective Cohort

Hicks et al published a prospective longitudinal study in 2005 evaluating long term BWS treadmill training in individuals with chronic SCI. Their goals were to determine the effects of a one year training program on functional walking ability and QOL in individuals with chronic SCI, along with an evaluation of whether gains made during this training were durable. Fourteen individuals with incomplete SCI AIS B (no motor activity below the LOI, but intact sensory system to the sacral nerve roots) and AIS C were enrolled in this study with a mean time since injury of 7.4 years. Twelve individuals with AIS C and two individuals with AIS B made up this cohort. Thirteen subjects completed the year-long trial completing three sessions of LT per week over 12 months for a total of 144 sessions. All subjects had a combined compliance rate of 78.8 +/- 7.8% over the year-long training period. All subjects improved their ability to walk on the treadmill from pre- to post-training to include
decreasing BWS (54% reduction), increasing treadmill training speed (180% increase), and increasing the distance walked in each treadmill session (335%). However, only six out of the 13 individuals who completed the trial were able to improve their OG walking ability. These subjects also demonstrated a statistically significant improvement in satisfaction with life (p=0.05) measured by the SWLS. The SF-36 is a multipurpose survey that measures eight domains of health including physical function, role limitations due to physical health, bodily pain, general health perceptions, vitality, social functioning, role limitations due to emotional problems and mental health and was used to show an improvement in satisfaction with physical function (p=0.03) in this study. Improvements in the SWLS and the SF-36 (physical function) were correlated to the improvements noted in treadmill walking ability. However, there was no significant change in perceived health also measured by the SF-36 or perceived ability to perform instrumental activities of daily living measured by the Instrumental Activities of Daily Living Index from pre- to post-training.

Follow-up to evaluate durability of gains was also an important goal of this study and the opportunity to continue training after formal study completion was built into the protocol. All subjects were given the opportunity to participate in treadmill training one time per week or two exercise sessions per week with study personnel for the eight months following study completion. The adherence to this training was drastically lower than the adherence to the original training at 22.5 +/-26.5%. Twelve out of the 13 individuals who completed this study returned for follow-up assessment approximately eight months after the study was completed. Results demonstrated a significant decline in treadmill walking performance in these 12 individuals while there were no changes in mean OG walking
scores in the six subjects who were able to ambulate at the eight month follow-up assessment. In terms of subjective well-being, there was a significant decrease in satisfaction with physical function (p=0.03) reported using the SF-36 at the follow-up assessment while satisfaction with life remained unchanged (SWLS). Overall, this study reported improved walking function in approximately 50% of subjects who completed 12 months of treadmill training with BWS. They also reported improved life satisfaction and satisfaction with physical function, that were all maintained over an eight month follow-up period, except satisfaction with physical functioning measured by SF-36, even though training compliance was much lower during the follow-up period than during the study period.

It was surprising that the authors included individuals with chronic motor complete SCIs (AIS B) in this study given that walking function was a primary outcome in this study and previous studies had not demonstrated OG walking benefits from treadmill training with BWS for individuals with motor complete injuries. However, psychosocial outcomes were also evaluated in this trial, which may be the primary reason the authors included individuals with AIS B injuries in the cohort as they were evaluating whether or not participation in this LT program would impact psychosocial outcomes even in individuals where improved walking function was not expected.

In the largest prospective observational cohort intensive LT study to date, the NRN Centers (Harkema et al) reported significant improvements in balance and walking measures in 196 individuals with motor incomplete SCI after completing a standardized intensive LT protocol initiated soon after discharge from inpatient rehabilitation across
seven outpatient rehabilitation centers. All participants were diagnosed with AIS grades C (non-functional strength below the LOI) and D (functional strength below the LOI) and completed at least 20 sessions of LT. LT in this study was defined as 60 minutes of treadmill training with BWS and manual assistance immediately followed by 30 minutes of OG walking training 5 days/week. Total number of sessions/number of weeks of therapy were different for all participants as this was based on an individual’s insurance policy and ability to make functional progress to justify continued therapy services. The primary outcome measures evaluated in this study included the BBS, 6minWT to evaluate walking endurance and the 10MWT to evaluate walking speed. One hundred thirty individuals enrolled were AIS D, while 66 were AIS C, and there was high variability in walking function among the patients at enrollment.

Patients received a median of 47 LT sessions in the study (20 minimum; 251 maximum) and were evaluated every 20 sessions along with pre- and post-discharge from the outpatient program. The authors reported statistically significant functional improvement from pre- to post-intervention in balance (p<.001) measured by the BBS, walking endurance measured by the 6minWT (p<.001) and walking speed measured by the 10MWT (p<.001). Over half of those enrolled improved in all three areas of walking while 87% improved in at least one of these areas. Magnitude of improvement was also significantly different between individuals with AIS C and D injuries with the latter demonstrating a better overall response to training. To better understand the impact of chronicity on response to training, the authors divided patients into one of the following three groups for analysis defined by time since injury: 1) Less than one year post-injury. 2)
one to three years post-injury. 3) Three or more years since injury. They found that time since SCI was not significantly associated with outcome measures at enrollment, but was related inversely to levels of improvement, as patients who were further out from their injury demonstrated less overall improvement than those who were enrolled soon after their injury. Although chronic patients did not demonstrate the degree of improvement that more acute patients did, they still demonstrated statistically significant improvements in functional outcomes from pre- to post-intervention. Twenty-four (12%) of all patients enrolled were categorized as non-responders as they showed no change or a decrease in each of the three functional outcomes. Twenty-two out of the 24 non-responders were non-ambulatory at the time of enrollment and were diagnosed with AIS C injuries again providing support that severity of injury may be the most important predictor in response to treatment. Overall, there was very high variability in functional abilities at enrollment among the 196 patients diagnosed with AIS C and D SCIs, but there was still a statistically significant improvement in functional walking outcomes among the cohort from pre- to post-intervention in response to an intensive LT program.

The authors also provide a good discussion regarding whether the changes demonstrated in this analysis are clinically relevant even though they are statistically significant. In terms of walking speed, clinical relevance is difficult to define as a 0.05m/s walking change may be clinically important to some (allowing them to reach a functional walking threshold that impacts their daily life) while the same change may not be meaningful to others. Further work needs to be done to understand clinical relevance in variety of cohorts after SCI. The authors also make a strong point that the individuals
analyzed in this study received more intense therapy in an outpatient setting than what is normally considered usual care and the far majority of participants were able to make significant walking improvements whether in the acute or chronic phases of recovery. Therefore, implementing this level of dosage and intensity as standard care after motor incomplete SCI may have a long lasting positive impact on the individuals who sustain these type of injuries each year.

In terms of study limitations, the authors acknowledge that this analysis did not address comparative effectiveness with this study as there was no intervention being compared to LT. However, they also discuss another well-known study by Van Hedel et al who evaluated responsiveness in the 10MWT and the 6 minWT and found that individuals with incomplete SCI who were ambulating one month post-injury did not demonstrate changes in these walking outcome measures in response to routine rehabilitation (often considered 1-2x/week for one hour sessions delivered by a single physical therapist). They also suggest that individuals with AIS C and D injuries should be analyzed separately in future studies as they may exhibit a different level of response to this type of training which did not occur in this study.

Morrison et al published a follow-up analysis to Harkema et al using a subset of 69 individuals who completed at least 120 sessions of LT and were among the 169 individuals included in the original study. These individuals completed 120 sessions of the intensive manual LT protocol (previously described) in 11.3 ± 9.3 months (mean ± SD). The authors reported significant improvements in all functional outcomes (previously described) and ISNCSCI motor scores (p <0.001) for all subjects over the course of 120 sessions. Only
three individuals out of the 69 failed to demonstrate improvements that surpassed the MDC on at least one outcome throughout the 120 sessions of intervention resulting in a non-responder rate of 4% (3/69). They reported an AIS C to D conversion of 51% and 6% regressing from D to C. The authors reported that walk tests (10MWT and the 6 minWT) were most responsive to change with 70% of all patients exceeding the MCID threshold of 0.15m/s over the 120 sessions with 80% of these individuals continuing to demonstrating clinically meaningful improvements at 6 and 12 month follow-up. They also reported that 69% of patients exceeded the MCID (39.6m) for the 6 minWT over the course of 120 sessions and 81% of these individuals continued to exceed the MCID for this measure at 6 and 12 month follow-up. The authors also projected out life time care cost reductions per person between $148,000 and $570,000 by reducing costs associated with home modifications, transportation and equipment for those individuals who were able to improve their walking and functional mobility.

The authors report that balance and walking gains were greatest after patients completed 60 sessions of LT. The authors proposed that limiting LT sessions to 40 would have denied detectable improvements in walking speed to approximately 30% of this sample while limiting therapy to 20 sessions would have limited approximately 60% of patients from achieving meaningful improvements in walking speed.

**Randomized Controlled Trials**

The first RCT comparing treadmill training with BWS to OG training in motor incomplete SCI during acute rehabilitation was published by Dobkin et al\(^3^6\) in 2006. A total of 146 subjects from six hospitals were enrolled in a single-blinded multi-center RCT and
were all within eight weeks (acute injuries) post incomplete SCI (AIS B, C, or D) with a FIM locomotion score of < 4 meaning they required at least moderate assistance to ambulate. In terms of intervention, both the experimental and control groups received standard inpatient and outpatient rehabilitation therapies for mobility and self-care skills for 12 weeks. In addition to this therapy, the experimental group also received an additional training session consisting of treadmill training with BWS (30 minutes) followed by 10-20 minutes of OG walking practice when feasible (once subject was able to assist with stepping and supporting weight). Treadmill training speeds were at a minimum of 0.72m/s with a goal of being greater than 1.07m/s. The control group also received an additional hour of mobility training for one hour per day with the specific amount of standing or stepping time dependent on each subject’s level of ability. Subjects who were not able to take steps yet spent the majority of this time in standing position with assistance while those who were able to take steps ambulated OG with physical assistance from two to three therapists, bracing and assistive devices. The control subjects were not allowed to use the treadmill or receive BWS. The training paradigm for both groups was focused on repetition, intensity, task difficulty and reinforcing successful skill acquisition. The primary outcome measures for this study were FIM-locomotion item (walking independence) and OG walking speed. These outcome measures were assessed at baseline and every two weeks for 12 weeks, post treatment (3 months) and 6 and 12 months after enrollment. Secondary outcomes including the BBS, WISCI (walking independence), LEMS, Ashworth Scale (hypertonicity) and the Medical Outcomes Study 54-Item Short Form Health Survey (SF-54) (perceived health-related QOL) were collected at baseline, three, six and 12 months.
These authors did not find any statistically significant differences at baseline between the control and experimental groups in regards to age, gender, race, time since injury or level of injury suggesting successful randomization. Outcome measures including FIM, LEMS, walking speed, walking distance, BBS and WISCI were also comparable at baseline. The subjects in this cohort were also highly disabled as only two of the 117 subjects who finished the study were able to walk 50 feet at baseline. The authors originally planned the FIM-locomotion item would be the primary outcome measure for comparison for AIS B and C subjects as these subjects were not expected to reach functional walking scores based on historically reported outcomes, meaning they would be unable to complete walking speed assessments. Walking speed was originally planned as the primary outcome measure for individuals with AIS D injuries at baseline. However, the authors had to change their study design and analysis plan as they were unable to enroll a sufficient number of subjects diagnosed with AIS D injuries into the trial while at the same time the majority of AIS C subjects in both groups reached functional walking scores which was far greater than what was predicted using historical outcomes. Therefore, the authors chose to combine AIS C and D subjects for the primary analysis using walking speed as the primary outcome.

A futility analysis was completed as the interim analysis revealing that to detect a conditional power of 80% for FIM-locomotion item, an additional 2500 subjects would have been needed and for a conditional power of 80% to detect a 20% difference in walking speed, an additional 4,000 AIS C and D subjects would have been needed. Therefore, enrollment was stopped at the interim analysis and results were reported only for those
who were enrolled at that time. The primary analysis reported for AIS B and C subjects was FIM-locomotion item. There was no statistical difference in outcomes between the control and experimental groups who completed at least six weeks of intervention. An analysis of AIS C and D subjects and walking speed revealed there was also no statistically significant difference in walking speed between experimental and controls groups at six months post enrollment. Again, these subjects demonstrated an unexpectedly high level of walking ability at this time point for both groups and fell within the range of functional community ambulation (1.1m/s). In terms of the secondary outcome measures, there was also no difference found in endurance, LEMS, BBS, WISCI score, Ashworth score and pain between these two groups. With further analysis of the AIS B subjects, it didn’t appear that either treatment intervention led to gains in OG walking, but those who did improve were enrolled soon after injury and converted to AIS C within the eight week enrollment period (were still considered AIS B for the analysis). Therefore, these authors conclude that those individuals who are still AIS B at eight weeks post-injury have a lower probability of achieving functional walking ability with either intervention.

An important discussion point in this trial was that even though there was not a statistically significant difference between control and experimental groups, both groups achieved walking abilities beyond what was expected based on previous literature and the clinical experience of the investigators.\textsuperscript{95,96} The authors also found that walking speeds for AIS C and D subjects were so much higher than predicted at six months that the hypothesized 20% difference used to calculate the power analysis would not have been clinically meaningful even if it had been present. There was a variety of possibilities
proposed by the authors of this trial for this misalignment of outcomes and prediction including the fact that there was no previous literature describing walking speeds achieved during inpatient rehabilitation for individuals with motor incomplete SCI. Also, the various SCI Model System Centers had reported very different statistics in terms of those who achieved functional walking abilities at discharge from inpatient rehabilitation, and the interaction of time between AIS score assignment could greatly affect these outcomes (assigning scores earlier rather than later could allow for an overestimation of outcome).

Finally, the design of this trial could have also been impactful in these findings.

In terms of trial design, both groups (control and experimental) were receiving two-fold the dosage of standing/stepping that was considered usual care for inpatient rehabilitation during this trial. Also, both groups were treated by a greater number of staff (physical therapists and aides) than what usually occurs in traditional rehabilitation. Therefore, patients assigned to the control group were getting stepping and standing practice they likely would not have received in traditional therapy due to the labor and number of staff required to deliver it safely. Individuals with motor incomplete SCIs who are not yet walking on their own (only two individuals in the control group and no individuals in the experimental group were walking on their own at baseline) are not generally provided with walking training/practice during traditional rehabilitation in the absence of technology (BWS) and/or extra staff to manage the labor and safety associated with doing this. For example, patients in traditional rehabilitation programs are often treated by one physical therapist who may not be able to provide walking practice for an individual who isn’t yet walking on their own due to labor and safety concerns. Therefore,
they may focus their rehabilitation program on more compensatory activities such as transfer training and wheelchair skills training. In summary, both groups were getting twice the amount of therapy that would have been given in traditional therapy and they were likely given significantly more upright mobility/walking practice because there was extra staff and technology associated with the design of the trial. The extra dosage and repetition of walking may have had an impact on this trial which reported individuals with motor incomplete SCI achieved far greater walking function than what had previously been reported.

Field-Fote et al reported preliminary walking outcomes as well as final walking outcomes from a single-blind RCT comparing four different LT approaches. The final analysis will be discussed in this review. A total of 74 individuals with chronic SCI (greater than one year) with minimal walking function were first stratified into four groups based on their pre-training LEMS (1) 1-10; 2) 11-21; 3) 22-32; and 4) 33-40) and then randomized within these strata to one of the following four LT approaches: treadmill training with BWS (TM); treadmill training with BWS and stimulation (TS); OG training with stimulation (OG); and treadmill training with BWS and robotic assistance (LR). Subjects trained five days per week (one hour sessions) x 12 weeks in all four groups. Training concepts for all groups included providing as little BWS as possible to achieve appropriate gait kinematics (< 30% BWS) and participants in all groups were encouraged to walk as far and fast as possible, but were allowed to rest as needed. The primary outcomes for this study were walking speed (10MWT) and distance (2minWT). LEMS was the secondary outcome measured in this trial. All outcome measures were completed just prior to training and after training had been
completed. All walking tests were completed without BWS and without assistance for stepping. Follow-up testing at six months was completed for a convenience sample of 10 subjects who had demonstrated at least a 0.05m/s improvement in walking speed in response to trial participation.

A total of 64 subjects completed this trial (86% completion rate) and were categorized as less impaired (LEMS >15 for at least one leg and >10 for the other leg) or more impaired (all others) for data analysis. There were no significant differences among the four training groups at baseline in terms of demographics, LEMS, walking speed and walking distance. Subjects demonstrated overall effects (small to medium) for speed (effect size index [d] =0.33 and distance [d=0.35]) from pre- to post-intervention training. Improvement in walking speed from pre-training to post-intervention was statistically significant for the OG, TS and TM groups, but not for the LR group. There was no statistically significant difference between all four LT groups in terms of walking speed changes although there was a moderate effect size for the OG group and only a small effect size for the TS and TM groups. In terms of walking distance/endurance, there was a statistically significant difference for the OG and TS groups, but not the TM and LR groups from pre-training to post-training. The effect size for walking distance was moderate for the OG group and small for the TS group. The OG group also demonstrated a statistically significant improvement in walking endurance over the other three groups. When analyzed per group, effect sizes for speed and distance were larger for the OG group (d=0.43 and d=0.40, respectively). Effect sizes for speed were the same for the TM and TS groups (d=0.28) and there was no effect for the LR group. The effect size for distance was greater
with the TS (d=0.16) than with the TM or LR groups for which there was no effect. In regards to LEMS, there was no significant differences among change scores between the groups. When analyzing groups stratified into more and less impaired (previously described above), the TS group had the largest proportion of participants who met or exceeded the minimal important difference (MID) of 0.05m/s\textsuperscript{89} for speed among the more impaired subjects while the OG group had the largest proportion of participants who met or exceeded the MID for distance within the least impaired group. Ten subjects completed follow-up testing six months after trial completion and walking speed was slower than at the end of the trial (average decrease of 0.06m/s), but remained faster than pre-training speeds (average increase of 0.09m/s).

An important point of discussion in this trial is that in opposition to the author’s original hypothesis, the OG group was associated with statistically significant improvements in walking distance over all of the treadmill groups and also had the greatest effect size for walking speed among the groups. The authors propose that the reason the OG group demonstrated the greatest improvements is because OG walking is task specific to the outcome being evaluated (OG walking speed and distance) while also requiring a greater demand for supraspinal input to activate voluntary step initiation and forward progression. In contrast, treadmill training is thought to primarily activate central pattern generators (CPGs) which are spinal segments that are capable, of self-producing, even in absence of descending or peripheral inputs, basic rhythmic, and coordinated locomotor movements.\textsuperscript{98} Supraspinal centers are also known to be involved in activating CPGs\textsuperscript{99,100} so training that places a demand on supraspinal centers may also result in CPG activation while the reverse
may not be true. These findings support the idea that voluntary effort and maximizing descending drive may be key components for improving walking function after SCI. One key limitation of this study was that none of the training groups incorporated a combined training approach that included both treadmill training (targeting CPG activation) as well as OG training (targeting supraspinal activation) which may have yielded results greater than the singularly focused groups in this study.

Alexeeva et al\textsuperscript{101} published a RCT in 2011 in which 35 adults with motor incomplete (AIS C or D) chronic (greater than a year post-injury) SCI were randomized into one of the following three groups: OG gait training with BWS using a fixed overhead track system (TRK); treadmill training with BWS (TM); and comprehensive physical therapy (PT). The PT group received a structured program delivered by a physical therapist that was individualized for each subject focusing on gait, balance, and functional activity such as strengthening, stretching and aerobic training. The TM group received ~30\% BWS while walking on a treadmill with the assistance of trainers (non-skilled) as needed. The TRK group also received ~30\% BWS while walking OG with the assistance of trainers (non-skilled) as needed. Subjects in the two BWS groups (TM and TRK) walked at a self-selected pace. All groups completed 13 weeks of training at a frequency of 3x/week (one hour per day). Subjects in the two BWS groups (TRK and TM) were not provided with input from a physical therapist during their training. The primary outcomes of this study included walking speed (10MWT), balance (Tinetti Scale\textsuperscript{102}), lower extremity muscle strength (LEMS), fitness (heart rate) and QOL measured by the Satisfaction with Abilities and Well-Being Scale\textsuperscript{103} (SAWS) and the SF-36.\textsuperscript{85} Subjects were randomized into one of the three groups at enrollment and
no significant differences were noted between groups at baseline. Outcome measures were evaluated just prior to enrollment and at the end of the 13 week training program. From pre-training to post-intervention, all groups demonstrated significant improvements in maximal walking speed and muscle strength. A significant improvement in balance was demonstrated in the PT and TRK groups, but not in the TM group. There was no significant difference observed from pre-training to post-intervention in fitness and QOL.

An important characteristic of this study is that the authors reported their goal for the study was not to design an intervention that would maximize functional recovery after chronic motor incomplete SCI, but rather to evaluate the ability of two interventions utilizing BWS (TRK and TM) to facilitate improvements in walking in the absence of a skilled clinician. The results demonstrated robust effects of the two interventions without PT involvement in the areas of maximum walking speed and lower extremity strength. However, only the PT group and the TRK group demonstrated significant improvements in balance while the TM group did not. This was the only outcome illustrating a significant difference among the three groups signifying the treadmill condition may not be the optimal environment for balance training. As was discussed in the previous review, treadmill training alone targets CPG activation of the nervous system which may strengthen the interneuronal connections associated with creating and maintaining a locomotor pattern, but does not require supraspinal drive/activation which is known to play a crucial role in maintaining balance and responding to balance perturbations. This study also evaluated the relationship between strength (LEMS) and walking speed and found there was no significant association between improvement in LEMS and walking speed which
supports the findings from previous studies examining this relationship.\textsuperscript{10,106} In summary, this study demonstrated that individuals with motor incomplete SCI may demonstrate improved walking ability following intensive training in a variety of conditions including those that do not utilize a skilled PT. However, it also demonstrated that the TM condition alone may not be optimal for improving balance in these individuals as it may not activate supraspinal centers which are important for maintaining balance. It also confirmed that improved walking ability is not always associated with improvements in QOL. The authors acknowledge that a combination of these interventions (TM, TRK and PT) targeting both CPG and supraspinal activation may have resulted in further benefit, but was not evaluated in the current study.

Adams and Hicks\textsuperscript{107} published a study in 2011 comparing the effects of treadmill training with BWS and manual assistance to tilt-table standing in individuals with chronic SCI. The primary outcome measure in this study was spasticity which is outside the scope of this review. However, secondary outcome measures that were also evaluated include perceived health and functioning using the Quality of Life Index Spinal Cord Injury Version III and functional mobility using the FIM Motor Subscale. The study design was a randomized cross-over with participants randomly assigned to complete four weeks of treadmill training with BWS or tilt-table standing with a four-week washout period between the interventions before completing the opposite training paradigm. Each participant served as their own control with the order of conditions randomly assigned. Interventions were matched in terms of dosage and frequency at 3x/week for four weeks. When evaluating functional mobility, treadmill training with BWS was more beneficial than tilt-table standing at the
same dosage and frequency in seven individuals with chronic (greater than one year) SCI demonstrating a large effect size of 1.27 in favor of treadmill training with BWS. In regards to perceived health and functioning, the treadmill training paradigm also appeared favorable to tilt-table standing with a moderate effect size of 0.50 in support of treadmill training. Even though this was a very small study with a primary outcome measure that is outside the scope of this review, the analysis provides further evidence that treadmill training with BWS may have a positive impact on functional mobility and perceived health and functioning in individuals with SCI. As with many of the studies, there was no long term follow-up provided for this cohort of individuals.

Hitzig et al\textsuperscript{108} published a RCT in 2013 evaluating a FES-assisted walking program to a non-FES walking program with the primary outcome measures being QOL and community participation. Twenty-seven individuals with chronic SCI (>18 months) were randomly assigned to a FES-assisted walking group (treadmill training with BWS and FES) or an aerobic/resistance training group and completed each intervention 3x/week for 16 weeks. Primary outcome measures included the following: SCIM\textsuperscript{109}, Satisfaction With Life Scale\textsuperscript{60} (SWLS), Lawton Instrumental Activities of Daily Living\textsuperscript{110} Craig Handicap Assessment Reporting Technique\textsuperscript{61} (CHART), Reintegration to Normal Living Index\textsuperscript{111} (RNLI) and perceptions of interventions from qualitative questions. There were no significant differences between groups at baseline in regards to these outcome measures and study evaluations occurred at baseline, four, six, and 12 months. At completion of the study, there were no significant differences reported between groups on any of the outcome measures. However, at the 12 month follow-up analysis, the FES group demonstrated a
significant increase (p<.01) on SCIM mobility subscores demonstrating improved mobility in the FES-assisted walking group in comparison to the aerobic/resistance training group. No other statistically significant differences were noted between groups in this study at this time period. Both groups reported positive gains in well-being from participating in these interventions per the SWLS and the RNLI, but again, no significant differences were seen in QOL or community participation between the two groups. This study supports that walking training with FES and BWS yields improved mobility in individuals with chronic SCI and supports improved QOL for individuals who participated in this type of training as well. Most importantly, 12 month follow-up evaluations supported the durability of these gains for the group who received treadmill training with BWS only. This was the first publication to report that treadmill training with BWS may have a longer carryover of gains than other types of LT interventions.

Jones et al\textsuperscript{64} published a RCT with a delayed treatment design in 2014 evaluating a 24 week activity-based therapy program in individuals with motor incomplete SCI (AIS C and D) that included the following training components: developmental sequencing; resistance training; repetitive motor activity; and task-specific LT. Algorithms were used to guide group allocation, utilization of FES, and LT progression. LT consisted of both treadmill training with BWS as well as OG walking training augmented with FES. Subjects were randomly assigned at enrollment to an experimental group which began the intervention within 2 weeks of enrollment or a control group which waited 24 weeks before starting the training program. Primary outcomes include neurologic function (ISNCSCI), walking speed and endurance (10MWT, 6 minWT), community participation (SCIM III and RNLI), and
metabolic function (weight, body mass index, and Quantitative Insulin Sensitivity Check). Significant improvements in neurologic function were noted between experimental and control groups \((p=0.004)\) (improvements in motor and sensory function not often measured in most LT studies) as well as walking speed \((p=0.036)\) and walking endurance \((p=0.002)\). No significant differences were noted in the outcome measures evaluating community participation and metabolic function between experimental and control groups after completing 24 weeks of an intensive activity-based therapy program. This study yielded significant improvements in walking function in 48 individuals with chronic motor incomplete SCI, but did not report significant gains in community participation and health measures. These results support that intensive training incorporating treadmill training with BWS as one component of a comprehensive activity-based therapy program may facilitate improved walking capacity in comparison to no therapy. It is unclear why this study is in contrast to previous studies such as Hitzig et al\(^{108}\) who reported a positive association between improved walking ability and improved psychosocial outcomes such as QOL and community participation.

Kapadia et al\(^{112}\) published an RCT in 2014 that evaluated a 16 week program (three days per week) of treadmill training with BWS augmented by FES to the lower extremities in comparison to an aerobic and resistance training program on gait, balance and functional mobility in individuals with motor incomplete SCI (AIS C and D). Results demonstrated a significant difference between groups on the functional mobility outcome, the SCIM mobility sub-score. Walking speed, endurance and balance improved in both groups, but no statistically significant differences were noted between groups in these areas. The
results from this trial support that individuals with motor incomplete SCI who participate in treadmill training with BWS may benefit from improved functional mobility. The additional impact of adding FES to treadmill training remains unclear as there was no comparison group of treadmill training without FES. It also demonstrates that alternative interventions that are considered less task specific for walking (aerobic training and resistance training) may also positively impact gait and balance outcomes after SCI.

Yang et al\textsuperscript{113} published a randomized crossover trial also in 2014 evaluating the contrasting therapy approaches of precision training and endurance training. Twenty-two participants with motor incomplete SCI were initially randomized to either the precision group (OG walking while stepping over obstacles and reaching targets) or the endurance group (treadmill training with BWS). Both groups trained 5x/week for two months followed by a two month washout period and then each group completed the alternate training program. Outcomes including walking speed, distance, and skill as well as depression, confidence and lower extremity strength were measured and compared after each training phase. The results of this trial demonstrated that both forms of training led to statistically significant improvements in various aspects of walking. The endurance training group (treadmill training with BWS) yielded larger improvements in walking distance for high functioning walkers (speed >0.5m/s) than the precision training group with no difference noted between groups who were categorized as low functioning walkers (speed <0.5m/s). The largest improvements in speed and distance occurred in the first month of training in both high and low functioning subjects. However, improvements in skill occurred during both types of training.
Three individuals in this study did not improve in any of the walking outcome measures irrespective of training approach. The authors did not discuss any possible patient characteristics that would account for this difference in response to treatment as baseline characteristics were similar between this group and those who improved in response to training. The authors were very surprised that treadmill training with BWS improved walking skill to a comparable degree as precision training in this population and concluded that treadmill training focusing on walking faster and longer may be sufficient to induce cortical tract plasticity. However, they also questioned whether their outcome measures were sensitive enough to detect changes in higher level aspects of gait challenging dynamic balance and obstacle management. The authors did not report on the other outcomes captured in this trial including depression, confidence and lower extremity strength. This trial demonstrates that individuals with motor incomplete SCI may benefit from a variety of training approaches, but that high functioning walkers may benefit most from treadmill training focused on improving speed and endurance. This trial supports that this patient population benefits from intensive training programs (five days per week) which is considerably more training than what is considered usual care (one to two days per week). Unfortunately, it did not provide any long term follow-up for these individuals to understand if these training approaches may also result in long term impact on function, but did report that participants in both groups demonstrated residual gains after completing the two month washout period.
Systematic Reviews

Merholz et al\textsuperscript{114} published a systematic review of LT in SCI in 2012. The goal of this systematic review was to assess the benefits of LT after traumatic SCI. They included RCTs which compared LT to a control of any other exercise or no treatment. The primary outcomes evaluated were walking speed and walking capacity at study completion. They reviewed five RCTs involving 309 subjects including three of the RCTs previously reviewed here (Alexeeva et al,\textsuperscript{101} Dobkin et al,\textsuperscript{36} and Field-Fote et al\textsuperscript{63}) and reported inconclusive results. They concluded that there is insufficient evidence to support that any one form of LT is superior to any other rehabilitation strategy focused on improving walking after SCI or that LT benefits individuals with SCI more than other types of rehabilitation. Although this review is helpful in understanding the lack of reported advantage between LT interventions, it does not address the comparison of intensive LT to usual care in terms of dosage and frequency. None of the RCTs that were analyzed for this review provided a comparison of intervention to no intervention. These reviews were all focused on either acute rehabilitation or during the chronic stages of recovery so it also does not address what type and dosage of training may be most efficacious to provide in the subacute phase of recovery (three to six months post-injury) which is generally when patients are involved in outpatient rehabilitation programs. Finally, this review is only focused on short term walking outcomes and does not address long term follow-up, psychosocial or health outcomes.

Morawietz and Moffat\textsuperscript{115} published a systematic review on the effects of LT after incomplete SCI in 2013. Their goal was to evaluate current LT approaches and to identify
the most effective interventions to promote walking recovery after incomplete SCI. They limited their review to RCTs and included a total of eight articles in their review and three of these RCTs were also included in the Cochrane review\textsuperscript{114} and were previously discussed in this review (Alexeeva et al,\textsuperscript{101} Dobkin et al,\textsuperscript{36} and Field-Fote et al\textsuperscript{63}). RCTs focused only on LT with robotic assistance were also included in this review. Walking capacity, speed, duration and quality were the primary outcomes evaluated in this review. After synthesizing the data, they reported slight improvements in gait parameters after treadmill training with BWS, and manual as well as robotic assistance in acute SCI. They also reported greater improvements in chronic SCI utilizing treadmill training with BWS augmented by FES and OG gait training augmented by FES than treadmill training with BWS and manual assistance, treadmill training with BWS and robotic assistance, or conventional PT. Overall, they reported that the evidence for LT after SCI is limited and that all approaches show some potential for improvement of ambulatory capacity without superiority of one approach over another. Similar to the previously discussed systematic review,\textsuperscript{114} this review also did not address LT effectiveness in regards in comparison to no therapy and it did not address psychosocial or health outcomes. These areas remain significant gaps in the literature.

**Summary of Gaps in the Literature**

In reviewing this literature, common themes emerged in terms of gaps in the current literature base. First, there is insufficient evidence to support that usual care is not sufficient to maximize recovery after motor incomplete SCI. Second, durability of gains achieved after participating in intensive LT during post-acute rehabilitation has not been
studied. Finally, the impact of intensive LT on psychosocial outcomes and re-
hospitalizations rates after motor incomplete SCI has not been adequately studied.

Insufficient evidence to support that usual care may not be sufficient to maximize
recovery after motor incomplete SCI. The status quo, as it pertains to post-acute
rehabilitation after motor incomplete SCI, generally does not focus on recovery of walking
for individuals who did not achieve the ability to walk during inpatient rehabilitation.
There’s a wide variety of treatment interventions provided at variable doses which often
define usual care after SCI during inpatient and outpatient physical rehabilitation. Many of
these approaches utilize a single physical therapist to provide education and skill-based
compensatory training. Usual care is also difficult to define in terms of frequency especially
after inpatient rehabilitation. It is often dictated by insurance benefit with many policies
being limited to 20 total visits/year as this is often seen as equivalent to Medicare’s
outpatient therapy cap.\textsuperscript{116,117} In summary, usual care often lacks interventions targeting
recovery of function in this unique patient population largely due to limited resources and
limited insurance benefit. This definition of usual care is likely pervasive throughout the
SCIMS Centers that are not also a part of the NRN as they are not known to have a
structured program that provides intensive LT after inpatient rehabilitation.

Limited efficacy for usual care during inpatient rehabilitation was first reported in
Dobkin et al\textsuperscript{36} where a comparison of two types of interventions focused on walking
recovery resulted in all subjects receiving two times the amount of training that was
considered usual care and yielded benefits that were far greater than historically reported
outcomes. These were the first authors to demonstrate that usual care is not sufficient to
maximize walking recovery during inpatient rehabilitation. This was an important conclusion from this study that was actually overshadowed by the fact that these authors expected treadmill training with BWS to be superior to OG walking training provided by two to three therapists. The publication focused on the lack of superiority between these interventions rather than on the potential for individuals with SCI to achieve greater outcomes when provided with a greater dosage of therapy.

In terms of post-acute rehabilitation (after discharge from inpatient rehabilitation), Field-Fote et al\textsuperscript{63} trained individuals who were on average >18 months post SCI 5x/week x 12 weeks using four different types of LT interventions. Walking ability for the individuals enrolled in this trial was considered stable at time of enrollment given they were all chronic (greater than year post-injury) and spontaneous recovery is not expected in this population after one year.\textsuperscript{19} The study did not report statistically significant differences in walking speed between these interventions, but three out of the four groups (robotic LT group did not improve) demonstrated a significant improvement from baseline to post treatment evaluation. Individuals in this study would have been receiving usual care for chronic SCI which is generally considered no therapy prior to enrollment and yet were still able to make significant improvements in walking function in response to intensive training offered at five days per week irrespective of specific intervention choice. The construct of these four interventions significantly differed from usual care in terms of dosing and specificity of walking recovery as most patients are no longer receiving therapy at one year post-injury. This highlights the limitations of usual care offered to individuals with SCI after inpatient rehabilitation.
Even when reducing training frequency from five days to three days per week, Alexeeva et al\textsuperscript{101} reported significant walking improvements in maximal walking speed and muscle strength in individuals who were on average 84 months post-injury and received training for 13 weeks in one of the following three groups: treadmill training with BWS; OG training with a BWS and comprehensive PT. This study also supports that individuals who participate in an intensive LT program even in the chronic stages of recovery have the ability to make meaningful walking and strength improvements. The training all three groups received in this study is likely greater than what is considered usual care at approximately seven years post SCI as most individuals with SCI are no longer receiving care at this time point. Hitzig et al\textsuperscript{108} compared FES-assisted OG walking to FES-assisted walking on a treadmill with BWS and also found no significant differences between walking groups. Again, they provided 3 times per week intensive training in the chronic SCI population (approximately 10 years post SCI) and demonstrated that both groups were able to make significant improvements in walking function adding further support that the current state of usual care after motor incomplete SCI may not allow individuals to maximize their recovery.

The previously reviewed publications provide evidence that usual care may not be sufficient to maximize recovery of walking during acute rehabilitation (greater than three months) and in the chronic stages of recovery (greater than one year), but we have insufficient evidence to make this conclusion for individuals who have completed inpatient rehabilitation and are less than one year post SCI. There are no current reports of a comparison between intensive LT and usual care in the subacute stages of recovery (greater
than three months and less than 12 months) which remains an important gap in the literature and needs to be better understood to provide the most efficacious interventions during outpatient PT. The previously discussed studies evaluating intensive LT in chronic SCI also did not provide a direct comparison to usual care by following a parallel arm which was not receiving intervention. In the largest prospective observational cohort intensive LT study to date, the NRN Centers (Harkema et al47) reported significant improvements in balance and walking measures in 196 individuals with motor incomplete SCI after completing an intensive LT protocol initiated soon after discharge from inpatient rehabilitation. Even though statistically significant gains in walking performance and balance were achieved in this cohort from pre- to post-intervention, efficacy from this data cannot be established because there was no control group provided for comparison. The current study will provide a one year post-injury comparison of individuals who received intensive LT only offered at six sites in the US to those who did not receive this treatment.

**The durability of gains achieved after participating in intensive LT during post-acute rehabilitation has not been adequately studied.** Only a few publications have addressed durability of gains after intensive LT. For those reports that have provided some follow-up, the follow-up time period has been variable (ranging from two months to one year) and appears to have been based on convenience without sound scientific rationale. The studies have generally reported only a convenience sample of subjects from the original study limiting generalizability to a larger population of individuals with SCI. Also, the majority of these studies only addressed the ability of subjects to maintain walking speed
gains; one study evaluated the durability of psychosocial outcomes; and only one other study evaluated functional independence with mobility at follow-up.

In regards to independence with functional mobility, Kapadia et al\textsuperscript{112} compared 16 weeks of treadmill training with BWS to 16 weeks of a combined aerobic/resistance training in 27 individuals with motor incomplete SCI and found both groups had improved, but no significant difference between groups in mobility scores immediately after training. However, during a 12 month follow-up evaluation, the group who had previously received treadmill training with BWS demonstrated significant improvements in mobility (SCIM mobility subscale) over the aerobic/resistance training group demonstrating durability of gains in the treadmill training group only. This small study leads us to question whether sustained effects may be more substantial after intensive LT than other types of interventions.

In regards to psychosocial outcomes, Hicks et al\textsuperscript{90} reported eight month follow-up on 14 individuals who completed one year of treadmill training with BWS. They found that individuals improved their OG walking ability, satisfaction with life and satisfaction with physical functioning after the year-long training. With regard to eight month follow-up, subject’s walking ability remained stable between end of study and follow-up evaluation, but the authors reported that subjects demonstrated a significant decrease in satisfaction with physical functioning at follow-up evaluation. This is an interesting finding with a variety of potential explanations including but not limited to the idea that an individual’s satisfaction with physical functioning is not directly related to actual walking performance; currently used measures evaluating walking function are not sensitive enough to detect a
decline in walking function; or that walking ability may not be the most significant predictor in satisfaction with physical function.

Yang et al\textsuperscript{113} evaluated two month durability of gains achieved in walking speed, endurance and skill from 8 weeks of treadmill training with BWS versus OG precision training both delivered at five days per week in 20 individuals with chronic motor incomplete SCI in a randomized cross-over study. As in many of the other previously discussed studies, both training groups demonstrated improvements in walking speed and skill after completing both endurance and skill training with walking endurance being the only measure that was statistically significant between groups with the advantage going to those who participated in treadmill training with BWS. Follow-up evaluation of each type of training occurred at the end of each washout period (two months) and subjects demonstrated excellent retention of walking speed, endurance and skill without a difference between intervention type. Although this is promising in terms of durability, two months is a relatively short time period and the clinical expectation is that these gains would be maintained for at least the first couple of months after study completion. Six and 12 month follow-up evaluations would have been very helpful in understanding the true durability of these gains.

In terms of walking speed only, Field-Fote et al\textsuperscript{63} reported approximately 20 month follow-up on a convenience sample of 10 individuals who met or exceeded the minimal detectable change (MDC) in walking speed of 0.05m/s at completion of the trial. As a group, they had an average improvement in walking speed of 0.15m/s at conclusion of the trial and during the follow-up evaluation demonstrated an average decline in walking speed.
of 0.06m/s from trial completion to follow-up evaluation. Therefore, on average this sample of 10 individuals were walking 0.09m/s faster at the follow-up evaluation than they were prior to the trial. Since this was only a small convenience sample out of the larger study population, the results are interesting, but not generalizable to a larger population of individuals receiving intensive treadmill training with BWS. Also, given that only walking speed was evaluated, it’s difficult to determine whether this final increase of 0.09m/s was a clinically relevant improvement for these 10 individuals.

Musselman et al\textsuperscript{88} reported three month follow-up for a case series of four individuals who completed a randomized cross-over study where all subjects started with three months of treadmill training with BWS and were then randomized to follow this with either OG walking training or another episode of treadmill training with BWS. The subjects were then switched to the opposite group for the final episode of treatment. All subjects initially met or exceeded the minimal clinically important difference for walking speed of 0.05m/s. The authors also reported that at follow-up, three out of the four subjects had retained on average (median) 92% of walking speed improvements gained during the active phase of the trial. This is an extremely small sample size with a fairly short follow-up period so even though speed gains were maintained in the majority of subjects at three months, there is limited generalizability to a larger population. Field-Fote et al\textsuperscript{86} also reported one year follow-up on a convenience sample of four out of 20 subjects who completed three months of treadmill training with BWS augmented by FES. On average all 20 subjects demonstrated an average increase in walking speed of 0.12m/s through the trial and three out of the four subjects evaluated at one year had maintained these walking speed
improvements. Again, this study suggests promising durability, but is too small to be
generalizable to a larger population.

In summary, the durability of gains obtained from intensive LT have not been
adequately studied. Few studies have reported on the maintenance of gains after intensive
LT, but most of these have reported short follow-up times on a much smaller sample of the
original study population. Maintenance of walking speed has been the focus of the majority
of studies that have reported follow-up while questions remain as to whether walking
speed improvements are the most important long term outcome from this intervention. To
better understand the true potential benefits from LT, it will be important to investigate the
long term impact (one year) that a bout of intensive LT has on functional independence,
mobility, and psychosocial outcomes.

The impact of intensive LT on psychosocial outcomes after motor incomplete SCI
has not been adequately studied. Despite the importance of psychosocial and community
participation outcomes after SCI, there is very limited data evaluating the impact of specific
rehabilitation interventions on these outcomes and the data that is available reports
variable outcomes. In a randomized cross-over design comparing treadmill training with
BWS to tilt table standing, Adams and Hicks\textsuperscript{107} reported improved QOL when individuals
completed treadmill training over tilt table standing with a moderate effect size of 0.50.
Although promising, this was a very small sample of seven individuals and results were
obtained immediately after finishing each intervention phase so does not speak to the long
term impact these interventions may have on QOL.
Alexeeva et al\textsuperscript{101} reported improved psychological outcomes in a RCT comparing 13 weeks of treadmill training with BWS to standard PT and to walking training with overhead BWS. The authors reported \textasciitilde80\% improvement in satisfaction with abilities and well-being that was consistent across all groups and was maintained at a one month follow-up evaluation. It appears from this study that intensive physical training regardless of approach demonstrated improved QOL scores, but one month is a very short follow-up period and does not speak to the long term durability of these gains. Also, perceived health was not changed from pre-treatment to post-treatment evaluation leading to a question whether the perception of health has an impact on QOL.

Hitzig et al\textsuperscript{108} evaluated community participation and QOL in 27 individuals with chronic motor incomplete SCI who completed either 16 weeks of treadmill training with BWS and electrical stimulation or aerobic/resistance training. There was no significant improvement in QOL or community participation in response to either training and there were no reported differences between groups. It is unclear why this study did not report an improvement in psychosocial outcomes when previous authors did. However, the two studies were using different outcome measures which may have contributed to inconsistent findings. Also, the authors of this study report that many of their subjects had very high community participation and QOL scores at baseline so the sample may have been compromised with individuals who were generally satisfied with their lives before the intervention. Finally, the authors also asked the subjects in this study open-ended qualitative questions post intervention and found very positive answers in regards to
improved mobility and QOL supporting a lack of potential sensitivity in the measures chosen to evaluate psychosocial outcomes in this study.

Jones et al\textsuperscript{118} reported modest gains in psychosocial outcomes (Reintegration to Normal Living Index) in a sample of 41 individuals with chronic motor incomplete SCI who completed 24 weeks of a multi-modal training program that included intensive LT in a delayed cross-over design. Effing et al\textsuperscript{87} reported limited to no improvement in psychosocial outcomes in a small pilot study of three individuals who completed 12 weeks of treadmill training with BWS. The authors provided no explanation for this other than the sample size was too small to draw any conclusions.

In contrast, another pilot study, Singh et al\textsuperscript{119} reported improved physical functioning and improved psychosocial outcomes after a program of intensive LT in seven individuals with motor incomplete SCI immediately following inpatient rehabilitation. These authors concluded there may be a positive impact on QOL, community transition and perceived health in response to intensive LT in addition to the previously reported mobility benefits. However, these short term benefits were reported in a study also with a very small sample size that did not consider the long term impact of this intervention on the psychosocial outcomes. Finally, Hicks et al\textsuperscript{90} reported significant improvements in QOL and satisfaction with physical function in 14 individuals who completed one year of treadmill training with BWS. Satisfaction with life scores were maintained at eight month follow-up while satisfaction with physical function scores were significantly reduced which suggests there may be other co-variates outside of physical function that have a significant impact on life satisfaction.
As the evidence in the previous review supports, treadmill training with BWS may have variable impact on psychosocial outcomes after SCI. Evaluating the impact using one year post-injury data on psychosocial outcomes between a group of individuals who received intensive LT and those who didn’t will be helpful in understanding this variability. Long term follow-up is needed to better understand the impact this intervention has on QOL and community participation as studies providing short term follow-up have reported variable outcomes.

The impact of intensive LT on health outcomes such as re-hospitalization rates after motor incomplete SCI has not been adequately studied. Re-hospitalization rates are high after SCI with 30-45% of individuals reporting being hospitalized one or more times annually due to SCI complications.\textsuperscript{18,120} Skelton et al\textsuperscript{120} reported on 186 patients who were prospectively enrolled in a trial evaluating health-care utilization during the first year after SCI. Telephone follow-up calls occurred at three, six, nine and 12 months post-injury to inquire about health care utilization. The authors reported that 45% of individuals were re-hospitalized during the first year after injury in this cohort. They also reported that those with C1-4 AIS A-C SCIs used the most health care services and those discharged home used less services overall than those discharged to other facilities. Age, sex, race and education were not associated with higher use of health care services in this cohort. The authors concluded that those individuals with greater neurologic impairment and not discharged home after inpatient rehabilitation had higher health care utilization overall. The authors did not ask about PT services or activity level in this study which may have been helpful in better understanding their association with re-hospitalizations.
DeJong et al.\textsuperscript{51} evaluated re-hospitalization rates one year after their SCI in 951 individuals with traumatic SCI who were discharged from six rehabilitation centers in the US. They found that 36.2\% of their respondents had been hospitalized at least one time over the previous year while 12.5\% were hospitalized at least twice during the same time frame. The average length of stay (LOS) was 15.5 days across all re-hospitalization episodes. Skin, respiratory and urinary tract infections were the three most common causes of re-hospitalization in this sample. The factors associated with increased odds of re-hospitalization included being a woman, having Medicaid as the main payer, and more severe injuries/co-morbidities. Intensive PT delivered during inpatient rehabilitation was the only factor associated with lower odds of re-hospitalization.

The authors also reported that those who were re-hospitalized during the first year after injury also reported more depression symptomology at 12 months than those who had not been re-hospitalized. This was the only report found that linked intensive PT delivered during inpatient rehabilitation to a reduction in re-hospitalization rate the first year after injury, though the specifics of the intervention are undefined and may or may not have included treadmill training with BWS. Therefore, understanding the impact of intensive LT delivered in outpatient rehabilitation on re-hospitalization rates during the first year after injury remains a current gap in the literature. Given the potential personal, societal and financial cost associated with re-hospitalization rates, this an important topic that needs investigated.
CHAPTER III

METHODS

Research Design and Data Collection

This dissertation is a retrospective analysis (nested case/control design) using data obtained from participants enrolled in the SCIMS database. “Cases” were defined as individuals with motor incomplete SCI who following discharge from inpatient rehabilitation completed at least 30 sessions of the NRN LT protocol. “Controls” were defined as individuals with motor incomplete SCI who received usual care following discharge from inpatient rehabilitation and did not receive any NRN LT sessions. Utilizing SCIMS data exclusively from the 6 centers offering the NRN program, “Form I” data for both groups (cases and controls) were collected at the point of discharge from inpatient rehabilitation by clinical evaluation and medical abstraction and were utilized to determine participant’s demographics and to characterize baseline functional independence as well as examine heterogeneity between groups. Outcome data in “Form II” are collected via interview at 1 year post-injury (+/- 182 days) and were obtained for both groups and used for comparison between groups. See Table 3.1 for inclusion and exclusion criteria for cases.

Exclusion criteria were utilized to identify those individuals who were not appropriate matched controls for this study (i.e., “no controls”) as they had some exposure to the NRN protocol, but do not meet the inclusion criteria for a case. Generally, these are individuals who were enrolled in the NRN protocol, but did not complete 30 sessions of training, none-the-less representing a confounding exposure to NRN. The NRN national data manager searched the database and provided patient episode numbers (both potential
Table 3.1 Inclusion/Exclusion Criteria

<table>
<thead>
<tr>
<th>Inclusion Criteria</th>
<th>Exclusion Criteria</th>
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<tbody>
<tr>
<td>• Diagnosed with motor incomplete SCI (AIS C or D)</td>
<td>• Diagnosed with motor incomplete SCI and completed less than 30 sessions of LT in the NRN</td>
</tr>
<tr>
<td>• Completed inpatient rehabilitation at SCIMS Center that was also an NRN Center</td>
<td>• Did not complete 30 sessions of LT within the first year post-injury</td>
</tr>
<tr>
<td>• Complete 1 year post-injury follow-up in the SCIMS database</td>
<td></td>
</tr>
<tr>
<td>• Completed at least 30 sessions of LT in the NRN within the first year post-injury</td>
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</table>

SCI = spinal cord injury; AIS = ASIA impairment scale
Figure 3.1 Data Retrieval Process

1. Cases and no controls identified from the NRN database
2. NRN patient numbers matched to SCIMS numbers at each site
3. All SCIMS no controls removed from SCIMS database before matching
4. Cases matched 1:1 with controls and full data set obtained of Form I and Form II data
cases and no controls) who met the above criteria to the representative NRN network site director. Each site director matched the patient episode numbers to each patient’s SCIMS database identification number. Each site then sent SCIMS numbers for both cases and no controls to the Principal Investigator of this study (Tefertiller). The Principal Investigator combined the SCIMS numbers for all cases and no controls from all sites and removed the no controls Model Systems numbers from the SCIMS database before matching. Controls were matched with cases in a 1:1 ratio. See Figure 3.1 for data retrieval process.

Controls were matched to cases based on age at injury, motor function (AIS classification), gender, year of injury, mode of mobility at discharge from inpatient rehabilitation, and rehabilitation facility (NRN site) as these factors may impact recovery rates.\textsuperscript{121} Matching was completed using a SAS macro (SAS 9.4).\textsuperscript{a} Two data sets were created for this process, one data set containing all cases and a second data set containing all potential controls. Each data set contained the variables used for matching (gender, AIS classification, age, injury year, mode of mobility at discharge from inpatient rehabilitation and rehabilitation facility) with the maximum difference allowed defined for each variable. This program selected one case at a time and then searched through the control data set (randomly ordered) and found a control that satisfies the criteria for matching each variable. When a match was found, the case and matched control data were written to a data set and the potential control data set was updated removing the used control. If no match was found then the case was written to a separate, no match, data set. The process was repeated for all cases and a summary report of the matching process was generated. See Table 3.2 Variable Matching.
<table>
<thead>
<tr>
<th>Variable</th>
<th>Matching</th>
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<tbody>
<tr>
<td>Age at Injury</td>
<td>All cases will be matched with controls within +/- 5 years</td>
</tr>
<tr>
<td>Gender</td>
<td>Female = Female</td>
</tr>
<tr>
<td></td>
<td>Male = Male</td>
</tr>
<tr>
<td></td>
<td>Other = Other</td>
</tr>
<tr>
<td>AIS Classification at time of discharge from</td>
<td>AIS C = AIS C</td>
</tr>
<tr>
<td>inpatient rehabilitation</td>
<td>AIS D = AIS D</td>
</tr>
<tr>
<td>Rehabilitation Hospital</td>
<td>All cases will be matched with controls from their specific site</td>
</tr>
<tr>
<td>Year of Injury</td>
<td>All cases will be matched with controls who sustained their SCI within +/- 5 years</td>
</tr>
<tr>
<td>Mode of Mobility at discharge from inpatient rehabilitation</td>
<td>Walking = Walking</td>
</tr>
<tr>
<td></td>
<td>Wheelchair = Wheelchair</td>
</tr>
</tbody>
</table>
Sample Size and Power Analysis

A power analysis was calculated using PASS 11 and the following known variables: sample size of 72 matched pairs, 80% power, and a significance level of $\alpha = 0.05$. This sample size has at least 80% power with a paired $t$-test to detect Cohen’s $d$-type effect sizes as small as 0.345 which are generally considered a small to moderate effect size. Effect size will be reported for comparison of continuous outcomes as a method to quantify the size of the standardized difference in means between two groups, is easily understood by clinicians who are the primary audience for this work, and can easily be used in meta-analyses. Using effect size to quantify the standardized mean differences between groups places the emphasis on the most important aspect of this comparison which is the size of the effect between groups rather than its statistical significance which is sample size dependent and may or may not be clinically meaningful. Given the small available sample size from this data set, effect size has the most utility and the interpretation may be clinically relevant.

Analysis Plan

SAS version 9.4 was utilized for all statistical analyses. A descriptive analysis of patient characteristics between those who are identified as cases and those who are matched controls was completed. A comparison of patient demographics included the following: SCI etiology, neurologic level of injury, age, gender, marital status, education, primary health insurance, cause of SCI, inpatient discharge ASIA Total motor index, inpatient rehabilitation discharge FIM mobility score, and inpatient rehabilitation LOS. The total
number of LT sessions completed was obtained for all cases from the NRN LT database and summarized using mean, median, minimum and maximum values.

One year outcome data for comparison included the following: satisfaction with life, community participation, re-hospitalizations, and mobility. For all comparisons, unadjusted models and adjusted models controlling for important patient and clinical factors were fit. Patient factors that were included in the models were marital status and education. The following clinical characteristics were also included in the models: inpatient discharge FIM motor score, ASIA Motor index total score, and inpatient rehabilitation LOS. See Table 3.3 One Year Outcome Data Variables.

**Analysis Plan for Research Aim 1 and Hypothesis**

Aim 1: Evaluate and compare one year post-injury mobility outcomes from the SCIMS database for individuals with motor incomplete SCI who received the NRN LT protocol (cases) in post- acute rehabilitation and matched controls who received usual care.

_H1_1: Individuals with motor incomplete SCI who received the NRN LT protocol will demonstrate higher FIM\textsuperscript{57} motor scores (total motor score; locomotion; transfer index; and stairs) in comparison to controls matched on age, gender, injury year, NRN center, motor function (AIS C or D) and mode of mobility at discharge from inpatient rehabilitation and adjusting for important patient and clinical characteristics.

The FIM \textsuperscript{57} will be the primary mobility outcome utilized to evaluate this hypothesis. The FIM is used as a measure of functional status at inpatient rehabilitation admission, discharge, and at 1 year post-injury. The FIM contains 18 items (13
Table 3.3 One Year Outcome Data Variables

<table>
<thead>
<tr>
<th>Outcome Measure</th>
<th>Item/Subscale</th>
<th>Psychometrics</th>
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<tbody>
<tr>
<td>Functional Independence Measure (FIM)</td>
<td>• Total motor score&lt;br&gt;• Transfer index&lt;br&gt;• Locomotion score&lt;br&gt;• Stair score</td>
<td>Valid and Reliable in SCI&lt;sup&gt;57,122&lt;/sup&gt;</td>
</tr>
<tr>
<td>Craig Handicap Assessment and Reporting Technique (CHART-SF)</td>
<td>• Physical Independence&lt;br&gt;• Mobility&lt;br&gt;• Social Integration&lt;br&gt;• Occupation</td>
<td>Valid and Reliable in SCI&lt;sup&gt;61&lt;/sup&gt;</td>
</tr>
<tr>
<td>Satisfaction With Life Scale (SWLS)</td>
<td>• Aggregate score</td>
<td>Valid in SCI&lt;sup&gt;60&lt;/sup&gt;</td>
</tr>
<tr>
<td>Re-Hospitalization Yes or No</td>
<td>• Number of times since discharge from inpatient rehabilitation&lt;br&gt;• Total number of days re-hospitalized since inpatient rehabilitation</td>
<td>NA</td>
</tr>
</tbody>
</table>
mobility and 5 cognitive items) with a maximum possible score of 126 which indicates complete independence and a minimum possible score of 18 indicating complete dependence. Tasks are rated on a seven point ordinal scale from complete dependence to complete independence (1-7). The FIM Total Motor Score is made up of 13 items that include the following: eating; grooming; bathing; upper body dressing; lower body dressing; toileting; bladder management; bowel management; bed to chair transfer; toilet transfers; shower transfer; locomotion; and stairs. The greater the FIM score on each item, the greater independence with mobility an individual possesses in that area. The FIM has been shown to be valid and reliable in SCI.\textsuperscript{122,123} Adequate correlation has been demonstrated between the mobility index which includes locomotion, bed to chair transfer, shower transfer, toilet transfer and stairs ($r = 0.733$) and the single locomotor item ($r = 0.454$) when scored by clinicians at discharge from rehabilitation and patient self-report at one month.\textsuperscript{122} Excellent correlation has also been reported between FIM motor score (13 items previously mentioned with scores ranging from 13 to 91) and the ASIA total motor score [10 UE and 10 LE motor scores from 0 (no motor activity) to 100 (normal motor function)].\textsuperscript{124} However, decreased sensitivity to detect change has been reported in SCI and expert opinion does not recommend using the FIM locomotor item in SCI research.\textsuperscript{125,126}

Linear mixed effects models were utilized to account for the paired nature of the matched sample. Initial unadjusted comparisons of FIM motor scores on the following items were analyzed between cases and matched controls using one year outcome data:

- **FIM Total Motor Score** which is an aggregate of all motor items assessed by FIM (scores ranging from 13-91 with higher scores denoting greater independence);
Locomotor item which is defined by the ability and assistance required to walk 50-150 feet (score range from 1-7 with higher scores denoting greater independence);

Transfer index which includes average assistance required for the following transfer items: bed to chair transfer, toilet transfer, and shower transfer (scores ranging from 3-21 with higher scores denoting greater independence);

Stair item defined by the ability and assistance required to ascend/descend one flight of steps (score range from 1-7 with higher scores denoting greater independence);

FIM Total Motor Score, locomotion, stairs and the transfer index were dependent variables in these models. Next, adjusted models were fit to compare FIM mobility outcomes on the previously discussed items between cases and controls after controlling for the important patient and clinical characteristics that were included in the analysis plan.

H2: At one year post-injury individuals with motor incomplete SCI who received the NRN LT protocol will demonstrate greater odds of being able to walk in the home, community and up a flight of stairs in comparison to controls matched on age, gender, NRN site, motor function (AIS C or D) and mode of mobility at discharge from inpatient rehabilitation reported in the following mobility-related outcome questions (response is either yes or no):

a) Ability to walk >150 ft. with or without a mobility aide within the home
b) Ability to walk with or without a mobility aide one street block outside the home
c) Ability to walk with or without mobility aide up one flight of steps
Logistic generalized linear mixed-effects models (assuming a binomial distribution and a logit link function) were fit for each mobility question previously mentioned (the ability to walk 150ft in the home; ability to walk one street block outside; and the ability to walk up one flight of steps) controlling for the relevant patient and clinical characteristics previously described in the analysis plan. This is equivalent to a logistic regression model that is able to account for the paired nature of the matched data.

**Analysis Plan for Research Aim 2 and Hypothesis**

Evaluate and compare one year post-injury re-hospitalization, QOL, and community participation for individuals with motor incomplete SCI who received the NRN LT protocol (cases) in post-acute rehabilitation and matched controls who received usual care (control).

\textbf{H}_2\textbf{1}: Individuals with motor incomplete SCI, who received the NRN LT protocol will report better QOL as measured by the SWLS\textsuperscript{60} in comparison to controls matched on age, gender, injury year, NRN center, motor function (AIS C or D) and mode of mobility at discharge from inpatient rehabilitation.

\textbf{H}_2\textbf{2}: Individuals with motor incomplete SCI, who received the NRN LT protocol will report better community participation as measured by the CHART-SF\textsuperscript{61} in comparison to controls matched on age, gender, injury year, NRN center, motor function (AIS C or D) and mode of mobility at discharge from inpatient rehabilitation.

\textbf{H}_2\textbf{3}: Individuals with motor incomplete SCI, who received the NRN LT protocol will report decreased number of re-hospitalizations and decreased numbers of days re-
hospitalized during the first year after SCI in comparison to controls matched on age, gender, injury year, NRN center, motor function (AIS C or D) and mode of mobility at discharge from inpatient rehabilitation.

QOL was compared using the Satisfaction with Life Scale (SWLS)\(^60\) between cases and controls. The SWLS has been validated in SCI.\(^58\) It contains five questions about life satisfaction including three in the present, one from the past and one in the future. It is completed via an interview format and all five items are scored on a seven point Likert scale from strongly agree (1) to strongly disagree (7) with the total score ranging from 5 to 35 (not satisfied to highly satisfied). Unadjusted and adjusted linear mixed effects models were completed using the SWLS total score as the dependent variable in the same manner as previously discussed for the FIM models and adjusting for the same patient and clinical characteristics.

The Craig Handicap Assessment and Reporting Technique - Short Form (CHART-SF)\(^61\) was utilized to evaluate community participation after SCI. The CHART-SF was designed to assess how people with disabilities function as active members of their communities. The CHART-SF contains 32 items based on the following six domains: physical independence; cognitive independence; mobility; occupation; social integration and economic self-sufficiency. Scores on each subscale range from 0-100 with higher scores indicating greater levels of community participation. The following subscales were analyzed independently between cases and controls as clinically they appear to be most closely associated with participation in PT interventions: physical independence; mobility; occupation and social integration. Scores on each subscale range from 0-100 with higher scores indicating a lesser
degree of disability or a greater degree of social and community participation. The CHART-SF is given via interview format and has been shown to be valid and reliable in SCI.\textsuperscript{61,127,128} Unadjusted and adjusted mixed effects models controlling for relevant patient and clinical characteristics were fit using the CHART-SF subscale scores as dependent variables in the same manner as previously discussed for the FIM models and adjusting for the same patient and clinical characteristics.

The number of times an individual has been re-hospitalized and the number of days they’ve spent re-hospitalized between discharge from inpatient rehabilitation and their one year post-injury follow-up is an indication of their overall health status. Percent differences were reported between groups for the number of re-hospitalizations occurring in the first year post-injury. Generalized linear mixed-effects models (assuming a Poisson distribution and a log link) were fit to compare the number of times an individual has been hospitalized between cases and controls and to account for the paired nature of this sample. An initial unadjusted comparison of total number of re-hospitalizations and total number of days re-hospitalized was completed between cases and matched controls from one year post-injury outcome data. Total number of re-hospitalizations and total number of days re-hospitalized were the dependent variables utilized in these models. In addition, an adjusted generalized linear mixed-effects model (assuming a Poisson distribution and a log link) controlling for the same patient and clinical factors previously described was fit for both numbers of re-hospitalizations and re-hospitalization days and presented as exponential mean ratios.
Revised Methods

Matching was initially proposed using the following variables: age (exact), gender (exact), injury year (exact), NRN center (exact) and motor function (exact: AIS C or D). However, some initial attempts at matching demonstrated the ability to match 42 pairs when using exact age and exact injury year. Therefore, the age range and injury year were increased to within 5 years as this allowed a greater number of matching pairs without compromising clinical differences based on age and rehabilitation focus. While continuing to investigate the number of potential cases that could be matched, it was decided to decrease the number of required LT sessions from 40 to 30 so that a larger pool of cases would be considered for matching. Clinically, these are individuals who have completed at least one 20 session block of NRN training which is often the baseline number of outpatient therapy services provided by many insurance companies.

After completing some initial frequency tables, it was noted that a substantially greater number of controls were discharged from inpatient rehabilitation with walking as their primary mobility status while a greater number of cases were discharged with wheelchair use as their primary means of mobility. Therefore, it was determined that cases and controls should also be matched on mode of mobility at discharge from inpatient rehabilitation along with age, gender, injury year, NRN center, and motor function (AIS C or D). A 1:3 ratio match between cases and controls was also initially proposed as a way to increase sample size and reduce variability within the control sample. However, once it was determined that matching needed to include mode of mobility, this was no longer possible.
and it was determined that a 1:1 match would be required to obtain a maximum number of appropriately paired cases and controls.

*A priori* covariates that were included in the models needed to be adjusted due to low frequencies of known data and high percentage of unknown data in multiple categories. Patient factors that were planned to be included in the model were family income and insurance benefit. However, 77% of family income and 66% of payer type were unknown so they could not be included in this analysis without significant loss of sample size. After completing a baseline demographic analysis, education level was found to be significantly different between the two groups (*p* = 0.044) and marital status was also significantly different between the two groups (*p* = 0.009). Therefore, both of these socio-demographic patient factors were included in the models in place of family income and payer type.

Clinical characteristics that were originally planned to be included in the models included the following: inpatient discharge FIM motor scores; and prior health care status (history of diabetes, high blood pressure, arthritis). However, prior health care status was also largely unknown (greater than 65%) in these groups. Baseline analysis between groups revealed a statistically significant difference between cases and controls in terms of how many days they spent hospitalized during inpatient rehabilitation so this clinical characteristic was used in place of prior health care status. Also, ASIA total motor index was also added to the models to account for varying neurologic levels of injury as matching on them (exact: cervical, thoracic, and lumbar) would have decreased the number of matching pairs considerably (72 to 45) which would have negatively affected the power of this analysis.
CHAPTER IV

RESULTS OF ANALYSIS

Seventy-two matched pairs were obtained from the SCIMS database. Individuals were matched based on the following characteristics:

- Age (+/- 5 years)
- Gender (exact, male or female)
- Time since injury (+/- 5 years)
- Primary mode of mobility at discharge from inpatient rehabilitation (exact, walking, wheelchair or equally using both)
- AIS classification (exact, C or D)
- Rehabilitation facility (exact, Craig Hospital, Shepherd Center, Magee Rehabilitation, TIRR Memorial Hermann, Kessler Institute of Rehabilitation, and Frazier Rehab Institute)

Even though there were 24,728 individuals with valid follow-up in the SCIMS database for potential matching, the ability to match pairs was notably limited by matching on rehabilitation facility as a couple of the NRN sites have only been SCIMS centers for a limited number of years including the following: Frazier (5 years) and Ohio State (3 years). Therefore, these two centers had a much lower pool of controls to match from than Magee Rehabilitation, Shepherd Center, TIRR and Craig Hospital which have been contributing data to the SCIMS database for 15, 37, 40 and 45 years respectively. See Figure 4.1 Subject Allocation and Matching.
Figure 4.1 Subject Allocation and Matching
The following describes the etiology among the total sample: 37.5% motor vehicle accidents; 30.6% falls; 14.6% sports accidents; 10.4% violent acts; and 6.9% other. Out of the 72 pairs, 33.3% (24 pairs) were diagnosed with AIS C injuries and 66.7% (48 pairs) diagnosed with AIS D injuries. The distribution of neurologic level of injury in the control group included the following: 40 cervical injuries (56.7%); 13 thoracic injuries (19.4%); 16 lumbar injuries (23.9%) and 3 (4.2%) were unknown. The distribution of neurologic level of injury in the case group included the following: 59 cervical (83.6%); 10 thoracic (14.9%); 1 lumbar (1.5%) and 2 unknown (2.8%). In regard to the primary means of mobility at discharge from inpatient rehabilitation, 9 pairs (12.5%) were walking while 62 pairs (86.1%) were using a wheelchair and 1 pair (1.4%) were equally walking and using a wheelchair.

Demographic differences were analyzed between paired cases and controls using a McNemar’s Test. Significant differences ($p<0.05$) were noted between cases and controls with more cases who were married, with a higher level of education, and who had private insurance. Cases completed a mean of 81.5 (SD = 53.3), a median of 60 (25th percentile = 40; 75th percentile = 110), and a minimum 30 and a maximum of 230 LT sessions. See Table 4.1 Demographics for Cases and Controls.

**Variables at Discharge from Inpatient Rehabilitation**

Paired $t$-tests were used for normally distributed continuous variables at discharge from inpatient rehabilitation to compare means; nonparametric Wilcoxon signed-rank test were used to compare medians for highly skewed data at discharge from inpatient rehabilitation. The following continuous variables were chosen *a priori* for comparison at discharge from inpatient rehabilitation between cases and controls as they were expected
to have an impact on recovery: age at injury; days hospitalized during inpatient rehabilitation; ASIA motor index total; and FIM motor scores. There were statistically significant differences at discharge from inpatient rehabilitation between the two groups in the following areas: days hospitalized ($p<0.001$); FIM Transfer Index ($p<0.001$); FIM Total Motor Score ($p<0.001$); and FIM Stairs ($p<0.001$). Cases were hospitalized during inpatient rehabilitation an average of 21.1 (SD=50.5) days longer than matched controls while their FIM Transfer Index was on average 2.7 (SD=7.0) points lower than controls. FIM Total Motor Score for cases was an average of 9.8 (SD=24.6) points lower than that of controls and FIM Stairs were 0.8 (SD=1.7) points lower for cases than controls. Therefore, after matching the cases required longer hospitalization and also discharged from inpatient rehabilitation with significantly lower mobility scores (FIM Total Motor Score, FIM Transfer Index and FIM Stairs) than controls. However, there was not a significant difference between locomotion scores at discharge from inpatient rehabilitation between the two groups [cases = 5.6 (SD=1.0); controls 5.6 (SD=1.1)]. In terms of ASIA motor index total score, there was not a significant difference between means for the two groups while the median score of the cases was 17.5 points lower than the median score of the controls. See Table 4.2 Variables at Discharge from Inpatient Rehabilitation.

**Unadjusted Outcomes**

Without adjusting for important co-variates, there were statistically significant differences at one year between cases and controls on the CHART-SF Mobility Subscale and the CHART-SF Social Integration Subscale with cases on average reporting higher scores than controls. No other outcomes were statistically significant in the unadjusted models.
Table 4.1 Demographics for Cases and Controls

<table>
<thead>
<tr>
<th>Variable</th>
<th>Label</th>
<th>Total</th>
<th>Case</th>
<th>Control</th>
<th>P-Value†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (n=144)</td>
<td></td>
<td>114 (79.2%)</td>
<td>57 (79.2%)</td>
<td>57 (79.2%)</td>
<td>n/a</td>
</tr>
<tr>
<td></td>
<td>Male</td>
<td>114 (79.2%)</td>
<td>57 (79.2%)</td>
<td>57 (79.2%)</td>
<td>n/a</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>30 (20.8%)</td>
<td>15 (20.8%)</td>
<td>15 (20.8%)</td>
<td></td>
</tr>
<tr>
<td>Marital Status (n=142)</td>
<td>Married or in relationship</td>
<td>61 (43.0%)</td>
<td>38 (53.5%)</td>
<td>23 (32.4%)</td>
<td>0.009*</td>
</tr>
<tr>
<td></td>
<td>Single, Divorced, Widowed, Other</td>
<td>81 (57.0%)</td>
<td>33 (46.5%)</td>
<td>48 (67.6%)</td>
<td></td>
</tr>
<tr>
<td>Education (n=135)</td>
<td>High School or lower</td>
<td>93 (68.9%)</td>
<td>38 (55.9%)</td>
<td>55 (82.1%)</td>
<td>0.001*</td>
</tr>
<tr>
<td></td>
<td>More than High School</td>
<td>42 (31.1%)</td>
<td>30 (44.1%)</td>
<td>12 (17.9%)</td>
<td></td>
</tr>
<tr>
<td>Primary Payer (n=56)</td>
<td>Private Insurance/Work Comp</td>
<td>45 (80.4%)</td>
<td>29 (96.7%)</td>
<td>16 (61.5%)</td>
<td>0.001*</td>
</tr>
<tr>
<td></td>
<td>Medicare/Medicaid/Veterans</td>
<td>11 (19.6%)</td>
<td>1 (3.3%)</td>
<td>10 (38.5%)</td>
<td></td>
</tr>
<tr>
<td>AIS classification (n=144)</td>
<td>AIS C</td>
<td>48 (33.3%)</td>
<td>24 (33.3%)</td>
<td>24 (33.3%)</td>
<td>n/a</td>
</tr>
<tr>
<td></td>
<td>AIS D</td>
<td>96 (66.7%)</td>
<td>48 (66.7%)</td>
<td>48 (66.7%)</td>
<td></td>
</tr>
<tr>
<td>Mode of Mobility (n=144)</td>
<td>Walking</td>
<td>18 (12.5%)</td>
<td>9 (12.5%)</td>
<td>9 (12.5%)</td>
<td>n/a</td>
</tr>
<tr>
<td></td>
<td>Wheelchair</td>
<td>124 (86.1%)</td>
<td>62 (86.1%)</td>
<td>62 (86.1%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Both</td>
<td>2 (1.4%)</td>
<td>1 (1.4%)</td>
<td>1 (1.4%)</td>
<td></td>
</tr>
</tbody>
</table>

†Based on McNemar’s Test; n/a due to matched sample; AIS = ASIA Impairment Scale
See Table 4.3 Unadjusted Comparisons of Continuous Outcomes; See Table 4.4 Unadjusted Comparison of Dichotomous Outcomes.

**Research Aim 1**

Evaluate and compare one year post-injury mobility outcomes from the SCIMS database for individuals with motor incomplete SCI who received the NRN LT protocol (cases) in post-acute rehabilitation and matched controls who received usual care.

**H₁₁:** Individuals with motor incomplete SCI who received the NRN LT protocol will demonstrate higher FIM$^{57}$ motor scores (total motor score; transfer index; locomotion and stairs) in comparison to controls matched on age, gender, injury year, NRN center, mode of mobility at discharge from inpatient rehabilitation, and motor function (AIS C or D) adjusting for important patient and clinical characteristics.

To evaluate Research Aim 1 (H₁₁), an initial unadjusted comparison between cases and controls was completed using paired t-tests for these normally distributed continuous outcome variables.

**FIM Total Motor Score**

Cases scored 0.3 (SD = 24.1) units higher on average ($p=0.925$) than controls on the FIM Total Motor Score in an unadjusted model at one year which was a non-significant difference favoring the cases. However, using a linear mixed-effects model controlling for marital status, education level, ASIA Motor Index total score at discharge from inpatient rehabilitation, FIM Total Motor Score at discharge from inpatient rehabilitation, and days hospitalized during inpatient rehabilitation, cases scored 9.9 units higher (95% CI = 4.0, 15.8)
Table 4.2 Variables at Discharge from Inpatient Rehabilitation

<table>
<thead>
<tr>
<th>Variable</th>
<th>Case Mean±SD</th>
<th>Median (IQR)</th>
<th>Control Mean±SD</th>
<th>Median (IQR)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at Injury</td>
<td>38.8±16.1</td>
<td>39 (29)</td>
<td>38.7±15.9</td>
<td>38 (30)</td>
<td>0.782&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Days Hospitalized</td>
<td>75.7±41.9</td>
<td>65 (50)</td>
<td>52.7±35.7</td>
<td>50 (34)</td>
<td>&lt;0.001&lt;sup&gt;b&lt;/sup&gt; *</td>
</tr>
<tr>
<td>ASIA Motor Index</td>
<td>70.7±106.1</td>
<td>59 (34)</td>
<td>69.1±21.1</td>
<td>76.5 (30.5)</td>
<td>0.901&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Total Score</td>
<td>11.0±5.0</td>
<td>12 (8)</td>
<td>13.7±5.3</td>
<td>15.5 (6)</td>
<td>0.002&lt;sup&gt;a&lt;/sup&gt; *</td>
</tr>
<tr>
<td>FIM Transfer Index</td>
<td>50.3±17.1</td>
<td>51.5 (24.5)</td>
<td>60.2±20.1</td>
<td>69 (28)</td>
<td>0.001&lt;sup&gt;a&lt;/sup&gt; *</td>
</tr>
<tr>
<td>FIM Total Motor Score</td>
<td>5.6±1.0</td>
<td>6 (0)</td>
<td>5.6±1.1</td>
<td>6 (0)</td>
<td>0.966&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>FIM Locomotion</td>
<td>1.7±1.3</td>
<td>1 (1)</td>
<td>2.6±1.9</td>
<td>1 (3)</td>
<td>&lt;.0001&lt;sup&gt;a&lt;/sup&gt; *</td>
</tr>
</tbody>
</table>

<sup>a</sup> paired t-test; <sup>b</sup> Wilcoxon signed-rank test; SD = standard deviation; IQR = interquartile range; FIM = Functional Independence Measure; ASIA = American Spinal Cord Injury Association; * = statistically significant difference
Table 4.3 Unadjusted Comparisons of Continuous Outcomes at One year Follow-Up

<table>
<thead>
<tr>
<th>Variable</th>
<th>Case Mean±SD</th>
<th>Control Mean±SD</th>
<th>Mean±SD of Difference</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>FIM Total Motor Score</td>
<td>73.1±16.0</td>
<td>72.8±21.0</td>
<td>0.3±24.1</td>
<td>0.925</td>
</tr>
<tr>
<td>FIM Transfer Index</td>
<td>16.8±5.2</td>
<td>16.7±5.8</td>
<td>0.1±7.2</td>
<td>0.882</td>
</tr>
<tr>
<td>FIM Locomotion Score</td>
<td>5.8±1.3</td>
<td>5.9±1.2</td>
<td>0.1±1.1</td>
<td>0.157</td>
</tr>
<tr>
<td>FIM Stairs</td>
<td>3.8±2.4</td>
<td>4.0±2.5</td>
<td>0.2±2.5</td>
<td>0.331</td>
</tr>
<tr>
<td>FIM Locomotion + Stairs</td>
<td>9.6±2.9</td>
<td>9.9±3.2</td>
<td>-0.2±3.0</td>
<td>0.585</td>
</tr>
<tr>
<td>Satisfaction with Life Scale Total Score</td>
<td>20.9±8.2</td>
<td>19.3±7.6</td>
<td>1.6±10.8</td>
<td>0.234</td>
</tr>
<tr>
<td>CHART - Physical Independence</td>
<td>71.5±35.1</td>
<td>81.9±28.8</td>
<td>-10.4±42.8</td>
<td>0.056</td>
</tr>
<tr>
<td>CHART - Mobility Total</td>
<td>87.6±17.6</td>
<td>76.1±27.4</td>
<td>11.5±28.5</td>
<td>0.002   *</td>
</tr>
<tr>
<td>CHART - Occupation Total</td>
<td>59.6±34.8</td>
<td>57.9±37.7</td>
<td>1.8±49.0</td>
<td>0.776</td>
</tr>
<tr>
<td>CHART - Social Integration</td>
<td>95.5±13.3</td>
<td>88.0±21.9</td>
<td>7.5±26.1</td>
<td>0.028   *</td>
</tr>
</tbody>
</table>

Based on paired t-test; SD = standard deviation; CHART = Craig Handicap Assessment and Reporting Technique Short Form; FIM = Functional Independence Measure; * = statistically significant difference
Table 4.4 Unadjusted Comparison of Dichotomous Outcomes at One Year Follow-Up

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total Pairs</th>
<th>Case Pair Yes (%)</th>
<th>Control Pair Yes (%)</th>
<th>Odds Ratio</th>
<th>Lower 95% CI</th>
<th>Upper 95% CI</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Walk 150ft Home</td>
<td>63</td>
<td>42 (66.7)</td>
<td>40 (63.5)</td>
<td>1.150</td>
<td>0.552</td>
<td>2.394</td>
<td>0.683</td>
</tr>
<tr>
<td>Walk 1 Block</td>
<td>63</td>
<td>37 (58.7)</td>
<td>36 (57.1)</td>
<td>1.067</td>
<td>0.526</td>
<td>2.165</td>
<td>0.847</td>
</tr>
<tr>
<td>Walk 1 Flight Stairs</td>
<td>63</td>
<td>36 (57.1)</td>
<td>37 (58.7)</td>
<td>0.937</td>
<td>0.462</td>
<td>1.901</td>
<td>0.842</td>
</tr>
<tr>
<td>FIM Indep Loco</td>
<td>57</td>
<td>51 (89.5)</td>
<td>54 (94.7)</td>
<td>0.472</td>
<td>0.112</td>
<td>1.989</td>
<td>0.257</td>
</tr>
<tr>
<td>FIM Indep Stairs</td>
<td>57</td>
<td>32 (56.1)</td>
<td>31 (54.4)</td>
<td>1.074</td>
<td>0.513</td>
<td>2.247</td>
<td>0.842</td>
</tr>
</tbody>
</table>

Based on McNemar’s Test; % = percent; ft = feet; Indep = Independent; loco = locomotion
Table 4.5 Unadjusted Comparison of Non-Parametric Data at One Year Follow-Up

<table>
<thead>
<tr>
<th>Variable</th>
<th>Case Median</th>
<th>Case Range</th>
<th>Case IQR</th>
<th>Control Median</th>
<th>Control Range</th>
<th>Control IQR</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Days Hospitalized</td>
<td>0 (0)</td>
<td>0,90</td>
<td>0,0</td>
<td>0 (0)</td>
<td>0,47</td>
<td>0,0</td>
<td>0.840(^b)</td>
</tr>
<tr>
<td>Number of Re-hospitalizations</td>
<td>0 (0)</td>
<td>0,2</td>
<td>0,0</td>
<td>0 (0)</td>
<td>0,3</td>
<td>0,0</td>
<td>0.100(^b)</td>
</tr>
</tbody>
</table>

\(^b\)Wilkcoxon signed-rank test; IQR = Interquartile Range; % = Percentile
on average at one year post-injury follow-up on FIM Total Motor Scores compared to controls ($p=0.002$). A between group effect size was estimated at 0.53. In addition, several covariates were found to have significant relationships with FIM Total Motor Scores at one year follow-up. The FIM Total Motor Score for those with above high school education was 7.6 units lower ($p=0.002$) than those with high school or lower education. Also, every one unit increase in FIM Total Motor Score at discharge from inpatient rehabilitation was associated with a 0.66 unit increase ($p<0.001$) in one year FIM score; while every one day increase in hospitalization in the inpatient rehabilitation unit was associated with a 0.16 unit decrease ($p<0.001$) in one year FIM Total Motor Score. See Table 4.6 Adjusted FIM Total Motor Score at One Year Follow-Up.

**FIM Transfer Index**

Cases scored 0.1 (SD=7.2) units higher on average ($p=0.882$) than controls on the FIM Transfer Index in an unadjusted model at one year which was a non-significant difference favoring the cases. However, after controlling for marital status, education level, ASIA motor index total score at discharge and FIM Transfer Index at discharge from inpatient rehabilitation, and days hospitalized during inpatient rehabilitation, cases scored significantly higher than controls by an average of 2.6 units (95% CI = 0.76-4.41) at one year follow-up on the FIM Transfer Index ($p=0.007$). The between group effect size was estimated to be 0.47. In addition, several covariates were found to have significant relationships with FIM Transfer Index scores at one year follow-up. A one unit increase in FIM Transfer Index at discharge from inpatient rehabilitation was associated with a 0.59 unit increase ($p<0.001$) in one year FIM Transfer Index scores; while every one day increase in hospitalization in the
Table 4.6 Adjusted FIM Total Motor Score at One Year Follow-Up

<table>
<thead>
<tr>
<th>Comparison</th>
<th>Mean Difference</th>
<th>SE</th>
<th>Lower 95% CI</th>
<th>Upper 95% CI</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases vs. Controls</td>
<td>9.987</td>
<td>2.918</td>
<td>3.996</td>
<td>15.798</td>
<td>0.002</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Covariates</th>
<th>Estimate</th>
<th>SE</th>
<th>Lower 95% CI</th>
<th>Upper 95% CI</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marital Status</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Married/Unmarried Couple</td>
<td>2.476</td>
<td>2.976</td>
<td>-3.356</td>
<td>8.308</td>
<td>0.411</td>
</tr>
<tr>
<td>Education Level</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Above High School</td>
<td>-7.557</td>
<td>3.154</td>
<td>-13.739</td>
<td>-1.375</td>
<td>0.022 *</td>
</tr>
<tr>
<td>ASIA Motor Index</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total Score at Discharge</td>
<td>-0.001</td>
<td>0.017</td>
<td>-0.035</td>
<td>0.032</td>
<td>0.936</td>
</tr>
<tr>
<td>FIM Total Motor Score, at Discharge</td>
<td>0.658</td>
<td>0.075</td>
<td>0.510</td>
<td>0.805</td>
<td>&lt;0.001 *</td>
</tr>
<tr>
<td>Days Hospitalized in the Systems Inpatient Rehab Unit</td>
<td>-0.158</td>
<td>0.040</td>
<td>-0.236</td>
<td>-0.080</td>
<td>&lt;0.001 *</td>
</tr>
</tbody>
</table>

N=112; SE = Standard Error; CI = Confidence Interval; FIM = Functional Independence Measure; ASIA = American Spinal Cord Injury Association; * = statistically significant difference (α = 0.05)
inpatient rehabilitation unit was associated with a 0.05 unit decrease ($p<0.001$) in one year FIM Transfer Index score. See Table 4.7 Adjusted FIM Transfer Index at One Year Follow-Up.

**FIM Locomotion and Stairs**

At one year, 42 cases (64.4%) and 38 controls (60.30%) reported walking as their primary means of mobility while 23 cases (35.40%) and 25 controls (39.70%) reported wheelchair use as their primary mode of mobility. Cases scored 0.2 (SD=3.0) units lower on average ($p=0.585$) than controls on the FIM Locomotion (locomotion and stairs) in an unadjusted model at one year which was a non-significant difference favoring the controls.

After controlling for marital status, education level, ASIA motor index total score at discharge, FIM Locomotion at discharge, and days hospitalized during inpatient rehabilitation, cases scored on average 0.58 (95% CI = -0.387, 1.543) units higher on FIM Locomotion (locomotion and stairs) than controls which was not statistically significant ($p=0.233$). The estimated effect size was 0.24. In addition, several covariates were found to have significant relationships with FIM Locomotion scores (locomotion and stairs). Every unit increase in FIM Locomotion score at discharge from inpatient rehabilitation was associated with a 0.35 unit increase ($p=0.009$) in one year FIM Locomotion score; while every one day increase in hospitalization in the inpatient rehabilitation unit was associated with a 0.021 unit decrease ($p=0.003$) in one year FIM Locomotion score. See Table 4.8 Adjusted FIM Locomotion and Stairs at One Year Follow-Up. Locomotion and stairs were analyzed separately and dichotomized into those individuals who were able to complete the task on their own (modified independent or independent) in comparison to those who needed assistance to complete the task (supervision, contact guard assist, minimal assistance,
Table 4.7 Adjusted FIM Transfer Index at One Year Follow-Up

<table>
<thead>
<tr>
<th>Comparison</th>
<th>Mean Difference</th>
<th>SE</th>
<th>Lower 95% CI</th>
<th>Upper 95% CI</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases vs. Controls</td>
<td>2.858</td>
<td>0.903</td>
<td>0.759</td>
<td>4.410</td>
<td>0.007</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Covariates</th>
<th>Estimate</th>
<th>SE</th>
<th>Lower 95% CI</th>
<th>Upper 95% CI</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marital Status</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Married/ Unmarried Couple</td>
<td>0.938</td>
<td>0.889</td>
<td>-0.804</td>
<td>2.680</td>
<td>0.298</td>
</tr>
<tr>
<td>Education Level</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Above High School</td>
<td>-1.172</td>
<td>0.954</td>
<td>-3.041</td>
<td>0.698</td>
<td>0.226</td>
</tr>
<tr>
<td>ASIA Motor Index</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total Score at Discharge</td>
<td>-0.003</td>
<td>0.005</td>
<td>-0.013</td>
<td>0.007</td>
<td>0.587</td>
</tr>
<tr>
<td>FIM Transfer Index, at Discharge</td>
<td>0.594</td>
<td>0.082</td>
<td>0.433</td>
<td>0.755</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Days Hospitalized in the Systems</td>
<td>-0.047</td>
<td>0.012</td>
<td>-0.071</td>
<td>-0.024</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Inpatient Rehab Unit</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>*</td>
</tr>
</tbody>
</table>

N=113; SE = Standard Error; CI = Confidence Interval; FIM = Functional Independence Measure; ASIA = American Spinal Cord Injury Association; * = statistically significant difference (α = 0.05)
Table 4.8 Adjusted FIM Locomotion and Stairs at One Year Follow-Up

<table>
<thead>
<tr>
<th>Comparison</th>
<th>Mean Difference</th>
<th>SE</th>
<th>Lower 95% CI</th>
<th>Upper 95% CI</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases vs. Controls</td>
<td>0.578</td>
<td>0.477</td>
<td>-0.387</td>
<td>1.543</td>
<td>0.233</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Covariates</th>
<th>Estimate</th>
<th>SE</th>
<th>Lower 95% CI</th>
<th>Upper 95% CI</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marital Status</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Married/Unmarried Couple</td>
<td>-0.349</td>
<td>0.509</td>
<td>-1.348</td>
<td>0.649</td>
<td>0.497</td>
</tr>
<tr>
<td>Education Level</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Above High School</td>
<td>-0.450</td>
<td>0.548</td>
<td>-1.524</td>
<td>0.624</td>
<td>0.416</td>
</tr>
<tr>
<td>ASIA Motor Index</td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total Score at Discharge</td>
<td>0.005</td>
<td>0.003</td>
<td>-0.001</td>
<td>0.011</td>
<td>0.141</td>
</tr>
<tr>
<td>FIM locomotion, at Discharge</td>
<td>0.350</td>
<td>0.127</td>
<td>0.101</td>
<td>0.599</td>
<td>0.009 *</td>
</tr>
<tr>
<td>Days Hospitalized in the Systems Inpatient Rehab Unit</td>
<td>-0.021</td>
<td>0.007</td>
<td>-0.035</td>
<td>-0.008</td>
<td>0.003 *</td>
</tr>
</tbody>
</table>

N=112; SE = Standard Error; CI = Confidence Interval; FIM = Functional Independence Measure; ASIA = American Spinal Cord Injury Association; * = statistically significant difference (α = 0.05)
moderate assistance and maximal assistance). Fifty-one (89.5%) cases and 54 (94.7%) controls reported they were able to walk without assistance at one year while 6 (10.5%) cases and 3 (5.3%) controls reported they needed assistance to walk. In the unadjusted comparison (odds of walking independently versus needing assistance, for cases relative to controls), the odds of cases walking independently was 0.472 (95% CI = 0.112, 1.989) comparison to controls which is a non-significant difference (p=0.257). The probability of walking independently was also modeled using a generalized linear mixed-effects model and the comparison between cases and controls was quantified using an adjusted odds ratio (odds of completing the task on their own versus needing assistance, for cases relative to controls) controlling for marital status, education level, ASIA motor index total score at discharge, FIM Locomotion at discharge, and days hospitalized during inpatient rehabilitation. In the adjusted model, cases had 1.51 (95% CI = 0.393, 5.786) greater odds of ambulating without assistance at one year than controls which was not a statistically significant difference (p=0.541). There were not any significant relationships between any of the covariates in the model to the odds of ambulating independently.

When evaluating stairs dichotomized into independence and needing assistance, 32 (56.1%) cases and 31 (54.4%) controls reported they were able to ascend a flight of stairs independently while 25 (43.9%) cases and 26 (45.6%) controls reported they required assistance. Utilizing an unadjusted odds ratio (odds of completing the task on their own versus needing assistance, for cases relative to controls) cases had 1.074 (95% CI = 0.513, 2.247) greater odds of ascending a flight of stairs without assistance in comparison to
controls which is a non-significant difference \((p=0.842)\). The probability of ascending a flight of stairs on their own was modeled using a generalized linear mixed-effects model and comparison between cases and controls were quantified using an adjusted odds ratio (odds of completing the task on their own versus needing assistance, for cases relative to controls) controlling for marital status, education level, ASIA motor index total score at discharge, FIM Locomotion at discharge, and days hospitalized during inpatient rehabilitation. Cases were 1.205 (95% CI = 0.407, 3.570) times more likely to ascend one flight of stairs without assistance than controls. This difference did not reach statistical significance \((p=0.727)\). Also, when examining the impact of covariates on the model, the adjusted odds ratio for hospitalization during inpatient rehabilitation was 0.98 \((p=0.027)\) for every day increase in hospitalization during inpatient rehabilitation. See Table 4.9 Adjusted Odds Ratio of FIM Locomotion at One Year Follow-Up and Table 4.10 Adjusted Odds Ratio of FIM Stairs at One Year Follow-Up.

**H\(_1\):** At one year post-injury individuals with motor incomplete SCI who received the NRN LT protocol will demonstrate greater odds of being able to walk in the home, community, and up a flight of stairs in comparison to controls matched on age, gender, NRN site, mode of mobility at discharge from inpatient rehabilitation and motor function (AIS C or D) reported on the following mobility-related outcome questions:

**Ability to walk >150 ft. with or without a mobility aide within the home**

At one year, 42 (66.7%) cases and 40 (63.5%) controls reported they were able to walk greater than or equal to 150ft in their home while 21 (33.3%) cases and 23 (36.5%) controls reported they were not able to complete this task. The odds of being able to walk
Table 4.9 Adjusted Odds Ratio of FIM Locomotion at One Year Follow-Up

<table>
<thead>
<tr>
<th>Comparison</th>
<th>Odds Ratio</th>
<th>Lower 95% CI</th>
<th>Upper 95% CI</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases vs. Controls</td>
<td>1.507</td>
<td>0.393</td>
<td>5.786</td>
<td>0.541</td>
</tr>
<tr>
<td>Covariates</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Marital Status</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Married/Unmarried Couple</td>
<td>1.584</td>
<td>0.413</td>
<td>6.071</td>
<td>0.506</td>
</tr>
<tr>
<td>Education Level</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Above High School</td>
<td>0.399</td>
<td>0.100</td>
<td>1.584</td>
<td>0.199</td>
</tr>
<tr>
<td>ASIA Motor Index Total Score at Discharge</td>
<td>1.003</td>
<td>0.986</td>
<td>1.020</td>
<td>0.736</td>
</tr>
<tr>
<td>FIM Mod I/Indep vs. Supervision/Assistance</td>
<td>1.069</td>
<td>0.222</td>
<td>5.142</td>
<td>0.934</td>
</tr>
<tr>
<td>Days Hospitalized in the Systems Inpatient Rehab Unit</td>
<td>0.993</td>
<td>0.977</td>
<td>1.009</td>
<td>0.377</td>
</tr>
</tbody>
</table>

N=113 CI = Confidence Interval; Mod I = Modified Independence; Indep = Independence; FIM = Functional Independence Measure; ASIA = American Spinal Cord Injury Association; * = statistically significant difference (α = 0.05)
Table 4.10 Adjusted Odds Ratio of FIM Stairs at One Year Follow-Up

<table>
<thead>
<tr>
<th>Comparison</th>
<th>Odds Ratio</th>
<th>Lower 95% CI</th>
<th>Upper 95% CI</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases vs. Controls</td>
<td>1.205</td>
<td>0.407</td>
<td>3.570</td>
<td>0.727</td>
</tr>
<tr>
<td><strong>Covariates</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Marital Status</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Married/Unmarried Couple</td>
<td>0.850</td>
<td>0.305</td>
<td>2.367</td>
<td>0.506</td>
</tr>
<tr>
<td>Education Level</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Above High School</td>
<td>0.747</td>
<td>0.254</td>
<td>2.198</td>
<td>0.199</td>
</tr>
<tr>
<td>ASIA Motor Index Total Score at Discharge</td>
<td>1.002</td>
<td>0.997</td>
<td>1.007</td>
<td>0.736</td>
</tr>
<tr>
<td>FIM Mod I/Indep vs. Supervision/Assistance</td>
<td>2.124</td>
<td>0.122</td>
<td>37.013</td>
<td>0.934</td>
</tr>
<tr>
<td>Days Hospitalized in the Systems Inpatient Rehab Unit</td>
<td>0.980</td>
<td>0.964</td>
<td>0.997</td>
<td>0.027 *</td>
</tr>
</tbody>
</table>

N=93 CI = Confidence Interval; Mod I = Modified Independence; Indep = Independence; FIM = Functional Independence Measure; ASIA = American Spinal Cord Injury Association; * = statistically significant difference;
greater than or equal to 150 feet in the home is 1.15 times greater (95% CI = 0.552 – 2.394) for cases than controls in the unadjusted model which is a non-significant difference (p=0.683). However, after fitting a generalized linear mixed-effects model, the odds of being able to walk greater than or equal to 150 feet in the home is 3.06 times greater (95% CI = 1.10 - 9.19) for cases than controls after adjusting for marital status, education, ASIA motor index total, FIM Total Motor Score at discharge from inpatient rehabilitation, and days hospitalized during inpatient rehabilitation. This represents a statistically significant difference between cases and controls (p=0.047). Also, when evaluating the impact of covariates on the outcome, FIM Total Motor Score at discharge from inpatient rehabilitation and days hospitalized during inpatient rehabilitation demonstrated a statistically significant effect on the outcome. Adjusted odds ratios were 1.05 (p=0.002) and 0.98 (p=0.042) times greater for every one unit increase in FIM Total Motor Score at discharge and for every one day increase hospitalization during inpatient rehabilitation, respectively. See Table 4.11 Adjusted Odds Ratio Walking 150ft in the Home at One Year Follow-Up.

**Ability to walk with or without a mobility aide one street block outside the home**

At one year, 37 (58.7%) cases and 36 (57.1%) controls reported they were able to walk one street block while 26 (41.3%) cases and 27 (42.9%) controls reported they were not. The odds of being able to walk one street block is 1.07 times greater (95% CI = 0.526 – 2.165) for cases than controls in the unadjusted model which is a non-significant difference (p=0.847). Utilizing a generalized mixed-effects model, the odds of walking one street block outside the home is 1.91 times greater for cases than controls (95% CI = 0.65, 5.56) after
adjusting for marital status, education, ASIA motor index total, FIM Total Motor Score at discharge from inpatient rehabilitation, and days hospitalized during inpatient rehabilitation. This is not a statistically significant difference between cases and controls \( (p=0.233) \). Also, the adjusted the odds ratio was 1.06 times greater \( (p=0.002) \) for every unit increase in FIM Total Motor Score at discharge from inpatient rehabilitation. See Table 4.12 Adjusted Odds Ratio Walking 1 Block Outside at One Year Follow-Up.

**Ability to walk with or without mobility aide up one flight of steps**

At one year, 36 (57.1\%) cases and 37 (58.7\%) controls reported they were able to walk up one flight of stairs while 27 (43.9\%) cases and 26 (41.3\%) controls reported they were not. The odds of being able to walk up a flight of stairs is 0.937 times \( (95\% \text{ CI } = 0.462 – 1.901) \) for cases in comparison to controls in the unadjusted model which is a non-significant difference \( (p=0.842) \). However, after adjusting for marital status, education, ASIA motor index total, FIM Total Motor Score at discharge from inpatient rehabilitation and days hospitalized during inpatient rehabilitation, the odds of walking up one flight of steps is 3.08 times greater for cases than controls \( (95\% \text{ CI } = 0.94, 10.10; \ p = 0.062) \). This is not a statistically significant difference. When evaluating the impact of covariates on the outcome, the FIM Total Motor Score at discharge from inpatient rehabilitation had a statistically significant impact on the outcome. The adjusted odds ratio was 1.07 times greater \( (p=0.002) \) for every unit increase in FIM Total Motor Score at discharge from inpatient rehabilitation. See Table 4.13 Adjusted Odds Ratio Walking One Flight of Stairs at One Year Follow-Up.
Table 4.11 Adjusted Odds Ratio Walking 150ft in the Home at One Year Follow-Up

<table>
<thead>
<tr>
<th>Comparison</th>
<th>Odds Ratio</th>
<th>Lower 95% CI</th>
<th>Upper 95% CI</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases vs. Controls</td>
<td>3.058</td>
<td>1.017</td>
<td>9.192</td>
<td>0.047 *</td>
</tr>
<tr>
<td>Covariates</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Marital Status</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Married/Unmarried Couple</td>
<td>1.642</td>
<td>0.597</td>
<td>4.516</td>
<td>0.342</td>
</tr>
<tr>
<td>Education Level</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Above High School</td>
<td>0.659</td>
<td>0.224</td>
<td>1.940</td>
<td>0.453</td>
</tr>
<tr>
<td>ASIA Motor Index Total Score at Discharge</td>
<td>1.000</td>
<td>0.994</td>
<td>1.005</td>
<td>0.957</td>
</tr>
<tr>
<td>FIM Total Motor Score, at Discharge</td>
<td>1.046</td>
<td>1.018</td>
<td>1.074</td>
<td>0.002 *</td>
</tr>
<tr>
<td>Days Hospitalized in the Systems Inpatient Rehab Unit</td>
<td>0.985</td>
<td>0.970</td>
<td>0.999</td>
<td>0.042 *</td>
</tr>
</tbody>
</table>

N=114; CI = Confidence Interval; FIM = Functional Independence Measure; ASIA = American Spinal Cord Injury Association; * = statistically significant difference
Table 4.12 Adjusted Odds Ratio Walking 1 Block Outside at One Year Follow-Up

<table>
<thead>
<tr>
<th>Comparison</th>
<th>Odds Ratio</th>
<th>Lower 95% CI</th>
<th>Upper 95% CI</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases vs. Controls</td>
<td>1.907</td>
<td>0.654</td>
<td>5.560</td>
<td>0.233</td>
</tr>
<tr>
<td><strong>Covariates</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Marital Status</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Married/Unmarried Couple</td>
<td>1.508</td>
<td>0.564</td>
<td>4.030</td>
<td>0.417</td>
</tr>
<tr>
<td>Education Level</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Above High School</td>
<td>1.292</td>
<td>0.449</td>
<td>3.723</td>
<td>0.637</td>
</tr>
<tr>
<td>ASIA Motor Index Total Score at Discharge</td>
<td>1.003</td>
<td>0.995</td>
<td>1.006</td>
<td>0.913</td>
</tr>
<tr>
<td>FIM Total Motor Score, at Discharge</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Days Hospitalized in the Systems Inpatient</td>
<td>0.995</td>
<td>0.981</td>
<td>1.008</td>
<td>0.455</td>
</tr>
<tr>
<td>Rehab Unit</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

N=114; CI = Confidence Interval; FIM = Functional Independence Measure; ASIA = American Spinal Cord Injury Association; * = statistically significant
Research Aim 2

Evaluate and compare one year re-hospitalization, QOL and community participation for individuals with motor incomplete SCI who received the NRN LT protocol (cases) in post-acute rehabilitation to matched controls (age, gender, injury year, NRN center, mode of mobility at discharge from inpatient rehabilitation and motor function) who received usual care (controls).

H$_2$1: Individuals with motor incomplete SCI, who received the NRN LT protocol will report better QOL as measured by the SWLS$^{60}$ in comparison to controls matched on age, gender, injury year, NRN center, mode of mobility at discharge from inpatient rehabilitation, and motor function (AIS C or D).

Life Satisfaction

Cases scored 1.6 (SD=10.8) units higher on average ($p=0.234$) than controls on life satisfaction using an unadjusted model at one year which is a non-significant difference favoring the cases. Using a linear mixed-effects model, on average, cases scored 3.98 units higher on the SWLS than controls at one year follow-up (95% CI = 0.679, 7.273) after adjusting for marital status, education level, ASIA total motor index score, FIM Total Motor Score, and days of hospitalization during inpatient rehabilitation. This is a statistically significant difference at $p=0.019$. The between group effect size was estimated to be 0.50. Also, every one day increase in hospitalization in the inpatient rehabilitation unit was associated with a 0.06 unit decrease ($p=0.006$) in one year life satisfaction score. See Table 4.14 Adjusted Life Satisfaction Scores.
Table 4.13 Adjusted Odds Ratio Walking One Flight of Stairs at One Year Follow-Up

<table>
<thead>
<tr>
<th>Comparison</th>
<th>Odds Ratio</th>
<th>Lower 95% CI</th>
<th>Upper 95% CI</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases vs. Controls</td>
<td>3.084</td>
<td>0.942</td>
<td>10.102</td>
<td>0.062</td>
</tr>
<tr>
<td>Covariates</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Marital Status</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Married/Unmarried Couple</td>
<td>0.786</td>
<td>0.268</td>
<td>2.303</td>
<td>0.663</td>
</tr>
<tr>
<td>Education Level</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Above High School</td>
<td>0.897</td>
<td>0.282</td>
<td>2.849</td>
<td>0.854</td>
</tr>
<tr>
<td>ASIA Motor Index Total Score at Discharge</td>
<td>1.001</td>
<td>0.996</td>
<td>1.007</td>
<td>0.636</td>
</tr>
<tr>
<td>FIM Total Motor Score, at Discharge</td>
<td>1.069</td>
<td>1.035</td>
<td>1.104</td>
<td>0.002*</td>
</tr>
<tr>
<td>Days Hospitalized in the Systems Inpatient Rehab Unit</td>
<td>0.986</td>
<td>0.969</td>
<td>1.003</td>
<td>0.114</td>
</tr>
</tbody>
</table>

N=114 CI = Confidence Interval; FIM = Functional Independence Measure; ASIA = American Spinal Cord Injury Association; * = statistically significant difference
**H₂**: Individuals with motor incomplete SCI, who received the NRN LT protocol will report better community participation as measured by the CHART-SF in comparison to controls matched on age, gender, injury year, NRN center, mode of mobility at discharge from inpatient rehabilitation, and motor function (AIS C or D).

**Community Participation**

Controls scored 10.4 (SD=42.8) units higher on average ($p=0.056$) than controls on the CHART-SF Physical Independence Subscale using an adjusted model at one year which is a non-significant difference favoring the controls. Using a linear mixed-effects model, there is no significant difference between cases and controls on the CHART-SF Physical Independence Subscale score at one year follow-up (difference = 0, 95% CI = -13.1, 13.1) after controlling for marital status, education, ASIA motor index at discharge from inpatient rehabilitation, FIM Total Motor Score, and days hospitalized during inpatient rehabilitation.

In addition, several covariates were found to have significant relationships with CHART-SF Physical Independence scores at one year follow-up. Every one unit increase in FIM Total Motor Score at discharge from inpatient rehabilitation was associated with a 0.49 unit increase ($p=0.004$) for one year CHART-SF Physical Independence score; while every one day increase in hospitalization in the inpatient rehabilitation unit was associated with a 0.21 unit ($p=0.017$) decrease in one year CHART-SF Physical Independence score. See Table 4.15 Adjusted CHART-SF Physical Independence Subscale at One Year Follow-Up.

Cases scored 11.5 (SD=28.5) units higher on average than controls on the CHART-SF Mobility Subscale using an unadjusted model at one year which was is a significant difference favoring the cases ($p=0.002$). After adjusting for important covariates, on
Table 4.14 Adjusted Life Satisfaction Scores at One Year Follow-Up

<table>
<thead>
<tr>
<th>Comparison</th>
<th>Mean Difference</th>
<th>SE</th>
<th>Lower 95% CI</th>
<th>Upper 95% CI</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases vs. Controls</td>
<td>3.976</td>
<td>1.633</td>
<td>0.679</td>
<td>7.273</td>
<td>0.019</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Covariates</th>
<th>Estimate</th>
<th>SE</th>
<th>Lower 95% CI</th>
<th>Upper 95% CI</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marital Status</td>
<td>-0.922</td>
<td>1.558</td>
<td>-3.976</td>
<td>2.132</td>
<td>0.557</td>
</tr>
<tr>
<td>Married/Unmarried Couple</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Education Level</td>
<td>-0.731</td>
<td>1.693</td>
<td>-4.048</td>
<td>2.587</td>
<td>0.668</td>
</tr>
<tr>
<td>Above High School</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ASIA Motor Index</td>
<td>-0.001</td>
<td>0.009</td>
<td>-0.019</td>
<td>0.017</td>
<td>0.897</td>
</tr>
<tr>
<td>Total Score at Discharge</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FIM Total Motor Score, at Discharge</td>
<td>0.046</td>
<td>0.040</td>
<td>-0.033</td>
<td>0.125</td>
<td>0.258</td>
</tr>
</tbody>
</table>
| Days Hospitalized in the Systems Inpatient Rehab Unit | -0.061 | 0.021 | -0.102 | -0.019 | 0.006 *

N=114; SE = Standard Error; CI = Confidence Interval; ASIA = American Spinal Cord Injury Association; FIM = Functional Independence Measure; * = statistically significant difference
average, cases scored 18.2 points higher than controls on the CHART-SF Mobility Subscale score at one-year post discharge which is also a statistically significant difference between the groups (95% CI = 10.2, 26.1; \( p < 0.001 \)). The between group effect size was estimated to be 0.79. In addition, several covariates were found to have significant relationships with the CHART-SF Mobility score at one year. Every one unit increase in FIM Total Motor Score at discharge from inpatient rehabilitation resulted in a 0.39 unit increase in CHART-SF Mobility score at one year (\( p < 0.001 \)); while every one day increase in hospitalization during inpatient rehabilitation was associated with a 0.14 unit decrease in one year CHART-SF Mobility score (\( p=0.015 \)). See Table 4.16 Adjusted CHART-SF Mobility Subscale at One Year Follow-Up.

Cases scored 1.8 (SD=49.0) units higher on average (\( p=0.776 \)) than controls on the CHART-SF Occupation subscale using an unadjusted model at one year which is a non-significant difference favoring the cases. However, after controlling for marital status, education, ASIA motor index at discharge from inpatient rehabilitation, FIM Total Motor Score, and days hospitalized during inpatient rehabilitation, cases scored, on average, 15.6 points higher than controls at one year after injury (95% CI = 2.07, 29.06; \( p=0.025 \)). This demonstrates a statistically significant difference between cases and controls. The between group effect size on the CHART-SF Occupational score was estimated to be 0.43. In addition, FIM Total Motor Score at discharge from inpatient rehabilitation had a significant impact on CHART-SF Occupational score at one year. For every one unit increase in FIM Total Motor Score at discharge, cases demonstrated a 0.62 unit increase in CHART-SF Occupational score.
at one year follow-up ($p=0.001$). See Table 4.17 Adjusted CHART-SF Occupational Subscale at One Year Follow-Up.

Cases scored 7.5 (SD=26.1) units higher on average ($p=0.028$) than controls on the CHART-SF Social Integration Subscale using an unadjusted model at one year which is a significant difference between groups favoring the cases ($p=0.028$). After controlling for marital status, education, ASIA motor index at discharge from inpatient rehabilitation, FIM Total Motor Score, and days hospitalized during inpatient rehabilitation, on average, cases scored 8.37 points higher than controls at one year follow-up (95% CI = 0.49, 16.26) on the CHART-SF Social Integration Subscale which demonstrates a statistically significant difference between cases and controls at $p=0.038$. The between group effect size on this measure was estimated to be 0.46. In addition, FIM Total Motor Score at discharge from inpatient rehabilitation had a significant impact on the CHART-SF Social Integration score at one year. For every one unit increase in FIM Total Motor Score at discharge from inpatient rehabilitation, there is a 0.21 unit increase in CHART-SF Social Integration score ($p=0.034$) at one year follow-up. See Table 4.18 Adjusted CHART-SF Social Integration Subscale at One Year Follow-Up.

H$_2$3: Individuals with motor incomplete SCI, who received the NRN LT protocol will report decreased number of re-hospitalizations and decreased numbers of days re-hospitalized during the first year after SCI in comparison to controls matched on age, gender, injury year, NRN center, mode of mobility at discharge from inpatient rehabilitation and motor function (AIS C or D).
Table 4.15 Adjusted CHART-SF Physical Independence Subscale at One Year Follow-Up

<table>
<thead>
<tr>
<th>Comparison</th>
<th>Mean Difference</th>
<th>SE</th>
<th>Lower 95% CI</th>
<th>Upper 95% CI</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases vs. Controls</td>
<td>0.0</td>
<td>6.492</td>
<td>-13.1</td>
<td>13.1</td>
<td>0.999</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Covariates</th>
<th>Estimte</th>
<th>SE</th>
<th>Lower 95% CI</th>
<th>Upper 95% CI</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marital Status</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Married/Unmarried Couple</td>
<td>3.149</td>
<td>6.222</td>
<td>-9.045</td>
<td>15.344</td>
<td>0.615</td>
</tr>
<tr>
<td>Education Level</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Above High School</td>
<td>6.381</td>
<td>6.755</td>
<td>-6.858</td>
<td>19.620</td>
<td>0.350</td>
</tr>
<tr>
<td>ASIA Motor Index Total Score at Discharge</td>
<td>0.033</td>
<td>0.037</td>
<td>-0.040</td>
<td>0.105</td>
<td>0.382</td>
</tr>
<tr>
<td>FIM Total Motor Score, at Discharge</td>
<td>0.487</td>
<td>0.161</td>
<td>0.171</td>
<td>0.802</td>
<td>0.004 *</td>
</tr>
<tr>
<td>Days Hospitalized in the</td>
<td>-0.211</td>
<td>0.085</td>
<td>-0.377</td>
<td>-0.045</td>
<td>0.017 *</td>
</tr>
<tr>
<td>Systems Inpatient Rehab Unit</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

N=116; SE = Standard Error; CI = Confidence Interval; ASIA = American Spinal Cord Injury Association; FIM = Functional Independence Measure; * = statistically significant difference
<table>
<thead>
<tr>
<th>Comparison</th>
<th>Mean Difference</th>
<th>SE</th>
<th>Lower 95% CI</th>
<th>Upper 95% CI</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases vs. Controls</td>
<td>18.2</td>
<td>3.942</td>
<td>10.2</td>
<td>26.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Covariates</td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Marital Status</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Married/Unmarried Couple</td>
<td>-1.934</td>
<td>4.027</td>
<td>-9.827</td>
<td>5.959</td>
<td>0.634</td>
</tr>
<tr>
<td>Education Level Above High School</td>
<td>7.304</td>
<td>4.351</td>
<td>-1.224</td>
<td>15.833</td>
<td>0.101</td>
</tr>
<tr>
<td>ASIA Motor Index Total Score at Discharge</td>
<td>0.004</td>
<td>0.024</td>
<td>-0.043</td>
<td>0.050</td>
<td>0.881</td>
</tr>
<tr>
<td>FIM Total Motor Score, at Discharge</td>
<td>0.389</td>
<td>0.102</td>
<td>-0.246</td>
<td>-0.031</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Days Hospitalized in the Systems Inpatient Rehab Unit</td>
<td>-0.138</td>
<td>0.055</td>
<td>0.189</td>
<td>0.590</td>
<td>0.015</td>
</tr>
</tbody>
</table>

N=115; SE = Standard Error; CI = Confidence Interval; ASIA = American Spinal Cord Injury Association; FIM = Functional Independence Measure; *= statistically significant difference
Table 4.17 Adjusted CHART-SF Occupational Subscale at One Year Follow-Up

<table>
<thead>
<tr>
<th>Comparison</th>
<th>Mean Difference</th>
<th>SE</th>
<th>Lower 95% CI</th>
<th>Upper 95% CI</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases vs. Controls</td>
<td>15.563</td>
<td>6.690</td>
<td>2.071</td>
<td>29.055</td>
<td>0.025 *</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Covariates</th>
<th>Estimate</th>
<th>SE</th>
<th>Lower 95% CI</th>
<th>Upper 95% CI</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marital Status</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Married/Unmarried Couple</td>
<td>12.452</td>
<td>6.618</td>
<td>-0.519</td>
<td>25.423</td>
<td>0.067</td>
</tr>
<tr>
<td>Education Level</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Above High School</td>
<td>3.642</td>
<td>7.242</td>
<td>10.553</td>
<td>17.837</td>
<td>0.618</td>
</tr>
<tr>
<td>ASIA Motor Index</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total Score at Discharge</td>
<td>-0.055</td>
<td>0.039</td>
<td>-0.131</td>
<td>0.022</td>
<td>0.169</td>
</tr>
<tr>
<td>FIM Total Motor Score, at Discharge</td>
<td>0.623</td>
<td>0.170</td>
<td>0.290</td>
<td>0.955</td>
<td>0.001 *</td>
</tr>
<tr>
<td>Days Hospitalized in the Systems Inpatient Rehab Unit</td>
<td>-0.186</td>
<td>0.095</td>
<td>-0.372</td>
<td>0.001</td>
<td>0.058</td>
</tr>
</tbody>
</table>

N=115; SE = Standard Error; CI = Confidence Interval; ASIA = American Spinal Cord Injury Association; FIM = Functional Independence Measure; * = statistically significant difference
Table 4.18 Adjusted CHART-SF Social Integration Subscale at One Year Follow-Up

<table>
<thead>
<tr>
<th>Comparison</th>
<th>Mean Difference</th>
<th>SE</th>
<th>Lower 95% CI</th>
<th>Upper 95% CI</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases vs. Controls</td>
<td>8.374</td>
<td>3.912</td>
<td>0.486</td>
<td>16.262</td>
<td>0.038</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Covariates</th>
<th>Estimate</th>
<th>SE</th>
<th>Lower 95% CI</th>
<th>Upper 95% CI</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marital Status</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Married/Unmarried Couple</td>
<td>6.246</td>
<td>3.725</td>
<td>-1.054</td>
<td>13.546</td>
<td>0.101</td>
</tr>
<tr>
<td>Education Level Above High School</td>
<td>3.744</td>
<td>4.062</td>
<td>-4.218</td>
<td>11.706</td>
<td>0.362</td>
</tr>
<tr>
<td>ASIA Motor Index Total Score at Discharge</td>
<td>-0.004</td>
<td>0.022</td>
<td>-0.047</td>
<td>0.039</td>
<td>0.866</td>
</tr>
<tr>
<td>FIM Total Motor Score, at Discharge</td>
<td>0.214</td>
<td>0.098</td>
<td>0.022</td>
<td>0.405</td>
<td>0.034*</td>
</tr>
<tr>
<td>Days Hospitalized in the Systems Inpatient Rehab Unit</td>
<td>0.031</td>
<td>0.054</td>
<td>-0.076</td>
<td>0.137</td>
<td>0.573</td>
</tr>
</tbody>
</table>

N=114; SE = Standard Error; CI = Confidence Interval; ASIA = American Spinal Cord Injury Association; FIM = Functional Independence Measure; * = statistically significant difference
Re-Hospitalization

Eight individuals (11.1%) from the case group were re-hospitalized between discharge from inpatient rehabilitation and the one year post-injury follow-up. Six of these individuals were hospitalized one time, while two were re-hospitalized twice for a total of 10 hospitalizations in the case group. Fifteen individuals (20.8%) from the control group were re-hospitalized during the same time frame; nine of them were hospitalized once with five being hospitalized twice and one person hospitalized three times in the first year for a total of 22 hospitalizations in the control group. The number of times individuals were re-hospitalized during the first year of injury and the number of days they were re-hospitalized were modeled using a generalized linear mixed-effects model assuming a Poisson distribution. The ratio of the mean number of re-hospitalizations (and the mean number of days re-hospitalized) was used to compare cases to controls. The mean number of re-hospitalizations for controls was 1.86 times greater than that of cases. The difference between case and control was not statistically significant (95% CI = 0.75, 4.65; \( p = 0.178 \)). However, when examining the impact of covariates, the mean number of re-hospitalizations for those married/unmarried couples was 3.0 (95% CI = 1.218, 7.610; \( p = 0.178 \)) times greater than that of single/divorced/separated/widowed patients which is a statistically significant difference (\( p = 0.021 \)). See Table 4.19 Adjusted Re-Hospitalization Numbers at One year Follow-Up

Out of the eight cases who were re-hospitalized, they were re-hospitalized a mean of 19.9 (SD=30.4) and a median of 4 days (25\textsuperscript{th} percentile = 3.5; 75\textsuperscript{th} percentile = 26.5) (Interquartile range 1 to 90). The 15 individuals in the control group were re-hospitalized a
mean of 9.1 days (SD = 11.7) and a median of 4 days (25\textsuperscript{th} percentile = 2.0; 75\textsuperscript{th} percentile = 14.0) (Interquartile range 1 to 47). In this case, the medians are better measures of central tendency than the means due to the skewness of the data. The (geometric) mean number of days re-hospitalized was 2.95 times greater for cases than controls (95% CI = 1.52, 5.71; \( p = 0.002 \)). In evaluating the impact of other covariates, the mean number of re-hospitalized days for those married/unmarried couples was 2.6 (95% CI = 0.372, 1.238; \( p = 0.021 \)) times greater than that of single/divorced/separated/widowed (\( p = 0.015 \)); the mean number of re-hospitalized days for those with high school or lower education was 5.5 times greater than those with above a high school education (\( p < 0.001 \)). See Table 4.20 Adjusted Re-Hospitalization Days at One Year Follow-Up.
Table 4.19 Adjusted Re-Hospitalization Numbers at One year Follow-Up

<table>
<thead>
<tr>
<th>Comparison</th>
<th>Mean Ratio</th>
<th>Lower 95% CI</th>
<th>Upper 95% CI</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Controls vs. Cases</td>
<td>1.863</td>
<td>0.746</td>
<td>4.654</td>
<td>0.178</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Covariates</th>
<th>Mean Ratio</th>
<th>Lower 95% CI</th>
<th>Upper 95% CI</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marital Status</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Married/Unmarried Couple</td>
<td>3.045</td>
<td>1.218</td>
<td>7.610</td>
<td>0.021   *</td>
</tr>
<tr>
<td>Education Level</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Above High School</td>
<td>0.533</td>
<td>0.192</td>
<td>1.484</td>
<td>0.234</td>
</tr>
<tr>
<td>ASIA Motor Index</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total Score at Discharge</td>
<td>0.998</td>
<td>0.988</td>
<td>1.008</td>
<td>0.675</td>
</tr>
<tr>
<td>FIM Total Motor Score, at Discharge</td>
<td>0.982</td>
<td>0.959</td>
<td>1.005</td>
<td>0.126</td>
</tr>
<tr>
<td>Days Hospitalized in the Systems Inpatient Rehab Unit</td>
<td>0.995</td>
<td>0.984</td>
<td>1.006</td>
<td>0.362</td>
</tr>
</tbody>
</table>

N=125; CI = Confidence Interval; ASIA = American Spinal Cord Injury Association; FIM = Functional Independence Measure; * = statistically significant difference;
Table 4.20 Adjusted Re-Hospitalization Days at One Year Follow-Up

<table>
<thead>
<tr>
<th>Comparison</th>
<th>Mean Ratio</th>
<th>Lower 95% CI</th>
<th>Upper 95% CI</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cases vs. Controls</strong></td>
<td>2.947</td>
<td>1.522</td>
<td>5.707</td>
<td>0.002</td>
</tr>
<tr>
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<td>0.988</td>
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<td>0.985</td>
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N=125; CI = Confidence Interval; ASIA = American Spinal Cord Injury Association; FIM = Functional Independence Measure; * = statistically significant difference;
CHAPTER V

DISCUSSION

Baseline Comparison

A comparison of cases and controls at the time of discharge from inpatient rehabilitation revealed statistically significant differences in the following areas: days of hospitalization during inpatient rehabilitation, FIM Transfer Index, FIM Total Motor Score, FIM Stairs, marriage/couple status, educational level, and insurance carrier. Cases spent a significantly greater number of days in inpatient rehabilitation while also discharging with less mobility and independence as noted by significantly lower FIM Transfer Index scores, FIM Total Motor Scores and FIM Stairs scores. Insurance requires that individuals must have medical reasons (infections, pressure injuries, and respiratory compromise) to remain in inpatient rehabilitation once the patient and family have been trained to safely provide care. Therefore, given that cases and controls were site matched, having the same discharge guidelines in each system of care, one can infer that the patients referred to the NRN likely had greater severity of injury and potentially more medical complications to justify a longer length of stay in inpatient rehabilitation. Previous literature supports the positive association of severity of injury and comorbidities to length of stay in SCI.129,130

These baseline differences were surprising and represent a potential selection bias that is not accounted for in the NRN protocol. All individuals who present with an AIS C or D injury are eligible for participation in the NRN while it appears that across the sites, those with the greatest functional impairment are more likely to be referred to this program instead of traditional rehabilitation programs. This is potentially due to the intense staffing
model (one PT and three technicians) and high technology utilization (treadmill system with BWS) provided in the NRN in comparison to traditional rehabilitation (generally one PT with limited technology). Individuals who are less functionally impaired (higher FIM Total Motor Scores) may be more commonly referred to a traditional outpatient therapy program where they can achieve their goals and improve mobility while only requiring the assistance from one therapist. This appears to be the most reasonable clinically relevant explanation for the lower scores in mobility/independence (lower FIM Total Motor Score, FIM Transfer Index and FIM Stairs) in cases versus controls at discharge from inpatient rehabilitation. Clinically and fiscally, this is important information to begin to understand who may benefit from this type of intensive and more costly program while also determining who may be able to participate in a less expensive therapy model while still maximizing their recovery after SCI.

Payer mix (type of health care insurance that paid for inpatient rehabilitation) was also significantly different between the two groups with more cases having private insurance and more controls having Medicare/Medicaid. Future investigations should include this variable for analysis given the limited outpatient therapy reimbursement associated with governmental payer sources as it’s difficult to financially support a program with an intensive staffing model if the majority of participants do not have private insurance. The analysis was unable to control for payer mix in these models due to the large number of missing data as 61.1% was unknown for the entire sample (58.3% cases unknown; 63.9% controls unknown). This may be an area of influence/bias that could not be controlled for in this analysis and should be included in future prospective studies.
There was a significantly higher number of couples (married or unmarried) in the case group in comparison to the control group while the individuals in the case group also had a significantly higher educational level than the control group. A plausible explanation for this difference may be due to the fact that there are only six NRN centers in the US providing this intervention. Therefore, many individuals must relocate to one of the six cities to complete the program and often need physical assistance and financial support of a significant other to live outside their home community and participate in the NRN program. In terms of education, higher levels of education may be an indicator of higher socioeconomic status allowing individuals who have the financial means to live outside their home community for months at a time to participate in the NRN program. Given that both education level and family support\textsuperscript{131,132} have been shown to be important factors impacting outcomes after SCI,\textsuperscript{131,132} these covariates were included in all models and their impact described in each of the analyses.

**Primary Results**

In initial unadjusted models, the only two outcomes that were significantly different between cases and controls were the CHART-SF Mobility Subscale score and the CHART-SF Social Integration Subscale score with differences favoring cases on both outcomes. Adjusted models yielded statistically significant differences favoring cases over controls on the following outcomes: FIM Total Motor Score; FIM Transfer Index; SWLS; CHART-SF Mobility, Occupation, and Social Integration subscales; and the odds of walking 150ft without assistance. Cases also demonstrated greater improvement over controls that did not reach statistical significance on the following outcomes: FIM Locomotion and Stairs
Research Aim 1 (H₁): FIM Total Motor Score, Transfer Index, Locomotion and Stairs

FIM Total Motor Score

There was not a statistical difference in FIM Total Motor Scores between cases and controls at one year post-injury in the unadjusted model (p=0.925). However, after controlling for additional relevant covariates, individuals who participated in the NRN protocol demonstrated greater overall independence with mobility than matched individuals who did not receive this intense LT program. This is the first literature in SCI comparing LT to usual care after inpatient rehabilitation rather than comparing LT to an alternate intervention. The FIM Total Motor Score is used to characterize how much assistance an individual needs to move in bed, eat, bathe, groom, transfer to and from multiple surfaces, and mobilize in their home and community. The cases in this study on average scored approximately 10 points higher on the FIM Total More Score than their matched controls. Unfortunately, a minimal clinically important difference has not been established for the FIM Total Motor Score for individuals who have motor incomplete SCI. However, a 10 point difference is suggestive of a level of improvement on almost all of the 13 items which would be clinically meaningful as being able to perform daily tasks with less
assistance may allow individuals with SCI to live more independently requiring less caregiver assistance.

In regards to the covariates that demonstrated a significant association to the outcome of this model, individuals with higher education scored significantly lower than those with a high school education/lower at one year follow-up. This was not expected and further investigation is warranted regarding the relationship between mobility and education. FIM scores at discharge from inpatient rehabilitation demonstrated a positive and significant association with FIM scores at one year follow-up. Although there is no plausible explanation for the impact of education on this model, FIM scores at discharge from inpatient rehabilitation have been shown to be predictive of FIM scores at one year follow-up. Cohen et al\textsuperscript{133} reported a one year increase of 0.76 units for every unit increase of FIM motor score at discharge from inpatient rehabilitation which is similar to the 0.66 unit increase found here. Longer lengths of stay (days of hospitalization during inpatient rehabilitation) were predictive of lower FIM Total Motor Scores at one year. Length of stay during inpatient rehabilitation and severity of injury has been shown to predict length of stay during inpatient rehabilitation and has also been shown to negatively impact an individual’s ability to make functional improvements at one year which is also similar to these results.\textsuperscript{129,130,133}

With regard to previous intensive LT literature, Alexeeva et al\textsuperscript{101} reported a baseline average FIM Total Motor Score of 66.3 (SD=17.2) in a cohort of 35 individuals with a chronic (>1 year) motor incomplete SCI prior to 13 weeks of LT with and without BWS. In response to training, both groups (with and without BWS) demonstrated on average a 2 point FIM
Total Motor score increase. In contrast, the control group in this current study
demonstrated a 12 point improvement while cases demonstrated a 23 point improvement
in FIM Total Motor Score over the first year after injury (unadjusted). Providing intensive LT
earlier versus later after injury has been reported to improve long-term outcomes. In addition, spontaneous recovery is likely responsible for some of the improvement in these
groups (both cases and controls) which is thought to be most impactful during the first 3
months post-injury. A medium effect size (0.53) was estimated between cases and
controls at one year post-injury with the magnitude of the treatment effect being greater
for cases than controls. Even though both groups (cases and controls) likely experienced
some degree of spontaneous recovery during that initial year after SCI, the cases
experienced a greater effect from treatment (LT) than controls (usual care).

In terms of the financial cost associated with SCI, Cohen et al reported that for
every 5 point increase in FIM Total Motor Score, the number of re-hospitalizations each
year reduces by 0.022, while the amount of personal care assistance decreases by 3.6%. Miller et al used these numbers to report that for every 5 point increase in FIM Total
Motor Score, annual direct costs associated with SCI decrease by about $25,000 in the first
year of injury and $4,000 annually thereafter. A 10 point FIM Total Motor Score difference
at one year between cases and controls was found in the current study, which using these
previously published numbers may result in a $50,000 decrease in direct costs the first year
after injury and an $8,000 decrease annually thereafter for those who received the NRN LT
protocol in comparison to those who received usual care. Given that the mean age at injury
in both groups in this study was 38 years old, the estimated length of survival for this cohort
is 35 years. Therefore, the potential lifetime savings based on this estimation is $330,000 for each individual and would result in approximately a $24 million dollar savings between cases and controls in this cohort over their lifetime. This would also result in an estimated $48 million dollar savings to the healthcare system if both groups were given the opportunity to participate and benefit from this intervention. This projection includes only the cost savings associated with re-hospitalization and caregiver assistance (Miller et al) and does not take into account additional savings associated with home modifications and equipment that were also reported in response to intensive LT by Morrison et al. This potential cost savings could justify and offset the expense of intensive LT after SCI and compel government agencies (Medicare and Medicaid) to pay for these interventions by demonstrating the long term decrease in burden placed on the US health care system. The cost of the NRN program at one SCIMS is approximately $8600 for every 20 sessions of therapy while traditional OP therapy is approximately $5800 for every 20 sessions for an estimated difference of $3,000 between interventions for every 20 sessions. The cases in this study completed a median of 60 LT sessions which results in a $9,000 increase in cost for NRN services in comparison to traditional PT. With an estimated $50,000 savings the first year after SCI due to a 10 point FIM Total Motor Score difference, the NRN intervention would result in a net cost savings of $41,000 the first year of injury in addition to the estimated $8,000 every year after. As previously stated, the initial greater cost of NRN therapy ($9,000) is easily justified with the $330,000 lifetime cost reduction for each individual in the case group.
**FIM Locomotion and Stairs**

In regards to FIM locomotion, locomotion and stairs were analyzed in combination using a linear mixed-effects model due to low numbers and cell counts that were encountered when attempting to evaluate each item separately. Non-significant differences were found between groups in the unadjusted model ($p=0.233$). Non-significant differences were also found in the adjusted model with cases scoring a half point higher than controls when the two tasks were combined for analysis. It’s difficult to determine whether there is a true difference between groups due to the small sample size and inability to analyze these items separately. It is also not possible to use FIM locomotor item to determine if there is a true difference in walking ability between groups as the reported numeric value does not distinguish whether they are walking or using a wheelchair as it only focuses on distance and assist level. For example, one individual may report they can mobilize in a wheelchair without assistance for 150ft which would score a 6 on the locomotor item while another individual reports they can walk 150ft using a walker without physical assistance and would also score a 6 on the same item. Therefore, previous literature has recommended not using this item of the FIM when attempting to capture functional change in walking ability.$^{125}$ More data is required in future investigations to evaluate if a true difference exists between groups (especially in regards to walking ability) and if so, whether or not there is a clinically meaningful difference.

Specific to walking, Dobkins et al$^{36}$ used FIM Locomotion as a primary outcome in a comparison of LT with BWS to conventional therapy during inpatient rehabilitation. They reported baseline locomotor FIM scores of 1.0 (SD=1-2) in their combined group of AIS C
and D injuries with 92% (22/24) of these subjects achieving a score of \( \geq 6 \) (modified independent) at 6 months post-injury. They did not find a statistically significant difference between the two treatment groups with both groups demonstrating impressive recovery likely heavily influenced by spontaneous recovery as individuals participated in this trial during the first three months post-injury. Kapadia et al\(^\text{112}\) reported no significant change in FIM locomotor scores between groups after one year of LT with and without FES (LT with FES 4.70 to 5.19 after one year of training; LT without FES 4.18 to 5.09). It’s difficult to compare these results to the results obtained in this analysis due to the differences in treatment design, but it does support small (less than 1 point) treatment effects using the FIM Locomotion item as the primary outcome measure. As previously discussed, the cases in this study demonstrated a 0.5 point improvement over controls using the adjusted model on the locomotor item which included both locomotion and stairs and was not statistically significant. This outcome is in line with the results of Kapadia et al\(^\text{112}\) demonstrating small changes associated with this one FIM item in response to LT. However, it is not ideal that locomotion and stairs items were combined for this analysis as cases demonstrated significantly lower scores on stairs at discharge from inpatient rehabilitation than controls which was not adjusted for in this analysis and could be confounding the outcome.

As previously discussed, FIM Locomotion and FIM Stairs could not be analyzed independently due to unequal/low cell counts, so adjusted odds ratios were completed comparing those individuals who reported being able to walk/climb 1 flight of steps without assistance (independent or modified independent) compared to those who required assistance (minimal assistance, moderate assistance, maximum assistance, total assistance).
A non-significant trend was found with cases demonstrating greater odds (1.5 times) of being able to walk without assistance than controls at one year post-injury. A non-significant trend was also found with cases demonstrating greater odds (1.2 times) of being able to climb a flight of steps than controls at one year post-injury. Although demonstrating greater odds of locomotion/stairs recovery, the differences between cases and controls were not statistically significant possibly due to limited sample size, large variability among the sample, and loss of power due to dichotomizing the variables.

In contrast, individuals in the case group had significantly greater odds of being able to walk 150ft in their home than controls. The discrepancy in significance between these two outcomes (walk 150ft vs. FIM locomotor item) may illustrate the lack of specificity associated with the FIM locomotor item which does not distinguish between walking and wheelchair as previously discussed. Also in regards to lack of FIM locomotor specificity, individuals may not have scored themselves as being independent with walking 150ft when asked on the FIM because they were considering both indoor and outdoor ambulation. However, when the question was more focused on walking indoor, it appears that individuals in the case group were more confident in answering they were able to do this without assistance. This also supports the fact that there were not statistically significant differences between cases and controls in regards to the outcomes of walking 1 street block and walking up 1 flight of stairs. Cases report a greater degree of independence while walking in their home than their matched controls, but do not report this same level of confidence when walking in the community and climbing stairs. It’s possible that if data had
not been missing (locomotion n=113; stairs n=93), statistically significant differences may have been observed.

Finally, both cases and controls were discharged from inpatient rehabilitation with a fairly high level of locomotor independence (both averaging slightly better than supervision level), but as previously discussed, this numeric value does not distinguish between walking and wheelchair. It only focuses on independence and distance travelled. Previous literature in traumatic brain injury has shown substantial ceiling effects using the FIM Locomotion item especially for groups with higher level walking abilities at multiple time points including discharge from inpatient rehabilitation as well as one and two year follow-up periods. Therefore, since this sample scored in the higher ranges of the FIM Locomotion item at discharge from inpatient rehabilitation, this item may not be able to adequately capture change in either group. Also, based on SCI expert evaluation, Jackson et al reported that the FIM Locomotion item had little utility and validity in SCI research. Anderson et al supported these conclusions while also reporting other outcome measures including the 10MWT, 6minWT, and WISCI II were more valid and sensitive to change in this population.

In regards to relevant covariates, increased FIM Locomotion scores at discharge from inpatient rehabilitation were significantly associated with increased FIM Locomotion scores at one year post-injury which is consistent with the study conducted by Horn et al which showed that FIM motor scores at discharge from inpatient rehabilitation were predictive of one year FIM motor scores. Also, increased length of stay during inpatient
hospitalization was significantly associated with a decrease in one year FIM Locomotion scores, which is also consistent with previous literature.\textsuperscript{129,130}

**FIM Transfer Index**

Outside of walking, being able to move from one surface to another independently is very impactful for overall mobility. In this study, statistically significant between group differences were found in the adjusted model with cases demonstrating improved ability to transfer to a variety of surfaces (bed, shower, and toilet). A medium effect size was estimated (0.47) demonstrating a greater effect from treatment in the cases. No other studies were found which evaluated the impact of LT on an individual’s ability to transfer to multiple surfaces that individuals with SCI encounter on a daily basis. The analysis of the impact of LT on transfers was included in this study as patients/families often report to their therapists that even if walking is not recovered after intensive LT, individuals often achieve greater independence when transferring out of their wheelchair to their bed, toilet and shower chairs which improves their daily independence and mobility. The inclusion of the transfer index in this study was also influenced by motor learning literature and the principle of transference. Kleim et al\textsuperscript{91} discuss transference as the likelihood that a less difficult skill like transfers become easier when treatment is focused on a more difficult skill such as walking. Hornby et al\textsuperscript{135} also described this idea as challenging patients with training tasks considered more difficult (walking and stair climbing) instead of tasks that are considered less difficult (bed mobility and transfers) as the more difficult training will also improve the less difficult tasks even though they were not the focus of training. He reported this “transference” is likely to occur from training tasks of greater difficulty to those of
lower difficulty while the same transference of skill does not occur when training of lower
difficulty tasks to higher difficulty tasks. This philosophy is consistent these results as the
treatment intervention for cases was focused on the intensive practice of walking so the
transference principle would predict the benefits from practicing the more difficult skill of
walking positively impacted the skill of transferring to multiple surfaces while not
translating to tasks considered more difficult than walking such as stair climbing.

Increased FIM Transfer Index scores at discharge from inpatient rehabilitation were
significantly associated with increased transfer index scores at one year, which is consistent
with previous literature supporting that FIM motor scores at discharge from inpatient
rehabilitation are predictive of FIM motor scores at one year after injury. Increased initial
length of stay (days of inpatient hospitalization) was also associated with a significant
decrease in FIM Transfer Index scores at one year, which is consistent with previous
literature. 

**FIM Stairs**

When evaluating one year outcomes on stair climbing, cases were more likely to
report they could climb a flight of stairs without assistance than controls (OR = 1.2, 95% CI =
0.4, 3.6), but this difference did not reach statistical significance. Individuals in the NRN LT
protocol focused the majority of their training on intensive walking on a treadmill and over
ground which likely didn’t include a significant amount of practice on stair climbing as this
task is not specifically included in the NRN protocol. As previously discussed, stair climbing
is considered a more difficult task than over ground walking so the benefits of this training
likely had less impact on stairs climbing than over ground walking. Cases were significantly
more dependent with stair climbing than controls at discharge from inpatient rehabilitation $(p<0.001)$ which was not controlled for in the model due to the number of covariates already being adjusted which may have impacted this outcome and should be considered in future analyses. Also, this outcome was dichotomized due to limited sample size also resulting in a loss of power. Length of stay (days hospitalized during inpatient rehabilitation) was the only covariate that had a significant impact on this outcome demonstrating more time spent in inpatient rehabilitation resulted in a decrease in the odds of an individual being able to independently climb a flight of steps at one year. This outcome is consistent with previous literature on length of stay and functional outcomes at one year.\textsuperscript{129}

**Research Aim 1 (H\textsubscript{12}): Odds of Walking in the Home, Community and Stairs**

When the individuals in this sample were asked if they could walk 150ft in their home at one year follow-up, cases were over three times more likely to be able to walk in the home at one year than matched controls $(OR = 3.06, 95\% CI = 1.1, 9.2)$, which also represents a statistically significant difference between the two groups in the adjusted model. Regarding the NRN protocol, patients generally spend a significant amount of time working on over ground walking in a gym environment which is often focused on improving independence with household mobility as this is a primary concern for insurance companies and including resource justification. Therefore, it seems reasonable that the largest reported difference in locomotion ability between cases and controls would occur within the household environment due to the repetition and specificity of the training environment for the cases.\textsuperscript{91}
Cases reported nearly 2 times greater odds of being able to walk one street block over controls (OR = 1.9, 95% CI = 0.7, 5.6) and were over 3 times more likely to walk up/down one flight of stairs than controls (OR = 0.9, 10.1). However, neither outcome demonstrated a statistically significant difference between groups in the adjusted model. Even though there is a difference observed favoring cases in both outcomes, it is likely the lack of statistical significance is due to low power (high variability and limited sample size). Also, due to the specificity of training for indoor walking that was previously discussed, it seems reasonable there would be less of an effect on outdoor mobility between cases and controls as the majority of the NRN LT protocol occurs inside a rehabilitation facility rather than out in a community setting. Stair climbing is a more difficult task than over ground walking and not specifically included in the NRN protocol so it’s likely cases spent much less time practicing this task in comparison to over ground walking indoors which again supports the concept of specificity of training.91 Also, cases were significantly more dependent with stair climbing than controls at discharge from inpatient rehabilitation which was not controlled for in the model due to the number of covariates already being adjusted which may have impacted this outcome. Individuals who have any walking impairment will likely feel more confident walking in a controlled indoor environment with less fear of falling rather than in the community where unexpected obstacles may arise and there’s a higher risk of falling. Currently, there’s no other literature that has directly evaluated these two constructs in individuals with motor incomplete SCI, so it is difficult to draw a supported rationale. However, from a clinical standpoint walking in the community and stair climbing are more difficult tasks than walking in the home. Individuals in the NRN protocol spend
much less time working on walking in the community and climbing stairs than walking household distances in a familiar environment. Therefore, specificity of training and limited power are likely the two most impactful factors explaining the trend for improvement noted in the cases in all three walking domains with only household mobility reaching statistical significance.

The two co-variates demonstrating the most significant impact on all mobility outcomes at one year post-injury are days hospitalized during inpatient rehabilitation and FIM Total Motor Score at discharge from inpatient rehabilitation. Individuals with higher FIM Total Motor Scores at discharge from inpatient rehabilitation demonstrated greater odds of being able to walk 150ft at one year whereas longer days of hospitalization during inpatient rehabilitation negatively impacted this ability at one year. FIM scores at discharge from inpatient rehabilitation have been shown to be predictive of mobility at one year follow-up\(^{133}\) and longer length of stay during inpatient rehabilitation has been associated with lower levels of mobility and independence at one year.\(^{129,130}\)

**Research Aim 2 (H21): Satisfaction with Life**

There were no significant differences between cases and controls in regards to satisfaction with life in the unadjusted model. However, in the adjusted model, cases reported significantly greater satisfaction with life in comparison to matched controls at one year post-injury (difference = 4.0, 95% CI = 0.7, 7.3) and this difference was associated with a medium effect size (0.5). While there is limited data available to evaluate whether a four point difference is clinically meaningful between cases and controls, a score of 20 on this measure indicates a neutral score of being neither satisfied nor dissatisfied with life.\(^{60}\) In the
adjusted model, cases who participated in the NRN had an average score (22.1) above the neutral cut-off meaning more satisfied with life while controls (18.1) scored below the neutral cut-off meaning less satisfied. The number of days hospitalized during inpatient rehabilitation was the only co-variate in the model demonstrating a statistically significant effect on the outcome with those who initially required more days of hospitalization reporting a lower quality of life at one year. This suggests that those who originally had greater severity of injury, medical complications/comorbidities early in rehabilitation may have continued to experience challenges over the first year after injury as health complications are significantly associated with decreased quality of life after SCI.\textsuperscript{130,136}

Riggins et al\textsuperscript{137} reported that individuals with SCI who were either able to maintain the ability to ambulate or who were able to achieve the ability to ambulate after inpatient rehabilitation reported higher SWLS scores\textsuperscript{60} than those who were unable to ambulate or lost the ability to ambulate over the first year of injury. The results of the current study support Riggins et al\textsuperscript{137} in that cases demonstrated greater odds of being able to ambulate at one year and also reported significantly higher SWLS\textsuperscript{60} scores than matched controls in the adjusted model. Alexeeva et al\textsuperscript{101} reported a statistically significant improvement in satisfaction with life across all LT groups from pre-training to post-training with the improvement persisting at 1 month follow-up. This improvement is consistent with the SWLS results observed in this study while this current analysis also suggests greater durability of effect considering most individuals complete the NRN program immediately after inpatient rehabilitation so are likely to complete SCIMS interview closer to six to nine
months post-intervention as there is a 6 month window on either side of the one year injury anniversary in which the outcome interview is completed.

In contrast, Hitzig et al\textsuperscript{108} did not report an improvement in satisfaction with life in either intervention group in their study (12 months of LT with and without FES). Their subjects were at least 18 month post-injury when they were enrolled in the study/intervention. Therefore, chronicity of injury may be an important difference between the improvement seen in this study and the lack of improvement noted in the Hitzig study. Also, their groups reported a baseline SWLS scores of 18.81 (7.17) and 20.18 (8.61) for cases and controls respectively. The cases in this study reported one year SWLS scores of 22.05 (1.04) with controls at 18.08 (1.20) demonstrating that the average score of cases at one year post-injury in this study are greater than the group estimates in the Hitzig\textsuperscript{108} study. In a case series of 14 individuals with chronic incomplete SCI, Hicks et al\textsuperscript{90} reported a 3.9 point improvement (19.7 to 23.6) in satisfaction with life in individuals in response to a year-long LT program which is very consistent with the results obtained in this study.

Research Aim 2 (H\textsubscript{2}2): Community Participation

Physical Independence Subscale

Community participation at one year was evaluated using four of the CHART-SF subscales. No difference in CHART-SF Physical Independence scores between cases and controls was found in both the unadjusted and adjusted models (difference = 0, 95% CI = -13.1, ES = xx). In general, the Physical Independence subscale measures an individual’s ability to be independent in their daily life, and the number of hours per day someone requires routine or occasional assistance (paid or unpaid) is a major component of this
subscales. Therefore, there doesn’t seem to be a difference in how much paid or unpaid assistance is being provided to these two groups. Personal preference and priorities may play a large role in this domain as individuals may decide to get assistance for something they can do independently to save time and energy that can be focused on other areas of their lives. For example, an individual with a cervical level of injury may decide to pay for caregiver assistance to complete their ADLs even though with enough time and physical burden, they have the ability to complete these activities without assistance. They may make decisions to pay for caregiver assistance for ADL management in exchange for being able to work a full day or spending quality time with family and friends.

Riggins et al\textsuperscript{137} reported CHART-SF Physical Independence scores for individuals who maintained the ability to ambulate one year after injury, transitioned from wheelchair to ambulation, transitioned from walking to a wheelchair, and who stayed at a wheelchair level at 91.4 (SD=22.9), 85.7 (SD=26.9), 61.5 (SD=42.1), and 58.5 (SD=39.7), respectively. The scores for both cases and controls in this study fall between the groups who achieved the ability to ambulate during the first year of injury and those who lost the ability to ambulate during the first year of injury in the Riggins study and demonstrates that scores from this analysis are consistent with other studies evaluating the impact of walking on community participation (CHART-SF). Gontkovsky et al\textsuperscript{128} reported normative data on 28 individuals with chronic SCI (64\% with motor complete SCI). In their sample, the mean score on the physical independence subscale was 47.0 (44.2) which is approximately 28 points lower than both cases and controls included in this study. The higher scores of this sample are likely at least partially due to the fact that the entire sample has motor incomplete
injuries and the majority of their sample had motor complete injuries. This difference supports the fact that individuals with motor incomplete injuries are generally able to achieve greater physical independence than those who have sustained motor complete injuries. Given that the standard error of measure (SEM) for this subscale is 8.2 points, there is not a meaningful difference between the two groups in this study which suggests that other factors may also impact this score such as economic wealth as well as personal choices regarding social roles and priorities.

The two co-variates found to be statistically associated with the outcome of this analysis were days hospitalized during inpatient rehabilitation and FIM Total Motor Score at discharge from inpatient rehabilitation. Horn et al demonstrated that initial days of hospitalization (rehabilitation length of stay) is significantly affected by severity of injury and preinjury comorbidities while also being predictive of one year outcomes which is consistent with one year data from this study. FIM motor scores at discharge from inpatient rehabilitation have been shown to be predictive the amount of assistance an individual with SCI requires at one year post-injury which is also consistent with the impact this variable has on this model.

**Mobility Subscale**

A significant difference was found on the CHART-SF Mobility Subscale in both the unadjusted and adjusted analyses as cases reported higher levels of mobility at one year than controls. A large effect size was calculated (0.79) between groups. This subscale focuses on an individual’s ability to effectively move in their environment by evaluating the following: how many hours per day they spend out of bed; how many days per week they
get out of the house; how many nights are spent away from home; accessibility of the home and the utilization of transportation. On average, cases scored 18.2 points higher than controls in this domain. The SEM for this subscale is 5.1 points so the difference found in this analysis is a true difference and is clinically meaningful. It suggests those who participated in the NRN protocol are more effective at mobilizing in their own community and maybe even traveling outside of their home community. It’s difficult to ascertain whether the cases are truly more effective with mobility or are just more confident in their ability to mobilize in different areas, but either way, this difference suggests they are getting out and about more than the controls in this study.

Riggins et al reported CHART-SF mobility scores ranging from 60.2 (SD= 26.5) to 85.7 (SD=19.7) for individuals who lost the ability to ambulate by one year post SCI to those who maintained the ability to ambulate at one year post SCI. The cases in this study scored higher than the individuals who maintained the ability to ambulate at one year while the controls scored between individuals who had lost and gained the ability to ambulate over the first year of injury. Again, this demonstrates that the scores obtained in this study are in line with previously published CHART-SF scores associated with mobility.

Cao et al reported mortality rates (per 1000 person years) for individuals with SCI who scored above 75 and those who scored below 75 on the CHART-SF Mobility Subscale as 13.93 and 31.77, respectively. The cases in this study reported an adjusted score of above the 75 point cut-off (92 points) at one year follow-up while the control group reported an adjusted score below the 75 point cut-off (74 points). Therefore, the difference in this
subscale may not only have a positive impact on mobility, but may also decrease mortality risk.

Additional covariates impactful to the model were days hospitalized and FIM Total Motor Scores at discharge from inpatient rehabilitation. Days hospitalized during inpatient rehabilitation was shown to have a significantly negative impact on CHART-SF Mobility scores at one year, again suggesting that individuals who required longer inpatient hospitalization likely had more medical complications/comorbidities that may have continued to negatively affect their mobility during the first year of injury. FIM Total Motor Scores at discharge from inpatient rehabilitation also significantly positively impacted one year mobility outcomes, which has been shown to predict one year motor outcomes.

**Occupational Subscale**

A significant difference was found between cases and controls on the CHART-SF Occupation subscale (difference = 15.6, 95% CI = 2.1, 29.1) and was associated with a medium effect size (0.43). This subscale focuses on how much time an individual spends gainfully employed, in school, homemaking, doing volunteer work, recreational activities and self-improvement activities. In this analysis, cases scored 15.6 points higher than their matched controls on the occupation subscale. The SEM for this subscale is 14.8 points so the difference found in this analysis is a true difference between groups and is clinically meaningful based on the effect size. Again, it’s difficult to determine exactly why cases demonstrate a greater ability to return to employment, volunteer, and recreational activities given they are not receiving any job training or career coaching in the NRN, but
does suggest a strong connection to their higher scores reported on the CHART-SF Mobility Subscale. Getting out of the house daily and even occasional/frequent travel are requirements of many jobs and volunteer positions. So, the fact that cases report a greater ability to do these tasks than the controls in this study suggests they may be more able to meet the requirements of a consistent job or volunteer position. The fact that cases are more likely to have a higher education level than controls could also suggest that they may have been more likely to have a pre-injury occupation that didn’t require physical labor which may be easier to return to after an injury. However, education was not a statistically significant covariate in this model so there is no direct support for this argument. Krause et al\textsuperscript{139} reported that individuals with SCI who have less severe injuries was more likely to be employed. However, the cases in this study were characterized as having more severe injuries (greater number of cervical injuries; greater time spent inpatient rehabilitation; lower FIM mobility scores at discharge from inpatient rehabilitation) and yet scored significantly higher on the occupation subscale than controls. Given that only 12% and 33% of individuals with SCI are employed one and 20 years after injury, respectively,\textsuperscript{13} interventions provided after SCI that increase the number of individuals returning to gainful employment may result in a significant reduction of those relying on social security and disability income which would also decrease the financial burden on the US government.

FIM Total Motor Score at discharge from inpatient rehabilitation was the only covariate in this model that had a significant impact on Occupational subscale scores at one year. Cohen et al\textsuperscript{133} reported that FIM scores at discharge from inpatient rehabilitation are significantly associated with the probability of engaging in paid work at one year post-injury.
Riggins et al\textsuperscript{137} reported CHART-SF Occupational scores for individuals with SCI one year post-injury ranging from 39.3 (SD=35.8) to 68.0 (SD=34.1). The cases in this study scored just below individuals in their study who had maintained the ability to ambulate over the first year of injury (approximately a 4 point difference) and the controls in this study scored just above individuals who maintained wheelchair mobility as their primary means of mobility through the first year of injury (approximately a 4 point difference). This demonstrates the results from this study are in line with previously published reports.

Being able to achieve gainful employment after SCI may have not only affect an individual’s socioeconomic status, but may also have an important impact on risk of mortality. Krause et al\textsuperscript{140} compared mortality risk between individuals with SCI who were unemployed, working 1-29 hours per week and those working greater than 30 hours per week and found an increased odds of mortality for the unemployed of 1.67 and 1.37 for the group working 1-29 hours per week. Therefore, finding interventions that increase the likelihood of returning to employment may be important for socioeconomic status as well as mortality risk.

**Social Integration**

Analysis of the CHART-SF Social Integration subscale also yielded a significant difference between cases and controls, with cases reporting higher social integration scores than controls (difference = 8.4, 95% CI = 0.5, 16.3) and was associated with a medium effect size (0.46). This subscale focuses on an individual’s ability to participate in and maintain customary social relationships. It evaluates how much regular contact they have with relatives, business associates, friends and initiating conversations with strangers. The SEM
for this subscale is 11.6 points\textsuperscript{127} and the cases in this study scored on average 8.4 points higher than controls. Even though there is a statistically significant effect with cases scoring higher than controls, it remains unclear whether this is a meaningful difference due to falling just outside the SEM for this subscale. Referring back to the mobility subscale, improved mobility may make it easier to maintain both personal and business relationships that are enhanced by face to face communication and time spent together. In regards to the impact of other covariates, FIM Total Motor Score at discharge from inpatient rehabilitation was the only co-variate in this analysis that had a significant impact on the Social Integration subscale scores at one year. An individual’s level of independence and mobility at discharge from inpatient rehabilitation is predictive of mobility and independence at one year\textsuperscript{133} which likely impacts an individual’s ability to get outside the home and maintain personal and business relationships that benefit from in person communication and nurturing.

Riggins et al\textsuperscript{137} reported CHART-SF social integration scores at one year post SCI of 73.4 (SD=31.2) and 88.7 (SD=21.7) for individuals who lost the ability to ambulate over the first year of injury to those who maintained the ability to ambulate over that same time period. The cases in this study on average scored considerably higher (22.6 points and 7.3 points) than the two previously mentioned groups in the Riggins study while the controls reported the same score as those who transitioned from wheelchair to walking (87.9) at one year post-injury demonstrating these scores are in line with previous literature focused on social integration after SCI.

Hitzig et al\textsuperscript{108} reported greater improvements in the CHART-SF Mobility subscale in individuals with chronic motor incomplete SCI who received LT in comparison to those who
received aerobic/resistance training. They did not report improvements on the physical independence, occupation or the social integration subscales. These results are similar to this analysis in that the mobility subscale was most positively impacted by the NRN intervention in this study and both groups in the Hitzig\textsuperscript{108} study demonstrated improvement in this subscale in response to an intensive training intervention. Neither this study nor Hitzig et al found a significant impact on the physical independence subscale in response to training supporting the idea that decisions about caregiver assistance may be more heavily impacted by priorities/economics than actual physical ability. Finally, a significant difference in social integration score was observed between cases over controls in this study while there were no within group differences found in the Hitzig study in response to LT or aerobic/resistance training. The sample in the Hitzig study was more chronic than the sample in this study and suggests those with more chronic injuries may have already established their social routine prior to participating in intensive physical training and that four months of training may not be enough to change those already established patterns. Harness et al\textsuperscript{141} reported a 12 point improvement in the CHART-SF total score in individuals with chronic SCI who participated in an intensive exercise program provided by physical trainers while only a 0.1 point improvement was noted in the control who participated in a self-regulated exercise routine. Although the authors of this study evaluated the CHART-SF total score and not individual subscales, it does support the concept that CHART-SF scores may improve in response to intensive physical training.
Research Aim 2 (H23): Re-Hospitalizations and Re-Hospitalized Days

Lower functional independence scores at discharge from rehabilitation, severity of injury (motor complete injuries and cervical injuries demonstrating greater health care utilization than motor incomplete and thoracic/lumbar injuries), indwelling catheters and lower socioeconomic factors (lower education and family income) are all factors that have been associated with increased rates of re-hospitalization during the first year after SCI.\textsuperscript{51,120,131,132} On average, cases in this analysis were re-hospitalized fewer times than controls over the first year of injury, but this difference did not reach statistical significance. This demonstrates a trend for controls to be hospitalized more often than cases but the analysis had a wide confidence interval which may be due to the small sample size so a larger study would help clarify whether or not there is a true difference between these groups. This data is in line with DeJong et al\textsuperscript{51} who reported that those individuals with SCI who received intensive physical therapy had lower odds of re-hospitalization during the first year of injury than those who did not receive intense physical therapy.

In terms of the impact of other covariates, those who were a couple (married or unmarried) were significantly more likely to be re-hospitalized than those who were single (divorced/separated/widowed). From a societal perspective, individuals who have a “significant other” in their life may be more influenced to seek medical assistance than those who are living on their own. Previous literature also suggests that lack of accessible transportation is a significant barrier to accessing health care when needed after SCI.\textsuperscript{132,142,143} Therefore, it seems reasonable that those with a significant other may also have more assistance for accessible transportation when they need to access healthcare.
which also supports the impact of this covariate in the current analysis. Another plausible explanation is the larger percentage of couples enrolled in the NRN in this study in comparison to the control group representing a group with increased length of stay and lower FIM scores, both associated with re-hospitalization. Previous literature has also reported that individuals with SCI who have lower levels of education are more likely to be re-hospitalized than those with higher levels of education.\textsuperscript{131,144} However, education was not a significant covariate in this analysis.

DeJong et al\textsuperscript{51} evaluated 870 consecutively enrolled individuals with traumatic SCI over their first year of discharge from six inpatient rehabilitation centers across the US and found that 36.2% of their sample required re-hospitalization at least one time during the 12-month follow-up period. They also reported that re-hospitalization was much higher among those individuals with cervical injuries AIS A-C classification (44%) while much lower for AIS D injuries (23.8%) and much higher for individuals who had Medicaid/Medicare as their primary payers. The percentage of individuals requiring re-hospitalization during the first year after injury in the current analysis was lower than what was previously reported for both the case group and the control group at 11.1% and 20.8% respectively. Some of the variability between the two studies may be explained by the fact that the current sample does not contain any motor complete injuries (AIS A or B) and is comprised of only motor incomplete injuries (AIS C 33.7%; AIS D 66.7%) which have been shown to require less health care utilization during the first year after injury.\textsuperscript{120,131} However, even after taking AIS classification into account, the percentage of individuals in this study (both AIS C and D) who required re-hospitalization during the first year was still less in both groups (cases and
controls) than the percentage of re-hospitalizations for AIS D participants alone in the DeJong study (cases in this study 11.1% in comparison to 23.8% in the DeJong study; controls in this study 20.3% in comparison to 23.8% in the DeJong study). Although there was a very low response rate on the question of primary payer in this study, only 20% of those who provided this information in this cohort reported Medicare/Medicaid is their primary payer with 80% being private insurance/workman’s compensation while those in the DeJong study reported 75% private insurance/workman’s compensation with 25% Medicare/Medicaid. Therefore, some of this variability is also likely due to differences in payer mix between the two studies as DeJong reported higher health care utilization for those individuals with Medicare/Medicaid as their primary payer. They also reported a high variability among the six centers that were involved in their study with those centers reporting re-hospitalizations ranging from 27.8% to 50%. Five out of six of their centers were also SCIMS Centers at the time of that study, but there was only one center that was involved in that study that was also involved in this study so some of these differences may also be attributed to site specific factors. Re-hospitalizations were not evaluated specific to each center in this study, but again, both our cases and controls reported numbers below those of the lowest reported facility in the DeJong study. Finally, the total number of participants in the current analysis is much smaller (144 to 870) which is also likely to have contributed the greatest variability between studies.

In a similar study, Sikka et al.\(^{145}\) reported 38% of 664 individuals with traumatic SCI (admitted from a level 1 trauma center) required re-hospitalization during their first year post-injury which is also a higher percentage than both cases and controls in the current
study. They completed retrospective chart reviews to examine health care utilization while this study relied on self-report using one year survey information which may be subject to interview and recall bias. This may explain some of the variability between the two studies while they also included individuals with AIS A and B injuries known to require more healthcare during the first year post-injury. Also, the data in the Sikka study was obtained from a center that is not a SCIMS Center, which could also account for the variability in percentage of re-hospitalization at one year.

Cao et al\textsuperscript{138} reported that re-hospitalization during the previous year may also have an important impact on the risk of mortality after SCI. They published mortality rates of 31.23 for individuals who reported being re-hospitalized in the previous year and only 13.64 for those who were not re-hospitalized in the previous year. Therefore, deploying therapeutic interventions that decrease the risk of re-hospitalization may be important for decreasing the overall mortality risk associated with SCI. In terms of the economic impact of hospitalization in this population, DeVivo et al\textsuperscript{146} reported that hospitals bill on average $40,000 for each hospitalization after SCI. Using this estimate, the case group in this study reported a total of 10 hospitalizations during the first year of injury suggesting a financial burden of $400,000 while the control group reported a total of 22 hospitalizations during the same timeframe suggesting a burden of $880,000. Therefore a $480,000 savings can be estimated in the case group in comparison to the control group. Interventions that have a positive impact on reducing hospitalizations each year will decrease the financial burden on individuals as well the overall health care system and further investigation should focus on
determining whether or not there is a clinically meaningful difference in re-hospitalizations associated with the NRN protocol using a larger sample size.

In regards to the number of days of re-hospitalization, cases were re-hospitalized significantly more days than controls (ratio of geometric means = 3.0, 95% CI = 1.5, 5.7). Being a couple and being less educated were significant factors that contributed to longer lengths of stay for re-hospitalizations. Patients often report that it can be difficult to advocate for themselves in the hospital environment so having a significant other who can also advocate for an individual’s needs may be helpful in obtaining a longer length of stay, especially in a climate where hospitals are often financially incentivized to limit lengths of stay. Krause et al\textsuperscript{131} reported that individuals with SCI who had a high school or lower education were significantly more likely to be re-hospitalized than individuals with college education. Although educational level did not reach statistical significance in the previous model (number of re-hospitalizations), it did show a trend that individuals with higher education were re-hospitalized fewer times than those with lower educational levels; this model (re-hospitalized days) showed a significant relationship as individuals with higher education were re-hospitalized for fewer days which is in line with findings from the previously reported research.\textsuperscript{131}

Sikka et al\textsuperscript{145} reported a median length of stay of 11 days when re-hospitalization was required during the first year of injury while DeJong et al\textsuperscript{51} reported an average mean length of stay of 15.5 days across all re-hospitalization episodes and the National SCI Statistical Center\textsuperscript{13} reports an average length of stay of 22 days for re-hospitalizations. The median length of stay for both cases and controls in the current analysis was four days.
Therefore, both groups in this study reported an average (median) of seven fewer days of re-hospitalization per episode in comparison to the Sikka study. This may be due to the fact that this entire cohort (cases and controls) were motor incomplete (AIS C and D) and completed their rehabilitation at a SCIMS center while those in the Sikka study did not. It is difficult to compare the current results with the DeJong study as they reported mean days rather than median days even though they also reported very high standard deviations suggesting that a non-parametric comparison may have been more appropriate for their analyses.

However, when making a relative comparison, there was a lower percentage of the current sample re-hospitalized during the first year of injury than the previous reports and the average number of days (median) for both groups in this study is lower than previously reported literature.\textsuperscript{12,13,51,145} The decrease in health care utilization in this cohort (cases and controls) is likely due to the continuum of SCI specialty care provided at SCIMS Centers and the fact that his entire sample has motor incomplete SCIs (AIS C and D).

The total cost of re-hospitalizations and re-hospitalized days should be the subject of further study. The direct financial impact associated with SCI during the first year of injury is high with estimates from $359,000 for individuals who are motor functional at any level of injury to $1.1 million dollars for individuals with high tetraplegia.\textsuperscript{13} Re-hospitalizations have been shown to be a significant contributor to direct costs associated with the first year after SCI\textsuperscript{12} so finding interventions/treatments that decrease re-hospitalization and re-hospitalization days could positively impact the financial health of an individual/family with SCI as well as our entire health care system. However, it’s important that re-hospitalization
analyses focus not only on the financial burden but also the emotional burden. Spending
time in the hospital may negatively impact an individual’s QOL so future analyses should
also include factors associated with QOL, long term health implications, and mortality risk to
better understand the impact of re-hospitalization number and days on individuals with SCI
as well as the impact on the global health care cost/burden. Additionally, programs like the
NRN have a cost to persons/payers and understanding the overall cost-benefit of these
interventions will continue to be an important part of their viability.

**Study Limitations**

There are several limitations to this investigation. The inability to know or account
for what types and dosing of interventions the control group received may limit the
generalizability of the results. There is a broad definition of usual care within this
therapeutic environment which could not be controlled for in this retrospective analysis.
This data is not collected and therefore, was not available in the SCIMS database. Given the
unique nature, resource requirements, and limited access to LT programs with attributes
similar to the NRN, any additional exposures to therapy under usual care does not represent
a significant comparative confound and this analysis provides the best available
comparative data to date. Arguably, the “control” data set likely includes many person’s
receiving additional therapy services, conventional or otherwise, beyond an actual
controlled “usual care” making these findings more meaningful. Regardless, the lack of rigid
controls in the entire data set should be part of the discussion of the translation of these
findings.
Limited power and missing data are both limitations to this study. Even though the study has 80% power to detect effect sizes as small as 0.342 with alpha at 0.05 for 72 pairs of cases and controls, there was a large amount of missing data in the majority of the analyses. Outcomes were analyzed with 93-125 subjects, but none of them included the full 144 subjects that were included in the power analysis. Using a mixed-effects model allowed for the inclusion of larger numbers of subjects in the analysis as it includes all cases and controls that were originally matched even if one of the pairs has missing data for that outcome and must be thrown out. Although this supports greater overall power for the study, it could also create a bias if more cases or more controls were inadvertently included in an analysis. Future prospective studies should be powered appropriately and take care to ensure missing data is limited.

In regards to matching for this study, individuals with lumbar injuries were included in the control group (24%) to maximize power even though only one case had a lumbar injury (1.5%). Individuals with lumbar injuries are expected to have higher levels of functional independence than individuals with cervical and thoracic injuries so a higher percentage of lumbar injuries in the control group may suggest a potential underestimation of the effect of the LT intervention. However, FIM Total Motor Score and ASIA total motor index at discharge from inpatient rehabilitation were also included in all of the models to account for the variability associated with severity of injury and FIM motor score was found to have a significant impact on the majority of models in this analysis. Future studies should evaluate these questions with a larger sample size allowing the ability to do an exact match on neurologic level (cervical, thoracic, and lumbar) as matching on neurologic level in this
study would have limited the sample size of a retrospective analysis with already limited power.

There are two areas of selection bias that are potential limitations of this study. The first is that all center data included in this study came from SCIMS centers which are well-established SCI specialty clinical centers with strong research agendas and clinical infrastructure. They are supported by government grant funding which is very different than the majority of non-SCIMS centers in the US. The second source of potential selection bias comes from being a part of the NRN. Patients in the NRN are encouraged to complete at least 40 sessions of LT which means that those who are actually enrolled in this protocol may have better insurance coverage than those who are not enrolled. Since this protocol is only delivered at six sites across the US, it often requires patients and families to live away from home to participate in it and free housing is not provided to these patients at any of the sites. Therefore, individuals who are able to participate in this program may also have better family support and higher family income than those who do not participate. Living with family/having a strong social network has been shown to be an important predictor of community integration. Unfortunately, 77% of the individuals in this study had “unknown” family income levels and 61% of all individuals in the analysis had “unknown” insurance type so those two co-variates could not be included in the models. Future studies should include both family income and payer type in the analysis to better understand how these factors impact who receives more intensive training and how that may influence outcomes after SCI. These areas of selection bias may limit the generalizability of these findings. Another threat to generalizability is the fact that the patients in this study have
inpatient rehabilitation lengths of stay that are much longer than what has previously been reported (73 days cases; 52 days controls; and 34 days National Statistical Center).  

Another limitation to this study is that the data contained in the SCIMS database in terms of functional capacity focuses largely on assistance required to complete an activity. In terms of mobility, the database contains information relating to independence associated with mobility-related activity such as walking, transferring to different surfaces and stair climbing. However, it does not contain any information with regards to how fast an individual is able to perform those activities and no information about the quality of those movements. Therefore, differences in independence with mobility between these two groups do not take into account other clinically meaningful differences that exist between the two groups in terms of the speed of walking and the quality of their movement pattern. For example, two individuals (one case and one control) could both score a 7 on the FIM locomotor item (able to walk independently) while one of them is walking at a speed of 0.5 m/s (may not be safe for walking across a busy intersection), while the other is walking at a speed of 1.2 m/s considered a safe speed for walking across a busy intersection. Likewise, one of these same individuals could have developed a walking pattern that was actually causing harm to their joints such as hyperextension of the knee due to weakness in the leg muscles while the other could be walking with an appropriate kinematic pattern and this analysis does not distinguish between them. Based on an evaluation by a multinational work group of experts in SCI, Anderson et al reported that FIM is most appropriate to measure burden of care and is not necessarily measuring functional recovery especially for individuals who exhibit higher levels of mobility. Therefore, this is an initial analysis focused
on burden of care and further prospective studies are warranted to address questions with more appropriate outcomes that directly assess recovery of walking speed, endurance and functional independence to provide a more discriminant analysis.

Given that all outcomes for the SCIMS database are gathered by a survey through interview format, there’s the potential of introducing interview and recall bias into this analysis. There may also be an inherent discrepancy in the data as FIM discharge scores were obtained by a licensed and trained health care professional while FIM one year data is obtained solely from the perspective of the patient. These interviews may be completed six months before or six months after the individual’s one year injury date which is a large window for data collection and is another limitation of this study. Future prospective studies should ensure equal data retrieval dates to minimize unwanted variability due to chronicity. It may also be difficult to generalize these results to a larger population of individuals with motor incomplete SCI due to the small sample size in this study. One of the primary goals of this study was to determine the one year impact of this intensive training in comparison to a more traditional approach. However, analyzing outcomes that are greater than one year will be important in future studies. Evaluation at five years, 10 years, and 15 years will provide a better understanding to determine whether the longer-term return on investment from this intervention is worth the initial high resource utilization for patients, families and hospitals. Multiple comparisons were not controlled for in this analysis due to the fact that it was not powered appropriately. Future prospective analysis should be of adequate power and should control for multiple comparisons.
Another potential limitation to this study is that individuals who had completed only 30 sessions of LT were included in the sample of cases as requiring more than 30 sessions for inclusion in the analysis would have significantly limited numbers resulting in decreased power. Morrison et al. reported that the majority of individuals who participated in an NRN LT program in their cohort demonstrated the greatest improvements in walking and balance after completing 60 sessions of LT and continued to demonstrate improvements through 120 sessions. Therefore, including individuals in this analysis who completed only 30 sessions of LT may be underestimating the treatment effect of this intervention.

Despite these limitations, this work provides a useful starting point for comparing the long term effects (greater than one year) of intensive LT in comparison to usual care. Even though this sample size is smaller than expected, all mobility outcomes were either significantly better for those who received intensive LT or at least demonstrated a trend for improvement for individuals who complete the NRN LT protocol in comparison to usual care. This may be useful information for patients and families who are faced with difficult decisions about care after SCI and it may also serve as a comparison for future studies with larger sample sizes and more rigid controls to evolve this area of study. This work adds a valuable contribution to the field of LT research by reporting Cohen’s d type effect sizes for all continuous outcomes. This standardizes the differences between groups making them more easily interpretable. These effect sizes can be used in future studies to compare the relative size of the treatment effect across different outcomes. The effect sizes estimated in this analysis are meaningful and may also be used in future Meta analyses.
Conclusion

The purpose of this dissertation was to begin addressing the current gaps in literature surrounding LT after SCI utilizing a focused comparison with usual care in the areas of mobility, life satisfaction, community participation, and re-hospitalization and represents a comprehensive analysis of the impact of NRN/intensive LT on one year outcomes obtained from the most comprehensive longitudinal database (National SCI Statistical Center) tracking outcomes after SCI. After controlling for important covariates, individuals with motor incomplete SCI who received an intensive LT training program reported better functional mobility and independence scores on all mobility outcomes at one year post-injury than controls who were matched from the same NRN site on age, gender, year of injury, AIS classification, and mode of mobility at discharge from inpatient rehabilitation. Individuals enrolled in this program had significantly longer inpatient rehabilitation lengths of stay than their matched controls and also had significantly lower functional mobility and independence scores at discharge from inpatient rehabilitation. This suggests that therapists and potentially hospital administrators are targeting individuals who present with more functional impairment and more medical complications to participate in NRN programs due to the rich staffing model and technology utilization. More staffing and advanced technology may allow individuals who are more impaired the opportunity to receive intensive walking training that may not be facilitated safely in a more traditional environment with one physical therapist and limited technology use. In contrast, individuals who have less medical complications (fewer inpatient rehabilitation days) and
are already making significant gains toward functional mobility and independence may not need a greater number of staff and more expensive technology to maximize their mobility.

Individuals who participated in the NRN protocol demonstrated significantly greater satisfaction with life than their matched counterparts after adjusting for important covariates. Although difficult to determine how clinically meaningful this change is, it does place the NRN group into a category of being more satisfied with life and the control group into a category of being less satisfied than neutral. Also, because SCI has been shown to negatively affect an individual’s satisfaction with life, even a small improvement may be clinically meaningful.

Individuals who received the NRN protocol also demonstrated significantly greater community participation than their matched controls in the areas of mobility, occupation, and social integration, while there was no difference noted in the area of physical independence. Being more mobile may facilitate greater confidence to access their community, travel, be employed and maintain social/business contacts, but it may not be a factor when determining how much daily assistance someone receives after an SCI. Daily assistance may be more influenced by economic factors and priorities and this is an area that should receive further study. As previously discussed, individuals who participated in the NRN reported significantly greater satisfaction with life scores than their matched controls at one year post-injury. This may also be due to the fact that they are also reporting improved mobility, social integration, occupational activity, and independence.

Finally, individuals who participated in the NRN demonstrated a trend for a decrease in the number of re-hospitalizations that occurred during the first year of injury which may
result in less health care utilization than the control group. However, this difference was not significant and should be evaluated in future studies with larger sample sizes. The NRN group also demonstrated a significantly higher number of re-hospitalized days than the control group which may result in higher health care utilization. Therefore, it’s difficult to understand the impact of these two variables on health care utilization and future research is warranted. The financial burden associated with SCI on both the patient/family as well as the entire health care system is an important area of study and continuing to investigate interventions that lower this financial burden should be a priority.

Overall, although this retrospective analysis of Model System’s data lacks high power; the majority of findings demonstrated that cases had a more favorable outcome at one year than controls after matching and further adjusting for important co-variates. Medium to large effect sizes were found favoring cases in the areas of FIM Total Motor Scores, FIM Transfer Index scores, satisfaction with life (SWLS), and community participation [CHART-SF (mobility, occupation, social integration)]. A small effect size was estimated for locomotion/stairs and zero effect size between groups was found on the CHART-SF Physical Independence Subscale. The most impactful covariates in these models include the following: days of hospitalization during initial rehabilitation; FIM motor discharge scores; education level and whether or not someone is part of a married/non-married couple. Future prospective studies with larger sample sizes should be conducted and should include information on family income and primary payers as these factors may also have a significant impact on outcomes after SCI. Caution should be taken when attempting to generalize these results to the SCI population as a whole as this entire sample
was obtained from persons with characteristic amenable to NRN training (or matched) within the SCIMS Centers. At last, this work substantially adds to the literature supporting the positive impact of intensive LT after motor incomplete SCI in the areas of mobility, life satisfaction, community participation and health care utilization and provides fundamental analyses (effect sizes) that may be utilized for comparison in future prospective studies.

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47. Harkema SJ, Schmidt-Read M, Lorenz DJ, Edgerton VR, Behrman AL. Balance and ambulation improvements in individuals with chronic incomplete spinal cord injury using locomotor training-based rehabilitation. *Archives of physical medicine and rehabilitation.* 2012;93(9):1508-1517.


