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Measuring Quality of Life and Function During Early Recovery in Adults with Traumatic Spinal Cord Injury

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Measuring Quality of Life and Function During Early Recovery in Adults with
Traumatic Spinal Cord Injury

by
Debra Hemmerle

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Measuring Quality of Life and Function During Early Recovery in Adults with

Traumatic Spinal Cord Injury

Debra Hemmerle

Abstract

Background

Traumatic spinal cord injury (SCI) is a tragic, life-altering event that can result in varying levels of handicap and disability. Recent initiatives have encouraged the use of patient-reported outcome measures to assess quality of life (QoL) alongside function in the SCI population. Given that most SCI research is conducted in the chronic population, little is known about the relationship between QoL and function throughout rehabilitation.

Purpose

The purpose of this research is to explore the relationship between measurements of QoL and function in adults with traumatic SCI during the early phase of recovery.

Methods

This dissertation study is an analysis of data from the ongoing prospective cohort study called Transforming Research and Clinical Knowledge in SCI (TRACK-SCI). Adult participants admitted with an acute traumatic SCI from December 2017 to October 2020 were eligible for this analysis (N=114). We explored associations between functional independence, health-related QoL, and overall QoL across two timepoints within the first year post-SCI. Functional independence was measured using the Spinal Cord Independence Measure III (SCIM-III), health-related QoL was measured using 11 Neuro-QoL Measurement System short forms, and overall QoL was measured using the International SCI QoL Basic Data Set (ISCI-QoL).

Results

We found that the most amount of variance in overall QoL was explained by the Neuro-QoL

Mental Health domain (R^2=0.43), followed by the Social Health domain (R^2=0.38). In a

backwards stepwise regression model, the only health-related QoL measures that maintained

significance with overall QoL at 6-12 months post-SCI were Depression and Satisfaction with

Social Roles/Activities (R^2=0.46). Overall QoL was not significantly associated with baseline

injury severity, functional independence, or physical function health-related QoL.

Conclusion

This early dissertation research suggests that depression and satisfaction with social roles might

be more important than measures of physical function in predicting overall QoL during the early

recovery phase after SCI.

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List of Abbreviations

ADL	Activities of daily living		**SCI**	Spinal Cord Injury
ISCI-QoL	International Spinal Cord Injury Quality of Life Basic Data Set		**SCIM-III**	Spinal Cord Independence Measure, Version III
LEMS	Lower extremity motor score		**SCIM-MOB**	SCIM-III mobility subtotal score
Neuro-QoL	Quality of Life in Neurological Disorders		**SCIM-SC**	SCIM-III self-care subtotal score
NQ-ADL	Neuro-QoL Upper Extremity Function (Fine Motor, ADLs) Short Form		**SCIM Total**	SCIM-III total score
NQ-ANX	Neuro-QoL Anxiety Short Form		**UEMS**	Upper extremity motor score
NQ-COG	Neuro-QoL Cognitive Function Short Form			
NQ-DEP	Neuro-QoL Depression Short Form			
NQ-EBD	Neuro-QoL Emotional and Behavioral Dyscontrol Short Form			
NQ-FTG	Neuro-QoL Fatigue Short Form			
NQ-MOB	Neuro-QoL Lower Extremity Function (Mobility) Short Form			
NQ-PAR	Neuro-QoL Participation in Social Roles and Activities Short Form			
NQ-PWB	Neuro-QoL Positive Affect and Well-being Short Form			
NQ-SAT	Neuro-QoL Satisfaction with Social Roles and Activities Short Form			
NQ-SGM	Neuro-QoL Stigma Short Form			
QoL	Quality of Life			

Chapter 1: Introduction

Background and Significance

Spinal cord injury (SCI) is a tragic and debilitating neurological condition that often results in substantial physiologic and psychosocial implications for the individual. There are nearly 18,000 new SCIs being treated each year in the United States, and roughly 300,000 persons currently living with SCI [1]. Depending on injury severity, the average SCI-related living expenses and health care costs are estimated to be $45k-$200k per year (not including costs acquired from loss of wages or productivity). SCI has historically been most prevalent among young men between 17 and 27 years old, yet recent epidemiological studies have reported a more bimodal distribution with a second peak occurring in persons over 60 years old [2]. Not surprisingly, the most common causes of SCIs are motor vehicle collisions (42%) and falls (27%) [1]. Since traumatic SCIs are caused by force (i.e. impact, jolt, twist or penetration to the body), most injuries occur in levels of the spine with the most mobility; over 50% of all SCIs are in the cervical spine, which are associated with much higher morbidities and functional impairments than those occurring in the thoracic or lumbar spine [2-4]. Depending on the location and severity of injury, chronic neuromuscular deficits can be classified into paraplegia or tetraplegia (affecting the lower two extremities or all four extremities, respectively) and complete or incomplete (absence or partial preservation of function below the level of injury, respectively) [5].

In the absence of a cure, rehabilitation is the primary treatment. SCI recovery is often conceptualized across three phases: acute, subacute, and chronic. While researchers have proposed different temporal demarcations, it is generally thought that the acute and subacute ("early") phases comprise the process of neuro-rehabilitation and the chronic ("late") phase of recovery begins once neuro-rehabilitation has plateaued [6]. Early recovery, which can last up to

two years from the time of injury, involves drastic changes to the environment (e.g. transitioning from acute hospital to rehabilitation facility, becoming familiar with adaptive equipment) and the individual (e.g. loss/delay of employment, post-traumatic stress and coping) [7, 8]. While individual and environmental adjustments are also present throughout chronic recovery, early recovery is especially representative of a time when many SCI survivors must redefine their self-image and reintegrate their life routines as they work toward a new functional baseline.

Functional Recovery in SCI

Due to improvements in medical treatments and technology, life expectancy after SCI has increased significantly over the past couple decades [2, 9]. Advancements in neurorehabilitation methods and assistive equipment have given many SCI survivors the opportunity to re-enter most, if not all, aspects of their pre-injury life. However, most survivors of SCI will experience some degree of long-term handicap or disability. Persons with SCI-related functional impairments have reported higher rates of perceived stigma, social isolation, and depression when compared to the non-injured population [10-12] Over 25% of persons employed at the time of their SCI will be unemployed a year after their injury, and the suicide rate is estimated to be as high as six times that of the general population [1, 13]. With some evidence to suggest there is a positive relationship between functional independence and psychosocial well-being, more research is needed to better understand the relationship between objective function and the subjective experience of functional recovery throughout all stages of SCI rehabilitation.

Function and *disability* are opposing umbrella terms that include a continuum of conditions throughout the dimensions of health, person, and environment [14]. The World Health Organization's (WHO) International Classification of Functioning, Disability & Health conceptualizes function in three levels: structural function (e.g. bowel, bladder, respiratory

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capabilities), individual function (e.g. task performance, independence with ADLs), and societal function (e.g. social engagement, community participation, vocational return). On the level of the individual, there exists personal factors that are relatively unchangeable (e.g. age, income level, developmental status) and psychological factors that are modifiable (e.g. affective response, intrinsic/extrinsic motivation) [15]. Outside of the individual, environmental supports and barriers exist as well. Environmental factors can be either physical (e.g. assistive devices, workplace building design) or social (e.g. family support, healthcare workers). Treatment models from physical, occupational and vocational therapies are designed to teach SCI survivors how to develop new skills and adapt necessary tasks to optimize their level of function. In the rehabilitation setting, functional recovery is marked by a patient's ability to participate in meaningful activities and improve performance through positive interactions with their environment [16].

Measuring Function in SCI. Return to function after SCI is marked by a patient's ability to participate in meaningful activities and improve performance through positive interactions with their environment [16]. Objective measurements of function in SCI vary in design from clinician-administered neurosensory exams to paper-and-pen quantitative inventories of symptoms. The gold standard for measuring severity of SCI, both in the acute and outpatient settings, is the International Standards for Neurological Classification of SCI (ISNCSCI) exam [17]. ISNCSCI exams, which must be performed in person by a trained clinician, gather necessary information on motor and sensory function. Scores are computed in an algorithm that produces an American Spinal Injury Association (ASIA) Impairment Scale severity score, or AIS grade, which ranges from A (complete injury) to E (no impairment). The ISNCSCI exam is widely used across all phases of care to detect functional changes in SCI over

time, however, there are many critiques to this methodology, including: lengthy exam time, scoring difficulties due to non-SCI related conditions (e.g. ventilators, sedating medication, pain), and difficulties associated with scheduling in-person exams in the setting of injury-related transportation limitations. Furthermore, although the ISNCSCI exam is often used as a method of measuring function, it does not measure function within the context of environment or assess patient-identified limitations to performing daily activities [18].

Questionnaires designed to take inventory of functional ability and performance may be considered an easier method for measuring functional outcomes in SCI, especially in the outpatient setting. Some inventories assess a specific area of functioning in SCI [i.e. the Walking index for SCI (WISCI) and the Graded Redefined Assessment of Strength, Sensation & Prehension (GRASSP)]; other inventories assess functioning across more broad elements of SCI recovery, such as independence, mobility, performance, and social integration [i.e. the Spinal Cord Independence Measure Version III (SCIM-III) and the Craig Handicap Assessment & Reporting Technique (CHART)]. While numerous assessments have been developed to quantify functional outcomes after SCI, far fewer have been developed to assess the quality of outcomes from the patient's perspective. Given the long-term deficits and increasing life expectancy post-SCI, the most holistic assessment of functional outcomes may require a deeper phenomenological exploration into the subjective patient experience of recovery.

Quality of Life in SCI

According to the WHO, quality of life (QoL) is defined as: "individuals' perceptions of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns" [14]. First conceptualized by the scientific community in the 1950's, QoL was not explored by SCI literature until the 1980's [19].

Comprehensive care plans in the rehabilitation setting will use QoL as a primary treatment objective to ensure that a patient's expectations for functional recovery are reflective of their personal preferences and values [20]. More frequently defined as simply "life satisfaction" or "subjective well-being," QoL has increasingly grown in popularity as a necessary endpoint in SCI outcomes research as well. Studies in the SCI population have found QoL to be associated with demographics such as younger age, higher income, and married status [21]. Health factors like pain, mobility, and co-morbid complications of SCI (e.g. re-hospitalizations, skin pressure ulcers) have shown negative associations with QoL outcomes [22, 23]. Of the studies that have shown a significant relationship between QoL and function after SCI, there are inconsistent findings on whether QoL is most strongly associated with fine motor function [11, 24], bowel/bladder function [25], or ambulatory status [26]. In chronic SCI, functional independence is consistently reported as a significant covariate of QoL [27-29].

Conclusions drawn from recent literature reviews have purported that variability in QoL outcomes are due to the research community's failure to systematically partition findings across SCI subpopulations (i.e. injury severity and duration) [19]. Likely due to the difficulty with enrolling study participants in the midst of a catastrophic life event, most QoL research has been conducted in community-dwelling persons who have lived with their SCI-related functional impairments for years or even decades. Studies showing insignificant or weak QoL-function relationships in chronic SCI have hypothesized the presence of latent moderating variables known to be related to time since injury (e.g. resilience, response shift effects, community integration) [30, 31]. Some have speculated that QoL has a positive linear relationship to years since injury, with the greatest QoL occurring decades after injury [32, 33]. There is also evidence of a strong link between post-SCI employment and QoL, which could mean the relationship is

more curvilinear with QoL starting to decrease after retirement age [34]. In the setting of limited longitudinal outcome data starting from the early recovery phase, it is even more difficult to know the true relationship between QoL and function in SCI.

Measuring Quality of Life in SCI. While most clinical researchers agree that measuring QoL is necessary to the assessment of outcomes, there remains disharmony among investigators as to how QoL should be measured in the SCI population. Wilson et al. published a review in 2011 that identified all common QoL outcome measures used in the SCI population. Of the 27 instruments identified, none were SCI-specific and only 4 had been validated in the SCI population [35]. The most widely used QoL assessment tool in SCI research is the Short Form 36 (SF-36), which was designed for use in the general population [36]. In order to detect meaningful changes throughout recovery, it is imperative that the tool used is appropriate for the population. SCI participants in qualitative studies have criticized SF-36 item interpretability due to narrow wording in the physical function domains and lack of appropriate response options [37]. For example, the SF-36 asks questions with regard to "walking" and "climbing stairs," and avoids any clarification on whether additional ways of mobilizing can be considered. Given the fact that many persons with permanent disability tend to separate their health status from their physical impairment, there likely exists discrepancies in item interpretation between patients and clinicians [38].

QoL is ontologically a subjective construct, making it difficult to measure solely from the clinician perspective. Where several reviews have exposed the lack of standardization among QoL measures in SCI research [26, 35, 38-40]; others have pointed out the inconsistent ways in which QoL is even operationalized [38, 41, 42]. Some researchers have attempted to infer QoL solely from clinician-administered assessments of a patient's health and functional status;

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however, this assumes that an improvement in health represents a direct improvement in the patient's QoL [38]. Although this methodology might be appropriate on an economic scale to assess disease burden between populations, it is likely not adequate in assessing individual patient experiences. As a result, knowledge of the relationship between QoL and function after SCI remains to be limited. Some studies have shown a positive correlation between QoL and function in SCI [43, 44]; others have shown no discernable difference in QoL between the chronic SCI and non-injured populations [30, 45].

Recent initiatives to improve and standardize QoL measures for the SCI population have been issued by multiple organizations, including the National Institute for Neurological Disorders and Stroke (NINDS), the National Center for Medical Rehabilitation Research, and the Department of Veterans Affairs [46]. As a result, methodological advancements in patient-reported outcome measures show a promising future for assessing QoL throughout disease-specific populations. First released in 2010, the NINDS-funded Quality of Life in Neurological Disorders (Neuro-QoL) measurement system offers a comprehensive and psychometrically sound methodology for measuring various facets of health-related QoL in adults living with neurological conditions [47]. An adaptation of the Neuro-QoL measurement system designed to be more relevant for use in individuals with SCI, called SCI-QoL, was just released in 2015 [13]. Both Neuro-QoL and SCI-QoL items banks were designed using Item Response Theory and can be administered via short form questionnaires or computer adaptive testing (CAT). This CAT technology allows for a more precise assessment of health-related QoL through the administration of questions generated from calculated relevancy. By using these more efficient and reliable methods for measuring a dynamic construct like QoL, more information can be

gained on the QoL-function relationship across SCI sub-populations, within various environmental contexts, and throughout the recovery trajectory.

Impact and Innovation

There is a need for more rigorous and generalizable studies examining the relationship between function and QoL in SCI. Since obtaining and maintaining study enrollments is difficult in patients with recent catastrophic injury, most existing publications on SCI outcomes use retrospective data, small sample sizes, or convenience samples of community-dwelling persons with chronic SCI. Given that the potential for functional advancements is highest during the first year post-SCI, there is an even greater need for literature reporting on QoL outcomes during the early recovery phase. It is possible that there are QoL-related constructs present during rehabilitation that – due to being relatively unexplored – have not been considered in SCI treatment plans. With a deeper understanding of the intersection between function and QoL immediately following injury, clinicians will be able to treat SCI patients more holistically across the entire care continuum.

Specific Aims

The objective of this research is to explore the relationship between measurements of function and QoL during the first year of recovery in adults with traumatic SCI. Specifically, this original research aims to:

1. Explore the psychometric properties of the Neuro-QoL Measurement System short forms in a traumatic SCI sample population during the first year following injury

2. Assess the relationships between objective measures of injury severity and functional independence with subjective measures of physical health-related QoL in a traumatic SCI sample population during the first year following injury

3. Determine how well overall QoL is predicted by baseline injury severity, functional independence, and health-related QoL at 6-12 months following traumatic SCI

The following chapters of this dissertation serve as detailed inquiries into the theoretical, empirical, and methodological approaches to understanding early relationships between QoL and function following traumatic SCI. Chapter 2 is an integrative review of literature identifying published associations between functional independence and QoL during the early recovery phase after SCI. Chapters 3 and 4 detail the design, methodological approach and study findings of primary research conducted under the major prospective study, Transforming Research & Clinical Knowledge in Spinal Cord Injury (TRACK-SCI) [48]. Chapter 5 synthesizes key study findings, summarizes strengths and limitations of the original research, and provides future direction for this expanding field of research.

Chapter 2: Integrative Review of Literature

Introduction

Studies in the SCI population have found QoL to be associated with demographics such as younger age, higher income, and married status [21]. Health factors like pain, mobility, and co-morbid complications of SCI (e.g. re-hospitalizations, skin pressure ulcers) have shown negative associations with QoL outcomes [22, 23]. Of the studies that have shown a significant relationship between QoL and function after SCI, there are inconsistent findings on whether QoL is most strongly associated with fine motor function [11, 24], bowel/bladder function [25], or ambulatory status [26]. Functional independence, or level of assistance required to perform daily living activities, is consistently reported as a covariate of QoL in chronic SCI [27-29]. Variability in QoL outcomes are likely due to the research community's failure to partition findings by injury severity and duration [19]. With a paucity of longitudinal outcome data starting from the early recovery phase, it is even more difficult to know the true relationship between QoL and function in SCI.

Literature reviews are an effective way of guiding future research by exposing relational themes between variables and across publications. Through the examination of SCI literature published over the last 10 years, this review aims to synthesize findings from the early recovery phase after SCI, and: (1) identify how QoL is defined and measured, (2) explore what is known about the relationship between QoL and functional independence, and (3) identify gaps in what is known about QoL and functional independence early in SCI recovery.

Methods

Operational Definitions. Due to the variability in how scientists operationalize QoL, the approach to a review of QoL measurement tools is more challenging than intuitive. To better

synthesize SCI outcomes across the various conceptualizations of QoL, the definition of "function" has been narrowed. While structural function (i.e. bowel, bladder, respiratory capabilities) and societal function (i.e. social engagement, community participation, vocational return) are important constructs in QoL research, this review will focus only on function at the level of the individual. More specifically, "function" is operationalized here as a measure of independence as assessed by either the Functional Independence Measure (FIM) or the Spinal Cord Independence Measure (SCIM). The FIM is widely used in rehabilitation medicine and disability research for measuring functional independence across a wide range motor and cognitive tasks. The SCIM was adapted from the FIM to more specifically assess the amount of assistance required by persons with SCI to complete activities if daily living (ADLs). The FIM and the SCIM have been shown to have excellent correlation [49, 50], and to have excellent interrater reliability across different patient settings (e.g. inpatient vs. outpatient) and administration techniques (e.g. clinician-administered vs. self-report) [49, 51]. Additionally, both the FIM and SCIM are recommended by the SCI Evaluation Database to Guide Effectiveness (EDGE) Task Force for use across acute, subacute, and chronic SCI populations [52]. It is the author's intention that by focusing only on functional independence with respect to ADLs, more iterations of QoL definitions and measurements can be considered in this review.

Table 2.1 *Integrative review search strategy*

Example Search Terms	Inclusion Filters	Exclusion Filters	Yield (N=)
TOPIC= ("spinal cord injury" OR "spinal cord injuries" OR "traumatic spinal cord injury" OR "spine injury" OR "spine trauma" OR "SCI" OR "tSCI") AND **TOPIC**= ("quality of life" OR "QoL" OR "life satisfaction" OR "subjective well-being" OR "patient-reported outcome" OR "PROM" OR "PRO") AND **TOPIC**= ("function" OR "functional outcome" OR "functional independence" OR "mobility" OR "FIM" OR "SCIM" OR "functional independence measure" OR "spinal cord independence measure")	**Species:** Human **Document Type:** Article **Language:** English **Population:** >/= 18 years old **Timespan:** 1/1/2010 – 12/31/2019	**Study Design:** Narrative, Case Report, Review, Controlled Trial, Abstract Only **Population:** <18 years old	**PubMed:** 213 **EMBASE:** 14 **Web of Science:** 427 **PsycInfo:** 129

Note: 1 = low risk of bias, 2 = moderate risk of bias, 3 = high risk of bias

Study Identification and Selection Process. Studies were initially identified through a methodological search of four electronic databases: PubMed, EMBASE, Web of Science, and PsycInfo. The initial search phrases included variations of "traumatic spinal cord injury," "quality of life," and function-related terms such as "functional outcome," "independence," and "mobility." Additional searches added in the terms "FIM" and "SCIM." A list of search terms used is displayed in Table 2.1. Given the increasing emergence and popularity of patient-reported outcome measures over the last 10 years, the literature search included human studies published between January 1, 2010 and December 30, 2019. Search criteria was further limited to exclude non-English publications and pediatric studies (majority of sample aged <18 years).

A publication was included in this review if it met the following criteria: (1) it was a primary source of literature reporting on original data by way of retrospective or prospective observational research; (2) the study sample was comprised of persons diagnosed with traumatic SCI only; (3) the study was limited to the non-acute setting (outpatient or rehabilitation facility) and collected outcome data within the first two years following SCI; (4) the study included functional independence as a primary variable, as measured by any version of the FIM or SCIM; and (5) the study reported results from at least one instrument previously identified as a QoL measurement tool. Studies were not included if they measured QoL using a single patient-reported question on overall health status or well-being. Publications were excluded if they were study protocols, narratives, case reports, reviews, or abstracts only. Psychometric studies, comparative effectiveness studies, or those focusing solely on pre-/post-intervention data were also excluded. Studies reporting only on data collected with qualitative methodology were excluded, although studies containing mixed methods were not initially excluded. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist was used as a

guideline to ensure thorough and systematic consideration of article data [53]. Figure 2.1 details

the study selection process with stepwise exclusion criteria.
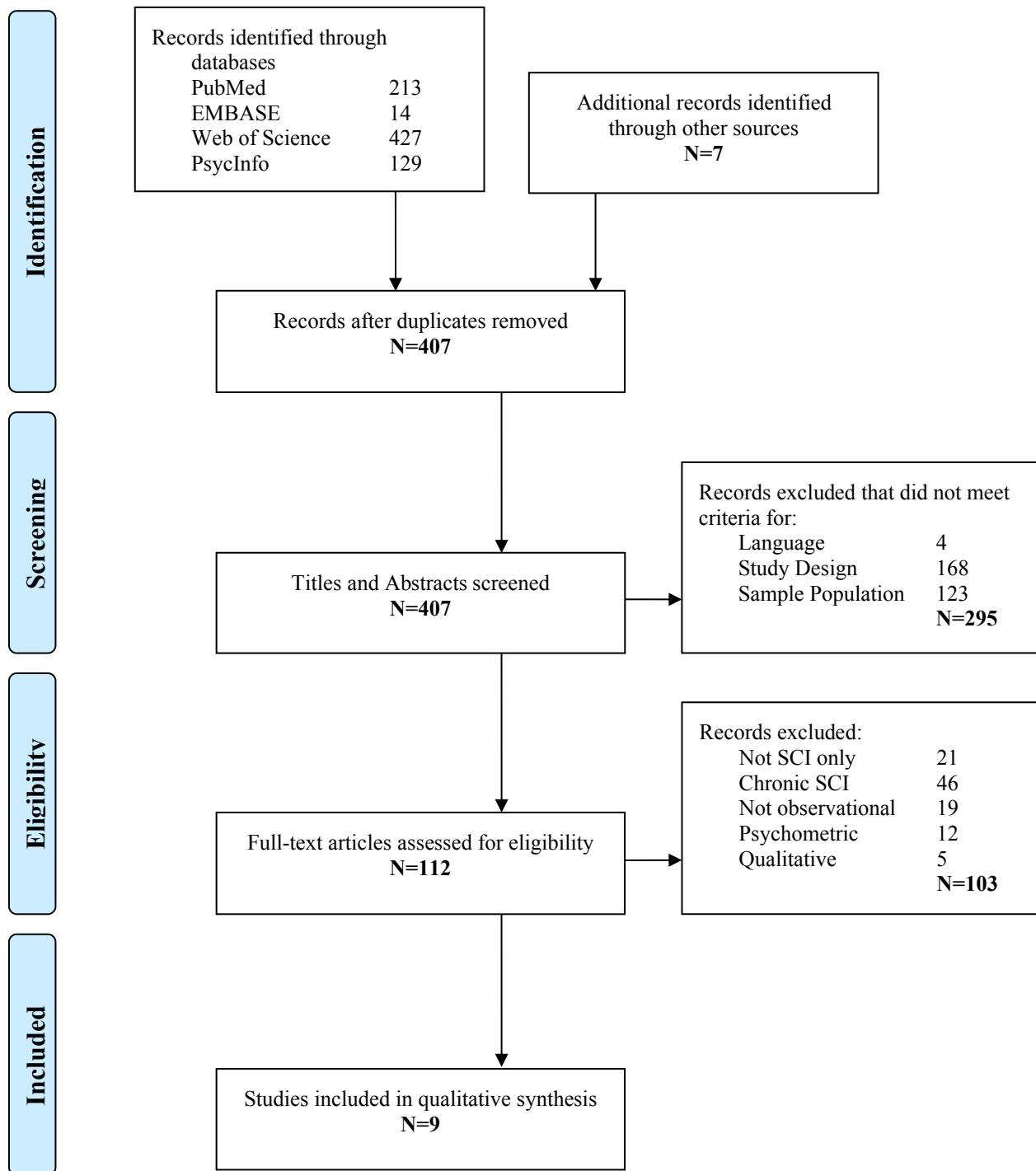
Figure 2.1 *PRISMA flow chart of study identification and selection for integrative review*

Data Extraction

Using a single reviewer, the following data was extracted, organized, and then analyzed: a) study attributes – study design, enrollment criteria, setting, purpose, and framework; b) sample characteristics – sample size, mean age, sex distribution, and injury severity; c) measurement characteristics – QoL definition, measurement tools used, data collection timepoints, and main outcome; and d) summary of study findings – reported associations between QoL and function, additional associated factors of QoL, and relevant study conclusions. To minimize bias and ensure appropriate collection of information, the Quality Assessment Tool for Quantitative Studies designed by the Effective Public Health Practice Project was used to evaluate the quality of included articles (Table 2.2) [54]. Table 2.3 presents a broad summary of study attributes, sample characteristics, and measurement characteristics. Table 2.4 summarizes the relevant findings from each study.

Table 2.2 *EPHPP¹ quality assessment tool for quantitative studies*

	A	B	C	D	E	F	G	H	I
Selection Bias	1	2	1	2	2	2	2	3	2
Study Design	2	3	3	2	2	3	3	2	2
Confounders	1	2	2	2	2	2	1	2	1
Blinding	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Data Collection	1	2	1	1	1	1	1	1	2
Withdrawals	2	3	1	2	1	2	2	2	3
Intervention	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Global Rating	1	3	2	1	1	2	2	2	2

¹ EPHPP = Effective Public Health Practice Project [54]
Note: A = Backus et al. (2013); B = Goulet et al. (2019); C = Hartoonian et al. (2014); D = Hilton et al. (2017); E = Hiremath et al. (2017); F = Mortenson et al. (2010); G = Rivers et al. (2018); H = Schwartz et al. (2018); I = Erosa et al. (2014)

Results

There were initially 783 articles identified through PubMed (n=213), EMBASE (n=14), Web of Science (n=427), and PsycINFO (n=129). An additional 7 articles were found from reference lists of other studies. After duplicates were removed, 407 titles and abstracts were reviewed for inclusion. If study suitability to the defined inclusion and exclusion criteria could not be determined from the abstracts alone, the full publication was then reviewed. The review of abstracts excluded 295 publications: 4 were not published in English, 168 did not meet inclusion criteria for study design (e.g. reviews or psychometric studies), and 123 did not meet inclusion criteria for study population (e.g. studies in animal models, pediatrics, or non-SCI). Of the remaining 112 articles, 103 were excluded after a full-text review: 21 were not SCI only, 46 were chronic SCI only, 19 were not observational studies, 12 were psychometric studies, and 5 were qualitative studies. Nine articles met the inclusion and exclusion criteria for this review.

Study Attributes. Out of the 9 studies included in this review, four were conducted in the United States (U.S.), four in Canada, and one in Australia. Four studies were cross-sectional in design, four were prospective cohort studies, and one was a retrospective cohort study. While all studies were published after 2010, one study used data that was collected starting in 1985 [55], and another used data that was collected starting in 1989 [56]. One study enrolled participants from an acute hospital, whereas the rest sampled participants from rehabilitation centers. Seven studies used multi-center data.

Sample Characteristics. Sample sizes ranged from 93 to 7,775 participants, with two of the studies having a sample size of less than 100 [22, 57]. Consistent with what is known about the target population, study samples were 75-89% male with a reported mean age of 35-49 years old. Baseline injury severities were not reported in two studies. The other seven studies reported

on injury severity using different scales, making this characteristic difficult to summarize. Of the studies that reported on injury severity using the gold standard American Spinal Injury Association Impairment Scale (AIS), AIS grades A through D were represented in each study. All but one study included the variable of QoL in their stated study purpose [57]. Five studies mentioned use of a theoretical framework; two studies used the International Classification of Functioning, Disability, and Health (ICF) model, one study used the Disability Creation Process (DCP) model, one study used the Canadian Model of Occupational Performance and Engagement (COMP-E), and one study used the Response Shift Theory.

Measurement Characteristics. Despite QoL being a variable of interest in all the studies, only three included an operational definition of QoL. An operationalization of QoL was inferred for the other studies by what measurement tool they selected for use. With these inferred QoL definitions, there were seven studies that conceptualized QoL to be the same as life satisfaction; the other two studies referred to QoL as either subjective or overall well-being. To measure QoL, the SWLS was used in 3 studies, the SF-36 in 3 studies, the LiSat-11 in 2 studies, the LSI in 1 study, the PWI in 1 study, and the QLI in 1 study (see Table 2.3 for list of abbreviations). In regard to measuring functional independence, seven studies used versions of the FIM and two studies used versions of the SCIM. Function and QoL data were collected over a variety of timepoints across the studies. Two studies collected data on both function and QoL at baseline and one year follow-up [22, 55]; one study collected functional data at baseline and QoL data at follow-up [58]; one study collected functional data at baseline and both function and QoL data at follow-up [30]; four studies collected functional and QoL data at the same timepoints during follow-up only [45, 57, 59, 60]; one study collected functional and QoL data at

different timepoints during follow-up only [56]. QoL was designated as a main outcome in six of the nine studies.

Summary of Study Findings. Despite consistent findings that certain personal factors are associated with functional independence, only one study stratified QoL results by injury severity [45]. Goulet et al. (2019) found QoL, as measured by SF-36 PCS, to have a strong association with functional independence in tetraplegics and a weak association with functional independence in paraplegics. There were three studies that did not find a correlation between functional independence and QoL at all [22, 57, 58] and two studies that found a weak correlation [56, 59]. One study found significantly lower QoL in SCI patients who were wheelchair-bound at follow-up compared to those that were ambulating, regardless of their ambulation status at discharge from rehabilitation [55]. One study found functional independence to have significant positive associations with physical health QoL (SF-36 PCS) and QoL as life satisfaction (LiSat-11), but a significant negative association with mental health QoL (SF-36 MCS) [60]. Schwartz et al. (2018) found a significant improvement in physical health QoL between 1- and 2-years post-SCI, but not in mental health QoL, QoL as life satisfaction, or functional independence [30].

There were similar findings across studies with regard to QoL covariates outside of function. Higher QoL scores were associated with higher baseline education [55, 58, 60], greater social participation [22, 56, 57, 59], greater family support [22, 55, 56, 60], and involvement in post-injury employment [55, 57, 59, 60]. Three studies found lower QoL scores to be associated with higher depression scores [55, 57, 59]; two studies found persons with more severe SCIs to report lower QoL scores [58, 60].

Table 2.3 *Summary of included papers*

Author (Yr) *Study Design*	Enrollment	Setting	Sample Characteristics (Mean±SD)	Summary of Purpose	QoL Definition	Measures	Timepoints	Primary Outcome(s)
Backus, et al. (2013) *Prospective Cohort*	Consecutive admissions 2007-2012, aged ≥12yrs	6 rehab centers in U.S.	N=1032 Age: 37.7±16.7 Sex: 81.2% male IS: C1-4 & AIS A-C (28.5%), C5-8 & AIS A-C (19.8%), T1-S5 & AIS A-C (36.1%), AIS D (15.6%)	To examine inpatient and post-discharge rehab services and the degree to which rehab services are associated with functional outcomes, social integration, and QoL Framework: NR	Life satisfaction[†]	FIM SWLS	Baseline & 1yr post-rehab 1yr post-rehab	Function, life satisfaction & community participation
Goulet, at al. (2019) *Cross-Sectional*	Consecutive admissions 2010-2016, C1-L1 SCIs post-surgery, aged ≥17yrs	1 level-1 trauma center in Canada	N=195 Age: 48.8±18 Sex: 79.7% male IS: AIS A (35.6%), B (9.6%), C (14.2%), D (40.6%)	To explore the relationships between specific functional abilities assessed by the SCIM and health-related QoL Framework: NR	Life satisfaction	SCIM SF-36	6-12mths post-SCI 6-12mths post-SCI	NR
Hartoonian, et al. (2014) *Cross-Sectional*	Within 1yr of injury, neuro deficit 2006-2011, aged ≥17yrs, completed inpatient rehab	SCIMS centers in U.S.	N=4976 Age: 39.1±16.4 Sex: 78.1% male IS: incomplete para (19.2%), incomplete tetra (37.1%), complete para (23.3%), complete tetra (15.4%)	To assess whether demographic, injury, health, and functional factors have the same predictive relation with symptoms of depression and which symptoms of depression are associated with QoL Framework: NR	Life satisfaction[†]	FIM SWLS	1-yr post-SCI 1-yr post-SCI	Somatic and non-somatic symptoms of depression
Hilton, et al. (2017) *Prospective Cohort*	Consecutive admissions 2010-2013, aged 15-65yrs, in EIVR	1 rehab center in Australia	N=97 Age: 35.1±14.9 Sex: 81.4% male IS: C1-4 & AIS A-C (10.3%), C5-8 & AIS A-C (23.7%), T1-S5 & AIS A-C (46.4%), AIS D (19.6%)	To explore the longitudinal outcomes following EIVR, and to assess the relationships between contextual factors and employment outcomes over time Framework: CMOP-E, ICF	Subjective well-being[†]	SCIM PWI	Baseline, 1yr & 2+yrs post-rehab Baseline, 1yr & 2+yrs post-rehab	Employment status
Hiremath, et al. (2017) *Retrospective Cohort*	Within 1yr of injury and neuro deficit, 1985-2012, aged ≥17yrs	21 SCIMS centers in U.S.	N=7,775 Age: 37±16.4 Sex: 78.9% male IS: NR	To assess QoL across changes in locomotion status at different timepoints, and to evaluate predictors of QoL at each timepoint Framework: ICF	Life satisfaction[†]	FIM SWLS	1-, 5-, & 10-yrs post-acute 1-, 5-, & 10-yrs post-acute	Life satisfaction, depression, & participation
Mortenson, et al. (2010) *Cross-sectional*	Consecutive admissions 1999-2003	2 rehab centers in Canada	N=93 Age: 39.5±14.8 Sex: 89% male IS: AIS A (28%), B (11%), C (11%), D (43%)	To examine predictors of post-rehabilitation QoL and their relationships Framework: DCP	Life satisfaction[†]	FIM QLI	3- & 15-mths post-rehab 3- & 15-mths post-rehab	QoL
Rivers, et al. (2018) *Cross-sectional*	Acute admission with L2 or higher SCI 2004-2014	RHSCI centers in Canada	N=340 Age: 41.6±17.3 Sex: 79.1% male IS: AIS A (34.78%), B (11.8%), C (16.3%), D (37.4%)	To analyze relations among injury, demographic, and environmental factors on function, QoL, and life satisfaction Framework: modified ICF	Life satisfaction and overall well-being	FIM SF-36 & LiSat-11	9-18mths post-rehab 9-18mths post-rehab	QoL and life satisfaction

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Table 2.3 *Summary of included papers, continued*

Author (Yr) *Study Design*	Enrollment	Setting	Sample Characteristics (Mean±SD)	Summary of Purpose	QoL Definition	Measures	Timepoints	Primary Outcome(s)
Schwartz, et al. (2018) *Prospective Cohort*	Acute admission 2004-2014	RHSCI registry centers in Canada	N=1125 Age: 33% aged 18-34yrs, mean NR Sex: 79% male IS: AIS A (34%), B (9%), C (16%), D (28%), unknown (13%)	To investigate post-SCI response shift effects in QoL over time Framework: Response Shift Theory	Health (physical, emotional, and social functioning) and well-being (a sense of meaning in one's life)	FIM SF-36 & LiSat-11	Baseline rehab, 1-, 2-, & 5-yrs post-SCI 1-, 2-, & 5-yrs post-SCI	Changes in function, life satisfaction, and QoL across all timepoints
Erosa, et al. (2014) *Prospective Cohort*	Acute admission 1989-1992, aged ≥17yrs, enrolled at 1yr follow-up	8 research centers in U.S.	N=144 Age: 37 Sex: 75% male IS: NR	To assess the mediating effects of participation on the predictive relationships of functional impairment, family satisfaction, and pain to QoL. Framework: NR	Life satisfaction[+]	FIM LSI	1yr post-SCI 5yrs post-SCI	Function & family satisfaction at 1yr; pain at 2yrs; life satisfaction & self-rated health at 5yrs

[+] QoL definition not explicitly given by study author. Operationalization implied from selected QoL measurement.

Note: yr(s) = year(s); mth(s) = month(s); QoL = quality of life; EIVR = early intervention vocational rehabilitation; IS = injury severity; AIS = American Spinal Injury Association Impairment Scale grade; para = paraplegia; tetra = tetraplegia; rehab = rehabilitation; SCIMS = SCI Model Systems; RHSCI = Rick Hansen Spinal Cord Injury; NR = not reported; CMOP-E =Canadian Model of Occupational Performance and Engagement; DCP = Disability Creation Process; ICF = International Classification of Functioning, Disability, and Health; FIM = Functional Independence Measure; SCIM = Spinal Cord Independence Measure; SWLS = Satisfaction with Life Scale; SF-36 = Medical Outcomes Study Short Form Health Survey 36-Item; PWI = Personal Well-being Index; QLI = Quality of Life Index; LiSat-11 = Life Satisfaction-11 Questionnaire; LSI = Life Satisfaction Index

Table 2.4 *Findings and study limitations*

Author (yr)	QoL-Function Findings	Other QoL Covariates	Additional Findings
Backus, et al. (2013)	⊘ No correlation: baseline mFIM with 1yr QoL ✓ Baseline cFIM with 1yr QoL (p=0.004)	↑QoL: college education ↓QoL: older age, AIS A-C, Medicaid or worker's compensation payer source	- Demographic and injury characteristics accounted for 9% of variance in 1yr SWLS, but 49% of the variance in 1yr FIM. - Significant positive relationship between acute rehab and 1yr FIM but no relationship with SWLS.
Goulet, at al. (2019)	✓ Moderate correlation: PCS with mSCIM (r=0.52), scSCIM (r=0.42) & SCIM (r=0.48) ✓ Strong correlation: PCS with mSCIM (r=0.56), scSCIM (r=0.52) & SCIM (r=0.54) in tetraplegics ✓ Weak correlation: PCS with mSCIM (r=0.39) in paraplegics ⊘ No correlation: MCS with SCIM	↑QoL: greater mobility and self-care independence in tetraplegics	- PCS was most strongly associated with mobility, followed by self-care and sphincter management
Hartoonian, et al. (2014)	✓ Weak correlation: mFIM with QoL (r=0.24)	↑QoL: greater participation in work, social, or physical activities ↓QoL: non-somatic symptoms of depression	- The correlation between mFIM and life satisfaction disappeared in their suggested model for predicting depression - The effect of function on QoL could be mediated by participation
Hilton, et al. (2017)	⊘ No correlation: SCIM with QoL at 2+yrs	↑QoL: greater social participation, perceived participation, autonomy, employment ↓QoL: greater anxiety and depression	- PWI predicts f/u employment status, but SCIM does not.
Hiremath, et al. (2017)	✓ Significantly lower QoL in AW compared to AA and WA groups at 1yr (p<0.oo1) ✓ Significantly lower QoL in WW compared to AA and WA groups at 1yr (p<0.oo1)	↑QoL: employment, education level over 12th grade, married status ↓QoL: loss of ambulation status, depression	- Individuals transitioning from ambulation to w/c use have lower QoL after 5 and 10 years than those who maintained w/c over time of improved from ambulating to w/c use.
Mortenson, et al. (2010)	⊘ No difference in QoL between 3- and 15-mths overall ⊘ No correlation between baseline mFIM & QoL at 3- or 15-mths	↑QoL: higher health competence, social participation, and mood (3mths); greater 3mth QoL, health competence, family support, and social participation (15mths)	- Personal factors explained most variance in QoL at 3- & 15-mths - Environmental factors explained more variance in QoL at 15mths than 3mths - Mood is significant predictor of QoL at 3mths but not 15mths
Rivers, et al. (2018)	✓ Significant positive association between QoL (on LiSat-11 and SF-36 PCS) and baseline mFIM (p<0.001) ✓ Significant negative association between mental health QoL (on SF-36 MCS) and baseline mFIM (p<0.001)	↑QoL: married status, employment ↓QoL: injury severity, higher age, less education, AIS A-C, and more co-morbidities	- Significant association between lower mFIM and higher mental health QoL could suggest a response shift effect
Schwartz, et al. (2018)	✓ Significant change in QoL (SF-36 Role Physical) between 1yr and 2yr follow-up ⊘ No significant change in QoL (Li-Sat-11 and SF-36 MCS) or in FIM scores between follow-ups	NR	- >95% had a FIM change <MCID over entire study period - True change improvement in QoL physical latent variable could indicate possible component of adaptation)
Erosa, et al. (2014)	✓ Weak correlation between FIM (1yr) & QoL (5yrs) (0.39) ✓ Mobility and family satisfaction are significant mediators between FIM and QoL	↑QoL: higher mobility, social integration, and family satisfaction	- Results of path analysis suggest that participation variables are mediators of relationship between function and QoL

Note: yr(s) = year(s); mth(s) = month(s); QoL = quality of life; rehab = rehabilitation; NR = not reported; FIM = Functional Independence Measure; mFIM = FIM motor score; cFIM = FIM cognitive score; SCIM = SCIM = Spinal Cord Independence Measure; mSCIM = SCIM mobility score; scSCIM = SCIM self-care score; SF-36 = Medical Outcomes Study Short Form Health Survey 36-Item; PCS = SF-36 physical component score; MCS = SF-36 mental component score; LiSat-11 = Life Satisfaction-11 Questionnaire; AW = change from ambulation to wheelchair status; AA = maintained ambulation status; WW = maintained wheelchair status; WA = change from wheelchair to ambulation status; MCID = minimally clinically important difference

Discussion

Despite there being limited research on QoL during early SCI recovery, the synthesis of QoL findings is especially difficult in the absence of standardized QoL definitions and measurement methodologies. No studies in this review used a conceptual model that contained QoL as a major domain or construct. Additionally, most studies did not stratify results by variables known to be associated with QoL and function, which likely impacted the generalizability of findings. For example, after Goulet et al. (2019) found a moderate correlation between QoL and function, further exploration in the QoL-function relationship revealed a strong correlation in tetraplegics and a weak correlation in paraplegics.

One interesting finding across multiple studies was the role of participation in functional and QoL outcomes. Erosa et al. (2014) and Hartoonian et al. (2014) found participation to be a mediator between functional independence and QoL. This suggests that participation, not disability, has a direct relationship with QoL and that any observed association between functional independence and QoL is via participation. More research examining this relationship could have a significant impact on the way that rehabilitation care is structured. In the setting of permanent functional disability, this could mean more possibilities for clinicians and caregivers to assist in promotion of QoL.

Limitations. Although systematic reviews are designated level-1 quality evidence, there are still limitations of this review to consider. First, the literature search was restricted to articles published in English, which may have excluded relevant studies in other languages. Widening the study period inclusion criteria to more than 10 years may yield additional studies, although a cursory search of studies published between 2000 and 2010 did not reveal any that would have met the other inclusion criteria. Additionally, the categories included in the methodological

assessment of studies, although based on previous research, was largely constructed by this author. More information might be gained from a review including studies with qualitative methodologies and studies exploring caregiver perceptions. Findings on factors of QoL during early SCI recovery should be taken with caution given the lack of standardization across QoL conceptualizations and the variety of instruments used.

Clinical Implications and Directions for Future Research. More longitudinal observational studies are needed to understand multivariate relationships between QoL and function in SCI. This author offers a few reasons for why QoL is relatively unstudied throughout early SCI recovery. First, it is reasonably very difficult to obtain and maintain enrollments in patients with a recent catastrophic injury. Second, disconnected healthcare systems like in the U.S. create a barrier to following patients through various levels of care and residencies. Finally, QoL has long been thought of as an endpoint – rather than a counterpoint – to other outcome measures [61]. It is probable that researchers who hold this conceptualization of QoL might assume that other outcomes are more important to address earlier in the recovery process. When measured alongside other outcomes, QoL can contribute to a more accurate assessment of patient health status – one that considers individual perspectives of well-being. It is possible that there are QoL-related constructs present during rehabilitation that – due to being relatively unexplored – have not been considered in SCI treatment plans. Until the relationship is better known, measuring QoL alongside objective measurements of independence and performance, throughout the entire recovery trajectory, may be the best approach to ensuring optimal patient outcomes. By considering QoL measurements immediately following injury, clinicians will be able to treat SCI patients more holistically throughout early recovery and rehabilitation.

Chapter 3: Design and Methods of Original Research

The Health-Related Quality of Life Conceptual Model

While some conceptual models have been referenced in SCI research, there is no widely adopted framework to underpin the intersection between QoL and function in SCI. Some relevant treatment models have been developed and adopted in practice, but many are institutionally specific and do not address components that span across the patient care continuum. Other treatment models focus on the essential objectives for achieving optimal function but disregard facets of the subjective patient experience, such as QoL.
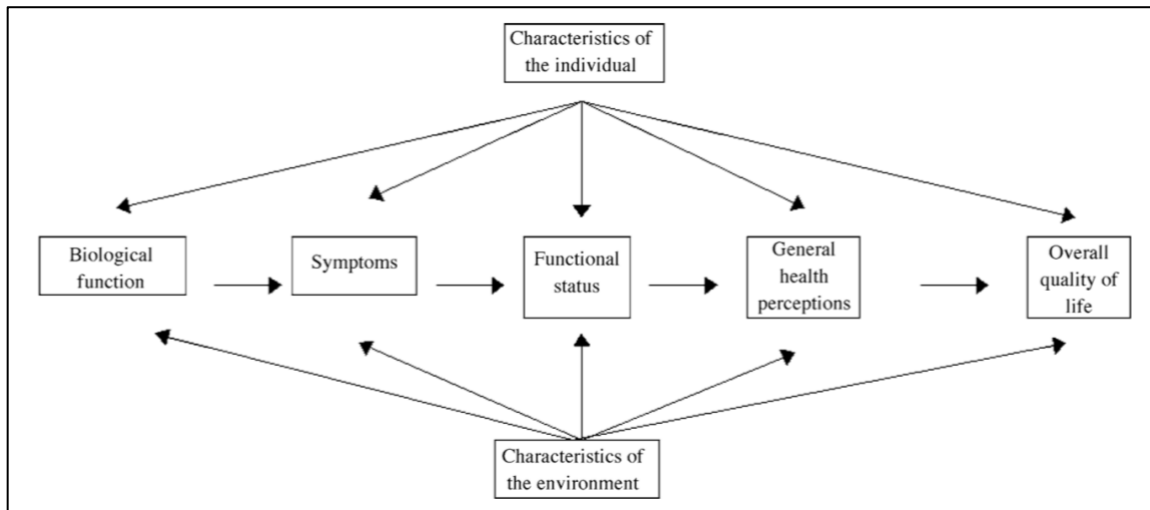
Figure 3.1 *Simplified representation of the original Health-Related Quality of Life Model* [15]

First introduced in 1995 by Drs. Wilson and Cleary, the Health-Related Quality of Life (HRQoL) model was developed as a conceptualization of whole-person health from a biopsychosocial perspective (Figure 3.1). According to Wilson and Cleary, the HRQoL model "categorizes measures of patient outcome according to the underlying health concepts they represent and proposes specific causal relationships between different health concepts" [61]. There are five classifications of patient outcome measures identified in the model: biological and

physiological variables, symptom status, functional status, general health perceptions, and overall QoL. There is a unidirectional relationship among the five types of patient outcome measures, such that they lie on a continuum of increasing biopsychosocial complexity.

The HRQoL model was chosen as a conceptual framework to underpin this original research because of its simplicity and flexibility in application to the SCI population. In a 2012 systematic review and critique of various QoL models, the HRQoL model was determined to be based on adequate empirical evidence with concepts that were consistently defined and "made sense" for real world applications [62]. In 2017, Ojelabi and colleagues conducted a systematic review of all studies that had applied the HRQoL model to chronic disease management [63]. Although this review did not include studies in SCI, it identified a wide range of patient populations that had used the HRQoL model for a framework in disease management (e.g. Coronary Artery Disease, Hodgkin's Lymphoma, Diabetes, HIV/AIDS, stroke, asthma). Pending future research into model components and the relationships between constructs, the HRQoL model still serves as a useful template for conceptualizing SCI outcomes and the relationships between them. The model's schematic representation of patient outcome measures as linear determinants of overall QoL provides a practical, baseline framework for hypothesis generation. The inclusion of subjective factors, like symptoms and general health perceptions, provides clinicians with a broader view of outcomes measurement – one that encompasses more than just physiological status.

Study Design

To further understand the relationship between function and QoL, I performed a longitudinal correlation study with data from hospital admission (baseline) and two follow-up timepoints in patients with SCI. This analysis of data is part of an ongoing, observational,

prospective cohort study called Transforming Research and Clinical Knowledge in SCI (TRACK-SCI). TRACK-SCI is a translational, multidisciplinary clinical research study that collects complex physiological and observational data from the emergency, operative, critical care, acute care, subacute care, and in-home settings throughout the first year of recovery after traumatic SCI [48]. A comprehensive list of all measures included in the TRACK-SCI study are presented in the Appendix (Table A.1). Variables include highly granular clinical data, imaging, biospecimens, and follow-up data using the National Institute of Neurological Disorders and Stroke (NINDS) common data elements (CDEs). Outcomes include data from various follow-up questionnaires administered at 3-, 6-, and 12-months post-injury and from in-person clinician assessments performed at 6- and 12-months post-injury. Institutional review board approval was obtained and remains active (UCSF Human Research Protection Program #15-16115).

Participants and Enrollment

Participants of the prospective Transforming Research and Clinical Knowledge in Spinal Cord Injury (TRACK-SCI) Study were considered for inclusion in this analysis. Patients presenting consecutively between December 2017 and October 2020 to one of two California level-1 trauma centers with an acute traumatic SCI were considered for enrollment. Additional inclusion criteria required hospital presentation within 24-hours of injury, imaging confirmation of both a documented neurologic deficit and a spine fracture or ligamentous injury, and ability to obtain consent from patient or proxy. When prioritization of quality care prevented our ability to get consent, emergency waiver was used and a designated patient advocate signed consent on the patient's behalf (IRB #15-16115). Patients were excluded from enrollment in TRACK-SCI if they were <18 years old, pregnant, in custody, or on a legal psychiatric hold. Enrolled participants received $50 compensation at each study time point (maximum total of $200).

Measurements

Demographic and Injury Characteristics. This analysis includes measures collected during the acute hospitalization and from each of the follow-up timepoints. Demographic, injury, and clinical data were collected from participant self-report and concurrent chart reviews. AIS grades were measured by trained clinical investigators using the ISNCSCI exam [17]. When acute ISNCSCI exams were not clinically feasible in the setting of patient intubation, sedation, pain, or undue burden, AIS grades were estimated by a neurosurgical attending. Patient-reported outcome measures were administered either in-person or over the phone at 3-, 6-, and 12-months post-injury. Given the accelerated participant attrition during the COVID-19 pandemic, the 6- and 12-month follow-up timepoints were collapsed for this analysis.

Spinal Cord Independence Measure III. Objective self-reported function was assessed at both the early (3 months post-injury) and late (6-12 months post-injury) follow-up timepoints using the self-report version of the Spinal Cord Independence Measure III (SCIM-III) [64, 65]. The SCIM-III assesses the amount of assistance required by persons with SCI to complete activities if daily living (ADLs). The inventory consists of 19 items across three subscales (self-care, respiration and sphincter management, and mobility), with a total maximum score of 100 indicating complete functional independence. I consider this inventory to be an objective measure because it generates a functional score without considering the respondent's own perspective of well-being.

The SCIM-III has repeatedly shown adequate-excellent internal consistency (Cronbach's alpha = 0.77-0.85) and interrater reliability across subscales (r = 0.90-0.94) [50]. TRACK-SCI uses the self-report version of the SCIM-III, which allows for administration of the inventory over the telephone when an in-person exam is infeasible. There is a total of 19 items across 3

subscales: Selfcare (SCIM-SC), Respiration and Sphincter Management (SCIM-RSM), and Mobility (SCIM-MOB). Functional independence is operationalized here using the SCIM-SC (0-20 points), the SCIM-MOB (0-40 points), and the SCIM-III total score (0-100 points).

Neuro-QoL Short Forms. Subjective health-related QoL was assessed at both the early and late follow-up timepoints using the short form versions of the Quality of Life in Neurological Disorders (Neuro-QoL) measurement system [66-68]. Neuro-QoL is a psychometrically robust collection of patient-reported outcome measures that assess physical, mental, and social domains of health-related QoL in persons with neurological disorders. Each questionnaire asks the respondent to assess their current level of difficulty with specific tasks using a 1-5 Likert scale (1 = unable to do, 5 = without any difficulty), or to assess their current level of satisfaction with their ability to perform these specific tasks. I consider these questionnaires to be subjective measures of function because they evaluate performance based on what is optimal to the respondent, not a population-based standard. Test-retest reliability among the Neuro-QoL short forms has been studied and confirmed in sample populations of participants with various neurological conditions [69].

International SCI Quality of Life Basic Data Set. The ISCI-QoL Basic Data Set is a measure of overall life satisfaction [70]. Using 10-point Likert scales between "completely satisfied" and "completely dissatisfied," this 3-item inventory asks the respondent to rate their own physical health, psychological health, and life as a whole. Each of the items added together creates an overall QoL score with a maximum value of 30.

Specific Aims and Hypotheses

Specific Aim 1. Although the Neuro-QoL measurement system is highly recommended to assess patient outcomes in the neurologic population, there currently exists no reliability or

validation testing in the traumatic SCI population. The first aim was to explore the psychometric properties of the Neuro-QoL Measurement System short forms in a traumatic SCI sample population during the first year following injury. I addressed Specific Aim 1 via the following sub-aims:

1.A. Assess reliability of Neuro-QoL short forms by analyzing score distributions (i.e. means, standard deviations, medians and ranges), floor and ceiling effects, internal consistency within measures, and test-retest reliability across two follow-up time points.

  Hypothesis. There will be strong internal consistency within all measures and strong test-retest reliability of measures between the two timepoints. Floor and ceiling effects may reveal limits of detection in health-related QoL changes.

1.B. Assess convergent and discriminant validity between the 11 Neuro-QoL short forms and the ISCI-QoL.

  Hypothesis. There will be strong positive correlations between shorts forms of the Physical Health domain and short forms of the Social Health Domain, but there will be little-to-no correlation between these and the short forms of the Mental Health domain. There will be moderate-to-strong correlations between each of the Mental Health short forms, with directionality depending on whether the questionnaire is designed to measure better health (i.e. Positive Affect & Well-being and Cognitive Function short forms) or worse health (i.e. Anxiety, Depression, Emotional/Behavioral Dysfunction, and Stigma short forms). I anticipate that all Neuro-QoL measures will be correlated with the ISCI-QoL.

Specific Aim 2. In persons with traumatic SCI, little is known about the relationship between function and QoL throughout the early recovery period when neuro-rehabilitation is the primary treatment focus. The second aim was to assess the relationship between objective measures of injury severity and functional independence with subjective measures of physical health-related QoL in a traumatic SCI sample population during the first year following injury. I addressed Specific Aim 2 via the following sub-aim:

> *2.A.*   Determine if baseline measures of injury severity [i.e. AIS grade, level of injury, upper extremity motor score (UEMS), and lower extremity motor score (LEMS)] and concurrent measures of functional independence (SCIM-SC, SCIM-MOB, and SCIM-III Total) are associated with Physical Health Neuro-QoL scores at 6-12 months post-SCI.
>
> *Hypothesis.* Physical Health Neuro-QoL scores will have a significant moderate-to-strong association with baseline injury severity and functional independence measures. I hypothesize that the strongest associations will be between the SCIM-SC and the NQ-ADL, and between the SCIM-MOB and the NQ-MOB.

Specific Aim 3. While little is known about the relationship between objective function and subjective function-related QoL after SCI, even less is known about how measures of function relate to overall well-being. Our third aim was to determine how well overall QoL is predicted by measures of baseline injury severity, functional independence, and health-related QoL at 6-12 months post-SCI. I addressed Specific Aim 3 via the following sub-aims:

> *3.A.*   Assess univariate relationships at 6-12 months post-SCI between: (1) baseline injury severity (i.e. AIS grade, level of injury, UEMS and LEMS) and the ISCI-QoL, (2) SCIM-III and the ISCI-QoL, and (3) Neuro-QoL and the ISCI-QoL.

Hypothesis. ISCI-QoL at 6-12 months post-SCI will have weak-or-no association

with the baseline injury severity measures and will have moderate-to-strong

positive associations with the SCIM-III and Neuro-QoL measures.

3.B. Assess multi-variable regression models between overall QoL and each of the

Neuro-QoL measurement domains at 6-12 months post-SCI.

Hypothesis. In a multi-variable regression model, the majority of variance in

ISCI-QoL will be explained by the Neuro-QoL Physical Health short forms, over

the Mental and Social Health short forms.

Statistical Approach: Specific Aim 1

TRACK-SCI Clinical Research Coordinators aided with data abstraction from the

medical record and RedCap database. STATA was used for data cleaning, curation and analysis.

I performed an analysis of missing data to determine the best method for maximizing the sample

size while minimizing bias. Amplified sample attrition was anticipated due to the COVID-19

pandemic and subsequent administrative holds on clinical research activities. The 6- and 12-

month timepoints were collapsed into one follow-up timepoint for analysis. If a participant

provided data at both 6- and 12-months, the latest of the two was used for analysis. Descriptive

statistics were calculated for all demographics, diagnostic etiologies, and levels of clinical

endpoints. Frequency distributions were assessed to identify any outliers or questionable data

points potentially representing data errors. Cross tabulations and Pearson *r* correlation matrices

were used to make comparisons between QoL scores. Regression analyses were performed to

determine any significant associations between measures of injury severity, functional

independence, health-related QoL and overall QoL. Significance was assessed at a type 1 error

level of $p<0.05$. Effect sizes – reported as coefficients of determination (R^2) – were used to

examine the proportion of variance explained by the analysis model. Multiple hypothesis protection was performed using Bonferroni's correction to control for family-wise error rate inflation.

Score Distributions. Score means, standard deviations, medians, and ranges were calculated for each Neuro-QoL measurement to evaluate the spread and normality of distributions. The percentage of missing items across all respondents were calculated to assess the difficulty of measurement completion. When possible, missing items were imputed using guidelines from the NINDS User Manual for Neuro-QoL Measures [71]. The percentage of minimum and maximum possible facet scores were calculated to assess for floor and ceiling effects.

Reliability. The study performed two tests of reliability: internal consistency and test-retest reliability. Cronbach's alpha was calculated to examine the internal consistency of each eleven Neuro-QoL short forms at 6-12 months post-SCI. Cronbach's alpha is an estimate of measurement error that assesses the strength of co-variance among measurement items [72]. Measures with a Cronbach's alpha > 0.70 were determined to have good internal consistency [73]. Pearson r correlation coefficients were used to assess test-retest reliability, which is a measure of score stability over time. The Pearson r correlations measured the stability of error variances between the early (3 months post-SCI) and late (6-12 months post-SCI) timepoints for each Neuro-QoL measure. Measures with Pearson r > 0.70 were determined to have good test-retest reliability between the two timepoints [74].

Validity. Convergent and discriminant validity was assessed at both follow-up timepoints using pairwise Pearson r correlation coefficients between the 11 Neuro-QoL measures and the ISCI-QoL measure of overall QoL. Convergent validity measures the extent to which the same

domain is measured by two different tools, whereas discriminant validity measures the extent to which two different tools are distinct [75].

Statistical Approach: Specific Aims 2 & 3

Univariate regression analyses were used to assess if injury severity measures [AIS grade, level of injury, upper extremity motor score (UEMS), lower extremity motor score (LEMS)] and functional independence measures (SCIM-III total score, self-care sub-score, and mobility sub-score) were significant predictors of Physical Health Neuro-QoL and ISCI-QoL scores at 6-12 months post-SCI. Univariate regression analyses were also used to assess if any of the 11 Neuro-QoL measures were significant predictors of the ISCI-QoL at 6-12 months post-injury. Finally, multi-variable regressions were performed to assess which of the Neuro-QoL short forms were the greatest predictor of overall QoL at 6-12 months post-SCI.

Chapter 4: Study Findings

Sample Characteristics

A diagram of participant enrollment and retention is displayed in Figure 4.1. There were 179 participants with traumatic SCI that were enrolled from the two California sites (127 from a San Francisco hospital and 52 from a Fresno hospital). Fourteen participants died during hospitalization and 19 electively withdrew from the follow-up portion of the study. Thirty-two participants (21.9%) had complete loss to follow-up despite multiple attempts to contact them, resulting in 114 participants who completed at least one of the three follow-up timepoints.

See Table 4.1 for sample demographics and injury characteristics. Participants were between 18 and 90 years old at the time of injury (mean age was 53 years old); about 40% were >60 years old and 70% were >40 years old. Three-quarters of the study population were men. Roughly half of the participants had paid employment, some college education, and were unmarried. The majority of SCIs were to the cervical spine (80.7%), resulted from fall-related trauma (50.0%) and were determined on ISNCSI exam to be incomplete injuries (72.8%).

Findings for Specific Aim 1

Aim 1 was to explore the psychometric properties of the Neuro-QoL Measurement System short forms in a traumatic SCI sample population during the first year following injury. Table 4.2 displays the Neuro-QoL descriptive statistics across two follow-up timepoints. At the 3-month follow-up, the rate of questionnaire completion was between 57% (NQ-PWB, N=65) and 68% (NQ-MOB, N=77). At 6-12 months post-SCI, questionnaire completion rates were between 63% (NQ-PWB, N=72) and 72% (NQ-ADL, N=82).
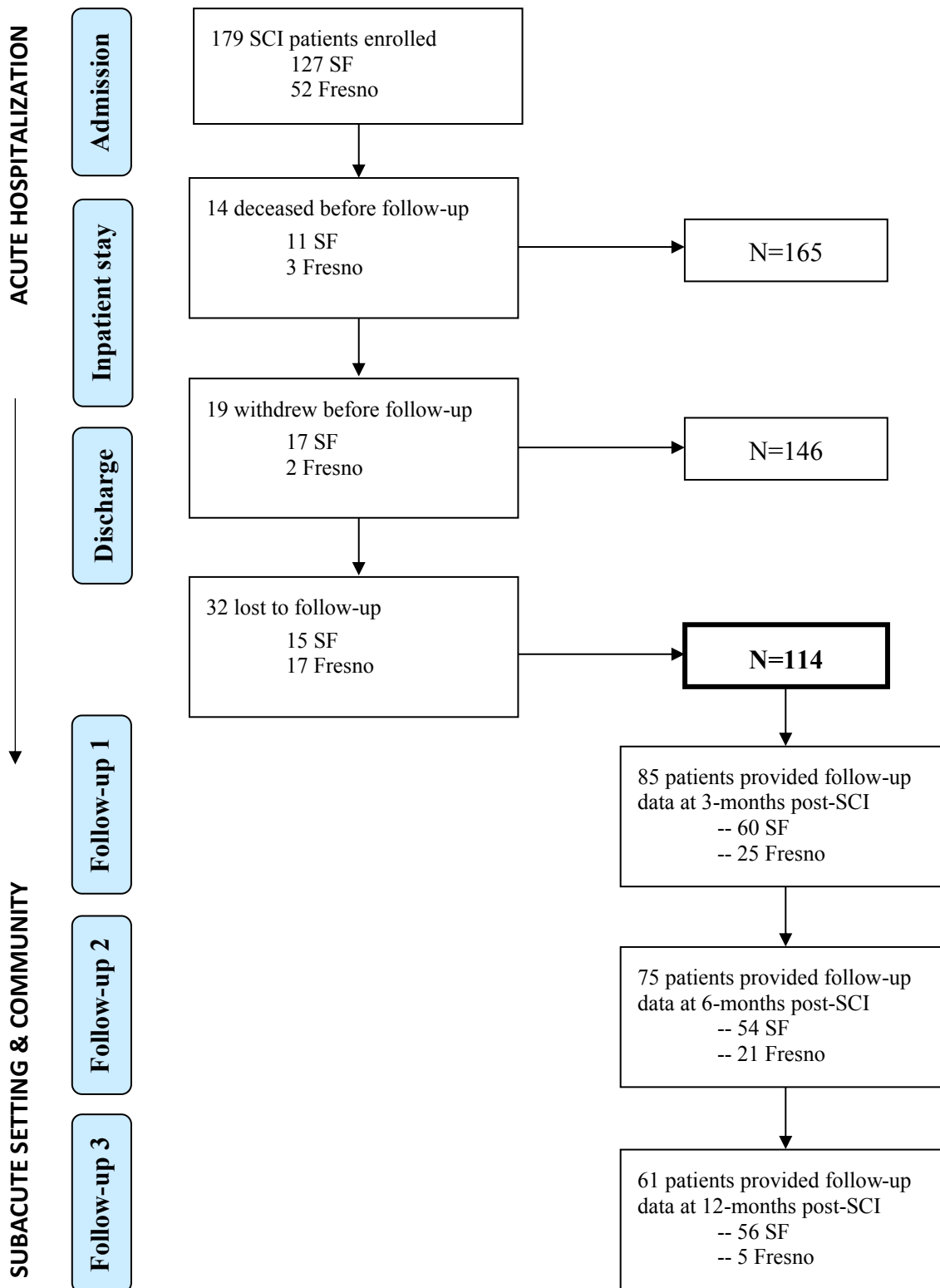
Figure 4.1 *Flow diagram of participant enrollment and retention*

Table 4.1 *Sample demographics and injury characteristics, N=114*

Characteristic	N *(%)* or Mean±SD
Age in years; *(min-max)*	53.2±19.3; *(18-90)*
Female	30 *(26.3)*
Education	
<13 years	15 *(13.2)*
13-16 years	57 *(50.0)*
17 years or more	29 *(25.4)*
Not reported	13 *(11.4)*
Living situation	
Alone	22 *(19.3)*
1-3 housemates	63 *(55.3)*
>4 housemates	28 *(24.6)*
Not reported	1 *(0.9)*
Marital status	
Married/partnered	49 *(43.0)*
Single/widowed/separated	58 *(50.9)*
Not reported	7 *(6.1)*
Employment	
Paid work	55 *(48.2)*
Student/homemaker	6 *(5.3)*
Retired	31 *(27.2)*
Unemployed	17 *(14.9)*
Not reported	5 *(4.4)*
Annual income	
<$25k	30 *(26.3)*
$25k to <$100k	19 *(16.7)*
$100K and over	25 *(21.9)*
Not reported	40 *(35.1)*
Injury mechanism	
Assault	14 *(12.3)*
Fall	57 *(50.0)*
Collision[1]	26 *(22.8)*
Other trauma[2]	9 *(7.9)*
Unknown	8 *(7.0)*
Level of injury	
Cervical	92 *(80.7)*
Thoraco-lumbar	19 *(16.7)*
Unknown	3 *(2.6)*
Baseline AIS[3]	
Complete	23 *(20.2)*
Incomplete	83 *(72.8)*
Unknown	8 *(7.0)*
Hospital LOS in days; *(min-max)*	15.0±13.1 *(2.6-93.5)*

[1] Includes bicycle vs. auto, bicycle vs. ground, pedestrian vs. auto, motorcycle collisions, and motor vehicle collisions
[2] Includes sports-related, leisure-related, or crushing injury
[3] Complete = AIS A, Incomplete = AIS B-E
Note: Level of injury and baseline AIS collected from latest motor-sensory exam prior to discharge from acute hospitalization

Table 4.2 *Neuro-QoL descriptive statistics at 3 months and at 6-12 months post-SCI*

Domain	Neuro-QoL Short Form Measure	Abbreviation	N	3 Months Mean ± SD	Median (min–max)	N	6-12 Months Mean ± SD	Median (min–max)
Physical Health-Related Quality of Life	Upper Extremity Function (Fine Motor, ADLs)	NQ-ADL	76	31.0 ± 9.9	35 (8–40)	82	31.2 ± 10.2	36 (8–40)
	Lower Extremity Function (Mobility)	NQ-MOB	77	24.8 ± 11.1	27 (8–40)	81	27.0 ± 10.6	28 (8–40)
	Fatigue	NQ-FTG	72	19.7 ± 7.8	18 (8–40)	75	19.2 ± 8.2	18 (8–40)
Mental Health-Related Quality of Life	Anxiety	NQ-ANX	74	15.6 ± 8.3	13 (8–38)	75	15.2 ± 7.6	13 (8–40)
	Depression	NQ-DEP	72	14.5 ± 8.3	11 (8–39)	75	12.2 ± 6.2	10 (8–40)
	Positive Affect & Well-being	NQ-PWB	65	34.1 ± 9.1	35 (12–45)	72	35.6 ± 8.1	37 (17–45)
	Emotional & Behavioral Dyscontrol	NQ-EBD	73	13.3 ± 6.1	11 (8–40)	75	15.1 ± 6.8	14 (8–40)
	Cognitive Function	NQ-COG	74	34.4 ± 6.3	37 (12–40)	76	34.4 ± 6.3	37 (15–40)
	Stigma	NQ-SGM	71	13.6 ± 6.9	11 (8–40)	75	13.9 ± 7.2	10 (8–36)
Social Health-Related Quality of Life	Participation in Social Roles & Activities	NQ-PAR	73	29.6 ± 8.8	30 (8–40)	75	32.3 ± 8.4	34 (8–40)
	Satisfaction with Social Roles & Activities	NQ-SAT	73	26.1 ± 9.6	29 (8–40)	75	29.2 ± 8.9	30 (8–40)

Note: For all Neuro-QoL measures, a higher score indicates more of the construct being studied. For example, a higher score on the NQ-ADL would indicate better health and a higher score on NQ-DEP would indicate worse health.

Score distributions and reliability measures are displayed in Table 4.3. Floor and ceiling effects were considered significant if greater than 15% [73]. There were significant floor effects noted within both follow-up timepoints for the Neuro-QoLs measuring: Mobility (14.8-16.9%), Anxiety (24.0-25.7%), Depression (34.7-38.7%), Emotional & Behavioral Dyscontrol (25.3-27.4%), and Stigma (30.7-38%). Of these, all measures except for Mobility demonstrated a significant right-sided skew (>1.0) to their score distributions. Significant ceiling effects were noted within both follow-up timepoints for the ADL (24.3-29%), Positive Affect & Wellbeing (18.5-22.2%), Cognitive Function (22.4-28.4%), and Participation with Social Roles/Activities (15.1-30.0%) Neuro-QoL measures. Of these, all measures except for Participation with Social

Roles/Activities had score distributions with a significant left-sided skew (<-1.0) within at least one of the timepoints. The only Neuro-QoL measurements that did not show floor or ceiling effects were Fatigue and Satisfaction with Social Roles/Activities. As hypothesized, there was very high internal consistency observed in each Neuro-QoL measures and across both timepoints. At 3 months post-SCI, internal consistency ranged from a Cronbach's alpha of 0.87 (Cognitive Function) to 0.96 (ADL and Mobility). At 6-12 months post-SCI, internal consistency ranged from a Cronbach's alpha of 0.87 (Cognitive Function) to 0.96 (ADL).

Table 4.3 *Score distributions and reliability of Neuro-QoL measures across two timepoints*

| Measure | Items | Range | 3 Months | | | | 6-12 Months | | | | |
			FE (%)	CE (%)	Skew	α	FE (%)	CE (%)	Skew	α	r
NQ-ADL	8	8-40	5.3	29.0	-0.95	0.96	8.5	24.3	-1.23	0.96	0.75
NQ-MOB	8	8-40	16.9	9.0	-0.21	0.96	14.8	11.1	-0.53	0.95	0.85
NQ-FTG	8	8-40	11.1	1.4	0.30	0.92	8.0	2.7	0.70	0.94	0.60
NQ-ANX	8	8-40	25.7	0	1.06	0.94	24.0	1.3	1.31	0.94	0.46
NQ-DEP	8	8-40	34.7	0	1.31	0.95	38.7	0	1.40	0.89	0.42
NQ-PWB	9	9-45	0	18.5	-0.59	0.95	0	22.2	-0.57	0.92	0.77
NQ-EBD	8	8-40	27.4	1.4	1.56	0.92	25.3	0	0.70	0.89	0.38
NQ-COG	8	8-40	0	28.4	-1.39	0.87	0	22.4	-1.21	0.87	0.30
NQ-SGM	8	8-40	38	1.4	1.69	0.90	30.7	0	1.35	0.89	0.61
NQ-PAR	8	8-40	1.4	15.1	-0.60	0.91	2.7	30.0	-1.05	0.93	0.47
NQ-SAT	8	8-40	8.2	8.2	-0.40	0.92	0	14.7	-0.54	0.89	0.61

Note: For all Neuro-QoL measures, a higher score indicates more of the construct being studied. For example, a higher score on the NQ-ADL would indicate better health and a higher score on NQ-DEP would indicate worse health. FE = floor effect; CE = ceiling effect; α = Cronbach's alpha; r = Pearson's correlation coefficient

See Table 4.4 for an assessment of convergent and discriminant validity using a pairwise Pearson *r* correlation matrix. As hypothesized, significant positive correlations were observed between the ADL and Mobility Neuro-QoLs at 3 months (*r*=0.55) and at 6-12 months (*r*=0.79), however, there were no significant correlations between Fatigue and the other two measures in

the Physical Health domain. All six of the Mental Health Neuro-QoL measures were significantly correlated with each other at 3-month follow-up, with magnitudes of association ranging from 0.34 (Cognitive Function and Emotional/Behavioral Dyscontrol) to 0.79 (Depression and Anxiety). At 6-12 months post-SCI, all correlations remained significant except for those between Cognitive Function and Depression (-0.16), Positive Affect & Wellbeing (0.21) and Emotional/Behavioral Dyscontrol (-0.30). Social Health Neuro-QoL measures had a significant positive correlation with each other at 3 months (0.75) and at 6-12 months (0.64).

Unlike I had hypothesized, only small-moderate significant correlations were observed between Physical Health and Social Health Neuro-QoLs across each follow-up timepoint (magnitude of associations between 0.38 and 0.60). Neither the Participation with Social Roles/Activities nor the Satisfaction with Social Roles/Activities measures had a significant correlation with the ADL Neuro-QoL at 3 months post-SCI (r=0.28 & 0.29, respectively). Overall QoL – measured by the ISCI-QoL – showed moderately significant correlations with Fatigue (r=-0.48 and -0.52), Anxiety (r=-0.52 and -0.50), Depression (r=-0.60 and -0.58), Positive Affect & Wellbeing (r=0.67 and 0.49), Cognitive Function (r=0.44 and 0.38), Stigma (r=-0.49 and -0.51), and Satisfaction with Social Roles/Activities (r=0.68 and 0.61) at each follow-up timepoint, respectively. The only measure that did not show a significant correlation with overall QoL in either timepoint was the ADL Neuro-QoL (r=0.10 and r=0.20, respectively).

Table 4.4 *Pairwise Pearson r correlation matrix of Neuro-QoL and ISCI-QoL measures within two follow-up timepoints*

		1	2	3	4	5	6	7	8	9	10	11	12	6-12 Months
Physical Health-Related QoL	1. NQ-ADL	1.00	**0.79**	-0.08	-0.06	-0.06	0.05	-0.06	0.18	-0.20	**0.60**	**0.48**	0.20	1. NQ-ADL
	2. NQ-MOB	**0.55**	1.00	-0.25	-0.20	-0.27	0.21	-0.20	0.29	-0.37	**0.54**	**0.57**	**0.41**	2. NQ-MOB
	3. NQ-FTG	0.10	-0.03	1.00	**0.74**	**0.64**	**-0.52**	**0.58**	-0.37	**0.60**	-0.38	**-0.58**	**-0.52**	3. NQ-FTG
Mental Health-Related QoL	4. NQ-ANX	0.03	-0.13	**0.68**	1.00	**0.76**	**-0.52**	**0.72**	**-0.36**	**0.60**	-0.28	**-0.52**	**-0.50**	4. NQ-ANX
	5. NQ-DEP	0.11	-0.14	**0.72**	**0.79**	1.00	**-0.58**	**0.58**	-0.16	**0.61**	-0.25	**-0.52**	**-0.58**	5. NQ-DEP
	6. NQ-PWB	0.06	0.13	**-0.59**	**-0.61**	**-0.71**	1.00	**-0.44**	0.21	**-0.48**	0.33	**0.53**	**0.49**	6. NQ-PWB
	7. NQ-EBD	-0.03	-0.12	**0.45**	**0.53**	**0.49**	**-0.39**	1.00	-0.30	**0.56**	-0.37	**-0.46**	**-0.38**	7. NQ-EBD
	8. NQ-COG	-0.01	0.08	**-0.54**	**-0.50**	**-0.51**	**0.58**	**-0.34**	1.00	-0.25	**0.35**	0.26	**0.38**	8. NQ-COG
	9. NQ-SGM	0.05	-0.26	**0.55**	**0.60**	**0.65**	**-0.47**	**0.45**	**-0.42**	1.00	-0.36	**-0.63**	**-0.51**	9. NQ-SGM
Social Health-Related QoL	10. NQ-PAR	0.28	0.32	**-0.47**	**-0.37**	**-0.38**	**0.44**	-0.16	**0.38**	**-0.38**	1.00	**0.64**	0.28	10. NQ-PAR
	11. NQ-SAT	0.29	**0.40**	**-0.55**	**-0.57**	**-0.59**	**0.59**	-0.32	**0.43**	**-0.51**	**0.75**	1.00	**0.61**	11. NQ-SAT
Overall QoL	12. ISCI-QOL	0.10	0.22	**-0.48**	**-0.52**	**-0.60**	**0.67**	-0.26	**0.44**	**-0.49**	**0.47**	**0.68**	1.00	12. ISCI-QOL
3 Months		1	2	3	4	5	6	7	8	9	10	11	12	

Note: Overall QoL measured using ISCI QoL Basic Data Set. Results in yellow measured at 3 months post-SCI. Results in blue measured at 6-12 months post-SCI: N=65-77. Results in blue measured at 6-12 months post-SCI: N=72-82. Values with boldface type are significant with Bonferroni corrected $p < 0.003$.

Table 4.5 *Univariate associations of Physical Health Neuro-QoL with baseline injury severity and concurrent SCIM-III scores*

Timepoint	Measure		NQ-ADL				NQ-MOB				NQ-FTG		
		N	Coef.	95% CI	R^2	N	Coef.	95% CI	R^2	N	Coef.	95% CI	R^2
Baseline	AIS Complete[1]	75	-7.62	(-13.59, -1.65)	**0.08**	74	-14.42	(-19.95, -8.90)	**0.27**	69	-0.91	(-6.17, 4.35)	0.00
	Cervical SCI[2]	79	-6.01	(-12.57, 0.56)	0.04	78	4.35	(-2.55, 11.27)	0.02	73	-2.10	(-7.44, 3.24)	0.00
	UEMS	69	0.37	(0.27, 0.47)	*0.44*	68	0.29	(0.16, 0.41)	*0.24*	64	0.02	(-0.09, 0.14)	0.00
	LEMS	67	0.20	(0.10, 0.30)	*0.19*	66	0.27	(0.18, 0.37)	*0.32*	62	-0.01	(-0.11, 15.72)	0.00
6-12 Month Follow-up	SCIM-III Total	81	0.30	(1.10, 1.44)	*0.65*	80	0.33	(0.29, 0.37)	*0.76*	75	-0.03	(-0.10, 0.04)	0.01
	SCIM-SC	81	1.27	(0.06, 0.17)	*0.73*	80	1.26	(1.06, 1.46)	*0.67*	75	-0.18	(-0.46, 0.09)	0.02
	SCIM-MOB	81	0.55	(0.44, 0.65)	*0.56*	80	0.67	(0.58, 0.75)	*0.77*	75	-0.10	(-0.23, 26.29)	0.03

[1] AIS complete (Grade A) *vs.* AIS incomplete (Grades B-E)

[2] Cervical level of injury *vs.* thoraco-lumbar level of injury

Note: Baseline measures are from latest motor-sensory exam prior to discharge from acute hospitalization. UEMS = upper extremity motor score; LEMS = lower extremity motor score. Boldface type indicates significance at p<0.05. Boldface type with italics indicates significance at p<0.001.

Findings for Specific Aim 2

Aim 2 was to explore the relationship between objective measures of injury severity and functional independence with subjective measures of physical health-related QoL in a traumatic SCI sample population during the first year following injury. See Table 4.5 for univariate associations of baseline injury severity measures and SCIM-III scores with Physical Health Neuro-QoL measures. Our hypothesis was correct in that there were moderate-to-strong significant associations between the ADL and Mobility Neuro-QoLs and the SCIM-III scores (r=0.75 to 0.88). The most variance in the ADL Neuro-QoL was explained by the SCI-III Selfcare sub-score (R^2=0.73), and the most variance in the Mobility Neuro-QoL was explained by the SCIM-III Mobility sub-score (R^2=0.77). There were only weak-to-moderate associations between the ADL and Mobility Neuro-QoLs and baseline injury severity measures (r=0.28 to 0.66). Incongruent with our hypothesis, there were no significant relationships observed between the Fatigue Neuro-QoL and any of the injury severity or SCIM-III measures.

Findings for Specific Aim 3

Aim 3 was to explore how well overall QoL – as measured by the International Spinal Cord Injury QoL Basic Dataset (ISCI QoL) – is predicted by baseline injury severity measures, functional independence, and physical health-related QoL at 6-12 months post-SCI. See Table 4.6 for univariate associations of baseline injury severity measures and SCIM-III scores with ISCI-QoL at 6-12 months post-SCI. As hypothesized, there were no significant associations between baseline injury severity measures and overall QoL. While I had hypothesized that there would be moderate-strong associations between SCIM-III scores and ISCI-QoL, there were no significant associations found. Table 4.7 displays univariate associations between the Neuro-QoL measures with overall QoL (ISCI-QoL). I hypothesized that all 11 Neuro-QoLs would be

strongly associated with the overall QoL, however, the ADL Neuro-QoL showed no significant association. Of the 10 Neuro-QoLs that were found to be significantly associated with overall QoL, variance explained ranged from 8% (Participation in Social Roles/Activities) to 37% (Satisfaction with Social Roles/Activities).

Table 4.6 *Univariate associations of ISCI-QoL with baseline injury severity and concurrent SCIM-III scores at 6-12 months post-SCI*

Timepoint	Measure	N	Coef.	SE	95% CI	R^2	p-value
Baseline	AIS Complete[1]	73	0.67	2.48	(-4.27, 5.61)	0.00	0.789
	Cervical SCI[2]	77	-1.98	2.50	(-6.97, 3.00)	0.01	0.430
	UEMS	67	0.06	0.06	(-0.06, 0.18)	0.02	0.321
	LEMS	65	0.06	0.05	(-0.03, 0.15)	0.03	0.207
6-12 Month Follow-up	SCIM Total	79	0.04	0.03	(-0.02, 0.11)	0.02	0.189
	SCIM Selfcare	79	0.21	0.13	(-0.05, 0.47)	0.03	0.116
	SCIM Mobility	79	0.09	0.07	(-0.04, 0.22)	0.02	0.180

[1] AIS complete (Grade A) vs. AIS incomplete (Grades B-E)
[2] Cervical vs. thoraco-lumbar level of injury
Note: Baseline measures are from latest motor-sensory exam prior to discharge from acute hospitalization. UEMS = upper extremity motor score; LEMS = lower extremity motor score.

Table 4.7 *Univariate associations of ISCI-QoL with Neuro-QoL short form questionnaires at 6-12 months post-SCI*

Neuro-QoL Domain	Measure	N	Coef.	SE	95% CI	R^2	p-value
Physical Health	ADL	77	0.16	0.09	(0.02, 0.34)	0.04	0.075
	MOB	76	0.29	0.08	(0.14, 0.44)	0.17	**<0.001**
	FTG	74	-0.44	0.09	(-0.61, -0.27)	0.27	**<0.001**
Mental Health	ANX	74	-0.46	0.09	(-0.64, -0.27)	0.25	**<0.001**
	DEP	74	-0.64	0.11	(-0.85, -0.43)	0.34	**<0.001**
	PWB	71	0.43	0.09	(0.25, 0.61)	0.24	**<0.001**
	EBD	74	-0.38	0.11	(-0.60, -0.16)	0.14	**0.001**
	COG	75	0.44	0.13	(0.19, 0.69)	0.14	**0.001**
	SGM	74	-0.49	0.10	(-0.69, -0.29)	0.26	**<0.001**
Social Health	PAR	74	0.23	0.09	(0.05, 0.42)	0.08	**0.015**
	SAT	74	0.49	0.08	(0.34, 0.64)	0.37	**<0.001**

Note: Overall QoL measured using the ISCI QoL Basic Data Set. All measures taken at 6-12 months post-injury. Boldface type indicates significance at p<0.05

Table 4.8 shows multi-variable regression models between overall QoL and each of the Neuro-QoL measurement domains at 6-12 months post-SCI. Due to its insignificance in the univariate model, the ADL Neuro-QoL was excluded as a predictor from the multi-variable model. I had hypothesized that the most amount of variance in overall QoL would be explained by Neuro-QoLs from the Physical Health domain. Unexpectedly, the most amount of variance in overall QoL was explained by the Neuro-QoL Mental Health domain (R^2=0.43), followed by the Social Health domain (R^2=0.38). The model with the Physical Health domain accounted for the least amount of variance in overall QoL (R^2=0.35). All 10 Neuro-QoL measures were included in a backwards stepwise regression model and revealed that the only Neuro-QoL predictors that maintained significance were Depression and Satisfaction with Social Roles/Activities (R^2=0.46).

Table 4.8 *Multi-variable regression models of Neuro-QoL domains predicting ISCI-QoL at 6-12 months post-SCI*

Neuro-QoL	Physical Health Model (N=74)			Mental Health Model (N=71)			Social Health Model (N=74)			Backwards Stepwise Regression (N=74)			
	Coef.	SE	95% CI	Coef.	SE	95% CI	Coef.	SE	95% CI	Coef.	SE	95% CI	p
MOB	**0.20**	**0.07**	**(0.06, 0.33)**										
FTG	**-0.38**	**0.08**	**(-0.55, -0.21)**										
ANX				0.06	0.17	(-0.28, 0.39)							
DEP				**-0.44**	**0.18**	**(-0.80, -0.86)**				**-0.38**	**0.12**	**(-0.62, -0.15)**	**0.002**
PWB				0.16	0.10	(-0.04, 0.37)							
EBD				0.08	0.14	(-0.21, 0.37)							
COG				0.22	0.12	(-0.03, 0.47)							
SGM				-0.21	0.13	(-0.46, 0.46)							
PAR							-0.13	0.10	(-0.33, 0.67)				
SAT							**0.56**	**0.10**	**(0.37, 0.76)**	**0.34**	**0.09**	**(0.17, 0.51)**	**<0.001**
R^2	0.35			0.43			0.38			0.46			

Note: All measures taken at 6-12 months post-injury. NQ-ADL excluded due to insignificance in univariate analysis. Boldface type indicates significance at p<0.05. Backwards stepwise regression includes all 10 Neuro-QoL measures.

Chapter 5: Discussion

Summary and Discussion of Findings

There were meaningful relationships noted in the univariate comparisons at 6-12 months post-SCI. While Neuro-QoL Fatigue is considered a QoL measure within the Physical Health domain, no significant relationships were found between this measure and the other Physical Health measures. Surprisingly, Fatigue was found to be significantly correlated with all other measures in the Mental Health and Social Health domains. Further analysis with factor comparisons may yield important information on whether Fatigue is appropriately placed within this Neuro-QoL measurement domain. Neuro-QoL measures in the Mental Health domain showed the lowest test-retest reliability; the strongest pairwise correlations across all domains were found among the Mental Health Neuro-QoLs at 3-months post-SCI, but these correlations became less strong and even insignificant in the second follow-up timepoint (6-12 months post-SCI). This could suggest that mental and emotional well-being during the first year following SCI is dynamic over time.

Variable associations with overall QoL at 6-12 months post-injury yielded the most interesting findings in this study. I was surprised to note that baseline injury severity and SCIM-III functional independence measures were not predictive of overall QoL at 6-12 months. Additionally, the only Neuro-QoL measure that was not predictive of overall QoL at 6-12 months was the ADL Neuro-QoL from the Physical Function domain. While the other Physical Function Neuro-QoL measures – Mobility and Fatigue – were strong univariate predictors of overall QoL, these relationships lost significance when placed in a multi-variable model of all Neuro-QoL measures. Depression and Satisfaction with Social Roles/Activities were the only two Neuro-QoLs that maintained significance among all other predictors. This could perhaps be an indication that

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constructs of mental and social well-being are more important factors of overall QoL during the early recovery phase following traumatic SCI.

There is enough evidence to suggest that function is a likely predictor of overall QoL, yet it is possible that there are more important factors to consider throughout the process of neurorehabilitation. Multiple studies have found a significant relationship between depression and QoL early in the recovery trajectory following SCI [55, 57, 59]. Our original research also confirms that depression is an important factor throughout neurorehabilitation, possibly even more so than physical and social function. Other studies have suggested participation as a mediator between function and QoL in early SCI recovery [22, 57, 59, 76]. While our study did not find participation to be significant within a multi-variable model, there were significant univariate relationships observed between participation and both physical function and overall QoL. Further analysis into the function-participation-QoL relationships during early SCI recovery may reveal important considerations for neurorehabilitation treatment models. With additional research on early recovery QoL, we may find that a greater and earlier focus on mental well-being after SCI leads to improved overall QoL.

Study Strengths and Limitations

There are multiple reasons for why this original research provides a vital contribution to the body of literature on SCI outcomes. QoL and function have been studied in persons with chronic SCI for decades; this dissertation offers a unique lens into various facets of QoL during early functional recovery. Following acute hospitalization, rehabilitation marks a critical time when providers have the greatest potential to influence a patient's well-being and assist them in setting the stage for life after injury. The findings of this study provide groundbreaking insight into the early influence of mental health factors, such as depression, on overall QoL in adults with a new

traumatic SCI. This novel research is further strengthened by the prospective multi-center design, the longitudinal data collection across all phases of care, and the extensive battery of outcome data provided by the TRACK-SCI study. This is the first study to report on validity and reliability statistics for Neuro-QoL short forms exclusively in the SCI population during the first year post-injury. Additionally, no study to date has analyzed 11 short form questionnaires from the Neuro-QoL Measurement System alongside time-matched measures of functional independence and overall QoL in the SCI population. Finally, the sample size of this dissertation research (N=114) is well above the median sample size for observational studies in the traumatic SCI population.

While this original research from the TRACK-SCI study offers a unique exploration into early recovery QoL after SCI, it is important to note a few study characteristics before findings can be generalized. First, there was a high lost to follow-up rate observed in our sample population. I anticipated this due to the understandable burden of enrolling in a research study in the setting of a catastrophic injury, and I found our study attrition to be consistent with previous observational studies exploring early recovery after traumatic SCI [77, 78]. While it is possible that a detailed analysis into missingness could reveal between-subject trends across those lost to follow-up, I would like to note that the last one-third of the study period took place during the COVID-19 pandemic when all clinical research activities were suspended. Second, our sample population was older than what is typically found in studies of this kind; there was a left-skewed age distribution (mean age of 53 years and max age of 90 years) with almost one-third (27.2%) being retired at the time of injury and one-half (50.0%) obtaining an SCI from a fall. This limitation could also serve as a strength in that it mirrors the observed trend toward an aging population and increasing number of fall-related SCIs in older adults [1]. Finally, in 9 out of the 11 Neuro-QoL questionnaire

distributions, there were significant skewing and floor/ceiling effects noted in the direction of better health.

Directions for Future Research

      Conceptual Modeling. Advanced statistics like structural equation modeling and latent factor analysis can provide a more rigorous approach to exploring dependencies among components of recovery after SCI. For example, Rivers et al. (2018) used path analysis to model the complex interactions among SCI-related medical comorbidities, function, health-related QoL, and life satisfaction [60]. Their proposed conceptual model resulted in five layers that were nearly identical to the five outcome classifications previously identified in the HRQoL model (see Figure 3.1). These advanced statistics not only build and support conceptual models, but they can also provide a template for future providers on how to better optimize QoL in early recovery after SCI. Unfortunately, these advanced statistical approaches were not appropriate for this dissertation study due to the fact that they require larger sample sizes to yield stable results. As the ongoing TRACK-SCI study continues to enroll participants, I look forward to the increasing feasibility of these methodologies in our future analyses.

      Patient-Reported Outcome Measures. Future inquiry into QoL early on in SCI rehabilitation will continue to expose elemental relationships that exist throughout the period of recovery when the most change occurs. I believe that this can best be addressed in two ways. First, future studies should prioritize the use of outcome measures that are specific to the SCI or neurological populations. Second, there needs to be a greater emphasis on the importance of collecting patient-reported outcomes and subjective QoL alongside objective measures of recovery. Previous research has incorrectly focused on the limitations of using subjective data in outcomes research, such as the difficulty in detecting meaningful health changes and the tendency

toward inflated self-reports of health status [79, 80]. I purport that patient-reported outcome measures, like the Neuro-QoL Measurement System, offer a unique lens into the patient experience that is necessary for identifying barriers to optimal health and recovery. Normalizing the use of these subjective measures will encourage providers to treat the whole patient rather than solely the disease states existing within a patient.

      Nursing Considerations. Currently, the majority of outcomes research in SCI is published in neurosurgery, physical therapy, occupational therapy, and physiatry journals. Perhaps one reason why there remains to be confusion about early determinants of QoL in SCI is because studies coming from the nursing perspective are relatively nonexistent. The nursing profession is rooted in the practice of assessing, guiding, and evaluating recovery as it relates to the subjective burden of illness and injury. According to nursing theorists Plummer et al. (2009), QoL in many ways is synonymous with health; both QoL and health include subjectivity and represent the overall experience of living with disease or injury [81]. Nurses are specially trained to consider holistic approaches to treatment goals and to prioritize theory-based care. Continued use of the HRQoL model as a framework in SCI research is one way to assist in the conceptualization of QoL throughout the dynamic process of functional recovery. As future research narrows the link between function and QoL during early recovery after SCI, patient-centered nursing perspectives can especially be of great use to the field.

Appendix

Table A.1 *TRACK-SCI study measures and CDEs*

Demographic & clinical	NINDS CDE General Core, version 1.0
	NINDS CDE Demographics, version 1.0
Health history	NINDS CDE Medical History, version 1.0
	NINDS CDE Prior and Concomitant Medications, version 1.0
	NINDS CDE Family History, version 1.0
	NINDS CDE Alcohol and Tobacco Use, version 1.0
	NINDS CDE Substance Use, version 1.0
Injury-related events	NINDS CDE Pre-Hospital Assessment, version 1.0
	NINDS CDE History of Injury, version 1.0
Assessments & examinations	NINDS CDE Acute Admission/Discharge, version 1.0
	NINDS CDE Rehabilitation Admission/Discharge, version 1.0
	NINDS CDE Clinical Assessment, version 1.0
	ASIA ISNCSCI Motor and Sensory Examination
	Clinical ZSFGH Muscle Strength Exams
Radiological imaging	3-T MRI
	NINDS CDE Magnetic Resonance Imaging, version 1.0
	NINDS CDE Diffusion Tensor Imaging, version 1.0
	CT
Outcomes & endpoints°	NINDS CDE Rehabilitation Therapies, version 1.0
	NINDS CDE Injury Spinal Intervention and Spinal Procedures Basic Data Set, version 1.0
	ISCoS ISCI Lower Urinary Tract Function Basic Data Set, version 1.0
	ISCoS ISCI Urinary Tract Infection Basic Data Set, version 1.0
	ISCoS ISCI Urodynamic Basic Data Set, version 1.0
	ISCoS ISCI Bowel Function Basic Data Set, version 1.1
	ISCoS ISCI Sexual Function Basic Data Set, version 1.0
	ISCoS ISCI Cardiovascular Basic Data Set, version 1.0
	NINDS CDE Upper Extremity Function (Fine Motor, ADL): Neuro-QoL SF, version 1.0
	ISCoS ISCI Upper Extremity Basic Data Set, version 1.1
	NINDS CDE Lower Extremity Function (Mobility): Neuro-QoL SF, version 1.0
	NINDS CDE Spinal Cord Independence Measure, version 3.0
	ISCoS ISCI Autonomic Dysfunction Following SCI (ADFSCI)
	ISCoS ISCI Quality of Life Basic Data Set, version 1.0
	NINDS CDE Cognitive Function: Neuro-QoL SF, version 2.0
	NINDS CDE Ability to Participate in Social Roles & Activities: Neuro-QoL SF, version 1.0
	NINDS CDE Satisfaction with Social Roles and Activities: Neuro-QoL SF, version 1.1
	NINDS CDE Anxiety: Neuro-QoL SF, version 1.0
	NINDS CDE Depression: Neuro-QoL SF, version 1.0
	NINDS CDE Emotional and Behavioral Dysfunction: Neuro-QoL SF, version 1.0
	NINDS CDE Positive Affect and Well-being: Neuro-QoL SF, version 1.0
	NINDS CDE Fatigue: Neuro-QoL SF, version 1.0
	NINDS CDE Stigma: Neuro-QoL SF, version 1.0
	Douleur Neuropathique 4
	Location of Pain & Pain Medication Questionnaire
	NINDS CDE Pain Quality and Intensity Questionnaire

° Outcome measurements collected at 3-, 6-, and 12-months
Note: NINDS = National Institute of Neurological Disorder and Stroke; CDE = Common Data Elements; ISCoS = International Spinal Cord Society; ISCI = International Spinal Cord Injury; SF = short form

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