The Effect of Robotic Walking and Activity-based Rehabilitation on Functional Capacity, Secondary Complications & Psychological Well-being in Individuals with Spinal Cord Injury (SCI)

BY

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DECLARATION

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LIST OF ABBREVIATIONS

SCI – Spinal Cord Injury

RCT – Randomized Control Trial

FDA – Food and Drug Administration

Qol – Quality of Life

ADL – Activity of Daily Living

MVA – Motor Vehicle Accident

ISNCSCI – International Standards for Neurological Classification of SCI

ASIA – American Spinal Cord Injury Association

TSI – Time Since Injury

LOI – Level of Injury

MRI – Magnetic Resonance Imaging Study

DXA – Dual Energy X-Ray Absorptiometry

BWSTT – Body-Weight-Supported Treadmill Training

RLT – Robotic Locomotor Training

ABT – Activity-Based Training

FES – Functional Electrical Stimulation

BDI – Beck Depression Inventory

STAI – State-Trait Anxiety Inventory

RPE – Rating of Perceived Exertion

MVC – Maximum Voluntary Contraction

DOMS – Delayed-Onset-Muscle-Soreness

BMD – Bone Mineral Density

FFSTM – Fat-Free Soft Tissue Mass

FM – Fat Mass

SAT – Subcutaneous Adipose Tissue

VAT – Visceral Adipose Tissue

FN – Femoral Neck

LEMS – Lower Extremity Motor Score

UEMS – Upper Extremity Motor Score

6MWT – 6-Meter Walk Test

10MWT – 10-Meter Walk Test

TUG – Timed-Up-and-Go Test

6MAT – 6-Minute Arm Ergometry Test

SCI-FAI – Spinal Cord Injury Functional Ambulatory Inventory

95% CI – 95% Confidence Interval

SD – Standard Deviation

ES – Effect Size

OR – Odds Ratio

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DISSERTATION ABSTRACT

Activity-based training (ABT) represents the current standard of care in neurological rehabilitation centers around the world. However, innovative rehabilitation techniques have been developed including robotic locomotor training (RLT). The conceptual basis for RLT initially appeared promising; a rehabilitation modality that removes the need for intensive assistance from therapists, whilst facilitating safe and effective over-ground ambulation. However, small sample sizes and a lack of homogeneity across studies have resulted in an underpowered evidence base supporting the efficacy of RLT for SCI rehabilitation. Thus, this randomized control pilot study aimed to investigate the effects of RLT compared to ABT on functional capacity, secondary complications, and psychological well-being in people with SCI after 24-weeks of rehabilitation.

Participants with chronic, traumatic motor incomplete SCI were randomized into two intervention groups: RLT (n = 8) and ABT (n = 8) groups. RLT involved solely walking in the Ekso bionic suit. ABT involved a variety of resistance, cardiovascular and flexibility training combined with regular weight-bearing in the standing position. Outcome measures, including functional strength, ambulatory function, pain, spasticity, bladder/bowel, bone density, body composition, quality of life (QoL) and depression were tested at baseline, 6, 12 and 24-weeks of the intervention.

There were no significant differences between the intervention groups for lower or upper extremity motor scores (UEMS effect size (ES) = 0.30; LEMS ES = 0.07), back strength (ES = 0.14) and abdominal strength (ES = 0.13) after training. However, both groups showed a significant increase of 2.00 points in UEMS and a significant increase in abdominal strength from pre- to post intervention. Only the RLT group showed a significant change in LEMS, with a mean increase of 3.00 [0.00; 16.5] points over time. Distance walked in the Functional Ambulatory Inventory (SCI-FAI) increased significantly ($p = 0.02$) over time only for the RLT group. Therefore, the RLT showed promising evidence for potentially inducing functional strength changes and improvements in ambulatory function after 24 weeks of training. There was some evidence to support RLT to induce bowel improvements in individuals with SCI and both interventions appeared to reduce urinary incontinence and improve bladder function ($p = 0.04$). Total spasticity and pain intensity were similar between groups ($p = 0.25$; $p = 0.96$). However, pain interference ratings significantly increased from pre-post intervention for both groups ($p = 0.05$). RLT prevented the progressive decline of bone mineral density usually occurring in the SCI population, as hip BMD was maintained during RLT; however, it was significantly reduced ($p = 0.04$) during ABT, with a mean reduction of 0.06 [-0.34, 0.22] g/cm^2 (5%) from pre to post intervention. No change in leg fat-free soft tissue mass (FFSTM) occurred between groups or over time

($p = 0.32$), however, there was a significant 7% increase in arm FFSTM over time for both groups ($p < 0.01$). The ABT group was more effective (ES = 1.02) in reducing central and peripheral adiposity, with a significant decrease in visceral adipose tissue (VAT) ($p = 0.04$) and gynoid FM ($p = 0.01$) over time. Both groups reported increased QoL and decreased depression ratings over time, with the RLT group having a significant change in the general life and physical health domains, $p = 0.03$, respectively.

This pilot trial offers promising evidence for the effectiveness of RLT for improving functional and ambulatory capacity, reducing secondary complications, and potentially improving QoL in people with incomplete SCI. Thus, this dissertation adds substantial weight to the lacking evidence base on the effects of RLT, by incorporating a large homogenous sample, comprehensive testing procedures and an extended intervention period within South Africa.

CHAPTER 1

Setting the scene for rehabilitation for individuals with spinal cord injury: A South African context

Certain components of the present chapter have been published in the *Journal of Rehabilitation Medicine* (2019) – DOI: 10.2340/16501977-2601.

1.1 Spinal cord injury

Spinal cord injury (SCI) is a devastating and life-altering condition which occurs as a result of incision, compression, contusion or ischemia of the spinal cord from the level of the foramen magnum to the cauda equina (1). SCI results in disturbances in signal conduction across and below the point of lesion, which consequently may lead to disrupted sensory, motor, and autonomic function and ultimately impacts an individual's physical, psychological, and social well-being (1,2). Aetiology of SCI can be classified as either traumatic or non-traumatic (1). Common traumatic causes include motor vehicle accidents, falls, sporting accidents and violence (3). Causes of non-traumatic injuries are extensive and include metabolic disorders, vascular diseases, neoplasia, inflammatory and autoimmune diseases, toxins, radiation, infection, motor neurone disease and syringomyelia (4).

1.2 SCI epidemiology

There is no reliable estimate of global SCI prevalence, as only a handful of high-income countries can provide national statistics, and data sources are so few and so methodologically varied that it is not possible to calculate reliable estimates (5). However, WHO (2020) estimates the annual global incidence at 40 to 80 cases per million population. Up to 90% of these cases are due to traumatic causes, though the proportion of non-traumatic appears to be growing (6). In South Africa, epidemiological data on SCI are also scarce, partly owing to the lack of a national registry and a coordinated system of care (3). However, a study by Joseph et al. (2015) provided the first population estimates of the incidence of traumatic SCI in South Africa, reporting a staggering rate of 75.6 per million persons, compared to the average global incidence rates estimated at 23 per million (7). Therefore, the SCI

incidence rates in South Africa have been reported as more than double those in developed nations (3). The main cause of SCI in South Africa was found to be interpersonal violence, which accounted for approximately 60% of all cases, followed by transport-related causes (26%) and falls (12%) (7) . In a recent study by Miseer and colleagues (2019) in which they considered the clinical profile of spinal pathology presenting to the Tygerberg Hospital Spinal Unit in South Africa, car accidents were the primary cause of traumatic injury, accounting for 48% of spinal trauma, with falls contributing a further 26% (8). Incidence of SCI varies depending on age, gender, region and occupation (6). In South Africa, men account for 85.5% of SCI reports, with the highest prevalence between 15-29 years of age (9,10).

1.3 SCI classification

The extent and severity of sensory, motor and/or autonomic loss from SCI depends not only on the level of injury to the spinal cord, but also on whether the lesion is "complete" or "incomplete" (5). According to the International Standards for Neurological Classification of SCI (ISNCSCI), a SCI is considered complete (AIS A) if there is no evidence of sensory or motor function in the sacral segments. This assessment is based on manual testing of deep anal pressure and voluntary contraction of the anal sphincter. While some sensory and or motor function is preserved below the level of injury in incomplete SCI (AIS B, C, D), including the lowest sacral segments S4-S5, it is no less serious and can still result in severe impairments (11). The ISNCSCI includes a motor exam (strength assessment of 10 key muscles), and sensory exam (light touch and pin prick testing of key points) to determine neurological level of injury and defines the level of injury as the lowest intact segment where the associated key muscle is graded a three (antigravity) or better (11,12). In general, the higher up the spinal cord the lesion occurs, the more extensive the range of impairments will be (5) (Table 1.1). Cervical SCI (C1-C8) commonly causes sensory and motor loss in the arms, body and legs, a condition called tetraplegia (the alternative term quadriplegia is now less used). SCIs are most common in the cervical region, with the C5 level being the most prevalent, as this segment of the spine is most susceptible to injury based on its anatomy and flexibility (11). In the population-based study of SCI in Cape Town, South Africa, by Joseph et al. (2015), of the 141 cases studied, injuries to the cervical area were the most common (53.1%) (13). Of these cervical injuries, 71.4% were incomplete, classified B,

C or D on the American Spinal Cord Injury Association (ASIA) Impairment Scale (AIS). Thus, the most common type of SCI in Cape Town is motor/sensory incomplete tetraplegia, which mimics the current global trends for SCI.

Table 1.1: Potential expected functional outcomes for individuals with complete cervical spinal cord injury.

	Function										
	Feeding	*Grooming*	*Upper limb dressing*	*Lower limb dressing*	*Bathing*	*Bed mobility*	*Weight shifts*	*Transfers*	*Wheelchair propulsion*	*Driving*	*Bladder & bowel*
C3-C4	Adapted equipment support	Dependent	Dependent	Dependent	Dependent	Dependent	Dependent	Dependent	Dependent unless powered chair	Unable	Dependent
C5	Independent with equipment after set-up	Independent with equipment after set-up	Requires assistance	Dependent	Dependent	Requires assistance	Requires assistance	Requires assistance	Short distances in manual chair with lugs or plastic rims on level surfaces	Unable	Dependent
C6	Independent with equipment	Independent with equipment	Independent	Requires assistance	Independent with equipment	Independent with equipment	Independent	Possibly independent with transfer board	Independent with manual chair on level surfaces with plastic rims	Adapted car	Independent with bowel; assistance for bladder
C7	Independent	Independent with equipment	Independent	Independent with equipment	Independent	Independent	Independent	Independent (except for floor transfers)	Independent (except curbs)	Adapted car	Independent
C8-T1	Independent	Independent	Independent	Independent	Independent	Independent	Independent	Independent	Independent	Independent	Independent

Adapted from Kirshblum S, Gonzalez, P Nieves, J et al. Spinal cord injuries (SCI). In: Cuccurullo SJ, ed. Physical medicine and rehabilitation board review. New York: Demos, 2004.

1.4 Economic impact of SCI

The management of SCI requires significant health care resources and can place a substantial financial burden on individuals, their families, and the community (2). Costs are largely due to a need for high-level acute care in the short-term and additional long-term costs related to medical equipment, consumable supplies, rehabilitation, special transport needs, personal assistance and home and vehicle adaptations (2,14,15). The main medical expenses stem from secondary complications associated with SCI, which are extensive including; neurogenic bladder, pressure ulcers, urinary tract infections, osteoporosis, pulmonary and cardiovascular complications (1,16,17). Thus, there is a substantial financial burden due to the expensive and prolonged treatment required owing to the person's lifelong dependence on medical care (18), accounting for costs ranging from $368,562 to $1,129,302 in the first year and $44,766 to $196,107 in further annual health care costs depending on the severity of injury (19). According to the Christopher and Dana Reeve Foundation, average medical expenses for paraplegia range from $518,000 per person, while in Canada, the lifetime economic burden is estimated to range from $1.5 to $3.0 million per individual with SCI (20). The Christopher and Dana Reeve Foundation report the average expenses as follows: for the 1st year, people with high tetraplegia can expect to pay about a $1 million for care. Low tetraplegia produces about $769,000 in medical expenses, while paraplegia costs about $518,000 (20). Injuries that produce incomplete motor function at any level cost an average of $347,000. Not only do the economic consequences of SCI include the direct costs of care, but also, the indirect costs resulting from loss of future productivity and wages, as many are unable to return to work (14).

Rehabilitation can ease this financial burden by decreasing the number of required hospitalizations and preventing secondary conditions associated with a SCI (15). Secondary complications are extensive in individuals with SCI, including neurogenic bladder and bowel, bone mineral density decline and fractures, pain, spasticity, autonomic dysfunction as well as psychological disorders (1,16). These secondary health complications are a frequent cause of morbidity and mortality for individuals with SCI and can lead to increased rates of rehospitalization and economic burden on individuals and hospitals

(16,21). Therefore, health systems need to be ready to respond to the numerous challenges following a SCI by providing access to specialized and comprehensive health services, including physical rehabilitation (22,23).

However, access to rehabilitation for people with disabilities remains problematic in South Africa (24). People with disabilities have unequal access to healthcare services, experience poorer levels of health and have more unmet health and rehabilitation needs compared to people without disabilities (25,26). South African community-based study by Maart and Jelsma (2014) found the proportion of unmet needs for services were as follows: 54% for home-based care; 34.5% for assistive devices; 28.9% for medical rehabilitation services; and 2.5% for health services (27). It has been documented that South Africans experience problems with accessing health and rehabilitative services due to inadequate finances (71%) and transport problems (72%) (7). Thus poorer people have an increased risk of injuries, and are most affected by the financial pressure resulting from injuries (15). Within South Africa, poverty is still a major problem and affects a large majority of the population and hence, access to health care is challenging for many. Due to widespread poverty, most people are dependent on social grants such as a disability grant. However, the maximum amount that can be claimed is R1 860 per month, which is considerably less than the average minimum wage of R 3 500 per month for 40-hour work week (28). Furthermore, this small amount often must support a whole family. Thus, the relationship between poverty and disability care calls for economic development as well as better allocation of resources in a resource-limited environment such as South Africa (18). Understanding the financial constraints to receiving adequate rehabilitation and treatment is essential to enhance the opportunities and quality of life (QoL) for those with disabilities in South Africa.

1.5 Physiological and psychological impact of SCI

Aside from the substantial economic burden of SCI, the other impacts that the injury has on an individual's life can be grouped under primary neurological effects and secondary health complications (1). The primary neurological effects of SCI include loss of sensory or motor control of the lower limbs, trunk and the upper limbs, as well as loss of autonomic regulation of the body (5). These changes can

lead to serious disability by impacting upon physical functioning and independence (1). Thus, people with SCI can experience a range of activity limitations and participation restrictions in areas such as mobility, self-care activities, education, employment, maintenance of social relationships, and participation in leisure activities (29). Individuals with SCI may face a transition regarding their roles as members of their households and participants in their communities (30). In addition to the motor-sensory loss, SCI affects the autonomic neurologic function of the body, resulting in multiple impairments which can affect breathing, heart rate, blood pressure, temperature control, and sexual function (5). Additional secondary health complications are extensive in individuals with SCI and include neurogenic bladder and bowel, urinary tract infections, pressure ulcers, orthostatic hypotension, osteoporosis, deep vein thrombosis, pain, spasticity, autonomic dysreflexia, pulmonary and cardiovascular problems (1).

SCI is a health condition that not only affects the individual physically but also has psycho-social consequences, as the overwhelming lifestyle changes that follow a SCI often make it difficult for individuals to adjust emotionally (23,31). Thus, from a psychological perspective, SCI can lead to elevated levels of depression and anxiety, lower QoL, and decreased life satisfaction compared to people without SCI (12,31–33). Overall, SCI is a life-altering and costly condition, with current data showing that SCI is associated with elevated morbidity and mortality rates as well as increased psychological complications, including higher suicide rates (5,34). This mortality risk varies widely by country income status and depends heavily on the availability of quality clinical care and rehabilitation services (5,22). Consequently, the sudden and significant changes brought about by SCI present an individual with numerous challenges including substantial physical, psychological and economic burdens (33,35,36). However, despite these difficulties, many individuals with SCI go on to live full, complete lives.

1.6 SCI rehabilitation modalities

After sustaining a SCI, individuals need to maintain their daily function, prevent secondary complications and maximise their QoL (1). Physical rehabilitation is required to address these goals

through facilitating functional recovery and independence (37,38). Rehabilitation is defined as "a set of measures that assist individuals, who experience or are likely to experience disability, to achieve and maintain optimum functioning in interaction with their environments" (5). Rehabilitation is a progressive, dynamic, goal-oriented process, which enables persons with impairment to reach their optimal mental, physical, cognitive and/or social functional level (39). The rehabilitative management of persons with SCI goes beyond promoting solely functional independence to encouraging participation in daily living in a way that promotes better QoL (30). Thus, rehabilitation is instrumental in enabling people with disability to return to their home or community, live independently, and participate in economic and social life (37). Rehabilitation as a form of medicine is a concept of growing popularity within academic, medical, and policy circles, as regular physical activity can alleviate, as well as prevent, a myriad of existing physical and psychological complications (33). Therefore, rehabilitation can help clinicians to bridge the gap that exists between inpatient treatment and successful community reintegration, by providing support through functional exercises, strength and endurance, altogether fostering independence and an active lifestyle within the individuals' community (39,40).

Functional rehabilitation after SCI involves training the body for the activities performed in daily life by training basic functions, skills and muscular and cardiovascular endurance (39,41). Current rehabilitation strategies are based on the concept of directing central nervous system plasticity facilitated by early, intensive, and task-specific therapies to enhance the natural recovery process of the body (41). These neuroplasticity changes can be defined as adaptations in the sensorimotor systems after the acute stage of SCI (41). After sustaining a SCI, neuroplasticity occurs within the nervous system through either the sprouting of new neurons or a change in conduction of spared neural pathways (42). This plasticity recovery can be facilitated through functional training and is dependent upon injury characteristics, quality of acute care and the type of rehabilitative interventions used (43). In combination with neuroplasticity, the prevention of secondary complications is a fundamental goal of rehabilitation within the SCI population. SCI results in physical deconditioning across the musculoskeletal and cardiovascular systems (1). This physical deconditioning is inevitable to a certain

degree, however with continued physical inactivity, the likelihood of secondary complications increases.

Exercise has been theorized to provide neuroprotective and neuro-regenerative effects in the central nervous system that enhance the performance of several biochemical processes which aid in protein synthesis and cellular survival for neuronal cells (44). In addition, regular weight-bearing in the standing posture also assists in combating the multitude of secondary complications experienced by individuals with SCI (45). Beyond physiological, there are also psychological benefits to upright standing therapy, including improved self-image and eye-to-eye interpersonal contact (45,46). Rehabilitation has been found to be beneficial in reducing length-of-stay in hospitals and decreasing re-admissions, thus mitigating the negative social and health risks associated with prolonged hospitalization. Rehabilitation may also accelerate the ability to return to education or employment and further reduces the costs related to ongoing care (47,48). Physical rehabilitation thus acts as a health promoting activity following SCI, as it has been identified as a means to alleviate or prevent many of the health and psychological well-being complications associated with SCI (35,49,50).

1.6.1 Activity-based Training (ABT)

The current standard of physical activity in neurological rehabilitation centres around the world is known as Activity Based Therapy (ABT) which refers to "interventions that target activation of the neuromuscular system below the level of the lesion, with the goal of retraining the nervous system to recover a specific motor task" (39). This training involves the use of resistance, cardiovascular and flexibility training combined with the traditional fundamental component of regular weight-bearing in the standing posture (45). Traditional equipment facilitates standing through the use of an external structure/standing frame to splint the lower limbs and trunk, allowing an individual to adopt the upright posture of standing against gravity (45) (Fig. 1.1).

Figure 1.1: Equipment used to facilitate standing in the upright position during Activity-based Training.

Images from EasyStand Website and permission granted from the individual for use of the picture.

1.6.2 Robotic Locomotor Training (RLT)

Another technique founded on the principles of neuroplasticity and automaticity has been recently developed, known as locomotor training. The premise of locomotor training is to provide the damaged nervous system with appropriate sensory input to stimulate remaining spinal cord networks to facilitate their continued involvement even when supraspinal input is compromised (51). Originally, body-weight-supported treadmill training (BWSTT), which was introduced in the early 2000's, was utilised as the gait training technique (52). It involves unloading a portion of the individual's weight above a motorized treadmill using a counterweight-harness system, whilst providing manual assistance to guide the individuals limbs into a regular gait cycle (53). BWSTT is an effective form of gait training and may be advantageous in the acute phase of rehabilitation when an individual does not have sufficient upper body strength to support their own bodyweight (52). One difficulty with BWSTT is the labour-intensiveness for therapists who are required to manually facilitate movement in each limb to achieve a reciprocal gait cycle (54,55). A promising development in the field of locomotor training is the introduction of wearable robotic exoskeletons, a technique known as Robotic Locomotor Training

(RLT). RLT includes wearable robotic exoskeletons which are relatively lightweight and small devices that essentially function as an orthosis (54). There are currently several exoskeletons in development and early clinical use, including Ekso^{TM}. Ekso^{TM} is a commercially available bionic suit that enables individuals with lower extremity weakness to stand up and walk with a natural, full weight-bearing, and reciprocal gait (Fig. 1.2). Walking is achieved when the user's weight shifts to activate sensors in the device, initiating steps (56). Battery-powered motors drive the legs, replacing deficient neuromuscular function (57). This approach uses active or passive activation of the neuromuscular system through repetitive functional tasks to promote functional reorganization of the neuromuscular system and "relearning" of walking patterns (58).

Figure 1.2: Overground robotic exoskeleton (Ekso GT) used during Robotic Locomotor Training.

Curtsey of Ekso Bionics Website

Given the improvements in muscle activity and functional ability associated with BWSTT, the expectation of neurorehabilitation with RLT is promising (56,59). Studies of lower extremity robotic exoskeletons have become more extensive and have been shown to be feasible and safe as a rehabilitation technique for people with SCI (56,60,61). Locomotor training is associated with functional improvements in several behaviours and body systems, and can be standardized and

implemented efficiently (58). A literature review shows that locomotor training successfully improves the recovery of stepping and there is evidence that anatomical and physiological changes promoted by training occur in the locomotor circuitry (62). RLT has also been reported to improve the physical capacity and QoL of individuals as well as time spent in the community (59). Evidence suggests that all locomotor training interventions are able to elicit changes, primarily through neuroplasticity, and no single intervention is superior (52).

Despite these potential benefits associated with RLT, using robotic devices has some disadvantages. These devices are very expensive relative to competing rehabilitation technology, with costs ranging from approximately $70 000 to $150 000 (R1 million – R2.3 million) in comparison to a standing frame at roughly $3163 (R48 404) (63). Therefore, the gap between the cost of robotic and conventional therapies is considerable (64). Furthermore, aside from the high initial purchase price, additional expenses of the robotic exoskeletons include the annual maintenance costs and training costs per physical therapist user (63). Robotic devices can also break down and need regular services and they require considerable effort from both the therapist and the individual in order to advance rehabilitation outcomes (58,65). Everything combined, the cost of ownership of a powered robotic exoskeleton adds to roughly $210,000 (R3.2 million) for two years. That is incredibly expensive, especially when you consider that this is an extra cost in addition to all the standard medical expenses such as hospital stays and other rehabilitation services. As most robotic suits are not covered by medical aids and health insurance, these advanced technologies are beyond many people's reach. The high cost of robot devices raises the question of its efficiency in comparison with other training strategies (66). In fact, two reviews of locomotor training have concluded that there is not sufficient evidence to either support or refute its usefulness as an intervention, especially in light of the additional cost above and beyond conventional therapies (67,68). Once there is substantial evidence for improvements in overall health and well-being, perhaps future investments could be placed on developing low-cost system alternatives.

1.7 Problem statement of thesis

Chronic out-patient rehabilitation for people with SCI does not fall within the standard of care in South Africa (69). In South Africa (population = 60 million) there are only 23 rehabilitation facilities, which include 17 spinal rehabilitation units. Most of these facilities are centred in urban and socio-economically advantaged areas, whereas most individuals within South Africa live in rural and socio-economically disadvantaged areas (7). Less than 20% of South Africans have medical aid or health insurance, indicating that more than 80% of the population depends on government funding for public healthcare (13). Only eight spinal rehabilitation units serve this sector, in which all government-funded healthcare SCI individuals receive short-term inpatient care for 10-16 weeks, and if resources allow, are referred to a single public neurological rehabilitation centre in Cape Town (Western Cape Rehabilitation Centre) (13). Collectively, this leads to long waiting lists for inpatient rehabilitation and early discharge from rehabilitation (30). The common occurrence of non-specialized care of SCI survivors in South Africa is alarming, especially as such care has shown to be related to a high mortality rate and the occurrence of preventable secondary complications (22). While life expectancy is beginning to approach that of the general population in developed countries, it is far from equal in developing countries, where morbidity and mortality rates are likely to remain high (5). People with SCI in low-income countries continue to die from preventable secondary conditions that are no longer a leading cause of death in high-income countries (5). Mothabeng (2011) observed that 48% of people with SCI will at some point be re-admitted to hospital for secondary health complications (30). This rehospitalisation occurs soon after discharge and is mainly attributed to people not coping with their injury in their communities, and more specifically with healthy living and maintaining adequate physical activity levels (30,49,70). In a study considering the clinical profile of spinal pathology presenting to the Tygerberg Hospital Spinal Unit in South Africa, a total of 349 individual patients were admitted to the Spine Unit over the one-year study period (8). In addition to the initial admission, 6% of patients required one re-admission and 1% of patients required two re-admissions, amounting to 27 re-admissions in total in that year.

As a consequence of poverty, many people with disabilities in South Africa are likely to live with limited access to appropriate healthcare and rehabilitation services (15). Studies examining living conditions amongst people with disabilities in Southern Africa found that individuals with disabilities and their households are worse off on many important indicators of living conditions, and they often live without optimal technical, medical or social support (71,72). This is illustrated in a study by Eide et al. (2011) which found that only 18% to 36% of individuals with disabilities in South Africa have access to assistive devices and services (72). Access to specialized healthcare services is not only a historic problem in South Africa, but it is further exacerbated by the lack of resources. Local medical facilities experience a high burden of trauma, and as South Africa is a middle-income country, resources are primarily focused on optimising acute care rather than out-patient support structures (73,74).

Therefore, government funded hospitals simply cannot cope with the amount of people requiring rehabilitation services. South Africa certainly can provide high quality inpatient care, but the demand from poor, uninsured communities is overwhelming, and the South African medical systems have to function under financial restraints with an emphasis on primary healthcare. Additionally, there are insufficient rehabilitation facilities, limited human and equipment recourses and a high patient to healthcare worker ratio. There is a need to develop the infrastructure and knowledge in South Africa to adequately provide for the long-term needs of all individuals with SCI; focusing on innovative rehabilitation that is targeted to promote optimal functioning, reduce secondary complications, and improve psychological well-being. This innovative rehabilitation may be costly, however, once efficacy is established, it will serve as a catalyst for the development of low-cost alternatives.

1.8 Lack of evidence-based SCI rehabilitation guidelines

Given that the development and use of powered exoskeletons is relatively new, the current evidence supporting their use and reported benefits has mostly been limited to single-intervention trials with few participants or single case reports (56,60). Thus far, there is no clear evidence for the effectiveness of RLT in terms of daily functional outcomes, such as body functions, health measures and community participation (66). Rehabilitation research on RLT has shown that these seemingly conceptually sound,

well-defined interventions are as likely to be no better, incrementally better, or incrementally worse than similar conventional ABT (75). These strategies, at best, are better than no intervention but not superior in conception, cost, or outcomes to other forms of goal-directed, progressive, and well-dosed therapy (75). Gaps in SCI literature are evident with regards to the lack of homogenous studies with inadequate sample sizes and varying methods, resulting in an underpowered evidence base supporting the efficacy of RLT (61,75,76). Moreover, the evidence available thus far has emerged from a broad spectrum of locomotor training programmes presenting substantial programme attribute variations (e.g., inpatient vs. community-based programmes, length of the programme, frequency and duration of the training sessions, content of the training, trajectory of the progression, assessment times, outcome measures) (77). Invariably, conclusions are that further research is needed to determine the optimal dosage, and the sub-group (injury level, severity, chronicity) that is more likely to benefit from the RLT interventions. It has been suggested that, given the widespread gaps in evidence-based knowledge, the multitude of positive effects associated with RLT are yet to be adequately supported (77,78). This lack of homogeneity is also noted in the many studies that report ABT to be a useful strategy in alleviating the negative health symptoms associated with SCI, in that they use different interventions, methods and outcome measures (35). Recent systematic reviews of rehabilitation interventions after SCI highlight similar issues, including the small number of randomized controlled trials (RCTs), the relatively small sample sizes in these trials, and the sub-optimal quality of clinical trials in this field.

In rehabilitation, the shortage of evidence-based practice has been a major barrier to advancing care for those living with SCI. A comprehensive investigation of all the available evidence is essential to support the clinical application of RLT for rehabilitation after SCI. Consequently, we conducted a systematic review that aimed to critically examine the effectiveness of over-ground powered exoskeletons as a tool for SCI rehabilitation by investigating ambulatory function, secondary health outcomes, including spasticity and pain, and user satisfaction from the current literature (61). Due to the lack of RCTs, analysis therefore included a total of 27 non-randomized, non-comparative, observational studies, representing 308 participants. The average intervention length was 12.1 ± 19.6 weeks and sessions were typically conducted three times per week for 60 minutes per session. Sample sizes ranged from 3 to 44

participants, with males accounting for 78% of the sample and a mean participant age of 40 ± 7 years. Most participants presented with chronic (>1 year) complete spinal cord injuries between T1 and T12 (Table 1.2).

Table 1.2: Baseline participant characteristics and Robotic Locomotor Training design of included studies.

PARTICIPANT CHARACTERISTICS								EXPERIMENTAL PROTOCOL				
Author	**Year**	**Sample size**	**Age (years; SD/range)**	**Sex**	**LOI**	**Injury type (ASIA category)**	**TSI (years)**	**Device**	**Intervention length**	**Total number of sessions**	**Session frequency (per week)**	**Session duration (minutes)**
Asselin et al.(79)	2015	8	46.0 ± 12.0	7 M, 1 F	T1 - T11	Complete (A)	4.6 ± 3.3	ReWalk	12 weeks	37 ± 13	3x	90
Baunsgaard et al.(80)	2018	52	47.0 (32.5–61.8)	36 M, 16 F	C5 - L2	Mixed	25% = < 1 year 75% = 13.7 (7.2–28.5)	Ekso	8 weeks	17 - 24	3x	60
Benson et al.(81)	2016	5	29.2 ± 7.3	5 M	C7 - L1	Mixed: 3A, 2C	3.3 ± 2.3	ReWalk	10 weeks	20	2x	120
Birch et al.(82)	2017	19	40.9 ± 5.8	14 M, 6 F	5(C4 - C8), 15(T1 - L5)	Mixed	8.1 (1- 52)	REX	Single session	1	1x	180
Esquenazi et al.(83)	2012	12	33.6 ± 13.1	8 M, 4 F	T3 - T12	Complete (A)	7.4 ± 7.6	ReWalk	8 weeks	24	3x	90
Evans et al.(84)	2015	5	42.0 ± 9.0	4 M, 1 F	T6 - T12	Complete (A)	11.0 ± 6.0	Indego	2 sessions	5 practice & 2 testing days	2x	30
Fineberg et al.(85)	2013	6	44.1 ± 12.8	5 M, 1 F	T1 - T11	Complete (A)	6.2 ± 4.5	ReWalk	5-6 months	NR	3x	120
Gagnon et al.(86)	2017	14	39.0 ± 10.8	9 M, 5 F	C6 - T10	Mixed	7.9 ± 8 years	Ekso	6 - 8 weeks	18	3x	60
Gagnon et al.(87)	2018	13	38.7 ± 10.9	9 M, 4 F	C6 - T10	Complete (A)	7.4 ± 7.8	Ekso	6 weeks	18	3x	60
Hartigan et al.(88)	2015	16	34.9 (18-51)	13 M, 3 F	C5 - L1	Mixed: 11A, 3B, 2C	NR	Indego	NR	5	NR	90
Karelis et al.(89)	2017	5	60.4 ± 6.1	4 M, 1 F	C7 - T10	Complete (A)	7.6 ± 4.6	Ekso	6 weeks	18	3x	60
Kolakowsky-Hayner et al.(54)	2013	7	29.8 ± 6.8	5 M, 1 F	T4 - T12	Complete (A)	< 1 year	Ekso	6 weeks	6	1x	60
Koyama et al.(90)	2016	5	46.2 ± 14.6	4 M, 1 F	T6 - T12	Complete (A)	11.2 ± 4.5	WPAL	2 years	NR	NR	90
Kozlowski et al.(91)	2015	7	36.0 (16-60)	7 M	C4 - T10	Mixed: 3A, 1B, 3C	< 1 year	Ekso	24 weeks	20 - 24	1x	120
Kressler et al.(92)	2014	3	30.3 ± 6.6	2 M, 1 F	T1 - T10	Complete(A)	> 1 year	Ekso	6 weeks	18	3x	60
Lonini et al.(93)	2016	4	37.0 ± 17.8	3 M, 1 F	T8 - T10	Complete (A)	10 months - 3 years	ReWalk	12 weeks	36	3x	60
Platz et al.(94)	2016	7	48.3 ± 10.2	5 M, 1 F	T5 - L1	Mixed: 6A, 1C	11.4 ± 10.1	ReWalk	4-5 weeks	20 - 25	5x	60
Sale et al.(55)	2016	3	36.0 ± 14.5	2 M, 1 F	T10 - L1	Mixed: 2A, 1C	NR	Ekso	5 weeks	20	4x	50

Sale et al.(95)	2018	8	43.2 ± 13.2	6 M, 2 F	T1 - L2	Mixed: 3A, 4B, 1C	NR	Ekso	5 weeks	20	4x	45
Spungen et al.(96)	2013	7	42.0 ± 12.0	6 M, 1 F	T1 - T11	Complete (A)	5.6 ± 4.1	ReWalk	NR	45 ± 20	3x	120
Stampacchia et al.(97)	2016	21	48.1 ± 12.3	17 M, 4 F	C7 - L2	Mixed: 12A, 2B, 7D	9.7 ± 8.1	Ekso	Single session	1	1x	40
Talaty et al.(98)	2013	12	33.6 ± 13.1	8 M, 4 F	T3 - T12	Completes (A)	7.4 ± 7.6	ReWalk	8 weeks	24	3x	90
Tanabe et al.(90)	2013	7	46.2 ± 11.7	6 M, 1 F	T6 - T12	Complete (A)	11.8 ± 5.3	WPAL	NR	2-11	NR	60
Tefertiller et al.(99)	2017	32	37	27 M, 5 F	T4 - L2	Mixed: 21 A, 5B, 6C	NR	Indego	8 weeks	24	3x	NR
Van Dijsseldonk.(100)	2017	12	42.0 (24–56)	7 M, 5 F	T4 - T11	Complete (A)	6.2 (2-23)	ReWalk	8 weeks	24	3x	90
Yang et al.(101)	2015	12	46.0 ± 12.0	10 M, 2 F	C7 - T11	Mixed: 9A, 2B, 1C	6.8 ± 5.4	ReWalk	NR	55 (12 - 102)	NR	120
Zeilig et al.(102)	2012	6	33.2 ± 10.5	6 M	T5 - T12	Complete (A)	5.0 ± 1.3	ReWalk	NR	13.7 ± 5.8	NR	50
Mean ± SD	-	*11 ± 9*	*40 ± 7*	*M: 8.7 ± 7.5* *F: 2.6 ± 3.2*	-	-	*6.8 ± 3.7*	-	*12.1 ± 19.6*	*21.0 ± 13.0*	*2.7 ± 1.0*	*79.8 ± 34.2*

LOI: level of injury; *TSI:* time since injury; *No. of ppt*: number of participants in chronic (>1 year) and acute (< 1 year) recovery phase; *M*: male; *F:* Female; *ASIA scale*: American Spinal Injury Association Impairment Scale (39); *SD*: standard deviation. *NR*: not reported in article; Calculation for mean ± SD for intervention length excluded the study outliers with single sessions/2-year periods. Reprinted with permission: Shackleton, C., Evans, R., Shamley, D., et al. (2019). Effectiveness of over-ground robotic locomotor training in improving walking performance, cardiovascular demands, secondary complications and user-satisfaction in individuals with spinal cord injuries: A systematic review. *Journal of Rehabilitation Medicine*, *51*(10), 723–733.

1.8.1 Ambulatory function

Ambulatory function involved outcomes of walking capacity, which included a) 6-Minute Walk Test (6MWT) that measures the distance and velocity walked over a 6-minute period and serves as an indicator of submaximal aerobic capacity; b) 10 Meter Walk Test (10MWT) that measures the velocity achieved during a 10m walk; c) Timed-Up-and-Go (TUG) Test that measures the time required to stand up, balance and sit down again. The meta-analyses performed on the relevant included studies showed that RLT can be used as an effective rehabilitation method to significantly improve walking capacity ($p < 0.001$). Positive pooled effects were found for the 6MWT [-0.94 (95% CI: -1.53, -0.36)], 10MWT [-1.22 (95% CI: -1.87, -0.57)] and TUG [0.74 (95% CI: 0.36, 1.11)] meta-analyses from pre to post RLT interventions (Fig. 1.3-1.5). The analyses indicated a general trend of improved walking capacity with more walking sessions, suggesting a training effect due to the increased proficiency in ambulating within the exoskeleton device over time (54). Longer training periods ensure repetitive task practice, improving performance through increased motor learning and neuroplasticity (3,8,16,17,29).

The average velocity achieved across the studies for the 6MWT ranged from 0.22m/s to 0.36m/s and the average velocity in the 10MWT ranged from 0.25m/s to 0.38m/s. A previous meta-analysis investigating a similar group of heterogeneous individuals, with various RLT protocols encompassing a wide range of training sessions, found a similar weighted mean gait velocity of 0.25 m/s (103). The review by Miller et al. (2016) (60) suggests that these gait velocities are encouraging for independent ambulation in home and community environments, while other authors argue that these velocities are not considered sufficient for community ambulation (101,104,105). Potentially, such differences in gait velocities exist between studies due to the variability in population, training methods and the outcome measures used for assessing walking performance. This inter-study variability is highlighted in the moderate to high heterogeneity scores of 27% and 60% for the 6MWT and 10MWT meta-analyses respectively performed in this review (Fig. 1.3 and 1.4).

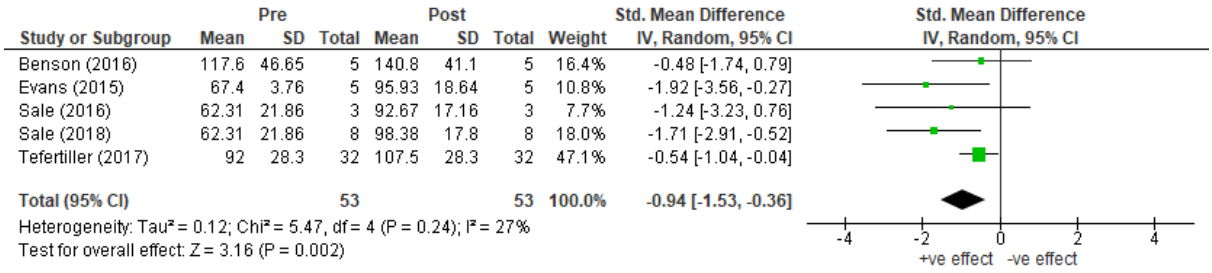

Figure 1.3: Effect of Robotic Locomotor Training on 6-Minute Walk Test distance using a random effects model.

6MWT: Six-minute walk test measured in meters (m)
Notes: Standardized mean difference of -0.94 (95% CI: -1.53, -0.36; I^2 =27%; p=0.002)
Reprinted with permission: Shackleton, C., Evans, R., Shamley, D., et al. (2019). Effectiveness of over-ground robotic locomotor training in improving walking performance, cardiovascular demands, secondary complications and user-satisfaction in individuals with spinal cord injuries: A systematic review. *Journal of Rehabilitation Medicine*, *51*(10), 723–733.

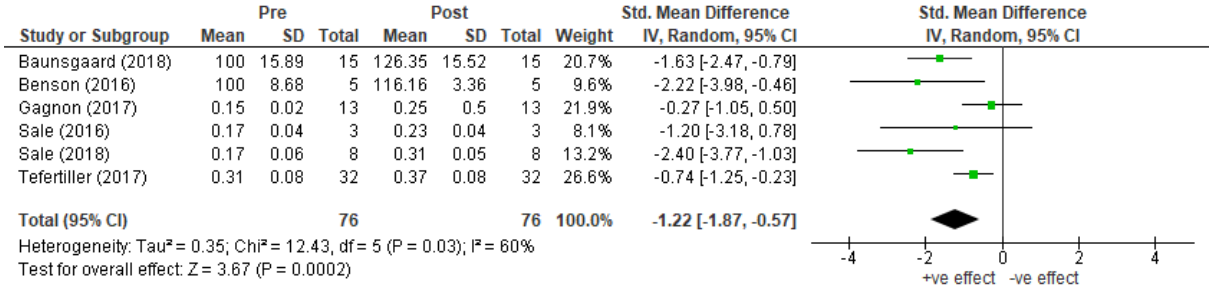

Figure 1.4: Effect of Robotic Locomotor Training on 10-Meter Walk Test speed using a random effects model.

10MWT: 10m walk test measured in velocity (m/s)
Notes: Standardized mean difference of -1.22 (95% CI: -1.87, -0.57; I^2 =60%; p=0.0002)
Reprinted with permission: Shackleton, C., Evans, R., Shamley, D., et al. (2019). Effectiveness of over-ground robotic locomotor training in improving walking performance, cardiovascular demands, secondary complications and user-satisfaction in individuals with spinal cord injuries: A systematic review. *Journal of Rehabilitation Medicine*, *51*(10), 723–733.

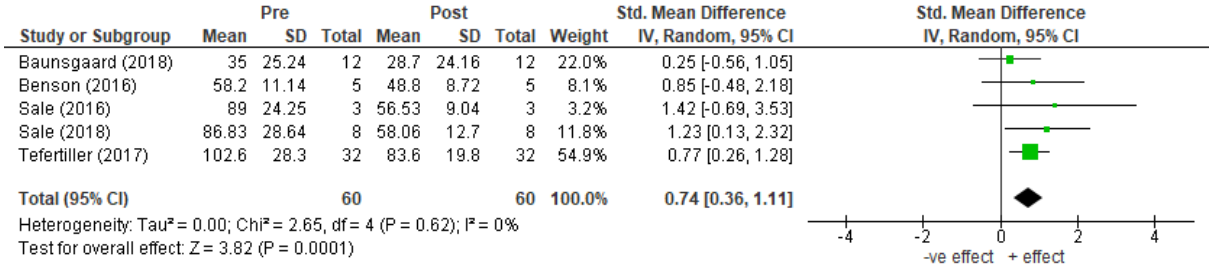

Figure 1.5: Effect of Robotic Locomotor Training on the Timed-Up-and-Go time using a random effects model.

TUG: Timed-up-and-go test measured in seconds (s)
Notes: Standardized mean difference of 0.74 (95% CI: 0.36, 1.11; I^2 =0%, p=0.0001)
Reprinted with permission: Shackleton, C., Evans, R., Shamley, D., et al. (2019). Effectiveness of over-ground robotic locomotor training in improving walking performance, cardiovascular demands, secondary complications and user-satisfaction in individuals with spinal cord injuries: A systematic review. *Journal of Rehabilitation Medicine*, *51*(10), 723–733.

1.8.2 Secondary complications

Weight-bearing activity and over-ground ambulation have been shown to reduce many of the secondary complications associated with SCI, by increasing body strength and aerobic capacity, minimizing declines in bone mineral density, improving circulation and countering the other health risks associated with prolonged sitting (55,60). Secondary complications, including spasticity and pain, were analysed in this systematic review which were measured using subjective ratings; Numeric Rating Scale of 0-10 for spasticity and 0-6 for pain as well as a VAS questionnaire. Clinical tests included the Modified Ashworth Scale and The Spinal Cord Assessment for Spastic Reflexes.

1.8.2.1 *Spasticity*

Spasticity is a long-term secondary complication of SCI that is experienced by 65–78% of individuals with SCI (1,16). Spasticity has the potential to negatively influence both physical functional and psychological well-being by restricting daily activity, inhibiting effective walking and selfcare, causing pain and fatigue, contributing to negative self-image and reducing overall QoL (16). The systematic review found that only five out of the 27 studies provided spasticity measures (Table 1.3). Two of the studies using clinical measures found significant improvements in spasticity from pre to post-walking (81,97), one showed reduced spasticity across the intervention (83) and one indicated no change (94). All the studies using self-reported measures indicated improvements in spasticity ratings across the intervention (83,92). The spasticity reduction was observed in previous case reports evaluating the training effects of using powered exoskeletons (78,83). Miller et al. (2016) also reported that clinically relevant improvements were found in self-reports for muscle spasticity in various other RLT studies (60). The decrease in spasticity following RLT might be explained by the activation of neuronal circuits involved in walking, which is able to reduce the under-regulated hyperactivation present in spasticity (97). Another cause of the decreased spasticity may be the effect of the mobilization of usually unused muscles, which leads to muscular fatigue and muscular fuse adaptation (83,97).

Table 1.3: Spasticity assessments in individuals with spinal cord injury using Robotic Locomotor Training.

	Clinical		Self-reported
	Spinal cord assessment tool for spastic reflexes	*Modified Ashworth scale*	*Numeric rating scale (0-10)*
Benson(81)		2 participants = mild spasticity pre - session was reduced post sessions (average decrease of 0.71) *	
Esquenazi(83)		T0 - T1 = spasticity reduced*	T0 - T1 = 3/11 reported reduced spasticity; none reported increased spasticity*
Kressler(92)	T0 - T1 = no change*		Post-trial = none to mild spasticity reported*
Platz(94)		T0 - T1 = no change*	
Stampacchia(97)		*Total lower limb score for 3 segments:* Pre - session = 4.0 [0.0–10.7] Post session = 2.0 [0.0–5.2] (p<0.001)	Pre - session = 2.0 [0.0–4.5] Post session = 0.0 [0.0–1.5] (p<0.001)

T0: Pre-intervention; *T1*: Post intervention; Significance: p<0.05. Note: studies with missing original data or level of significance – indicated by *.

1.8.2.2 *Pain*

Chronic pain is one of the most frequent secondary complications experienced by people with SCI, with up to 80% of individuals reported to suffer from it (16,106). Chronic pain may lead to functional disability, emotional dysfunction and may impact negatively on community participation and QoL (16,107,108) Majority of the studies in the systematic review reported pain intensity to decrease during and after the use of the robotic exoskeletons (54,81,83,92,97), however, three studies reported no change in pain perceptions (55,95,102) (Table 1.4). The decreased pain reports could be attributed to the improved psychological benefit of walking again (97), endogen endorphins activated by the walking exercise (97) and reduced muscular spasticity (81,97).

Table 1.4: Pain assessments in individuals with spinal cord injury using Robotic Locomotor Training.

	Visual analogue scale (VAS)	Numeric Rating Scale (NRS 0 -6)
Benson(81)	Pre - post sessions = improved pain intensity (VAS = +0.19) *	
Esquenazi(83)	T0 - T1 = 5/12 participants reported a combined 28x that pain was reduced*	
Kolakowsky-Hayner(54)	Post session =No significant pain reported*	
Kressler(92)		T0 - T1 = reduction in pain severity scores (average of -1.3 to 1.7 difference) ($p<0.05$) *
Sale(55)	T0 = 3.333 ± 4.041 T1 = 3.00 ± 3.464 No significant change ($p>0.05$)	
Sale(95)	T0 = 1.00 ± 2.83 T1 = 0.88 ± 2.47 No significant change ($p>0.05$)	
Stampacchia(97)	Pre - session: 6.0 [4.5–7.0] Post - session: 2.0 [0.0–4.0] ($p = 0.002$)	
Zeilig(102)	Pre-session = 1.77 ± 0.92 Post-session = 1.71 ± 1.02 No significant change ($p>0.05$)	

T0: Pre-intervention; *T1*: Post intervention; Significance: $p<0.05$. Note: studies with missing original data or level of significance – indicated by *.

1.8.3 User satisfaction and quality of life (QoL)

The positive relationship between physical activity and subjective QoL has been documented in individuals with SCI and hence, it is predicted that an exercise-based intervention will assist in improving an individual's mood state (109–111). However, as RLT is a particularly novel form of physical activity, its effect on psychological and QoL outcomes is largely unclear. There are proposed psychological and social benefits to standing, including improved self-image, eye-to-eye interpersonal contact and increased independence (55,78,92,96). The review (Table 1.5) showed that the majority of studies found that the users felt safe and comfortable in the exoskeleton device and had tendencies towards strong positive comments regarding the acceptability and emotional/health benefits of the training process (55,82,83,86,94,95,97,102). Benson et al. (2016) showed that QoL improved by 4 points after partaking in a RLT intervention (81). Improvements in QoL, psycho-emotional stability and wellness were also been reported post intervention by Platz et al. (2016) (94).

Table 1.5: User satisfaction assessments in individuals with spinal cord injury using Robotic Locomotor Training.

	Questionnaires	Satisfaction (VAS 1-5)	Acceptability (VAS 1-7)
Benson(81)	*ATD-PA scale:* T0 to T1 = increase in QoL subscale (+4 points; SD 4.2)* T0 = 41; T1 = 34 (Mean device form score)* *ADAPSS score:* Average decrease in disability appraisal across all domains* = -3 points		
Birch(82)			15 out of 16 statements = > 90% +ve response 1 statement = -ve response (transfer ability)
Esquenazi(83)		3/11 subjects = improved spasticity 1/11 subjects = use of device caused fatigue 5/11 subjects = improved bowel regulation All subjects = no pain from the device	
Gagnon(86)	*VAS (0-100):* 95.7 ± 0.7% = satisfied with the locomotor training program 79.6 ± 17% = positive ability to learn to perform sit–stand and walk with the device 67.9 ± 16.7% = perceived some health benefits 16.7 ± 8.2% = reported no fear of developing secondary complications or risks linked to the use of the device 91.3 ± 0.1% = felt motivated to engage in a regular physical activity program		
Platz(94)	*SF-12v2 score:* T0 to T1 = increase in physical function (0.38 [0.01–0.76])* *Baseline scores:* Physical functioning = lower than norm Mental component = higher psycho-emotional stability than norm		
Sale(55)		All 10 statements = > 3 score	
Sale(95)		9 out of 10 statements = > 3 score 1 statement = < 3 (safety of device)	
Stampacchia(91)			*+ve sensations:* Comfort, 6.0 [6.0– 6.0] Enjoyment, 6.0 [6.0–7.0] Advantages, 5.0 [5.0–6.0] Motivation, 6.0 [6.0–7.0] Suggest, 6.0 [6.0–7.0] *-ve experiences:* Pain, 2.0 [1.0–2.0] Fatigue, 3.0 [2.0–5.0]
Zeilig(96)		8 out of 10 statements = > 3 score 2 statements = < 3 score (bowel and wearing the device)	

ATD-PA: Assistive Technology Device Predisposition Assessment; *ADAPSS:* Appraisals of DisAbility: Primary and Secondary Scale; *SF-12v2:* SF-12v2 Health Survey*; VAS*: Visual analogue scale. Note: studies with missing original data or level of significance – indicated by *.

In conclusion, the systematic review shows that RLT appears promising as a tool to offer comprehensive care to individuals with SCI. The review indicates that RLT can provide individuals with SCI the ability to walk safely while possibly improving their ambulatory capacity as well as reducing negative health complications, including spasticity and pain. However, the effect of RLT on psychological well-being and QoL is understudied and requires more extensive investigation. In particular, there have been increasingly more calls for the use of measures that capture subjective QoL as an outcome for rehabilitation efficacy (112–115). As evident in the review, there is an underpowered evidence base regarding the efficacy of RLT, primarily due to the heterogeneity in the study characteristics and small sample sizes. Additional large clinical trials with sufficient rehabilitation durations as well as adequately powered homogenous studies are required to better understand these effects of RLT on individuals with SCI.

1.9 Rationale for thesis

RLT is a particularly novel form of physical activity and hence, its effect on functional capacity, secondary complications, bone health and psychological outcomes is still largely unclear. In aiming to advocate for rehabilitation for individuals with SCI in South Africa, where there is currently a lack of specialized health and rehabilitation services, this study had to investigate innovative technologies that could not only enhance functional and psychological benefits but also reduce the prevalence of secondary complications that are so common among the SCI population. To our knowledge, there are currently no RCTs within this field of over-ground exoskeleton research. Thus, due to the novelty of such a trial in South Africa, the investigation commenced as a pilot RCT. The preliminary results of this randomized controlled pilot study aim to add depth to the literature using homogenous SCI groups with comparable lesion levels and a long intervention period (24 weeks) with inclusive testing procedures. In addition to the protocol strengths of the trial, the research also aided in meeting the needs of investigating health, functioning and the psychological well-being of survivors of SCI within the context of a low to middle-income country where limited research has been conducted.

1.10 Aims

The aim of this randomized controlled pilot study was to evaluate the effect of Robotic Locomotor Training (RLT) compared to Activity-based Training (ABT) during a 24-week rehabilitation programme in individuals with SCI. The study aimed to measure 1) functional capacity 2) secondary complications and 3) psychological well-being of individuals with SCI when exposed to 24 weeks of RLT or ABT. The inclusion of all three aforementioned aims is a first within this field of research and thus, will provide a preliminary understanding of these outcomes during an extended rehabilitation programme.

1.10.1 Objectives

The objectives of this study were to evaluate and compare the effect of RLT and ABT programmes over a 24-week period on:

1. Functional capacity
    a. Spinal Cord Injury Functional Ambulatory Index (SCI-FAI)
    b. 6-Minute Walk Test (6MWT)
    c. 6- Minute Arm-ergometer Test (6MAT)
    d. Handgrip strength
    e. Isometric abdominal and back strength
    f. ISNCSCI Motor and Sensory Scores

2. Secondary complications
    a. Spasticity – Modified Ashworth Scale
    b. Pain – International Pain Basic Data Set
    c. Bladder and bowel complications – International Lower Urinary Tract Function Basic Data Set, International Bowel Function Basic Data Set

3. Psychological well-being and quality of life
    a. One-on-one interviews
    b. Quality of life – International SCI Quality of Life Basic Data Set
    c. Depression – Beck Depression Inventory
    d. Anxiety – State - trait Anxiety Inventory

1.11 Expected Outcomes

The literature supports the expectation that the ABT group will show improvements in functional capacity (49), and psychological outlook (109). However, the effect of RLT on these outcomes is less clear. According to the literature, although limited, one would hypothesize that improvements in functional capacity and mobility from performing RLT, would likely be similar to those found in other robotic interventions (54,55,78,116,117). Furthermore, evidence suggests the potential for alleviating secondary complications that occur after SCI through physical activity (49). Thus, although the specific effect of RLT on health-related benefits is largely unknown (92), it is hypothesised the RLT would impact spasticity, pain as well as bladder and bowel function.

RLT is a particularly novel form of physical activity and hence, its effect on psychological outcomes is largely unclear. However, based on the positive evidence surrounding physical activity and psychological outcomes, and the unique features of RLT training such as eye-to-eye contact, one can hypothesize that there is a potential for improving the psychological outlook of individuals engaging in RLT.

1.12 References

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CHAPTER 2

Robotic Locomotor Training and Activity-based Training after spinal cord injury: study design and methodology

2.1 Introduction

This chapter outlines the novel study design and methods of the pilot randomized control study (RCT) on which all subsequent chapters are based. This study was a collective effort between three research institutions (University of Cape Town, Cape Peninsula University of Technology, Stellenbosch University) in the Western Cape, South Africa. The study aimed to measure 1) functional capacity 2) secondary complications and 3) psychological well-being of people with chronic SCI over a 24-week intervention. This trial is registered with the Pan African Clinical Trials Registry (PACTR201608001647143).

2.2 Study design

2.2.1 Pilot randomized control trial (RCT)

The aim of this pilot RCT was to investigate the effect of RLT compared to ABT during a 24-week rehabilitation programme in individuals with SCI. It is a first within SCI research to investigate the long-term effects of these rehabilitation modalities across functional capacity, prevention of secondary health complications and psychological outcomes. The data collected for this study formed part of a larger study providing a comprehensive understanding of these training modalities for SCI rehabilitation. The cardiovascular and positive paradigm psychological outcomes for people with SCI, together with the role of hope are not reported in this thesis. These outcomes were investigated by a fellow PhD student (Rob Evans, 2021) who shared the same cohort (See Appendix 2.1 for the full testing schedule). The data presented in this dissertation, however, remains unique to this thesis. Although RCTs are the gold standard for scientific research, they can create methodological, ethical and practical challenges when applied to interventional SCI studies (118). As a result, researchers often

use experimental research designs which describe preliminary effects and provide translational research insights into real-world scenarios (119–121). The increased practicality may ensure that evidence generation is not hindered by the requirement to adhere to often unobtainable study designs (119). Furthermore, within low and middle-income countries, a full-scale RCT may not always be feasible due to human resources, equipment, and financial restraints. When a context does not allow for the implementation of an RCT, pilot trials can describe evidence of effectiveness in everyday clinical contexts. To upscale this pilot study to a full-scale RCT, a significant amount of rehabilitation equipment, facility space and human resources would be required. It is envisaged that the insights of this pilot trial will assist in the design and efficacy of future large-scale clinical trials in a similar setting. The 24-week length of this trial was significantly longer than the standard of care (8-16 weeks) offered by both private medical insurers and the support systems within the public health sector of South Africa (7). This study aimed to provide preliminary evidence to demonstrate that a full RCT could be undertaken in a South African context, as to the author's knowledge, this is the first pilot RCT within this field of exoskeleton research using large homogenous groups. Thus, this RCT was performed to determine the efficacy of RLT in comparison to ABT in improving a range of rehabilitation outcomes and as a pilot to assess the feasibility of implementing a similar larger-scale intervention in the future.

2.2.2 Mixed-methods approach

This study used a mixed methods design, by collecting, analysing, and "mixing" both quantitative and qualitative data to understand our research problem more completely (122,123). Researchers have recognized that in many instances the use of both qualitative and quantitative methods are required to tease out and illuminate different dimensions of this complexity (122). Since perceptions of psychological well-being are context-specific and filled with subjective meanings, mixing methods would seem to be especially appropriate in this type of research (113,124). This study used an embedded (nested) mixed method design in which the quantitative and qualitative data were collected concurrently, analysed separately, and then merged during the interpretation phase of results. This is a popular design in health science research in which quantitative and qualitative approaches are embedded to provide new insights or more refined thinking (122). In this study, the quantitative analyses

considered the numeric data from the functional capacity, secondary complications, and the psychometric outcomes, while the secondary qualitative approach was used to collect text data through individual semi-structured interviews to determine the lived experiences and perceptions of the participants involved in the trial. Thus, the qualitative data within the intervention helped to understand the specific subtopic of how the participants experienced the interventions, with focus on the participants' perceptions of the benefits to QoL achieved during rehabilitation, as well as the experienced barriers and facilitators to participation in the intervention. Therefore, by using both methods, we provided a detailed data set and a comprehensive interpretation of that data to obtain a more complete picture of the interventions and participant experiences over the 24-weeks.

2.2.3 Study setting

This study was performed in a neurological private practice called the *Walking with Brandon, Therapy & Beyond Rehabilitation Centre*, based in the multi-disciplinary Sport Science Institute of South Africa, Cape Town, Western Cape, South Africa. The ambient temperature within the rehabilitation centre was set at 22 degrees centigrade and 50% humidity. The access to the building, all floors in the building, including the bathrooms, rehabilitation practice, gym, as well as the parking facilities were wheelchair accessible.

2.3 Study protocol

2.3.1 Participant recruitment

To reduce heterogeneity, the most common subgroup of SCI in Cape Town was recruited, namely motor incomplete with a neurological level of injury between C1-C8 (cervical injury) (13). The recruitment process is provided in detail in Figure 2.1 and spanned a period of 18 months. Seventeen participants with chronic (> 1 year) traumatic motor incomplete tetraplegia (AIS B, C, D) were recruited via a media release (Appendix 2.2). Participants were randomly assigned via number generation (Microsoft Excel) to either the RLT or ABT intervention group. The principal investigator conducted this procedure and

informed participants of their assigned rehabilitation group. A physician was included in the rehabilitation team to oversee clinical concerns and advice on acceptance/withdrawal from the interventions. One participant discontinued the intervention after being enrolled in the RLT group for three weeks. Persistent right leg weakness necessitated a magnetic resonance imaging study (MRI) which provided images consistent with the diagnosis of a tibial stress fracture. Only baseline measures had been recorded for the participant which may have been confounded by an existing stress fracture. Thus, the participant was excluded from all analyses and received treatment for the fracture outside of the trial protocol. Each participant provided written informed consent for screening and prior to the study interventions (Appendix 2.3). All participants were provided with transport to attend screening, testing, rehabilitation intervention sessions and post-trial access. Post-trial rehabilitation was provided to the participants according to the Declaration of Helsinki. All participants received an additional three months of twice weekly rehabilitation, whereby the individuals had access to the rehabilitation modalities used in both RLT and ABT interventions, regardless of which intervention they were originally assigned to.

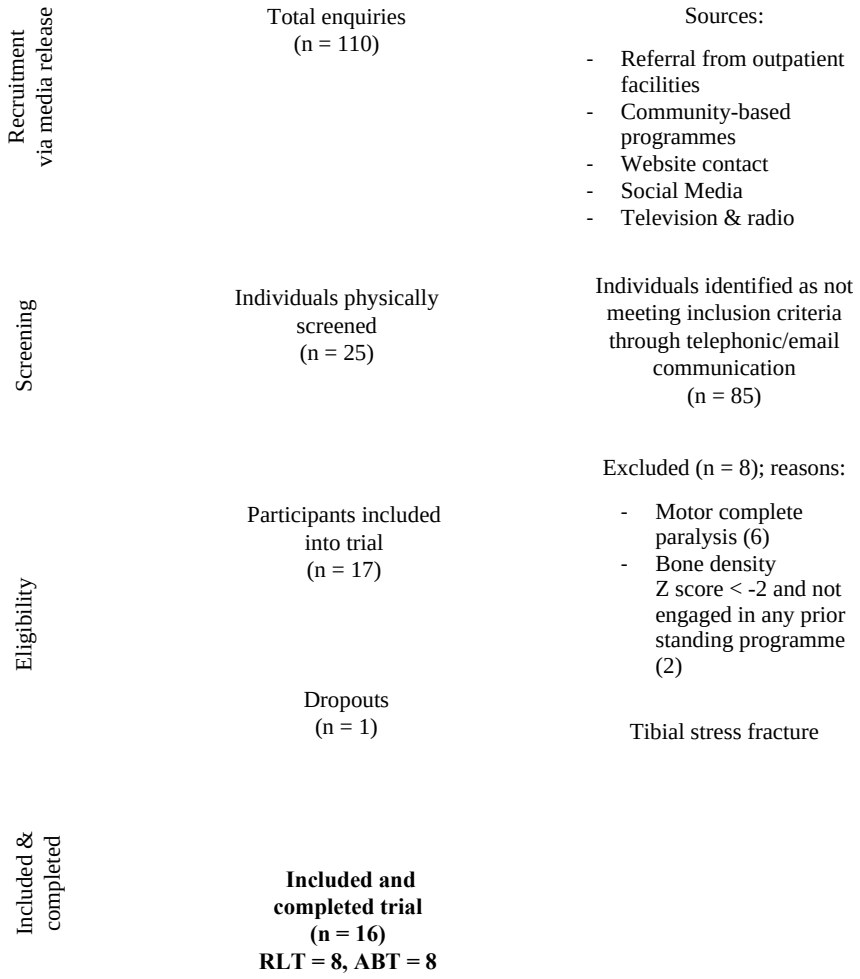

Figure 2.1: Recruitment of participants into the pilot randomized control trial.

2.3.2 Participant pre-screening

Participants were assessed to ensure they complied with the inclusion/exclusion criteria of the study (Appendix 2.4). The intensive pre-screening assessment involved three different visits to the Sports Science Institute of South Africa, Cape Town, to cover an in-depth four-stage reliability and safety process. All specialists involved in pre-screening of participants were in collaboration with the investigators. The four-stage pre-screening consisted of 1) Participants' basic anthropometrics were measured, 2) Participants underwent Dual Energy X-ray Absorptiometry (DXA) screening of one hip (left or right) and lumbar spine to analyse bone mineral density, muscle and fat mass, 3) Participants were medically screened by a rehabilitation Doctor (Vincent Pallotti Hospital), to ensure individuals

were safe to perform the rehabilitation programme, 4) Participants were screened and briefed by experienced psychologists, specialized in disability research (Stellenbosch University) regarding their psychological well-being, understanding of the realistic outcomes of partaking in the rehabilitation intervention, as well as mental preparation for the physical rehabilitation sessions. Thereafter, an experienced and robotic walking trained Biokineticist assessed the participants on their ability to safely walk in the robotic suit. This screening (Appendix 2.5) covered a range of aspects regarding joint range of motion, spasticity, strength, and further medical screening.

2.3.3 Interventions

All intervention sessions were conducted by trained biokineticists (fellow PhD candidate, Robert Evans, and myself) within the *Walking with Brandon Foundation, Therapy & Beyond Rehabilitation Centre* based at the Sport Science Institute of South Africa, Cape Town. Biokinetics is a clinical profession focused on improving physical functioning and health through exercise rehabilitation as a treatment modality (125). All participants were instructed to maintain their normal levels of physical activity outside of the intervention sessions, and refrain from starting new exercise programmes. Participants were asked to inform the research team if they started any form of new medical or psychological treatment. By refraining from increasing the amount of habitual physical activity or altering their psychological support, the effect of the respective intervention was better controlled for.

2.3.3.1 *Robotic Locomotor Training (RLT)*

Locomotor training relied on solely standing and walking in the Ekso GT (Variable Assist Model) bionic suit. Participants performed sessions three times per week, allowing for sufficient rest between sessions. Each session was approximately 60 minutes long and the intensity of the sessions varied between participants and as the participant adapted during the programme. The first five minutes of the session served as a warm-up, stretching, and mobilising the participant in preparation to walk in the suit. Intensity levels during the session ranged from:

- Standing time: 15 - 40 minutes
- Walking time: 10 - 30 minutes

- Steps taken: 50 - 1000 steps

The Ekso GT exoskeleton is equipped with variable assist software which can provide three different levels of walking assistance for the participant and four different modes of stepping (Appendix 2.6). Variable assist allows for motor power to be dynamically adjusted to the user's capabilities, with the overall aim of mimicking a natural gait pattern. Progression included lowering the level of assistance from the exoskeleton and increasing the number of steps per session. This progression was faster or slower in some participants, as training was specific to the capacity of each individual and followed their learning pace rather than a predetermined timetable. As the participant progressed through the various modes, the objectives to meet during sessions included: improved walking performance with step triggering, coordinating step timing and foot clearance, and safe and effective stopping. Across all modes, crutch/walker placement for balance and limb advancement was a fundamental skill.

2.3.3.2 *Activity-based Training (ABT)*

Activity-based Training (ABT) represents the current standard of care provided in advanced neurological rehabilitation centres around the world (126). The form of ABT used in the intervention was adapted from the *Beyond Therapy* model used by the Shepherd Centre and can be described as a six-stage process (Therapy & Beyond Rehabilitation Programme – Appendix 2.7). The six stages include: Stage I – Prehabilitation, Stage II – Muscle Recruitment, Stage III – Posture & Joint Stability, Stage IV – Resistance & Endurance Training, Stage V – Pre-Gait, Stage VI – Gait Training. The stages of ABT were not linear in design but rather recursive, where progression went back and forth as needed. Progress was determined by the treating biokineticist according to the ability of the participant to meet the demands required within each stage of rehabilitation. Sessions were conducted three times per week and were approximately 60 minutes in duration. Five minutes of the session was allocated to transfers and setting up of the various apparatus. ABT involved resistance, cardiovascular and flexibility training combined with regular weight-bearing in the standing position. The approximate standardized time allocation for each session was as follows:

- Warm-up & mobility: five minutes
- Resistance training: 30 minutes
- Cardiovascular training: 20 minutes.

2.3.4 Data Collection

Data were collected between February 2017 and May 2018. Major data collection time-points were at 0, 6, 12 and 24 weeks. Table 2.1 illustrates the data collection schedule for the full testing protocol throughout the 24-week intervention. A summary of the outcome variables is provided below and will be described in depth in each subsequent chapter:

2.3.4.1 *Functional capacity outcomes:*

a) Isometric handgrip strength

b) ISNCSCI impairment scale (motor and sensory scores)

c) Isometric abdominal and back strength

d) Six-Minute Arm Ergometry Test (6MAT)

e) Spinal Cord Injury Functional Ambulatory Index (SCI-FAI)

f) Six-Minute Walk Test (6MWT)

g) Borg's Rating of Perceived Exertion (RPE)

2.3.4.2 *Secondary complication outcomes:*

a) Spasticity (Modified Ashworth Scale)

b) Pain (International SCI Pain Data set)

c) Bladder and bowel function (International Lower Urinary Tract Function Basic Data Set, International Bowel Function Basic Data Set)

2.3.4.3 *Bone density and body composition outcomes*

a) Bone mineral density (BMD)

b) Body composition and distribution

2.3.4.4 *Psychological well-being outcomes:*

a) Depression (Beck Depression Inventory (BDI))

b) Anxiety (State-trait Anxiety Inventory (STAI))

c) Quality of Life (International SCI Quality of Life Basic Data Set)

d) One-on-one interviews

Table 2.1: Testing periods for outcome variables collected during the 24-week intervention.

			Weeks						
	Screening	**Baseline**	**4**	**6**	**8**	**12**	**16**	**20**	**24**
Informed consent	X								X
Anthropometry	X								
ISNCSCI	X								X
Medical screening	X								
Bone density and body composition (DXA)	X								X
Bio, physio, doctor screening	X								
Psychological interviews (qualitative)	X		X		X	X	X	X	X
Psychometric questionnaires		X		X		X			X
Isometric strength test		X		X		X			X
6MAT		X		X		X			X
Spasticity		X	X	X	X	X	X	X	X
Handgrip		X				X			X
Lower Extremity Motor Score (LEMS)		X				X			X
Rating of Perceived Exertion (RPE)		X		X		X			X
SCI-FAI		X		X		X			X
Lower Urinary Tract Infection Basic Data Set		X		X		X			X
Bowel Function Basic Data Set		X		X		X			X
International SCI Pain Data Set		X		X		X			X

ISNCSCI: International Standards for Neurological Classification of Spinal Cord Injury; *DXA:* Dual-Energy X-Ray Absorptiometry for bone mineral density and body composition; *Bio:* biokineticist, *Physio:* physiotherapist, *Doctor:* physician specialising in SCI (All three groups involved in final screening of participants and confirming inclusion and exclusion criteria); *Psychometric questionnaires*: International SCI Quality of Life Basic Data Set; Beck Depression Inventory, State-Trait Anxiety Inventory; *6MAT:* Six-minute Arm Ergometry Test; *SCI-FAI*: Spinal Cord Injury Functional Ambulation Index.

2.3.5 Ethical approval

Ethical approval was granted by the University of Cape Town, Human Research Ethics Committee (384/2016 – Appendix 2.8). Signed informed consent was obtained from participants prior to data collection. Coded participant names and de-identified data were securely stored on password protected computers. The medical liability of this trial was covered by the general insurance of the University of Cape Town. All researchers followed the Good Clinical Practice Guidelines of South Africa, in accordance with the Declaration of Helsinki (127), Guidelines for Good Clinical Practice in the Conduct of Clinical Trials in Human Participants in South Africa (128) and The Department of Health: Ethics in Health Research: Principles, Structures and Processes (129).

2.3.6 Statistical analysis

All data were analysed using statistical software (R, R Core Team, Auckland, New Zealand and Prism 8, GraphPad Software Inc, California, USA). Normality distribution of the data were assessed using the Shapiro-Wilks test. Linear mixed effect models assessed continuous responses which were measured at four time points (0, 6, 12 and 24 weeks). These models formally compared the effect of the group interventions across the total 24-week period and tested for any changes over time. To account for the within subject association between repeated measures, subject specific random effects were included. Due to small sample sizes, it was not possible to fit nonlinear time trends; hence only a linear time effect over the entire 24-week period was considered. Response profiles were illustrated using plots of means and half-width 95% confidence intervals (CI) for observed data; 95% CI were displayed as half-width to address the poor visibility of graph components caused by an overlap between full-width intervals. Non-parametric data was assessed using the Mann Whitney U and Wilcoxon Signed Rank tests to determine the group and time main effects. The Mann-Whitney U assessed whether the change in pre- and post-measurements were different between the ABT and RLT group; Null hypothesis (H0): The distribution of the change between pre- and post-measurements is the same for both groups. The Wilcoxon Signed Rank were used to determine differences between pre- and post-time points within a group; Null hypotheses (H0): The median difference, between two paired samples is equal to zero.

Significance was accepted at a $p < 0.05$. Outliers in data were determined by model diagnostics to quantify the influence of an individual using Cook's distance plots and standardised DF Beta plots. Magnitude-based inferences of change (effect size) were calculated according to Cohen's d. A Cohen's d of zero denotes no effect, whereas ranges from 0.2-0.5, 0.5-0.8 and >0.8 represent small, medium, and large effects, respectively. Whitehead et al. (2015) suggests that a pilot sample size of 10 per treatment group be reached for large effect sizes > 0.8. Due to 8 participants in each group, we aimed to reach larger effect sizes of 0.9 for clinical significance. Statistical analyses for the separate outcomes will be explained in the subsequent chapters.

Qualitative data were analysed using a thematic content analysis with a data-driven and inductive approach to coding (130), with initial coding done independently by two researchers. The initial codes identified by the two researchers were then reconciled by a third person, so that triangulation of themes could be achieved. Themes were then grouped into superordinate and subordinate themes, which were then independently reviewed and verified by a third author.

2.3.7 Limitations

We were limited in our sample size due to the limited number of therapists and time available to perform the labour-intensive rehabilitation and testing, limited facility space, and financial constraints (mainly due to the costs of transport for all participants to attend rehabilitation session) posed by the trial. A clear financial budget is required to conduct a full-scale RCT in future. Only one female participant was recruited for this trial, which serves as a limitation of this study by providing uncertainty regarding the application of these findings to other women with SCI. In addition, this study did not have a true experimental control in which no exercise was performed. Although an equivalent control group may be the experimental ideal, it is not feasible when conducting exercise interventions within the SCI population due to health and ethical implications. Although the small sample size was restrictive for making inferences from the results and limits the generalizing of these findings to the larger SCI population, it may still provide important preliminary information for researchers to expand upon.

2.3.8 Conclusions

This chapters describes the aim, study design, participant recruitment, interventions, data collection and data analysis of the pilot RCT underpinning this thesis. The methods described are unique in the field of SCI rehabilitation due to the study's long intervention duration (6-months), comprehensive testing procedures, inclusion of a control group (ABT), and a homogenous sample within the context of a middle-income country. This chapter serves as a point of reference for the methodology on which the findings of all subsequent chapters are based.

2.4 References

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CHAPTER 3

Robotic training for recovery of functional capacity in individuals with chronic spinal cord injury

3.1 Introduction

SCI is accompanied by a host of health-related issues, which are in part due to the direct effects of the injury, while others are secondary in nature and attributable to the resultant loss of muscle mass and a decrease in neuromuscular activity (131). Perhaps the most significant of the changes in muscle morphology and physiology is paralysis, which occurs almost instantly after injury and may last for a lifetime (132). After SCI, paralysed muscles exhibit decreased fibre diameter, reduced voluntary contraction force, abnormal increases in muscle tone, decreased metabolism, delayed conversion of slow-twitch to fast-twitch fibres, and a cross-sectional skeletal muscle area comprised mainly of Type I fibres (50,126,132). In addition to the substantial muscle atrophy, there is also decreased oxidative capacity, alterations in transmembrane ionic exchange, and decreased blood flow in muscles below the lesion level (133–136). These physiological changes often result in considerable neuromuscular fatigue, decreased muscle strength, physical and cardiovascular deconditioning and the reduced ability to voluntarily activate affected skeletal muscles (132,133,137).

Muscle weakness and physical deconditioning secondary to partial paralysis, can limit the ability to perform activities of daily living (ADLs), such as transfers, self-care activities, activities at work, household chores, and ambulation activities (138–142). Muscle atrophy and weakness in the upper limbs can profoundly reduce hand function which is considered an important determinant of QoL in the SCI population (143–145). Since handgrip is an integral part of ADLs, individuals with SCI frequently rank improvement in hand and upper limb function as a top functional priority, above walking and bowel or bladder function (141–143,146). Another priority for functional recovery after SCI is the ability to ambulate. People with SCI describe the inability to walk as one of their most devastating disabilities (147). Partial paralysis of the lower limb muscles can affect the ability to walk, as SCI

disrupts motor commands to the spinal locomotor circuitry and often severely limits the ability to coordinate muscles (144,148). Thus, muscular strength and conditioning are important health-related components of physical capacity and play a vital role in improving functional performance and psychological well-being (132). Sedentary behaviour and inactivity have also been linked to increased disability, and increased risk for cardiovascular disease and metabolic disorders (132,149). Consequently, functional outcomes are regarded as the outcome measures of choice in clinical trials, as improving functional capacity could substantially reduce health costs, improve QoL, improve ADL capacity, as well as reduce the risk of physical deconditioning and associated diseases (131,144,145,150,151). Therefore, there is a need to investigate rehabilitation interventions that promote recovery of functional capacity in people with chronic SCI, with the hopes of decreasing disability and subsequently, improving health and QoL (131,132,137).

3.1.1 Physical rehabilitation

Physical activity has become the most important quantifiable means for functional recovery after SCI (50,152,153). Previously, rehabilitation practices were largely based on the prevailing assumption that neural and functional recovery was limited in persons with chronic SCI (137). However, recent evidence indicates that neuroplasticity can be induced even years after injury (154,155). Research into neural recovery after SCI suggests that neural circuits in the spinal cord shutdown due to paralysis, but these circuits may be reactivated with physical training (126). This potential for retraining is based on activity-dependent plasticity driven by intensive, repetitive, task-specific sensory input to spinal networks (156). Several reviews suggest that exercise improves many aspects of physical health and fitness after SCI (157–159). Mitigating the harmful effects of muscle deconditioning is a key priority for health professionals working with persons with SCI and is usually the primary goal for most SCI rehabilitation programmes (132). Therefore, it is crucial that rehabilitation strives to maximize locomotor ability and functional capacity after SCI by increasing strength, endurance, and cardiorespiratory fitness (145,160). However, despite the importance for both upper extremities strengthening and walking capacity after SCI, very few studies have examined strength and functional

acquisition through targeted training (140,150). Understanding and developing therapies to promote functional recovery in the SCI population is challenging, given the extreme heterogeneity in presentation and response to treatment in this population (161). Thus, the potential for training-induced changes in muscle strength and its effect on functional capacity after incomplete SCI is under studied (137).

3.1.1.1 *Activity-based Training (ABT)*

A cornerstone of SCI rehabilitation is exercise therapy to enhance function and independence (141). One such therapy, is ABT, which specifically refers to interventions that provide activation of the neuromuscular system below the level of lesion to retrain the nervous system to recover a specific motor task (126,141). The combination of weight training, cardiovascular training and walking within ABT elicits encouraging changes in functional capacity and muscular strength (126,140,162,163). Traditionally, strength training for SCI is focused on the upper extremities to facilitate transfers and other essential ADLs. In two companion review articles examining the effects of exercise training on fitness parameters, the authors supported the benefits of participating in twice weekly resistance training (3 sets of 8–10 repetitions) to improve muscular strength using free weights, elastic bands, plate-loaded machines, and functional electrical stimulation (158,164). This prescription is consistent with findings that a multi-day, multi-set resistance training programme is effective for improving muscular strength and endurance of targeted muscles in persons with SCI (140,159,165–167). Currently, ABT is the standard of care for neurological rehabilitation globally (39).

3.1.1.2 *Robotic Locomotor Training (RLT)*

Locomotor training is a rehabilitation intervention that promotes motor relearning after SCI by providing sufficient afferent input to the nervous system to reproduce walking kinematics (147). RLT as a rehabilitative strategy has been used successfully to improve ambulatory function and secondary complications for many people with acute and chronic incomplete SCI; however, varied results are reported (53,168–173). Furthermore, most studies that focus on the effects of locomotor training on muscle activity and locomotor function, primarily focus on treadmill and body-weight support training

and not over-ground RLT (53,174–176). However, translation of the training principles beyond the treadmill environment has been developed and studied as a vital component of a locomotor training programme by several researchers (169,177–179). According to the literature, although limited, one would hypothesize that improvements from performing over-ground RLT would likely be similar to those found in other robotic interventions (54,78,116,117).

However, a systematic review by Morawietz & Moffat (2013) compared the effects of conventional gait training (parallel bars), BWSTT, and RLT and concluded that all interventions were beneficial, but no technique was superior (52). Furthermore, a Cochrane Library review suggested insufficient evidence to decide whether one of the over-ground or supported robotic training methods is superior to conventional ABT (67). Dobkin et al. (2012) showed RLT to not be superior to exercise or progressive over-ground gait training in improving functional status for those with neurological conditions (75). In addition, to our knowledge, no RCT has investigated the functional strength gains after over-ground RLT.

Research investigating the impact of robotic walking on physical conditioning parameters are beginning to emerge, but due to a limited number of RCTs on the topic, its effects on walking and functional capacity in people with SCI are unclear (180). Thus, in people with SCI, beneficial effects on functional rehabilitation outcomes from locomotor robotic devices cannot be strongly demonstrated. Additional research is needed to identify if any functional benefits might exist with this treatment modality, as well as to provide a consensus on the optimal duration and intensity of treatment required to observe changes (132,180). Stronger evidence is needed to inform the development of future evidence-based recommendations for RLT programme Thus, this study aimed at filling these knowledge gaps by performing a pilot RCT comparing the effects of RLT and ABT on functional capacity benefits in people with chronic incomplete SCI over a long duration intervention of 24 weeks.

3.2 Aims

The aim of this chapter was to explore the training effects of 24 weeks of RLT compared to ABT on functional capacity in persons with chronic incomplete SCI. Focus was given to the long-term changes (>12 weeks) in muscular strength, endurance capacity, and walking performance.

3.2.1 Objectives

The objectives were to compare and describe the changes in functional outcomes of RLT and ABT interventions over a 24-week period on:

1) *Muscle strength:*
    a) Isometric handgrip strength
    b) ISNCSCI impairment scale
    c) Isometric abdominal and back strength

2) *Endurance capacity:*
    a) 6-Minute Arm Ergometry Test (6MAT) distance and rating of perceived exertion (RPE)

3) *Walking capacity:*
    d) Spinal Cord Injury Functional Ambulatory Index (SCI-FAI)
    e) 6-Minute Walk Test (6MWT) distance and RPE

3.3 Methods

Comprehensive methods of the study protocol, including the RLT and ABT interventions, are provided in Chapter 2 of this thesis. Under supervision of a Biokineticist, all 16 participants performed the functional capacity assessments, which included handgrip strength, abdominal and back isometric maximal voluntary contractions, the six-minute arm test (6MAT) and the SCI Functional Ambulatory

Index (SCI-FAI) at baseline and at 6, 12, and 24 weeks. The six-minute walk test was performed by the eight participants in the RLT group at baseline, 6, 12 and 24 weeks. The ASIA motor and sensory exam was performed by a well-experienced SCI rehabilitation physician at baseline and week 24. Specific methods pertaining to the functional performance analyses are described below:

3.3.1 Muscle strength testing

3.3.1.1 *Handgrip strength*

Handgrip strength was measured using a hand-held dynamometer (Camry Electric Hand Dynamometer Model EH101) to measure the maximum isometric strength of the hand and forearm muscles. The participants held the dynamometer, with the arm at right angles and the elbow by the side of the body. Testing was performed on both the left and right hand. The handle of the dynamometer was adjusted if required to ensure the base rested on the first metacarpal (heel of palm), while the handle rested on middle of the four fingers. The participants were required to squeeze the dynamometer with maximum isometric effort, while limiting other body movement. The participants were encouraged with verbal cueing to provide a maximum effort. Handheld dynamometry is a valid and reliable measure of upper body strength as well as mobility limitations (181).

3.3.1.2 *International Standards for Neurological Classification of Spinal Cord Injury (ISNCSCI) impairment scale*

The International Standards for Neurological Classification of Spinal Cord Injury (ISNCSCI) (Appendix 3.1), commonly referred to as the ASIA Exam, was developed by the *American Spinal Injury Association* (ASIA) as a universal classification tool for SCI based on a standardized sensory and motor assessment, with the most recent revision published in 2019 (American Spinal Injury Association, 2019). The exam involves a motor and sensory examination to determine a neurological level of injury and whether the spinal injury is complete or incomplete. There are five AIS classifications, from AIS A (complete, no motor or sensory function in sacral segments S4-S5) to AIS E (a person with initial deficits who has normal motor and sensory function at the time of

assessment) (35). The ISNCSCI Sensory and Motor examinations are reliable when conducted by a trained examiner and are validated for injury classification in SCI population (182,183).

3.3.1.2.1 Motor assessment

The motor assessments were conducted in the supine position and involved a subjective grading of the strength of ten key muscles on each side of the body. ASIA muscle grades were assigned to each muscle, ranging from 0 (no detectable contraction) to 5 (full range of movement against maximum resistance). Scores were summed to give a total possible score of 50 for the upper extremities and 50 for the lower extremities. Previously, a total motor score of 100 for all extremities was calculated, but construct validity of the motor score as a measure of recovery following SCI and as an outcome measure for clinical trials, is greater when upper extremity and lower extremity are scored independently (182,183). Thus, the motor scores were separated into upper extremity (UEMS) and lower extremity motor scores (LEMS), each representing a maximal 50-point subset of the ASIA motor score (151).

3.3.1.2.2 Sensory assessment

Sensory scores were tested bilaterally using light touch and pin prick discrimination. A cotton tip applicator was used for light touch and either a pen tip or safety pin for pin prick. Appreciation of sensation at the key points representing each dermatome was made in comparison to sensation on the participant's cheek as a normal frame of reference. Pin prick and light touch sensation of each of the 28 points was separately scored on a 3-point scale (0, 1 and 2), with 2 representing normal sensation. Scores were summed to give a total possible score of 56 for pin prick and light touch respectively, resulting in a maximum possible sensory score of 112.

3.3.1.3 *Isometric dynamometry*

The peak isometric force of abdominal flexion (rectus abdominus) and back extension (erector spinae and latissimus dorsi) were measured using the abdominal attachment on the dynamometer (Biodex System3). Dynamometry set-up was standardized for each participant according to abdominal and leg length, with the dynamometric axis positioned at the third lumbar vertebral body to minimize error with

repeated measures (184). The participants' hips, thighs, knees, and upper body were firmly strapped into the dynamometer to prevent compensatory movements. Each individual had a standardised dynamic trunk warm up period prior to the start of the maximal voluntary contraction (MVC) trial. The warmup included three isometric contractions at 50, 70 and 90% of maximum contraction. The isometric strength tests included three MVCs of five seconds each, separated by two-minute rest intervals. During the MVCs, participants were verbally motivated and received post contraction feedback on the level of force generated to encourage them to reach their full potential in a subsequent attempt. MVCs were performed for abdominal flexion and back extension, with 10-minute rest period between the two protocols.

3.3.2 Endurance test

3.3.2.1 *6-Minute Arm Ergometry Test (6MAT) and Rating of Perceived Exertion (RPE)*

The 6-minute Arm Ergometry Test (6MAT) (Appendix 3.2) involved six minutes of submaximal exercise on a standard arm cycle ergometer at a constant power output. The aim was to attain a steady heart rate of 60% - 70% of age-predicted maximum heart rate. Set up of the arm ergometer was standardised for each participant according to their ergometer height and hand position. This test has proven to be a reliable and valid measure of cardiovascular fitness and upper body strength in individuals with SCI (185). The Borg Rating of Perceived Exertion (RPE) (Appendix 3.3) and the distance covered was recorded on completion of the test.

3.3.3 Walking test

3.3.3.1 *Spinal Cord Injury Functional Ambulatory Inventory (SCI-FAI)*

The SCI-FAI (Appendix 3.4) is an observational gait assessment instrument that includes timed (2-minute walk test) gait biomechanics, community ambulation and assistive device measures (186). It is the only SCI ambulatory outcome measure that includes an assessment of the quality of the gait pattern. Participants performed a 2-minute walk test with one of various levels of assistance (parallel bars,

walker, crutch, or cane) whilst being video recorded (1-minute lateral view, 1-minute anterior view). A blinded independent assessor retrospectively scored the video footage. The SCI-FAI is a reliable, valid and sensitive measure of walking ability in individuals with spinal cord injury (187). Gait analysis using this instrument is equally reliable whether the observation is performed live or from videotaped records (187). Outcome measures of this test included the distance walked, the technique score and the device score.

3.3.3.2 *6-Minute Walk Test (6MWT) and RPE*

Participants in the RLT group performed the 6MWT while secured in the exoskeleton. The 6MWT is a valid and reliable functional test (188) that can be used to determine the efficacy of the locomotor intervention and the functional status of the participant. The objective of the test was to cover as much distance as possible within a six-minute time frame. The 6MWT was standardised and performed exclusively in the 'Pro-Step adaptive' mode. The distance walked and the RPE was recorded directly after the test was completed.

3.3.4 Statistical analysis

All data were analysed using statistical software (R, R Core Team, Auckland, New Zealand and Prism 8, GraphPad Software Inc, California, USA). Normality of the data were assessed using the Shapiro-Wilks test. Linear mixed effect models assessed continuous responses for the parametric functional capacity outcomes and Mann Whitney U and Wilcoxon Signed Rank tests were used to determine the group and time main effects for the non-parametric outcomes (motor and sensory scores). Significance was accepted at a $p < 0.05$. Outliers in data were determined by model diagnostics to quantify the influence of an individual using Cook's distance plots and standardised DFBeta plots. If the individual altered the statistical significance of the data, this individual was considered an outlier and removed from the data. Magnitude-based inferences of change (effect size) were calculated according to Cohen's d. More details on these statistical methods can be found in Chapter 2 of this thesis.

3.4 Results

3.4.1 Participant characteristics

A total of 16 participants, aged 19 – 60 years (mean ± SD: 38.4 ± 14.3), with chronic (>1 year) traumatic motor incomplete SCI (C1-C8; ASIA C-D) were included in the trial (Table 3.1). RLT and ABT groups were statistically matched at baseline for age and time since injury. There was, however, a trend towards a lower time since injury in the ABT group (p = 0.10). Motor vehicle accidents accounted for 63% of injury aetiology in both groups, whilst stabbing, gunshot, rugby, motorcycle, mountain bicycle and diving accounted for 12.5% each. Only one female qualified for inclusion into the trial.

Table 3.1: Participant characteristics of the Robotic Locomotor Training and Activity-based Training groups.

Group	Participant	Age (years)	Time since injury (years)	Neurological level of injury	AIS category	Aetiology	Sex
RLT	1	27	9	C6	D	Stabbing	Male
	2	33	15	C6	C	MVA	Male
	3	32	3	C5	D	MVA	Male
	4	46	26	C4	D	Gunshot	Male
	5	55	4	C5	D	MVA	Male
	6	43	23	C6	C	MVA	Male
	7	56	15	C4	C	MVA	Male
	8	32	15	C7	C	Sport - Rugby	Male
	Average	40.5 ± 11.2	13.8 ± 8.2				
ABT	9	26	2	C6	C	MVA	Male
	10	46	20	C6	D	MVA	Female
	11	50	8	C7	D	MVA	Male
	12	19	2	C5	C	MVA	Male
	13	47	3	C4	D	Motorcycle	Male
	14	29	10	C5	C	MVA	Male
	15	60	2	C5	C	Mountain bike	Male
	16	30	11	C4	C	Diving	Male
	Average	38.4 ± 14.3	7.3 ± 6.4				

RLT: Robotic Locomotor Training (n = 8); *ABT*: Activity-based Training (n = 8); *MVA:* motor vehicle accident. Values quoted as mean ± SD. No significant difference between groups for age and time since injury (p = 0.10).

3.4.2 Participant adherence to the intervention

High levels of compliance were demonstrated by the participants. Participants had an average adherence of 93.9 ± 6.2% of all available sessions. The participant with the lowest adherence achieved 83.3%, whilst three participants achieved a 100% adherence rate. There was no statistical difference in the adherence rate between groups. Reasons for missing sessions were diverse (Fig. 3.1). Pathophysiological reasons such as bowel complications, urinary tract infections, baclofen pump complications and skin abrasions were localised to a few participants but occurred repetitively throughout the trial. Logistical reasons such as unreliable transport, work, personal and study commitments were more widely spread across participants. Only one session was interrupted by an exoskeleton malfunction.

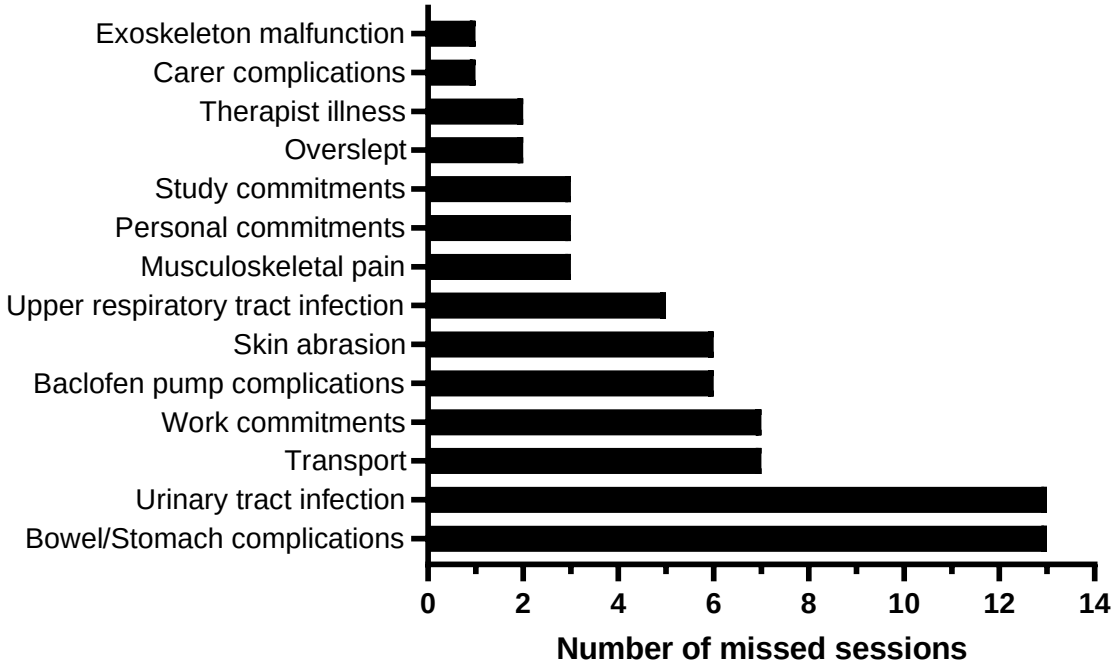

Figure 3.1: Reasons for missed rehabilitation sessions during the 24-week intervention.

Notes: Overall, 72 sessions missed of 1152 total – 6.25%.

Table 3.2 summarizes pre- and post-intervention functional capacity results for all participants separated into the RLT and ABT groups. Considerable variability was noted across the functional outcomes in response to the interventions, as indicated by the large standard deviations in Table 3.2. Effect sizes were calculated to demonstrate the clinical effects of the interventions between groups.

Table 3.2: A summary of functional performance characteristics between the Robotic Locomotor Training and Activity-based Training groups.

	RLT			**ABT**			***Effect size***	
Functional outcomes	*Pre*	*Post*	Δ *[95% CI]*	*Pre*	*Post*	Δ *[95% CI]*	*Pre*	*Post*
Right handgrip (kg)	11.42 ± 14.24	11.74 ± 14.60	0.31 [-1.67; 2.30]	4.26 ± 4.42	4.99 ± 5.33	0.72 [-0.70; 2.15]	0.67	0.61
Left handgrip (kg)	8.49 ± 13.40	8.85 ± 14.39	0.36 [-1.83; 2.55]	5.79 ± 5.99	7.09 ± 5.74	1.30 [-0.83; 3.45]	0.26	0.16
UEMS	31.00 ± 11.00	33.00 ± 10.00	2.12 [0.87; 3.38]	28.00 ± 10.00	30.00 ± 10.00	1.75 [-1.21; 4.71]	0.29	0.30
LEMS	16.00 ± 11.00	19.00 ± 14.00	3.75 [0.09; 7.41]	16.00 ± 13.00	18.00 ± 14.00	2.50 [-0.20; 5.20]	0.00	0.07
Pin prick sensory score	82.00 ± 14.00	87.00 ± 16.00	5.25 [-6.52; 17.02]	66.00 ± 16.00	70.00 ± 17.00	4.00 [-0.24; 8.24]	**1.06**	**1.03**
Light touch sensory score	83.00 ± 16.00	88.00 ± 19.00	4.88 [-1.63; 11.38]	79.00 ± 28.00	81.00 ± 26.00	1.62 [-1.34; 4.59]	0.18	0.31
Abdominal flexion (Nm)	11.75 ± 8.89	18.79 ± 18.14	3.52 [-4.83; 1.86]	10.98 ± 10.03	20.82 ± 12.54	9.84 [1.03; 18.65]	0.08	0.13
Back extension (Nm)	44.14 ± 32.87	68.21 ± 76.52	24.07 [-14.15; 62.29]	47.19 ± 29.93	78.55 ± 66.16	16.99 [-3.26; 37.13]	0.10	0.14
6MAT distance (km)	1.05 ± 0.66	1.11 ± 0.66	0.06 [-0.05; 0.16]	1.04 ± 0.61	1.18 ± 0.60	0.14 [0.00; 0.29]	0.02	0.11
6MAT RPE	15.25 ± 2.87	16.88 ± 2.17	1.62 [-0.03; 3.28]	14.88 ± 2.10	13.88 ± 3.80	-1.00 [-3.72; 1.72]	0.15	**0.97**
SCI-FAI distance (m)	2.57 ± 5.18	3.54 ± 5.84	0.98 [-0.57; 2.52]	3.12 ± 5.30	10.17 ± 13.31	7.05 [1.24; 12.87]	0.10	0.65
SCI-FAI technique score	5.00 ± 5.73	8.00 ± 6.74	3.00 [0.06; 5.94]	6.38 ± 7.25	8.25 ± 8.89	1.88 [0.16; 3.59]	0.21	0.03
SCI-FAI device score	2.50 ± 2.98	3.00 ± 2.83	0.50 [-1.11; 2.11]	3.50 ± 3.82	4.00 ± 4.41	0.50 [-0.14; 1.14]	0.29	0.27
6MWT distance (m)	68.33 ± 11.30	109.92 ± 19.67	41.60 [22.63; 60.57]	-	-	-	-	-
6MWT RPE	13.88 ± 2.53	13.38 ± 2.92	-0.50 [-2.56; 1.56]	-	-	-	-	-

RLT: Robotic Locomotor Training group (n = 8); *ABT:* Activity-based Training group (n = 8); *kg;* kilograms; *UEMS:* upper extremity motor score; *LEMS:* lower extremity motor score; *motor and sensory score;* ISNCSCI (ASIA) Impairment Scale (AIS); *Nm;* newton meters; *6MAT:* 6-Minute Arm Ergo Test; *km;* kilometres; *RPE;* rating of perceived exertion; *SCI-FAI;* Spinal Cord Injury Functional Ambulatory Index; *m:* meters; *6MWT:* 6-Minute Walk Test*; Pre:* week 0 measurement; *Post:* week 24 measurement. Data presented as mean ± SD; Δ *(95% CI):* mean difference ± 95% confidence interval. Effect sizes (ES) between ABT and RLT groups at pre- and post-intervention: Bold represents a large effect size. - indicates not applicable.

3.4.3 Strength capacity

3.4.3.1 *Handgrip strength*

There were no significant differences between groups for left and right handgrip strength, with p-values of 0.96 (ES = 0.16) and 0.64 (medium ES = 0.61) respectively. No significant changes from pre to post intervention were detected for either group, with a change of 0.31 Kg and 0.32 Kg for right-sided grip strength, and 0.36 Kg and 1.30 Kg for left sided grip strength for the RLT and ABT group, respectively.

3.4.3.2 *International Standards for Neurological Classification of Spinal Cord Injury (ISNCSCI) impairment scale*

3.4.3.2.1 Motor scores

There were no significant motor score differences between the ABT and RLT groups for LEMS (p = 0.75; ES = 0.07). However, only the RLT group showed a significant change in LEMS from pre (16.00 ± 11.00) to post intervention (19.00 ± 11.00) (p = 0.05) with a mean increase of 3.75 [0.09; 7.41] points post intervention (Fig. 3.2).

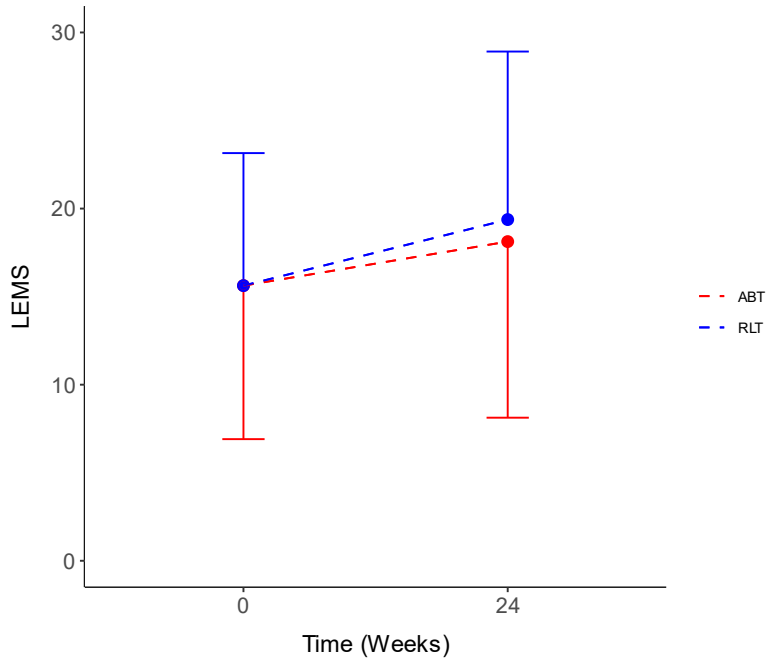

Figure 3.2: Lower extremity motor scores for the Robotic Locomotor Training and Activity-based Training groups at baseline and week 24.

RLT: Robotic Locomotor Training (n = 8); *ABT*: Activity-based Training (n = 8); *LEMS*: lower extremity motor score measured in ASIA exam. Data presented as observed mean ± half-width 95% CI. Modelled linear estimates shown as superimposed lines (predicted mean).

There were no significant motor score differences between the ABT and RLT groups for UEMS (p = 0.9; ES = 0.30). However, the RLT group showed a significant change in UEMS from pre (31.00 ± 11.00) to post (33.00 ± 10.00) (p = 0.03) intervention, with a mean difference of 2.12 [0.87; 3.38] points post intervention (Fig. 3.3).

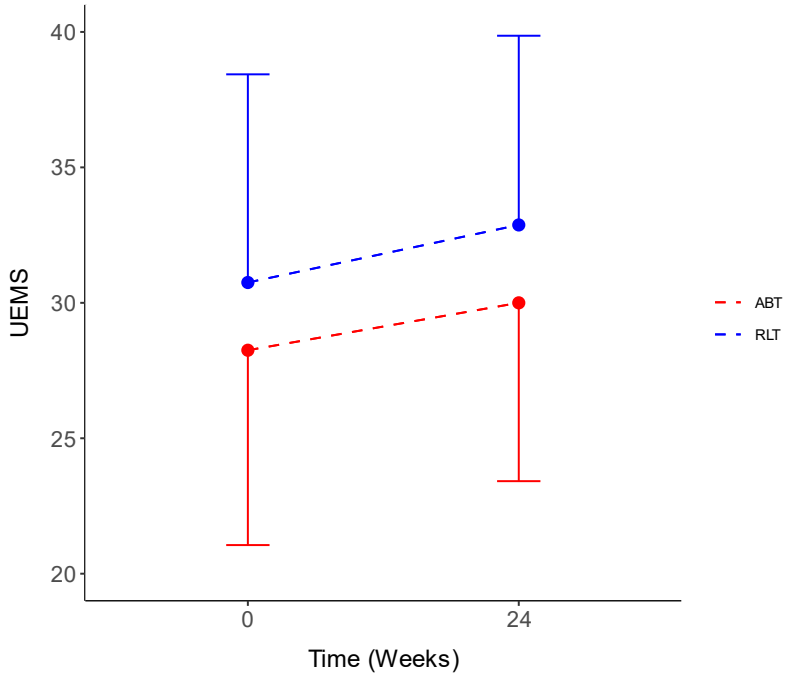

Figure 3.3: Upper extremity motor scores for the Robotic Locomotor Training and Activity-based Training groups at baseline and week 24.

RLT: Robotic Locomotor Training (n = 8); *ABT*: Activity-based Training (n = 8); *UEMS*: upper extremity motor score measured in ASIA exam. Data presented as observed mean ± half-width 95% CI. Modelled linear estimates shown as superimposed lines (predicted mean).

A proportion of 69% (n = 11) of the total participants showed an increase in LEMS from pre to post intervention (Fig. 3.4A). Within each group respectively, 75% (n = 6) of the participants experienced an improvement in LEMS over time, with one individual in the RLT group achieving as much as a 15-point difference over the 24 weeks (Fig. 3.4A). Similarly, 69% (n = 11) of the participants experienced an increase in UEMS score over time, with six individuals showing improvements in the ABT group and five in the RLT group (Fig. 3.4B). Interestingly, no individuals in the RLT group experienced a decrease in UEMS score (3 individuals showed no change in score) compared to the ABT group in which two individuals decreased in score, with one individual declining by 6 points post intervention.

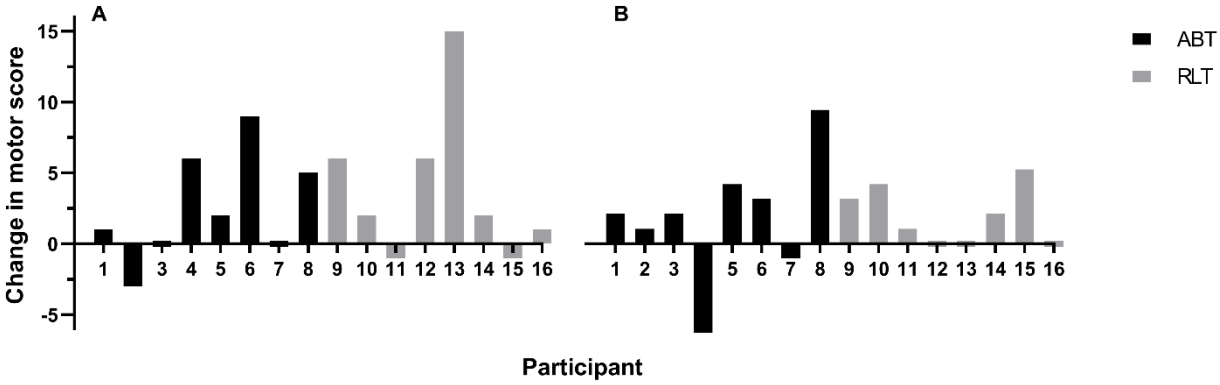

Figure 3.4: Individual participant (n = 16) changes in A) lower extremity motor score and B) upper extremity motor score from pre to post intervention.

RLT: Robotic Locomotor Training group (n = 8); *ABT:* Activity-based Training group (n = 8); *Change in motor score:* difference between pre (week 0) and post (week 24) score; *UEMS:* upper extremity motor score; *LEMS:* lower extremity motor score.

3.4.3.2.2 Sensory scores

No statistically significant differences in sensory scores were evident between the groups or over time. Pin prick scores did however demonstrate large effect sizes between groups at baseline (ES = 1.06) and 24 weeks (ES = 1.03). Effect size estimates thus suggest that the RLT group had larger sensory scores at baseline (82.00 ± 14.00) and 24 weeks (87.00 ± 16.00) in comparison to the ABT group (baseline: 66.00 ± 16.00; 24 weeks: 70.00 ± 17.00). Despite neither intervention resulting in statistically significant changes over time, several participants within both groups experienced improvements in sensory scores (Fig. 3.5). A clear pattern of responders versus non-responders was evident in sensory scores with eight participants showing no changes in pin prick score and seven participants showing no changes in light touch sensation. Interestingly, it appears that the RLT group was more responsive to sensory alterations compared to the ABT group (Fig. 3.5), which was highlighted by the large effect sizes (Table 3.2). However, sensation over time decreased in two participants in the RLT group, with P14 showing a decrease of 25 points for pin prick score and P12 by 9 points for light touch score.

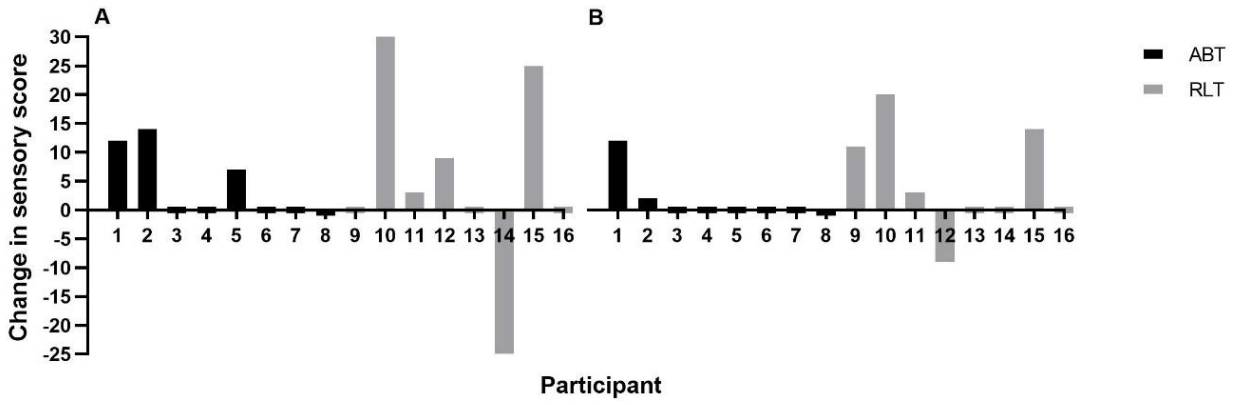

Figure 3.5: Individual participant (n = 16) changes in A) Pin prick and B) Light touch sensory scores from pre to post intervention.

RLT: Robotic Locomotor Training group (n = 8); *ABT:* Activity-based Training group (n = 8); *Change in sensory score:* difference between pre (week 0) and post (week 24) score; *A:* Pin prick sensory score; *B:* Light touch sensory score.

3.4.3.3 *Abdominal and back strength*

There were no significant group differences for back extension (p = 0.90; ES = 0.14) or abdominal flexion strength (p = 0.30; ES = 0.13). Although non-significant, there was a trend towards an increase (p = 0.08) in back strength over time for the RLT and ABT group, with improvements of 24.07 [-14.15; 62.29] and 16.99 [-3.26; 37.13] Nm from pre to post intervention, respectively (Fig. 3.6). There was also a significant change in abdominal strength from pre to post intervention (p = 0.02), with a mean increase of 3.52 [-4.83; 1.86] Nm and 9.84 [1.03; 18.65] Nm for the RLT and ABT group, respectively (Fig. 3.7). The large range in torque scores from 0.05 – 53.12 Nm and 0.44 – 238.25 Nm for overall abdominal strength and back strength respectively, indicate the high variability in response to training.

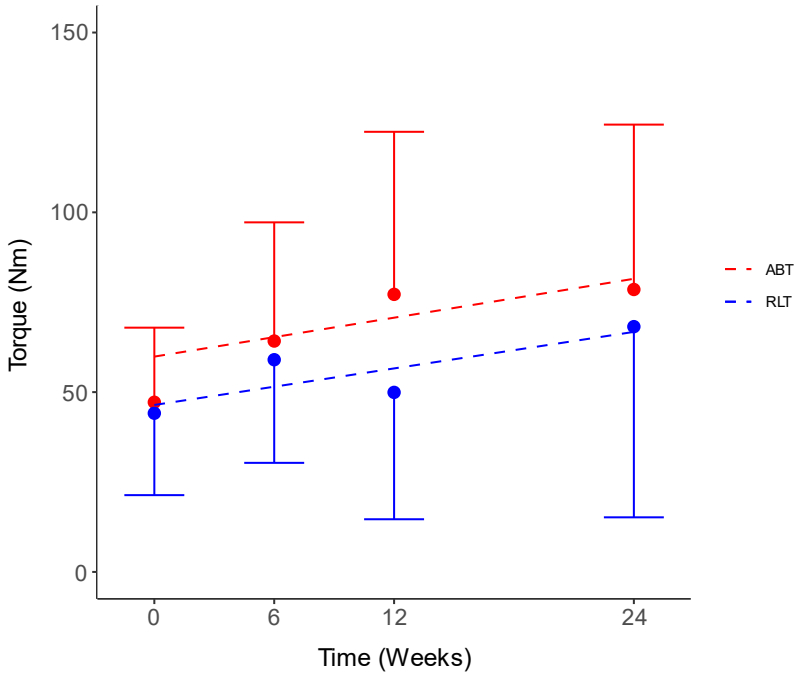

Figure 3.6: Back strength produced during extension for the Robotic Locomotor Training and Activity-based Training groups over time.

RLT: Robotic Locomotor Training (n = 8); *ABT*: Activity-based Training (n = 8); *Torque*: measured in Newton-meters (Nm). Data presented as observed mean ± half-width 95% CI. Modelled linear estimates shown as superimposed lines (predicted mean).

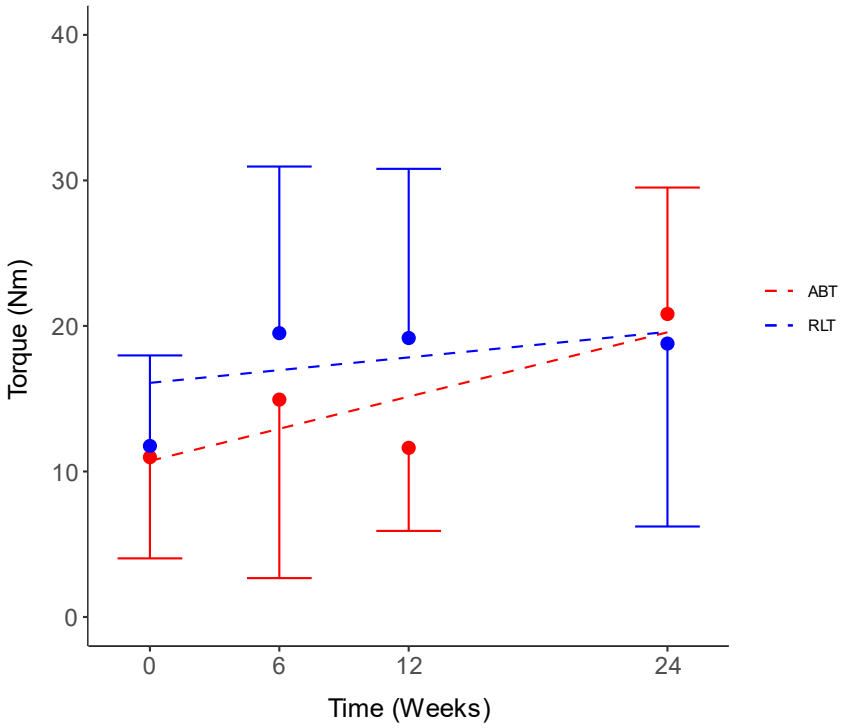

Figure 3.7: Abdominal strength produced during flexion for the Robotic Locomotor Training and Activity-based Training groups over time.

RLT: Robotic Locomotor Training (n = 8); *ABT*: Activity-based Training (n = 8); *Torque*: measured in Newton-meters (Nm). Data presented as observed mean ± half-width 95% CI. Modelled linear estimates shown as superimposed lines (predicted mean).

3.4.4 Endurance capacity

3.4.4.1 *6-Minute Arm Ergo (6MAT)*

There were no significant differences between the ABT and RLT groups for 6MAT distance (p = 0.20; ES = 0.11). Although non-significant, there was a trend towards increased distance over time for both groups (p = 0.09). Categorical analysis of the time points showed that a significant improvement in distance was achieved for the ABT group from baseline to week six (p = 0.03). However, thereafter, no significant improvements were noted for either group over time. There were no significant between-group (p = 0.15) or time differences (p = 0.30) in 6MAT RPE for the ABT and RLT groups. However,

a large effect size did indicate a clinically relevant difference between groups at week 24 (ES = 0.97). Thus, the perception of effort to complete the test was greater over time for the RLT group, with an increased RPE rating of 1.62 [-0.03; 3.28] compared to the decreased rating of the ABT group of -1 [-3.72; 1.72] over time (Fig. 3.8).

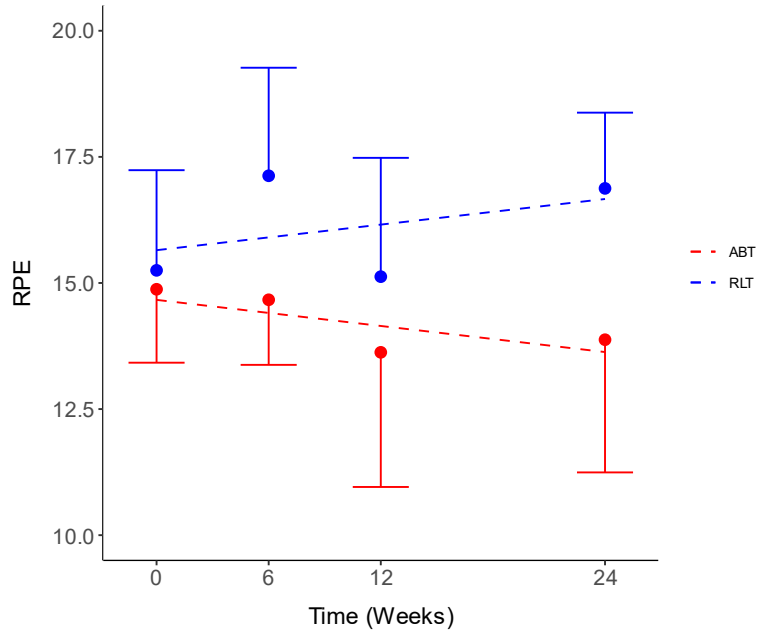

Figure 3.8: Rating of perceived exertion for the Robotic Locomotor Training and Activity-based Training groups over time.

RLT: Robotic Locomotor Training (n = 8); *ABT*: Activity-based Training (n = 8); *RPE:* rating of perceived exertion during the 6MAT test, measured with Borgs Scale. Data presented as observed mean ± half-width 95% CI. Modelled linear estimates shown as superimposed lines (predicted mean).

3.4.5 Walking capacity

3.4.5.1 *Spinal Cord Injury Functional Ambulatory Inventory (SCI-FAI)*

There were no significant between-group differences for the ABT and RLT groups over time for distance walked (medium ES = 0.65). However, there was a significant improvement in distance walked in the SCI-FAI test over time (p =0.02), with an increase of 0.98 [-0.57; 2.52] m and 7.05 [1.24; 12.87]

m for the RLT and ABT group, respectively. The larger mean difference reported in the ABT group may be due to the outlier (participant 5) within this variable. P5 in the ABT group walked substantially further than all the other participants across all time points, with a maximum walking distance of 50 m compared to the others who scored between 0 and 25 m during the interventions (Fig. 3.9). When this outlier was removed from the summary statistics, the average distance walked in the ABT group was 1.51 ± 2.91 at baseline and 7.74 ± 9.83 post intervention. Thus, the mean difference between pre- and post-intervention distance was 6.23 m when the outlier was removed compared to the 7.05 m when the outlier was included in the calculation. The removal of the outlier resulted in no significant difference in pre- and post-SCI-FAI distance in the ABT group ($p = 0.47$). It is relevant to note that six ($n = 4$ ABT; $n = 2$ RLT) of the 16 participants were non-ambulatory from baseline and continued to be so for the length of the intervention. However, two participants in the RLT group who were non-ambulatory at baseline, both managed to achieve an improved distance of 2.44 m and 0.82 m by week 24. SCI-FAI device score and technique score remained unchanged for both interventions over time ($p = 0.43$ and 0.15) (Table 3.2). However, a single participant in the ABT group progressed from walking in the parallel bars to using a walker frame by week 24.

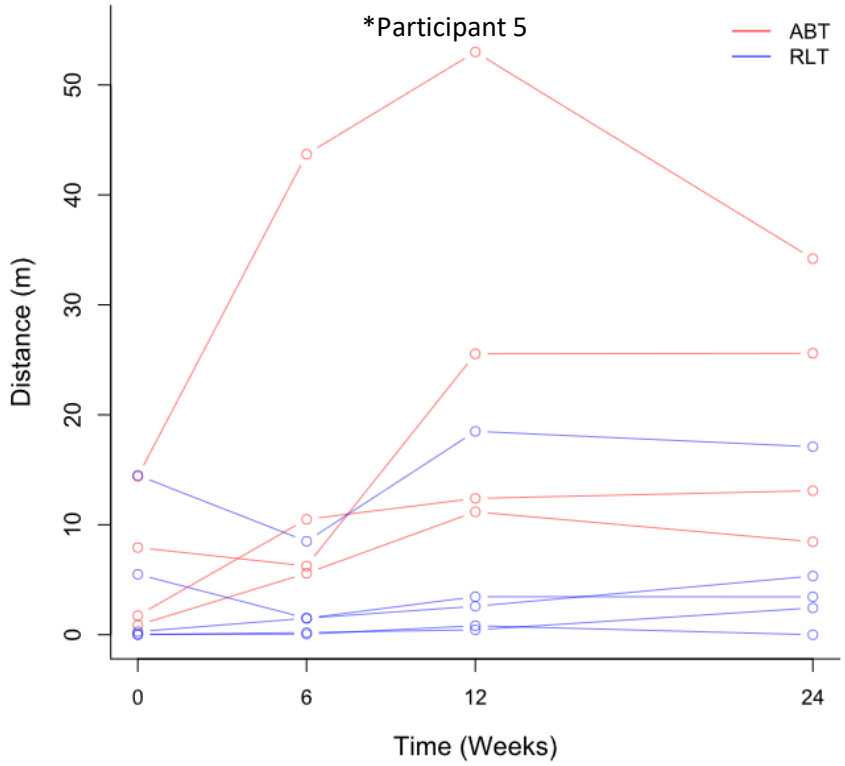

Figure 3.9: Individual participant (n = 16) SCI-FAI distance in the Robotic Locomotor Training and Activity-based Training groups over time.

RLT: Robotic Locomotor Training (n = 8); *ABT*: Activity-based Training (n = 8); *Participant 5:* single individual in the ABT group; *Distance:* measured in meters.

3.4.5.2 *6-Minute Walk Test (6MWT)*

No group comparisons could be made for the 6MWT, as only the RLT group performed this test in the robotic suit. There was a significant increase in distance walked over time ($p < 0.01$) (Fig. 3.10), with a mean increase of 41.60 [22.63; 60.57]m from pre to post intervention. Interestingly, no significant change in RPE was reported ($p = 0.79$) over time for this test.

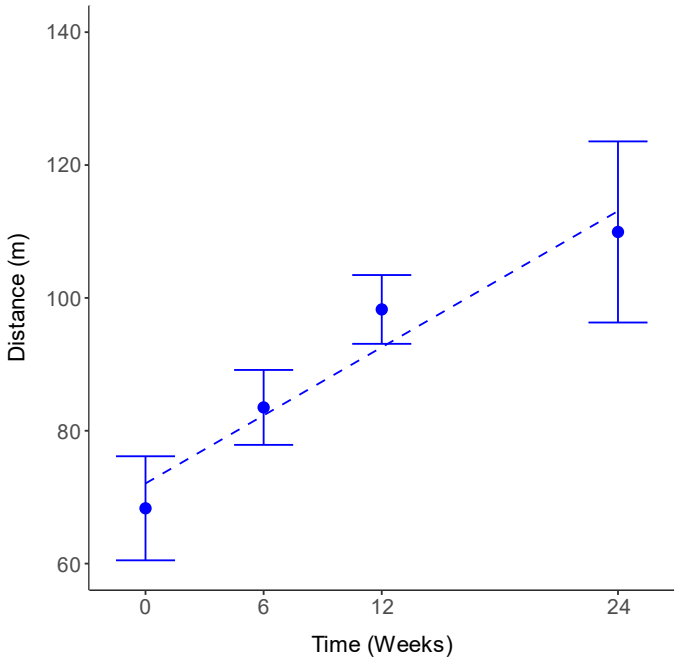

Figure 3.10: Distance walked during the 6-Minute Walk Test for the Robotic Locomotor Training group over time.

RLT: Robotic Locomotor Training (n = 8); *6MWT*: 6-Minute Walk Test; *m:* meters. Data presented as observed mean ± 95% CI. Modelled linear estimates shown as superimposed line (predicted mean).

3.5 Discussion

This randomized pilot study explored the effects of RLT in comparison to ABT on functional capacity in people with chronic incomplete SCI. Both RLT and ABT lead to functional improvements after SCI. However, the RLT group observed pre- to post improvements in a larger number of functional outcomes, which may suggest a potentially greater impact of treatment with the robotic exoskeleton on functional status. Thus, the results of this novel trial support the clinical effectiveness of RLT in improving functional capacity in individuals with SCI, as RLT had a significant effect on individual's upper and lower extremity motor scores, sensory scores, and ambulatory function. However, both RLT and ABT showed significant increases in trunk strength and arm ergo distance over time. In the following, we discuss the main findings with respect to each of these aspects.

3.5.1 Muscle strength

3.5.1.1 *Lower extremity motor score (LEMS)*

There were no between-group differences for LEMS in this study (ES = 0.07). A key finding of this study was that the participants in the RLT group experienced a significant increase in LEMS, with a mean change of 19% over time. Buehner et al. (2012) agree with these findings, after they evaluated motor outcomes after six months of RLT in adults with chronic incomplete SCI (ASIA C) (147). Locomotor training induced a significant 21% improvement in LEMS ($P < 0.001$) post intervention (147). Another study by Khan et al. (2019) involved 12 participants with chronic (> 1 year) motor complete or incomplete SCI, who were trained in the ReWalk for 12 weeks. Two out of the three participants with motor incomplete injuries showed clinically meaningful improvements in ASIA muscle strength for lower extremities (189). Increases in muscle strength are likely attributed to increased muscle fibre regeneration, increased muscle cross-sectional area and an increased ability to voluntarily activate affected skeletal muscles due to improved motor unit activation (50,137,190). However, motor recovery is dependent on the intensity, task specificity and goal-orientated approach of the training method, with overload and specificity being key principles for success (50,141,145,191).

Overload states that for an effect of training to occur, a system or tissue must be challenged with an intensity, duration, and frequency of exercise to which it is not adjusted. The principle of specificity indicates that the training effect is limited to the system and tissues involved in the activity (141). As RLT was more ambulatory- specific and involved more repetitive movement compared to the ABT intervention, lower limb strength may have been targeted more effectively in this group. Harness et al. (2008) suggests that the amount of time spent load bearing has a significant relationship with LEMS (131). This is perhaps also indicative of why the RLT group showed significant changes in LEMS, as the amount of time spent load bearing was greater than the ABT group. Additionally, Kloosterman et al. (2009) has suggested that feedback about performance (augmented and intrinsic) is the single most important variable for motor learning (141). Therefore, the afferent cues provided through

proprioceptive and auditory feedback during RLT may have stimulated lower-extremity activity and increased neural pathways for the RLT group. By providing spatial auditory biofeedback for the lateral and forward weight-shifting movements while using the exoskeleton, the participants may have become more aware of their body's position in space through improved sensorimotor integration (192). Thus, cues given by both the device as well as verbal feedback on step count and level of assistance from the therapist, could have aided in improving motor learning for the RLT group compared to the ABT group. Several sociodemographic factors and injury related characteristics including age, sex, race, level and severity of neurologic impairment, and time since injury can also influence motor recovery and capacity (58,139,141,191,193). Given that neural plasticity is most prominent in the first several years post injury, it is important to note that the ABT group has a trend towards shorter time since injury compared to the RLT group. Although not statistically different, the shorter time since injury in the ABT group may be a contributing factor to the improvements seen in the functional capacity of this group. Deeper analysis into this relationship should be performed in future investigations.

3.5.1.2 *Upper extremity motor score (UEMS)*

There were no between-group differences for UEMS in this study (ES = 0.30). However, the RLT group displayed significant increases in UEMS over time, whereas the ABT group experienced no improvements in UEMS throughout the trial. To our knowledge, no research into UEMS after lower limb RLT has been documented. However, evidence suggests that the exercise training must be intensive and task-specific in order to drive the neuroplastic changes required for restoration of targeted functional skills (132,194). Thus, it is quite surprising that the RLT group experienced improvements in upper limb strength, as robotic training is focused solely on the lower limbs for walking function. However, these changes in UEMS after RLT may be attributed to the fact that locomotor training requires active participation from the user to move and use a gait aid while maintaining standing balance.

ABT interventions have shown mixed effects on upper extremity function in individuals with chronic SCI (141,146). Significant improvements in upper extremity strength were reported by Hicks et al. (2003) with a twice weekly standardized arm exercise protocol (195) and clinical observations by Ginis et al. (2012) found that resistance training for 12 weeks, once per week, resulted in a 60-320% increase in muscular strength for different upper extremity muscle groups (196). The results of these studies demonstrate that participation in intensive and regular resistance training may produce significant increases in muscular strength in people with SCI. However, no significant changes in upper limb strength were reported by the ABT group in the current study. A lack of strength improvements was also reported by Jayaraman (2013) who found that conventional progressive resistance exercise did not show any differences in strength measures following training (190). Consideration should be given to the specificity and overload of the ABT training programme in order to provide reason for a lack of statistical change post intervention (132). Due to the diversity of exercises available within ABT, which includes upper and lower resistance training, core stability exercises, crawling, standing posture and walking function, training was possibly not specific enough to the upper body to induce significant UEMS changes.

3.5.1.3 *Abdominal and back strength*

There was no between-group difference in isometric trunk strength within this study. However, there was a significant change in abdominal strength from pre to post intervention for both the RLT and ABT group. A non-significant trend towards an increase in back strength was also shown over time for both groups. Thus, these results indicate that 24 weeks of an exercise intervention can produce back and abdominal strength improvements for people with SCI, but differences between exercise types (RLT vs ABT) could not be determined. The effects of RLT on abdominal and back strength are currently unknown, to our knowledge no RLT studies have reported on these outcomes.

However, in able-bodied individuals, the trunk muscles are rhythmically activated during walking to maintain upper body steadiness (197). Similarly, RLT requires active participation from the user to shift

their centre of mass forward and laterally in order to trigger the initiation of each step and to maintain an erect posture (197,198). It should be expected, therefore, that the alternating weight-shifting and standing balance required in the exoskeleton could help build and re-train the trunk musculature in people with SCI (197). This increase could also be brought about by strengthening of the existing muscle fibres and their firing rates. Thus, the increased trunk strength facilitated by RLT may be responsible for the higher torque produced during the isometric abdominal and back extension tests after 24 weeks of training. Not only are RLT studies on core and back strength limited, but to our knowledge, no other ABT studies have used dynamometry to test abdominal and back strength in individuals with SCI.

Only one study by Petrosky et al. (2005) investigated these strength measures in a SCI population, but they used another testing method; a strain gauge force sensor (199). They examined back and core strength in 14 participants with disabilities, including seven with paraplegia, before and after one month of training using three abdominal exercises and one lower back exercise accomplished from a wheelchair. The average strength increased by 72% ($p < 0.01$) in the abdominal muscles and 62% ($p < 0.01$) in the back muscles from pre to post training. Furthermore, dynamic trunk control is a well-known requirement for successful gait performance (198) and is essential for stability during sitting and to perform other daily functional activities (200). Therefore, participants in the ABT group would also have needed to engage the trunk muscles during walking to maintain postural stability and standing balance. This focus on improving trunk control is evident in our study, with the ABT group's improved abdominal and back strength post intervention.

3.5.2 Endurance capacity

3.5.2.1 *6-Minute Walk Test (6MAT)*

This study showed that after 24 weeks of either ABT or RLT training, there was a trend towards improved 6MAT distance. Improved arm ergometry distance relies on both an increase in muscle strength as well as muscle endurance in order to produce force over multiple repetitions for the required

six minutes (132). Similar improvements in endurance capacity were reported by Jacobs et al. (2001) who showed that individuals with paraplegia were able to improve their upper limb endurance by 29.7% after completing a circuit training exercise programme for 12 weeks (166). A similar study found that individuals who participated in a programme which consisted of ABT twice per week for nine weeks, showed a significant increase of 81% in submaximal arm ergometer power output compared to a control group that did not participate in exercise (111). Improved endurance performance after training is likely due to neural adaptations, as resistance training is generally not associated with increases in capillary density, which suggests that oxygen diffusion and delivery in the working musculature remains at pre-training values (145).

There were no changes in RPE over time within this study possibly due to the varying degrees of autonomic incompetence for people with SCI. When responding to exercise, individuals with SCI may have higher heart rate and oxygen consumption than people without SCI when exercising at the same work intensities. Therefore, the unique physiologic responses to activity of SCI individuals may challenge the use of the Borg Scale as a valid tool for assessing their integrated exertional responses (201). Other factors such as loss of sensation, physical imbalance during exercise, and level of conditioning might also disrupt the interaction between somatic cues and physiologic responses to physical exertion that form the foundation of the Borg RPE model (201).

3.5.3 Ambulatory function

3.5.3.1 *SCI-FAI and 6-Minute Walk Test (6MWT)*

This study showed no significant between-group differences for the ABT and RLT groups over time for walking capacity. However, there was a significant improvement in distance walked in the SCI-FAI test for the RLT group, with an increase of 0.98 m from pre- to post intervention. The removal of the outlier, P5 (ABT group), resulted in no significant difference in pre- and post-SCI-FAI distance in the ABT group. Additionally, the two participants in the RLT group who were non-ambulatory at baseline,

both managed to become ambulatory after training, with achievements of 2.44 m and 0.82 m by 24 weeks, whereas the four non-ambulatory individuals in the ABT group remained so throughout the intervention.

The 6MWT also indicated a clear increase in ambulatory function within the exoskeleton over time, with a significant change of 41.60 m walked for the RLT group from pre to post intervention. Studies of locomotor training have demonstrated that recovery of walking and balance function can occur for individuals months and even years after incomplete SCI (58,202). Restoration of motor function is based on the fundamental concept that repeated execution of motor tasks induces plasticity and functional and structural reorganization of neuronal circuits in the injured spinal cord (203–205). Thus, four mechanisms have been proposed to explain how RLT may assist in gait recovery of those with SCI: 1) providing external proprioceptive cues, 2) enhancing the automatic spinal control of locomotion, 3) improving postural control during walking and 4) promoting reconditioning and muscle strengthening of the lower limbs (55). The learning effect of walking must also be considered for improvements in walking capacity, as functional activities can also be improved by learning and using compensatory strategies (141).

Several studies suggest that there are conflicting results for the training potential of robotic devices and there is no compelling evidence that robot-assisted gait re-education improves walking function more than other rehabilitative strategies (66,203,206). Some studies have reported improvements in walking abilities in incomplete SCI participants with the use of RLT (95,207–209) while other studies have found that RLT does not determine better outcomes than traditional ABT rehabilitation (169,210). Our preliminary findings from this pilot study have shown RLT to improve ambulatory function in more participants compared to the ABT. Therefore, larger RCTs are recommended to confirm these results.

3.5.4 Limitations

As the functional status of the same AIS category SCI has been shown to be highly variable, perhaps alternatives to subject enrolment based on AIS category should have been considered. Other methods to achieve homogeneity of the SCI participants have been suggested, including stratification by LEMS or by initial ability to walk (211). Another limitation was the need to standardize the ABT programme for purposes of the clinical trial. In practice, ABT tends to be highly individualized based on functional abilities, exercise limitations and preferences of the participant. This degree of individualization in a clinical trial would lead to virtually uninterpretable results, we therefore standardized the therapy as best as possible, according to the Therapy and Beyond guidelines. Although this standardization may have limited the potential impact of ABT compared with its use in clinical practice, it did yield valid information about the effects of ABT more generally. These limitations need to be considered when designing future RCTs with larger samples and intervention durations.

3.5.5 Conclusion

The results of this trial offer promising evidence for the effectiveness of RLT for improving functional capacity in people with incomplete SCI. RLT appeared to induce larger pre- to post intervention changes in strength for the upper and lower limbs, and increased ambulatory function compared to the ABT group. Although neither group showed significant changes in sensation post intervention, it appears that the RLT group was more responsive to sensory alterations. However, neither intervention was superior regarding changes in trunk muscle strength, with both ABT and RLT groups experiencing improvements in abdominal and back torque production. This trial highlights the possibility that RLT can ameliorate the loss of function secondary to disuse or lack of neuromuscular activity in persons with SCI. The results offer encouraging evidence that RLT interventions can be implemented within a clinical setting to promote recovery of both strength and ambulatory function in individuals with incomplete chronic SCI. These preliminary data highlight the possibility of neuroplasticity after an incomplete SCI, and that rehabilitation needs to focus not just on compensation for impairment but on maximizing the person's potential for functional capacity recovery. Restoring functional ability will lead to an equivalent increase in independence, and in turn, will have a profoundly positive effect on

the adverse psychological, social, and economic factors associated with the SCI population. However, future large-scale RCTs should be performed in order to substantiate the preliminary results of this trial.

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CHAPTER 4

More than paralysis: The secondary complications of chronic spinal cord injury during ABT and RLT interventions

4.1 Introduction

SCIs often result in functional impairments due to the physical deconditioning across the musculoskeletal and cardiovascular systems (1). In the previous chapter, we showed that RLT could potentially be used as a rehabilitation modality to improve physical strength and walking capacity in those with SCI. However, aside from these functional capacity outcomes, another key intention of SCI rehabilitation is to minimise and prevent secondary health complications. These secondary complications include pain, spasticity, neurogenic bladder and bowel, urinary tract infections, pressure sores, orthostatic hypotension, autonomic dysreflexia, osteoporosis, respiratory and cardiovascular concerns, obesity and diabetes (1,16,17). In a prospective, South African-based cohort study, the prevalence of selected secondary medical complications showed that a total of 50.3% of acute SCI individuals had one or more secondary complications (9). By neurological level, the mean number of complications per individual was 1.0, 0.8 and 0.3 for those with cervical, thoracic and lumbar lesions, respectively (9).

These secondary health complications are a frequent cause of morbidity and mortality for individuals with SCI and can lead to increased rates of rehospitalization, loss of employability and social engagement and decreased QoL (16). Thus, secondary complications place a significant burden on health care systems when compared with the general population due to rehospitalizations, long-term care admissions, home care services and physician contacts (21). In the study conducted by Mothabeng (2011), 48% of the participants were re-admitted due to one or more secondary complications associated with SCI (30). Being readmitted to hospital can undermine rehabilitation gains, as once individuals are readmitted, additional therapy is often required to regain strength, endurance and physical function which may be lost whilst hospitalized (21). Rehospitalization can also be very disruptive to

psychological well-being and diminish an individual's ability to live actively and independently (212). Secondary conditions are associated with reduced odds of job retention and acquisition due to interruptions with work, education and interpersonal relationships (21). Management of secondary complications thus increases care needs and utilisation of healthcare resources (213).

Therefore, the prevention of secondary complications is a fundamental goal of rehabilitation management within the SCI population. Despite the prevalence of these complications in the SCI population, they are not always managed effectively and the evidence for physical rehabilitation treatments is limited (213). This chapter will focus on three most common secondary complications experienced in SCI namely, spasticity, pain and bladder and bowel function.

4.1.1 Spasticity

Damage to the upper motor neurons within the central nervous system can cause intermittent or sustained involuntary activation of muscles, known as spasticity (1,213). Spasticity is a common symptom of neurological damage with chronic SCI, affecting approximately 70% of individuals (1,16,214,215). It has been suggested that the American Spinal Injury Association (ASIA) classification of SCI (severity) and level of injury may predict the likelihood of developing spasticity (214). In individuals with cervical SCI, 93% of those diagnosed as ASIA A and 78% of those diagnosed as ASIA B–D reported having symptoms of spasticity, whereas in individuals with thoracic SCI, 72% of those diagnosed as ASIA A and 73% of those diagnosed as ASIA B–D reported symptoms of spasticity. The greater incidence of upper motor neuron injury associated with higher-level injuries results in an increased tendency for spasticity development in these individuals (214).

Spasticity has the potential to cause significant physical disability and reduce QoL by restricting ADLs, inhibiting effective walking and selfcare, causing pain and fatigue, disturbing sleep, contributing to the development of contractures, reducing self-image as well as complicating the role of the caretaker and rehabilitation efforts (214,215). Despite the potential negative impacts, symptoms of spasticity can

sometimes assist functioning by increasing stability in sitting and standing, facilitating the completion of activities and transfers, increasing muscle bulk and increasing peripheral circulation (16,213). These possible benefits of spasticity can reduce the risk of other secondary complications, such as muscle atrophy, oedema and osteopenia and reduce cardiovascular risk factors including deep vein thrombosis (214,215). Therefore, management of spasticity requires a comprehensive approach involving a multidisciplinary team in which the benefits of treatment are weighed against the possible usefulness of the spasticity (213,214,216).

One such treatment approach is physical therapy, which plays an essential role in the initial treatment of spasticity as well as in the long-term routine of SCI care (216). Regular standing and active exercises have both shown improvements in passive range of movement, posture, circulation, muscle strengthening and reduced stress and fatigue, which in turn aid in reducing spasticity symptoms (17). Both static and active standing may increase inhibition of the stretch reflex, reduce motor neuron excitability and subsequently reduce spasticity in individuals with SCI (17,46,217).

4.1.2 Pain

Chronic pain is a common secondary complication for up to 80-90% of individuals with SCI (16,106,111,215). Pain is reported to be severe and/or disabling in 30%–40% of these individuals, affecting their physical functioning beyond levels attributable to the SCI (111). Pain is also ranked as one of the most disabling consequences of SCI, as it severely interferes with daily activities and independence, community participation, sleep and quality of life (1,16,218). Pain management in people with SCI is complex and usually requires a multifaceted approach involving a variety of therapeutic strategies (106,218,219). One of the most commonly reported treatment methods for reducing pain is physical therapy, including exercise, stretching and various other physical modalities (219,220). Perceptions of pain play a large role in exercise adherence in individuals with SCI. Therefore, pain relief may not only improve functioning and QoL, but it may also increase the likelihood of

exercise adherence in individuals with SCI and in turn, potentially alleviate many of the secondary health complications associated with SCI (218,221).

4.1.3 Bladder and bowel function

Bladder and bowel function are perceived as one of the top priorities for functional recovery for the general SCI population (143,222). Bladder complications include reduced capacity, poor voiding and increased incontinence (223). Bowel dysfunction includes ulcers, gastroesophageal reflux, autonomic dysreflexia, pain, distention, diverticulosis, haemorrhoids, nausea, constipation, diarrhoea and incontinence (219). Incontinence in particular has been noted as the most problematic, effecting physical functioning and social interaction which in turn has tremendous impacts on QoL (222–224). Bladder and bowel control are provided by the sacral portion of the spinal cord and are regulated by the autonomic nervous system (225). The sympathetic and parasympathetic components work together to regulate the bladder, reproductive organs, and the lower part of the intestines or colon (225). SCI can result in disrupted autonomic control and a loss in descending modulation and communication between the brainstem and the lumbosacral cord, in turn reducing bladder and bowel function (223,225,226).

Neurogenic bladder and bowel can be a disturbance for both physical and psychological well-being for individuals with SCI, restricting social activities, independence levels and QoL (227). Thus, regular monitoring and suitable management for this dysfunction are important to prevent long-term health complications and provide a better QoL for those with SCI (1,16). RLT, which has been shown as an effective tool for improving post-SCI motor outcomes, could potentially also be used as a management strategy for improving urinary and bowel complications (60,61). Given the existing overlap of the lumbosacral spinal circuitries controlling pelvic-visceral and locomotor functions, RLT may play a role in augmenting bladder and bowel function for those with SCI (223).

4.1.4 The effect of rehabilitation on secondary complications

Physical training, such as Activity-based Training (ABT) is important for regaining motor and sensory function after SCI and is considered a viable treatment for several secondary consequences after SCI (49,228,229). Evidence collected from a variety of training modalities supports the ability of exercise to reduce multisystem disease in persons with SCI by promoting mobility and functioning, preventing musculoskeletal deterioration and bone density loss and enhancing cardiovascular functioning and blood flow (92,228). Evidence further suggests that habitual exercise reduces fatigue, pain, weakness and neurological deficits that accompany aging with disability (49). Exercise thus acts as a health promoting activity following SCI, aiding in the prevention of secondary complications (49,195,221).

Additionally, weight-bearing activity and over-ground ambulation, such as Robotic Locomotor Training (RLT), show promise as a rehabilitation modality to attenuate the risk of developing secondary complications, due to the ability of overground robots to deliver both high-quality and quantity repetitions of therapeutically meaningful movements (56). RLT may reduce many of these health concerns by increasing body strength and aerobic capacity, minimizing declines in bone mineral density, improving circulation and countering the other health risks associated with prolonged sitting (60,61,230). However, there is substantial debate in the literature regarding the effectiveness of RLT. Research has found RLT to be an effective rehabilitation strategy for improving functional motor outcomes in individuals with SCI (60,61,223). However, although RLT may enable the development of small functional changes after training, these changes are similar compared with other physical interventions (59,75,223). Results from a study by Dobkin and colleagues (2012) showed that more conventional ABT produced similar results in strength, walking speed and distance, physical functioning, quality of life, and dependence on assistive aids (75). Thus, the question remains whether RLT is superior in conception, cost, and outcomes to other forms of goal-directed, progressive, and well-dosed ABT?

Furthermore, most of the RLT studies to date have focused on robotic devices as clinical training tools to improve motor function, yet they have overlooked the other possible health benefits of the intervention (65). RLT programmes are expected to produce numerous musculoskeletal, cardiorespiratory, endocrine-metabolic and psychological beneficial effects in the SCI population (56,86). In cases where functional change is nonsignificant, concurrent changes in health, such as cardiovascular function, muscle composition, metabolism, bone and fat mass, quality of life and depression, may be of considerable value to people with SCI (29,214). Some evidence points to the positive effect of RLT on these secondary complications following SCI, especially the perceived benefits on lower extremity spasticity and bowel movement (55,83,94,102). However, perspectives as related to satisfaction with RLT programmes and the effects on other secondary health concerns have rarely been documented (86). Moreover, very little is known about secondary complications for those with SCI within a South African context. Only one previous study assessed secondary complications in South African healthcare, reporting solely on the prevalence of pressure ulcers in persons with cervical lesions (18). Therefore, the impact of RLT on these non-locomotor functions remains largely unknown. This knowledge gap hinders the allocation of resources necessary for addressing secondary complications that negatively impact the individual (9,223).

Although the evidence for RLT is compelling, there are several methodological flaws that require consideration. There is large variability in the outcomes across the studies of locomotor training which is attributed to small samples, non-standardized protocols, heterogeneity in samples and ineffective assessment measures (77,231). Studies also vary considerably in their use of RLT, from time after injury, length of sessions, amount of cumulative sessions, density of treatment, use of co-treatments, and type of training (231). The heterogeneity in studies, particularly with respect to the variety of outcome measures used and the different types of intervention, make it difficult to synthesize and use this information to guide clinical practice. Thus, given the widespread gaps in the evidence-based knowledge of RLT, no real consensus has yet emerged on how best to develop and deliver RLT

programmes and to what extent the proposed programmes meet the needs and expectations of individuals with chronic SCI.

Although RLT serves as a promising therapeutic tool for treating secondary complications after SCI, there is insufficient evidence to draw conclusions about its effectiveness in persons with SCI (56,66). A strong evidence base for the prevention and effective management of secondary complications will be essential for future breakthroughs in SCI health and well-being. Therefore, continued experimental research and rigorous studies are required to study the extent to which physical activity, specifically as related to RLT, mitigates comorbidity risk, so that exercise guidelines and prescriptions can be developed to prevent secondary conditions (196).

4.2 Aims

This chapter aimed to describe the secondary complications experienced by individuals with SCI when exposed to 24 weeks of ABT or RLT interventions. These secondary complications included pain, spasticity, and bladder and bowel changes in relation to rehabilitation. A more descriptive approach is used in this chapter due to the non-parametric nature of the outcomes presented.

4.2.1 Objectives

To describe the secondary complications experienced by individuals with SCI during 24 weeks of ABT and RLT. The following were measured over 24 weeks of rehabilitation at baseline, 6-, 12- and 24-week intervals:

1. *Spasticity (Modified Ashworth Scale):*
    a) Total spasticity
    b) Upper spasticity
    c) Lower spasticity

d) Primary spasticity location

2. *Pain (International SCI Pain Data set):*

    a) Average total pain intensity

    b) Pain interference scores for three domains (Daily activity, mood, and sleep)

    c) Primary pain location

3. *Bladder and bowel function (International Lower Urinary Tract Function Basic Data Set, International Bowel Function Basic Data Set):*

    a) Urination frequency

    b) Bladder incontinence

    c) Bowel incontinence

    d) Defaecation frequency

    e) Defecation time

4.3 Methods

Comprehensive methods of the study protocol, including the RLT and ABT interventions, are provided in Chapter 2 of this thesis. Methods pertaining to the secondary complications' analysis are contained below. All 16 participants were included in the secondary complication analysis. Outcome measures for this chapter included spasticity, pain and bladder and bowel function.

4.3.1 Spasticity

Spasticity was measured in all participants using the Modified Ashworth Scale (MAS) (Appendix 4.1), developed by Bohannon and Smith in 1986. The MAS has been shown to be a reliable tool in SCI populations (232) and it is the most widely used assessment tool to measure resistance to limb movement in a clinical setting (216). Assessment techniques were standardized, including the speed of

assessment and adequate training prior to assessment. Scores ranged from 0 – 4: a score of 0 indicated no resistance and a score of 4 indicated rigidity. Tests were performed at 0, 6, 12 and 24 weeks of the rehabilitation programmes. Medication remained stable throughout the intervention period, except for a single participant who experienced a Baclofen pump blockage, resulting in Baclofen withdrawal and the medical implications thereof. This participant was hospitalized, and the blockage resolved with complete recovery on discharge. This complication resulted in six sessions being missed in total for this participant.

4.3.2 Pain and bladder & bowel questionnaires

Validated health-related questionnaires were used to measure pain and bladder and bowel function at 0, 6, 12 and 24 weeks (233,234). These questionnaires included.

4.3.2.1 *International SCI Pain Basic Data Set Version 2:*

This questionnaire (Appendix 4.2) was used to determine the intensity, location and type of pain that participants experienced, and the subsequent impact of that pain on three domains: A) Daily activities; B) Mood; C) Sleep (233).

4.3.2.2 *International Lower Urinary Tract Function Basic Data Set:*

This questionnaire (Appendix 4.3) was used to assess bladder health and function (235). Specific categories of this questionnaire included:

a) Urinary method
b) Bladder medications
c) Average number of urinations per day (in last week)
d) Average frequency of urinary incontinence (in last 3 months)
e) Improvements in urinary function (in the last year)

4.3.2.3 *International Bowel Function Basic Data Set:*

This questionnaire (Appendix 4.4) was used to assess bowel health and function (236). Specific categories of this questionnaire included:

a) Defecation method

b) Bowel medications

c) Average defecation time (in the last month)

d) Average defecation frequency (in the last month)

e) Average frequency of faecal incontinence (in the last three months)

4.3.3 Statistical analysis

All data were analysed using statistical software (R, R Core Team, Auckland, New Zealand and Prism 8, GraphPad Software Inc, California, USA). Linear mixed effect models assessed continuous responses which were measured at four time points (0, 6, 12 and 24 weeks). Categorical responses were analysed cross-sectionally using a Fisher's exact test at each time point. In the cases where a response was binary, an odds ratio (OR) of the RLT group to the ABT group was calculated. More details on these statistical methods can be found in Chapter 2 of this thesis.

4.4 Results

4.4.1 Spasticity

Figure 4.1 shows that the modelled difference in total spasticity at baseline between the groups was 9.45 units, p-value of 0.09. Thus, there was no significant difference in total spasticity scores between the RLT and ABT groups at baseline or over time ($p = 0.250$). However, both groups experienced small changes in spasticity over time: the ABT group experienced a slight trend of increasing scores over time with a rate of change of 0.11 ($p = 0.40$), while in contrast the RLT group had a rate of change of -0.03 ($p = 0.44$) and hence, experienced a slight decreasing trend over time (Fig. 4.1).

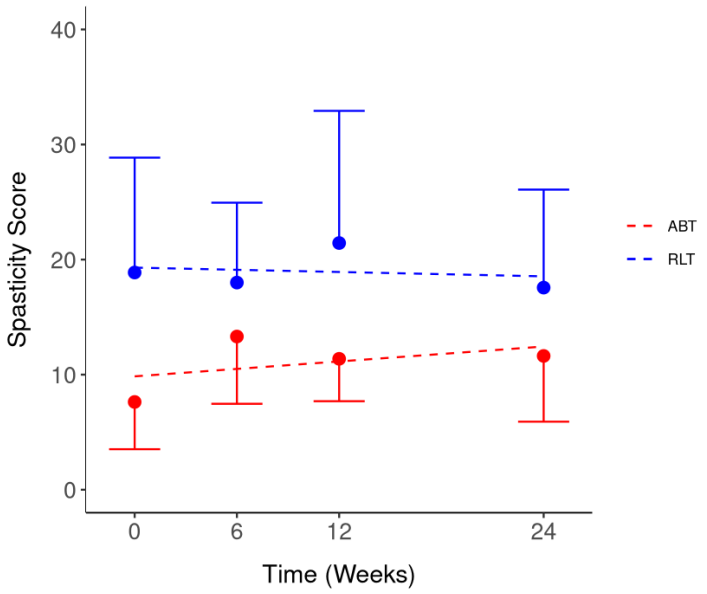

Figure 4.1: Total spasticity scores for the Robotic Locomotor Training and Activity-based Training groups over time.

RLT: Robotic Locomotor Training (n = 8); *ABT*: Activity-based Training (n = 8); *Spasticity score*: sum of scores for 22 tested body areas (combined right and left side) using Modified Ashworth Scale. Data presented as observed mean ± half-width 95% CI. Modelled linear estimates shown as superimposed lines (predicted mean). * No significant differences in spasticity scores at baseline (p = 0.09).

The opposing spasticity trends between the groups are evident in the mean percentage differences from pre to post trial for both groups for spasticity scores for the 22 measured body areas (Table 4.1). The RLT group had reduced spasticity scores over time with changes of 10%, 3% and 8% for total, upper and lower spasticity, respectively. However, the ABT group had a greater rate of change, with increased spasticity scores over time, with changes of 52%, 21% and 62% for total, upper and lower spasticity, respectively. Although there was no significant difference between groups for the total spasticity score (p = 0.250), there was a strong trend towards a significant group difference for lower body spasticity, with the RLT group having higher scores over time compared to the ABT group (p = 0.066) (Table 4.1). The RLT group showed higher variability in individual spasticity scores over time compared to the ABT group. At baseline, scores were recorded between 1.0 – 15.0 for the ABT group and between 5.0

– 41.5 for the RLT group, whereas at 24 weeks, ranges were 1.0 – 28.0 for the ABT group and 2.0 – 41.5 for the RLT group.

Table 4.1: Spasticity characteristics for the Robotic Locomotor Training and Activity-based Training groups at baseline and week 24.

	RLT			**ABT**		
Spasticity	*Pre*	*Post*	Δ (%)	*Pre*	*Post*	Δ (%)
Total body	18.88 ± 14.41	17.56 ± 12.29	-10	7.62 ± 5.93	11.62 ± 8.25	52
Upper body	4.56 ± 6.68	4.44 ± 7.03	-3	1.75 ± 2.55	2.12 ± 1.81	21
Lower body	14.31 ± 10.95	13.12 ± 8.44	-8	5.88 ± 4.16	9.50 ± 7.37	62

RLT: Robotic Locomotor Training (n = 8); *ABT*: Activity-based Training (n = 8); *Pre:* week 0 measurement; *Post:* week 24 measurement; Δ *(%):* mean percentage change from pre to post. Data presented as mean ± SD.

Figure 4.2 illustrates the spasticity scores per measured body area for both groups summed over the four testing periods (0, 6, 12 and 24 weeks). Across all participants, the area of highest spasticity over time was the ankle plantar-flexor muscles followed by the knee flexors. Interestingly, the third worst spasticity area was the adductors for the RLT group and the wrist extensors for the ABT group. Figure 4.2 highlights the group differences in measured spasticity, with the RLT having constantly higher scores across all body areas compared to the ABT group.

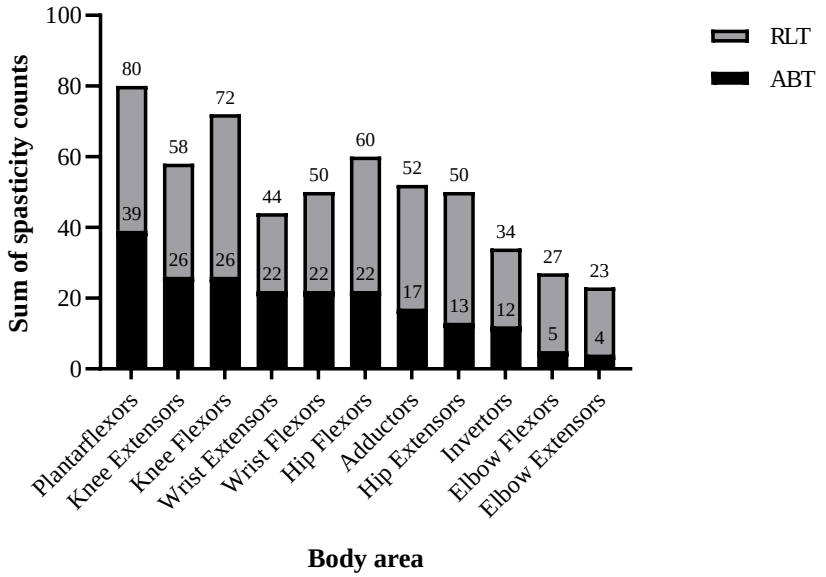

Figure 4.2: Totalled spasticity counts for the 11 measured body areas for the Robotic Locomotor Training and Activity-based Training groups.

RLT: Robotic Locomotor Training (n = 8); *ABT*: Activity-based Training (n = 8); *Spasticity count*: number of people who experienced a spasticity score > zero for a body area, summed over the four time points; *Spasticity score:* measured using Modified Ashworth Scale.

4.4.2 Pain

The responses to the pain questionnaire showed that approximately 81% (n = 13) of the participants experienced pain at baseline, whereas by week 24, 100% (n = 16) of the participants experienced pain. There was no significant difference between the RLT and ABT groups over time for pain intensity ($p = 0.96$) and pain interference ratings ($p = 0.61$). However, the average pain intensity tended to increase over time across all participants, with a combined mean pain intensity score of 4.0 ± 2.5 and 5.8 ± 1.5 at baseline and 24 weeks respectively (Fig. 4.3). There was a mean increase in pain intensity of 26% and 46% for the RLT and ABT group respectively from pre to post trial (Table 4.2).

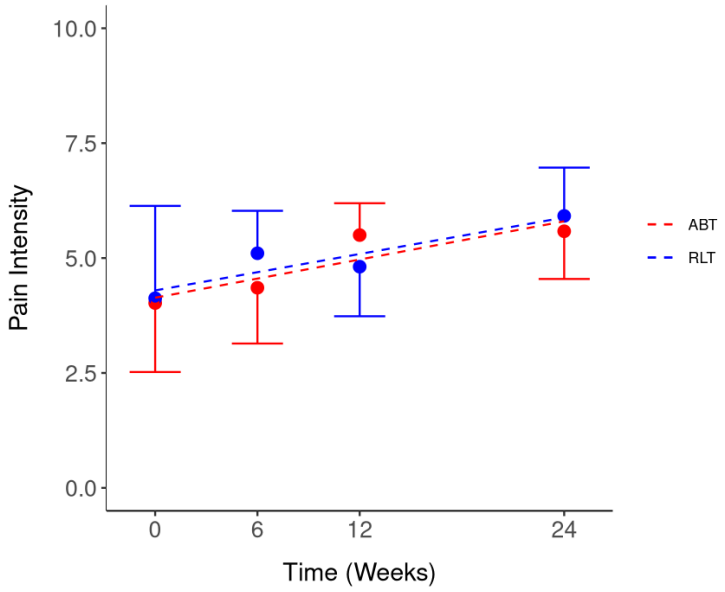

Figure 4.3: Average pain intensity score for the Robotic Locomotor Training and Activity-based Training groups over time.

RLT: Robotic Locomotor Training (n = 8); *ABT*: Activity-based Training (n = 8); *Pain intensity score (0-10):* averaged over number of pain locations reported in the International SCI Pain Basic Data Set Version 2. Data presented as observed mean ± half-width 95% CI. Modelled linear estimates shown as superimposed lines (predicted mean).

There was no significant difference between the RLT and ABT groups over time for pain interference ratings (p = 0.61). However, both groups reported pain to interfere in an increasing manner with the three measured domains over time (Fig. 4 A, B, C). There was a significant time effect for pain interference for the daily activity domain (Fig. 4.4A and Table 4.3) (p = 0.05) with a combined increase in pain interference of 2.19 units over time across all participants.

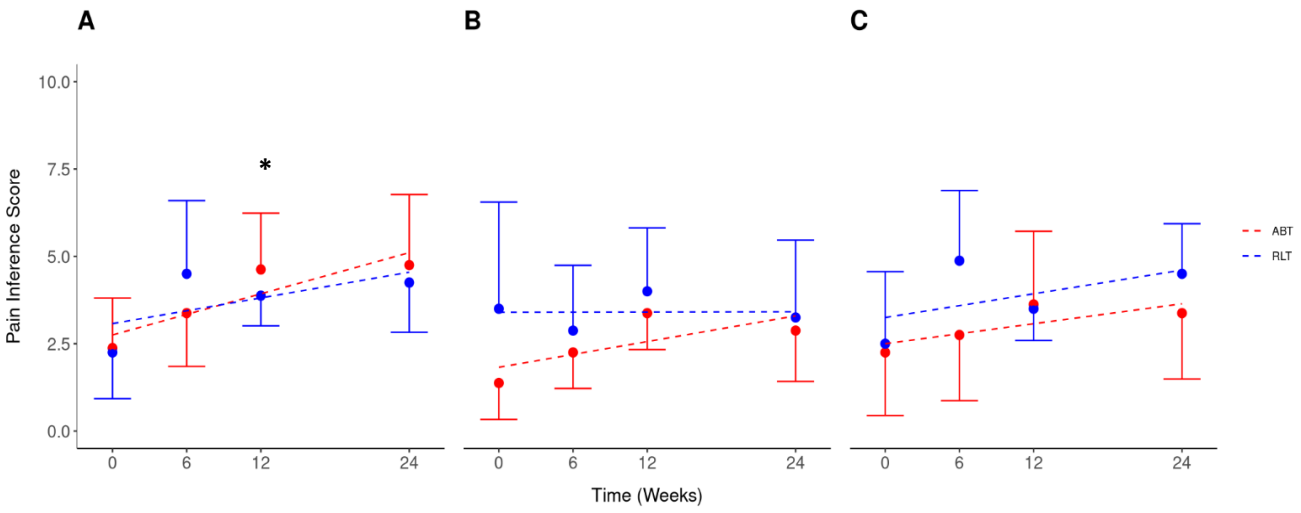

Figure 4.4: Pain interference scores across A) daily activity, B) sleep, and C) mood domains for the Robotic Locomotor Training and Activity-based Training groups over time.

RLT: Robotic Locomotor Training (n = 8): *ABT*: Activity-based Training (n = 8); *Pain interference score (0-10)*: International SCI Pain Basic Data Set Version 2; *Pain intensity score (0-10):* averaged over number of pain locations reported in the International SCI Pain Basic Data Set Version 2. Data presented as observed mean and half-width of 95% CI. Modelled linear estimates shown as superimposed lines (predicted mean). *Significant increase in pain experienced in the daily activity domain over time (p =0.05).

The ABT group had an increase in pain interference scores of 99%, 109%, and 50% for the daily activity, sleep, and mood domain, respectively. The RLT group had an increase in pain interference scores of 85% and 69% for the daily activity and mood domain respectively, but no change in the sleep domain (0% change).

Table 4.2: Pain characteristics for the Robotic Locomotor Training and Activity-based Training groups at baseline and week 24.

	RLT			ABT		
Pain	*Pre*	*Post*	Δ (%)	*Pre*	*Post*	Δ (%)
Intensity	4.15 ± 2.71	5.70 ± 1.56	26	4.02 ± 2.16	5.58 ± 1.50	46
Activity interference	2.33 ± 1.80	4.33 ± 1.94	85	2.38 ± 2.07	4.75 ± 2.92	99
Sleep interference	3.11 ± 4.28	3.11 ± 3.02	0	1.38 ± 1.51	2.88 ± 2.10	109
Mood interference	2.56 ± 2.79	4.33 ± 2.00	69	2.25 ± 2.60	3.38 ± 2.72	50

RLT: Robotic Locomotor Training (n = 8); *ABT*: Activity-based Training (n = 8); *Pre:* week 0 measurement; *Post:* week 24 measurement; Δ *(%):* mean percentage change from pre to post. Data presented as mean ± SD.

Most of the perceived pain was related to the musculoskeletal system. The body area experiencing the highest pain scores overall was the shoulder for the ABT group and the lower back for the RLT group (Table 4.3). The ABT group experienced a higher concentration of reported pain areas, with the neck and shoulder areas dominating. The shoulder area appeared to be a point of concern from baseline whereas there was an increase in the number of people who reported their necks as being painful from week 0 to week 24. The RLT group experienced a noticeable variability in the reported pain areas over time, with only the lower back and upper arm being reported as pain areas at both week 0 and week 24.

Table 4.3: Primary pain complaint area reported for the Robotic Locomotor Training and Activity-based Training groups at baseline and week 24.

	ABT		RLT	
Pain area	*Pre*	*Post*	*Pre*	*Post*
Shoulder	4	3		1
Neck	1	3	1	
Lower back	1		2	2
Buttocks	1	1	1	
Wrist		1		
Upper arm			2	1
Upper leg/thigh				2
Foot/toe				1
Hip				1
None	1		2	

RLT*:* Robotic Locomotor Training (n = 8); *ABT*: Activity-based Training (n = 8); *Pre:* week 0 measurement; *Post:* week 24 measurement; Data presented as frequency count of number of participants that reported that area of pain. *Pain areas:* Listed in the International SCI Pain Basic Data Set Version 2. *Note:* Additional body areas were available for selection on the pain questionnaire, but data above only presents those that were reported.

4.4.3 Bladder & bowel function

As shown in Table 4.4, for both groups, suppositories were the main defecation method used (50%), followed by normal defecation (31%) and lastly by staining/bearing down (19%). Intermittent catheterization, either by self or attendant was used by most of the participants (44%) as the chosen urinary method, followed by indwelling catheters (31%). Bladder and bowel medication were documented at baseline, with no changes occurring throughout the trial (Table 4.4).

Table 4.4: Baseline descriptive bladder and bowel characteristics of the Robotic Locomotor Training and Activity-based Training groups.

Group	Participant	Age (years)	Time since injury (years)	Neurological level of injury	AIS category	Aetiology	Sex	Urinary method	Defecation method	Bladder medication	Bowel medication
RLT	1	27	9	C6	D	Stabbing	Male	Normal voiding	Normal	None	None
	2	33	15	C6	C	MVA	Male	Intermittent self-catheterization	Straining/bearing down	None	None
	3	32	3	C5	D	MVA	Male	Transurethral indwelling	Suppositories	None	None
	4	46	26	C4	D	Gunshot	Male	Intermittent catheterization by attendant	Suppositories	None	Oral laxatives
	5	55	4	C5	D	MVA	Male	Normal voiding	Normal	None	Oral laxatives
	6	43	23	C6	C	MVA	Male	Intermittent self-catheterization	Suppositories	Bladder relaxants, sphincter/bladder neck relaxants, antibiotics	Oral laxatives
	7	56	15	C4	C	MVA	Male	Condom catheter	Suppositories	None	None
	8	32	15	C7	C	Sport - Rugby	Male	Intermittent self-catheterization	Normal	None	Oral laxatives
	Average	40.5 ± 11.2	13.8 ± 8.2								
ABT	9	26	2	C6	C	MVA	Male	Suprapubic indwelling	Suppositories	None	Oral laxatives
	10	46	20	C6	D	MVA	Female	Normal voiding	Normal	None	None
	11	50	8	C7	D	MVA	Male	Transurethral indwelling	Normal	Bladder relaxants	Oral laxatives
	12	19	2	C5	C	MVA	Male	Intermittent catheterization by attendant	Straining/bearing down	Bladder relaxants	None
	13	47	3	C4	D	Motorcycle	Male	Intermittent catheterization by attendant	Suppositories	None	Oral laxatives
	14	29	10	C5	C	MVA	Male	Suprapubic indwelling	Straining/bearing down	Bladder relaxants, sphincter/bladder neck relaxants, antibiotics	Oral laxatives
	15	60	2	C5	C	Mountain bike	Male	Intermittent self-catheterization	Suppositories	bladder relaxants, antibiotics	Oral laxatives
	16	30	11	C4	C	Diving	Male	Transurethral indwelling	Suppositories	Bladder relaxants, antibiotics	Oral laxatives
	Average	38.4 ± 14.3	7.3 ± 6.4								

RLT: Robotic Locomotor Training (n = 8); *ABT*: Activity-based Training (n = 8); *MVA:* motor vehicle accident. Values quoted as mean ± SD. No significant difference between groups for age and time since injury (p = 0.10).

No significant differences were found in bladder and bowel function between the ABT and RLT groups at baseline. Both groups experienced approximately four urinations per day and had monthly urinary incontinence. Neither group experienced faecal incontinence at baseline. The RLT group experienced slightly longer defecation times compared to the ABT group but defecation frequency was equivalent, with more than two occurrences per week for both groups. No significant group differences were found for the bladder and bowel outcomes over time, except for improvements in urinary function ($p = 0.04$). An evaluation of the change in urinary function over all time points showed a significant difference between groups occurring at week 24, as illustrated in the final column of the mosaic plot in Figure 4.5A. This highlights the need to have longer intervention periods to induce improvements in urinary function. Fisher's exact test for this time point reported a p-value of 0.04, which suggests that the type of intervention (i.e., group effect) had a significant influence on the odds of urinary change. The OR at this time point was 0.26, indicating that the RLT group was less likely to have an improvement in bladder function compared to the ABT group.

Both groups tended to show a pattern of decreasing urinary incontinence over time (Fig. 4.5B). There were no changes noted for faecal incontinence, defecation time or defecation frequency between groups over time. However, investigating the mosaic plot in Figure 4.5C, it shows that overall, more individuals in the RLT group experienced defecation times of 0 – 5 minutes and >60 minutes compared to the ABT group. Therefore, the ABT group was more consistent in their defecation time responses, whereas the RLT group showed high variability. It does appear that the RLT group had fewer individuals in the >60 minutes category over time. Figure 4.5D shows an increase over time in the number of RLT individuals experiencing a defecation frequency of once per day.

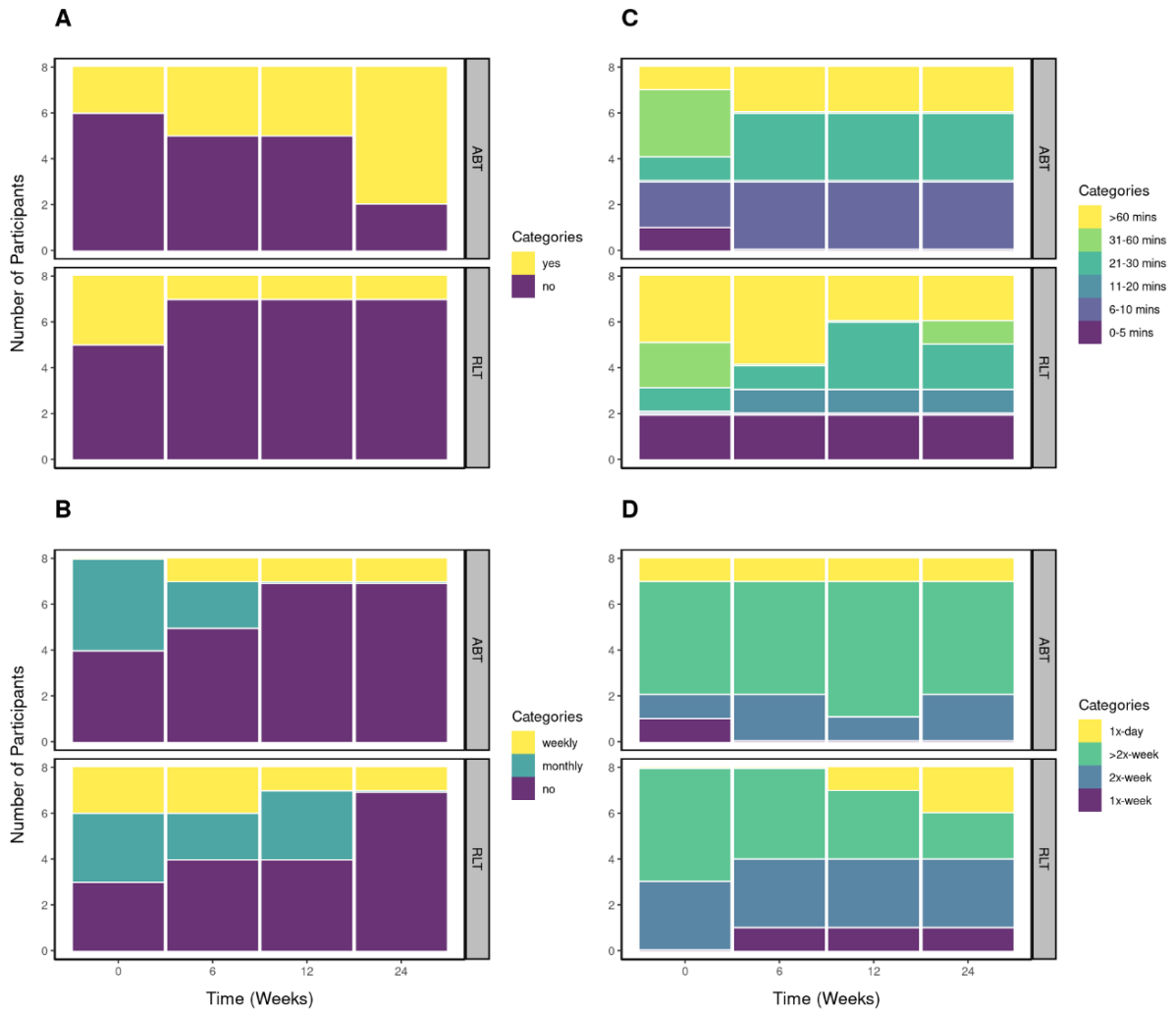

Figure 4.5: A) Improvement in urinary function, B) frequency of urinary incontinence, C) defecation time, and D) defecation frequency, for the Robotic Locomotor Training and Activity-based Training groups over time.

RLT: Robotic Locomotor Training (n = 8); *ABT*: Activity-based Training (n = 8); *Bladder function:* International Lower Urinary Tract Function Basic Data Set. Improvements in bladder function were taken for the previous year, hence why change can be seen at week 0; *Bowel function:* International Bowel Function Basic Data Set; *Mins:* minutes.

4.5 Discussion

The goals of neurological rehabilitation focus on diminishing the negative impact of impairments, preventing secondary complications and enhancing the well-being and independence of individuals with SCI (222). This study aimed to describe the effects of ABT and RLT on secondary complications,

in which we discuss the emerging trends that were noted over the 24-week interventions for spasticity, pain, and bladder and bowel function.

4.5.1 Spasticity

The beneficial effects that physical therapy modalities have on spasticity for individuals with SCI is well-established (1,17,46,49,61,217,228,237,238). Despite the proposed benefits of physical activity on spasticity, the current study showed no statistical changes in total spasticity scores between the RLT and ABT group ($p = 0.25$) or within each group over time ($p = 0.17$). Although neither intervention had a statistical impact on spasticity, spasticity scores did differ between the groups over time, indicating the possible clinical relevance of the interventions. The RLT group had reduced spasticity scores over time with changes of 10%, 3% and 8% for total, upper and lower spasticity respectively and the ABT group had increased spasticity scores over time, with changes of 52%, 21% and 61% for total, upper and lower spasticity, respectively (Table 4.1).

Some small-scale exoskeleton studies have found reductions in spasticity post RLT (44, 57, 41, 42,27). A systematic review also reported that clinically relevant improvements were found in self-reports for muscle spasticity in various other RLT studies (60). A total of 14 prospective studies representing 111 participants were included in the analysis. In five of the included studies, 38% (95% CI: 19%–59%) of participants reported decreases in spasticity with exoskeleton training (54,83,91,92,102). Other studies have found no change in spasticity symptoms after RLT (39, 32,43,56). However, no studies reported a worsening of spasticity post RLT intervention. Hence, there is significant conflicting evidence regarding the effect of RLT on spasticity in persons with SCI, but majority of studies indicate a positive effect of RLT on spasticity in these individuals (56). Additionally, spasticity depends on the type, site, and duration of injury as well as other influencing factors that can trigger or aggravate spasticity symptoms, such as caffeine, lack of sleep, heat changes and pharmacological options (216,232). These various contributing factors could be potential confounding variables adding to the inconsistent spasticity responses found within this study.

4.5.2 Pain

Chronic pain after SCI has been found to be prevalent in approximately four out of five individuals with SCI (16). Thus, it is not surprising that majority of the participants in this study experienced pain at baseline and throughout the study. The high prevalence and increasing intensity of pain observed in this study is consistent with previous results documented in a SCI population (239–241). This study found no statistical differences in pain intensity between the ABT and RLT groups ($p = 0.96$), nor did it find any improvements in pain levels after 24 weeks of training ($p = 0.15$).

ABT has been confirmed as an effective approach to reduce pain levels in the SCI population (60,220,230,242). Current evidence on the effect of RLT on pain is limited to case studies or investigations with small sample sizes, but may indicate a potential positive effect within a SCI population (56,60). A recent review of RLT on secondary complications reported that five of the eight included studies indicated significant reductions in pain intensity both within an exercise session and across the intervention (61). Contrary to these positive findings, the current study did not find a beneficial effect of either exercise intervention on reported pain ratings. Both pain intensity and the perceived interference of that pain on three different domains of life increased over time for both the ABT and RLT groups (Fig. 4.3 and 4.4). The increased perceptions of pain intensity within this study could possibly be due to the high intensity and frequency of exercise sessions within the groups. Chronic fatigue, burnout and staleness, and an imbalance between training versus recovery may have occurred due to this over-reaching (243,244). The rigidity of adhering to the intervention protocol, as followed from the Therapy & Beyond programme, did not allow the Biokineticist's to adjust the training programme accordingly. It is well documented that this type of training can cause increased fatigue and chronic muscle or joint pain due to an increase in the exercise load over time (243,245).

Another plausible explanation for the increasing perceptions of pain reported in both groups was due to an increase in musculoskeletal pain caused by muscle stiffness above the level of injury (246,247). This delayed-onset-muscle-soreness (DOMS) is a common occurrence following bouts of unaccustomed

strenuous physical activity and can result in muscle tenderness and debilitating pain symptoms (246). Thus, training of new skills, utilising often unused muscle groups, might have led to stressed muscles during training which was experienced by the participants as an increase in pain levels (238,247). Additionally, if the participant is experiencing spasticity, this could also contribute to pain development, as spasticity is often accompanied by pain possibly due to functional nerve entrapment in the muscles (232,238). Subsequently, this pain and related pain-induced sleep disturbances can lead to excess fatigue, which in turn creates stress and further increases spasticity and discomfort (238).

The shoulder has been reported to be the joint most commonly associated with pain above the level of injury in individuals with SCI (247–249). Alm et al. (2008) showed that based on a pain-related questionnaire of 88 people with SCI, 67% of participants reported a history of shoulder pain since becoming a wheelchair user (249). As manual wheelchair propulsion and wheelchair-related daily activities place a substantial load through the upper extremities and due to the shoulder's complex functional anatomy and limited muscle mass, it is especially at risk for overuse injuries (247). Therefore, it is expected that the ABT group in our study rated the shoulder as the most painful area, due to the high levels of upper body utilization within this training modality. RLT participants may also have encountered upper body pain attributed to the performance of a new exercise modality that uses the upper extremities for support in the Ekso bionic suit (54). However, in the current study, the RLT group rated the lower back as the site of greatest pain. Lower back pain is common within a SCI population, with a prevalence of between 50 and 70% (248). Kolakowsky-Hayner et al. (2013) reported that two of the seven participants reported the presence of minimal lower back pain with use of the exoskeleton (54) and another study in which 217 participants were required to indicate painful areas on a drawing, indicated the back area was most frequently (61.8%) effected (241). Several studies have reported on the relationship between the presence of pain and poor mood, reduced health and the ability of pain to interfere significantly with daily functioning (107,250). This was also evident in the current study which showed an increase in the perception of pain interference with life domains over time, particularly for activities of daily living (Fig. 4.4A). As this pain is a potential cause of daily activity and mood

limitations, upper extremity pain prevention and management programmes should be a focus for all rehabilitation sessions for individuals with SCI.

4.5.3 Bladder and bowel function

Despite the impact of bladder and bowel dysfunction on other medical complications and QoL for those living with SCI, there is still remarkably little research on this prominent issue (251). However, walking and running in the able-bodied population have been associated with reduced constipation and reduced bowel transit time (252). Therefore, considering the repetitive walking nature of RLT, improvements in bowel and bladder function might be a likely benefit (223). Additionally, the use of powered exoskeletons has been hypothesized to improve bowel function based on previous studies investigating the benefit of both upright posture and mobility on intestinal motility (56).

In the current study, the RLT experienced no faecal incontinence and had more frequent defections over time (Fig.4.5). Several studies using powered exoskeletons have found similar improvements in bowel function following robotic walking (83,91,102,223,253). Furthermore, a systematic review on the clinical effectiveness of powered exoskeleton-assisted walking in people with SCI found in three studies, 61% (95% CI: 20%–95%) that participants reported improvements in bowel movement regularity with exoskeleton training (60). However, other case series found no improvements in participants bowel regulation and functioning after being involved in RLT programmes (55,86,94). Similar improvements in bladder function are expected from RLT, as Hubscher and colleagues (2018), documented significant increases in bladder capacity, voiding efficiency and detrusor contraction time as well as significant decreases in voiding pressure post- RLT training relative to baseline in all (n = 8) participants (223). The benefits in bladder and bowel control with RLT are thought to be associated with the increased sensory information to the spinal cord generated through task-specific stepping and loading as well as activation of abdominal musculature which increases in colonic motility (92,96,223). Regular aerobic and resistance training may also reduce these health concerns in individuals with SCI, as training can induce changes in the local neural circuitry and enhance neuromuscular plasticity which

has shown to increase bladder capacity, decrease bowel regime time and decrease incontinence (50,254).

The ABT group experienced greater benefits in bladder control compared to the RLT group, in that they showed a tendency of decreased urinary incontinence over time as well as a significant improvement in bladder function (Fig. 4.5). Various non-activity related factors can also influence bladder and bowel function in individuals with SCI including, level of injury, extent of disability/completeness of cord injury, duration of injury and level of care available to the person (1,16). Additionally, intake of diuretics and various medications can also affect dysfunction (16,255). Therefore, both RLT and ABT interventions may positively benefit the neural circuitries controlling urogenital and bowel functions in persons with SCI (92,96,223), but effective management should ensure individualized training based on the type of dysfunction, as well as these unique categorizing qualities.

4.5.4 Limitations

A limitation of this study lies with the completion of the questionnaires. The accuracy of the responses may have been affected by the participants interpretation and subjective understanding of the questions due to the medical terminology used. In addition, the participants were required to complete the questionnaires in their own time outside of the rehabilitation setting. It is suggested that for future studies, the questionnaires be completed in the rehabilitation setting to avoid the possible distractions and mental fatigue that may have occurred at home, with the assistance of a research investigator to answer queries if required.

4.5.5 Conclusion

This chapter showed that both interventions, particularly ABT, appeared to aid in reducing urinary incontinence and can improve bladder function. There was some evidence to support RLT to induce bowel improvements in individuals with SCI. However, the interventions were not as promising for reducing other key secondary complications, such as pain and spasticity. The interventions did not

improve spasticity but did prevent a worsening of symptoms, yet pain tended to have increased over time, likely due to increased musculoskeletal stiffness and fatigue. Although the outcomes of this chapter may not have been statistically significant, small alterations in these measures may hold clinical relevance for people with SCI and should be investigated further. Addressing secondary complications is a priority for individuals with SCI and thus, clinicians ought to consider these health concerns as a key determinant in selecting effective rehabilitations strategies post SCI. Accurate management of secondary complications is crucial to allow individuals with SCI the opportunity to live a full, productive, and comfortable life as well as to reduce healthcare utilization and medical costs.

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CHAPTER 5

Mitigating bone density decline and adverse body composition in individuals with SCI: is robotic walking effective?

5.1 Introduction

Chapter 4 considered the effect of RLT on three common secondary complications including spasticity, pain, and bladder and bowel function. However, there are several other secondary complications related to the morbidity and mortality of those with SCI, including indices of bone health and body composition. As a consequence of sustaining a SCI, motor function can be severely limited. This results in an extreme form of immobilization and disuse of the paralysed extremities below the level of the lesion (256). The reduction in muscle contractions and a redistribution of the gravitational forces applied to the skeleton initiates a cascade of degenerative changes, including the well-known secondary complications affecting bone density, including osteoporosis; and body composition changes, including muscle atrophy and obesity (16,256).

5.1.1 Bone mineral density

Bone mineral density (BMD) is a measure of the amount of minerals contained in a certain volume of bone (16). BMD is used as an indicator to determine decreased bone mass in order to diagnose osteoporosis. Osteoporosis is a condition characterized by low bone mass and deterioration of the skeletal microarchitecture (16,257). In clinical practice, individual BMD values are compared with a reference value (Z-score) from a healthy, age and sex-matched control group to determine if BMD is within a normal range or indicative of osteopenia or osteoporosis (258). The International Soceity of Clinical Densitometry (ISCD) official positions (2019) criteria for BMD interpretation classify females prior to menopause and males <50 years old as "within expected range for age" (Z-Score above -2.0) or "below expected range for age" (Z-Score at or below -2.0). These values are however, based on normative data for the average able-bodied population. Currently, there is a lack of normative data surrounding bone density guidelines for individuals with SCI. According to Abderhalden et al. (2017),

“It remains unclear whether DXA-derived BMD measurements can predict fractures in a SCI population and there is no information on fracture risk based on WHO bone density categories following SCI” (259). Manufacturer-established standard protocols for bone density measurement at the knee as well as a large, SCI- specific normative datasets are needed (258).

In persons with SCI, a significant decrease in BMD is often presented below the level of injury, as the rate of bone resorption is accelerated and the rate of new bone formation is decreased after injury (258,260). A decrease in BMD of up to 33% can occur within the first three to four months and up to 50% within the first three years post SCI (49,235,257,261). In addition, the long bones in the lower extremity undergo substantial cortical thinning following SCI (260). The loss of bone mass in people with SCI is more prominent in the lower limbs than in the whole body, due to the lack of loading and muscular tension on the bones below the lesion (262). Demineralisation occurs predominantly in areas rich in trabecular bone, such as the distal end of the femur and the proximal tibia, while the regions which are rich in cortical bone, such as the spine, are partially preserved (263,264). Shields and colleagues (2005) compared spine, hip, and knee BMD of 11 people with complete SCI with sex and age-matched able-bodied controls, with an average age of 41 ± 12 years and an average duration of injury of 10.2 ± 9.1 years. Results showed that across all hip regions, the SCI group had significantly lower BMD than the able-bodied controls. Baseline hip BMD was approximately 0.6 g/cm^2 and 0.9 g/cm^2 for the SCI and able-bodied groups, respectively. However, there was no significant difference between the groups for lumbar spine BMD, with both groups measuring 1.0 g/cm^2 (265).

The large bone loss after SCI can lead to an increased risk of bone fractures, serving as a significant health risk for this population (89,261,266). Long-term follow-up data suggest that as many as 50% of people with SCI sustain a low-impact or an osteoporotic fracture at some point following their injury (267). These fractures often occur spontaneously and have serious health implications since they severely reduce independence and mobility and result in significant medical complications, such as pressure ulcers, autonomic dysreflexia and joint contractures (267). Complications arising from

fractures and their treatment can lead to long-term hospitalization, increased costs, and further disability (268).

BMD loss after SCI is partly caused by a decrease in mechanical loading as a result of reduced or complete loss of muscle function and weight-bearing activity (1,89). Alterations in neural innervation of bone and several endocrine changes after SCI can also influence BMD loss in those with SCI (16,29,89,269). Demographic and injury related factors such as, sex and aging, the level and severity of the lesion, and the duration of injury can additionally contribute to the extent of BMD decline (16,235,260,261,263). Drug treatments and the occurrence of spasticity are additional contributors to changes in bone mineral content after SCI injury (29,263).

5.1.2 Body Composition

An additional complication associated with a sedentary lifestyle following SCI is adverse changes in body composition (257,270). Body composition refers to the relative amount or percentage of different types of body tissue (bone, adipose tissue and lean muscle mass) that are related to health (162). After SCI, the body undergoes changes in composition and metabolism due to decreased physical activity levels and consequently, reduced daily energy expenditure (271). As a result, individuals with SCI have significantly decreased fat-free soft tissue mass (FFSTM) and increased fat mass (FM) compared to the average population (89,162,271). The average cross-sectional area of skeletal muscle after SCI has been reported to decrease by as much as 45-80% (162,257). Body fat can increase to more than 30% in individuals with chronic SCI, and there is a tendency for central obesity characterized by deposition of subcutaneous adipose tissue (SAT) and visceral adipose tissue (VAT) (89,257).

Previous studies have identified that people with SCI have 8.5% to 13% more adipose tissue per unit body mass than able-bodied individuals (266,272,273). In a study by Edwards et al. (2008), FM was quantified using Computed Tomography (CT) scan measurements in 15 young men and women with chronic SCI and compared to 15 age-, gender-, and waist circumference-matched able-bodied controls.

At the same waist circumference, the SCI group had a 58% greater mean VAT and a 48% greater mean ratio of VAT: SAT than that of able-bodied controls. This was likely due to abdominal muscle atrophy and subsequent increases in the proportion of FM to FFSTM post SCI (274). Measurement of body adiposity can help objectively identify the presence of obesity wherein specific threshold values are either met or exceeded. A healthy body fat relative to bodyweight (percentage body fat) is 15% for adult men and 23% for adult women. Individuals with body fat levels exceeding 25% for men and 32% for women are classified as obese and, as such, are at greater risk for certain diseases (275). The World Health Organization recognizes obesity as a global and increasing problem for the general population. Because of their reduced physical functioning, people with SCI face additional challenges for maintaining an appropriate whole-body energy balance, and thus, the majority of people with SCI are classified as overweight or obese (275).

In the SCI population, reported adiposity ranges from 25 -35% body weight which is consistent with the able-bodied classifications of being overweight, and prevalence of obesity varies from 40 to 66% (29,276,277). However, sex, ethnicity, age, physical activity level and disease states are important determinants of body composition (266). Specific to people with SCI, the duration of injury and level and completeness of injury can also impact body composition (266). Increased adiposity is closely related to an increased risk of coronary artery disease, diabetes and metabolic syndrome (89,257). VAT in particular, is strongly associated with all-cause mortality in different clinical populations (162,206,278). This increased risk of cardiovascular and metabolic complications within this population can lead to poorer functional outcomes, increased secondary complications, decreased psychological well-being and increased healthcare costs (220,271,279). Furthermore, physical inactivity exacerbates metabolic abnormalities and functional limitations related to SCI, increases perceived difficulty of exercise, and contributes to low motivation for physical activity, all of which create a reinforcing cycle of inactivity and associated adverse body composition (206,280).

5.1.3 The effect of physical rehabilitation on BMD

Currently, there are no comprehensive exercise interventions that have consistently demonstrated efficacy for preventing or reversing the dramatic bone loss occurring after SCI that can easily be implemented in the clinical setting (269,281). In general, there is a paucity of adequately powered studies evaluating the longitudinal benefits of exercise interventions on BMD (258). However, the importance of mechanical loading on bone health has long been recognized. In 1892, Julius Wolff published his influential work "The Law of Bone Transformation", in which he theorized that bone adapts its external shape and internal structure in response to the mechanical forces it is required to support, a concept that has become known as Wolff's Law (269).

In the able-bodied population, ABT in which there is mechanical loading of the bone, has been shown to increase BMD, cortical thickness, and bone strength by remodelling of bone at the site of greatest mechanical strain (162,206). Resistance training produces mechanical stress in the skeleton and enhances osteoblast activity which promotes bone health and density (282). Thus, resistance exercise and weight-bearing activities in which there is axial loading of the bones, such as passive standing (standing frame or tilt table) or various aided-walking systems, have been considered vital in preventing BMD decline for people with SCI by stimulating the osteogenic effects for bone mass deposit (16,282,283).

To date, RLT has been used primarily for studying walking parameters and performance, but the potential for these systems to increase muscle activation and weight-bearing in the upright posture is plausible (89). Growing research suggest that this exercise modality may also improve indices of health status including bone density, as the weight-bearing activity stimulates and creates an ideal stress environment to promote bone remodelling according to Wolff's Law (267,284). However, as RLT is a relatively new rehabilitation technology, few studies have investigated its effects on BMD for people with SCI. In a recent systematic review by Shackleton et al. (2019), only one study evaluated SCI-related changes in BMD in response to RLT (89). Tibial bone density increased by 14.5% for the five

participants, a finding which was not statistically significant but clinically relevant in a population who generally experiences a steady decline in their bone density (89). Thus, the use of RLT may present a promising therapeutic tool to overcome changes in BMD, but currently, there is a lack of powered studies addressing the influence of RLT on bone health in the SCI population (78,92). Additionally, there is a lack of published evidence-based guidelines defining the optimum time and frequency of weight-bearing activity required to maintain bone health during SCI rehabilitation (46,196,285) and there are no standardized treatment guidelines for the management of osteoporosis in individuals with SCI (45,262,263,286).

5.1.4 The effect of physical rehabilitation on body composition

Due to the many harmful effects of obesity on health, adequate monitoring and management of obesity in persons with SCI is clinically important (276). Exercise is a widely recognized and effective counter-measure for obesity in all populations by increasing daily energy expenditure and increasing lean muscle mass as metabolically active tissue (132,287). Resistance exercise creates muscle hypertrophy by promoting an increase in systemic growth factors and muscle protein synthesis (282). Thus, there is supporting evidence that regular physical activity is associated with greater FFSTM and lower FM for individuals with SCI (162,287).

Individuals with tetraplegia who participated in at least 150 minutes per week of physical activity had significantly lower total and regional FM compared to individuals with tetraplegia who were not physically active (278). In individuals with paraplegia, eight weeks of upper extremity resistance training resulted in an increase in upper extremity FFSTM and a decrease in FM (288). However, most existing trials are considered underpowered because of small sample sizes and the heterogeneity of the studied population (162). Despite signs pointing toward the benefits of exercise for improving body composition in those with SCI, by increasing energy balance, increasing muscle hypertrophy and reducing obesity-related health hazards, a clear consensus on the type, frequency, duration and intensity of exercise needed to achieve clinically meaningful improvements has yet to be determined (158). As

robotic exoskeleton devices are emerging technologies, they have not been thoroughly investigated for their utility in improving physical conditioning following SCI (132). There is a need to strengthen the current level of evidence linked to physical therapy interventions, including RLT, and to explore the impact of a longer intervention period of 24 weeks, in overcoming SCI-related changes in bone density and body composition.

5.2 Aims

This chapter aimed to compare the effects of RLT and ABT interventions on bone density and body composition in individuals with chronic SCI. Focus was given to changes in BMD, lean muscle mass and adiposity after 24 weeks of rehabilitation.

5.2.1 Objectives

The objectives of this chapter were to evaluate the effects of RLT and ABT interventions over a 24-week period on:

1. *Bone mineral density (BMD,* g/cm^2)
    a) Spinal BMD
    b) Total hip BMD
    c) Total femoral neck BMD

2. *Body composition and distribution*
    a) Whole-body and regional fat-free soft tissue mass (FFSTM) (kg)
    b) Whole-body, regional, and central fat mass (FM) (kg)
    c) Distribution of fat mass: gynoid FM (kg), visceral fat (VAT) (cm^2) and subcutaneous fat (SAT) (cm^2)

5.3 Methods

Comprehensive methods of the study protocol, including the RLT and ABT interventions, are provided in Chapter 2 of this thesis. All 16 participants were included in the analysis. Specific methods pertaining to the bone density and body composition analyses are described below.

5.3.1 Body weight

Body weight of the participants was measured in kilograms (kg) on a 900 x 600 mm AMTI force platform (AMTI, Watertown, MA, USA). Body weight of the subject was determined by subtracting the weight of the chair from the total mass.

5.3.2 Dual Energy X-ray Absorptiometry

Dual Energy X-ray Absorptiometry (DXA) (Hologic QDR, MA, USA) was used to measure bone density and body composition. DXA is considered by the World Health Organization as the "gold or criterion standard" to diagnose osteoporosis and is a well-accepted and reliable measure of body composition (261,289). A whole- body DXA scan was performed during pre-intervention screening (week 0) and again post-trial (week 24). Participants were required to remove all clothing and jewellery, wearing only their undergarments and a cotton gown for the scan. All scans were performed by the same radiographer who followed standardized procedures given by the DXA device manufacturers.

5.3.2.1 *Bone mineral density (BMD)*

BMD was measured at the following sites: whole body, lumbar spine, left and right hip, and left and right femoral neck. BMD of each region was analysed in g/cm^2. Z-scores were assessed as a pre-intervention screening tool to ensure participant's bone density were within safe ranges as prescribed by Ekso. The recommended guidelines regarding bone density for safe walking within the exoskeleton are a Z score of > -2. This is an FDA approved value to ensure minimal risk of stress fractures while walking in the suit. However, according to the 2019 ISCD bone density guidelines, there is no established threshold BMD value below which weight-bearing activities are absolutely contraindicated. There is a lack of evidence to support a T-score or Z-score cut-off as a contraindication for safe

participation in rehabilitation interventions (258). There is contradictory evidence on the risk of gait training on fracture risk, with some studies having reported fractures due to upright weight-bearing and gait training activities, while other studies using these gait training modalities reported no fractures (258). Thus, fracture risk should be evaluated on a case by case basis by the rehabilitation team based on BMD and clinical risk factors of the individual participant (258). In the current study, participants with low BMD Z- scores (< -2) were referred for clinical assessment to the study physician who, following clinical evaluation, confirmed it possible to proceed with the rehabilitation interventions.

5.3.2.2 *Whole-body bone mineral density*

Participants were evaluated in the supine position, feet rotated slightly inwards and supported with a band to prevent movement. The arms were pronated ensuring not to touch the torso. The head was positioned straight with the chin slightly elevated. The participant was positioned within the scan limits of the table. If a limb was outside the scan borders for the region of interest, values from the contralateral side were replicated. Scans were excluded from full analysis if a movement artefact was present in any limb.

5.3.2.2.1 Lumbar spine bone mineral density

Participants were evaluated in the supine position with legs elevated on a block to maintain 90 degrees of flexion for the hip and knees. The evaluation included the four lumbar vertebral bodies (L1–L4). In the case of vertebral artefacts causing technical limitations for all four vertebrae analysis, such as scoliosis, spine instrumentation or lumbar osteo-degeneration, at least two vertebrae were included in the analysis.

5.3.2.2.2 Bilateral hip bone mineral density

Bilateral hip measurements were evaluated, compiled from the femoral neck, trochanters, and intertrochanteric regions. Participants were evaluated in the supine position with the feet rotated 45 degrees and strapped into the femoral positioning.

5.3.2.3 *Body composition*

Parameters of body composition, including estimates of appendicular and total body fat-free soft tissue mass (FFSTM) (kg) and fat mass (FM) (kg), percent fat mass (%), trunk/limb fat mass ratio, android/gynoid ratio, trunk fat mass (kg), percentage trunk fat (%), VAT (cm^2), and SAT (cm^2) were obtained based on total body DXA data acquisition. In vivo precision, expressed as a percentage coefficient of variation (% CV), was 0.7% and 1.67% for FFSTM and FM, respectively.

5.3.3 Statistical analysis

All data were analysed using statistical software (R, R Core Team, Auckland, New Zealand and Prism 8, GraphPad Software Inc, California, USA). Non-parametric statistical tests, Mann Whitney U and Wilcoxon Signed Rank, were used to determine the group and time main effects on bone density and body composition between pre- and post-measurements. Significance was accepted at a $p < 0.05$. Percentage differences were calculated from pre to post intervention, with clinical significance accepted at > 5% (89). Magnitude-based inferences of change (effect size) were calculated according to Cohen's d. More details on these statistical methods can be found in Chapter 2 of this thesis.

5.4 Results

5.4.1 Participant characteristics

There were no significant differences between the ABT and RLT group at baseline for body weight, percentage whole-body fat mass and whole-body BMD values (Table 5.1). Although non-significant, the ABT group appeared to have slightly higher body weight and percentage fat mass compared to the RLT group. Whole-body Z-scores indicated that seven participants (ABT: n = 5; RLT: n = 2) were below the recommended guideline for healthy BMD of -2, indicating that these seven participants were classified as being "below the expected range for age". According to able-bodied classifications for obesity, having fat mass of >25% for men and 32% for women, 11 participants in this trial classified as being clinically obese.

Table 5.1: Bone density and body composition characteristics of the Robotic Locomotor Training and Activity-based Training groups.

Group	Participant	Body weight (Kg)	Total body fat (%)	Whole body BMD (g/cm^2)	Whole body Z-score
RLT	1	63.6	27.3	1.050	-1.6
	2	64.8	19.0	1.065	-1.4
	3	62.5	14.9	1.132	-0.7
	4	85.1	33.1	0.893	-3.2
	5	81.7	43.2	0.692	-1.4
	6	71.3	34.9	0.974	-2.3
	7	73.8	38.2	0.942	-2.3
	8	52.4	18.4	0.996	-2.2
	Average	69.4 ± 10.7	28.6 ± 10.4	0.97 ± 0.13	
ABT	9	84	40.6	0.965	-2.6
	10	63	28.4	0.952	-1.5
	11	95.8	31.8	1.150	-0.3
	12	63	28.4	0.952	-1.5
	13	99.7	43.3	1.350	1.4
	14	51.7	24.4	1.088	-1.2
	15	108.5	34.0	0.514	-2.5
	16	81.9	43.9	0.873	-3.7
	Average	81.0 ± 20.2	34.4 ± 7.4	0.98 ± 0.24	

RLT: Robotic Locomotor Training (n = 8); *ABT*: Activity-based Training (n = 8); *BMD:* bone mineral density. Values quoted as mean ± SD. *Note:* Participants with low BMD Z- scores (> -2) were referred for clinical assessment to the study physician who, following clinical evaluation, confirmed that it was possible to proceed with the rehabilitation interventions, as suggested in the ISCD official position on bone density guidelines for SCI research (258).

5.4.2 Bone mineral density

There were no significant differences between the RLT and ABT groups for spinal (ES = 0.08), hip (ES = 0.22) and FN (ES = 0.09) BMD (Table 5.2). There were no changes (0%) in spinal BMD for either group over time (p = 0.86). However, there was a significant decrease in BMD in the ABT group for both the total hip (p = 0.04) and FN (p = 0.05) measurements, with a mean difference of 0.03 [-0.29, 0.23] (3%) and 0.06 [-0.34, 0.22] g/cm^2 (5%) from pre to post intervention, respectively. No significant changes in these BMD sites were found for the RLT group over time, p = 0.55, respectively.

5.4.3 Body composition

There were no significant group differences between the ABT and RLT interventions for all body composition outcomes (Table 5.2). Effect size estimates, however, suggest that the RLT group had a

lower gynoid FM at baseline (2.84 ± 1.13 kg; ES = 1.02) in comparison to the ABT group (4.16 ± 1.45 kg). Appendicular FM also demonstrated large effect sizes between groups at baseline (ES = 1.14) and 24 weeks (ES = 1.04). This group difference in appendicular FM is highlighted by the 9% decrease for the ABT group compared to the negligible (0%) decrease in the RLT group post intervention. There was a significant 7% increase in arm FFSTM over time for both the ABT ($p < 0.01$) and RLT ($p < 0.01$) group, with a mean increase of 0.35 [-1.32, 2.02] kg and 0.34 [-0.86, 1.54] kg from pre to post intervention respectively (Table 5.2). However, no change in leg FFSTM occurred for either group over time ($p = 0.32$). The ABT group showed a significant 15% decrease in VAT ($p = 0.04$) and 13% decrease in gynoid FM ($p < 0.01$) over time, with a mean decrease from pre to post intervention of 23 [-108.39, 62.39] cm^2 and 0.54 [-1.77, 0.69] kg, respectively.

Table 5.2: A summary of bone mineral density and body composition characteristics between the Robotic Locomotor Training and Activity-based Training groups.

	RLT					ABT							
DXA outcomes	*Pre*	*Post*	Δ *[95% CI]*	*% Δ*	*p*	*Pre*	*Post*	Δ *[95% CI]*	*% Δ*	*p*	Δ *group p*	*Effect size (Pre)*	*Effect size (Post)*
Bone mineral density (g/cm^2)													
Spinal BMD	0.97 ± 0.09	0.97 ± 0.10	0.00 [-0.09, 0.09]	0	0.94	0.98 ± 0.13	0.98 ± 0.15	0.00 [-0.14, 0.14]	0	0.94	0.96	0.09	0.08
Hip BMD	1.25 ± 0.07	1.24 ± 0.08	0.01 [-0.08, 0.06]	1	0.55	1.23 ± 0.27	1.20 ± 0.25	0.03 [-0.29, 0.23]	3	**0.04***	0.13	0.10	0.22
Femoral neck BMD	1.15 ± 0.14	1.13 ± 0.14	0.02 [-0.16, 0.12]	2	0.55	1.21 ± 0.30	1.15 ± 0.27	0.06 [-0.34, 0.22]	5#	**0.05***	0.16	0.26	0.09
Fat Mass													
Whole-body FM (kg)	18.53 ± 9.18	18.29 ± 8.32	0.24 [-8.83, 8.34]	1	0.64	25.93 ± 10.60	23.46 ± 9.57	2.47 [-12.37, 7.43]	10#	0.25	0.38	0.75	0.58
Appendicular FM (kg)	7.86 ± 3.20	7.85 ± 3.03	0.010 [-3.06, 3.04]	0	0.84	12.15 ± 4.28	11.03 ± 3.11	1.12 [-4.79, 2.55]	9#	0.19	0.44	**1.14**	**1.04**
Trunk FM (kg)	10.67 ± 6.19	10.37 ± 5.60	0.30 [-6.79, 6.19]	3	0.38	13.78 ± 6.91	12.43 ± 6.74	1.35 [-8.04, 5.34]	10#	0.15	0.28	0.47	0.33
Whole-body fat (%FM)	28.62 ± 10.36	28.18 ± 9.56	0.44 [-10.25, 11.3]	2	0.67	34.79 ± 7.13	32.47 ± 5.33	2.32 [-4.43, 9.07]	7#	0.46	0.40	0.69	0.55
Appendicular fat (% FM)	44.56 ± 6.35	44.76 ± 6.90	0.20 [-6.29, 6.69]	0	0.84	49.04 ± 9.20	49.97 ± 9.69	0.93 [-8.33, 10.19]	2	0.25	0.57	0.57	0.61
Trunk fat (% FM)	55.44 ± 6.35	55.24 ± 6.90	0.20 [-6.69, 6.29]	0	0.84	50.96 ± 9.20	50.03 ± 9.69	0.93 [-10.19, 8.33]	2	0.25	0.57	0.57	0.62
Gynoid FM (kg)	2.84 ± 1.13	2.82 ± 1.21	0.20 [-1.17, 1.13]	1	0.55	4.16 ± 1.45	3.62 ± 1.03	0.54 [-1.77, 0.69]	13#	**0.01***	0.28	**1.02**	0.71
Subcutaneous fat (cm^2)	172 ± 103	170 ± 100	2 [-101.48, 97.48]	1	0.25	244 ± 115	227 ± 108	17 [-126.32, 92.32]	7#	0.55	0.88	0.66	0.55
Visceral fat (cm^2)	144 ± 100	142 ± 104	2 [-101.98, 97.98]	1	0.74	152 ± 92	129 ± 82	23 [-108.39, 62.39]	15#	**0.04***	0.08	0.08	0.14
Fat - free soft tissue mass (kg)													
Whole-body FFSTM	41.34 ± 3.96	41.94 ± 4.63	0.60 [-3.62, 4.82]	1	0.15	43.11 ± 11.45	43.91 ± 12.51	0.80 [-10.95, 12.55]	2	0.46	0.96	0.21	0.21
Appendicular FFSTM	17.96 ± 2.26	18.30 ± 2.38	0.34 [-1.93, 2.61]	2	0.54	19.65 ± 6.32	20.01 ± 6.73	0.36 [-6.04, 6.76]	2	0.46	0.88	0.36	0.34
Leg FFSTM	12.78 ± 2.03	13.20 ± 2.35	0.42 [-1.73, 2.57]	3	0.38	14.50 ± 4.79	14.77 ± 5.16	0.27 [-4.61, 5.1]	2	0.64	0.51	0.47	0.39
Arm FFSTM	5.10 ± 1.21	5.44 ± 1.24	0.34 [-0.86, 1.54]	7#	**0.01***	5.24 ± 1.65	5.59 ± 1.75	0.35 [-1.32, 2.02]	7#	**0.01***	0.96	0.10	0.76

RLT: Robotic Locomotor Training group (n = 8); *ABT:* Activity-based Training group (n = 8); *BMD:* bone mineral density; *FM:* fat mass; *FFSTM:* fat-free soft tissue mass; *kg:* kilograms; *% FM;* percentage FM; *Pre:* week 0 measurement; *Post:* week 24 measurement. Data presented as mean ± SD; Δ *(95% CI);* mean difference ± 95% confidence interval; *% Δ:* percentage change from pre to post intervention; *Statistical significance accepted at $p < 0.05$; #Clinical significance accepted at > 5% change over time. Effect size: between groups for pre- and post-respectively; Bold represents large effect size.

Figure 5.3 shows individual participant changes from pre to post intervention for whole-body and appendicular FFSTM and FM for the ABT and RLT groups. FFSTM measurements show that majority of participants experienced an increase in whole-body and appendicular lean muscle, while all measured areas of FM tended to decrease over time for most participants. Figure 5.3A shows that 62.5% of the participants (ABT: n = 4; RLT: n = 6) had improvements in whole-body FFSTM, with those individuals showing an average increase of 5.7% for the ABT group and 3.5% for the RLT group from pre to post intervention. Figure 5.3B shows that 62.5% of the participants (ABT: n = 5; RLT: n =5) had improvements in appendicular FFSTM, with a respective average increase of 5% for both groups. FM measurements (Fig. 5.3C and 5.3D) show that 69% (ABT: n = 6; RLT: n = 5) and 62.5% (ABT: n = 5; RLT: n = 5) of the participants showed improvements in whole-body FM and appendicular FM, respectively. Those that had a decrease in whole-body FM, showed an average improvement of 16.9% for the ABT group and 9.7% for the RLT group. For those that had improvements in appendicular FM, there was an average decrease of 17.1% and 10% for the ABT and RLT group, respectively. Figure 5.3E shows that 69% (ABT: n = 6; RLT: n = 5) of the participants had improvements in trunk FM, with an average decrease of 20.9% and 11.4% for those individuals in the ABT and RLT group, respectively.

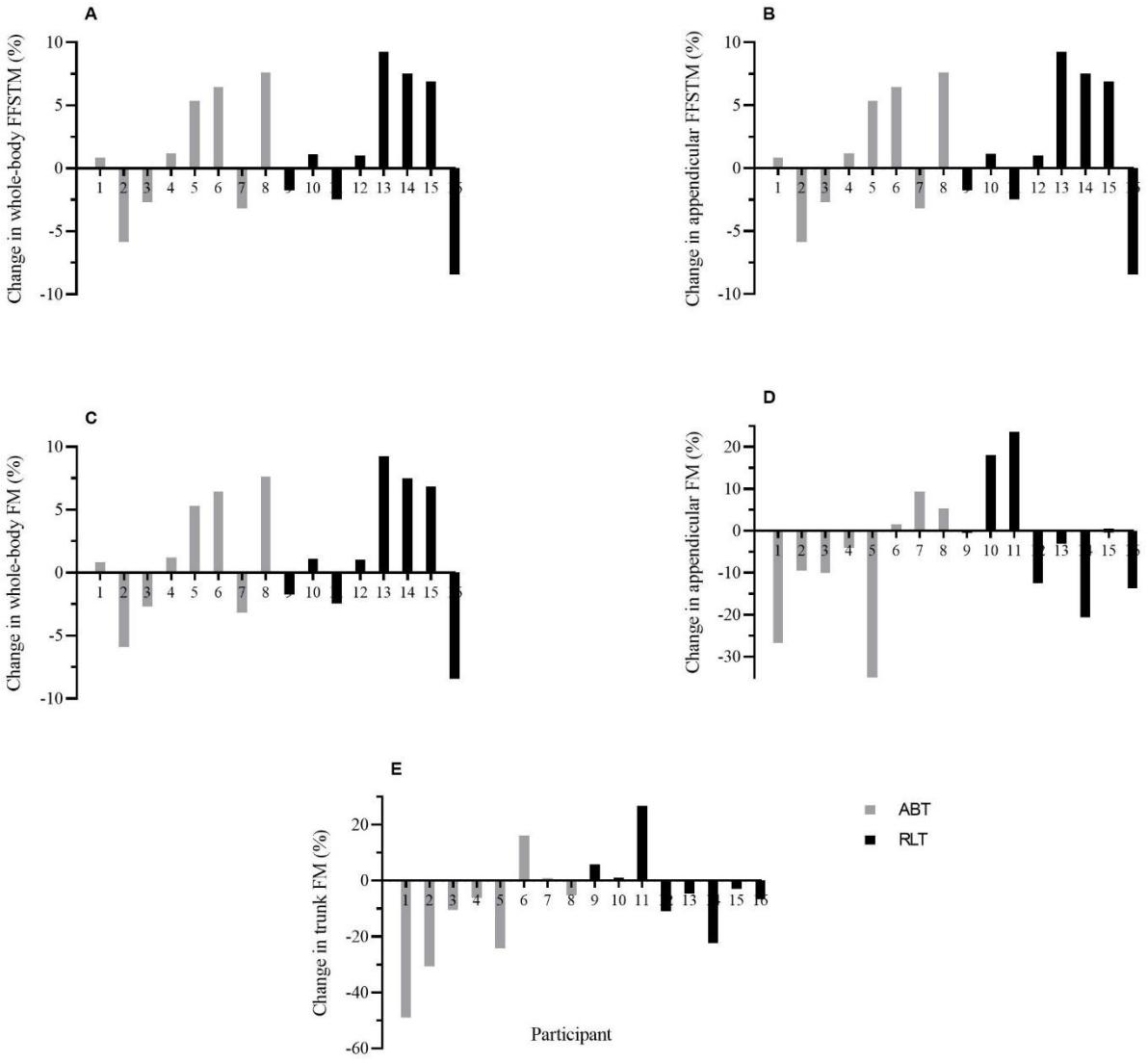

Figure 5.3: Individual participant (n = 16) changes in A) whole-body FFSTM, B) appendicular FFSTM, C) whole-body FM, D) appendicular FM, and E) trunk FM over time.

RLT: Robotic Locomotor Training; *ABT:* Activity-based training; *FFSTM:* fat-free soft tissue mass (lean muscle mass); *FM:* fat mass; *Whole-body:* full body; *Appendicular:* arms and legs only; *A:* whole-body FFSTM; *B:* regional FFSTM; *C:* whole-body FM; *D:* regional FM; *E:* trunk FM. Data presented as individual (n = 16) percentage change from pre to post intervention for the ABT group (participants 1-8) and the RLT group (participants 9-16).

5.5 Discussion

This randomized controlled pilot study explored the effects of RLT in comparison to ABT on bone density and body composition in people with chronic incomplete SCI, over an intervention period of 24

weeks. The results of this novel trial support the clinical effectiveness of RLT in preventing BMD decline in individuals with SCI. However, it appears that conventional ABT may be the better intervention to mitigate adverse changes in body composition in a SCI population. In the following, we discuss the main findings with respect to each of these aspects.

5.5.1 Bone mineral density

5.5.1.1 *Spinal bone mineral density*

No changes in spinal BMD were noted between groups ($p = 0.96$; ES = 0.09) or over time within this study. A lack of change in the cortical bone of the spine is expected, as BMD adaptations typically occur in regions rich in trabecular bone, as they have the greatest bone remodelling potential (263,269,290). In addition, spinal BMD may not have shown changes with the exercise interventions, as studies have found that lumbar spine BMD is preserved regardless of standing, potentially due to the axial loading that occurs while seated in a wheelchair (264,286).

5.5.1.2 *Hip bone mineral density*

The main finding of this study showed that there was a significant reduction in hip and FN BMD in the ABT group over time, with a change of 0.03 [-0.29, 0.23] and 0.06 [-0.34, 0.22] g/cm^2 from pre to post intervention, with p-values of 0.04 and 0.05, respectively. However, the RLT group showed no changes in these BMD measures across the 24 weeks ($p > 0.05$). Therefore, despite both the ABT and RLT interventions involving regular standing and weight-bearing, BMD was only preserved in the RLT group. However, the highest rate of bone mineral loss occurs in the first 1–2 years post-injury (29,291). Thus, the more severe bone loss in the ABT group may possibly be accounted for by the four individuals who are three years or less post injury, compared to the single individual in the RLT group. Therefore, although the groups are statistically balanced at baseline for time since injury, the ABT group's mean injury duration is lower and there are more participants within the three-year window.

5.5.1.3 *Effects of dynamic loading on bone mineral density*

Although there are a multitude of factors influencing the pathophysiology of SCI-related BMD decline, the loss of mechanical loading to bone is considered to be a key component (269). Therefore, reintroduction of load and mechanical stress, through passive standing or by various aided-walking systems, may be a viable strategy for preventing or reducing bone loss after SCI (286,292,293). Dudley-Jarvoski et al. (2012) (290) compared post-SCI BMD of the distal femur in individuals with SCI who received three doses of bone compressive loads: 0% (no standing), 40% (passive standing), and 150% (quadriceps activation while standing). Quadriceps loading during stance yielded better results over three years of training than the two lower dose levels and no significant differences emerged between passive standing and no standing. As passive standing was not sufficient to produce BMD changes, the results of this study confirm that muscular loads in stance are needed to offer a bone-sparing stimulus to the lower limbs following SCI (290).

Other studies are in agreement, demonstrating that dynamic loading of the skeleton is more effective than static loading in terms of bone mass (293). A pilot study considering the benefits of RLT on BMD in five people with chronic complete SCI (C7 - T10) found that after six weeks of RLT, three times per week, tibial bone density increased by 14.5% (89). This finding was not statistically significant but clinically relevant in a population who generally experiences a steady decline in their bone density. As dynamic loading to the skeleton seems critical to maintaining or preventing BMD loss, this may provide reason for why the RLT group's bone density was persevered. The repetitive dynamic loading of RLT was effective in preventing BMD decline in people with SCI because, as Wolff's Law suggests, the skeleton responds to mechanical loading by increasing cortical bone at the site of greatest mechanical strain (267,282).

5.5.1.4 *Effects of training parameters bone mineral density*

Contrary to our findings that passive standing in the ABT group did not improve BMD, a prospective study of 54 individuals with SCI showed that those who performed passive daily standing had less BMD loss in the lower extremities after two years compared with those who did not perform standing (294).

However, it is relevant to consider that the participants in this study were in the acute phase of injury and additionally, were required to stand for one hour or more per day for at least five days per week, over two years, for bone effects to be observed. Two systematic reviews (281,295) concluded that of the small number of studies that demonstrated that mechanical loading might be beneficial for the skeleton after SCI, a common component was long-term (six months or greater), higher dose programmes (five times per week). Karimi et al. (2012) (296) showed that standing and walking with an orthosis must be done lifelong and must be repeated several times a week to yield effects on bone osteoporosis. From the evidence gathered by Zehnacker et al. (2007) (297), the effectiveness of strength training in the hip and spine sites is related to the intensity of the training; the exercise requires high loads (70-90% of a maximum repetition) for 8-10 repetitions of 2- 3 sets performed at least for 1 year, 3 times a week for 45- 70 minutes per session. Strain patterns must be atypical and because bone cells rapidly become desensitized to prolonged loading, periods of rest are required between sessions to maximize osteogenic potential (298,299).

Therefore, these studies suggest that BMD benefits for people with SCI rely on exercises that can produce dynamic loading that are delivered with enough transitional force, enough frequency and for sufficiently long durations to stimulate new bone formation (257,282,298,300). These parameters further highlight why RLT may have been more effective in BMD maintenance compared to ABT, as the robotic walking resulted in more frequent and longer time periods of unusual force distribution in the skeletal system. The passive standing in the ABT group may not have provided sufficient stimulus to elicit osteogenic effects in those participants, as constant stimulation can lead to desensitization of the bone to the applied mechanical forces (267,284). Similarly, Goemare et al. (1994) (301) reported that solely standing will not prevent bone loss at the proximal hip and a number of other studies have shown no significant impact of passive standing on lower limb BMD in individuals with chronic SCI (257,300,302).

5.5.2 Body Composition

This study showed that there were no group differences in the body composition variables over the 24 weeks of rehabilitation. However, ABT improved body composition by decreasing FM and positively altering adiposity distribution whereas, the RLT group did not experience any significant changes in FM or its distribution over the 24-week intervention. Both groups increased FFSTM in the upper extremities but neither group showed changes in lower body lean muscle mass over the 24 weeks.

5.5.2.1 *Fat mass*

This study showed that ABT was effective in altering adverse body composition in people with SCI over 24 weeks of rehabilitation. There were significant decreases in VAT (15%) and gynoid FM (13%) in the ABT group from pre to post intervention. ABT has previously been identified as a rehabilitation tool that mechanically loads skeletal muscle to increase lean mass and decrease FM in different clinical populations, including SCI (155,303). In agreement with these findings, D' Oliveira et al. (2014) (278) showed that resistance exercise practiced at least three times a week for at least three months was sufficient to promote positive changes in FM, especially for central adiposity. However, a review of 69 studies concluded that the evidence is mixed regarding the effects of exercise on body composition because studies have yielded inconsistent results that are difficult to interpret and synthesize given methodologic limitations and inconsistencies (158). In addition, there are many complex physiologic, metabolic, and biochemical mechanisms that can mediate changes in body composition, acting as confounders for changes related to exercise interventions (132).

Some exercise interventions have failed to produce significant reductions in FM for people with SCI, with the exception of some low powered functional electrical stimulation (FES) studies (158). Astorino and colleagues (2015) evaluated six months of ABT in 17 individuals with SCI. Despite high compliance to training across all participants, no change in body weight or body fat was exhibited (304). A paper by Fischer et al. (2015), reviewed studies using resistance training circuits for people with SCI and found that based on the results of seven included studies (140,145,166,195,305–307), there was no

evidence to support changes in body composition following upper body circuit resistance training. Although ABT has been recommended as a promising therapeutic strategy to counter the adverse changes in body fat (282), currently limited evidence is available examining the effects of RLT on body composition after SCI.

To our knowledge, no RCTs have examined the effects of over-ground RLT on body composition in people with SCI. However, based on small case-series, RLT has been suggested to be a viable strategy for the reduction of FM in individuals with SCI. Karelis et al. (2017) evaluated body composition changes with RLT in people with SCI and observed body composition changes in five participants after six weeks of robotic walking included a decrease in total, leg and appendicular FM (89). Total body adipose tissue was reduced by 5% in these individuals post training. In a case-series, a single participant with incomplete SCI, performed RLT 1 x per week for 16 weeks (206). The participant presented with a modest decrease in FM. Contrary to these case-series, the current study found no effect of RLT on FM after 24 weeks of training. Exercise regimes need to be intense and of sufficient frequency to result in a decrease in total FM, and it has been suggested that a locomotor training frequency of two to three times a week likely does not result in enough energy expenditure for the energy balance equation to change (266,308). Another reason for why RLT did not induce changes in FM in the current study, could be due to the intensity of training. A systematic review concerning different types of exercise intensities on weight loss in able-bodied adults showed that high intensity interval training provided greater absolute reductions in FM compared to moderate intensity long duration training (309).

Within the current study, ABT sessions typically involved variations of resistance training and cardiovascular training whereas RLT involved exclusively walking in the exoskeleton. Thus, ABT may have produced a greater reduction in FM compared to RLT, as ABT consisted of high volume interval training which would have increased total daily energy expenditure by raising the resting basal metabolic rate and physical activity-associated energy expenditure of the participants in the group (266,304).

5.5.2.2 *Fat-free soft tissue mass*

Both the ABT and RLT interventions were successful in promoting positive changes in FFSTM in the upper body over time ($p < 0.01$). ABT is the key strategy used for strengthening the upper limb muscles of people with paraplegia and thus, increases in arm FFSTM were expected due to the high levels of upper body utilization within this training modality (165). RLT participants may also have encountered upper body increases in FFSTM attributed to the performance of a new exercise modality that uses the upper extremities for support within the Ekso bionic suit. Upper body muscle strength can be attributed to the fact that locomotor training requires active participation from the user to move and use a gait aid while maintaining standing balance. Despite the improvements in upper body FFSTM for both groups during the trial, no changes in lower limb FFSTM were measured for either group over time. As ABT does not solely target the leg muscles, its inability to promote muscle hypertrophy in the lower limbs is not surprising (165,304). The effect of RLT on FFSTM is less clear, as to our knowledge, no RCTs have evaluated the effect of over-ground RLT on body composition outcomes.

However, RLT may increase FFSTM of the lower limbs, as the repetitive movement of walking can trigger neuroplasticity changes due to rewiring of the motor cortex, which in turn enhances muscle hypertrophy (43). The spinal circuitry responds to sensory input, adapts behavioural output appropriately, and can induce permanent modifications in this system with repetition: the spinal cord can learn (51). Locomotor training after incomplete SCI promotes improved corticospinal drive to muscles of the lower limbs that correlates with improved locomotor function. This increased corticospinal drive could come from plasticity occurring in the cortex or in the descending pathways themselves (43). This effect of RLT on muscle gain for individuals with SCI was evident in a case-study by Karelis et al. (2017) who evaluated body composition changes of five individuals in response to six weeks of thrice weekly RLT. Observed changes after six weeks of walking included an increase in leg and appendicular FFSTM (89). Repetition is not the only factor effecting the induction of neural plasticity, as the intensity of stimulation also plays a role (310). Low-intensity stimulation can induce a weakening of synaptic responses (long-term depression), whereas higher intensity stimulation will

induce long-term potentiation (310). Consequently, the majority of SCI studies in which increases in lower body FFSTM occurred, are characterized by functional electrical stimulation (304). Therefore, the intensity of the RLT stimulation in this study may not have been high enough to cause lean muscle adaptation below the SCI lesion level.

Although neither the ABT nor the RLT intervention produced lower limb hypertrophy over time, they did prevent a worsening of muscle atrophy over the 24 weeks. Thus, the lack of change in leg FFTSM in response to both exercise interventions can be viewed as a desirable outcome considering that usually, lean muscle tends to decrease over time in the SCI population.

5.5.2.3 *Individual variability in body composition*

Data from able-bodied individuals exhibit varying responses to identical regimens of training whether it be resistance-based or aerobic in origin (304). As SCI research is typically characterized by heterogenous populations, it is likely that similar individual differences in exercise adaptation exist in the SCI population (304). In the current study, there was large variability in the alterations in body composition, as some participants showed marked declines in FFSTM and FM, whereas others showed a relative maintenance or increase in these outcomes (Fig. 5.3). Fat loss in response to exercise training varies between individuals, even when differences in compliance to the exercise programme are accounted for (158,278,279,311). It has been suggested that individual differences in compensatory adjustments to the increased exercise energy expenditure may be responsible for this variability noted in body composition changes.

Data reported by Astorino and colleagues (2015) showed that participants who had improved FFSTM were sedentary upon entering the study, so it would be anticipated that a new exercise stimulus may promote FFSTM accretion, whereas those who typically lost FFSTM were habitual exercisers prior to the onset of SCI (304). Therefore, daily activity level and participation in leisure-time physical activity prior to entering the study may be an important aspect of body composition responses to exercise.

Furthermore, although participants completed the same modality of training and minimum training frequency and duration, the specific programmes were individualized for each participant based on their tolerance to exercise, so were somewhat different across individuals.

Fischer et al. (2015) suggests that SCI classification can effect individual changes in body composition, possibly due to the differences in spasticity levels and daily physical capacity (162). Additionally, demographic variables, such as age, sex and ethnicity have been shown to be important influences in determining body composition (96,162,258,304). Dietary intake must also be considered as an explanation for the marked variability in body composition changes, as healthy dietary intake may result in lowering the percentage of FM, increasing lean muscle growth and reduce the associated co-morbidities in people with SCI (162,304). A combination of these habits together with predisposed genetic factors and hormonal contributions may explain the large variance noted in body composition changes within this study.

5.5.3 Limitations

Several limitations to the study should be noted. This study considered the BMD measurements of the hip and spine. However, since the distal femur and proximal tibia are the most common sites of fracture post SCI (258), an effort should be made to assess the impact of interventions at these specific sites. Additionally, future research should consider caloric intake or dietary outcomes, as this could affect energy balance and result in excess body fat accumulation. Furthermore, neither calcium intake, vitamin D concentrations or melatonin concentrations were assessed within this study. As these variables can impact bone resorption and formation, perhaps they should be investigated in future trials as an additional outcome of interest.

5.5.4 Conclusions

This study offers novel insights into the effect of RLT and ABT on bone density and body composition in individuals with a traumatic cervical motor incomplete SCI over a 24-week intervention. In summary, to assist clinicians in identifying optimal exercise regimens to attenuate the risk of osteoporosis and

improve body composition in this population, we translate the findings of this study into practical suggestions:

1) *Bone mineral density*

   RLT prevented the progressive decline of BMD usually occurring in this population group. Therefore, RLT may act as an effective rehabilitation tool for preventing the development of osteoporosis and BMD decline in individuals with SCI.

2) *Fat mass*

   ABT resulted in significant reductions in central adiposity (gynoid and VAT) and showed clinically significant reductions in all other measures of FM. Thus, if reducing adiposity is the goal of the rehabilitation programme, then ABT may be more effective compared to RLT. ABT may serve as an effective rehabilitation strategy to reduce total body FM and improve adiposity distribution, reducing the risk of chronic disease in this population.

3) *Lean muscle mass*

   Both ABT and RLT interventions improved upper body FFSTM. Neither intervention resulted in lower extremity muscle gain, but both prevented further muscle atrophy over time. Therefore, both interventions appear equally promising in promoting upper extremity muscle gain and preventing lower body muscle atrophy.

Despite proposing different interventions to address specific BMD and body composition goals, considering the myriad of secondary complications associated with SCI, a multifaceted treatment approach, including both ABT and RLT, could likely be the most successful scenario; however, this would need to be assessed in a future study. Given the associated health risks for cardiovascular and metabolic syndromes after SCI, more rigorously designed studies are needed to examine the effects of various doses of exercise types on these key health concerns. Research studies would need to design

more structured exercise trials that build on previous research and maintain a higher-level of sample and protocol homogeny. This will provide a stronger evidence base that will help support the translation of these findings into evidence-based best practice. Therefore, a larger sample sized RCT over a longer intervention period is warranted.

5.6 References

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CHAPTER 6

Psychological well-being after 24 weeks of exercise rehabilitation in individuals with spinal cord injuries

6.1 Introduction

In Chapters 3 – 5, the effect of RLT on functional capacity and major secondary health concerns were examined, encompassing several physiological rehabilitation outcomes of people with SCI. However, it is also relevant to consider the psychological outcomes of training as a fundamental requirement for rehabilitation post SCI. Individuals with SCI not only experience the trauma of the spinal injury itself, but a further series of multiple traumas associated with losses as the consequences of the physical injury become apparent (143). These resultant losses and overwhelming lifestyle changes that follow SCI often affect the individual's psychological and social functioning and make it difficult for individuals to emotionally adjust to their everyday lives (29,31,312). Research shows that people with SCI have a higher risk of negative mental health outcomes, including anxiety, depression, feelings of helplessness, higher levels of distress and lower levels of QoL (32,37,227,313,314). Longitudinal research suggests that almost 30% of people with SCI have clinically elevated levels of anxiety (313) and approximately 20% to 30% report significant depressive symptoms (34,315,316). The major concern linked to these depressive symptoms is suicide, as individuals with SCI are reported to be three to five times more likely to commit suicide compared to the general population (34,317). Furthermore, suicide is the leading cause of death in individuals with SCI younger than 55 years, where 75% of suicides occur within the first five years following injury (12).

Due to the poor psychological status associated with SCI, the ability to cope successfully with rehabilitation may be adversely affected, leading to poor rehabilitation outcomes (12,318). Negative psychological symptoms are also associated with decreased adherence to rehabilitation regimens (315,319). Therefore, in order to provide comprehensive treatment and individual care, it is of utmost

importance that rehabilitation staff can recognise and understand depression and anxiety symptoms (319). However, rehabilitation staff have been shown to inaccurately perceive the nature and degree of the emotional states and psychological distresses of SCI individuals. Staff tend to overestimate the prevalence of negative emotional problems, while underestimating the individuals' optimism and coping ability (320,321). Furthermore, people with SCI also tend to report lower QoL scores than able-bodied individuals (112,143).

QoL is a person-oriented and a multi-dimensional construct, which considers subjective appraisals of one's situation as well as objective and observable aspects (32,321,322). Consequently, there are large individual differences in reported ratings of emotional well-being among people with SCI (111,323). These differences are influenced by numerous demographic and psychosocial factors, including culture, age, social engagement and economic status (32,324,325). For example, older adults with physical disabilities are more likely to report symptoms of depression and lower QoL than younger persons (321,326). Subjective experiences, such as beliefs, attitudes and expectations can also influence the adjustment process after SCI and are expected to impact QoL (325). Secondary heath complications, such as pain and bladder and bowel incontinence, should also be considered to effect psychological states amongst people with SCI (32,321).

6.1.1 Physical activity and psychological well-being

Research in the able-bodied and some clinical populations have shown that regular physical activity is associated with improvements in a wide range of psychological outcomes, including depression and QoL (111,327). Some have even reported that exercise may be as effective as psychological interventions and drug therapy in treating depression, as it reduces stress and anxiety, improves body image, elevates self-efficacy, self-esteem, self-confidence, and prevents negative thoughts (327). Despite the relevance of psychological well-being for most populations, it remains a complex and fairly underexplored topic in SCI literature (222,315,328). There is a lack of systematic studies on the effects

of long-term exercise training on psychological well-being and other aspects of QoL in persons with SCI. To the authors knowledge, only a single quantitative RCT, by Hicks et al. (2003), has been performed on psychological well-being of people with SCI after exercise training. They investigated the effects of nine months of twice weekly resistance exercise on QoL for 23 people with SCI (exercise group: n = 11; control group: n = 12). The exercise group reported less stress, fewer depressive symptoms, improved QoL and greater satisfaction with their physical appearance and functioning, than the control group ($p < 0.05$) (111). Hicks et al. (2003) therefore, suggests that exercise can and should be used as a therapeutic modality for improving psychological well-being among people with SCI. As RLT is a novel form of physical activity, its effect on psychological outcomes remains uncertain.

The positive link between physical activity and psychological outcomes, with the unique features of RLT training, such as eye-to-eye contact (Chapter 1, Section 1.6), highlights the potential for improving the psychological outlook of individuals engaging in RLT (329). Previous case studies have shown that participating in gait training has the potential to improve self-image, decrease depression and create positive changes in emotion (330,331). Moreover, Stampacchia et al. (2016) reported positive changes in emotions and overall QoL for 21 individuals with SCI following only a single session (7–25 min) of walking in the Ekso powered exoskeleton (97). In a small case report by Cruciger et al. (2016), both participants (10 and 19 years; AIS A) reported increased health-related QoL scores for all eight domains of the Short Form Health Survey (SF-36) over 12 weeks of training (332). Similarly, a case study involving one individual with paraplegia, reported increased scores in six out of eight areas of the SF-36 following six months of rehabilitation with the ReWalk powered exoskeleton (333). Thus, despite being low powered with small sample sizes, these few studies show that the use of robotic exoskeletons may improve QoL and psychological well-being for people with SCI.

The contextual factor of the current study should also be considered for its possible impact on the psychological outlook of those involved in this research trial. Not only is the RLT technology new, and

currently expensive, but this pilot study was conducted in South Africa, a country which has, in common with many other low and middle-income countries, a relative lack of access to rehabilitative services in general (73,74,334,335). Most people with SCI in these contexts will have access to limited acute care, but it is uncommon to receive follow-up out-patient rehabilitation, due to reasons such as overstretched health systems, unaffordable rehabilitation rates, and unavailability of accessible transport (335,336). In South Africa, it is rare for a person with a SCI to be part of a rehabilitation study where they are provided any form of traditional exercise therapy. Thus, part of what becomes of interest in our study, is not only that they have access to a novel rehabilitation technology (i.e. bionic exoskeleton) but that they have access to care which is not universally available, which may in itself have psychological meaning for participants (337). Thus, in order to provide comprehensive SCI treatment and rehabilitation, and achieve the essential goal of improved QoL, it is critical that depression and anxiety and their link to both physical and health outcomes, are recognised and explored in full. This study aimed to investigate the psychological outcomes from participating in a pilot RCT investigating 24 weeks of novel RLT rehabilitation in people with chronic SCI within a low-middle income context.

6.2 Aims

This chapter aimed to determine the effect of RLT and ABT on psychological well-being in individuals with SCI prior to and following a 24-week rehabilitation intervention. The psychometric outcomes included self-reported markers of depression, anxiety and QoL.

6.2.1 Objectives

The objectives of this study were to evaluate and compare the psychological impact of ABT and RLT interventions over a 24-week period on:

1. Depression *(Beck Depression Inventory (BDI))*

2. Anxiety *(State-trait Anxiety Inventory (STAI))*

a) State anxiety

b) Trait anxiety

3. QoL *(International SCI Quality of Life Basic Data Set)*

a) Life as a whole/general life

b) Physical health

c) Emotional well-being

6.3 Methods

Comprehensive methods of the study protocol, including the ABT and RLT interventions, are provided in Chapter 2 of this thesis. Methods pertaining to the psychometric analysis are contained below. All 16 participants were included in the psychometric analysis. Traditional psychological studies into the effects of trauma on human beings have concentrated on identifying the negative, psychopathological consequences of life changing events. Thus, this study focused on the psychometric analysis of participant's negative emotional outcomes, including depression, anxiety and QoL. Self-report measures are widely used in the SCI literature to assess a participant's mental and emotional state (338). Therefore, validated psychological questionnaires were used to measure psychological well-being at 0, 6, 12 and 24 weeks (339,340). The questionnaires included:

6.3.1 Beck depression inventory (BDI)

This validated questionnaire (Appendix 6.1) was used to measure different markers of clinical depression. It consisted of 21 questions with four available score ratings per question: 0, 1, 2, 3 each indicating increasingly higher levels of depression symptoms. The individual scores of the 21 questions were added to provide a total depression score, with the lowest possible score of 0 and the highest possible score of 63. A score of 17 or higher indicated evidence of clinical depression, suggesting that medical treatment may be required (341).

6.3.2 State-Trait Anxiety Inventory (STAI)

This validated questionnaire (Appendix 6.2) was used to assess two types of anxiety markers: Trait and State. Trait anxiety referred to the relatively stable individual differences in anxiety proneness. State anxiety referred to the transitory emotional state in response to a threatening situation (Spielberger, 2010). The inventory comprised of two separate self-report scales: the trait anxiety scale; consisting of 20 statements, assessed how people ***generally*** felt. Each question had four choices to rate the ***frequency*** of their feelings: (1) almost never; (2) sometimes; (3) often; (4) almost always. The state anxiety scale: consisting of 20 statements, evaluated how respondents felt ***in the moment***. Each question had four choices to describe the ***intensity*** of their feelings: (1) not at all; (2) somewhat; (3) moderately so; (4) very much so. Anxiety scores for both sub-scales could vary from a minimum of 20 to a maximum of 80, with a higher score indicative of greater anxiety. A cut point of 39–40 was used to detect clinically significant symptoms for the state anxiety scale (342).

6.3.3 International SCI Quality of Life Basic Data Set

This validated questionnaire (Appendix 6.3) was used to assess average QoL in the past four weeks across three domains: A) life as a whole (general life); B) physical health; C) psychological well-being. This data set is part of the International SCI Data Sets project which is an effort by the International Spinal Cord Society (ISCoS) and the American Spinal Injury Association (ASIA) to create internationally recognized and endorsed standard data sets relevant to SCI populations (321). Scores were rated on a scale ranging from 0 (completely dissatisfied) to 10 (completely satisfied). A higher score indicates greater perceptions of QoL (321).

6.3.4 Statistical analysis

All data were analysed using statistical software (R, R Core Team, Auckland, New Zealand and Prism 8, GraphPad Software Inc, California, USA). Linear mixed effect models assessed continuous responses which were measured at four time points (0, 6, 12 and 24 weeks). Categorical responses were analysed cross-sectionally using a Fisher's exact test at each time point. Magnitude-based inferences of change

(effect size) were calculated according to Cohen's d. Relationships between the variables were assessed using linear regression analyses and correlation matrices. More details on these statistical methods can be found in Chapter 2, Section 2.3.6 of this thesis.

6.4 Results

Table 6.1: Psychometric characteristics for the Robotic Locomotor Training and Activity-based Training groups at baseline and week 24.

	RLT			**ABT**			**Effect size**	
Psychological outcomes	*Pre*	*Post*	*%Δ*	*Pre*	*Post*	*%Δ*	*Pre*	*Post*
Depression	8.75 ± 7.17	5.50 ± 3.55	-59	10.12 ± 8.69	9.88 ± 11.26	-2	0.17	0.52
State anxiety	47.12 ± 7.02	48.38 ± 5.32	3	46.38 ± 5.53	45.00 ± 4.93	-3	0.12	0.66
Trait anxiety	46.88 ± 5.79	50.12 ± 5.87	6	46.52 ± 3.27	44.62 ± 5.40	-4	0.08	**0.98**
General QoL	6.25 ± 2.31	8.62 ± 1.40	27	6.75 ± 2.31	7.50 ± 1.60	10	0.22	0.75
Physical QoL	6.62 ± 1.69	8.62 ± 1.19	23	6.50 ± 2.27	7.12 ± 2.30	9	0.06	**0.82**
Psychological QoL	8.00 ± 1.69	8.25 ± 1.83	3	7.12 ± 2.53	7.75 ± 2.12	8	0.41	0.26

RLT: Robotic Locomotor Training (n = 8); *ABT:* Activity-based Training (n = 8); *Pre:* week 0 measurement; *Post:* week 24 measurement. Data presented as mean ± SD; *%Δ:* mean percentage change from pre to post. Effect size: between groups for pre- and post-respectively; Bold represents large effect size.

6.4.1 Depression

There were no between-group differences in markers of depression over time (p = 0.20; ES = 0.52). However, the RLT group showed a trend of decreasing depression (p = 0.09), with a total decrease in score of 3.25 units from pre to post intervention (Fig. 6.1). As seen in Table 6.1, this decreasing trend for the RLT group correlated to a considerable mean reduction in depression of 59% over time, whereas the ABT group experienced a negligible decrease of 2% over time (p = 0.88). The ABT group indicated substantially more response variability at each time point, indicated by the larger standard deviations in Table 6.1.

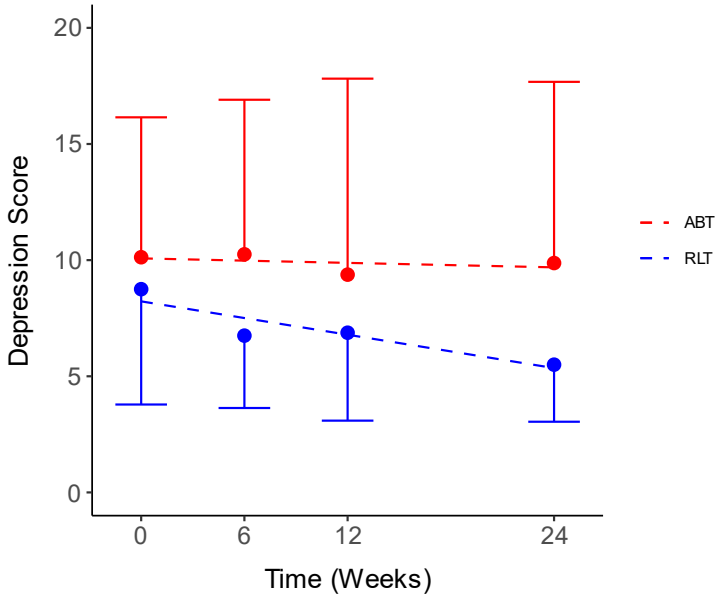

Figure 6.1: Self-reported depression for the Robotic Locomotor Training and Activity-based Training groups over time.

RLT: Robotic Locomotor Training (n = 8); *ABT:* Activity-based Training (n = 8); *Depression score (0-63)*: Beck depression inventory (BDI*).* Data presented as observed mean ± half-width 95% CI. Modelled linear estimates shown as superimposed lines (predicted mean). No significant difference between the groups at baseline (p = 0.65).

Figure 6.2 illustrates the individual variability in depression scores for all 16 participants. This shows that overall, the participants reported depression scores ranging from 1 to 25, with average (mean ± SD) pre- and post-intervention scores of 10.12 ± 8.69 and 9.88 ± 11.26 reported for the ABT group and 8.75 ± 7.17 and 5.50 ± 3.55 for the RLT group respectively (Table 6.1). However, there was a single outlier, participant 6, in the ABT group who reported substantially higher depression scores throughout the intervention (Fig. 6.2). When participant 6 was removed from the calculation, the average depression scores for the ABT group at pre- and post-intervention were 7.57 ± 5.22 and 6.14 ± 4.22. Thus, without P6 skewing the data for the ABT group, the resultant mean percentage change in depression increased from 2% to 23% across the 24 weeks.

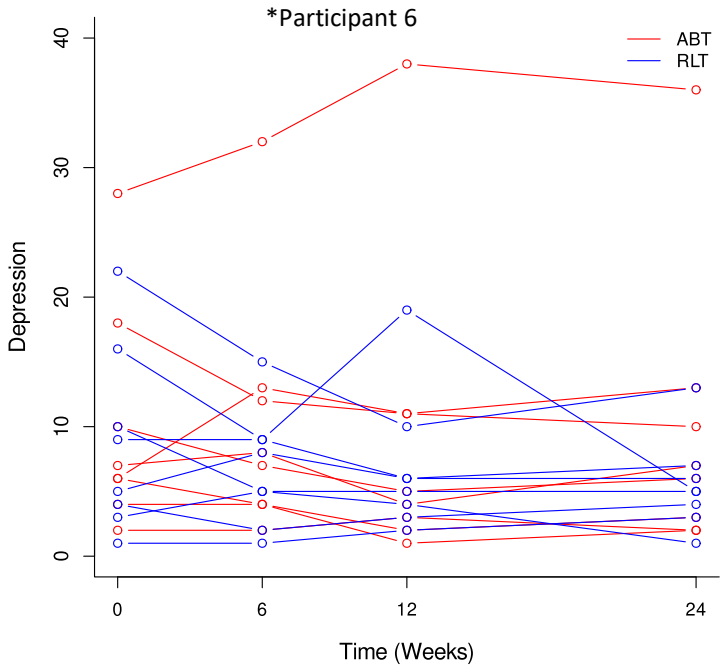

Figure 6.2: Individual participant (n = 16) depression scores over time.

RLT: Robotic Locomotor Training (n = 8); *ABT:* Activity-based Training (n = 8); *Participant 6:* Single individual in the ABT group; *Depression score (0-63)*: Beck depression inventory (BDI)*;* * Outlier.

Majority of the participants across both groups fell within the range of scores considered as the "normal category" of depression, with a few people reporting "mild" to "moderate" depression symptoms according to the questionnaire. The RLT group showed no "severe" depression scores over time, whereas the ABT group did from week six onwards. This is due to P6 in the ABT group, who reported to have high markers of depression throughout the intervention with scores of >31 across all time points (Fig. 6.3). This participant was screened prior to the intervention by trained psychologists and was cleared to participate in the trial. This participant, like the others in this study, received psychological support from the trained psychologist throughout the intervention period, and was encouraged to contact the psychologist during external rehabilitation hours to receive additional emotional support as required. The psychological state of the participants was overseen by the psychologist and any concerning

information was passed onto the Biokineticist's if deemed necessary, while still upholding the ethical guidelines stipulated.

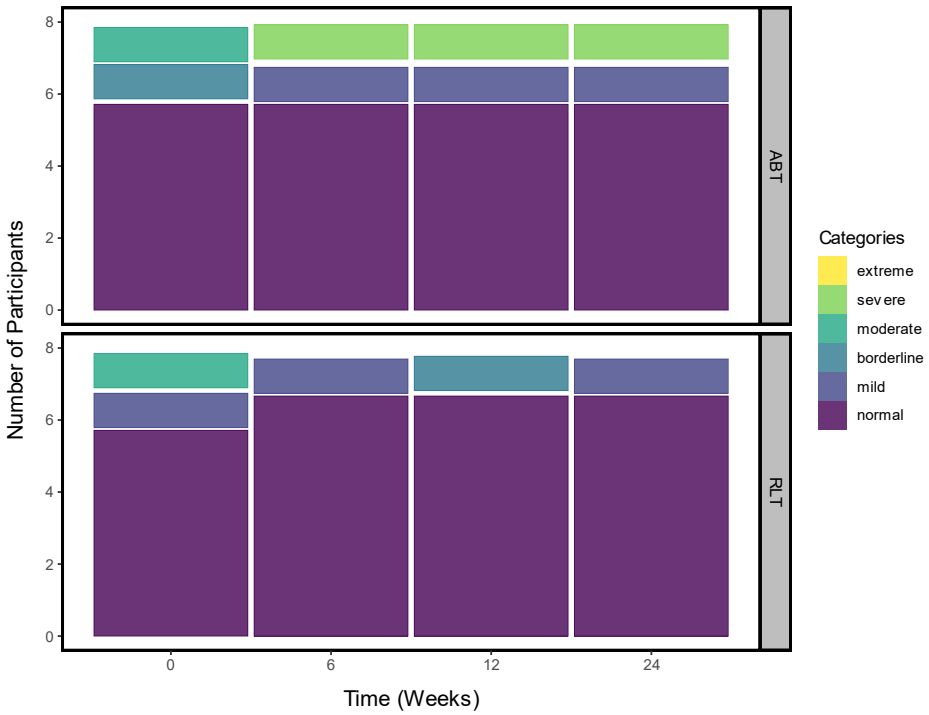

Figure 6.3: Depression categories for Robotic Locomotor Training and Activity-based Training groups over time.

RLT: Robotic Locomotor Training (n = 8); *ABT:* Activity-based Training (n = 8); *Depression score (0-63)*: Beck depression inventory (BDI)*; Categories:* 0-10: considered normal, 11-16: mild mood disturbance, 17-20: mild depression, 21-30: moderate depression, 31-40: severe depression, >40: extreme depression. Significant outlier evident in ABT group = severe depression category (31 – 40).

6.4.2 Anxiety

There were no differences in markers of state anxiety between the ABT and RLT groups (p = 0.59) or over time (p = 0.67) (Fig. 6.4A). However, as seen in Table 6.1, although both groups experienced a non-significant mean change in state anxiety from pre to post intervention, the RLT group had increased scores, while the ABT group showed decreased scores over time (ES = 0.66). Similarly, markers of trait anxiety (Fig. 6.4B) tended to increase for the RLT group and decrease for the ABT group over time (ES = 0.98), resulting in a notable interaction effect between the two interventions and time (p = 0.06). The

RLT group had an average trait anxiety score of 46.88 ± 5.79 at baseline, with an increase of 6% post intervention, while the ABT group had an average trait anxiety score of 46.52 ± 3.27 at baseline, with a decrease of 4% post intervention.

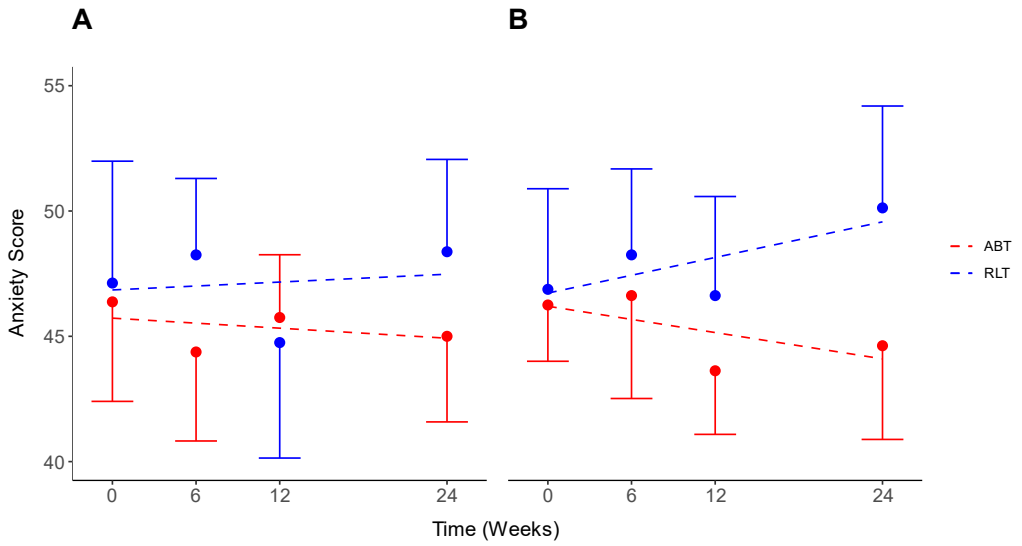

Figure 6.4: Self-reported anxiety scores for A) state anxiety, and B) trait anxiety, for the Robotic Locomotor Training and Activity-based Training groups over time.

RLT: Robotic Locomotor Training (n = 8); *ABT:* Activity-based Training (n = 8); *Anxiety Score (20 -80):* State-trait anxiety inventory (STAI); *A:* State anxiety; *B:* Trait anxiety. Data presented as observed mean ± half-width 95% CI. Modelled linear estimates shown as superimposed lines (predicted mean). * No significant difference between groups at baseline for state or trait anxiety (p = 0.65 and p = 0.82 respectively).

The relationship between reported state and trait anxiety for both intervention groups is shown in the regression analysis in Figure 6.5. There was a strong relationship between the ABT group's state and trait anxiety scores (r^2 = 0.71; p = 0.05). However, no correlation existed between the anxiety scores for the RLT group (r^2 = 0.35; p = 0.40). Additionally, the RLT group's anxiety responses were more variable than those of the ABT group, illustrated by the larger 95% CIs (Fig. 6.5).

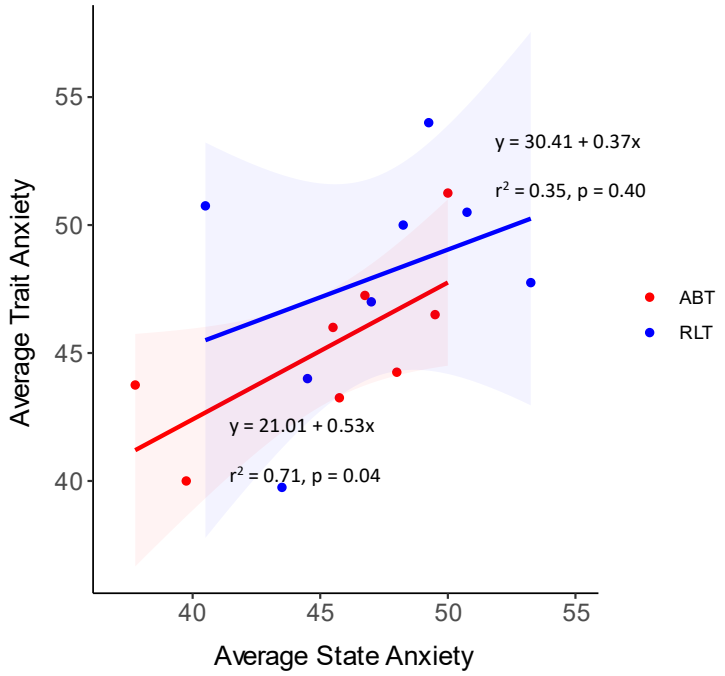

Figure 6.5: Relationship between trait and state anxiety for the Robotic Locomotor Training and Activity-based Training groups.

RLT: Robotic Locomotor Training (n = 8); *ABT*: Activity-based Training (n = 8); *Anxiety Score (20 - 80):* State-trait anxiety inventory (STAI). Data presented a scatterplot of the average scores over the four time points (week 0, 6, 12 and 24) for each group, with corresponding regression lines, equations and ± 95% CI (shaded areas).

6.4.3 Quality of Life

Both the ABT and RLT groups showed a trend of increasing perceptions of QoL over time, across all three domains: A) general life, B) physical health, C) psychological well-being (Fig. 6.6). The RLT group showed a trend of a greater rate of change in QoL for two domains, A) general life and B) physical health, compared to the ABT group (ES = 0.75; ES = 0.82). In general life, the ABT group experienced slight increasing trend with a rate of change of 0.03 (p = 0.25), while the RLT group experienced a more notable trend, with a greater rate of change of 0.09 (p = 0.14). The experience was similar for physical health with a rate of change of 0.02 and 0.08 (p = 0.48, p = 0.12) for the ABT and RLT group, respectively. For psychological well-being, there was no difference between the two groups (p = 0.75). This greater trend of change in QoL for the RLT group is also shown in Table 6.1, in which the RLT group had mean increased changes of 27%, 23% and 3% for the three respective domains, whereas, the ABT group had mean increased changes of 10%, 9% and 8% respectively.

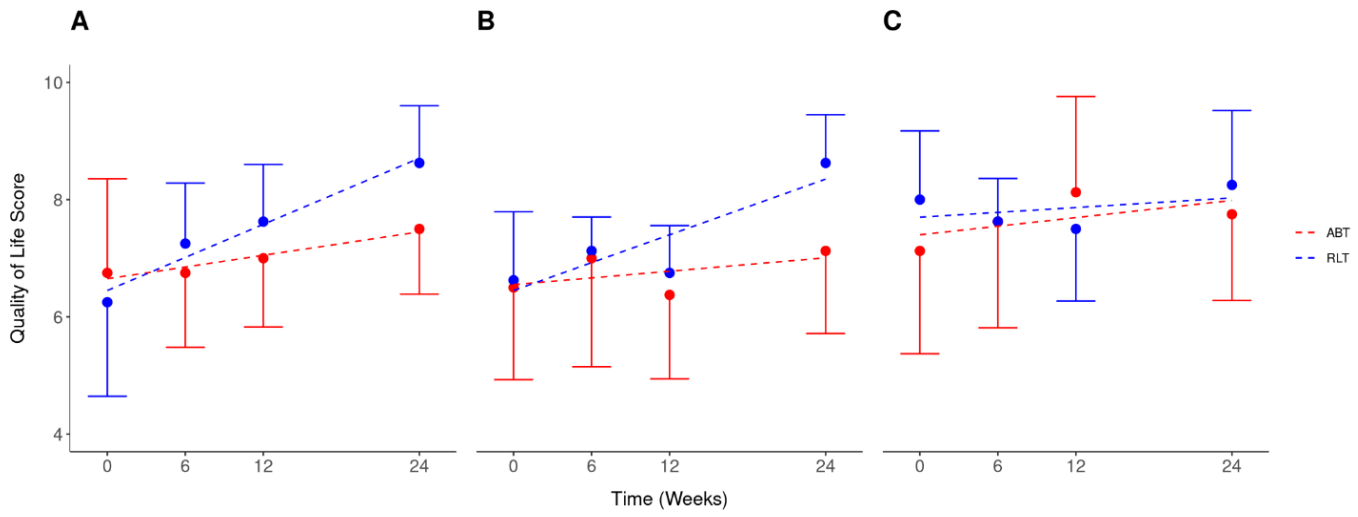

Figure 6.6: Self-reported quality of life for A) general life, B) physical health, and C) psychological health, for the Robotic Locomotor Training and Activity-based Training groups over time.

RLT: Robotic Locomotor Training (n = 8); *ABT:* Activity-based Training (n = 8); *Quality of life score (0-10)*: International SCI Quality of life (QOL) Basic Data Set; *A*: life as a whole*; B:* physical health; *C*: psychological health. Data presented as observed mean ± half-width 95% CI. Modelled linear estimates shown as superimposed lines (predicted mean).

As previously mentioned, a single participant in the ABT group skewed the markers of depression data by scoring significantly higher depression rates than the others in the study (Fig. 6.2 and 6.3). This outlier, participant 6, also scored consistently well below the group average in the other psychometric measures, including state anxiety and QoL. The outlier's scores in comparison to the rest of the participants in the ABT group are shown in Figure 6.7.

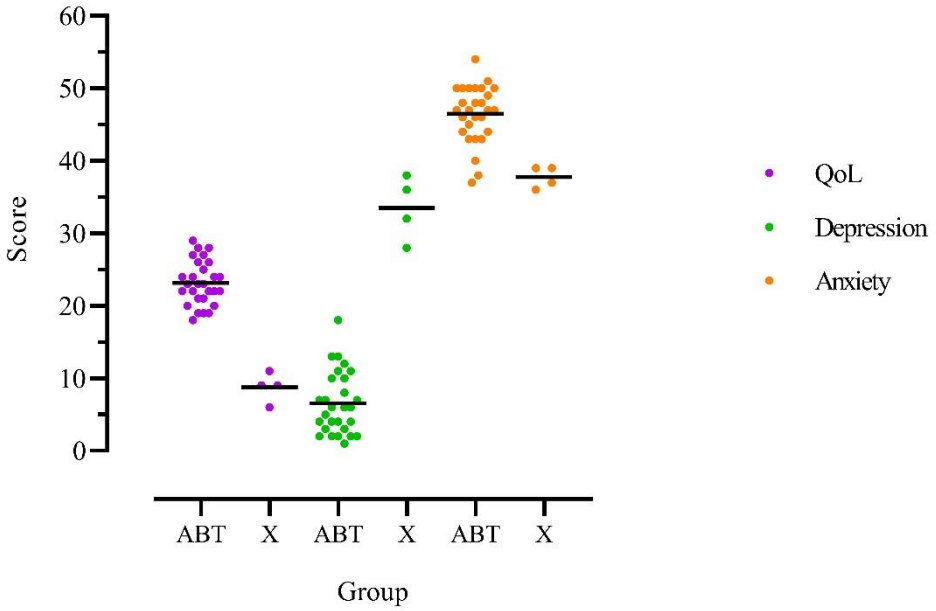

Figure 6.7: Scatterplot of individual participant (n = 8) scores for quality of life, depression, and state anxiety for the Activity-based Training group.

ABT: Activity-based Training group (n = 7); X*:* participant 6 (n = 1); *QoL:* quality of life. Data presented as individual responses across all time points (0, 6, 12 and 24 weeks) with mean shown by solid bar. Scores of a single ABT outlier (participant 6) have been placed alongside the remaining ABT group values.

6.5 Discussion

This study aimed to assess the psychometric outcomes of people with SCI after 24 weeks of ABT and RLT interventions. Previous research has focussed on psychological well-being as a key outcome in determining the efficacy of physical rehabilitation (157,343). It is suggested that health promotion and increased physical activity may improve psychological well-being, including feelings of depression, anxiety and QoL in people with SCI (309,343).

6.5.1 Depression

Although nonsignificant, the current study showed a decreasing trend in markers of depression of 3.25 units for the RLT group over time. This decrease in depression score accounts for a 59% improvement for the RLT group from baseline to week 24. This decrease in depression post RLT may hold important

clinical relevance for people with SCI, however, there was no change in reported depression for the ABT group over time. The lack of improvement in depression ratings for the ABT group was likely due to the outlier, participant 6, who skewed the group data by scoring well above the average for the markers of depression throughout the intervention. With the effects of P6 removed, the ABT group showed a mean decrease in reported depression of 23% from pre to post intervention. Literature shows that physical exercise can improve depression in clinical and nonclinical populations (309). Latimer et al. (2004) tested depression in a group of chronic SCI participants who reported an average depression score of 10.45 ± 8.30 at baseline. The current study showed similar results with an average depression score of 8.75 ± 7.17 and 10.12 ± 8.69 for the RLT and ABT group, respectively. In a study using the BDI to assess depression in people with SCI, 42% of the participants at week 6 were above the cut-off score of 14, which dropped to 26% of the participants by week 18 (317). Previous studies attribute this positive outcome of exercise on depression levels to physiological and neurobiological mechanisms (309). Aerobic training, such as that carried out during the ABT and RLT interventions, can improve cardiorespiratory fitness, which stimulates neurotrophins, oxygen and energy supply to the brain and the synthesis and release of endocannabinoids. These changes can inhibit the hypothalamic– pituitary–adrenal axis, leading to a reduction in cortisol release and, consequently, of the psychological stress response (309).

6.5.2 Anxiety

The average state and trait anxiety at baseline were 46.38 ± 5.53 and 46.52 ± 3.27 for the ABT group and 47.12 ± 7.17 and 46.88 ± 5.79 for the RLT group, respectively. According to the normative data for working able-bodied males used in the STAI test, average state anxiety is 35.72 ± 10.40 and average trait anxiety is 34.89 ± 9.19 (344). Therefore, the anxiety scores of both groups within this study were greater than the able-bodied norms presented. As previous studies have reported that individuals with SCI show higher incidences of anxiety when compared with able-bodied persons, it was not unexpected that the individuals in this study would have higher anxiety scores than these norms. However, comparisons of our data with expected values within a SCI population is challenging, as there is

significant variation in study designs, protocols and included samples among the literature (321,327). Nevertheless, all participants in this study would be considered to have significant anxiety concerns, as a cut-point of 39–40 is normally used for clinically significant symptoms of a state of anxiety (345). Previously published data shows that participation in physical activity reduces anxiety symptoms in people with SCI (346,347). However, the current study found that only the ABT group experienced reduced anxiety levels from pre to post intervention, with a decrease of -3 and -4 points for state and trait anxiety scores, respectively. The modelled responses of markers of anxiety for the RLT group (Fig. 6.4) showed higher trait anxiety scores (increase of 3 points) and a slight trend of increasing state anxiety scores (increase of 6 points) from pre to post intervention. These responses can be explained by Spielberger et al. (1983), who identifies that individuals with high levels of trait anxiety would be more susceptible to stress, thus responding to situations with more frequent and greater intensity state anxiety than those with low trait anxiety (348). Hence, in the RLT group, the increased trait anxiety may have led to a subsequent increase in state anxiety over time.

There is a strong correlation between trait and state anxiety, as high anxiety proneness is likely to result in elevated state anxiety responses during stressful situations (344). The trait inventory STAI presents items that describe symptoms of anxiety and others that show absence of anxiety. However, some authors have suggested that the items that try to display absence of anxiety may in fact evaluate levels of dysphoric mood that are mostly associated with depression, rather than with anxiety (348,349). Thus, rather than being considered a measure of specific proneness to anxiety as originally proposed, trait anxiety should be considered a measure of general vulnerability to emotional disorder and depression (348,349). However, this was not apparent in our study, as the RLT group had notable decreases in depression and yet, reported substantially higher anxiety scores over time. In general, higher correlations between state and trait anxiety are predicted in social situations and lower correlations in physical situations (344,348). Therefore, perhaps this explains why no correlation was found between the two anxiety scores for the RLT group (Fig. 6.5), as this group may have experienced more anxieties associated with the exposure of a new physical stimulus with the novel training technique of RLT. A

systematic review by Naidoo et al. (2020) further describes the possibility of the research burden (i.e., the psychological, physical, and financial burdens) placed on participants during a RCT (350). Elevated state anxiety in our sample may, in part, be explained by the exposure to a unique and demanding research environment for participants who otherwise experienced social isolation and a lack of access to rehabilitation (350,351). However, mood and anxiety problems are often long-standing and difficult to shift. It is very possible that the participants who reported higher markers of depression and anxiety faced a range of other stressors in their daily lives, which remained unaltered by the exercise interventions. Heightened distress may be triggered by various concerns; physical health and the ongoing fears of secondary complications, relationship satisfaction and social and occupational impairment to name a few (349,352). These factors together with the unique cultural, race, economic and interpersonal differences of the participants in this study, make it plausible that psychological well-being could differ considerably among the individuals regardless of the effect of the interventions (345).

6.5.3 Quality of life

The current study presented trends of increased perceptions of QoL for both the RLT and ABT group over time (Fig. 6.6). Therefore, it is plausible that the psychological well-being of individuals involved in this study improved regardless of the intervention type. These preliminary results add to previous findings that link engagement in physical activity with improved health and QoL (196). A 9-month RCT showed that individuals with SCI who participated in a twice-weekly supervised exercise training reported greater QoL and less stress and pain than the non-exercising control cohort (221). Physically active individuals with SCI report a comparatively better QoL within physical, psychological and social fields than their inactive counterparts (322). This was reported in our study in which there appeared to be improvements not only in the general life QoL but also in the physical and emotional domains. Standing and ambulation in particular, have been linked to improved psychological well-being and QoL in people with SCI (21,45). There are many psychological and social benefits to standing, including improved self-image, eye-to-eye interpersonal contact and increased independence, all of which contribute to building QoL (92). Wheelchair-dependent individuals enjoy and value the normalizing

experience of seeing themselves upright and participating in the walking motion (29). A study of 21 participants with SCI indicated that all had positive emotions and improved overall QoL following a single session of 7-25 min of walking in the Ekso powered exoskeleton (97). Eng et al. (46) reported that the prevalent benefit of standing was a feeling of well-being reported by 87% of the respondents. Thus, the increased QoL reported by all participants in this study could be attributed to the improved psychological benefit of standing and even walking again (97).

In addition, quality relationships and providing or receiving social and emotional support, can improve psychological well-being in people with SCI (212). The availability of emotional support provides positive experiences and increased stability for people with SCI (317,353). It can also help to buffer the impact of stressful events, possibly by enhancing perceived control and coping capacity (317). Within the South African context, most individuals with SCI do not receive out-patient rehabilitation, let alone the opportunity to exercise in a large multi-disciplinary training setting. Due to the lack of neurological specific rehabilitation centres in South Africa, most of the participants in this trial were unfamiliar with training in groups or alongside others with similar conditions. Consequently, the effect of regular social participation and interpersonal support, provided by the rehabilitation setting, may have led to improved psychological QoL for the participants in this study (refer to Chapter 7, Theme 2).

This study also showed possible improvements in QoL related to physical health domain. For individuals with SCI, many ADLs are physical in nature (e.g., transferring, wheeling, eating). As a result, individuals who lack the physical capacity to perform basic ADLs may judge these tasks as stressful because of feelings of helplessness due to an inability to cope with the demands of daily living (250). Thus, the achievement of physical goals over the 24-week interventions may have led to increased perceptions of physical QoL, greater satisfaction with physical ability and improved self-image and self-efficacy (212,322,353).

6.5.4 Heterogeneity in psychological well-being

These data suggest that people with SCI could derive some psychological benefits from an exercise training programme, as seen through trends of reduced depression and increased QoL. However, heterogeneity in symptom severity and response to exercise is well-established (34,354). Research has repeatedly demonstrated clear trajectories of individual differences in psychological outcomes across time following traumatic events such as SCI (323). Although aversive life events are highly distressing and often potentially debilitating, it is clear that not everyone reacts the same way (32,323). Some people are overwhelmed and unable to function normally for years after the event, while others continue functioning normally soon after the trauma (323). The effects of various socio-demographic and secondary health complications can influence depression and life satisfaction post SCI (32,323). Individuals who suffer from continuing medical problems post SCI have a higher chance of a psychological diagnosis by reducing self-esteem due to a lack of privacy and dignity, limiting participation in physical activities and reducing social engagement (212,223,251). Pain in particular has been suggested to mediate changes in mood, stress and self-esteem (111,196). Negative psychological states are also linked to higher incidences of secondary complications due to the self-neglect and feelings of worthlessness experienced by those with SCI (316). However, causation remains unresolved: does the depression exacerbate the complication or does experiencing the complication make the individual depressed (34)? Many studies support the idea of 'feedback loops', where increased secondary complications following SCI may in turn accentuate the initial depression and vice versa (34,250). However, in this study, although there were increases in pain levels, no change in spasticity measures and limited improvements in bladder and bowel control (Chapter 3), both groups experienced a clear increase in QoL over time for all life domains (Fig. 6.1). However, varying prevalence and severity of health concerns among the participants could have contributed to the large variability in the psychometric outcomes measured in this study.

6.5.5 Limitations

Response bias caused by reluctance to express negative emotions or dissatisfaction to others may have been a concern during baseline testing, as questionnaires were answered in front of the tester. However, once participants understood the questionnaires satisfactorily, this bias was reduced through self-administered questionnaires for the remaining test periods. However, it is recommended that questionnaires be completed in the rehabilitation setting to avoid distractions at home and to allow for clarification of question terms if required. Another limitation was the insufficient statistical power (small sample) to make meaningful inferences. Thus, the results of this trial should be interpreted with caution, as we simply discussed the trends noted in the data. However, although no statistically significant changes were reported, these preliminary trends in values are interesting and worth reporting for understanding psychological well-being for people with SCI in future pilot trials or RCTs. It also indicates that perhaps qualitative assessments may be of better value for these outcome measures.

6.5.6 Conclusion

In summary, the results of this study demonstrate that physical activity in the form of ABT and RLT, is possibly associated with trends towards better psychological status in individuals with chronic SCI. This study established that both interventions tended to increase perceptions of QoL and decrease depression ratings over time. However, RLT did result in increased trait anxiety symptoms over time, possibly due to the exposure to a new environment and novel training stimulus, together with individual variations in sociodemographic and secondary complications. The results highlight the importance of depression being addressed early and effectively to optimize the reduction of secondary complications and to develop guideline-based recommendations and emerging best practices for depression care. Confirmation of the positive effects of physical activity on subjective well-being can provide yet another motivation for the development of interventions to increase activity in this very inactive population. Not only will physically active people with SCI improve their health and reduce their risk for secondary complications, but they may also experience improved psychological status. The assessment of rehabilitation success, therefore, should not only involve physiological parameters but

also psychological outcomes. Future large-scale RCTs should further investigate these preliminary psychometric findings and should consider the limitations of the questionnaires.

6.6 References

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CHAPTER 7

The lived experience of participating in a spinal cord rehabilitation intervention in South Africa

7.1 Introduction

The previous chapters (Chapter 3 - 6) have all considered primary SCI rehabilitation outcomes using a quantitative approach. However, many researchers are suggesting that in order to bridge the gap between the everyday needs of the individuals with SCI and the rehabilitation being performed, one should consider the perspectives and opinions of the participants involved in the trials. According to Hammel and colleagues (2007), "if rehabilitation services are to be evidence-based, relevant and effective in meeting the needs of people with SCI, they must be informed by the perspectives of those people who have experience of both SCI and rehabilitation: people with SCI". Consequently, the following chapter considers the lived experiences of participants using a qualitative approach of understanding.

There is growing consensus that QoL is a fundamental need for persons with SCI, particularly because life expectancy of these individuals has increased substantially over the past 30 years (355). QoL is a person-oriented and multidimensional construct primarily based on a person's subjective appraisal of their physical, functional, emotional, and social well-being that might be affected by disease, disability, and its treatments (32,321,322,324). QoL relies on performing tasks such as ADLs, having relationships, reducing secondary health issues, and engaging in social activities and occupations corresponding with one's life stage, goals, and values (356). There is encouraging evidence to support the benefits of exercise rehabilitation and leisure-time physical activity on the physiological (158,195,357) and overall psychosocial (195,254,358) function of individuals with SCI, by increasing functional independence and QoL, and promoting social and community engagement (359). Despite the health-related benefits of exercise, it can be a challenge for people with SCI to adhere to exercise and to maintain a physically active lifestyle (360,361). The global estimate for physical activity for able-

bodied adults is approximately 70% (362), and according to 2014 results, the prevalence of physical activity in South African adults specifically, is estimated to be approximately 51 -59% (363). However, people with SCI are more likely to lead physically inactive lives than most other clinical populations (10,364,365), with only 50% of individuals with SCI currently reporting to meet recommended exercise guidelines (358,366).

Rehabilitation and leisure-time physical activity are hindered by several barriers for people with disability. Not only do they face significant financial, transportation and mobility barriers, but their susceptibility to a variety of secondary health problems, illness, and injury also create frequent barriers to adherence (162,271,365). Additionally, emotional and psychological barriers have been reported to prevent participation in exercise for persons with a SCI (162,356). These psychological barriers include a lack of motivation and energy, depression and anxiety, needing assistance and fear of a new environment (162,356). People with SCI must also learn to identify, manage, and overcome numerous discriminatory, intrapersonal and informational barriers to sports and exercise participation (356). Factors working against these barriers to facilitate exercise participation have also been identified, including improvements in health and fitness (367) and the role of peer and family support (356,368). Social support plays a key role in both physical and emotional progress after SCI and individuals who report greater support, perceive themselves to be better adjusted to their injury, experience less emotional distress and report greater QoL and life satisfaction (369–371).

Currently, there is a scarcity of large-scale trials that target physical activity and psychology among those with SCI (372). Of the studies that have considered the psychological factors following SCI, most have used psychometric methods, not qualitative investigation (373,374). Yet, the use of structured psychiatric interviews in addition to validated screens is accepted as best practice and qualitative evidence is increasingly being used as a basis for evidence-based practice (113,313,373). A comprehensive understanding of people's experiences and perspectives in overcoming physical disability and rehabilitation requires extensive investigations that are traditionally done by qualitative

research (361,375,376). However, the few studies that have been conducted on the lived experiences of persons with SCI (360,368,377) were mostly conducted in North America, Europe, Asia, and other high-income countries. Limited research has been conducted in low- and middle-income countries to explore the experiences of persons with SCI and the impact of these experiences on their functioning and general well-being (378). The lack of qualitative studies that sought the perspective of the participants, particularly in a low-middle income setting, has motivated this study to explore the lived experiences of adults with SCI while involved in a rehabilitation trial in South Africa. To the best of the authors' knowledge, there are currently no published data on the experiences of persons with SCI involved in a longitudinal rehabilitation intervention in South Africa.

7.2 Aims

While existing literature has tended to take a quantitative approach, the aim of this qualitative study was to describe the lived experiences of participants (n = 16) involved in a pilot RCT for individuals with SCI in Cape Town, South Africa. This chapter provides an account of the participants' perceptions of the benefits to QoL achieved during rehabilitation, as well as the experienced barriers and facilitators to participation in the intervention.

7.3 Methods

7.3.1 Data collection

This qualitative chapter is descriptive and will describe participants' perceptions and experiences without trying to make definitive claims about differences between the two groups or changes over time. Data were collected via in-depth semi-structured individual interviews. Interviews were conducted by registered psychologists, using open ended questions, and providing space for participants to communicate freely. At baseline, 60-minute interviews were conducted to assess psychological preparedness for the intervention and to manage the participants' expectations. Every four weeks within the trial, 30-minute interviews were conducted to assess the participants lived experiences of the

interventions. In the interviews at the end of the intervention (week 24), a final interview (lasting approximately 60 mins) was conducted, where participants were asked about their experience of participating, the perceived benefits of the intervention, as well as any difficulties experienced and how these were overcome. They were invited to give critical feedback and make recommendations for how the intervention might have been improved or made more participant centred. Interviews were audio recorded and transcribed verbatim. Interviews were conducted by a psychologist who has a clinical interest in resilience to physical disability and injuries. The Biokineticist's (myself and fellow PhD candidate, Robert Evans) who performed the initial coding of the data also employed a clinician's mindset to interpret the interviews.

7.3.2 Data analysis

Data were analysed using a thematic content analysis with a data-driven and inductive approach to coding (130), with initial coding done independently by two researchers. Analysed interviews included the five within-trial interviews (each four weeks apart) and the final concluding interview post intervention. Sentences and phrases were initially analysed using NVivo computer software (QSR International, 2020) and an open coding method. The initial codes identified by the two researchers were then reconciled by a third person, so that triangulation of themes could be achieved. Themes were then grouped into superordinate and subordinate themes. In this way three main themes were identified, namely: 1) perceptions of benefits to QoL outside of the trial, 2) perceived barriers to sustained participation in the intervention, and 3) perceived facilitators to sustained participation in the intervention. The following strategies were used to improve the trustworthiness and credibility of the findings (379): all authors reviewed the themes to ensure that they accurately reflected the interview content; two authors conducted a confirmability audit to ensure that all interpretations were supported by interview data; verbatim quotes have been included to provide evidence for the findings; and data from all 16 interviews are included in an effort to avoid cherry-picking quotes from a selected sub-sample of interviews.

7.3.3 Data management

Data were collected by registered psychologists in a private setting. De-identified data were securely stored on password protected computers. Procedures were implemented to refer participants for psychological assessment and treatment if they expressed any distress because of the intervention or the interviews, or if they exhibited any signs of psychopathology. Participant names have been removed to protect participants' privacy and all identifying descriptions have been changed for the purpose of anonymity.

7.4 Findings

Despite differences in age, life situations, severity of and time since injury, three overarching superordinate themes and multiple subordinate themes were identified in this thematic content analysis. The themes are outlined below with representative quotes taken from as broad a range of the sample as possible.

7.4.1 Theme 1: Benefits to quality of life (QoL) outside of the trial

The participants frequently mentioned how they experienced the physical benefits of the trial to translate to improved QoL within their everyday lives, with three subordinate themes emerging: enhanced functional independence; reduced secondary complications; and improved psychosocial and emotional well-being.

7.4.1.1 *Enhanced functional independence*

Participants referred to how the rehabilitation interventions "helped them help themselves" and how they were able to "do things on their own and see things on their own."

P16: "You go back to home and when you got home and you reflect just on that day and say, wow, I was did it again, and so it's give me like an independence, like it's make me feel like I can do things for myself, and that independence, to be independent like if you know, it's a huge thing. Even if you are able bodied."

Several participants mentioned the ease of transferring as a perceived benefit of the trial.

P1: "Ja, well for instance, like at home now, I always used to use a plank to get onto the wheelchair. Now I just hop onto the wheelchair from by bed to my wheelchair. If I am going out and we go and eat something, and we are sitting at a table, I can't fit by the table. Then I can climb into the chair."

P7: "I am getting stronger, transferring is easier."

P10: "But ja, getting into my chair from the floor, has become easier than usual."

Other benefits related to the ease of performing activities of daily living, such as dressing, doing chores and bathing.

P1: "Like dressing, the dressing has become easy, things that I could do before, but it has become easier. Because you find ways to do things differently. Each time."

P5: "And now I am like, after this weekend, after this talk I had with myself. I can hold a broom, I can use the broom to keep myself upright, and like do some broom work, do some sweeping. I can do a lot now."

P4: "I mean I am walking much better, well I am taking more steps now than I could, it's not functional really, but I mean it has aided me in my functionality, kind of, making getting in and out of the bath easier. Because all of these exercises are exactly the types of things that I need to do to get into the bath, using whatever lifts and things. So that has made it so much easier, now I can get in and out like a little chick, in and out, before it was ok, I have got to watch my arm and lift my legs, and now it is so much easier, so it has helped in other ways ja."

Participants also highlighted the importance of how achieving "small things" in the rehabilitation period in turn contributed significantly to the achievement of important daily tasks and ease of life outside of the interventions.

P1: "A simple think like opening a door. I couldn't open a door before hey. It's a small little difference, but, it's a small little thing but it makes a big difference."

P5: "So now you just saw me touching my face? I couldn't do that, like two months or even a month ago, I couldn't do that."

Another commonly reported benefit was increased mobility and freedom. One participant was able to stop using their wheelchair and progressed to walking with a standing frame. Thereafter, the participant

was able to use a quad cane while walking, and even achieved climbing stairs.

P5: "I am going to be mad at her for taking my chair away from me, actually both chairs and she almost took my frame away because she's like started to make me walk with this cane thingy with the four legs. And today, I got up on the steps."

Other participants mentioned how they could not only stand at home on their own, but how they developed a greater desire to be more mobile and attempt more functional tasks.

P11: "To try and stand and use my legs more, because I have this one calliper, and I would just stand, but now I actually want to move around more. That I can do things, normally I just wouldn't try."

P3: "I can walk with a walking frame in the house, which I did now, was it last week. From the frame and into the seat, bit more freedom."

One participant prior to the trial was pushed in his wheelchair. After the intervention, he could not only push his own chair, but was also able to push himself to town and back for groceries.

P1: "It is it changes your life a lot. I mean, I push to town, it takes me like five minutes, to get to town, five, six minutes to get to town, I push my wheelchair all the way to town. Wherever I go, they say hi JC how's it going? How's it going? It's good, it's good. You know."

Another participant was able to use public transport for the first time and travel alone with no support or assistance. He mentioned how the increased independence gave him the opportunity and ability to be mobile.

P16: "I develop more skills, like it makes me also very, very independent. Like um, because of this to come here, travelling and stuff. It's easier ja, yoh, it feels for me like yes, I know I got the ability in me, to like do things for myself, before I get here, but that, um, you see but um, there is so much things that I discover about myself during this six months, it's like um, wow, yes Charles you can go with public transport, yes Charles you can push a lot of distance. It laid a foundation now in my life, that I can do it. I am mobile, I can do it."

7.4.1.2 *Reduced secondary complications*

Participants reported changes in their physical health through reductions in common secondary complications associated with SCI. Several participants mentioned improvements in bladder and bowel function throughout the intervention.

P15: "My urine when I start walking was, dark, and I don't understand what's going on. Whether it's the walking, the legs, the more I walk the more my urine came clearer and clearer and clearer."

P7: "Over the study, I have had two UTI's. Which is like a record for me, I usually have like once a month. So it's gotten much better."

P9: "Bowel, definitely stronger, definitely."

P13: "But nowadays, I said to my wife, I need to go to the toilet, so I can get there, without using anything. And then we spoke about it, me and Rob before, so I go more regularly. Not waiting 2 days or 3 days to go. I go on a regular basis without using anything."

P4: "Great, even like my bowel system seems to be improving because of it."

Additionally, some participants reported improved sleep patterns.

P14: "Ja, because I sleep better. I sleep better because now, I feel tired and then I go to sleep. I sleep much better."

P10: "It's also like I have been going through a lot of changes lately, ah, because back home I normally only sleep about three to four hours a night. And all of a sudden I am sleeping way too much, to the norm."

P9: "Sleep pattern? Ja, it has, I sleep better, I sleep deeper, no my sleeping is good. It has changed because I am sleeping more."

Three participants reported changes in sexual functioning and libido throughout the intervention. Some experienced more desire and interest in sexual activity, while others were able to perform sexually for the first time in years.

P4: "So this was kind of also, you know interesting to me. That I have been thinking more about sex since starting the programme. I am pleasantly surprising myself. So I don't know if that is it, maybe because I am more physical, my body's working so I have more faith

in it, so that is kind of cool. And so I have made a date with somebody, I haven't been on a date with anybody, I have not been with anybody for a long, long, long time."

P5: "Another thing that I needed to tell you is, something that's a very personal thing. It is not easy for me to talk about. But my care giver, my wife is my care giver, alright, so it's like a couple of times now, in the last two to three weeks, ja, three weeks tops, I have been waking up like a young man. I have been like waking up with an erection, it's like yoh! Another thing that they said, will be impossible. It's impossible!"

P9: "My sex drive is a lot better. It could be due to having a girlfriend now or because of the intervention. It could be a bit of both because the circulation is changing the body again, which I didn't have in the past. Because it has changed, I am not saying it is because of the suit or the research, but it could possibly be."

7.4.1.3 *Improved psychosocial and emotional well-being*

Not only did participants experience a reduction in physical secondary complications, but several participants spoke of the perceived impact of the interventions on reducing negative psychological complications, including stress and depression.

P8: "Also, I mentioned this to you the last time that, my body just feels like way better, and in the end, like I feel way happier that emotionally because of just pain being taken away."

P2: "And I think it has also helped a bit with my mood. I feel like more relaxed."

P6: "This has been really, it's if I still feel low, it's not nearly as regular or as long as it was. I was a bit all over the place and now I can see light at the end of the tunnel."

P14: "I stress a lot less, um, there are no, everything is, well coming to a bit of a kind of peace. Kind of like coming right and getting more relaxed."

Many participants experienced new life meanings and changes in their perspective and behaviours.

P5: "But what I have found here, in this programme, it changed my whole way of looking at life. No, I am actually glad I mentioned it, I don't know how to explain it, it's like, I am a better person now because of this. In ways that I can't explain, I see the world from a whole different pair or spectacles. But I can already feel it, this place has really changed my life. I appreciate life more now. Um, I'm like more like appreciative of lots of things, life in general."

P16: "Ja, and just to be here for say like 2 months, it's really changed my whole attitude, my body language, it's like in a new world that I am living now, because of this. My mind-set is transformed, I am a new person."

A positive outlook on life appeared to be a product of the trial. Collectively, participants were more likely to make 'optimistic' statements, with more positive attitudes and improved moods. They started believing in themselves and had improved confidence within other aspects of their lives. Reaching physical goals within the trial also encouraged some participants to have a more optimistic view of their intervention progress and motivated them to pursue higher goals.

P16: "It's a new chapter. It's like fireworks that's going on here inside of me, while I am talking, just knowing that yoh, anything is possible if you just can put your mind, if you just like renew your mind-set. And just build on positive thinking's and stuff, then anything is possible."

P4: "Ja, ok, I can do it and every time when it happened, all the time, and so that's like a continuous you know, adding, you know building my self-confidence, esteem and just confirmation that yes you can do it, ja."

P6: "I feel better about myself, since I have been coming. Big learning curve, big positive, for me."

P5: "Because now because of all this, I'm now like I have found ways, to uplift myself like, because of what happened here, it's like I'm, I became this pessimist which I never thought I would become pessimist, but I am now back to being my old self, I am an optimist. She is like lifting my spirits, she is like, yoh, she is like really, really making me believe in myself, I am capable of even more that what happened now."

P1: "And it gives you more confidence."

P12: "It makes me think of maybe I can do something more and maybe, you know."

P9: "I think doing the programme has made me more confident. Coming out of my house every day. I am in and out, I am here, socialising with people."

P11: "It has given me more confidence to try and more motivation as well."

Participants felt that over-coming the physical obstacles within the intervention improved their self-confidence and ability to tackle other challenges within their personal lives.

P4: "It does, because you know initially you don't know, well I didn't know I could do these things, and so just the fact that, you know, after being able to do it, and learning to do it and doing it so well, that I can do it, it makes me think that I can tackle other challenges that I think that I would not be able to take on. Some of the exercises have been hard, but

that's part of it, for me some of the challenges were, I have got a lot of issues happening in my personal life, and so having to deal with that, um, you know this actually made it easier to deal with my other challenges."

P16: "Ja, so when I come and experience all this stuff and I see this stuff and I must go through this and that, then yoh, and it makes me so like become a stronger person and the way how I do the things and when I figure out some, because it's like a puzzle!"

7.4.2 Theme 2: Perceived facilitators of sustained participation in the intervention

Within the main theme of the factors that facilitated participation during the trial, two dominant subordinate themes were identified: inter-personal support; and contributing to research.

7.4.2.1 *Inter-personal support*

The most prominent facilitator to participation was the perception of the various forms of support during the trial, both in the receiving and providing of it. Participants felt that the relationships with others influenced their performance and emotions, and the comradery with fellow participants in the study served as a strong motivator for continued participation and effort during the interventions.

P4: "I think for me it was fantastic to see all these guys that are in a similar situation to I am, and just to see them accomplish, to be able to do something that they couldn't do before. Um, that you know comradery, that pure support and understanding. Um, ja, so it been, quite, I am liking it I am really liking it. I like the interaction with the people. I like seeing the other guys, I like the participants, also being able to, I can see their excitement, and when they are exhausted it is like so cool to see other people also achieving and you know."

P13: "I mean, just meeting the other guys, and see maybe you think, that I am bad, and ah, I don't want to, not really, then you see people that's in a much badder state than you are, and those people has got hope. They want to, they are positive, now why can't I be?"

P16: "And you see the other guys, with the glints in their eyes and how they are liking it also."

Not only did participants bond and engage with fellow participants, but many formed interactions with other private clients within the rehabilitation setting. These relationships seemed to allow participants to relate to other people's situations and to find inspiration from one another.

P14: "It gives an opportunity to meet other people and experience other people in the same situation

as you."

P16: "Motivation is locked up in that hour, meeting new people, seeing new disabled people, how they cope daily, how they, so that is also locked up in that hour, so, ja."

P6: "And he also, just chatting to him was so inspirational. Just to hear a different experience and a different side of things."

It was noted that individuals could share their stories with one another and receive feedback and recommendations from those that were in similar situations, thus, offering assurances and support during the trial.

P12: "I spoke to him, he was nervous as well, so to calm him a little bit and tell him what's it's about, and how it's going to be and how he's going to feel physically. It's good that I helped him, because talking to him helps me."

P14: "The psychological side and the physical side and whatever they give you. It is something which even like with other patients, because I am not like the only patient, because there is there patients, because by talking to them and sharing their experiences, then it's something that helps the other patients and it helps me and then you share, your experience. It's quite and then you get to know people, and then you get in contact."

P1: "He is great friend of mine you know, and also one of the guys that helped me change my mentality. He said to me, how can you ask a nurse for help, when you know you can do it yourself. I looked at him, straight at him, this was in February, January. He said you can do it yourself you know. And I didn't believe him until now."

Exercising in a large multi-disciplinary setting involving other people with disabilities, as well as able-bodied gym members and even athletes and sports teams seemed to impact how the participants viewed themselves and emerged as a significant facilitator to improved motivation among the participants in this study.

P5: "The air was like laden with potential, like opportunities, that guy was like, I was like intoxicated with this positivity, the opportunities and everything here, the whole vibe in this place, the people, everybody in here you can see they are very driven, they are like, they have a purpose, and you can see all of them now they are sticking to it, and they are putting their all into it."

P2: "Whereas here it's everyone, people who have Scoliosis or rugby players, they gym just there, so. Ja, you are not isolated. That's why I actually like where this gym is placed, and ja.

You feel more, more, I don't know normal I guess. Not hidden away in some little physio rehab thing."

P6: "It's been brilliant, I absolutely, I find this place, you come inside here, and it's just so inspiring. Ja. I don't why, I don't know, I was just saying to Rob, the gym, it's not really different to any Virgin Active Gym. But there is just something about it, that's inspiring. Coming down here and seeing athletes and rugby players and things training here, it's brilliant. I love it."

P1: "So like before, like coming here, and speaking to other people and working with Rob and working with Claire, and you working with, you know, a whole spectrum of different kinds of people, there is nothing like this anywhere else in South Africa, really, you know, and your mind set and your mentality changes."

Several participants commented on the importance of the bond between the participant and their therapist. This relationship fostered friendship and intimacy, which acted as a motivator to sustained participation in the study. The positive relationship with the therapists allowed participants to press forward with their training, take the lead in the rehabilitation programme and push toward new goals.

Tiny: "And I just think the whole approach, um, Rob and Claire are really positive people, well I found them positive. It encourages you to try harder and work harder."

P6: "I said to Rob, that, his continuous encouragement it helps a lot, with therapy, wanting to reach and try and achieve that goal because when I was in government, it was just you are there and your therapist is there for rehabilitation, that all. This is like a whole different perspective, it's like someone is encouraging you and motivating you."

P5: "Ja, it's not about that thingy within and all that, something inside that just like keeps on believing, I think it's all about this environment here. About other people, people like Claire, Rob and all of you guys, it's like people who like know, not believe you, know that anything is possible if you just believe."

One participant's quote reinforces the sense of belonging that the participants felt during the trial due to the perceived relationship with the therapists.

P3: "Rob and Claire are great, so they make the experience fun, so they make you feel at home."

7.4.2.2 *Making a contribution to research*

Several participants mentioned that playing a role in the greater research project served as motivation to continue with their adherence to the programme. They wanted to have a positive impact on the outcomes of the study and on the exercise recommendations for others with similar injuries.

P3: "This will benefit other people so that's the main aim. I gave into the programme, not just for myself, to benefit others also."

P4: "Because I know myself, I know that I would, you know, push myself. I knew that there were going to be benefits for me, you know, goals and it is not only myself, it's everybody else, it's bigger than just me."

P8: "And I don't feel that I could just break that commitment. And I think it would be so unfair, not, it doesn't only affect me, it affects Claire, it affects Rob, it affects the research they're doing."

P10: "It's also why I am participating in the programme, that's why I applied. Is to do my part. I am laying the paving for somebody else."

P1: "So I can't let him down, on his stuff, it's important not only for him but for you guys as well. Otherwise you've got no research."

7.4.3 Theme 3: Perceived barriers to sustained participation in the intervention

Within the main theme of the barriers to participation during the interventions, two key subordinate themes were identified: pain and fatigue as a result of the trial; and personal challenges encountered during the trial.

7.4.3.1 *Pain and fatigue as a result of the trial*

All the participants in the study reported pain of varying degrees as part of the ramifications of their injury as well as the physical demands of the interventions.

P8: "The first time I used the arm, my shoulder was so sore, it's like I couldn't sleep and when I came home. It was so much painful."

P15: "But you see, when I walk, that lot of steps, my legs is sore! It's sore. My muscles! So that was a challenge for me, a genuine challenge. It was tough and I have problems with my muscles, it was painful, it was sore."

P10: "For the past two, three weeks I have had serious pain in my hamstring and calf and upper thigh."

P13: "Ja well I feel pain, constant pain."

P6: "You know this pain thing, is also when you think, ah, as I said, go this evening to go out, go down to the beach, I know that by the time 5 o'clock comes my arms are so sore that I can't sit in the chair properly."

Another commonly reported symptom of the intervention was the effect of fatigue, with some participants describing pure exhaustion post exercise.

P8: "I'll just say that the exercise has just made me like, sometimes really exhausted."

P3: "I really feel this is working because after a session I am really knackered you know. And my wife is always laughing at me when I get home, after a bath when I sit at the table, my head is down."

P6: "I don't think I have ever been so tired in all my life. When I got home I felt so tired I thought I was going blind."

P10: "And I was on Tuesday when I got home, I was, knackered, man down, out."

P9: "I literally roll out of here sometimes when I have finished walking, I will be finished, I am completely now, I am finished. Ja, I sit now and I am ja, just wait, just like ten minutes wait, my whole body needs to come right."

P11: "I normally get tired at home when I stand, but I didn't know I was going to be this tired."

P13: "After the session, ask my wife. Sometimes I sit there in the chair and I go to sleep. Ja, because it is very tiring."

7.4.3.2 *Personal challenges encountered during the trial*

During the trial, several external challenges of a personal nature arose as barriers to the participants adherence and well-being. Although not the most prevalent concern mentioned by participants, financial constraints may be the most important concern due to its impact on the ability of two participants to adhere to the trial.

P1: "But it does, it is starting to play a role on us. Because we you know we have fun, we go out and do this, and we keep it in moderation, but it's not easy for us, to attend the programme. I could easily, just say, give up and walk away and say, ok I'm done with the programme. I can't, I'm done, I am just going to give up and go home. I want to go back home. The financial pressure is literally it's eating, it's eating us alive."

P10: "Ah well the financial stress and all of that. I had a couple of near break-down points, just reached those points, if I could actually find somebody to take me to the airport I would have been gone."

Together with the financial difficulties that these two participants experienced, a lack of stable accommodation was another barrier that they experienced. These two participants could not afford the quadriplegic homes that they were originally staying in and thus, tended to move between various accommodations in the Cape Town area.

P1: "I had some up and downs in between. Not having accommodation, it's very difficult at the moment. Literally one little bag. This backpack and another backpack, that's all I got. So I don't know where I live next, next week, maybe I live somewhere else again. You know?"

P10: "Well we are a month behind on rent where I live now. That is, that is what's been stressing me out, is how I'm going to pay. The fighting, the indecisiveness, just lack of stability and everything, is just, it gets too much. It kind of gets to you."

There is a lack of accessible and available public transport for people with disabilities in South Africa. Therefore, many of the participants relied on the private transport company, provided by the study, to bring and return them to their exercise sessions. This transport company was one of only three companies in the Western Cape that were validated and approved to transport individuals with wheelchairs. A reported barrier to continued participation among the participants was the standard of service provided by this company.

P14: "It seems like it a bit of a problem for these transport people, because the boss himself doesn't really understand what the situation with the drivers, because the call centre is very bad."

P7: "Sometimes transportation is late and things like that."

P8: "I think this is not a, ok, it is part of the rehab, because we are transported here, it's just that I feel part of it is that, you know the company that is currently transporting us I sometimes feel that as disabled individuals, it's like we, I am at that point where I feel that the respect or, because we are disabled, because, let me rather speak for myself. I am disabled, they are starting to think basically nothing of it because in the beginning, when we came here, I would be fetched at 8 o'clock at home, arrive 9 o'clock. My session would be done. But now, its like I was picked up 10 o'clock and then because they now starting to cater for the private people and I think they also being money hungry, they fetch this one, took this one here, pick that one up. I left here 10 o'clock and I arrived 3 o'clock at home. So Friday it's like I am taking a trip around the world to here to there."

One participant lived too far away to make use of the transport provided by the private company. Thus, this participant used public transport via multiple buses to arrive at the exercise sessions. This was a barrier to participation for this participant due the long hours and energy required to get to and from each session.

P16: "Ja, so actually for one day, it's take me five hours just to be on the road to travel yes, sometimes the travelling is like very difficult because say on the raining days, some stuff, sometimes the buses is not wheelchair friendly, and I must ask people to help me. Evens to get, I ask someone to get me over the road to the bus stop and all that kind of stuff ja. It's quite an inconvenience. Taking time, it takes energy."

Another common barrier was the difficulty in balancing work and study life with the commitment of three times per week of exercise for the trial. This was reported as a source of added stress and unnecessary time consumption to the busy lives of the participants.

P8: "Because you know, you going to come with, in the end, the academia, you know, you might have that stressing you out and the deadlines, are you going to have that hanging over your head. It's just that, I must say I feel a bit overwhelmed with everything that is going on so, but, I am trying to make it work, I'll be honest with you."

P3: "I am a bit stressed about the work because not being there, it's, because you know you have got deadlines to meet, it is a bit of a stress. Ja, just balancing it, that's been a challenge."

P6: "I decided I will give it a good go for the last couple of weeks. Jeez, it just takes up so much time. Getting here and getting back, is long. And when I get back, I am so clapped. It takes me an hour sometimes two hours to recover sometimes. And then the day is just about gone, you know. And in terms of work, that doesn't really do a heck of a lot."

7.5 Discussion

There is a need to develop a holistic approach to SCI recovery, in which the perspectives of those involved in the rehabilitation interventions are understood. Thorough investigations should delve into the benefits, challenges and facilitators that may hinder or enhance progress of rehabilitation after sustaining a SCI. The present study contributes to the limited existing literature and aimed to understand the lived experiences of people with SCI during a 24-week rehabilitation intervention within a South African context. A qualitative approach was used, as these methods allowed a deeper investigation of the subjective experiences of the participants, with three superordinate themes identified: perceived benefits to QoL outside of the trial, perceived facilitators to sustained participation in the intervention, and perceived barriers to sustained participation in the intervention.

7.5.1 Perceived benefits to QoL outside of the trial

QoL has become the ultimate goal of rehabilitation following SCI and a key outcome in determining the effectiveness of rehabilitation programmes for people with SCI (113,374). DeLisa (2002) suggests that reducing the gap between traditional outcome measures and the needs of people with SCI requires research to be guided by those outcomes that are valued most highly by SCI survivors (380). However, few qualitative studies explored QoL following SCI from survivors' perspectives (113).

Within the current study, the participants remarked on how the interventions provided them with benefits far beyond those of just physical well-being. Several respondents in this study attributed enhanced QoL through better functioning, reduced secondary complications and improved psychological well-being to participation in the trial. The current study showed that physical activity became an important and integral component of life for the participants and was reported to impact their "abilities to regain their independence". Participants highlighted that the rehabilitation intervention allowed them to become more proficient at certain ADLs, such as mobility activities and basic self-care, being able to perform these tasks with less difficulty and in less time. Thus, the participants became less reliant on assistance from others to perform tasks, which in turn, afforded them more freedom,

autonomy, and independence. Gaining independent function and physical recovery after SCI has been reported to bring personal and familial happiness, freedom, self-confidence, promotion of ADLs, better QoL, and better communication with other people (361,381). This emphasis of physical functioning was also clear in respondents' narratives in previous literature (382,383). Restoring any physical functioning will lead to an equivalent increase in independence, and this will have a profoundly positive effect on QoL by impacting on the adverse psychological, social, and economic factors associated with the SCI population (143).

Another benefit to QoL reported by the participants in this study was the reduced secondary complications, especially bladder and bowel complications. These benefits in bladder and bowel function varied from improvements in sensation, better voiding capacity and even requiring less medication for control. In addition to improved bladder and bowel function, participants also reported enhanced sexual functioning and libido, better sleep patterns, and reduced adverse psychological outcomes, such as less depression and stress, all of which form crucial components of QoL. Reducing these secondary health concerns can have a profound impact on QoL for people with SCI, as research has shown that the most desired outcomes for SCI rehabilitation include improved sexual function, regaining bladder and bowel function, reducing pain, and eliminating autonomic dysreflexia (143,384). The prevention and treatment of secondary complications not only contributes to improving QoL, but also improving the rehabilitation process, functional independence, social engagement and reducing morbidity and mortality (16,385).

Furthermore, involvement in the current study was an important tool by which participants were able to reconstruct their identity and personality in a positive way. The rehabilitation interventions assisted in the construction of a positive new identity for many participants, noting that, through the achievement of new goals, the participants were able to redefine themselves in terms of their self-perceptions and their abilities. Participants in this trial also emphasized that the interventions provided a discovery of "I can do this!" attitude, enabling enhanced self-confidence and efficacy for other goals and challenges

within their external lives. Results of other earlier studies have echoed these findings, with physical activity improving people's perceptions of their abilities, which is of particular relevance for individuals with a negative self-concept (386,387). Thus, the interventions within this study provided the participants with a way of reconnecting with their previous selves, enhancing autonomy, and providing an ongoing positive meaning to their lives. As previously noted by Nowakowska-Domagała (2017), positive psychosocial factors can significantly affect the QoL of people with SCI (388). Helping an individual to become aware of the positive outcomes that may have arisen from the exercise experience may build self-esteem and self-efficacy as well as overall psychological health (374). Therefore, although the primary aim of rehabilitation is to improve functioning and reduce impairment, it may also indirectly affect psychosocial well-being, thus in turn targeting QoL (388).

7.5.2 Perceived facilitators to sustained participation in the intervention

The present study found that personal, social, and situational factors can possibly play an important role in influencing the QoL and psychosocial well-being of participants involved in rehabilitation trials. The role of giving and receiving of support was continually mentioned by participants, as they noted several ways in which the interactions and attitudes of others affected their adherence and participation in the intervention. The participants said their involvement in the trial provided the opportunity to socialize and meet new people who had sustained similar injuries, had been through rehabilitation, and were willing to share stories and information about living life with a SCI. For many people with disabilities, the connections, and relationships among and between others with disabilities have proven to be an invaluable source of information, support, and companionship (389). There is a sense of sameness and ease when associating with peers who have had similar life experiences and understand disability from an experiential point of view (389). These findings are consistent with other studies, which have reported the value of non-specific psychological and emotional support through the input of peer support and social interaction (360,389–391).

The most interesting relationship that was highlighted in the current study was the interactions between participant and therapist. The way in which therapists communicate with, and relate to the individuals has been perceived by the individuals to influence rehabilitation outcomes and commitment (382,383,392,393). The attitudes of healthcare providers are perceived as negative when limitations are emphasised and goal predictions are inaccurate, and positive if the therapist adopts an enabling approach, allowing the individuals to explore goals and envision possible opportunities (375). This is reflected in the current study in which participants frequently mentioned that the relationship with the therapist was caring, friendly and encouraging, which motivated them to adhere to the exercises and improve their performance within the intervention. Lastly, the state of the clinical facility and other organizational factors can influence participant experiences and have a large impact on the efficiency of rehabilitation interventions (394). For individuals discharged from inpatient rehabilitative settings, accessing exercise and locomotor therapy in a clinical setting may reinforce a "sickness model" and consequently, have the potential to negatively impact on rehabilitation outcomes and societal re-integration (395). In contrast, going to a gym setting has been found to provide individuals with a sense of psychological respite from the stresses associated with living with a disability (396). Participants in this study mentioned feeling motivated by the integrated gym setting in which the rehabilitation occurred. They reported the environment to be positive and encouraging and remarked that able-bodied gym users were also motivated by seeing their rehabilitation in progress. Participants saw the integrative rehabilitation setting as fostering an inclusive environment that allowed them to feel motivated, excited, and comfortable from the moment they entered the building. In agreement, Vennedy et al. (2020) reported that a welcoming atmosphere and a feeling of being respected within the setting were perceived as facilitators of participation in physical activity programmes. Therefore, it is important for rehabilitation professionals to recognize the connections people have within and beyond the rehabilitation setting, as these may impact their attitudes, experiences and performance within a trial (397).

Another perceived facilitator to sustained participation in the intervention was the desire to contribute and be actively involved in the research process. When asked about their motivation to participate, many participants talked about the importance of giving back to the SCI community and contributing to advanced research within this population. Similar perspectives were reported in a systematic review by Naidoo et al. (2020) who showed that participants involved in RCTs perceived altruistic benefits to their participation, including "paying it forward to future generations", "giving back to the health care system", "contributing to future research", and how it "feels good to do good" (350). This is a particularly interesting theme, given that people with disabilities are often viewed as inferior and are associated with incapacity, as the public assume that persons with severe disabilities are dependent on others physically, economically, socially, and psychologically (398). The public perception is that people with disabilities may not be able to achieve or perform as much as those without disabilities (399). Due to these perceptions that society has regarding the potential of people with disabilities, this population tends to be economically inactive and less socially engaged (399,400). Negative perceptions can lead to lack of opportunities and work, low self-esteem, and isolation, and consequently to stigmatization, marginalization, and recurring negative health outcomes that prolong the discomfort of people with disabilities.

South Africa has been characterised by great number of discriminatory practices in the past, some of which persist today. In particular, persons with disabilities have generally had difficulties in exercising their fundamental social, political and economic rights (400). However, the participants in this trial had the desire to participate and commit to an intensive, time-consuming, physically, and emotionally draining exercise programme in order to contribute to future research. This directly contradicts the biased attitudes and unjustified perceptions to how these people and their capabilities are currently being perceived in South Africa. The participants enhanced their autonomy, ensured they were useful, and broke the prejudiced social and attitudinal barriers towards disability.

7.5.3 Perceived barriers to sustained participation in the intervention

One of the most well documented barriers to exercise adherence for people with SCI is pain (169,401). Worsening pain, which is often the result of the prescribed intervention (378), often deters participants from complying with prescribed training programmes. Most of the participants in this study verbalized varying degrees of pain from light muscle aches to debilitating pain that effected the ability to work and prevented engaging in social activity. This pain was most likely of a musculoskeletal nature due to the performance of new exercises and general muscle stiffness from the training load within the intervention as discussed in Chapter 4 of this thesis. Another common barrier to sustained participation was the high levels of fatigue reported by the participants throughout the trial. Fatigue is an important concern for people living with SCI, as it may contribute to decline in function and mobility, loss of independence and reduced QoL (402). However, this fatigue was expected in the participants due to the 'muscular fatigue' associated with exercise training (402,403). Fatigue can result from reduced energy, disuse, or overuse (403) and thus, it is no surprise that participating in a lengthy task requiring constant cognitive attention and physiological intensity resulted in tiredness for the participants in this trial.

Aside from the pain and fatigue experienced by participants in this study, external challenges tended to act as more influential barriers to sustained participation. Financial constraints, sub-optimal transport services, and family and work commitments were considered the key reasons for demotivation to participation in the interventions. The participants opinions within this study echo previous research which identified health issues, transport and accessibility, work schedules, family dependents and childcare, financial and time constraints as barriers to physical activity and participation within the SCI population (366,401). Transportation issues rate highly as a challenge for people with disabilities in South Africa, which can be related to cost, affordability, accessibility and attitudes of passengers and the drivers themselves (336). Research with people with disabilities and taxi drivers in the Durban area of South Africa, highlighted that minibus-taxi drivers often refused to provide transport services to people with physical disabilities, due to seeing them as less economically viable (404,405). People with disabilities take longer to board the taxi and thus, compromise the driver's ability to transport more

able-bodied customers, in turn reducing their profits (405) It is evident that stereotypes and discriminatory practices are still visible in society towards people with disabilities and their right to access transportation in South Africa (406).

Furthermore, South Africa, along with most low- to middle-income countries, lacks a comprehensive public transport system that is troubled by regular worker strikes and unreliable schedules. Limited provision for individuals with physical disability is provided through strained government services such a 'Dial-a-ride', resulting in the majority of people with a SCI not being able to attend health and rehabilitation appointments (405). Additionally, high unemployment rates amongst the South African population with disability result in little to no access to private transport (407). This was evident in the current study, in which participants relied on a private transport company, provided by the trial, to attend and return from exercise sessions. Despite the high cost of this transport, the standard of service provided by the company, who were themselves operating with limited resources, affected some of the participants experience of participating in the study. Thus, this transport company struggled to accommodate the substantial logistical requirements needed to timeously transport participants in wheelchair accessible vehicles to this clinical trial (three times per week for 24 weeks).

In addition to the transport concerns, financial difficulties were hugely impactful on adherence to the trial, especially considering the already substantial burden that SCI has on the finances of the individual and their family (388). Financially, initial and long-term medical costs are extremely burdening and, unfortunately, large proportions of people living with paralysis are not able to return to full-time work and, thus, are dependent upon government assistance (143). There is a well-recognised link between poverty and disability (406,408,409), which is further exacerbated by the statistics in South Africa, showing that people with disabilities are less likely to be employed than their non-disabled counterparts (406,410). Statistics pertaining to the employment of persons with disabilities in South Africa show that the working sector in South Africa is absorbing fewer than expected persons with disabilities into its workforce, with eight out of ten people with disabilities being unemployed (411). This is due to several

factors including discriminatory attitudes and practices, past ineffective labour legislation, inaccessible and unsupportive work environments, inadequate access to information, and inaccessible or unaffordable transport. Linked to employment is income, which in turn determines the welfare of individuals living with SCI (412). Poverty and disability interact with one another to produce experiences of marginalisation which are likely to reinforce negative outcomes like loss of income, lower levels of education, and lower levels of health and well-being (336,406).

Thus, the financial difficulties that participants experienced during this intervention are commonly reported (350), given the struggle to maintain stable accommodation during their participation in this study, while also dividing their time and focus from job and study opportunities, which are already more difficult to attain based on their disability. Therefore, the reports of transport and financial constraints to adhere to this study highlight the experiences of people living with disabilities in South Africa. These topics raised by the participants in the trial give us insight into the important disability and social welfare concerns of those living with SCI in South Africa and reveal the need to address these issues if future exercise trials are to be successfully undertaken.

7.5.4 Limitations

A limitation to the qualitative approach used within this study is that it relies on the involvement and interpretation of the researchers, who may have had biased views and whose own personal characteristics may have impacted the data collection and coding. Exploring personal narratives depends on the research question raised, and in the present study, the semi-structured interviews explored a resilience-oriented perspective, probably influencing the narratives presented. Another possible bias to the analysis is that the participants wanted or felt a need to contribute to the research. Thus, the more conscientious participants who might have ordinarily dropped out of the trial for various reasons, may have felt obliged to stay on to benefit others in a similar situation and to further research. This chapter indicated unforeseen complications to participant adherence to the interventions, including financial constraints and the standard of service provided by the transport company. At this point, our

analyses are preliminary and thus, more longitudinal qualitative research, exploring the perceptions and experiences of those involved in SCI interventions is warranted to better understand the lived experience of individuals with SCI in South Africa.

7.5.5 Conclusions and clinical implications

The use of qualitative research in this study allowed the investigation of an under-researched topic by adding depth and richness to the understanding of the perspectives of people with SCI involved in a rehabilitation intervention within South Africa. The holistic approach to rehabilitation calls for the involvement of individuals' views about what matters to them to inform clinical practice and to identify potential target outcomes for interventions. This qualitative chapter highlighted the role that physical activity and the perceived successes, barriers and facilitators play in prompting and integrating both positive and negative experiences. Rather than focus on traditional physiological outcomes, we can target QoL outcomes, and specifically target outcomes that are important and meaningful for participants living with SCI. While exploratory in nature, the themes that emerged in this preliminary pilot study may guide future quantitative and qualitative research with larger sample sizes in a similar low-middle income setting. Future research involving larger samples would further enhance our understanding of the experiences of persons with SCI and the impact of such experiences on their overall physical functioning and QoL.

7.6 References

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CHAPTER 8

Translating the science into recommendations for SCI rehabilitation and directions for future research

8.1 Introduction

This thesis has described the motivation for (Chapter 1), design and methodology (Chapter 2), and findings (Chapter 3-7) of a pilot RCT concerned with the effects of 24 weeks of RLT and ABT for people with SCI on these key outcomes. To our knowledge, this is the first pilot RCT within this field of RLT research using homogenous groups and an extended intervention period. Previous interventions documented in the literature typically have a duration of 6-12 weeks with, to our knowledge, an absence of RCTs focusing on over-ground exoskeletons and SCI (61,92,116,117,413,414). To extend its novelty, this pilot trial was conducted within a low-middle-income country, South Africa, in which there is currently a lack of rehabilitation research for those living with SCI.

Researchers often strive to implement RCT's as the gold-standard of experimental research. However, within these low and middle-income countries, a full-scale RCT may not always be feasible due to a lack of human and equipment resources, and financial constraints. RCTs can be very expensive, especially when conducted in clinical settings that require transportation, extensive staff time, and laboratory resources (415). Additionally, there are several other challenges in implementing such interventions in individuals with disabilities, including the difficulty in obtaining an adequate sample size and the ethical concerns involved in randomization into a true control group in which treatment is withheld. The limitations and challenges experienced in this pilot study will assist in the planning and design of future full RCTs, especially in a South African setting. This chapter aims to summarise and translate the findings of the previous chapters into evidence-based recommendations for SCI rehabilitation and research. Additionally, the feasibility of performing a full-scale RCT will be discussed based on the following aspects of the pilot trial: 1) sample size calculation 2) recruitment and retention rates 3) adherence rates 4) adverse complications and safety 5) cost-efficacy of RLT.

8.2 Summary of findings

The effect of RLT and ABT on key outcome measures was investigated in the previous chapters of this thesis (Chapters 3-7). A summary of the main clinical findings as related to 1) functional capacity, 2) secondary complications, 3) bone mineral density and body composition, 4) psychological well-being, and 5) lived experiences are presented below:

8.2.1 Functional capacity

Table 8.1: Summary of the functional capacity outcomes for the Robotic Locomotor Training and Activity-based Training groups over time.

RLT:	ABT:
↑ upper and lower motor score	↑ back strength
↑ back strength	↑ abdominal strength
↑ abdominal strength	≠ walking distance (SCI-FAI)
↑ walking distance (SCI-FAI)	↑ arm ergo distance
↑ arm ergo distance	≠ sensation
≠ sensation	≠ handgrip
≠ handgrip	

↑: increase; ↓: decrease; ≠: no change; *green*: positive change (improvement); *red*: negative change (worsened); *blue*: no change.

The results of Chapter 3 offer promising support for the effectiveness of RLT for improving functional capacity in people with incomplete SCI. RLT was successful in inducing strength changes in both the upper and lower limbs after 24 weeks. Furthermore, RLT was effective in producing increased ambulatory function compared to the ABT intervention.

8.2.2 Secondary complications

Table 8.2: Summary of the secondary complications for the Robotic Locomotor Training and Activity-based Training groups over time.

RLT:	ABT:
↑ pain	↑ pain
↑ bowel frequency	↑ bladder function
↓ urinary incontinence	↓ urinary incontinence
≠ spasticity	≠ spasticity

↑: increase; ↓: decrease; ≠: no change; *green*: positive change (improvement); *red*: negative change (worsened); *blue*: no change.

Chapter 4 suggested that RLT induced better bowel improvements and had a similar effect on reducing urinary incontinence compared to ABT. However, ABT resulted in better bladder functioning over 24 weeks of training. Neither intervention reduced pain or spasticity after 24 weeks of training. However, both interventions prevented a worsening of spasticity symptoms. Therefore, these results suggest that RLT could potentially alleviate some bladder and bowel difficulties and may prevent worsening of spasticity symptoms over time.

8.2.3 Bone density and body composition

Table 8.3: Summary of the bone mineral density and body composition indices for the Robotic Locomotor Training and Activity-based Training groups over time.

RLT:	ABT:
≠ spinal BMD	≠ spinal BMD
≠ hip BMD	↓ hip BMD
≠ fat mass	↓ fat mass
≠ adiposity distribution	↓ visceral adiposity
↑ upper body lean muscle mass	↓ gynoid fat mass
≠ lower body lean muscle mass	↑ upper body lean muscle mass
	≠ lower body lean muscle mass

↑: increase; ↓: decrease; ≠: no change; *green*: positive change (improvement); *red*: negative change (worsened); *blue*: no change.

Chapter 5 indicated that RLT prevented the progressive decline of BMD usually occurring in the SCI population. Therefore, RLT may act as an effective rehabilitation tool for preventing the development of osteoporosis and BMD decline in individuals with SCI. RLT was as effective as ABT in improving upper body strength, however, it was not effective in reducing fat mass or changing adiposity distribution. Neither intervention resulted in changes in lower body lean muscle mass.

8.2.4 Psychological well-being

Table 8.4: Summary of the psychometric outcomes for the Robotic Locomotor Training and Activity-based Training groups over time.

RLT:	ABT:
↑ anxiety markers	↓ anxiety markers
↑ quality of life markers	↑ quality of life markers
↓ depression markers	≠ depression markers

↑: increase; ↓: decrease; ≠: no change; *green*: positive change (improvement); *red*: negative change (worsened); *blue*: no change.

Chapter 6 showed that both interventions increased perceptions of QoL over the intervention period, with the RLT group showing a greater change in the general life and physical domains compared to the ABT group. The RLT group showed a significant decrease in markers of depression over time, however, they also experienced increased markers of trait anxiety compared to the ABT group.

8.2.5 Lived experiences

Table 8.5: Summary of the lived experiences of the participants during the intervention period.

Themes across participants:
↑ quality of life:
↑ physical independence
↑ emotional well-being
↓ secondary complications
↑ comradery and inter-personal support
↑ feelings of making a positive contribution
↑ pain and fatigue
↑ difficulties with time management and work/study balance
↑ financial constraints
↑ transport complications

↑: increase; ↓: decrease; ≠: no change; *green*: positive change (improvement); *red*: negative change (worsened); *blue*: no change.

Although Chapter 7 did not compare the RLT and ABT groups, it still provided valuable insight into the lived experiences of the SCI sample involved in the interventions. This chapter showed that QoL is a vital rehabilitation outcome for individuals living with SCI and revealed possible challenges and facilitators to being part of an exercise trial within South Africa. These opinions also revealed potential points to address from a feasibility perspective if a full-scale RCT would be performed. Thus, the thematic findings indicate that rehabilitation goals post SCI should not only consider physiological and functional recovery but should also consider the fundamental goal of improving QoL.

8.3 Feasibility of conducting a full-scale RCT

This investigation was undertaken as a pilot RCT to assess the feasibility of potentially performing a full-scale RCT in future. In order to consider the possibility of a large-scale investigation, key feasibility criteria are presented below:

8.3.1 Sample size calculation

This pilot study was unable to provide a sample size calculation due to the sparse and under-powered research available on RLT interventions. Additionally, the diversity and number of outcome variables tested over the intervention period meant that accurate effect sizes would rely on individual outcome calculations, which was out of the scope of the current pilot trial. In total, 17 individuals with motor incomplete tetraplegia were included in this pilot trial (Chapter 2, Fig. 1). Recruiting a larger sample to account for dropouts proved problematic, primarily due to limited resources and the highly specific inclusion and exclusion criteria of the trial. Multi-centre clinical exercise trials are necessary for achieving adequate statistical power and for generalizing findings to certain disability groups and, ideally, to certain subgroups within a specific disability (415). However, within low -middle income countries, such as South Africa, there are limited out-patient rehabilitation facilities which restricts the possibility of performing cross-centre trials. This study was performed in one of two, out-patient rehabilitation facilities (the other being used in a private therapy/rehabilitation practice) in our country that is equipped with a robotic suit for over-ground walking rehabilitation. Thus, in South Africa there are no multi-centred rehabilitation programmes that allow researchers to collate data, which limits large sample sizes for future RCTs.

8.3.2 Recruitment and retention rates

As indicated in Chapter 2 (Fig. 2.1), seventeen individuals were eligible to participate in the study after undergoing a successful screening process. To our knowledge, there are no other RCTs addressing overground RLT within a South African context and of those case series that have been performed on RLT outcomes, all have utilised relatively small sample sizes ranging from 3 to 44 participants (mean ± SD: 11 ± 9) (61). Thus, this sample size of 17 is one of the largest documented in this field of research.

The city of Cape Town in South Africa, where the trial was conducted, has an alarmingly high incidence of traumatic SCI, namely 75.6 per million population (13) as compared to the global average of 23 per million population (3). Therefore, a larger sample could certainly be recruited, however, due to limited equipment and human resources within this pilot trial, participants were split into two intakes of a maximum of eight participants each, taking a total of 18 months to complete the trial. In future RCTs, if human and equipment resources would allow, more individuals could be recruited per intake. Otherwise, one could extend the data collection period to allow for more intakes to be incorporated into the trial.

Only one individual was withdrawn from the study due to a right tibial stress fracture after three weeks of the RLT intervention. The participant had a Brown-Sequard SCI and was ambulatory over short distances with poor right sided sensation and a heavy reliance on the stronger right leg. It is hypothesised that the RLT further aggravated an already overloaded right lower limb. The lack of sensation in this limb resulted in no prior symptoms of overload and the most common lower limb fracture sites after SCI are the proximal tibia and distal femur (416). A DXA scan was therefore not sufficient to screen and identify this complication. Screening for foot and ankle fractures prior to initiating rehabilitation interventions is strongly encouraged (258). Thus, the high recruitment and retention rates within this pilot RCT support the possibility of performing a future full-scale RCT.

8.3.3 Adherence rates

This pilot trial indicated a total adherence rate of 93% over the 24-week interventions (Chapter 3, Fig. 3.1). High levels of compliance were demonstrated by the participants, with an average adherence of 93.9 ± 6.2% of all available sessions. The participant with the lowest adherence achieved 83.3%, whilst three participants achieved a 100% adherence rate. There was no statistical difference in the adherence rate between groups. Therefore, high adherence rates within this pilot trial support the possibility of achieving similarly high participant compliance rates in a full-scale RCT, especially if transport is provided to the participants.

8.3.4 Adverse complications and safety

Training within both interventions was intensive and fatiguing, but there were no severe risks within the rehabilitation protocol. Participants exposed to this trial had potential risk of fractures, sprains, bruises, skin irritations, cardiovascular complications and orthostatic hypotension with both ABT and RLT interventions (1). However, the exoskeleton has previously been tested for safety and feasibility (FDA class 2; CE Class IIa device) and found to be safe for individuals with SCI (54). A 30m galvanized steel safety tether was installed to mitigate the risk of falls. All personnel involved were trained in first aid and a dedicated physician was on emergency call within the facility. From a psychological perspective, the research team acknowledged that participating in over-ground walking in an exoskeleton or activity-based rehabilitation could trigger very strong emotions in some participants and that this effect was not underestimated (417). Ongoing monthly monitoring of participant's psychological well-being was performed by a trained psychologist to identify and safeguard against mood disturbances. The capabilities and limitations of both interventions were discussed with the participants before starting the trial.

A single participant discontinued the programme due to a tibial stress fracture within the first three weeks of the RLT intervention. During the recruitment for the trial, the mean total hip BMD across those recruited was a Z-score of -2.25 ± 0.73. The bone density levels required for safe walking within the exoskeleton, a Z-score of > -2 has been recommended. This value had been approved and adopted by the FDA to ensure minimal risk of stress fracture while walking in the exoskeleton. However, this value is based on normative data for the average healthy population (418). The lowest BMD Z-score, of -3.8, was recorded for an ABT participant who experienced no adverse events. The participant who was excluded after three weeks due to a right tibial stress fracture had a satisfactory total right hip BMD Z-score of -1.1. Consequently, it is apparent that a cut off BMD value to determine eligibility within the trial is challenging, as values are currently based on able-bodied norms. However, a BMD cut-off value of below 0.6 g/cm^2 of the knee joint has been used in previous SCI studies and may provide a useful absolute cut-off value for future RCTs (419,420). There were no other adverse complications or

injuries within the intervention period, indicating the safety of performing RLT and ABT for people with SCI. Several previous reports have also demonstrated that exoskeleton training is safe for users with SCI (79,103,206,413).

8.3.5 Cost-effectiveness of RLT

The preliminary results of this pilot trial indicate that RLT may potentially be as effective as the gold standard ABT currently used in rehabilitation facilities around the world. This study suggests that RLT could be used as an effective rehabilitation modality to improve both physical and psychological functioning, together with reducing bladder and bowel complications in those with chronic SCI. However, it appears that RLT may not be advised for reducing obesity among this population, as the traditional ABT was more effective in reducing full-body fat mass and central adiposity after 24 weeks. Neither intervention altered lower body lean muscle, spasticity, or pain. Therefore, it is our recommendation that based on the initial results of this pilot trial, locomotor training can be used safely and effectively for SCI rehabilitation in individuals with chronic incomplete SCI to improve strength parameters, improve walking function, reduce bladder and bowel complications, prevent BMD decline, and enhance psychological well-being. However, the results are less clear on the effects of RLT on other secondary health concerns, including pain, spasticity, and obesity. Thus, before clinicians are justified in the higher resource investment for access to specialized robotic locomotor equipment and facilities, a large-scale, high powered RCT is required to confirm the findings and increase generalizability. Whilst the feasibility of performing a RCT of this nature within the South African context would be promising, the relevant financial and resource constraints of such a low-middle income setting should be addressed.

There is still a limited accessibility to exoskeletons in clinical settings, partly because of their unaffordability and the high level of training required before use, and these concerns may interfere with accessibility in developing countries (420). However, it has been suggested that there is potential for new robotic technology to be cost saving if the cost of an exoskeleton could be offset by a decreased

need for rehabilitation personnel to conduct the labour-intensive demands of rehabilitation (63). Costs would also decrease as the hours of possible use of the exoskeleton increased (64).The price of exoskeletons is also proposed to be reduced with increased numbers of emerging brands in the market and studies demonstrating their efficacy (63). Several robotic device companies are entering the market with substantially lower price points than that of the device used in this study, e.g., $40,000 instead of $150,000 (63). Concerns for cost-effectiveness of such services should take into account improved treatment effectiveness, and savings from prevented secondary complications (24). There are recognized benefits of RLT on spasticity, physical capacity, bowel movement and QoL after SCI (420,421). Hence, if the potential health benefits of the exoskeleton system are confirmed, healthcare utilization and costs, as well as caregiver burden, will decrease, while social participation and life satisfaction will increase. Future studies investigating the benefits of RLT will provide a better understanding of the balance between health and social benefits and the economic costs.

8.4 Recommendations for research and suggestions for future studies

This pilot RCT was undertaken in order to provide preliminary results to investigate the effect of RLT as a rehabilitation modality for people with SCI, and to establish the feasibility of a performing a large-scale RCT in future within the context of a low-to-middle income country. With these preliminary results in mind, suggested clinical and research recommendations are provided to address the uncertainties within this pilot trial to prepare for future definite trials and enhance SCI evidence-based practice. Therefore, based on the findings of this study, five key recommended areas for future SCI research and treatment are presented below, as well as brief suggestions for improving the protocol in future studies:

8.4.1 Focus on secondary health complications as a rehabilitation and research outcome

Individuals with SCI in low-income countries continue to die from preventable secondary conditions that are no longer a leading cause of death in high-income countries (5,22). Management and treatment of secondary complications not only affects the functional and psychological well-being of the

individual but also impacts healthcare utilization and costs, as well as caregiver burden (222,223). Addressing secondary complications is a priority for people with SCI and thus, clinicians ought to consider these health concerns as a key determinant in selecting effective rehabilitations strategies post SCI. There is a growing interest and need from a public health perspective for clinicians, researchers, hospital administrators, and health insurance providers to develop and support strategies to minimize secondary health complications following SCI to reduce both the individual and healthcare burden (87). In fact, based on the available evidence, adapted physical activity programmes incorporating standing and walking with a robotic exoskeleton could potentially alleviate the development of musculoskeletal (421), cardiorespiratory (96,132), and endocrine-metabolic (421) secondary health conditions and complications. Hence, there is a need to develop and test such programmes that integrate an overground walking component, especially in publicly funded healthcare environments where morbidity and mortality rates from secondary complications remain high (87).

8.4.2 Focus on psychological and qualitative aspects of rehabilitation and research

Physical complications of SCI seem to attract more attention from health-care providers but currently, depression is one of the most common diseases throughout the world, has a high recurrence rates and is a significant risk factor for suicide, especially in the SCI population (34,327). Therefore, depression represents a substantial financial and health-care burden (34). Effective treatment of psychological diseases can mitigate the effects of depression in SCI, which in turn can reduce secondary health concerns and all cause morbidity and mortality (5). Improved psychological status can ensure better exercise adherence, allowing for further improved long-term health outcomes (313). Thus, addressing psychological well-being for people with SCI should be a priority for rehabilitation in order to alleviate the individual's burden and reduce overall health-care costs.

In particular, there is a lack qualitative research among SCI and rehabilitation studies, especially within a South African context (372,378). Future psychological research should investigate the opinions and perspectives of those involved in the rehabilitation programmes, as currently there is a mismatch

between the desired outcomes of participants and the outcomes usually targeted by clinicians (380). Qualitative research will help to identify innovative strategies and critical success factors for strengthening health systems to meet the needs of people with disabilities (24). Furthermore, an in-depth analysis of participants experiences can allow for their inclusion into the planning, implementation, and monitoring of goals and for progressing rehabilitation programmes to ensure an individual-centred approach to recovery.

8.4.3 Develop and validate a SCI specific measure for bone mineral density and assessment

Clinical care for people with SCI has been previously limited by the lack of consensus derived guidelines or standards regarding DXA-based diagnosis of osteoporosis, fracture risk prediction, or monitoring response to rehabilitation therapies (258). Issues that could be addressed in future research include a recommendation as to the most appropriate method of measuring bone parameters in people with SCI, determination of an index of fracture risk after SCI, whether bone density can be positively affected by RLT, and identification of the optimal dosage of mechanical loading for maintenance or improvement of bone density in those with SCI. Recommendations based on early evidence suggest that a BMD below 0.6 g/cm^2 of the knee joint (*i.e.*, distal femur and proximal tibia) or T-scores less than 3.5 standard deviations at the hip joints or femoral neck can be used as cut-offs to exclude individuals from participating in standing activities (420). However, these cut-offs do not guarantee that fractures at any of these sites may not occur (291,422).

Additional guidelines for BMD assessments are provided by the International Society of Clinical Densitometry who established the Official Positions for bone density assessment by dual-energy X-ray absorptiometry in individuals with SCI (258). The panel suggest that a mandate for reporting the presence or absence of fractures is needed for all studies implementing rehabilitation interventions in individuals with SCI. All future studies with DXA derived BMD outcomes should report means and ranges of both bone density and T-scores, as well as information about other conditions following the guidelines in this position statement. The future of routine densitometry in the SCI population is

dependent on the development of normative databases and improved cut-off values for fracture at the distal femur and proximal tibia using both DXA and advanced imaging methods (422). This standardization is needed to allow determination of BMD cut offs and other criteria for safety in future trials (258). Furthermore, future prospective cohort studies are required that account for risk factors for fracture, such as completeness of lesion, age at injury, duration of injury, to permit the development of SCI-appropriate algorithms validated in the clinical environment that predict fracture risk (422).

8.4.4 Develop and validate a SCI specific measure for obesity and assessment

Obesity, defined by excess body fat accumulation, is associated with diabetes, cardiovascular disease and all-cause mortality (162,206,421). Thus, identification of obesity can lead to appropriate interventions and improved health outcomes. However, currently, there is no standardized obesity classification in individuals with SCI (423,424). Body mass index (BMI) is an anthropometric measure of weight adjusted for height (kg/m^2) often used to classify obesity (276). The World Health Organization (WHO) and Centres for Disease Control and Prevention (CDC) define obesity as having a BMI of 30 kg/m^2 or more, however, this value may not be valid for certain segments of the population including those living with SCI (424). Furthermore, since BMI underestimates adiposity in individuals with SCI, it is not sensitive for detecting obesity status and is a poor predictor of mortality in this population (276,292,425–428).

Adjusted BMI classification cut-offs have been proposed for the SCI population to account for the changes in body composition after injury; however, they have not yet been validated in a large population (424,425). Similarly, it has been proposed that waist circumference (WC) may be an indicator of obesity-related comorbidities, but there are currently no SCI-specific cut-off points that have been validated (424,429,430). Research is needed to determine and validate obesity classification specific to SCI due to physiological changes that occur following injury. Exoskeletons may facilitate reducing obesity concerns after SCI by helping to decrease sitting time, increase level of physical activity and improve parameters of body composition after SCI (420). However, there is still limited

evidence to support the positive effects of RLT on parameters of body composition. Future research on this topic should focus on developing a SCI specific screening tool in order to more accurately identify risk and provide timely intervention.

8.4.5 Address and improve accessibility of transport for people with disabilities

A review by Bright (2018) has shown that in general, access to rehabilitation services is poor in many low-to-middle income countries (335). Chapter 1 of this thesis further discussed the concerns regarding equitable healthcare for people with SCI within a South African context. Expanding on this chapter, a recent study found that persons with disabilities in South Africa were more likely to have poorer physical accessibility to healthcare, due to lack of health insurance, the use of public healthcare facilities, and longer traveling times, compared to persons without disabilities (25). Similarly, Badenhorst et al. (2021) found that in the public system within South Africa, quality of care, waiting time and availability of healthcare providers, transport and availability of stock were identified as the main barriers to receiving treatment and rehabilitation (431). The participants expressed that they had challenges related to limited availability and inaccessibility of transport to attend rehabilitation centres. These findings are consistent with those of Kahonde et al. (2010) and De la Cornillere (2007), who reported that individuals in the Western Cape, South Africa, encountered problems of inaccessible and inefficient transportation services to attend rehabilitation appointments (432,433). Vergunst et al. (2017) also reported that transport-related issues were especially prominent among the participants living in rural Madwaleni, South Africa, with four of the top five barriers to rehabilitation having to do with transport (26). These findings mimic the transport challenges encountered by the participants in this trial (Chapter 7).

The issue of transport points to a need for a coordinated response between the Departments of Health and Transport so that rehabilitation can be made available as a core component of essential healthcare. The need for affordable and accessible transport in developing countries cannot be overemphasised as a means of increasing equitable access to health services. Sherry (2014) suggested strategies to improve

transport, including dedicated transport services for people with disabilities (e.g. Dial-a-Ride), transport vouchers, and partnerships with local public transport providers (24). Ensuring better accessibility and affordability of transport for people with disabilities would be of significant value in reducing healthcare and rehabilitation inequities and facilitating better participant adherence in future RCTs.

8.5 Suggestions learnt from the pilot RCT to improve future studies

a) There may have been potential over-exertion within both groups during the study, and therefore, it is recommended that future studies use a fatigue scale, such as the Fatigue Severity Scale (FSS) over time, and Rating of Perceived Exertion (RPE) within each session, to monitor for fatigue symptoms.

b) Although no changes in spasticity were detected using the Ashworth scale, several participants commented on the benefits of exercise on reducing their spasms. As the Ashworth Scale relies on subjective ratings of spasticity from an examiner, it is recommended that future studies additionally use a participant subjective rating scale for spasticity, such as Penn Spasm Frequency Scale (PSFS) to detect clinically meaningful changes.

c) As QoL appears to be a fundamental goal for people with SCI, it is suggested to use a more in-depth questionnaire for this measure, such as the SF-36 for measuring Health Related Quality of Life.

d) Sexual function is a perceived priority for functional recovery for the general SCI population and thus, it is suggested that this is investigated within the secondary complications outcomes. A questionnaire such as the International Spinal Cord Injury Male Sexual Function Basic Data Set or the International Index of Erectile Function (IIEF) for males or the Female Sexual Function Index (FSFI) and the Sexual Function Questionnaire (SFQ) for females could be used in future.

e) Dietary intake and blood markers, such as Vitamin D and Calcium concentrations are recommended to be monitored in future studies to address the confounding influence on bone formation and resorption.

f) Qualitative discussion highlighted participants enhanced functional independence and yet there was no questionnaire for this outcome. Thus, it is recommended that a scale such as the Spinal Cord Functional Independence Measure (SCIM) or Quadriplegia Index of Function (QIF) is used to monitor subjective changes in functional capacity for participants.

g) Since the distal femur and proximal tibia are the most common sites of fracture post SCI, it is recommended that these sites be measured specifically in the DXA to determine the BMD of the most vulnerable areas, as opposed to the hip and spine.

h) It is suggested that trained psychologists perform the initial questionnaires to avoid any self-consciousness or response bias in front of the treating Biokineticists, which may alter participant responses.

i) Post-intervention follow up is recommended to address exercise adherence rates and to assess the maintenance of gains after the programmes.

8.6 Conclusion

Exoskeleton training may be a safe and feasible approach for rehabilitation in individuals with SCI. The current pilot RCT demonstrates feasibility of an over-ground powered exoskeleton in 16 individuals with chronic incomplete SCI. RLT has the potential to transform rehabilitation following SCI; however, it is still premature to make clear recommendations about their clinical use after SCI. The results from this study could be used to support the design of an larger full-scale RCT to determine the effects of RLT on functional outcomes, secondary complications, and psychological well-being. Studying the effects of this rehabilitation modality in a large-scale RCT will provide future insights on the full

applicability of this technology in persons with tetraplegia. Incorporating RLT into outpatient standardized care is possible, and based on the preliminary results of this pilot trial, may contribute positively to functional independence and QoL post SCI. However, in order to upscale this pilot study to a full-scale RCT, a significant amount of rehabilitation equipment, facility space and human resources would be required. With a lack of such resources in a low-to-middle income setting, pragmatic trials utilising lower-cost exoskeletons may prove to be more feasible.

The insights gained from this pilot study will contribute to the body of knowledge on rehabilitation for those living with SCI, shed light on the benefits of RLT and the possible factors influencing rehabilitation care. Furthermore, clinicians and policy makers will be able to utilise the preliminary findings of this study to inform health promoting policies and to improve the model of care for persons living with SCI in South Africa. Every effort should be made to create equitable healthcare and rehabilitation for all persons with SCI in South Africa and globally.

8.7 References

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APPENDICES

Appendix 2.1: Full schedule of the variables collected during the 24-week study (including aims from fellow PhD candidate)

	Screening	Baseline	4 Weeks	6 Weeks	8 Weeks	12 Weeks	16 Weeks	20 Weeks	24 Weeks
Informed Consent	X								X
Anthropometry	X								
ISNCSCI	X								X
DXA	X								X
Bio, Physio, Doctor Screening	X								
Psychological Interviews (Qualitative)	X		X		X	X	X	X	X
Psychometric Questionnaires (positive and negative paradigm)		X		X		X			X
Isokinetic Strength Test		X		X		X			X
Doppler Ankle Blood Flow		X	X	X	X	X	X	X	X
Spasticity		X	X	X	X	X	X	X	X
Heart Rate		X	X	X	X	X	X	X	X
Blood Pressure		X	X	X	X	X	X	X	X
Heart Rate Variability		X		X		X			X
6-Minute Walk Test		X		X		X			X
Handgrip		X				X			X
Lower Extremity Motor Score (LEMS)		X				X			X
Surface Electromyography (sEMG)		X				X			X
Rating of Perceived Exertion		X		X		X			X
SCI-FAI		X		X		X			X
International SCI QOL Basic Data Set		X		X		X			X
Mod. Lower Urinary Tract Infection Basic Data Set		X		X		X			X
Mod. Bowel Function Basic Data Set		X		X		X			X
International SCI Pain Data Set		X		X		X			X
PARA-SCI		X		X		X			X

Appendix 2.2: Media release recruitment poster

UNIVERSITY OF CAPE TOWN

IYUNIVESITHI YASEKAPA • UNIVERSITEIT VAN KAAPSTAD

Spinal Cord Injury Rehabilitation Research Project

PARTICIPANTS WANTED FOR UCT RESEARCH

Study outline

This research project aims to study the effect that different exercise training programs have on individuals with spinal cord injury. We will specifically focus on changes in muscle activity, functional capacity, health-related benefits and psychological well being.

Those interested in participating should:

- Have an incomplete cervical spinal cord injury (C1-C8)
- Have muscle activation below the C4 level
- Injury occurred more than 12 months ago
- Be 18 - 65 years old
- Be a maximum of 100kg
- Generally healthy and injury free

Testing & Rehabilitation Procedures:

- Two pre-screening sessions, which include:
  - Medical screening with a Rehabilitation Doctor
  - Bone density scan
  - Medical screening with a Psychologist
- A one-on-one, Biokineticist supervised, 24-week rehabilitation program (3 sessions per week) at the Sport Science Institute of South Africa.
- A 3-hr visit at baseline, 12 and 24 weeks for various non-invasive tests and measurements

Benefits of participating include:

- Extensive medical and health assessment free of charge
- 24-Week spinal cord injury rehabilitation program supervised by a qualified Biokineticist, free of charge (with continued access after the research)
- Transport to and from the Sport Science Institute of South Africa, free of charge

To sign up or find out more, please contact:

Robert Evans
Email: UCTSciRehab@gmail.com
Cell: 072 985 243

essm

University of Cape Town
Division of Exercise Science and Sports Medicine
Department of Human Biology, Faculty of Health Sciences

LANDER & PURSAD BIOKINETICISTS

Division of Exercise Science and Sports Medicine

Department of Human Biology

Faculty of Health Sciences

University of Cape Town

PRE-SCREENING

INFORMED CONSENT

Research Project:

The effect of robotic walking and exercise activity-based rehabilitation on muscle activity, health-related benefits, functional capacity, and psychological well-being in persons with spinal cord injury (SCI).

This study will be carried out by investigators from the University of Cape Town, University of Stellenbosch & Cape Peninsula University of Technology, South Africa.

WHY HAVE I BEEN ASKED TO PARTICIPATE?

We are inviting you to take part in this research study, as you are a healthy individual with an incomplete cervical spinal cord injury. This study will compare the effects of walking in a robot suit and normal rehabilitation exercises on the body. The information in this form explains what you will need to do if you agree to take part. Please ask the researcher to explain anything that you do not understand. Only you can decide if you want to take part and, if you choose to say no or to stop the study at any time, it will not affect your medical treatment in any way.

WHAT IS THE PURPOSE OF THIS STUDY?

In some people, exercises may improve the quality of life in people with incomplete spinal cord injuries. Robot suits have been made to help people with spinal cord injuries perform walking exercises. We however do not know if these robot suits are better than normal exercises. This research is being done to compare the effects of walking in a robot suit and normal rehabilitation exercises on people with an incomplete spinal cord injury. If you agree to participate in this study you will need to come to the spinal cord injury rehabilitation centre at the Sports Science Institute of South Africa (SSISA) in Newlands, Cape Town, 3 times a week for 45 minutes each, for 24 weeks. An authorised vehicle that can safely transport you with your wheelchair will be arranged if you need transport to and from the SSISA. During the study, the following will be measured: changes in your muscle, blood flow, heart rhythm, bone

density, your daily functional abilities e.g., how easy it is for you to perform every day functions including going to the toilet, your level of pain and your moods.

WHO CAN PARTICIPATE IN THIS STUDY?

In order to participate in this study,

1) You need to weigh less than 100kg and have a standing height of 157cm – 188cm

2) Your hipbone density needs to be high enough to safely maintain your body weight. We assess this by a hipbone scan.

3) You need to be assessed by our doctor to ensure it is safe for you to exercise

4) You need to be assessed by our biokineticist and physiotherapist to ensure it is safe for you to exercise

5) You need to be assessed by our psychologist to determine your mental wellness and understanding the objectives of this study with using exercise therapy as a tool for rehabilitation.

WHAT HAPPENS I DO NOT PASS THE ABOVE CRITERIA?

Unfortunately, if you do not pass all the above criteria, it is not safe for you to take part in the study.

WHAT HAPPENS IF I PASS THE ABOVE CRITERIA?

If you pass the above criteria it means that you may safely perform the exercises in the study. Your name will be randomly placed into either the group doing robotic suit exercise or normal exercise. You will then be given a specific consent form explaining what your exercise programme is about and the researcher will explain and answer all your questions. Only when you agree and sign this specific consent form will you then start the exercise programme.

WHAT DOES THE SCREENING INVOLVE?

1) You will have to be weighed on a force plate while sitting in your wheelchair.

2) You will have to be transferred onto a bed where an X-Ray scanner will scan your hips

3) You will have to perform a 60-minute medical assessment with our study doctor

4) You will have to perform a 60-minute assessment with our study Biokineticist and physiotherapist

5) You will have to be assessed by our study psychologist. This visit may take up to 2 hours.

WHAT ARE THE RISKS AND BENEFITS TO BEING SCREENED?

The DEXA scan has minimal radiation exposure, a cross-country flight will expose you to more radiation than a DEXA scan.

A qualified biokineticist will ensure that you are safely transferring in and out of your wheelchair. There are no other risks to participating in these screening measurements.

You will be provided with the outcomes of the medical assessments.

WHAT HAPPENS IF I GET HURT TAKING PART IN THIS STUDY?

This research study is covered by an insurance policy taken out by the University of Cape Town if you suffer a bodily injury because you are taking part in the study.

The insurer will pay for all reasonable medical costs required to treat your bodily injury, according to the SA Good Clinical Practice Guidelines 2006, which are based on the Association of the British Pharmaceutical Industry Guidelines. The insurer will pay without you having to prove that the research was responsible for your bodily injury. You may ask the lead investigator for a copy of these guidelines.

The insurer will *not* pay for harm if, during the study, you:

- Use medicines or other substances that are not allowed
- Do not follow the investigator's instructions
- Do not tell the investigator/study doctor that you are experiencing unwanted side effects
- Do not take reasonable care of yourself

If you are harmed and the insurer pays for the necessary medical costs, usually you will be asked to accept that insurance payment as full settlement of the claim for medical costs. However, accepting this offer of insurance cover does not mean you give up your right to make a separate claim for other losses based on negligence, in a South African court.

WHAT HAPPENS TO ANY INFORMATION COLLECTED FROM THIS STUDY?

All information collected from the study will be recorded and stored in secured files with access only given to the research team. When results are published your name will be coded to ensure no personal data is exposed.

AGREEMENT:

I have read the pre-screening informed consent sheet and I understand what is needed to see if I am a candidate to join this research study. Having had the opportunity to ask any questions I might have regarding the study, and satisfied with the answers, I consent to perform the pre-screening for the study

WRITTEN CONSENT TO PARTICIPATE

I,_____(PLEASE PRINT) voluntarily agree to perform **Pre-screening assessments** for the UCT Division of Exercise Science and Sports Medicine research project titled 'The effect of robotic walking and exercise activity-based training on muscle activity, health-related benefits, functional capacity and psychological well-being in persons with spinal cord injury (SCI)', performed at the Sport Science Institute of South Africa, based in Cape Town.

The screening process and what is required of me as a participant has been explained in detail to me.

Participant Name (Please Print): _____

Participant Signature (Pre-screening):_____**Date:**

Investigator Signature (Pre-screening):_____**Date:**_____

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Prof Wayne Derman (Stellenbosch University)
Prof Leslie Swartz (Stellenbosch University)
Prof Jason Bantjies (Stellenbosch University)
Dr Laurie Rauch (University of Cape Town)

Please feel free to contact the Human Research Ethics Committee (HREC) if you have any questions or concerns regarding your rights or welfare as a research participant.

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Division of Exercise Science and Sports Medicine

Department of Human Biology

Faculty of Health Sciences

University of Cape Town

EXERCISE-BASED REHABILITATION PROGRAMME

INFORMED CONSENT

Research Project:

The effect of robotic walking and exercise activity-based rehabilitation on muscle activity, health-related benefits, functional capacity, and psychological well-being in persons with spinal cord injury (SCI).

This study will be carried out by investigators from the University of Cape Town, University of Stellenbosch & Cape Peninsula University of Technology, South Africa.

1) WHY HAVE I BEEN ASKED TO PARTICIPATE?

We are inviting you to take part in this research study, as you are a healthy individual with an incomplete cervical spinal cord injury (SCI). This study will compare the effects on the body of walking in a robot suit and conventional rehabilitation exercises. Please read the information in this letter very carefully as it explains the details of the project and how you could be involved. Please ask the researcher to explain anything that you do not understand. Only you can decide if you want to take part and, if you choose to say no or to stop the study at any time, it will not affect your medical treatment in any way.

2) WHAT IS THE PURPOSE OF THIS STUDY?

In some people, exercises may improve the quality of life in people with incomplete spinal cord injuries. Robot suits have been made to help people with spinal cord injuries perform walking exercises. We however do not know if these robot suits are better than normal exercises. This research is being done to compare the effects of walking in a robot suit and normal rehabilitation exercises on people with an incomplete spinal cord injury. If you agree to participate in this study you will need to come to the spinal cord injury rehabilitation centre at the Sports Science Institute of South Africa (SSISA) in Newlands, Cape Town, 3 times a week for 45 minutes each, for 24 weeks. An authorised vehicle that can safely transfer you with your wheelchair will be arranged if you need transport to and from the SSISA. During the study, the following will be measured: changes in your muscle, blood flow, heart rhythm, bone density, your daily functional abilities e.g., how easy it is for you to perform every day functions including going to the toilet, your level of pain and your moods.

3) WHO CAN PARTICIPATE IN THIS STUDY?

In order to participate in this study, we needed to ensure that you were able to safely take part in the exercise programme. We therefore asked you to be assessed to ensure that you.

1. Weighing less than 100 kg and have a standing height of 157cm – 188cm
2. Have a hipbone density that was high enough to safely maintain your body weight. We assessed this with a hipbone scan.
3. Have been assessed by our medical doctor to ensure it is safe for you to exercise
4. Have been assessed by our biokineticist and physiotherapist to ensure it is safe for you to exercise
5. Have been assessed by our psychologist to determine your mental wellness and understanding of the objectives of this study with using exercise therapy as a tool for rehabilitation.

4) WHAT HAPPENS NOW THAT I PASSED THE ABOVE CRITERIA?

If you passed the above criteria it means that you may safely perform the exercises in the study. Your name will be randomly placed into either the group doing robotic suit exercise or normal exercise. You will then be given a specific consent form explaining what your exercise programme is about and the researcher will explain and answer all your questions. Only when you agree and sign this specific consent form will you then start the exercise programme.

5) WHAT EXERCISE REHABILITATION WILL I NEED TO COMPLETE?

We have randomized you to perform the exercise-based rehabilitation programme.

6) WHAT DOES TAKING PART IN THE EXERCISE-BASED REHABILITATION INVOLVE?

The activity-based rehabilitation programme is the current standard of care given in advanced neurological rehabilitation centres around the world. During sessions you will perform a combination of weights, endurance and stretching training. You will exercise 3 times a week for 45 minutes over 24-weeks. The amount and difficulty of training will change as you get fitter and stronger. You will be challenged to work hard and will always be supervised by a biokineticist. You may ask to stop a session at any time. It is important to follow the investigators instructions and to immediately tell us if you have a skin irritation or pain during or after a session.

Difficult training can cause strong emotions, the study's psychologists will be available to help you handle these emotions. You can carry on with any previous rehabilitation when participating in the study, but you may not start any new rehabilitation other than that given to you in the study. We also ask that you do not start any type of new psychological counselling while participating in the study.

In order for us to assess your progress in the rehabilitation programme we need to perform certain tests. The tests are described in detail below:

7) WHAT DOES THE TESTING SESSIONS INVOLVE?

You will need to visit the Sport Science Institute of South Africa (SSISA) for a 3–4-hour long testing session at the start of the study, and then at week 6, week 12 and week 24 of your rehabilitation programme. At week 6, you will need to take part in a shorter testing period lasting for approximately 1.5 hours. The investigator will explain each measurement to you. Please ask questions if you do not fully understand.

7.1) Resting measurements [30 minutes]

You will lie down on a padded table and have your resting heart rate recorded using a chest belt. Spasticity will then be measured in the legs by stretching the muscles. Your ankle flexibility will be tested whilst measuring how active your calf muscles are. Blood flow will be measured by listening to the blood flow in the vessels using an amplifier. Lastly, the strength in your legs will be measured by asking you to push/pull against resistance.

7.2) Fitness measurements [30 minutes]

Your fitness test will be 2-minutes of assisted walking and 6-minutes of arm cycling. For the 2-minutes of assisted walking you will use different types of assistance including either the parallel bars, walker, crutch, or cane. Your heart rate, blood pressure and rating of effort will be recorded during the test.

7.3) Muscle activity and strength [90 minutes]

Your muscle activity will be measured using electrodes (sticky pads) that are connected to a computer which will measure the amount of muscle activity in your arms, trunk, and leg muscles.

Your abdominal and back strength will be measured using the Biodex machine (measures muscle force). Your hips, thighs, knees, and upper body will be firmly strapped, to secure you. You are required to push against the machine as hard as you can with only your abdominals and then only your back.

Handgrip will be measured using a grip strength reader, where you will need to hold the handgrip and grip the machine as hard as you possibly can with your right and then your left hand.

7.4) Dual-energy x-ray absorptiometry (DXA) [20 minutes]

Your hip X-ray will be performed before and after your 24-week rehabilitation programme. The scan is used to measure the amount of bone, muscle & fat in your body. You will have to be transferred onto a bed where the X-Ray scanner will scan your hips

7.5) Questionnaires [60 minutes]

You will complete five questionnaires about your health and six questionnaires about your mental wellness. These questionnaires are electronic and have been placed onto a handheld tablet for easy completion.

7.6) One-on-one interview [45 minutes]

A psychologist will interview you before you start your rehabilitation, and then again after 12 and 24-weeks. The first interview will focus on your experience of your disability and your feelings of joining the rehabilitation programme. The next two interviews will focus on your experience in the study and thoughts about the future. You will also be asked to keep a voice diary during the rehabilitation programme where you record your thoughts (recorder supplied) about your rehabilitation at the end of each week.

8) WHAT ARE THE BENEFITS AND RISKS TO TAKING PART IN THE STUDY?

If you agree to take part in the study, you will be given supervised rehabilitation in a robotic suit 3 times a week for 24 weeks. If you have no means of transport to and from sessions, we will arrange for an authorised vehicle to safely transport you with your wheelchair. You will receive medical and psychological assessments at the start, 6 weeks, halfway (12 weeks) and at the end (24 weeks) of rehabilitation. There will always be a psychologist available whenever you feel the need to discuss or communicate your emotions in a safe space.

When finishing the study, you will still be able to continue to perform rehabilitation. You may attend rehabilitation clinics for 12-weeks after the study. Clinics will be held every Wednesday afternoon (1pm-5pm) and Saturday morning (9am-1pm). If you are unable to access transport to the clinics, then the research team will arrange your transport.

You will also be given an equipment hamper (resistance bands, dumbbells, exercise ball etc.) to take home and use for your home-based exercise routine. You are encouraged (but it is not compulsory) to exercise a minimum of 3 sessions per week after finishing the study. These 3 sessions will be one robotic walking session, one exercise rehabilitation session and one home-based session.

It is important to know that by joining this study you are at risk of potential fractures, sprains, bruises, skin irritations, cardiovascular complications and fainting with rehabilitation. Emergency procedures have been put into place to lower these risks. All people that will be monitoring you are trained in first-aid and there is a dedicated doctor and psychologist on stand-by. The DEXA scan has minimal radiation exposure, a cross-country flight will expose you to more radiation than a DEXA scan.

The measurement of muscle activity bears no risk; however, your skin might be irritated from shaving your hair and placement of the electrodes. A qualified biokineticist will ensure that you are safely transferring in and out of your wheelchair.

9) WHAT HAPPENS IF I GET HURT TAKING PART IN THIS STUDY?

This research study is covered by an insurance policy taken out by the University of Cape Town if you suffer a bodily injury because you are taking part in the study.

The insurer will pay for all reasonable medical costs required to treat your bodily injury, according to the SA Good Clinical Practice Guidelines 2006, which are based on the Association of the British Pharmaceutical Industry Guidelines. The insurer will pay without you having to prove that the research was responsible for your bodily injury. You may ask the lead investigator for a copy of these guidelines.

The insurer will *not* pay for harm if, during the study, you:

- Use medicines or other substances that are not allowed
- Do not follow the investigator's instructions

- Do not tell the investigator/study doctor that you are experiencing unwanted side effects
- Do not take reasonable care of yourself

If you are harmed and the insurer pays for the necessary medical costs, usually you will be asked to accept that insurance payment as full settlement of the claim for medical costs. However, accepting this offer of insurance cover does not mean you give up your right to make a separate claim for other losses based on negligence, in a South African court.

10) WHAT HAPPENS TO ANY INFORMATION COLLECTED FROM THIS STUDY?
All information collected from the study will be recorded and stored in secured files with access only given to the research team. When results are published your name will be coded to ensure no personal data is exposed.

CONSENT FOR TAKING PART IN THE REHABILITATION AND TESTING PROCEDURES

1. **Familiarization:** I will be shown how to use all the equipment for testing procedures one week before starting the rehabilitation programme. I will be free to ask any questions about the equipment used.

2. **Rehabilitation programme:** The length of rehabilitation will be 24 weeks. During this time, I will need to visit the Sport Science Institute of South Africa (SSISA) 3 times a week for the full 24-weeks. Rehabilitation sessions will be 45 minutes long. My rehabilitation programme will be exercise-based activity.

3. **Testing procedures:** I understand that I will be needed to come into SSISA for a 3–4-hour long testing session at the start of the study, and at 12 and 24 weeks of the rehabilitation programme - the details of which have been explained to me. Additionally, I will need to come in for a shorter testing period of 1.5 hours at 6 weeks.

4. I understand that I will be given an audio recorder to keep a voice diary during my rehabilitation where I can record my thoughts at the end of each week.

AGREEMENT:

I have read the informed consent letter and understand what is expected from me during the study. I understand all possible risks and know that I may stop the study at any time, without giving a reason. I understand that the investigators may also remove me from the study at any time if it is necessary. I understand that all my results from the study will be recorded and stored. All my personal results will remain private, my name will not be printed anywhere. Having had the chance to ask any questions about the study, and happy with the answers, I consent to the rehabilitation and testing involved in this study.

WRITTEN CONSENT TO PARTICIPATE

I,_____(PLEASE PRINT) voluntarily agree to participate in the UCT Division of Exercise Science and Sports Medicine research project titled 'The effect of robotic walking and exercise activity-based training on muscle activity, health-related benefits, functional capacity and psychological well-being in persons with spinal cord injury (SCI)', performed at the Sport Science Institute of South Africa, based in Cape Town.

Participant Name (Please Print): _____

Participant Signature (Enrolment): _____ **Date** _____

Investigator Signature (Enrolment): _____ **Date:** _____

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Prof Leslie Swartz (Stellenbosch University)
Prof Jason Bantjies (Stellenbosch University)
Dr Laurie Rauch (University of Cape Town)

Please feel free to contact the Human Research Ethics Committee (HREC) if you have any questions or concerns regarding your rights or welfare as a research participant.

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Division of Exercise Science and Sports Medicine

Department of Human Biology

Faculty of Health Sciences

University of Cape Town

ROBOTIC WALKING REHABILITATION PROGRAMME

INFORMED CONSENT

Research Project:

The effect of robotic walking and exercise activity-based rehabilitation on muscle activity, health-related benefits, functional capacity, and psychological well-being in persons with spinal cord injury (SCI).

This study will be carried out by investigators from the University of Cape Town, University of Stellenbosch & Cape Peninsula University of Technology, South Africa.

1) WHY HAVE I BEEN ASKED TO PARTICIPATE?

We are inviting you to take part in this research study, as you are a healthy individual with an incomplete cervical spinal cord injury (SCI). This study will compare the effects on the body of walking in a robot suit and conventional rehabilitation exercises. Please read the information in this letter very carefully as it explains the details of the project and how you could be involved. Please ask the researcher to explain anything that you do not understand. Only you can decide if you want to take part and, if you choose to say no or to stop the study at any time, it will not affect your medical treatment in any way.

2) WHAT IS THE PURPOSE OF THIS STUDY?

In some people, exercises may improve the quality of life in people with incomplete spinal cord injuries. Robot suits have been made to help people with spinal cord injuries perform walking exercises. We however do not know if these robot suits are better than normal exercises. This research is being done to compare the effects of walking in a robot suit and normal rehabilitation exercises on people with an incomplete spinal cord injury. If you agree to participate in this study you will need to come to the spinal cord injury rehabilitation centre at the Sports Science Institute of South Africa (SSISA) in Newlands, Cape Town, 3 times a week for 45 minutes each, for 24 weeks. An authorised vehicle that can safely transfer you with your

wheelchair will be arranged if you need transport to and from the SSISA. During the study, the following will be measured: changes in your muscle, blood flow, heart rhythm, bone density, your daily functional abilities e.g., how easy it is for you to perform every day functions including going to the toilet, your level of pain and your moods.

3) WHO CAN PARTICIPATE IN THIS STUDY?

In order to participate in this study, we needed to ensure that you were able to safely take part in the exercise programme. We therefore asked you to be assessed to ensure that you.

1. Weighing less than 100 kg and have a standing height of 157cm – 188cm
2. Have a hipbone density that was high enough to safely maintain your body weight. We assessed this with a hipbone scan.
3. Have been assessed by our medical doctor to ensure it is safe for you to exercise
4. Have been assessed by our biokineticist and physiotherapist to ensure it is safe for you to exercise
5. Have been assessed by our psychologist to determine your mental wellness and understanding of the objectives of this study with using exercise therapy as a tool for rehabilitation.

4) WHAT HAPPENS NOW THAT I PASSED THE ABOVE CRITERIA?

If you passed the above criteria it means that you may safely perform the exercises in the study. Your name will be randomly placed into either the group doing robotic suit exercise or normal exercise. You will then be given a specific consent form explaining what your exercise programme is about and the researcher will explain and answer all your questions. Only when you agree and sign this specific consent form will you then start the exercise programme.

5) WHAT EXERCISE REHABILITATION WILL I NEED TO COMPLETE?

We have randomized you to perform the robotic suit rehabilitation programme.

6) WHAT DOES TAKING PART IN THE ROBOTIC SUIT REHABILITATION INVOLVE?

All of your rehabilitation will be in the Ekso^{TM} robotic walking suit. The suit can be safely and effectively used on people with spinal cord injuries. You walk in the suit by moving your weight sideways and forwards. These movements turn on sensors in the feet, which make the legs move with motors.

You will walk 3 times a week for 45 minutes over 24-weeks. The amount and difficulty of walking will change as you get fitter and used to the suit. You will be challenged to work hard and will always be supervised by a biokineticist when using the suit. You may ask to stop a walking session at any time. It is important to follow the investigators instructions and to immediately tell us if you have a skin irritation or pain during or after walking.

Walking in the suit may trigger very strong emotions; the study's psychologists will be available to help you handle these emotions. You can carry on with your previous rehabilitation when participating in the study, but you may not start any new rehabilitation other than the robotic

walking. We also ask that you do not start any type of new psychological counselling while participating in the study.

In order for us to assess your progress in the rehabilitation programme we need to perform certain tests. The tests are described in detail below:

7) WHAT DOES THE TESTING SESSIONS INVOLVE?

You will need to visit the Sport Science Institute of South Africa (SSISA) for a 3–4-hour long testing session at the start of the study, and then at week 6, week 12 and week 24 of your rehabilitation programme. At week 6, you will need to take part in a shorter testing period lasting for approximately 1.5 hours. The investigator will explain each measurement to you. Please ask questions if you do not fully understand.

7.1) Resting measurements [30 minutes]

You will lie down on a padded table and have your resting heart rate recorded using a chest belt. Spasticity will then be measured in the legs by stretching the muscles. Your ankle flexibility will be tested whilst measuring how active your calf muscles are. Blood flow will be measured by listening to the blood flow in the vessels using an amplifier. Lastly, the strength in your legs will be measured by asking you to push/pull against resistance.

7.2) Fitness measurements [30 minutes]

Fitness tests will include 2-minutes of assisted walking, 6-minutes of arm cycling as well as three different tests in the robotic suit. The tests in the robotic suit will be a six-minute walk test, a sit-to-stand test and a 10-meter walk test. Your heart rate, blood pressure and rating of effort will be recorded during the six-minute walk test. During the sit-to-stand and 10m walk test, we will place 12 reflective markers on certain parts of your body, these markers will then be captured by 12 cameras in the room. An animated image of your body will be produced on the computer, this will help us to measure the way your body moves in the robotic suit.

7.3) Muscle activity and strength [90 minutes]

Your muscle activity will be measured using electrodes (sticky pads) that are connected to a computer which will measure the amount of muscle activity in your arms, trunk, and leg muscles.

Your abdominal and back strength will be measured using the Biodex machine (measures muscle force). Your hips, thighs, knees, and upper body will be firmly strapped, to secure you. You are required to push against the machine as hard as you can with only your abdominals and then only your back.

Handgrip will be measured using a grip strength reader, where you will need to hold the handgrip and grip the machine as hard as you possibly can with your right and then your left hand.

7.4) Dual-energy x-ray absorptiometry (DEXA) [20 minutes]

Your hip X-ray will be performed before and after your 24-week rehabilitation programme. The scan is used to measure the amount of bone, muscle & fat in your body. You will have to be transferred onto a bed where the X-Ray scanner will scan your hips

7.5)

Questionnaires [60 minutes]
You will complete five questionnaires about your health and six questionnaires about your mental wellness. These questionnaires are electronic and have been placed onto a handheld tablet for easy completion.

7.6) One-on-one interview [45 minutes]

A psychologist will interview you before you start your rehabilitation, and then again after 12 and 24-weeks. The first interview will focus on your experience of your disability and your feelings of joining the rehabilitation programme. The next two interviews will focus on your experience in the study and thoughts about the future. You will also be asked to keep a voice diary during the rehabilitation programme where you record your thoughts (recorder supplied) about your rehabilitation at the end of each week.

8) WHAT ARE THE BENEFITS AND RISKS TO TAKING PART IN THE STUDY?
If you agree to take part in the study, you will be given supervised rehabilitation in a robotic suit 3 times a week for 24 weeks. If you have no means of transport to and from sessions, we will arrange for an authorised vehicle to safely transport you with your wheelchair. You will receive medical and psychological assessments at the start, 6 weeks, halfway (12 weeks) and at the end (24 weeks) of rehabilitation. There will always be a psychologist available whenever you feel the need to discuss or communicate your emotions in a safe space.

When finishing the study, you will still be able to continue to perform rehabilitation. You may attend rehabilitation clinics for 12-weeks after the study. Clinics will be held every Wednesday afternoon (1pm-5pm) and Saturday morning (9am-1pm). If you are unable to access transport to the clinics, then the research team will arrange your transport.

You will also be given an equipment hamper (resistance bands, dumbbells, exercise ball etc.) to take home and use for your home-based exercise routine. You are encouraged (but it is not compulsory) to exercise a minimum of 3 sessions per week after finishing the study. These 3 sessions will be one robotic walking session, one exercise rehabilitation session and one home-based session.

It is important to know that by joining this study you are at risk of potential fractures, sprains, bruises, skin irritations, cardiovascular complications and fainting with rehabilitation. Emergency procedures have been put into place to lower these risks. All people that will be monitoring you are trained in first-aid and there is a dedicated doctor and psychologist on stand-by. The DEXA scan has minimal radiation exposure, a cross-country flight will expose you to more radiation than a DEXA scan. The measurement of muscle activity bears no risk; however, your skin might be irritated from shaving your hair and placement of the electrodes.

A qualified biokineticist will ensure that you are safely transferring in and out of your wheelchair.

9) WHAT HAPPENS IF I GET HURT TAKING PART IN THIS STUDY?

This research study is covered by an insurance policy taken out by the University of Cape Town if you suffer a bodily injury because you are taking part in the study.

The insurer will pay for all reasonable medical costs required to treat your bodily injury, according to the SA Good Clinical Practice Guidelines 2006, which are based on the Association of the British Pharmaceutical Industry Guidelines. The insurer will pay without you having to prove that the research was responsible for your bodily injury. You may ask the lead investigator for a copy of these guidelines.

The insurer will *not* pay for harm if, during the study, you:

- Use medicines or other substances that are not allowed
- Do not follow the investigator's instructions
- Do not tell the investigator/study doctor that you are experiencing unwanted side effects
- Do not take reasonable care of yourself

If you are harmed and the insurer pays for the necessary medical costs, usually you will be asked to accept that insurance payment as full settlement of the claim for medical costs. However, accepting this offer of insurance cover does not mean you give up your right to make a separate claim for other losses based on negligence, in a South African court.

10) WHAT HAPPENS TO ANY INFORMATION COLLECTED FROM THIS STUDY?

All information collected from the study will be recorded and stored in secured files with access only given to the research team. When results are published your name will be coded to ensure no personal data is exposed.

CONSENT FOR TAKING PART IN THE REHABILITATION AND TESTING PROCEDURES

1) **Familiarization:** I will be shown how to walk in the robotic suit and how to use all the equipment for testing procedures, one week before starting the rehabilitation programme. I will be free to ask any questions about the equipment used.

2) **Rehabilitation programme:** The length of rehabilitation will be 24 weeks. During this time, I will need to visit the Sport Science Institute of South Africa (SSISA) 3 times a week for the full 24-weeks. Rehabilitation sessions will be 45 minutes long. My rehabilitation programme will involve walking in a robotic suit.

3) **Testing procedures:** I understand that I will be needed to come into SSISA for a 3–4-hour long testing session at the start of the study, and at 12 and 24 weeks of the rehabilitation programme - the details of which have been explained to me. Additionally, I will need to come in for a shorter testing period of 1.5 hours at 6 weeks.

4) I understand that I will be given an audio recorder to keep a voice diary during my rehabilitation where I can record my thoughts at the end of each week.

AGREEMENT:

I have read the informed consent letter and understand what is expected from me during the study. I understand all possible risks and know that I may stop the study at any time, without giving a reason. I understand that the investigators may also remove me from the study at any time if it is necessary. I understand that all my results from the study will be recorded and stored. All my personal results will remain private, my name will not be printed anywhere. Having had the chance to ask any questions about the study, and happy with the answers, I consent to the rehabilitation and testing involved in this study.

WRITTEN CONSENT TO PARTICIPATE

I,_____(PLEASE PRINT) voluntarily agree to participate in the UCT Division of Exercise Science and Sports Medicine research project titled 'The effect of robotic walking and exercise activity-based training on muscle activity, health-related benefits, functional capacity and psychological well-being in persons with spinal cord injury (SCI)', performed at the Sport Science Institute of South Africa, based in Cape Town.

Participant Name (Please Print):_____

Participant Signature (Enrolment):_____Date_____

Investigator Signature (Enrolment):_____ Date:_____

Primary Investigator (Supervisor)
Dr Yumna Albertus
Email: yumna.albertus@uct.ac.za
Phone: (021) 650 4560

Student Investigator
Robert Evans & Claire Shackleton
Email: *RobertEvansSA@gmail.com*;
Claireshackleton13@gmail.com
Phone: 072 985 2435

Co-investigators
Dr Sacha West (Cape Peninsula University of Technology)
Prof Wayne Derman (Stellenbosch University)
Prof Leslie Swartz (Stellenbosch University)
Prof Jason Bantjies (Stellenbosch University)
Dr Laurie Rauch (University of Cape Town)

Please feel free to contact the Human Research Ethics Committee (HREC) if you have any questions or concerns regarding your rights or welfare as a research participant.

UCT Faculty of Health Sciences Human Research Ethics Committee (HREC)
Room E52-24, Old Main Building, Groote Schuur Hospital, Observatory, 7925
Phone: (021) 406 6338
Fax: (021) 406 6441
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Prof. Marc Blockman
Phone: (021) 406 6338
Email: Mark.Blockman@uct.ac.za

Appendix 2.4: Inclusion and exclusion criteria

Inclusion criteria:

- Male or female individuals with a SCI (traumatic)
- Individuals between 18 and 65 years old
- English speaking (Does not need to be 1st language but must be fluent)
- Chronic (>1yr) spinal cord injury
- Motor/Sensory incomplete (AIS B, C, D), with a neurological level of injury (NLI) between C1-C8 (cervical injury) as determined by the International Standards for Neurological Classification of SCI (ISNCSCI)
- Reliant upon a wheelchair as their primary mode of mobility
- Sufficient anthropometrics and range of motion (ROM) to achieve a normal, reciprocal gait pattern within the Ekso™ suit
    - Standing height: 157cm – 188cm
    - Maximum hip width: 42cm
    - Upper leg length (Femur): 51cm to 61.4cm
    - Lower Leg length (Tibia): 48cm to 63.4cm
    - Maximum weight: 100 kilograms
    - Hip extension greater than or equal to 5 degrees
    - Knee extension less than or equal to 12 degrees
    - Ankle dorsiflexion greater than or equal to 0 degrees
- Sufficient upper extremity (UE) strength to use a front wheeled walker (FWW) either by manual muscle testing (MMT) (minimum triceps strength bilaterally of 3/5, shoulder abduction/adduction and flexion/extension 4/5) and/or by functional standing test with FWW. Participants with impaired hand function may use cuff grips.
- Demonstrate adequate trunk stability and upper extremity strength to utilize Ekso™ bionic walking suit as evidenced by the ability to complete a level (or near level) surface wheelchair to mat transfer with minimal assistance.
- Medically stable and cleared by a physician for full weight-bearing locomotor training including 15-minute standing frame trial to assess standing tolerance.
- Severe osteoporosis: DXA Z score < -2 of the hip or lumbar spine

Exclusion criteria:

- Sensory Incomplete (AIS B) with a neurological level of C1-3

- Non-traumatic SCI
- Have trained in a robotic exoskeleton in the past
- Performing any other form of locomotor training
- Clinically Depressed (Beck Depression Inventory)
- Any medical issue that in the opinion of the investigating team precludes full weight-bearing locomotor training, including but not limited to:
    - Heart or respiratory comorbidity
    - Spinal instability (or spinal orthotic unless cleared by physician)
    - Acute deep vein thrombosis (DVT) with activity restrictions
    - Stoma bag
    - Severe, recurrent autonomic dysreflexia (AD) requiring medical intervention
    - Heterotopic ossification (HO) in the lower extremities resulting in ROM restrictions at the hips or knees
    - Two or more pathological fractures in the last 48 months in a major weight-bearing bone (femur or tibia) in the lower extremity
    - Hip subluxation (x-rays will be obtained for individuals injured prior to 10 years of age.
- Any medical issue that in the opinion of the investigating team would affect participant safety either due to cognitive deficits/impulsivity, intolerance to mild exercise or other factors
- Any issue that in the opinion of the investigating team would confound results such as a concurrent neurological injury or disorder (other than SCI)
- Modified Ashworth Scale (MAS) = 4 in any of the lower extremity joints (i.e., scored a 4 on the scale (indicating rigidity in the joint) when testing joint movements in lower extremities (hip flexion/extension, hip adduction/abduction, knee flexion/extension, ankle dorsi/plantar flexion)
- Skin integrity issues in areas that contact the device (including abdominal ostomies) or that would prohibit sitting
- Pregnancy
- Z scores outside of recommended range (<-2)

FORM 4: PATIENT SCREENING

Date: _____

Patient Name: _____ **Patient ID:** _____ **Physical Therapist Name:** _____

***For any item that results in a "NO" answer, indicate a plan of action for determining patient appropriateness for continuing with session.**

SCREENING QUESTIONS		YES	NO	COMMENTS	PLAN*	INITIALS
ROM: Hip	Does patient have sufficient ROM of both hips? (5 degrees of extension; 110 degrees of flexion)	○	○			
ROM: Knee	Does patient have sufficient ROM of both knees? (Full extension to 110 degrees of flexion)	○	○			
ROM: Ankle	Does patient have sufficient ROM of both ankles? (0 degrees of DF to 25 degrees of PF)	○	○			
ROM: Shoulder	Does patient have sufficient ROM of both shoulders? (50 degrees of shoulder extension)	○	○			
Measurement	Do the patient's skeletal length and width measurements fit within the guidelines/limitations of the Sizing Chart?	○	○			
	Are the legs symmetrical?	○	○			
Strength	Does patient have sufficient UE strength to safely use assistive device(s)?	○	○			
	Does patient have sufficient hand strength to safely use the Crutch interface?	○	○			
Spasticity	Does patient have Modified Ashworth Scale (MAS) scores of less than three (3) in both lower extremities?	○	○			
Mobility Skills	Is patient independent with static sitting balance?	○	○			
Medical	Is patient free of any skin integrity (past/present) that may interfere with wearing Ekso?	○	○			
	Is patient free of any other medical concerns that may prevent standing/walking? (Examples: orthostatic hypotension in standing, autonomic dysreflexia, LE fracture risk, High Blood Pressure)	○	○			
	Is patient medically a candidate for walking in other devices?	○	○			
Communication	Can patient safely follow directions and clearly express pain?	○	○			
IS IT SAFE AND APPROPRIATE TO PROCEED WITH AN EKSO TRIAL?		○	○			

⚠ **If patient has "NO" in ROM and/or Spasticity but deemed safe/suitable for Ekso trial, reassessments of both conditions must be made before each subsequent Ekso session.**

Appendix 2.6: Robotic Locomotor Training (RLT) settings: Ekso GT

The RLT intervention utilised the Ekso GT Variable Assist Model, which has been used in previous research (55,57). This model of exoskeleton is equipped with variable assist software which provides three different levels of walking assistance:

1) *Bilateral Max Assist*: Using Bilateral Max Assist, the Ekso suit provides full power to both legs. No strength is required from the participant, as only proper balance and weight shifts are required to achieve walking.
2) *Adaptive Assist*: When working in Adaptive Assist, participants with any amount of lower extremity strength contribute what they can to their walking efforts. Ekso dynamically adjusts to produce a smooth, consistent gait. Feedback is provided to the therapist about the amount of power needed from Ekso for participants to complete each step in a specified amount of time.
3) *Fixed Assist*: Using Fixed Assist, either leg of the Ekso contributes a fixed amount of power (levels 0-100%) to help participants complete steps in a specified amount of time. Values are established using information gained while walking in Adaptive Assist and assigned by the Biokineticist, allowing the clinician to explore the impact of various interventions on rehabilitation goals.

Locomotor training within the Ekso, is further divided into four modes of stepping:

1) *FirstStep mode:* A Biokineticist controls steps with a button push, input into the device is required for every transition. This first mode allows the Biokineticist to slowly move through the individual stages of the gait cycle.
2) *ActiveStep mode:* The participant takes control of initiating their steps via buttons on the crutches or walker. This semi-advanced mode uses input from the sensors in creating safeguards to prevent incorrect stepping. For example, to transition from the right foot step phase to the left foot step phase, Ekso analyses input to see that the right foot has progressed forward, and that the participant has shifted their weight both laterally and forward over the right foot. If these criteria are not in place, stepping will not occur when the participant presses the step button.
3) *ProStep mode:* Steps are fully automated by Ekso. The participant achieves the next step by moving their hips forward and shifting them laterally (the device recognizes that the user is in the correct position and steps). In addition to these guards, foot sensor information is evaluated to identify that the feet are correctly loaded to allow for a safe step.
4) *ProStep Plus mode:* Steps are triggered by the user's weight shift (*ProStep*) plus the initiation of forward leg movement. This mode as well as *ProStep* closely mimic a natural weightbearing, reciprocal gait pattern.

Appendix 2.7: Activity- based Training (ABT) intervention: Therapy & Beyond Rehabilitation Programme

Stage I – *Pre-habilitation*: The goal of Stage I is to prepare the participant for the intensive rehabilitation programme to follow. Blood pressure control is crucial in the initial phases. Muscles in spasm/contracture cannot function in an ideal length-tension relationship and must be stretched/released. It is important to note that not all spasticity is negative; it may assist in maintaining joint stability and muscle mass in some instances. The participant must be clear of secondary complications such as pressure sores and severe autonomic dysreflexia before progressing past this stage.

Examples:

- Stretching
- Standing frame
- Tilt table

Stage II – *Muscle Recruitment:* Regeneration of damaged nerves as well as neuroplasticity ('re-wiring') allows the nervous system to regain function that was lost due to injury. The nervous pathways that are used in the latter stages of rehabilitation are developed. As improvements occur within the nervous system, the participant's ability to recruit muscle fibres improves. This stage requires intense concentration from the participant to cognitively re-connect with the neurons that activate muscular contractions.

Examples:

- Reformer
- Passive range of motion with co-activation of agonist muscle

Stage III – Posture & Joint Stability: The body cannot move effectively through single muscle contractions; it must function as a kinetic chain. Correct posture and core stability must be developed from which to generate force in the limbs. An example of posture development is sufficient lower back and abdominal support to maintain a natural curvature of the spine. An example of joint stability is sufficient co-activation of the hamstrings and quadriceps to adequately support the knee joint. This stage is crucial before a participant can become weight-bearing.

Examples:

- Plinth exercises
- Swiss ball exercises
- Quadruped position exercises
- Tall kneeling exercises
- Supported chair seated exercises

Stage IV – *Resistance & Endurance Training*: The goal in Stage IV is to initiate muscle contractions whilst in a stable posture developed in Stage III. The strength to perform activities of daily living independently should be developed. Strength, endurance & co-ordination to facilitate a functional gait

are also of key importance. The therapist's task is to help clients do the work, not to do the work for them.

Examples:

- Resistance training
    - TheraBand, dumbbell, suspension training, bodyweight
- Cardiovascular training
    - Arm ergometry, boxing, rowing, cycling

Stage V – *Pre-Gait:* The aim within Stage V is to improve coordinated movement. The participant is in a transition as they have the function needed to move and control their legs and arms, but do not have the strength, balance, endurance and/or co-ordination to walk unaided. Sound gait technique should be developed to avoid a poor and inefficient gait pattern during the final stage.

Examples:

- Crawling
- Hydrotherapy
- Locomotor training

Stage VI – *Gait Training*: The objective of Phase VI is to provide advanced functional gait training for participants who are able to walk with or without adaptive aids. Sound gait technique and the endurance to maintain this technique are once again emphasized. The training programme in Stage IV is unique to each participant's individual goals. While one person may want to get upright and walk in a shopping centre, another may want to go beyond that and partake in competitive sports.

Examples:

- Parallel bars
- Resisted walking
- Treadmill/elliptical/stairs

Appendix 2.8: Ethical approval

UNIVERSITY OF CAPE TOWN
Faculty of Health Sciences
Human Research Ethics Committee

Room E53-45 Old Main Building
Groote Schuur Hospital
Observatory 7925
Telephone [021] 406 6626
Email: shurelta.thomas@uct.ac.za
Website: www.health.uct.ac.za/fhs/research/humanethics/forms

23 May 2018

HREC REF: 718/2017

Dr Y Albertus
Sport Science Institute
Human Biology

Dear Dr Albertus

PROJECT TITLE: THE ACUTE EFFECT OF ROBOTIC WALKING AND EXERCISE -BASED REHABILITATION ON HEALTH-RELATED BENEFITS, FUNCTIONAL CAPACITY AND PSYCHOLOGICAL WELL-BEING IN INDIVIDUALS WITH SPINAL CORD INJURY (SCI)- LINKED TO 362/2016 (MSc Candidate - Ms C Shackleton)

Thank you for submitting your response to the Faculty of Health Sciences Human Research Ethics Committee received on 9 May 2018.

It is a pleasure to inform you that the HREC has **formally approved** the above-mentioned study.

Approval is granted for one year until the 30 May 2019.

Please submit a progress form, using the standardised Annual Report Form if the study continues beyond the approval period. Please submit a Standard Closure form if the study is completed within the approval period.
(Forms can be found on our website: www.health.uct.ac.za/fhs/research/humanethics/forms)

Please quote the HREC REF in all your correspondence.

Please note that the ongoing ethical conduct of the study remains the responsibility of the principal investigator.

Please note that for all studies approved by the HREC, the principal investigator **must** obtain appropriate institutional approval, where necessary, before the research may occur.

The HREC acknowledge that the student, Claire Shackleton will also be involved in this study.

Yours sincerely

Signature Removed

PROFESSOR M BLOCKMAN
CHAIRPERSON, FHS HUMAN RESEARCH ETHICS COMMITTEE
Federal Wide Assurance Number: FWA00001637.
Institutional Review Board (IRB) number: IRB00001938

This serves to confirm that the University of Cape Town Human Research Ethics Committee complies to the Ethics Standards for Clinical Research with a new drug in patients, based on the Medical Research Council (MRC-SA), Food and Drug Administration (FDA-USA), International Convention on Harmonisation Good Clinical Practice (ICH GCP), South African Good Clinical Practice Guidelines (DoH 2006), based on the Association of the British Pharmaceutical Industry Guidelines (ABPI),and Declaration of Helsinki (2013) guidelines.
The Human Research Ethics Committee granting this approval is in compliance with the ICH Harmonised Tripartite Guidelines E6: Note for Guidance on Good Clinical Practice (CPMP/ICH/135/95) and FDA Code Federal Regulation Part 50, 56 and 312.

Patient Name _____

Examiner Name _____ Date/Time of Exam_____

INTERNATIONAL STANDARDS FOR NEUROLOGICAL CLASSIFICATION OF SPINAL CORD INJURY

ASIA American Spinal Injury Association

ISCOS

MOTOR

KEY MUSCLES (scoring on reverse side)

	R	L	
C5	☐	☐	Elbow flexors
C6	☐	☐	Wrist extensors
C7	☐	☐	Elbow extensors
C8	☐	☐	Finger flexors (distal phalanx of middle finger)
T1	☐	☐	Finger abductors (little finger)

UPPER LIMB TOTAL (MAXIMUM) ☐ + ☐ = ☐ (25) (25) (50)

Comments:

L2	☐	☐	Hip flexors
L3	☐	☐	Knee extensors
L4	☐	☐	Ankle dorsiflexors
L5	☐	☐	Long toe extensors
S1	☐	☐	Ankle plantar flexors

(VAC) Voluntary anal contraction (Yes/No) ☐

LOWER LIMB TOTAL (MAXIMUM) ☐ + ☐ = ☐ (25) (25) (50)

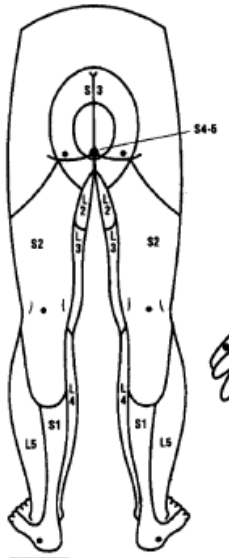
LIGHT TOUCH / PIN PRICK

	LT R	LT L	PP R	PP L
C2				
C3				
C4				
C5				
C6				
C7				
C8				
T1				
T2				
T3				
T4				
T5				
T6				
T7				
T8				
T9				
T10				
T11				
T12				
L1				
L2				
L3				
L4				
L5				
S1				
S2				
S3				
S4-5				
TOTALS (MAXIMUM)	☐ (56)	☐ (56)	☐ + ☐ = (56)	☐ + ☐ = (56)

SENSORY

KEY SENSORY POINTS

0 = absent
1 = altered
2 = normal
NT = not testable



• Key Sensory Points

(DAP) Deep anal pressure (yes/No) ☐

PIN PRICK SCORE (max: 112) ☐

LIGHT TOUCH SCORE (max: 112) ☐

NEUROLOGICAL LEVEL *The most caudal segment with normal function*	SENSORY R ☐ L ☐ MOTOR R ☐ L ☐	**SINGLE NEUROLOGICAL LEVEL** ☐	**COMPLETE OR INCOMPLETE?** ☐ *Incomplete = Any sensory or motor function in S4-S5* **ASIA IMPAIRMENT SCALE (AIS)** ☐	*(In complete injuries only)* **ZONE OF PARTIAL PRESERVATION** *Most caudal level with any innervation*	SENSORY R ☐ L ☐ MOTOR R ☐ L ☐

This form may be copied freely but should not be altered without permission from the American Spinal Injury Association.

REV 04/11

Appendix 3.2: 6-Minute Arm Test (6MAT)

Procedure:

(Adapted from Hol AT et al. Reliability and validity of the six-minute arm test for the evaluation of cardiovascular fitness in people with spinal cord injury. Arch Phys Med Rehabil, 88:489-95; Methods, with permission from Elsevier Publishing)

Heart rate measurements are continually recorded throughout the study. Blood pressure should be measured before and after the test.

Before the study commences, ask your subjects to empty their bladders to minimize any episodes of autonomic dysreflexia.

Subjects are asked to complete a single, 6-minute stage of submaximal exercise on a standard arm cycle ergometer. The power output (PO) is selected for each individual based on their manual muscle strength, ASIA motor score and physical activity level (see table below). The aim is to attain a steady heart rate of 60%-70% of age-predicted maximum heart rate or a rating of 11-15 on the Borg RPE scale.

PO selection:

<u>For subjects with tetraplegia:</u>

Set PO to 10W if: Power wheelchair user OR ≤ grade 4 wrist extension
Set PO to 15W if: Manual wheelchair user
Set PO to 20W if: Manual wheelchair user AND grade 5 wrist extension AND physically active (engaged in physical activity at least 3 times a week as measured by PASIPD)

<u>For subjects with paraplegia:</u>

Set PO to 30W if: female – inactive
Set PO to 40W if: female – active OR male – inactive
Set PO to 50W if: female – competitive athlete OR male: active
Set PO to 60W if: male – competitive athlete

An increase of 5 W/min for individuals with tetraplegia and 10 W/min for paraplegia are provided. The final steady-state heart rate is averaged over the last 30 sec of the 6 minute test.

6-MAT Worksheet

Participant Name: _____Date:_____

6-MAT

Ergo Height: _____

Handle Position: _____

Initial Power Output (PO):_____Watt

Increase in power output for each minute:_____Watt/minute

During the final 30 seconds of the test

Baseline Outcome Variables of Heart Rate:_____beats/minute

Borg Scale - Ratings of Perceived Exertion (RPE): _____ (6-20 points)

Appendix 3.3: Borg Rating of Perceived Exertion (RPE) Scale

Borg Categorical RPE SCALE

0	**Nothing at all**	
0.5	**Very, very weak**	**(**just noticeable)
1	**Very weak**	
2	**Weak**	(light)
3	**Moderate**	
4	**Somewhat strong**	
5	**Strong**	(heavy)
6		
7	**Very strong**	
8		
9		
10	**Very, very strong**	(almost max)

- **Maximal**

Borg RPE Scale Instructions

While exercising, we want you to rate your perception of exertion, i.e., how heavy and strenuous the exercise feels to you. The perception of exertion depends mainly on the strain and fatigue in your muscles and on your feeling of breathlessness.

The scale goes from 0 to 10, where 0 means "no exertion at all" and 10 means 'almost maximal exertion". Try to appraise your feeling of exertion as honestly as possible, without thinking about what the actual physical load is. Don't underestimate it, but don't overestimate it either. It's your own feeling of effort and exertion that's important, not how it compares to someone else.

Appendix 3.4: SCI Functional Ambulatory Inventory (SCI-FAI)

SCI Functional Ambulation Inventory (SCI-FAI)

Name: Session: Date:

PARAMETER	CRITERION	L	R	
A. Weight shift	shifts weight to stance limb	1	1	
	weight shift absent or only onto assistive device	0	0	
B. Step width	swing foot clears stance foot on limb advancement	1	1	
	stance foot obstructs swing foot on limb advancement	0	0	
	final foot placement does not obstruct swing limb	1	1	
	final foot placement obstructs swing limb	0	0	
C. Step rhythm (relative time needed to advance swing limb)	at heel strike of stance limb, the swing limb:			
	begins to advance in <1 second *or*	2	2	
	requires 1–3 seconds to begin advancing *or*	1	1	
	requires >3 seconds to begin advancing	0	0	
D. Step height	toe clears floor throughout swing phase *or*	2	2	
	toe drags at initiation of swing phase only *or*	1	1	
	toe drags throughout swing phase	0	0	
E. Foot contact	heel contacts floor before forefoot *or*	1	1	
	forefoot or foot flat first contact with floor	0	0	
F. Step length	swing heel placed forward of stance toe *or*	2	2	
	swing toe placed forward of stance toe *or*	1	1	
	swing toe placed rearward of stance toe	0	0	
	Parameter total			Sum /20

ASSISTIVE DEVICES		L	R	
Upper extremity balance/weightbearing devices	None	4	4	
	Cane(s)	3	3	
	Quad cane(s), Crutch(es) (forearm/axillary)	2	2	
	Walker	2		
	Parallel bars	0		
Lower extremity assistive devices	None	3	3	
	AFO	2	2	
	KAFO	1	1	
	RGO	0	0	
	Assistive device total			Sum /14

TEMPORAL/DISTANCE MEASURES				
Walking mobility (typical walking practice as opposed to W/C use)	Walks …			
	regularly in community (rarely/never use W/C)	5		
	regularly in home/occasionally in community	4		
	occasionally in home/rarely in community	3		
	rarely in home/never in community	2		
	for exercise only	1		
	does not walk	0		
	Walking mobility score			Sum /5
Two-minute walk test (distance walked in 2 minutes)	Distance walked in 2 minutes = ...		feet/minute	meters/minute

AFO: ankle-foot orthosis; KAFO: knee-ankle-foot orthosis.

Appendix 4.1: Modified Ashworth Scale

Scoring

Grade	Description
0	No increase in muscle tone
1	Slight increase in muscle tone, manifested by a catch and release or by minimal resistance at the end of the range of motion when the affected part(s) is moved in flexion or extension
1+	Slight increase in muscle tone, manifested by a catch, followed by minimal resistance throughout the remainder (less than half) of the ROM
2	More marked increase in muscle tone through most of the ROM, but affects part(s) easily moved
3	Considerable increase in muscle tone, passive movement difficult
4	Affected part(s) rigid in flexion or extension

1. **Modified Ashworth Results: Sample Form**

Muscle Tested	Score (Choose one for each muscle tested)
	☐ 0 ☐ 1 ☐ 1+ ☐ 2 ☐ 3 ☐ 4
	☐ 0 ☐ 1 ☐ 1+ ☐ 2 ☐ 3 ☐ 4
	☐ 0 ☐ 1 ☐ 1+ ☐ 2 ☐ 3 ☐ 4
	☐ 0 ☐ 1 ☐ 1+ ☐ 2 ☐ 3 ☐ 4
	☐ 0 ☐ 1 ☐ 1+ ☐ 2 ☐ 3 ☐ 4

Appendix 4.2: International Spinal Cord Injury Pain Basic Data Set

INTERNATIONAL SPINAL CORD INJURY PAIN BASIC DATA SET

DATA COLLECTION FORM – Version 2.0

Date of data collection: YYYY/MM/DD

Have you had any pain during the last seven days including today?
No Yes

If yes:

Please note that the time period during the last week applies to all pain interference questions.

In general, how much has pain interfered with your day-to-day activities in the last week?
No interference 0 - 1 - 2 - 3 - 4 - 5 - 6 - 7 - 8 - 9 - 10 Extreme interference

In general, how much has pain interfered with your overall mood in the last week?
No interference 0 - 1 - 2 - 3 - 4 - 5 - 6 - 7 - 8 - 9 - 10 Extreme interference

In general, how much has pain interfered with your ability to get a good night's sleep?
No interference 0 - 1 - 2 - 3 - 4 - 5 - 6 - 7 - 8 - 9 - 10 Extreme interference

How many different pain problems do you have?
1; 2; 3; 4; ⩾5

Please describe your three worst pain problems:

Worst pain problem:

Pain locations /sites (can be more than one, check all that apply): right (1), midline (1), or left (L)	**R**	**M**	**L**	**Type of pain** **Intensity** and **duration of pain** **Treatment of pain**
Head				**Type of pain (check one):**
Neck/shoulders				**Nociceptive**
throat				Musculoskeletal
neck				Visceral
shoulder				Other
Arms/hands				
upper arm				**Neuropathic**
elbow				At-level SCI
forearm				Below-level SCI
wrist				Other
hand/fingers				
Frontal torso/genitals				**Other**
chest				
abdomen				**Unknown**
pelvis/genitalia				
Back				**Intensity** and **duration of pain:**
upper back				**Average pain intensity in the last week:**
lower back				0 = no pain; 10 = pain as bad as you can imagine
Buttocks/hips				0; 1; 2; 3; 4; 5;
buttocks				6; 7; 8; 9; 10
hip				
anus				
Upper leg/thigh				**Date of onset:** YYYY/MM/DD
Lower legs/feet				
knee				
shin				**Are you using or receiving any treatment for your pain problem?**
calf				No Yes
ankle				
foot/toes				

Second worst pain problem:

Pain locations /sites (can be more than one, check all that apply): right (1), midline (1), or left (L)	**R**	**M**	**L**	**Type of pain** **Intensity** and **duration of pain** **Treatment of pain**
Head				**Type of pain (check one):**
Neck/shoulders				
throat				**Nociceptive**
neck				Musculoskeletal
shoulder				Visceral
				Other
Arms/hands				
upper arm				**Neuropathic**
elbow				At-level SCI
forearm				Below-level SCI
wrist				Other
hand/fingers				
Frontal torso/genitals				**Other**
chest				
abdomen				**Unknown**
pelvis/genitalia				
Back				
upper back				**Intensity** and **duration of pain:**
lower back				**Average pain intensity in the last week:**
Buttocks/hips				0 = no pain; 10 = pain as bad as you can imagine
buttocks				0; 1; 2; 3; 4; 5;
hip				6; 7; 8; 9; 10
anus				
Upper leg/thigh				**Date of onset:** YYYY/MM/DD
Lower legs/feet				
knee				
shin				**Are you using or receiving any treatment for your pain problem?**
calf				No Yes
ankle				
foot/toes				

Third worst pain problem:

Pain locations /sites (can be more than one, check all that apply): right (1), midline (1), or left (L)	**R**	**M**	**L**	**Type of pain** **Intensity** and **duration of pain** **Treatment of pain**
Head				**Type of pain (check one):**
Neck/shoulders				
throat				**Nociceptive**
neck				Musculoskeletal
shoulder				Visceral
				Other
Arms/hands				
upper arm				**Neuropathic**
elbow				At-level SCI
forearm				Below-level SCI
wrist				Other
hand/fingers				
Frontal torso/genitals				**Other**
chest				
abdomen				**Unknown**
pelvis/genitalia				
Back				
upper back				**Intensity** and **duration of pain:**
lower back				**Average pain intensity in the last week:**
Buttocks/hips				0 = no pain; 10 = pain as bad as you can imagine
buttocks				0; 1; 2; 3; 4; 5;
hip				6; 7; 8; 9; 10
anus				
Upper leg/thigh				**Date of onset:** YYYY/MM/DD
Lower legs/feet				
knee				
shin				**Are you using or receiving any treatment for your pain problem?**
calf				No Yes
ankle				
foot/toes				

Appendix 4.3: Lower Urinary Tract Function Basic Data Set

Date of data collection: YYYYMMDD

Urinary tract impairment unrelated to spinal cord lesion:
☐ No ☐ Yes, specify_____ ☐ Unknown

Awareness of the need to empty the bladder:
☐ No ☐ Yes ☐ Not applicable ☐ Not known

Bladder emptying:	Main	Supplementary
Normal voiding	☐	☐
Bladder reflex triggering		
Voluntary (tapping, scratching, anal stretch, etc.)	☐	☐
Involuntary	☐	☐
Bladder expression		
Straining (abdominal straining, Valsalva's manoeuvre)	☐	☐
External compression (Credé manoeuvre)	☐	☐
Intermittent catheterization		
Self-catheterization	☐	☐
Catheterisation by attendant	☐	☐
Indwelling catheter		
Transurethral	☐	☐
Suprapubic	☐	☐
Sacral anterior root stimulation	☐	☐
Non-continent urinary diversion/ostomy	☐	
Other method, specify_____	☐	☐

☐ Unknown

Average number of voluntary bladder emptyings per day during the last week __

Any involuntary urine leakage (incontinence) within the last three months:
☐ No ☐ Yes, average daily ☐ Yes, average weekly ☐ Yes, average monthly
☐ Not applicable ☐ Unknown

Collecting appliances for urinary incontinence:
☐ No ☐ Yes, condom catheter/sheath
☐ Yes, diaper/pad
☐ Yes, ostomy bag
☐ Yes, other, specify_____
☐ Unknown

Any drugs for the urinary tract within the last year:
☐ No ☐ Yes, bladder relaxant drugs (anticholinergics, tricyclic antidepressants, etc.)
☐ Yes, sphincter/bladder neck relaxant drugs (alpha adrenergic blockers etc.)
☐ Yes, antibiotics/antiseptics: ☐ For treatment of urinary tract infection
☐ For prophylactic reasons
☐ Yes, other, specify_____
☐ Unknown

Surgical procedures on the urinary tract:
☐ No ☐ Yes, supra-pubic catheter insertion, date last performed YYYYMMDD
☐ Yes, bladder stone removal, date last performed YYYYMMDD
☐ Yes, upper urinary tract stone removal, date last performed YYYYMMDD
☐ Yes, bladder augmentation, date last performed YYYYMMDD
☐ Yes, sphincterotomy/urethral stent, date last performed YYYYMMDD
☐ Yes, botulinum toxin injection, date last performed YYYYMMDD
☐ Yes, artificial sphincter, date last performed YYYYMMDD
☐ Yes, ileovesicostomy, date last performed YYYYMMDD
☐ Yes, ileoureterostomy, date last performed YYYYMMDD
☐ Yes, continent catheterizable valves, date last performed YYYYMMDD
☐ Yes, sacral anterior root stimulator, date performed YYYYMMDD
☐ Yes, other, specify_____ , date performed YYYYMMDD
☐ Unknown

Any change in urinary symptoms within the last year:
☐ No ☐ Yes ☐ Not applicable ☐ Unknown

Appendix 4.4: International Bowel Function SCI Basic Data Set

Defecation method and bowel care procedures (within the last four weeks):

	Main	Supplementary
Normal defecation	☐	☐
Straining/bearing down to empty	☐	☐
Digital ano-rectal stimulation	☐	☐
Suppositories	☐	☐
Digital evacuation	☐	☐
Mini enema (Clysma ⩽150 ml)	☐	☐
Enema (>150 ml)	☐	☐
Colostomy	☐	☐
Sacral anterior root stimulation	☐	☐
Other method, specify_____	☐	☐

☐ Unknown

Average time required for defecation (within the last four weeks):

☐ 0–5 min ☐ 6–10 min ☐ 11–20 min ☐ 21–30 min
☐ 31–60 min ☐ More than 60 min ☐ Unknown

Frequency of defecation (within the last four weeks):

☐ Three times or more per day ☐ Twice daily ☐ Once daily
☐ Not daily but more than twice every week
☐ Twice every week ☐ Once every week
☐ Less than once every week, but at least once within the last four weeks
☐ No defecation within the last four weeks
☐ Not applicable ☐ Unknown

Frequency of fecal incontinence (within the last three months):

☐ Two or more episodes per day ☐ One episode per day
☐ Not every day but at least once per week
☐ Not every week but more than once per month
☐ Once per month
☐ Less than once per month ☐ Never
☐ Unknown

Date performed: YYYYMMDD ☐ Unknown

Gastrointestinal or anal sphincter dysfunction unrelated to the spinal cord lesion:
☐ No ☐ Yes, specify_____ ☐ Unknown

Surgical procedures on the gastrointestinal tract:
☐ No
☐ Appendicectomy, date performed YYYYMMDD
☐ Cholecystectomy, date performed YYYYMMDD
☐ Colostomy, date last performed YYYYMMDD
☐ Ileostomy, date last performed YYYYMMDD
☐ Other, specify: _____, date last performed YYYYMMDD
☐ Unknown

Awareness of the need to defecate (within the last four weeks):
☐ Normal (direct)
☐ Indirect (For example: Abdominal cramping or discomfort—Abdominal muscle spasms—Spasms of lower extremities—Perspiration—Piloerection—Headache—Chills)
☐ None
☐ Unknown

Need to wear pad or plug (within the last three months):
☐ Daily use ☐ Not every day but at least once per week
☐ Not every week but at least once per month
☐ Less than once per month ☐ Never
☐ Unknown

Medication affecting bowel function/constipating agents (within the last four weeks):
☐ No
☐ Yes, anticholinergics
☐ Yes, narcotics
☐ Yes, other, specify: _____
☐ Unknown

Oral laxatives (within the last four weeks):
☐ No
☐ Yes, osmotic laxatives (drops)
☐ Yes, osmotic or bulking laxatives (tablets or granulates)
☐ Yes, irritant laxatives (drops)
☐ Yes, irritant laxatives (tablets)
☐ Yes, prokinetics
☐ Yes, other, specify:_____
☐ Unknown

Perianal problems (within the last year):
☐ None ☐ Haemorrhoids ☐ Perianal sores ☐ Fissures ☐ Rectal prolapse
☐ Other, specify_____ ☐ Unknown

Appendix 6.1: Beck Depression Inventory

1.		
	0	I do not feel sad.
	1	I feel sad
	2	I am sad all the time and I can't snap out of it.
	3	I am so sad and unhappy that I can't stand it.
2.		
	0	I am not particularly discouraged about the future.
	1	I feel discouraged about the future.
	2	I feel I have nothing to look forward to.
	3	I feel the future is hopeless and that things cannot improve.
3.		
	0	I do not feel like a failure.
	1	I feel I have failed more than the average person.
	2	As I look back on my life, all I can see is a lot of failures.
	3	I feel I am a complete failure as a person.
4.		
	0	I get as much satisfaction out of things as I used to.
	1	I don't enjoy things the way I used to.
	2	I don't get real satisfaction out of anything anymore.
	3	I am dissatisfied or bored with everything.
5.		
	0	I don't feel particularly guilty
	1	I feel guilty a good part of the time.
	2	I feel quite guilty most of the time.
	3	I feel guilty all of the time.
6.		
	0	I don't feel I am being punished.
	1	I feel I may be punished.
	2	I expect to be punished.
	3	I feel I am being punished.
7.		
	0	I don't feel disappointed in myself.
	1	I am disappointed in myself.
	2	I am disgusted with myself.
	3	I hate myself.
8.		
	0	I don't feel I am any worse than anybody else.
	1	I am critical of myself for my weaknesses or mistakes.
	2	I blame myself all the time for my faults.
	3	I blame myself for everything bad that happens.
9.		
	0	I don't have any thoughts of killing myself.
	1	I have thoughts of killing myself, but I would not carry them out.
	2	I would like to kill myself.
	3	I would kill myself if I had the chance.
10.		
	0	I don't cry any more than usual.
	1	I cry more now than I used to.
	2	I cry all the time now.
	3	I used to be able to cry, but now I can't cry even though I want to.

11.

0	I am no more irritated by things than I ever was.
1	I am slightly more irritated now than usual.
2	I am quite annoyed or irritated a good deal of the time.
3	I feel irritated all the time.

12.

0	I have not lost interest in other people.
1	I am less interested in other people than I used to be.
2	I have lost most of my interest in other people.
3	I have lost all of my interest in other people.

13.

0	I make decisions about as well as I ever could.
1	I put off making decisions more than I used to.
2	I have greater difficulty in making decisions more than I used to.
3	I can't make decisions at all anymore.

14.

0	I don't feel that I look any worse than I used to.
1	I am worried that I am looking old or unattractive.
2	I feel there are permanent changes in my appearance that make me look unattractive
3	I believe that I look ugly.

15.

0	I can work about as well as before.
1	It takes an extra effort to get started at doing something.
2	I have to push myself very hard to do anything.
3	I can't do any work at all.

16.

0	I can sleep as well as usual.
1	I don't sleep as well as I used to.
2	I wake up 1-2 hours earlier than usual and find it hard to get back to sleep.
3	I wake up several hours earlier than I used to and cannot get back to sleep.

17.

0	I don't get more tired than usual.
1	I get tired more easily than I used to.
2	I get tired from doing almost anything.
3	I am too tired to do anything.

18.

0	My appetite is no worse than usual.
1	My appetite is not as good as it used to be.
2	My appetite is much worse now.
3	I have no appetite at all anymore.

19.

0	I haven't lost much weight, if any, lately.
1	I have lost more than five pounds.
2	I have lost more than ten pounds.
3	I have lost more than fifteen pounds.

20.

0 I am no more worried about my health than usual.
1 I am worried about physical problems like aches, pains, upset stomach, or constipation.
2 I am very worried about physical problems and it's hard to think of much else.
3 I am so worried about my physical problems that I cannot think of anything else.

21.

0 I have not noticed any recent change in my interest in sex.
1 I am less interested in sex than I used to be.
2 I have almost no interest in sex.
3 I have lost interest in sex completely.

INTERPRETING THE BECK DEPRESSION INVENTORY

Now that you have completed the questionnaire, add up the score for each of the twenty-one questions by counting the number to the right of each question you marked. The highest possible total for the whole test would be sixty-three. This would mean you circled number three on all twenty-one questions. Since the lowest possible score for each question is zero, the lowest possible score for the test would be zero. This would mean you circles zero on each question. You can evaluate your depression according to the Table below.

Total Score	Levels of Depression
1-10	These ups and downs are considered normal
11-16	Mild mood disturbance
17-20	Borderline clinical depression
21-30	Moderate depression
31-40	Severe depression
over 40	Extreme depression

A PERSISTENT SCORE OF 17 OR ABOVE INDICATES THAT YOU MAY NEED MEDICAL TREATMENT. IF YOU HAVE ANY CARDIAC CONCERNS, PLEASE CONTACT CARDIOVASCULAR INTERVENTIONS, P.A. at 407-894-4880

Appendix 6.2: State-Trait Anxiety Inventory

DIRECTIONS:

A number of statements which people have used to describe themselves are given below. Read each statement and then circle the appropriate number to the right of the statement to indicate how you feel *right* now, that is, *at this moment*. There are no right or wrong answers. Do not spend too much time on any one statement but give the answer which seems to describe your present feelings best.

	NOT AT ALL	SOMEWHAT	MODERATELY SO	VERY MUCH SO
1. I feel calm	1	2	3	4
2. I feel secure	1	2	3	4
3. I am tense	1	2	3	4
4. I feel strained	1	2	3	4
5. I feel at ease	1	2	3	4
6. I feel upset	1	2	3	4
7. I am presently worrying over possible misfortunes	1	2	3	4
8. I feel satisfied	1	2	3	4
9. I feel frightened	1	2	3	4
10. I feel comfortable	1	2	3	4
11. I feel self-confident	1	2	3	4
12. I feel nervous	1	2	3	4
13. I am jittery	1	2	3	4
14. I feel indecisive	1	2	3	4
15. I am relaxed	1	2	3	4
16. I feel content	1	2	3	4
17. I am worried	1	2	3	4
18. I feel confused	1	2	3	4
19. I feel steady	1	2	3	4
20. I feel pleasant	1	2	3	4

DIRECTIONS

A number of statements which people have used to describe themselves are given below. Read each statement and then circle the appropriate number to the right of the statement to indicate how you *generally* feel. There are no right or wrong answers. Do not spend too much time on any one statement but give the answer which seems to describe how you generally feel.

	ALMOST NEVER	SOMETIMES	OFTEN	ALMOST ALWAYS
21. I feel pleasant	1	2	3	4
22. I feel nervous and restless	1	2	3	4
23. I feel satisfied with myself	1	2	3	4
24. I wish I could be as happy as others seem to be	1	2	3	4
25. I feel like a failure	1	2	3	4
26. I feel rested	1	2	3	4
27. I am "calm, cool, and collected"	1	2	3	4
28. I feel that difficulties are piling up so that I cannot overcome them	1	2	3	4
29. I worry too much over something that really doesn't matter	1	2	3	4
30. I am happy	1	2	3	4
31. I have disturbing thoughts	1	2	3	4
32. I lack self-confidence	1	2	3	4
33. I feel secure	1	2	3	4
34. I make decisions easily	1	2	3	4
35. I feel inadequate	1	2	3	4
36. I am content	1	2	3	4
37. Some unimportant thought runs through my mind and bothers me	1	2	3	4
38. I take disappointments so keenly that I can't put them out of my mind	1	2	3	4
39. I am a steady person	1	2	3	4
40. I get in a state of tension or turmoil as I think over my recent concerns and interests	1	2	3	4

Appendix 6.3: International SCI Quality of Life Basic Data Set

INTERNATIONAL SPINAL CORD INJURY DATA SETS
QUALITY OF LIFE BASIC DATA SET – DATA FORM (Version 1.0)

Date performed: (YYYYMMDD) _____/_____/_____ Unknown

1. Thinking about your own life and personal circumstances, how satisfied are you with your life as a whole in the past four weeks? Please use a scale ranging from 0 (completely dissatisfied) to 10 (completely satisfied). You can use 0 or 10 or any number in between.

Completely dissatisfied Completely satisfied

☐0 ☐1 ☐2 ☐3 ☐4 ☐5 ☐6 ☐7 ☐8 ☐9 ☐10

2. How satisfied are you with your physical health in the past four weeks? Please use a scale ranging from 0 (completely dissatisfied) to 10 (completely satisfied). You can use 0 or 10 or any number in between.

Completely dissatisfied Completely satisfied

☐0 ☐1 ☐2 ☐3 ☐4 ☐5 ☐6 ☐7 ☐8 ☐9 ☐10

3. How satisfied are you with your psychological health, emotions and mood in the past four weeks? Please use a scale ranging from 0 (completely dissatisfied) to 10 (completely satisfied). You can use 0 or 10 or any number in between.

Completely dissatisfied Completely satisfied

☐0 ☐1 ☐2 ☐3 ☐4 ☐5 ☐6 ☐7 ☐8 ☐9 ☐10