INNOVATIVE SPINAL CORD INJURY REHABILITATION IN THE CONTEXT OF A MIDDLE-INCOME COUNTRY: A PILOT RANDOMISED CONTROL STUDY INVESTIGATING PHYSIOLOGICAL AND PSYCHOLOGICAL EFFECTS.

BY

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This dissertation is presented for the degree
DOCTOR OF PHILOSOPHY
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In collaboration with the
Division of Orthopaedic Surgery, Stellenbosch University,
Department of Psychology, Stellenbosch University &
Department of Sport Management, Cape Peninsula University of Technology

Supervisors:
Dr. Yumna Albertus, Dr. Sacha West, Prof. Wayne Derman
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This dissertation is dedicated to the three participants that have since passed away, in part due to the COVID-19 pandemic. Your smiles and laughter will forever be in our hearts.

PROLOGUE:

The study underpinning this dissertation was a collaborative effort between three research institutions, (University of Cape Town, Cape Peninsula University of Technology and Stellenbosch University) in the Western Cape, South Africa. The overall study aimed to measure, 1) functional effects, 2) prevention of secondary complications, and 3) psychological well-being. This is a first within this field of research, specifically in South Africa, providing a comprehensive understanding of each participant completing the trial.

The multi-factorial nature of the study and numerous outcome measures (*Appendix 1*) provided sufficient depth for two Doctoral students to base their dissertations on its findings. This dissertation is focused upon findings relating to feasibility, cardiovascular and positive psychological outcomes. The second Doctoral student's dissertation has focused upon functional outcomes, secondary complications and negative psychological outcomes. The full methods of the study can be viewed on the Pan African Clinical Trials Registry (PACTR201608001647143).

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DECLARATION:

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Faculty of Health Sciences, Department of Human Biology,

Division of Exercise Science and Sports Medicine

I, Robert William Evans, hereby declare that the work on which this dissertation is based is my original work (except where acknowledgements indicate otherwise) and that neither the whole work nor any part of it has been, is being, or is to be submitted for another degree in this or any other university.

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Date: 15/03/2021

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2. **Evans RW**, Shackleton C, West S, Rauch L, Derman W, Albertus Y. Improvements in Cardiovascular Efficiency Over 24-weeks of Robotic Locomotor Training in Persons With SCI. *Archives of Physical Medicine and Rehabilitation*. 2019 ACRM Annual Conference, Chicago, USA. Dec 1;100(12):e184.

3. **Evans RW**, Bantjes J, Shackleton CL, West S, Derman W, Albertus Y, Swartz L. “I was like intoxicated with this positivity”: the politics of hope amongst participants in a trial of a novel spinal cord injury rehabilitation technology in South Africa. *Disability and Rehabilitation: Assistive Technology*. 2020 Sep 3:1-7.

4. **Evans RW**, Shackleton C, West S, Derman W, Rauch HG L, Baalbergen E, Albertus Y. Robotic locomotor training leads to cardiovascular changes in individuals with incomplete spinal cord injury over a 24-week rehabilitation period: a randomized controlled pilot study. *Archives of Physical Medicine and Rehabilitation*. 2021 (In Press)

I confirm that I have been granted permission by the University of Cape Town’s Doctoral Degrees Board (DDB) to include the above publications in my dissertation, and where co-authorships are involved, my co-authors have agreed that I may include the publications.

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City/Country: Chicago, USA

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Authors: **R, Evans**; C, Shackleton; S, West; Y, Albertus - Presented by Dr. Yumna Albertus

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Title of Contribution: Improvements in cardiovascular efficiency over 24-weeks of rehabilitation using robotic locomotor training in persons with spinal cord injury (SCI).

Authors: **R, Evans**; C, Shackleton; S, West; Y, Albertus

City/Country: Cape Town, South Africa

Title of Proceeding: 2018 SANRA/SASCA Conference

Title of Contribution: The first exoskeleton-based RCT on the African Continent: Lessons learnt & preliminary results within a sample of incomplete tetraplegics.

Authors: **R, Evans**; C, Shackleton; S, West; Y, Albertus

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Authors: **Evans, R.W.**

City/Country: Cape Town, South Africa

ABSTRACT:

A spinal cord injury (SCI) is life-altering, resulting in neurological deficits and a multitude of secondary complications. South Africa holds one of the highest traumatic SCI incidence rates in the world, where the social need for SCI prevention and rehabilitation is immense. Robotic locomotor training (RLT) is a novel rehabilitation technique that may improve health and well-being after SCI. A systematic review was conducted across 27 studies and 308 participants to explore the systemic effects of RLT. This review demonstrated that RLT shows promise as a tool for improving neurological rehabilitation outcomes; providing individuals with a SCI the ability to walk safely while improving their walking performance, as well as potentially improving cardiovascular outcomes and psychosocial factors. However, the studies reviewed were non-controlled with small, heterogenous sample sizes. Further high-powered, randomised controlled trials, with homogenous samples, are required to investigate these effects. If widespread adoption of these new technologies is to occur, sound evidence demonstrating efficacy and long-term cost saving is required.

This dissertation aimed to explore some of these under-researched areas in a sample of sixteen persons with incomplete tetraplegia. Areas of focus included, 1) rehabilitation feasibility, adherence, and research challenges in an under-resourced environment 2) cardiovascular functioning and adaptation to a rehabilitation programme, and 3) psychological well-being. We implemented two interventions, robotic locomotor training (RLT) and activity-based training (ABT), over a 24-week pilot randomised control trial.

Adherence to the interventions was high (93.9 ± 6.2%). Challenges to the study's feasibility included: ethical approval, medical clearance, transport and limited human/financial resources.

Cardiovascular parameters demonstrated that efficiency of exoskeleton walking improved during the intervention. RLT may be more effective than ABT in improving cardiac responses to orthostatic stress, with standing heart rate at 24-weeks being significantly lower in the RLT group (75.1 ± 15.0 beats/min) compared to the ABT group (95.6 ± 12.6 beats/min). Standing and RLT had similar effects on the parasympathetic nervous system, whilst both interventions were limited in their effect on brachial and ankle blood pressure.

Despite experiencing past trauma, participants possessed psychological resources including resilience, self-efficacy and post-traumatic growth which contributed to high perceptions of quality of life. The use of an exoskeleton may have had a greater positive impact on subjective psychological well-being. Expectations of participants entering the study centred around regaining the ability to walk again, despite past experiences and medical advice suggesting otherwise. Hope aids in buffering against negative emotions, however, a thin line exists between supporting high expectations and confronting unrealistic hope. Initial high expectations of recovery decreased and became more realistic during the intervention.

This dissertation demonstrates potential physiological and psychological benefits that RLT provides. Despite this potential, barriers exist in the use of RLT in low- and middle-income countries such as South Africa, primarily due to a lack of financial and human resources. The development of lower-cost exoskeletons would lessen the burden of conducting large-scale trials and increase the likelihood of adopting these innovative rehabilitation tools into current standard of care practices.

LIST OF ABBREVIATIONS:

10MWT:	10-Meter Walk Test
6MAT:	Six-minute Arm Ergometry Test
6MWT:	Six-minute Walk Test
ABPI:	Ankle Brachial Pressure Index
ABT:	Activity-based Training
AD:	Autonomic Dysreflexia
ADAPSS:	Appraisals of Disability: Primary and Secondary Scale
AIS:	American Spinal Injury Association Impairment Scale
ANOVA:	Analysis of Variance
ANS:	Autonomic Nervous System
ASIA:	American Spinal Injury Association
ATD-PA:	Assistive Technology Device Predisposition Assessment
BDI:	Beck Depression Inventory
BMD:	Bone Mineral Density
BP:	Blood Pressure
BPM:	Beats per Minute
BWSTT:	Body-weight Supported Treadmill Training
CD-RISC 25:	Connor-Davidson Resilience Scale
CE:	Conformitè Europëenne
CI:	Confidence Interval
CPG:	Central Pattern Generator
CS:	Clinical Significance
CSE:	Core Self-evaluation
CV:	Coefficient of Variation
DEXA:	Dual Energy X-ray Absorptiometry
ES:	Effect Size
FDA:	Food and Drug Administration (USA)
HR:	Heart Rate
HRV:	Heart Rate Variability
i:	Indoor Walking
ISNCSCI:	International Standards for Neurological Classification of SCI
LOI:	Level of Injury
m:	Meters
MAD:	Median Absolute Deviation

min:	Minute
mm:	Millimetre
mmHg:	Millimeters of Mercury
MRI:	Magnetic Resonance Imaging
MSES:	Moorong Self-Efficacy Scale
MVA:	Motor Vehicle Accident
NLI:	Neurological Level of Injury
NTSCI:	Non-traumatic Spinal Cord Injury
o:	Outdoor Walking
PARA-SCI:	Physical Activity Recall Assessment – Spinal Cord Injury
PEDro Scale:	Physiotherapy Evidence Database Scale
PTGI:	Post-traumatic Growth Inventory
PTSD:	Post-traumatic Stress Disorder
QoL:	Quality of Life
r:	Pearson Correlation Coefficient
RC:	Reliable Change
RCI:	Reliable Change Index
RCSC:	Reliable and Clinically Significant Change
RCT:	Randomised Control Trial
RLT:	Robotic Locomotor Training
RMSSD:	Root Mean Square of Successive Differences
ROM:	Range of Motion
RPE:	Rating of Perceived Exertion
s:	Percentage Change Measured in Seconds
SAI:	State Anxiety Inventory
SCI QoL-BDS:	Spinal Cord Injury Quality of Life Basic Data Set
SCI:	Spinal Cord Injury
SD:	Standard Deviation
SF-12v2:	SF-12v2 Health Survey
SRM:	Standardised Response Mean
STD RR:	Standard Deviation of the R-R Interval
THBI:	Total Heart Beat Index
TSCI:	Traumatic Spinal Cord Injury
TSI:	Time Since Injury
v:	Velocity
VAS:	Visual Analogue Scale

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CHAPTER 1

Review of the Literature

A paradigm shift from palliative care to activity-based therapies after spinal cord injury: The introduction and potential effectiveness of over-ground exoskeletons on cardiovascular health and psychological well-being.

Certain components of the present chapter have been published in the *Journal of Rehabilitation Medicine* (2019) – Shackleton C, **Evans R**, Shamley D, West S, Albertus Y. 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*. 2019 Nov 5;51(10):723-33. DOI: 10.2340/16501977-2601

1.1. Historical Development of Spinal Cord Injury Rehabilitation:

A spinal cord injury (SCI) is a devastating and life-altering condition which occurs as a result of incision, compulsion or contusion of the spinal cord from the level of the foramen magnum to the cauda equina[1,2]. SCI results in disruption of signal conduction across and below the point of lesion, which consequently leads to motor, sensory and/or autonomic impairment and functional restrictions[1,3]. Aetiology of SCI can be classified as either traumatic (TSCI) or non-traumatic (NTSCI). Common TSCI causes include motor vehicle accidents (MVA), falls, sporting accidents and violence[4]. Causes of NTSCI are extensive and include metabolic disorders, vascular diseases, neoplasia, inflammatory and autoimmune diseases, toxins, radiation, infection, motor neurone disease and syringomyelia[5].

The impact that a SCI has on an individual's life can be grouped under primary neurological effects and secondary complications[1,6]. The primary neurological effects of SCI, particularly paralysis of voluntary muscles, can lead to serious disability by impacting upon physical functioning and independence. The ability of an individual to work independently and engage socially is also hampered by neurological deficits[7]. Secondary complications are extensive in individuals with SCI and include neurogenic bladder and bowel, urinary tract infections, pressure ulcers, orthostatic hypotension, osteoporosis, deep vein thrombosis, spasticity, autonomic dysreflexia, pulmonary and cardiovascular problems as well as depressive disorders[8–10].

The Edwin Smith papyrus, an ancient Egyptian physician textbook dating back to 1700BC, described SCI as an ‘‘ailment not to be treated’’[11]. This palliative approach persisted over centuries and may still exist today were it not for the pioneering efforts of Sir Ludwig Guttman.

Guttman was a German-born British neurologist who was instrumental in the creation of specialized spinal units such as Stoke Mandeville Hospital which cared for injured soldiers returning to England during and after World War II[12]. Guttman pioneered a comprehensive model of care which focused upon the prevention and treatment of SCI related secondary complications, active rehabilitation and community reintegration[13]. Through these interventions, Guttman demonstrated that individuals with SCI were able to successfully reintegrate into the community, live a fulfilling life and even partake in competitive sports. Guttman's use of sport as a rehabilitative tool led to the first Paralympic Games in 1948. The 2012 London and 2016 Rio Paralympic Games provided global exposure for athletes with disabilities and have solidified the Paralympic Movement in numerous nations.

This Paralympic Movement has shifted societal views and the treatment of individuals with disabilities[14]. Improved treatment of persons with disabilities in low- and middle-income countries has been slower than high-income countries, however, this is likely due to reduced availability of capital and human resources required to enact change rather than societal views[15]. A global minority does, however, still hold strong prejudices against people with disabilities which may be associated with religious beliefs that portray disability as a curse for some form of wrongdoing[16,17].

Notable positive milestones in the global perception of disability include the United States of America introducing the Disabilities Act (ADA) of 1990 which prohibits discrimination based on disability. The USA Fitness and Athletic Equity Law for Students with Disabilities also ensures students with disabilities are given equal opportunities to compete in school athletics[18]. Within a local context, South African policy has seen the implementation of the Integrated Disability Management and Rehabilitation Pathway document[19]. This document states that persons with a SCI should receive adequate acute care, high-intensity inpatient rehabilitation and between one and three hours of outpatient rehabilitation per week. With this progression in government policy and societal inclusion, the goals of SCI rehabilitation in the 20th and 21st century have also shifted. Palliative care has made way for a focus on facilitating functional recovery and independence, promoting community-integration and economic independence, as well as enhancing quality of life[20,21]. The future of SCI treatment and rehabilitation is promising[2]. Acute treatment is advancing though various techniques, including neuroprotective drugs, neural scaffolds and stem cells[6,22]. Rehabilitation techniques are also set to advance through modalities such as brain-computer interfaces, virtual reality and robotics[23–25]. These advances in acute care and rehabilition are likely to support the achievement of better long-term outcomes after a SCI.

1.2. SCI in the South African Context:

South Africa holds one of the highest traumatic SCI incidence rates in the world, where the annual crude incidence was found to be 75.6 per million persons[26], compared to the global incidence rate estimated at 23 per million[4]. In South Africa, men account for 85.5% of these cases, peaking between 19-28 years of age with interpersonal violence presenting as the main injury source (59.3%)[26]. As a result of this high incidence rate, prevention and rehabilitation of SCI in South Africa should be of key importance. South Africa, along with many other low- and middle-income countries, faces a high and at times overwhelming demand for medical care from poor, medically uninsured communities[15,27]. Less than 20% of South Africans have medical insurance, indicating that the vast majority of the population depends on government funding for healthcare[26]. Additionally, the South African public healthcare system faces a quadruple burden of disease (maternal, new-born and child health; HIV/AIDS and tuberculosis

(TB); non-communicable diseases; and violence and injury) and has to function under financial restraints with an emphasis on primary healthcare[28]. The COVID-19 pandemic has placed further pressure on the South African health care system to prioritise primary healthcare, to the potential detriment of individuals with disabilities[29]. Outpatient rehabilitation is limited, well below the one-to-three hours advocated for in the Integrated Disability Management and Rehabilitation Pathway document[19,30]. Post-discharge, individuals suffering a SCI are unlikely to reach the full potential of their recovery and functional capacity. Lowered functional capacities reduce independence and increase the emotional and financial burden placed upon the individual and community.

In the government-funded healthcare system, standard of care for patients with SCI involves short-term in-patient care for 10-16 weeks. The length and intensity of care is dependent upon the patient's needs and amount of funding available from financial bodies such as the Department of Health, Road Accident Fund and Workman's Compensation Fund. Within the Western Cape Province in South Africa, only 40% of SCI patients (approximately 420 annually) are referred to a single rehabilitation centre in Cape Town (Western Cape Rehabilitation Centre)[26]. Referral for rehabilitation is based on factors such as age, potential for recovery and motivation. At present, chronic outpatient rehabilitation does not fall within the standard of care in South Africa[31]. Pressured healthcare facilities prioritize community reintegration with little time available to improve patient's physical capacity or functional outcomes[15]. Many individuals return to their communities without structured exercise routines, resulting in minimal levels of physical activity. There is a stark need to develop the infrastructure and knowledge in South Africa to adequately provide for the long-term needs of all individuals with SCI.

1.3. Recovery after SCI: the Role of Activity-based Therapies:

Neuroplasticity is the primary driver of functional recovery following SCI. It occurs within the nervous system through either the sprouting of new neurons or a change in conduction of spared pathways[32]. These processes were once thought to only occur during childhood, however, research in the 20th century has provided comprehensive evidence of neuroplasticity in all stages of life[3]. One of the major aims of rehabilitation after SCI is to illicit neuromuscular recovery through neuroplasticity. Recovery via neuroplasticity is dependent upon injury characteristics, quality of acute care and the type of rehabilitative interventions[33].

This plasticity can be enhanced and directed through functional training. Activity-based therapies aim to invoke neural retraining through task-specific movements whereby intense, repetitive practice is enhanced by appropriate sensory cues[34]. Kleim & Jones (2008) provide ten principles of experience-dependent plasticity, namely, 1) use it or lose it, 2) use it and improve it, 3) specificity, 4) repetition matters, 5) intensity matters, 6) time matters, 7) salience matters, 8) age matters, 9) transference and 10) interference[35]. Through these principles the level of success is dependent on the neural networks reaching a sufficient state of excitability to execute the desired task. Activity-based therapies comprise of resistance, aerobic, flexibility and gait training that is adapted to the abilities of the patient[34]. It is widely accepted that these forms of exercise both enhance recovery and promote the long-term health of individuals living with SCI[36].

Activity-based therapies typically include regular weight bearing, including standing[37]. Standing assists in combating a multitude of secondary complications experienced by individuals with SCI and is particularly effective in the maintenance of joint range of motion[38].

Beyond the physiological benefits, there are also psychological benefits to standing, including improved self-image and eye-to-eye interpersonal contact[39–41]. 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[38]. Calipers may also be used to splint the legs and facilitate walking in those with adequate trunk functioning[42]. Calipers can, however, be cumbersome and adherence to their use declines over time[43,44].

Body-weight-supported treadmill training (BWSTT) was first introduced in the early 2000's and provides a safe and controlled environment for gait retraining[45,46]. It involves unloading a portion of a patient's weight above a motorized treadmill using a counterweight-harness system, whilst providing manual assistance to guide the patients limbs into a regular gait cycle[47]. BWSTT and conventional gait retraining both demonstrate similar improvements in ambulatory function, without one approach being superior[45]. User satisfaction with BWSTT may be impacted by discomfort experienced by patients within harness systems, as well as the labour-intensiveness for therapists who are required to manually facilitate movement in each limb to achieve a reciprocal gait cycle[48–50].

1.4. Robotics and Over-ground Exoskeletons:

In order to reduce the strain placed on therapists, as well as enhance the volume and intensity of training, the first widely adopted treadmill-based powered exoskeleton, the Lokomat (Hocoma, Switzerland), was developed. The Lokomat has been widely used and researched since the early 2000's[51–54]. Robot-assisted technology has advanced in recent years to move away from treadmill-based designs to over-ground powered lower limb exoskeletons, including those provided by Ekso Bionics[55–58]. The Ekso GT is a commercially available robotic exoskeleton that enables individuals with lower extremity weakness to stand up and walk with a natural, full weight bearing, and reciprocal gait. Walking is achieved by the user's shift in weight to activate sensors in the device, which initiate steps. Battery-powered motors drive the legs, replacing deficient neuromuscular function[59].

Figure 1.1: Ekso GT Exoskeleton (Courtesy of Orthopedic Design & Technology Magazine).

Over-ground walking, or robotic locomotor training (RLT), is hypothesized to more closely mimic the forward propulsion required in the natural gait cycle with higher trunk muscle activation produced in over-ground exoskeletons when compared to the Lokomat[60]. Four mechanisms have been proposed to explain how RLT may assist in recovery of those with neurological disease: 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[49].

Secondary health complications and their ability to increase mortality rates are a major concern following SCI[61,62]. Evidence suggests that RLT may have the potential to alleviate various secondary complications such as cardiovascular deconditioning, spasticity, pain and bowel function[63,64]. Benson et al. (2006) reported that participants who reported mild spasticity pre-session, experienced a slight improvement post session[57]. Esquenazi et al. (2012) also demonstrated clinically relevant improvements in self-reports for muscle spasticity[65]. Reported pain has been shown to decrease during and after use of the robotic exoskeletons, with Sale et al. (2016) indicating as much as a 9% decrease in pain post RLT[49,66]. Self-reported bowel function has also shown potential for improvement[65,66].

Despite these promising benefits, various caveats exist around the adoption and use of exoskeletons. The largest barrier, particularly in low- and middle-income countries, is the technology's costly price tag[67]. In comparison to other forms of locomotor training, over-ground exoskeletons do, however, have the potential to be cost effective. Locomotor techniques such as BWSTT have high staffing requirements (up to three staff versus the single staff member required to operate an overground exoskeleton)[68]. Despite this potential cost saving in comparison to existing technologies, the majority of rehabilitation facilities in low- and middle-income countries do not have any form of locomotor training and limited financial resources to invest in new technologies[15,30]. If resources allow, adoption relies on evidence demonstrating a long-term cost saving that off-sets the initial high cost. This evidence is yet to be collected, with the systemic and musculoskeletal effects of RLT not yet adequately supported by scientific evidence through large-scale trials[63].

Randomized control trials are the gold standard of scientific evidence, however, they can create methodological, ethical and practical challenges when applied to interventional SCI studies[69].

For example, a non-exercising control group is often standard practice within a RCT, yet the ethical implications of withdrawing access to exercise for individuals with SCI are significant[70]. As a result of these challenges, researchers often choose pragmatic alternatives which may be a more accurate representation of real-world scenarios but have lower scientific rigor[69].

The SCI literature exploring RLT is diverse, ranging from small pragmatic case studies to robust multi-centre trials[71,72]. Heterogeneity in research designs has made interpretation of key outcome measures challenging. The following sections below provide a synthesis of this diverse literature, largely involving uncontrolled quasi-experimental interventions. Specific focus is given to cardiovascular and psycho-social outcomes after SCI and the effects of robotic locomotor training.

1.5. Cardiovascular Function after SCI:

A common secondary complication following SCI is cardiovascular disease, whereby individuals have a fourfold increase in the likelihood of developing cardiac dysfuncton[73]. A contributing factor to this high incidence is the disruption of autonomic nervous system (ANS) functioning below the neurological level of injury[74]. SCI at the cervical or high thoracic area, particularly above the splanchic sympathetic outflow (T5 - T6 level), is known to impair ANS control of the heart[75]. Reduced sympathetic activity due to a loss of supraspinal control is met with unopposed parasympathetic outflow from the unaffected vagus nerve[76]. The level of impairment experienced is modulated by the completeness and region of the SCI[77].

ANS dysfunction is particularly evident in the SCI population when changing posture from supine to standing. During this postural transition, arterial baroreceptors are unloaded, resulting in sympathetic activation and vagal withdrawal in uninjured persons to maintain blood pressure. If autonomic dysfunction due to SCI is present, then the sympathetic response to standing may be insufficient to prevent orthostatic hypotension from occurring[78]. This results in symptoms where dizziness, blurry vision, weakness and syncope may be experienced. Chronic sympatho-vagal imbalances may cause cardiac abnormalities including dysrhythmias, particularly bradycardia[79]. In addition, further cardiac deconditioning and coronary heart disease may occur due to reductions in physical activity levels[80,81]. A recent meta-analysis by Williams et al. (2019) demonstrated evidence for reduced left ventricular mass, size and volumes as well as altered systolic and diastolic function in individuals with SCI compared with able-bodied individuals[82]. The chronic 'unloading' of the heart results in increased mortality risk for persons post-SCI, thus early recognition and accurate management of cardiovascular dysfunction is vital[80,83]. As health-care systems become increasingly cognizant of financial sustainability, the management of cardiovascular disease post-SCI is one area of research that could provide evidence of significant cost-saving[84].

The ability to quantify changes in autonomic function and associated cardiovascular health after SCI is important, but can be challenging due to the complex nature of ANS dysfunction[85]. A practical measurement to investigate autonomic function is heart rate variability (HRV), which evaluates the changes in time intervals between heart beats, known as the inter-beat interval[86]. An international task force developed HRV guidelines in 1996, recommending the use of various HRV indices to reflect ANS functioning[87]. Two overlying processes are responsible for short-term HRV measurements. The first being the complex relationship between sympathetic and parasympathetic branches of the ANS. The second involves heart rate regulatory mechanisms which include respiratory sinus arrhythmia, the baroreceptor reflex and rhythmic changes in vascular tone[88]. Short term HRV assessment is considered a valid and a clinically practical measure of autonomic function in people with SCI[89]. The physiological interpretation for numerous HRV indices, however, remains unclear and hence caution should be exercised in their isolated interpretation[90].

1.5.1. The Effect of Robotic Locomotor Training on Cardiovascular Function and Walking Capacity:

Consistent physical activity is known to generate chronic adaptations in cardiovascular functioning[91]. Activity-based training (ABT) is a form of physical activity that promotes functional recovery, utilising major muscle groups at a sufficient intensity to confer cardiovascular benefits[92]. RLT has also been shown to increase heart rate above sitting or standing values[56,57,66,93]. The cardiac load during RLT is analogous to light-moderate exercise and can thus also be regarded as a health-promoting activity[63,94].

Despite acute changes in heart rate (HR) during RLT, intervention studies have been unable to demonstrate chronic changes in HR over time[72,93,95,96] – *Table 1.1*. Chronic cardiovascular benefits from RLT are plausible due to the possibility of an improved metabolic profile[95]. Evidence suggests that individuals who engage in regular physical activity have lower body mass indexes (BMI) and fat mass, higher total daily energy expenditure and both lipid profiles and glucose homeostasis are improved[97–100]. Numerous robotic interventions have demonstrated varying levels of functional improvements, however, there is a paucity in evidence for chronic cardiovascular benefits as a result of RLT[48,101–103].

Postural changes, such as those experienced during standing and RLT, also cause alterations in heart rate and blood pressure but have a more transient effect[104]. RLT provides a unique postural stimulus when considering the involvement of the central pattern generator (CPG). The CPG is a circuitry of interneurons within the spinal cord that is responsible for the basic rhythmic alternating muscle activity involved in locomotion[105,106]. A primary component of the CPG circuitry is the reticulospinal extra-pyramidal tract which is also involved in the regulation of basal sympathetic tone[107]. It could thus be hypothesised that by engaging the CPG during locomotion, the vascular tone and blood pressure changes of individuals engaging in RLT may differ from other forms of physical activity. Transient benefits from RLT may include an attenuation of orthostatic hypotension, primarily due to the muscle pump offered by the calf musculature, either through voluntary activation or the myotatic reflex[108]. Current evidence describing the effect of RLT on blood pressure (BP) is however unclear. Two interventional RLT studies have demonstrated a significant increase in BP from pre to post session[57,66], whilst another two studies have shown no change[93,96] – *Table 1.1.*

Table 1.1: Cardiovascular outcomes in individuals with spinal cord injury using Robotic Locomotor Training

	Heart Rate (bpm)	**Blood Pressure (mmHg)**	**RPE**
Asselin [56] **(N = 8)**	Walking (118 ± 21) Sit (70 ± 10) Stand (81 ± 12) (p<0.001)		Average post 6MWT = 10 ± 2*
Baunsgaard [93] **(N = 52)**	HR increased by 15 - 21% from sit to walk (p<0.001) T0 - T1 = no significant change (p>0.05)*	Within session = no significant change (p>0.05)* T0 - T1 = no significant change (p>0.05)*	T0 – T1 = significant decrease (p = 0.001)*
Benson [57] **(N = 5)**	Post session = higher HR (+9 beats per minute) compared to pre-sessions*	Post session = higher systolic BP (+4 mm/hg) than pre-session*	
Evans [95] **(N = 5)**	T0 = 121 ± 30 T1 =142 ± 35 No significant change (p>0.05)		
Kozlowski [66] **(N= 7)**	Pre - session = 71 to 104 range Post session = 78 to 108 range*	Pre - post session = increased systolic pressures*	Pre - session = 6 - 13 range Post session = 7.5 – 18.5 range*
Kressler [72] **(N = 3)**	T0 = 166.6 ± 24.0 T1 = 172.6 ± 5.13 No significant change (p>0.05)		
Sale (2016) [49] **(N = 3)**			T0 = 3 ± 3.464 T1 = 1.667 ± 1.155 No significant change (p>0.05)
Sale (2018) [109] **(N = 8)**			T0-T1 = No significant change (p>0.05)* Indoor: 1.50 ± 1.07 – 1.63 ± 1.41 Outdoor: 2.38 ± 1.60 – 1.75 ± 1.28*
Spungen [96] **(N = 7)**	T0 = 89 ± 17 T1= 106 ± 25 No significant change* Mean HR = highest for 6MWT compared to the other areas of walking session*	T0 = 136 ± 16/ 70 ± 6 T1 = 124 ± 18/ 70 ± 10 No significant change*	T0 = 15 ± 2 T1 = 8 ± 1 Significant change*

Abbreviations: bpm: Beats per minute; mmHg: Millimetres of mercury; RPE: Rating of perceived exertion; 6MWT: Six-minute walk test; Significance: $p < 0.05$. Studies with missing original data or level of significance – indicated by *. *Published in Journal of Rehabilitation Medicine by Foundation for Rehabilitation Information*[63].

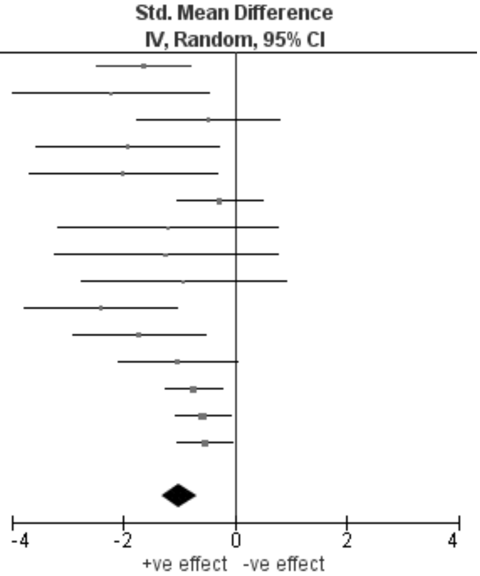
The cardiovascular benefit of exoskeleton use may, paradoxically, lower over time as individuals improve in their biomechanical efficiency and reduce the metabolic cost of walking[66]. Walking efficiency is traditionally measured using open-loop spirometry, however, the total heart beat index (THBI) calculated from continuous heart rate data is a simple and valid alternative to gas analysis[110,111]. Efficiency is improved via a significant learning effect, developed firstly through trust in the ability of the exoskeleton and therapist to safely support the user, and secondly through an optimization of the user's biomechanics synchronizing with those of the exoskeleton. Kozlowski (2015) demonstrated a rapid improvement in RLT ability whereby all but one participant could stand, walk, and sit with no more than minimal assistance, and half did so by session eight[66]. Meta-analysis of 6MWT and 10MWT performance across 15 quasi-experimental testing sessions reported significant improvements ($p<0.00$) in speed and distance with a positive pooled effect of -1.00 (95% CI: -1.32, -0.68)[63] – *Table 1.2*.

Walking performance depends on multiple factors, including the level and extent of injury[49,112], time since SCI[55] and level of assistance provided[113]. Individuals with more neurological preservation of their spinal cord are more likely to achieve greater velocities, and more recent injuries are likely to experience a faster rate of neuroplasticity and recovery[35]. The link between improved walking capacity and cardiovascular benefits from RLT are evident[94], however, the level of evidence is relatively limited and needs to be supported by randomised control trials with longer intervention periods.

Table 1.2: Effect of Robotic Locomotor Training on walking performance using a random effects model

	Pre			Post				Std. Mean Difference
Study or Subgroup	**Mean**	**SD**	**Total**	**Mean**	**SD**	**Total**	**Weight**	**IV, Random, 95% CI**
Baunsgaard 10MWTs	100	15.89	15	126.35	15.52	15	8.8%	-1.63 [-2.47, -0.79]
Benson 10MWTs	100	8.68	5	116.16	3.36	5	2.9%	-2.22 [-3.98, -0.46]
Benson 6MWT	117.6	46.65	5	140.8	41.1	5	5.0%	-0.48 [-1.74, 0.79]
Evans 6MWT	67.4	3.76	5	95.93	18.64	5	3.2%	-1.92 [-3.56, -0.27]
Evans 6MWTv	0.19	0.01	5	0.27	0.05	5	3.1%	-2.00 [-3.68, -0.33]
Gagnon 10MWT	0.15	0.02	13	0.25	0.5	13	9.7%	-0.27 [-1.05, 0.50]
Sale (2016) 10MWT	0.17	0.04	3	0.23	0.04	3	2.3%	-1.20 [-3.18, 0.78]
Sale (2016) 6MWTi	62.31	21.86	3	92.67	17.16	3	2.3%	-1.24 [-3.23, 0.76]
Sale (2016) 6MWTo	69.23	28.13	3	97.67	20.11	3	2.7%	-0.93 [-2.77, 0.90]
Sale (2018) 10MWT	0.17	0.06	8	0.31	0.05	8	4.4%	-2.40 [-3.77, -1.03]
Sale (2018) 6MWTi	62.31	21.86	8	98.38	17.8	8	5.4%	-1.71 [-2.91, -0.52]
Sale (2018) 6MWTo	73.21	26.9	8	99.13	20.1	8	6.5%	-1.03 [-2.10, 0.03]
Tefertiller 10MWTi	0.31	0.08	32	0.37	0.08	32	14.4%	-0.74 [-1.25, -0.23]
Tefertiller 10MWTo	0.32	0.08	32	0.37	0.09	32	14.6%	-0.58 [-1.08, -0.08]
Tefertiller 6MWT	92	28.3	32	107.5	28.3	32	14.6%	-0.54 [-1.04, -0.04]
Total (95% CI)			**177**			**177**	**100.0%**	**-1.00 [-1.32, -0.68]**

Heterogeneity: Tau² = 0.12; Chi² = 21.58, df = 14 (P = 0.09); I² = 35%
Test for overall effect: Z = 6.13 (P < 0.00001)



Abbreviations: 6MWT: Six-minute walk test measured in meters; 10MWT: 10-meter walk test measured in velocity; v: Velocity; s: % change measured in seconds; i: Indoor walking; o: Outdoor walking.

1.6. Psychological Well-being after SCI:

SCI often occurs unexpectedly and creates a large psychological burden[114]. Individuals with a SCI not only experience the trauma of the injury itself, but a further series of multiple traumas as the consequences of the physical injury become apparent[115]. The overwhelming lifestyle changes that follow a SCI often make it difficult for individuals to emotionally adjust[116]. Maladjustment raises concerns regarding the occurrence of psychological disorders, such as depression and anxiety[116,117]. People with SCI may have a higher risk of anxiety, feelings of helplessness and higher levels of distress[118]. These negative emotions are related to lower levels of adjustment to SCI and decreased life satisfaction[119,120].

Depressive disorders usually emerge within the first month following the injury and the prevalence appears to decline with time[117]. Depression is linked to higher incidences of secondary health problems such as pressure sores and urinary tract infections due to the self-neglect and feelings of worthlessness experienced[121,122]. The major concern linked to these depressive symptoms following SCI is suicide, whereby individuals with SCI are reported to be three to five times more likely to commit suicide as compared to the general population[123,124]. Furthermore, Kirshblum et al. (2007) state that suicide is the leading cause of death in individuals with SCI that are younger than 55 years, and that 75% of suicides occur within the first 5 years following injury[117].

Due to their potential to cause harm, the negative, psychopathological consequences of life changing events have traditionally being the focus of psychological research[125]. This approach is often reactionary, with care been provided once a specific pathology has been identified[126]. Furthermore, grief and loss psychology describe a series of stages that lead to adjustment[127,128]. These stages suggest that depression and grief are prerequisites before positive adjustment can occur; hope in the face of a catastrophic injury may be seen as denial within this paradigm[129].

Despite the significant psychosocial challenges facing individuals with an SCI, interestingly, the majority report a high quality of life (QoL)[130–133]. Research questions have evolved over time to not only explore psychopathology, but also recognize the opportunity for growth and positive outcomes with trauma[134]. This positive psychology paradigm aims to identify the qualities that help individuals thrive, as opposed to focusing on their weaknesses (e.g. depression, anxiety, stress)[135]. Concepts linked to the positive psychology paradigm such as resilience, post-traumatic growth and self-efficacy may explain how individuals are able to maintain high perceptions of quality of life post-injury[132,136,137]. Under this paradigm the attitude that an individual adopts towards their SCI is extremely important to the outcomes of their rehabilitation.

Hope is an integral part of the positive psychology paradigm with Snyder et al. (1991) defining hope as the belief that one can find pathways to desired goals, and have the agency to use those pathways[138]. This model was simplified by the phrase: The will (agency) and the ways (pathways) of goal attainment. Pathways thinking involves constructing feasible routes to achieve goals. In the context of disability and SCI, various difficulties and barriers may be experienced on the path to goal achievement. Adaptation and the generation of alternative pathways becomes essential to maintaining hope with a SCI[139,140]. Some individuals are inherently more hopeful which may be related to traits from other positive psychology constructs that they possess[141]. Core self-evaluation (CSE) theory combines the qualities of self-esteem, self-efficacy, emotional stability and locus of control[142]. CSE describes the foundation of an individual's self-appraisal and is a key aspect of hope through the generation of agency and pathway thinking[143].

The phenomenon of hope within the SCI population has been widely documented[144–147]. Hope and its associated goal directed agency results in strong positive outcomes[139,146,148], and is seen as essential to recovery from physical trauma[149,150]. Lohne (2008) describes a battle between hope and suffering, whereby hope can serve as a turning point away from anguish, not unlike the buffering hypothesis[152]. The buffering hypothesis describes hope's role in providing a reprieve from the suffering associated with SCI, having the potential to lift an individual out of a state of despair and suicidality[153,154]. Hope, however, can be a contentious issue within the clinical environment. Therapeutic treatment often brings hope of improvement, which may improve psychological well-being if favourable outcomes are experienced[155]. Unsubstantiated hope may, however, inflate expectations and lead to disappointment when those expectations are not met[156]. Monitoring of individuals expectations when commencing therapeutic treatment, especially in the SCI population who have an increased prevalence of mood and anxiety disturbances compared to the general population, is therefore of great importance[157]. Substantial qualitative literature has been published on hope and expectations of recovery, however, quantitative measurement of these constructs remains challenging[144,158]. The ability to screen and measure expectations of recovery when entering a clinical trial may aid in preventing future negative effects on mental health[159,160].

1.6.1. Robotic Locomotor Training and Psychological Well-being:

The positive relationship between physical activity and subjective quality of life has been well documented in individuals with SCI, and hence it is envisaged that an exercise-based intervention will assist in improving individual's mood state[161–163]. RLT is a particularly novel form of physical activity and hence its effect on psychological outcomes is largely unclear. Within this field researchers need to be weary of 'techno-optimism' where the perceived benefits of a technology may be inflated in comparison to the actual physiological benefits[164]. Perceptions can thus be misaligned with the current state of evidence. Despite this potential misalignment, based on the positive evidence surrounding physical activity and psychological outcomes, and the unique features of RLT training such as improved self-image, eye-to-eye contact and increased independance[49,72,96,102], one can hypothesize that there is a potential for improving the psychological outlook of individuals engaging in RLT. Benson et al. (2016) showed that quality of life (QoL) improved by an average of 4 points after 20 RLT training sessions over a 10-week period[165]. Improvements in QoL regarding physical abilities have also been reported by participants with thoracic and lumbar SCI after a 5-week intensive intervention by Platz (2016)[115] – *Table 1.3*.

Feelings of safety and comfort directly relate to an individual's emotional experience[167]. The use of an exoskeleton for an individual who has been a wheelchair user for multiple years can be an exciting but also fearful experience[168]. The multi-site RAPPER II trial demonstrated positive responses to 15 of the 16 statements relating to device acceptability amongst 20 participants[71]. Numerous other studies have also found that users felt safe and comfortable in the device and had tendencies towards strong positive comments regarding acceptability and the rehabilitation process[49,65,109,166,167,169,170] – *Table 1.3*.

Table 1.3: User satisfaction of individuals with spinal cord injury using Robotic Locomotor Training

	Questionnaires	Satisfaction (VAS 1-5)	Acceptability (VAS 1-7)
Benson[57] (N = 5)	*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[71] (N = 19)			15 out of 16 statements = > 90% +ve response 1 statement = -ve response (transfer ability)
Esquenazi[65] (N = 12)		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[169] (2017) (N = 14)	*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[166] (N = 7)	*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 (2016)[49] (N = 3)		All 10 statements = > 3 score	
Sale (2018)[109] (N = 8)		9 out of 10 statements = > 3 score 1 statement = < 3 (safety of device)	
Stampacchia[170] (N = 21)			*+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[167] (N = 6)		8 out of 10 statements = > 3 score 2 statements = < 3 score (bowel and wearing the device)	

Abbreviations: 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. Studies with missing original data or level of significance – indicated by *. *Published in Journal of Rehabilitation Medicine by Foundation for Rehabilitation Information*[63].

In studies that described adverse events (*Figure 1.2*), 22.9% of all participants (n = 208) reported that they experienced minor skin abrasions or irritations[48,57,65,93,96,112,166,171–173]. There were multiple reports of other mild adverse events including musculoskeletal pain[48,57,166,172], syncope[65,93,174] and joint pain/oedema[48,65,166,173,174]. Less frequently reported concerns included torso bruising, pressure ulcers and sensory complications[93,112,173]. There were two incidents of small bone fractures, one of the talus[57], one of the calcaneus[174] as well as one reported ankle sprain[173]. Numerous studies within a systematic review[63], however, did not report on adverse events[56,58,95,113,169,170,175,176]. Most of the adverse events were managed with alterations to the exoskeleton, including adjustment of device dimensions and additional padding[166,171]. Despite minor adverse events occurring, all studies agreed that RLT was a safe rehabilitation technique to use in individuals with SCI.

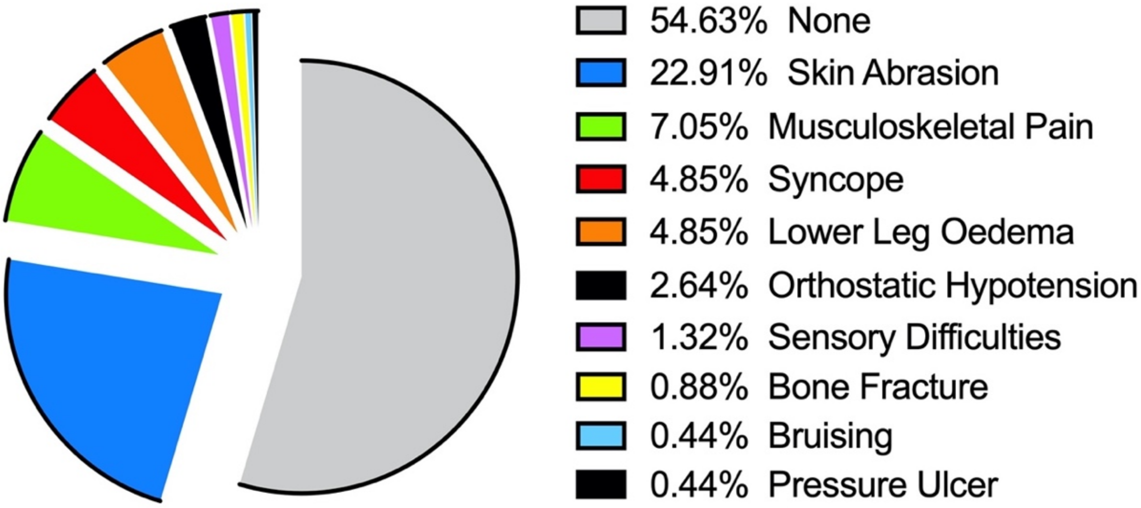


Figure 1.2: Percentage of adverse events reported in individuals with spinal cord injury using Robotic Locomotor Training. Total = 103 adverse events within the reported sample of 208 participants; Individual participants may have experienced more than one adverse event. *Published in Journal of Rehabilitation Medicine by Foundation for Rehabilitation Information*[63].

Despite positive perceptions and feelings of safety among individuals with SCI, the expectations of participants starting exoskeleton-based interventions need to be appropriately managed[168]. Benson et al. (2016) showed in their sample of five participants, with varying forms of SCI, that participants initially had positive expectations of using the exoskeleton with an average device form score on the ATD-PA of 41 points. However, not all these expectations were met, as the average study end-point score after 10-weeks was 34[57] – *Table 1.3*. Kinnett-Hopkins (2020) also discussed dissatisfaction expressed by participants who were unable to make use of the exoskeleton independently and safely[40]. Unrealistic initial expectations and hopes of taking part in a RLT program may play an important role in user satisfaction, particularly when expectations may not be met[177]. Participants volunteering for a research trial may also have inherently higher levels of motivation and expectation than the broader SCI population as they are willing to put themselves in a new and challenging environment[178]. Interestingly, Kwon (2012) demonstrated that 15-30% of their SCI sample would participate in a clinical trial regardless of the risk of complications[156]. Therapeutic misconception is thus a considerable reality in SCI trials with the need for careful communication to avoid potentially unrealistic expectations.

1.7. Conclusion:

Significant advancements in the field of SCI rehabilitation have been made in the last century. RLT is a promising new rehabilitation tool that aims to offer more comprehensive care for patients with SCI, however, it is yet to be widely incorporated into SCI standard of care practices due to a lack of robust scientific evidence. This literature review indicates that RLT can provide individuals with SCIs the ability to walk safely while improving their walking performance, as well as potentially improving cardiovascular outcomes and psychosocial factors. However, further large scale, homogenous trials are needed. Regardless of efficacy, there are still barriers that may exist when using RLT in low- and middle-income countries such as South Africa, primarily due to a lack of financial and human resource

PROBLEM STATEMENT:

The conceptual basis for robotic locomotor training (RLT) appears promising; a rehabilitation modality that removes the need for intensive assistance from therapists whilst facilitating safe and effective over-ground ambulation[48]. However, this novel and innovative rehabilitation modality is yet to be adequately supported by robust scientific evidence[179]. Previous research has compared the effects of conventional gait training (parallel bars), body-weight supported treadmill training (BWSTT) and RLT and concluded that all interventions were beneficial, suggesting no technique was superior[45]. Whereas other small clinical trials and case series have demonstrated positive effects of RLT on multiple domains such as walking capacity, cardiovascular and psycho-social outcomes[165,180,181]. Cardiovascular benefits from RLT are plausible but intervention studies have been unable to demonstrate chronic changes[72,93,95,96]. With the unique features of RLT training such as improved self-image and eye-to-eye contact[49,72,96,102], one can hypothesize that there is a potential for improving psychological outlook. The role of expectations when entering an interventional study may also impact upon psychological outlook, but are yet to be explored within a SCI trial. Small sample sizes and a lack of homogeneity across studies has resulted in an underpowered evidence base supporting the efficacy of RLT[63,179].

Large clinical trials with sufficient rehabilitation durations as well as adequately powered homogenous samples are thus required to better understand the effect of RLT. The feasibility of such large-scale trials is unknown in resource limited low- and middle-income countries. This dissertation aims to evaluate the feasibility of conducting a randomised control trial (RCT) within a middle-income country, and in the process add insight into the fragmented evidence base currently describing the effects of RLT. We aimed to address the gaps in the literature by introducing a longer intervention duration (6-months), a homogenous group and inclusion of a comparison activity-based training group.

RESEARCH QUESTIONS OF THIS DISSERTATION:

Question 1:

What is the feasibility of and challenges faced when conducting a SCI randomised control pilot trial evaluating cardiovascular and psychological outcomes within a middle-income country such as South Africa?

Question 2:

What is the effect of robotic locomotor training on various cardiovascular indices in individuals with SCI, over a 24-week intervention period?

Question 3:

Are psychosocial factors altered in individuals with SCI during a 24-week exercise-based intervention?

Question 4:

What are individuals with SCI lived experiences of a 24-week intervention through a narrative of hope?

CHAPTER 2

Study Design & Methodology

2.1. Introduction:

The purpose of this chapter is to provide an outline of the novel study protocol on which all subsequent chapters are based. The study in this dissertation aimed to measure 1) study feasibility and rehabilitation adherence 2) cardiovascular functioning and 3) psychological well-being in individuals with SCI during a 24-week exercise-based intervention. The methods and outcome measures relating to this dissertation are contained below.

2.2. Methods:

2.2.1. Study Design:

The overarching aim of the study was to describe the effect of robotic locomotor training (RLT) compared to activity-based training (ABT) during a rehabilitation programme in individuals with incomplete SCI. We implemented a 24-week pilot randomised control trial (RCT), allowing the measurement of both short and long-term physiological and psychological effects of the rehabilitation methods.

2.2.2. Research Ethics Approval:

Ethical approval was granted by the University of Cape Town, Human Research Ethics Committee (384/2016 – *Appendix 2*). 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[70], Guidelines for Good Clinical Practice in the Conduct of Clinical Trials in Human Participants in South Africa[182] and The Department of Health: Ethics in Health Research: Principles, Structures and Processes[183].

2.2.3. Participant Recruitment and Selection:

To reduce heterogeneity, the most common subgroup of SCI in Cape Town, South Africa was recruited, namely motor incomplete (AIS C, D), with a neurological level of injury between C1-C8 (cervical injury)[26]. The recruitment process is provided in detail in *Figure 2.1* and spanned a period of 18 months. Inclusion and exclusion criteria are detailed in *Table 2.1*. The research team acknowledged this pilot study's limitations in human and equipment resources, hence the target sample size was sixteen participants with eight in each intervention group. Seventeen participants with chronic (> 1 year) traumatic motor incomplete tetraplegia were recruited and assigned via random number generation (Microsoft Excel) to the RLT or ABT intervention groups. One participant did not complete the intervention, the details of which will be discussed in Chapter 3. Each participant provided written informed consent prior to the study (*Appendix 3*). All participants were provided with private transport to attend screening, testing, intervention sessions and post-trial access.

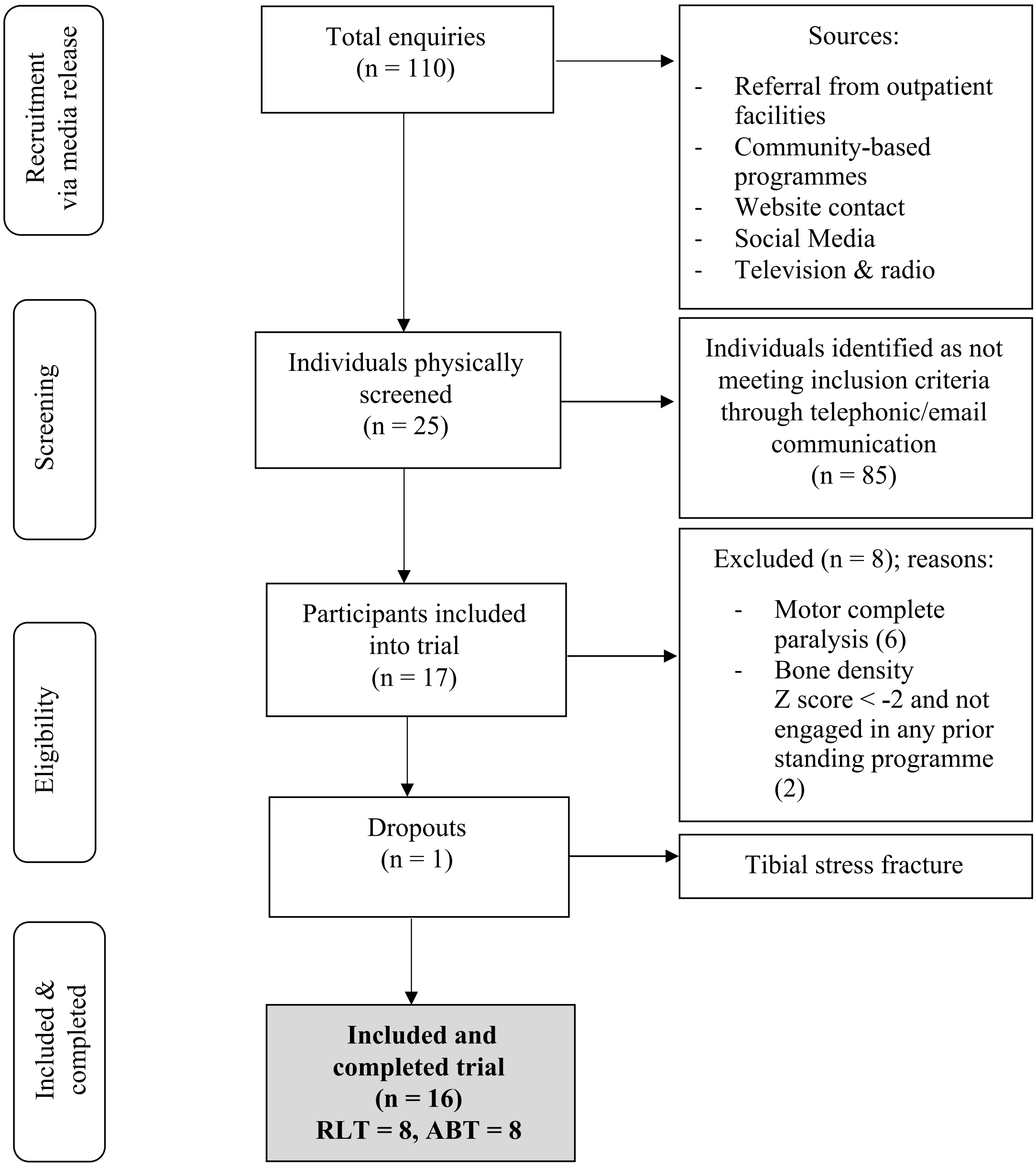


Figure 2.1: Recruitment and selection of participants into the trial.

Table 2.1: Participant Inclusion and Exclusion criteria:

Inclusion Criteria:	**Exclusion Criteria:**

- Male or female individuals between 18 and 65 years old
- Chronic (>1yr) spinal cord injury
- Motor incomplete (AIS C, D), with a neurological level of injury (NLI) between C1-C8 (tetraplegia) as determined by the International Standards for Neurological Classification of SCI (ISNCSCI)
- Reliant upon a wheelchair as the primary mode of mobility
- Sufficient anthropometrics and range of motion (ROM) to achieve a normal, reciprocal gait pattern within the Ekso GT^{TM} suit
- Medically stable and cleared by a physician for full weight bearing locomotor training including 15-minute standing frame trial to assess standing tolerance.
	- Non-traumatic SCI
	- Have trained in a robotic exoskeleton in the past 12-months
	- Psychopathology which may be exacerbated by inclusion into the trial
	- Modified Ashworth Scale (MAS) = 4 in any of the lower extremity joints
	- Skin integrity issues in areas that contact the device
	- Pregnancy
	- Severe osteoporosis
	- 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
	    - 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
	- 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)

2.2.4. Screening:

The following pre-assessment screening steps were conducted: 1) Participants' skeletal length and range of motion of the hips and lower limbs were taken to ensure they met the dimension limits of the exoskeleton; 2) Participants underwent Dual Energy X-ray Absorptiometry (DEXA) screening of both hips and lumbar spine to analyse bone mineral density; 3) Thereafter, participants were medically screened by a physician specialising in spinal cord injury rehabilitation; 4) Participants discussed their expectations of the intervention and were screened for any psychopathology such as mood disturbances or post-traumatic stress disorder (PTSD) by psychologists with special interest in disability.

Psychological screening was deemed necessary in order to ensure that participants did not commence the intervention with unrealistic expectations, and that they were not vulnerable to being traumatised by an intervention which may not increase their functional ability. PTSD is commonly associated with SCI, and in the South African context individuals are unlikely to have received treatment beyond their in-patient care[184]. To limit confounding factors, participants were asked to refrain from starting any psychological intervention outside of the trial. Psychological support was readily available and mandatory one-on-one sessions were conducted with the study psychologist every four weeks.

2.2.5. Risks to Participation:

The Ekso GT 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[48]. Participants ran the potential risk of fractures, sprains, bruises, skin irritations, cardiovascular complications and orthostatic hypotension with both forms of rehabilitation. A 30m galvanized steel safety tether was installed to mitigate the risk of falls. All personnel involved were trained in first-aid and there was a dedicated physician always on emergency call within the facility.

Based on clinical experience, the research team (including psychologists) 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 should not be underestimated. Ongoing monthly monitoring of participant's mental health was performed by a psychologist to identify and safe-guard against mood disturbances. We discussed both the capabilities and limitations of robotic locomotor and activity-based training to the participants before starting the trial.

2.2.6. Interventions:

All intervention sessions (RLT and ABT) were conducted by fellow PhD candidate Claire Shackleton and I (trained Biokineticists within the Walking with Brandon Foundation, Therapy & Beyond centre based at the Sport Science Institute of South Africa). Biokinetics is a clinical profession where the scope of practice is to improve physical functioning and health through exercise rehabilitation[185].

2.2.6.1. Robotic Locomotor Training:

Robotic locomotor training (RLT) took part exclusively using the Ekso GT exoskeleton. This model is equipped with variable assist software, allowing motor power to be dynamically adjusted to the users capabilities[186]. The device settings in which each participant walked was determined by the attending Ekso certified biokineticist, 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. Progression was faster or slower in some participants as training followed their natural learning pace.

Participants performed intervention sessions three times per week, allowing for sufficient rest by avoiding scheduling sessions on consecutive days. Each session was a maximum of 60 minutes in duration. Intensity levels ranged from: standing and walking time: 10 - 50 minutes, and steps taken: 50 - 1800 steps.

Figure 2.2: Example of a RLT session *(Patient consent provided).*

2.2.6.2. Activity-based Training:

Activity-based training (ABT) represents the current standard of care provided in advanced outpatient neurological rehabilitation centres around the world[19]. The form of ABT used in the intervention was adapted from the *Beyond Therapy*[187] model used by the Shepherd Centre and can be described as a six-stage process (Therapy & Beyond Rehabilitation Programme – *Appendix 4*). 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 are not linear in design but rather recursive, where progression is 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 60 minutes in duration. The approximate standardized time allocation for each session was as follows: warm-up & mobility: 5 minutes; resistance training: 20-30 minutes; cardiovascular training: 20-30 minutes. Upper and lower body resistance training was performed using bodyweight exercises and various apparatus including bands, wrist weights, dumbbells and cables. Gait retraining, without a treadmill or robotic assistance, was also performed in the ABT group. Five minutes was allocated for transfers and setting up of various apparatus.

Figure 2.3: Example of an ABT session *(Patient consent provided)*.

Total training time was matched between the two groups. Participants in both RLT and ABT groups were instructed to maintain their normal levels of physical activity outside of the intervention.

2.3. Data Collection:

Data were collected at 0, 6, 12 and 24-weeks of the interventions. All testing was conducted within the same rehabilitation centre with the climate controlled at 22 degrees centigrade and 50% humidity. Whitehead et al. (2015) suggests that a pilot sample size of 10 per treatment arm be reached for large effect sizes > 0.8[188]. Due to 8 participants in each group, we aimed for larger effect sizes for clinical significance throughout the research chapters. *Table 2.1* illustrates the data collection schedule for the outcome measures discussed within this dissertation. The study's full data collection schedule is contained within *Appendix 1*.

Table 2.2: Schedule of variables collected during the 24-week rehabilitation interventions

	Screening	Baseline	4 Weeks	6 Weeks	8 Weeks	12 Weeks	16 Weeks	20 Weeks	24 Weeks
Informed Consent	X								
Medical Screening	X								
Psychological Interviews (Qualitative)	X		X		X	X	X	X	X
Psychometric Questionnaires[1]		X		X		X			X
Doppler Ankle Blood Flow		X		X		X			X
Heart Rate		X		X		X			X
Blood Pressure		X		X		X			X
Heart Rate Variability		X		X		X			X
6-Minute Walk Test[2]		X		X		X			X
Rating of Perceived Exertion		X		X		X			X

1. *Psychometric Questionnaires = International SCI QOL Basic Data Set[189], CD RISC-25[190], Moorong Self-Efficacy Scale[191], Post-Traumatic Growth Inventory[192], Beck Depression Inventory[193], State-Trait Anxiety Inventory[194].*
2. *6-minute walk test (6MWT) is exclusive to participants in the RLT group.*

2.3.1. Cardiovascular Function:

Cardiovascular changes were evaluated during four physiological perturbations (testing conditions) in this study; 1) supine positioning at rest, 2) standing at rest, 3) six-minute arm ergometry test (6MAT) and 4) six-minute walk test (6MWT). These tests were conducted at baseline, and at 6, 12 and 24-week intervals.

2.3.1.1. Testing procedure:

Cardiovascular indices were initially measured at rest in a supine position with the participant lying passively on a plinth. Following this measurement, participants were then moved to a standing position which was performed using an EasyStand Evolv (Minnesota, USA) standing frame where the participant's ankles, knees, hips and torso were supported. Data was recorded for five-minutes in the supine and standing postures with all physiological perturbations separated by a five-minute resting interval. Lastly, a 6MAT[195] (Technogym, Italy) was conducted while seated, starting at a power output of 15 Watts and increasing by 5 Watts each minute until completion of the test. The 6MWT was performed in a separate session for the participants in the RLT group. The 6MWT[196] was conducted in the Ekso GT exoskeleton, hence the ABT group did not perform this test. The cardiovascular indices were measured for the duration of both the 6MAT and 6MWT.

2.3.1.2. Cardiovascular Measurements:

2.3.1.2.1. Brachial and Ankle Blood Pressure:

Resting brachial blood pressure was measured whilst supine using a clinically validated Omron M3 blood pressure monitor[197]. Resting ankle systolic pressure of the posterior tibial or dorsalis pedis artery was measured in the supine position, using a manual blood pressure cuff and handheld ultrasound Doppler system (Sonotrax Vascular, Hamburg, Germany), and the ankle brachial pressure index (ABPI) was calculated[27,28]. It is important to note that blood pressure and heart rate can vary considerably, measured using the coefficient of variation (CV), in individuals with tetraplegia who experience autonomic dysreflexia[198].

2.3.1.2.2. Heart Rate and Heart Rate Variability (HRV):

Heart rate and HRV was recorded during the aforementioned physiological perturbations using a Faros device (Bittium, Finland). Participants spent two-minutes in each perturbation before recording to allow the body time to adapt to the posture. Testing perturbations were separated by a five-minute interval. Variables included in the HRV analysis were the standard deviation of the R-R interval (STD RR) and root mean square of successive differences (RMSSD)[88,199].

2.3.1.2.3. Cardiovascular Efficiency:

Cardiovascular efficiency was measured during the 6MAT and 6MWT using the Total Heart Beat Index (THBI; calculated by dividing the total number of beats during exercise by the total distance travelled in that time period)[110]. The THBI is a cardiovascular efficiency metric that has been used within the SCI population and is a valid alternative to gas analysis[200].

2.3.2 Psychological Well-being:

In addition to initial screening and ongoing monitoring of participant's psychological well-being, empirical data collection was conducted through both quantitative and qualitative methods.

2.3.2.1 Quantitative Psychological Well-being:

Psychometric questionnaires were completed at four time points during the intervention: 0, 6, 12 and 24-weeks (*Appendix 6*). At baseline, researchers explained and were on hand to assist participants in completing paper versions of questionnaires. Questionnaires were then adapted into a *Google Docs* format, with further time-points being completed electronically. Outcomes of interest included: quality of life, resilience, self-efficacy, post-traumatic growth, markers of depression, markers of anxiety and expectations of recovery.

2.3.2.1.1 Quality of Life:

The International SCI Quality of Life Basic Data Set (SCI QoL-BDS) was used to assess perceived quality of life over the last month for three domains: a) Life as a whole; b) Physical health and; c) Psychological well-being[189]. Scores were rated on a scale ranging from 0 (completely dissatisfied) to 10 (completely satisfied) with a total QoL score averaged across the three domains. The SCI QoL-BDS has shown to have good reliability and validity for use in the SCI population[201–203].

2.3.2.1.2 Resilience:

The Connor–Davidson Resilience Scale (CD-RISC 25) was used to assess participants' levels of resilience[190]. The CD-RISC 25 comprises 25 statements relating to how one has felt over the past month. The response scale has a 5-point range: 0 (not true at all), 1 (rarely true), 2 (sometimes true), 3 (often true), and 4 (true nearly all of the time). Scores are added up to a maximum score of 100, meaning high resilience. The CD-RISC 25 along with the shortened CD RISC 10 have been recommended for use within the SCI rehabilitation setting[204].

2.3.2.1.3 Self-Efficacy:

The Moorong Self-Efficacy Scale (MSES) was used to assess participants' levels of self-efficacy[191]. The MSES is a 16-item scale rating confidence in performing everyday activities on a 7-point Likert scale with a maximum score of 112. The scale is specifically designed for individuals with SCI, comprising 3-factors: social function self-efficacy, personal function self-efficacy and general self-efficacy[205]. It is internally consistent, responsive and stable, and demonstrates good concurrent, convergent, and discriminant construct validity[191].

2.3.2.1.4 Post-traumatic Growth:

The Post-Traumatic Growth Inventory (PTGI) was used to assess participants' levels of post-traumatic growth[134]. The PTGI is a 21-item scale, rating growth on a 5-point Likert scale with a maximum score of 105. The scale assists in determining how individuals cope with the aftermath of trauma, and reconstruct their perceptions of self, others and the meaning of events. Both the full scale and the separate subscales of the PTGI have been shown to have good internal reliability. Test–retest reliability of the scale has been reported to be adequate and applicable to the SCI population[206,207].

2.3.2.1.5 Depression:

The Beck depression inventory (BDI) was used to assess participants' symptoms of depression[193]. The BDI is a 21-item scale measuring different symptoms of clinical depression using a 4-point Likert scale (0-3) with a maximum score of 63. The BDI is able to discriminate between subtypes of depression and differentiates depression from anxiety[208]. The scale is considered an acceptable measure of depression within the SCI population[114,209–211].

2.3.2.1.6 Anxiety:

The State Anxiety Inventory – Form Y-1 (SAI) was used to assess participants' levels of state anxiety[194]. The SAI is a 20-item scale within the State-Trait Anxiety Inventory with a maximum score of 80. This sub-scale aims to measure (emotional) state rather than (personality) trait anxiety. This SAI is an acceptable measure of anxiety within the SCI population[211–214].

2.3.2.1.7 Expectation Visual Analogue Scale (VAS-Expectation):

The VAS-Expectation (*Figure 2.4*) contained two ratings: a) Current perceived physical function and b) Perceived physical function in one-year. Each rating is scored on a separate 100mm numeric VAS (0-10), with 0 representing no function and 10 representing full function. The participant is asked to mark a vertical line on the VAS that best represents their perceptions. Rating a) is subtracted from rating b) with the difference calculated providing an Expectation Score. This Expectation Score is representative of the individuals anticipated (positive) gain or (negative) loss of physical function in the coming year. The VAS-Expectation will be discussed in further detail in *Appendix 5*.

2.3.2.2 Qualitative Psychological Well-being:

Qualitative data for this dissertation were collected via in-depth semi-structured individual interviews prior to starting the intervention, and six-months later after completing the intervention. Interviews were conducted by registered psychologists, using open-ended questions and providing space for participants to communicate freely[215]. Sessions lasted approximately 60-minutes and were audio recorded and transcribed verbatim. The overall study included additional interviews at 4-week intervals. These interviews were shorter in duration (15-30min) and served to monitor and identify any mood disturbances.

In the baseline interviews, participants were asked about the nature of their SCI, how it occurred, and how they had adjusted to the resulting impairments. They were also asked about their motives for joining the study, their expectations of the intervention, and their understanding of the aims of the research. They were asked about their psychological resources and to identify potential benefits of and barriers to their participation, as well as how these barriers might be overcome. They were also screened for symptoms of psychopathology. In the final interviews, upon conclusion of the intervention, participants were asked about their experience of participating, the perceived benefits of the intervention, whether or not their expectations had been met, as well as any difficulties experienced and how these were overcome. Participants were invited to give critical feedback and make recommendations for how the intervention might have been improved or made more client centred. Finally, they were asked what advice they would give to individuals who participated in these kinds of interventions in the future.

2.4. Statistical Analysis:

In this dissertation data were analysed using statistical software (Statistica 13, Statsoft Inc. Tulsa. Oklahoma, USA & Prism 8, GraphPad, California, USA). A broad statistical overview is provided below with further detail provided within each chapter.

Significance was accepted at a p value of < 0.05. Normality was assessed using Shapiro-Wilks tests. A combination of one-way and two-way repeated measures analysis of variance (ANOVA) were used across the outcome measures. Sphericity was not assumed when conducting the ANOVAs and hence p-values were adjusted according to the Greenhouse-Geisser correction. 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[216]. Outliers were excluded according to the median absolute deviation (MAD) method, using a 3*MAD conservative approach[217].

Qualitative data were analysed using an open-ended data-driven and inductive approach. Codes were identified using thematic analysis[218], 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. Grouping into superordinate themes was performed, which were then independently reviewed and verified by a third author.

2.5. Conclusion:

This chapter describes the aim, study design, participant recruitment and selection, interventions, data collection and statistical analysis of the pilot RCT underpinning this dissertation. 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 comparison group and context of a middle-income country. This chapter serves as a point of reference, providing the methods on which the findings of all subsequent chapters are based.

CHAPTER 3

Feasibility of implementing a pilot randomised control trial in individuals with Spinal Cord Injury in South Africa: Adherence to rehabilitation and challenges experienced.

3.1. Introduction:

The SCI population has many unique characteristics which can create a multitude of challenges for researchers in the field of exercise and rehabilitation science[69]. The diversity of SCI is evident across 28 possible levels of injury to the spinal nerves and four levels of severity according to the American Spinal Injury Association (ASIA) scale[219]. Therefore, in its most simple classification there are a total of 112 different categories of SCI. To illustrate this diversity, in two individuals classified with the same injury (C4 ASIA C tetraplegia), one may require an electric wheelchair and maximal assistance with activities of daily living, whilst the other may be able to live independently and even walk short distances with assistive devices[220].

Randomised control trials (RCTs) are the gold standard of scientific enquiry, comparing the effectiveness of two different treatments, one experimental and one comparison or control treatment. Participants are randomly assigned to either group, thereby reducing multiple sources of bias[221]. Despite the strength of RCTs, their stringent requirements can be difficult - if not impossible - to apply within SCI trials, thus leading to a call for more pragmatic approaches within SCI rehabilitation research[69]. Increased practicality may ensure that evidence generation is not hindered by the requirement to adhere to often unobtainable study designs. Quasi-experimental research designs can provide translational research insights into real-world clinical environments[69,222–225]. Single case experimental designs using small numbers of patients provide an example of a study design that is well suited to the rehabilitation environment. Researchers should recognize the potential of quasi-experimental designs to describe experimental effects and facilitate future RCTs that evaluate levels of efficacy[226]. The most common challenges experienced in experimental SCI trials relate to 1) sampling; 2) study design; 3) control group and 4) clinical inference. These factors are predominantly attributed to the wide diversity of SCIs and limited resources available for SCI focused research[227]**.**

A major global priority of SCI research is to establish the efficacy of activity-based rehabilitation in improving recovery through neuroplasticity[228]. If SCI research is challenging in high-income countries that have optimal resources, then what chance does a complex rehabilitation trial have of success in a middle-income country? The feasibility of such trials is largely unknown due to the sub-optimal systems of care and paucity of rehabilitation research in developing nations[229].

South Africa implemented its own National Rehabilitation Policy and approved the United Nations Convention on the Rights of Persons with Disabilities in November 2007. Within this policy, between one and three hours of outpatient rehabilitation should be received per week, focusing on community integration and social participation[30]. Implementation of this policy has unfortunately been sub-optimal. A low-income community-based study in Cape Town, South Africa conducted in 2014 demonstrated a high percentage of unmet rehabilitation needs. The percentages of unmet needs included: 54% for home-based care; 34.5% for assistive devices; 28.9% for medical rehabilitation services; and 2.5% for health services. Two major barriers were identified, namely inadequate finances (71%) and transport problems (72%), which restricted access to services[230]. These unmet needs illustrate the immense social need for outpatient rehabilitation within South Africa and many other low- and middle-income countries[15,231].

3.2. Aims:

The aim of this chapter is to describe how this pilot randomised control trial evaluated the feasibility of implementing and performing a larger scale RCT in a middle-income country such as South Africa. The pilot RCT evaluated the effects of robotic locomotor training (RLT) compared to activity-based training (ABT) during a 24-week rehabilitation programme in individuals with SCI. The feasibility criteria we highlight are the challenges and lessons learned regarding: 1) recruitment and adherence, 2) ethical approval, 3) screening procedures, 4) transport, and 5) human and financial resources.

3.3. Methods:

3.3.1. Interventions:

Detailed methods of the trial are provided within Chapter 2. In brief, RLT and ABT interventions consisted of three sessions per week, 60-minutes each, for 24-weeks and were overseen by biokineticists. RLT involved only walking in an Ekso GT exoskeleton. Volume of walking ranged from: standing and walking time: 10 - 50 minutes; steps taken: 50 - 1800 steps. ABT consisted of a combination of resistance, cardiovascular and flexibility training in various postures. Gait retraining, without a treadmill or robotic assistance, was also performed in the ABT group.

3.3.2. Statistical Analysis:

All data were analysed using statistical software (Statistica 13, Statsoft Inc. Tulsa. Oklahoma, USA & Prism 8, GraphPad, California, USA). Significance was accepted at a P value of < 0.05. Adherence rates were calculated based on a total of 72 sessions available to participants during the 24-week trial.

3.4. Results:

3.4.1. Recruitment:

A total of 110 enquiries were received for participation in the trial (*Figure 2.1* – Chapter 2). Enquires were screened according to the trial's inclusion/exclusion criteria and 25 individuals qualified to be physically screened. Eight individuals were excluded after physical screening and a total of 17 participants were included into the trial, with a successful recruitment ratio of 15.5% (17/110). One participant discontinued the intervention after being enrolled in the RLT group for 3-weeks. Persistent right leg weakness necessitated a magnetic resonance imaging (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.

As shown in *Table 3.1*, RLT and ABT groups were equivalent at baseline with regard to age and time since injury. There is however a trend towards a reduced time since injury in the ABT group ($p = 0.10$). Motor vehicle accidents accounted for 62.5% of injury aetiology whilst stabbing, gunshot, rugby, motor-cycle, mountain bicycle and diving accounted for 12.5% each. Only one female qualified for inclusion into the trial.

Table 3.1: General characteristics of participants in the RLT and ABT intervention groups

	Participant	Age (years)	Time since injury (years)	Total hip BMD (z-score)	Neurological level of Injury	AIS category	Aetiology	Sex
RLT group	Participant 1	27	9	-2.8	**C6**	D	Stabbing	Male
	Participant 2	33	15	-3.0	**C6**	C	MVA	Male
	Participant 3	32	3	-2.6	**C5**	D	MVA	Male
	Participant 4	46	26	-3.1	**C4**	D	Gunshot	Male
	Participant 5	55	4	-2.3	**C5**	D	MVA	Male
	Participant 6	43	23	-2.5	**C6**	C	MVA	Male
	Participant 7	56	15	-3.0	**C4**	C	MVA	Male
	Participant 8	32	15	-2.9	**C7**	C	Sport - Rugby	Male
	Average	41 ± 11	13 ± 8					
ABT group	Participant 9	26	2	-2.2	**C6**	C	MVA	Male
	Participant 10	46	20	-1.7	**C6**	D	MVA	Female
	Participant 11	50	8	-1.3	**C7**	D	MVA	Male
	Participant 12	19	2	-2.3	**C5**	C	MVA	Male
	Participant 13	47	3	-0.9	**C4**	D	Motor-cycle	Male
	Participant 14	29	10	-3.4	**C5**	C	MVA	Male
	Participant 15	60	2	-3.5	**C5**	C	Mountain bike	Male
	Participant 16	30	11	-3.8	**C4**	C	Diving	Male
	Average	38 ± 14	7 ± 6	2.6 ± 0.8				

Data presented as mean ± SD. RLT = robotic locomotor training; ABT = activity-based training; MVA = motor vehicle accident; AIS – ASIA Impairment Scale; BMD = bone mineral density (lowest z-score of total BMD in either the left or right hip tabulated). No significant differences ($p < 0.05$) in age or time since injury between RLT and ABT groups.

3.4.2. Adherence:

High adherence levels were demonstrated by the participants with an average adherence of 93.9 ± 6.2% for 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

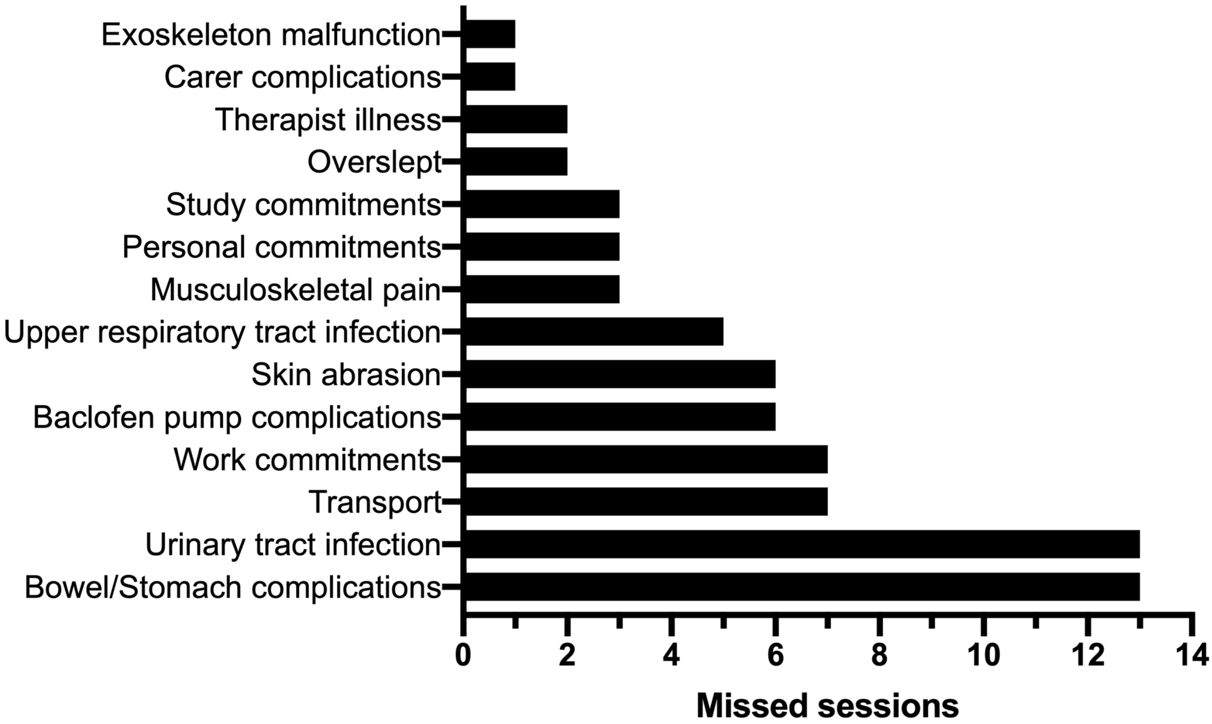


Figure 3.1: Reasons for missed sessions affecting adherence to rehabilitation. Overall 72 sessions missed of 1152 total – 6.25%.

3.4.3. Challenges:

Table 3.2 below represents a summary of the challenges experienced during this pilot randomised control trial that may impact upon the feasibility of conducting a future large-scale RCT in South Africa.

Table 3.2: A summary of Challenges Experienced During the Trial

Challenge	Description
Ethical Approval	Post-trial access. A period of 12-weeks was provided to satisfy the requirements of the Declaration of Helsinki and reintegrate the individual back into the community setting.
Screening procedures	Lack of normative data supporting bone density guidelines for individuals with spinal cord injuries. Recommended to perform a lower limb MRI for ambulatory individuals and distal femur or proximal tibia DEXA scan using threshold of BMD $< 0.6 g/cm^2$.
Transport	Little to no access to public transport for wheelchair users. Reliance on private companies carries a significant financial burden with the potential for sub-optimal service levels.
Human Resources	Limited trained clinicians who are experienced in SCI. This restricts the total number of participants that can be enrolled in the study as well as impacting on bias (blinding) when outcome measures are being assessed.
Financial Resources	The cost of an exoskeleton is approximately R2.8 million ($168 000) which exceeds the research budget of many projects conducted in middle-income countries. Additional equipment and facility space carry further costs required to expand sample sizes and upscale to a full RCT.

3.5. Discussion:

This chapter describes the recruitment, adherence and challenges faced in conducting a pilot RCT evaluating the effects of RLT and ABT in individuals with SCI over a 24-week period. To our knowledge, this is the first pilot RCT within this field of overground exoskeleton research using homogenous groups and an extended intervention period. To extend its novelty, the trial was conducted within the middle-income country of South Africa. The feasibility of the trial faced multiple challenges relating to: 1) recruitment and adherence, 2) ethical approval, 3) screening procedures, 4) transport, and 5) human and financial resources. These challenges may be significant in informing feasibility when implementing a novel intervention comparable to this study. They will be discussed below with the aim of sharing our insights and lessons learnt to assist in enhancing the quality and efficiency of future trials.

3.5.1. Recruitment and Adherence:

From an initial 110 enquiries, seventeen participants were recruited via referral from outpatient facilities, community-based programmes, website contact, social media, television and radio. This provided a recruitment ratio of 15.5%. Recruitment ratios vary significantly within the SCI literature and are largely dependent on the stringency of study designs and inclusion/exclusion criteria[232]. Average recruitment ratios across four previous SCI trials ranged from 3-63% with a mean ratio of 25%[233–236]. This trial's recruitment ratio of 15.5% can thus be regarded as below average. The strict inclusion and exclusion criteria used to recruit a homogenous sample, specifically that of incomplete tetraplegia, reduced the likelihood of a high recruitment ratio and that a candidate would qualify for inclusion.

3.5.2. Adherence:

Participants' adherence to both the RLT and ABT interventions was exceedingly high (93.9 ± 6.2%). Adherence to SCI interventions described previously in the literature ranged between 9% and 96%, with a mean adherence of 56%[237–241]. The perceived value gained from an intervention plays a major role in adherence rates[232]. Within our cohort, the majority of participants did not have access to adequate medical care or rehabilitations services, a problem that is endemic in low- and -middle income countries[15]. The opportunity of taking part in this study served as a potent motivator for participants to remain committed and disciplined in their attendance of intervention sessions[242]. The provision of transport alleviated a major external barrier to attendance and further supported the high adherence rates. Altruism is also a motivating factor for contributing to clinical trials[242]. Altruistic factors such as participants wanting to help others and support their peers were evident within the cohort and will be discussed further in Chapter 6.

3.5.3. Research Ethics:

Due to the novel research protocol and unique population studied, numerous protocol revisions were required from the initial application until final ethical approval was granted by the University of Cape Town, Human Research Ethics Committee (HREC).

Post-trial care is one of the most significant ethical challenges related to conducting research on a vulnerable population group. As quoted in the Declaration of Helsinki[70]: "The protocol should describe arrangements for post-trial access by subjects to interventions identified as beneficial in the trial or access to other appropriate care or benefits." It was hypothesized that both interventions would be beneficial for participants[45,243]; thus post-trial access in both RLT and ABT groups was provided to all participants.

Post-trial provision for participants was initially interpreted by the ethics committee as providing continuous, indefinite access to the interventions (RLT & ABT) within the trial. However, the financial and human resource implications of open-ended care were not feasible in the context of a middle-income country. The research team thus motivated that post-trial care be undertaken within the ambit of the World Health Organisation definition of rehabilitation as: "a progressive, dynamic, goal-oriented and often time-limited process, which enables an individual with an impairment to identify and reach his/her optimal mental, physical, cognitive and social functional level"[21]. The rehabilitation process is thus not open-ended, but may focus on specific interventions for a limited period of time[244]. A finite 12-week post-trial care period was thus proposed by the research team. The major aim within this 12-week period was to foster independence and successfully reintegrate the individual back into the community setting.

Capri & Coetzee (2012) state that, "The preferencing of the interests of vulnerable people and groups in ways that enable them to change the conditions of their vulnerability is paramount to a human rights perspective"[245]. Potential participants were thus given the autonomy to understand and consent to a finite period of rehabilitation; with the knowledge that the rehabilitation offered would come to an end. The ethics committee was satisfied with the proposed post-trial provision and ethical approval was granted.

Within the post-trial care period of 12-weeks, any rehabilitation modality, including the exoskeleton, could be utilised. This 12-week period was the average trial period used in previous studies[64]. After the post-trial period, participants were provided with informational packs and home-based exercise routines. Of the initial 17 participants, 14 chose to continue receiving one-on-one rehabilitation outside of the research study, paying a nominal income-graded fee. Future studies should consider the significant financial and human resources required to ensure continued post-trial access to innovative technologies[246].

3.5.4. Screening Procedures: Bone Density:

An intensive screening process, as described in Chapter 2, was used within the trial to ensure participants' safety. A major component of this screening was Dual Energy X-ray Absorptiometry (DEXA) screening of both hips and lumbar spine to analyse bone mineral density (BMD). While walking within an exoskeleton, significant loading of the lower limbs in the upright position occurs[113]. A risk of bone stress injury is present if osteoporosis has been diagnosed, or speed/intensity of loading (steps taken) is increased too rapidly. The Ekso™ recommended guidelines regarding bone density for safe walking within the exoskeleton are a Z-score of > -2.

This value has been approved and adopted by the FDA to ensure minimal risk of stress fracture while walking in the exoskeleton. This value is however based on normative data for the average able-bodied population[247]. Currently there is no established threshold BMD value below which weight-bearing activities are absolutely contraindicated after SCI[248]. During the recruitment for the trial, the mean total hip BMD across those recruited was a Z-score of -2.6 ± 0.8. If the cut-off of a Z-score of < -2 was strictly adhered to, recruitment for a sample of eligible individuals with chronic SCI would be significantly reduced and challenging.

Thus, participants who had Z scores < -2 were assessed on an individual basis. In order for them to be included into the trial, they had to be engaged in a consistent standing programme prior to participation, and clearance was required from the trial's physician who provided medical oversight. A clinical risk-benefit analysis was performed by the physician[249]. The lowest hip BMD Z-score included into the trial was that of -3.8, this participant was in the ABT group and experienced no adverse events.

Interestingly, a participant who was excluded after 3-weeks due to a right tibial stress fracture had a satisfactory total right hip BMD Z-score = -1.1 at initiation of the trial. The participant had a Brown-Sequard type 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 possibly the RLT further aggravated an already overloaded right lower limb, and the lack of sensation in this limb resulted in bone stress. The most common lower limb fracture sites after SCI are the proximal tibia and distal femur, as was the case with this participant[250]. A DEXA scan of the hip and lumbar spine is not sufficient to screen and identify this complication. Only an MRI of the right knee would have alerted researchers that the participant should not have been included into the trial. Upon providing an incident report to the Human Research Ethics Committee, we thus recommend a thorough medical examination which may include a knee MRI for individuals who are ambulatory and at risk of overuse injuries be included in preliminary assessments. Future studies should also expand DEXA screening to include the proximal tibia and distal femur in all participants. A BMD value of $0.6 g/cm^2$ has been used in previous studies and may provide a useful threshold value[251]

3.5.5. Transport:

High unemployment rates amongst the South African population with disability results in little to no access to private transport[252]. South Africa, alongside many countries such as Egypt, Morocco, India, Mexico and Cambodia, lack a disability inclusive public transport system[253,254]. The South African local taxi industry also does not see individuals with disabilities as economically valuable, resulting in further marginalisation[255]. Limited provision for individuals with physical disability is provided through strained government services such as ‘dial-a-ride’, resulting in the majority of people with a SCI not being able to attend health and rehabilitation appointments, nor seek employment[30]. Public services are therefore unable to accommodate the substantial logistical requirements needed to timeously transport participants in wheelchair accessible vehicles to a clinical trial (three times per week for 24 weeks)[255].

Research studies are thus forced to rely on costly private transport companies in order to transport participants in a reliable and safe manner. Within this trial, approximately 1280 individual screening, intervention and testing sessions were conducted across the 17 participants. This equates to 2560 trips by a private transport company, amounting to a considerable expense. The burden of inaccessible public transport needs to be factored into the budget considerations for future research studies in similar low- and middle-income settings. Despite the high cost, sub-optimal service levels were provided by the transport company in this study who themselves were operating with limited resources.

3.5.6. Possibility of Bias due to Limited Human and Financial Resources:

The Physiotherapy Evidence Database (PEDro) scale, based on the Delphi List[256], is routinely used to guide the design of physical rehabilitation trials. Items 5-7 of the PEDro scale pertain to the blinding of participants, therapists and assessors of key outcomes. Blinding procedures are necessary to minimize bias within a trial but can require significant human resources to implement. In order for participants to be blinded to their group allocation, each intervention should be conducted in isolation from the other. As interventions are best run concurrently, this can be achieved through careful management of participant intervention session times or access to two separate rehabilitation areas. This was not possible within this trial due to a lack of human resources and equipment availability.

Blinding of rehabilitation professionals poses another challenge in robotic locomotor research as it is clearly evident which participants are engaging in RLT. Assessors of key outcomes thus cannot be involved in the intervention as they will be exposed to the group allocation of each participant. Within this trial it was however not possible to satisfy the requirements of items 5 and 6 of the PEDro scale, relating to blinding of participants and therapists. The rehabilitation techniques used in the RLT and ABT groups ran concurrently, thus each group was aware of the other's treatment (not blinded). Furthermore, biokineticists who administered the interventions were aware as to which group the participant belonged to (not blinded).

Measures used to mitigate bias included counselling each group before commencing their respective intervention. Expectations of participants were managed by providing evidence that both interventions were equivalent in their efficacy. Health professionals administering intervention sessions were rotated halfway (12-weeks) into the intervention. Lastly, both intervention arms had the same amount of contact time with the investigators, biokineticists, physician and psychologists. Involvement in the study did carry significant psychological meaning to participants, which will be discussed further within Chapter 6 of this dissertation.

3.6. Future Research:

Researchers often strive to implement RCT's as the gold-standard of experimental research. Within low- and middle-income countries, a full-scale RCT may not always be feasible due to human resource and financial restraints. When the implementation of a full-scale RCT is not feasible, it is important to note that a pragmatic approach can describe evidence of effectiveness in everyday clinical contexts[257,258]. 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. This could be provided by a multi-centre trial[69]. However, with a lack of large funding and resources in a middle-income setting, at present, pragmatic trials utilising lower-cost exoskeletons may prove to be more feasible.

3.7. Conclusion:

The pilot RCT protocol described is unique as the research was conducted in a middle-income country (South Africa), consisted of a long intervention duration (6-months), comprised of wide-ranging testing procedures and included a homogenous comparison group. The challenges experienced in the current study included; ethical approval, medical screening, transport, and limited human and financial resources, which affected the blinding of participants and biokineticists. Despite these challenges, the trial was successfully completed. However, these challenges need to be addressed when considering the feasibility of conducting future large scale RCTs. We suggest that in order to upscale the study to a full RCT, the following would enhance feasibility: a) pre-assessment criteria to include lower limb MRIs for ambulatory individuals at risk of overuse injury, as well as mandatory proximal tibia/distal femur DEXA scans, b) development of a public transport system for individuals with disabilities or substantial research funding for the provision of private transport, c) additional human and financial resources to ensure adequate blinding, and d) utilising lower-cost exoskeletons to lessen the burden of conducting large-scale trials and increase the likelihood of adoption into current standard of care practices.

In the following chapters (4-6), the experimental results relating to cardiovascular and psychological outcome measures will be discussed. Despite the pilot nature of the trial, the study design strengths, high adherence rates and low dropout rate provided the research team with the opportunity to collect rich data and gain novel insights into the effects of both the RLT and ABT interventions.

CHAPTER 4

Robotic locomotor training leads to cardiovascular changes in individuals with incomplete spinal cord injury over a 24-week rehabilitation period.

Certain components of the present chapter have been published in the *Archives of Physical Medicine and Rehabilitation* (2021). Evans RW, Shackleton C, West S, Derman W, Rauch HG L, Baalbergen E, Albertus Y. Robotic locomotor training leads to cardiovascular changes in individuals with incomplete spinal cord injury over a 24-week rehabilitation period: a randomized controlled pilot study. *Archives of Physical Medicine and Rehabilitation*. 2021 (In Press).

4.1. Introduction:

A spinal cord injury (SCI) has far reaching impacts on an individual's life. One is required to rapidly adapt to both the primary neurological effects and secondary complications of the injury[1]. A common secondary complication in SCI is cardiovascular dysfunction both at rest and during exercise[73]. A contributing factor to the dysfunction is cardiac deconditioning due to reduced physical activity levels[80,81], and the effect of the injury on the autonomic nervous system (ANS)[74]. This can lead to reduced sympathetic activity due to a loss of supraspinal control with resultant unopposed parasympathetic outflow from the unaffected vagus nerve[76]. Chronic sympatho-vagal imbalance may consequently cause cardiovascular abnormalities including dysrhythmias, particularly bradycardia with concomitant hypotension[79].

The ability to maintain a supported standing posture for individuals with SCI is challenging due to the significant orthostatic stress involved, increasing the cardiovascular demand necessary to maintain blood pressure[38,104]. This increased demand when standing provides an acute neurohumoral cardiovascular response[104]. Consistent physical activity in the form of aerobic and resistance training is able to generate longer lasting cardiovascular adaptations and mitigate pathology[63,91,92]. Physical activity guidelines for individuals with SCI, suggest utilising major muscle groups providing sufficient intensity to improve metabolic profiles and induce cardiovascular benefits[97–100,259].

Activity-based training (ABT) is a form of physical activity characterized by repetitive activities to promote recovery below the level of lesion[34,187]. It is commonly used in rehabilitation and its cardiovascular response has been well established in persons with SCI[260]. Robotic locomotor training (RLT), which is also a form of physical activity, is a promising but costly rehabilitative tool for the SCI population[93,261]. RLT possesses unique attributes including an increased volume of stepping, larger lower limb muscle activity and engagement of the central pattern generator, a neuronal network producing the oscillating signals involved in locomotion[94,262–264]. In comparison to other forms of physical activity, RLT may have a unique impact on the cardiovascular responses of individuals with SCI. A recent systematic review, conducted by Shackleton et al. (2019), highlighted an absence of RCTs using homogenous groups and limited evidence for cardiovascular benefits from performing RLT. With an average intervention period of 9.5 ± 6.3 weeks, the reviewed studies are unable to provide a comprehensive understanding of the long-term cardiovascular adaptation. There is therefore a need to conduct a pilot RCT with a homogenous sample over a longer intervention period (24-weeks) to determine the effect of RLT on cardiovascular function.

4.1.1. Aim:

The primary aim of this pilot study was to evaluate the effect of RLT and ABT on participant's cardiovascular indices (brachial and ankle blood pressure, heart rate and heart rate variability responses) over a 24-week intervention. A secondary aim was to examine changes in cardiovascular efficiency during submaximal exercise tests over the 24-weeks of the RLT and ABT interventions. We hypothesised that the effect of RLT on cardiovascular indices may differ from that of ABT due to the unique stimulus that RLT provides.

4.2. Methods:

The recruitment of participants, interventions and outcome measures are discussed in detail in Chapter 2 of this dissertation. Participant characteristics are summarized in *Table 3.1* – Chapter

3. A brief repetition of the methods pertaining to the cardiovascular outcome measures is provided below.

4.2.1. Testing Procedures:

Cardiovascular changes were evaluated during four physiological perturbations (testing conditions) in this study; 1) supine positioning at rest, 2) standing at rest, 3) six-minute arm ergometry test (6MAT) and 4) six-minute walk test (6MWT); conducted at 0, 6, 12 and 24-week intervals. Data was recorded for five-minutes in the supine and standing positions with the physiological perturbations separated by a five-minute resting interval.

Cardiovascular indices were measured at rest in a supine position with the participant lying passively on a plinth. Participants were then moved to a standing position which was performed using an EasyStand Evolv (Minnesota, USA) standing frame where the participant's ankles, knees, hips and torso were supported. Lastly, a 6MAT[195] (Technogym, Italy) was conducted while seated starting at a power output of 15 Watts and increasing by 5 Watts each minute until completion of the test. The 6MWT was performed in a separate session for the participants in the RLT group. The 6MWT[196] was conducted in the Ekso GT exoskeleton, hence the ABT group did not perform this test. All testing was conducted within the same rehabilitation area with the climate controlled at 22 degrees centigrade and 50% humidity.

4.2.2. Cardiovascular Measurements:

4.2.2.1. Brachial and Ankle Blood Pressure:

Resting brachial blood pressure was measured whilst supine using a clinically validated Omron M3 blood pressure monitor[197]. Resting ankle systolic pressure of the posterior tibial or dorsalis pedis artery was measured in the supine position. A manual blood pressure cuff and handheld ultrasound Doppler system (Sonotrax Vascular, Hamburg, Germany) was used, and ankle brachial pressure index (ABPI) calculated[27,28]. Blood pressure and heart rate can vary considerably, measured using the coefficient of variation (CV), in individuals with tetraplegia who experience autonomic dysreflexia[198]. The CV across blood pressure findings was: baseline - 13%; 6-weeks – 15%; 12-weeks – 12% and 24-weeks – 16%.

4.2.2.2. Heart Rate and Heart Rate Variability (HRV):

Heart rate and HRV using a Faros device (Bittium, Finland) was recorded during the aforementioned physiological perturbations. Participants spent two-minutes in each perturbation before recording, to allow the body time to adapt to the posture. The CV across heart rate findings was: baseline - 17%; 6-weeks – 17%; 12-weeks – 18% and 24-weeks – 17%. Short term HRV assessment provides a valid and a clinically practical measure of autonomic function in people with SCI[89]. Variables included in the HRV analysis were standard deviation of the R-R interval (STD RR) and root mean square of successive differences (RMSSD)[88,199].

4.2.2.3. Cardiovascular Efficiency:

Cardiovascular efficiency was measured during the 6MAT and 6MWT using the Total Heart Beat Index (THBI; calculated by dividing the total number of beats during exercise by the total distance travelled in that time period)[110]. The THBI is a cardiovascular efficiency metric that has been used within the SCI population and is a valid alternative to gas analysis[200].

4.2.3. Statistical Analysis:

Comprehensive methods of the statistical analysis are contained in Chapter 2. HRV analysis was conducted on constant 150 second segments using AcqKnowledge[265] & Kubios[266] software. Comparisons of physiological perturbations (supine rest, standing, 6MAT and 6MWT) were performed using a two-way repeated measures ANOVA. Changes in cardiovascular efficiency during the 6MWT were performed using a one-way repeated measures ANOVA. Sphericity was not assumed when conducting the ANOVAs and hence p-values were adjusted according to the Greenhouse-Geisser correction. Magnitude-based inferences of change (effect size) were calculated according to Cohen's d[216]. Whitehead et al (2015) suggests that a pilot sample size of 10 per treatment arm be reached for large effect sizes > 0.8[188]. Due to 8 participants in each group, we aimed for larger effect sizes for clinical significance. Outliers were excluded from the HRV data according to the median absolute deviation (MAD) method, using a 3*MAD conservative approach[217].

4.3. Results:

4.3.1. Brachial and Ankle Blood Pressure

No statistically significant differences between groups or over time were evident for changes in brachial systolic and diastolic blood pressure, ankle systolic pressure or ABPI in the RLT and ABT groups over the course of the intervention. Effect size (ES) estimates did however demonstrate large differences in ABPI between RLT and ABT groups; with lower ABPI shown in the RLT group at baseline (ES = 1.05) and 24-weeks (ES = 1.02) *(Table 4.1)*.

Table 4.1: Comparison of supine systolic and diastolic blood pressure, ankle systolic pressure and ankle-brachial pressure index between robotic locomotor training and activity-based training groups.

Variable	Time	RLT (n = 8)	ABT (n = 8)	p-value	Effect Size
Systolic blood pressure (mmHg)	Baseline	138.13 ± 17.04	126.38 ± 13.52	0.48	0.76
	6-Weeks	133.50 ± 17.03	122.50 ± 11.21	0.48	0.76
	12-Weeks	133.13 ± 10.99	128.86 ± 12.45	0.93	0.36
	24-Weeks	133.50 ± 21.28	126.63 ± 10.47	0.90	0.41
Diastolic blood pressure (mmHg)	Baseline	82.75 ± 11.61	80.50 ± 11.99	0.99	0.19
	6-Weeks	82.63 ± 11.25	75.50 ± 8.82	0.55	0.71
	12-Weeks	83.63 ± 12.74	82.38 ± 6.30	0.99	0.12
	24-Weeks	83.63 ± 15.97	81.25 ± 6.50	0.99	0.19
Ankle systolic pressure (mmHg)	Baseline	114.25 ± 20.77	119.13 ± 17.07	0.82	0.34
	6-Weeks	111.38 ± 20.38	116.00 ± 28.56	0.86	0.31
	12-Weeks	122.88 ± 32.14	121.75 ± 19.40	0.97	0.19
	24-Weeks	100.75 ± 14.70	116.50 ± 21.95	0.91	0.27
Ankle brachial pressure index (ABPI)	Baseline	0.83 ± 0.10	0.94 ± 0.11	0.14	**1.05**
	6-Weeks	0.84 ± 0.16	0.94 ± 0.17	0.69	0.61
	12-Weeks	0.91 ± 0.18	0.94 ± 0.10	0.99	0.21
	24-Weeks	0.76 ± 0.13	0.92 ± 0.18	0.23	**1.02**

Data presented as mean ± SD. Bold represents large effect size. RLT = robotic locomotor training; ABT = activity-based training

4.3.2. Heart Rate:

In the supine position, no statistically significant differences in heart rate between groups or over time were evident. Effect size estimates however suggest that the RLT group had a lower supine heart rate at 6-weeks (58.7 ± 5.5 beats/min; ES = 0.90) and 24-weeks (59.9 ± 6.0 beats/min; ES = 0.81) in comparison to the ABT group (6-weeks: 64.8 ± 7.9 beats/min; 24-weeks: 66.3 ± 9.4 beats/min). In the standing position, heart rate at 24-weeks was significantly higher in the ABT group (95.6 ± 12.6 beats/min) compared to the RLT group (75.1 ± 15.0

beats/min) ($p = 0.05$). During the 6MAT, no significant differences in heart rate were evident *(Table 4.2)*.

Heart rate responses to physiological perturbations within the RLT and ABT groups both showed significant changes between perturbations and over time ($p < 0.01$) *(Figure 4.2a)*. 6MAT mean heart rate in the RLT group at baseline, 6, and 24-weeks was significantly higher ($p < 0.05$) compared to supine values at the same time points *(Figure 4.2a)*. Within the ABT group, 6MAT and standing heart rate values were significantly higher than supine values at all time points with no changes over time within a perturbation ($p < 0.05$) *(Figure 4.2*a).

In the RLT group, at baseline, mean heart rate during the 6MWT (121.8 ± 21.5 beats/min) was significantly higher ($p < 0.05$) than both supine (62.30 ± 7.4 beats/min) and standing (80.9 ± 18.2 beats/min) perturbations. *(Figure 4.2a)*. 6MWT mean heart rate decreased from baseline to 12-weeks (102.7 ± 25.8 beats/min) ($p = 0.01$) and remained similar at 24-weeks *(Table 4.2)*.

Table 4.2: Comparison of supine, standing, 6-minute arm ergometry test and the 6-minute walk test heart rate and heart rate variability measures in the robotic locomotor training and activity-based training groups from baseline to 24-weeks.

Variable	Time	Supine				Standing				6-Minute Arm Ergometry Test				6-Minute Walk Test
		ABT	RLT	p1	Effect size	ABT	RLT	p2	Effect size	ABT	RLT	p3	Effect size	RLT
Heart rate (beats/min)	Baseline	64.17 ± 6.07	62.30 ± 7.44	0.60	0.28	91.88 ± 13.21	80.87 ± 18.20	0.57	0.69	103.87 ± 21.82	99.10 ± 21.52	0.99	0.22	121.78 ± 21.53
	6-Weeks	64.81 ± 7.86	58.66 ± 5.54	0.11	**0.90**	87.98 ± 13.54	80.64 ± 20.64	0.88	0.42	105.13 ± 19.17	94.98 ± 17.19	0.74	0.56	107.37 ± 34.54
	12-Weeks	62.91 ± 8.75	60.11 ± 9.10	0.55	0.31	81.95 ± 5.18	79.36 ± 24.42	0.99	0.15	97.37 ± 13.70	94.08 ± 22.56	0.99	0.18	102.67 ± 25.82
	24-Weeks	66.34 ± 9.38	59.93 ± 6.02	0.15	**0.81**	95.58 ± 12.61	75.14 ± 14.96	0.05*	**1.47**	107.97 ± 19.06	98.83 ± 19.06	0.84	0.48	104.02 ± 37.09
STD RR (ms)	Baseline	25.98 ± 12.84	36.33 ± 19.11	0.69	0.64	10.49 ± 2.95	17.31 ± 8.15	0.26	**1.11**	7.69 ± 4.63	10.59 ± 5.53	0.77	0.57	9.66 ± 5.31
	6-Weeks	32.77 ± 29.37	77.75 ± 66.78	0.16	**0.87**	14.46 ± 8.81	17.93 ± 7.95	0.90	0.41	5.64 ± 1.52	12.01 ± 5.86	0.11	**1.49**	13.08 ± 5.66
	12-Weeks	38.95 ± 37.92	63.43 ± 59.72	0.85	0.49	23.42 ± 14.12	16.62 ± 11.47	0.79	0.53	8.98 ± 5.94	8.15 ± 4.82	0.99	0.15	13.94 ± 5.94
	24-Weeks	28.15 ± 10.91	54.41 ± 61.24	0.77	0.59	10.14 ± 3.32	14.93 ± 7.48	0.50	**0.83**	7.15 ± 3.13	11.13 ± 7.42	0.64	0.70	13.22 ± 7.78
RMMSD (ms)	Baseline	28.66 ± 13.29	34.87 ± 15.39	0.89	0.43	9.14 ± 3.17	16.78 ± 7.15	0.12	**1.38**	7.78 ± 2.87	10.53 ± 4.14	0.54	0.77	13.19 ± 6.47
	6-Weeks	34.36 ± 29.91	42.41 ± 16.61	0.95	0.33	12.26 ± 5.13	16.40 ± 8.90	0.77	0.57	7.34 ± 2.03	12.69 ± 5.47	0.16	**1.30**	16.93 ± 9.02
	12-Weeks	26.64 ± 9.95	45.24 ± 31.99	0.99	0.02	20.38 ± 11.46	14.68 ± 7.61	0.72	0.59	10.28 ± 7.00	8.48 ± 2.98	0.95	0.33	17.76 ± 8.15
	24-Weeks	28.94 ± 11.68	31.20 ± 13.68	0.99	0.18	10.07 ± 2.52	13.37 ± 5.62	0.57	0.76	8.51 ± 2.64	10.58 ± 4.58	0.79	0.55	17.52 ± 11.72

ABT = activity-based training, RLT = robotic locomotor training, p1 = supine comparison of ABT and RLT, p2 = standing comparison of ABT and RLT**,** p3 = 6-minute arm ergometry test comparison of ABT and RLT. Data presented as mean ± SD (n = 8 in each group). * $p \leq 0.05$. Bold represents large effect size.

4.3.3. Heart Rate Variability:

During the supine, standing and 6MAT perturbations, no statistically significant differences between groups or over time were evident in the measured HRV indices (STD RR and RMSSD). Effect size estimates however suggest that the RLT group had a higher supine STD RR at 6-weeks (77.75 ± 66.78ms) in comparison to the ABT group (32.77 ± 29.37ms; ES = 0.87). Furthermore, effect sizes also showed increased HRV in the RLT group during standing and 6MAT perturbations at 6- and 24-weeks (*Table 4.2*).

HRV comparison within the ABT group showed significant differences between physiological perturbations ($p < 0.01$), primarily due to elevated supine values. *(Figure 4.1b and 4.1c)*. At baseline and 24-weeks, supine STD RR and RMSSD were significantly higher than in both standing and 6MAT perturbations ($p < 0.05$) *(Figure 4.1b and 4.1c*). In the RLT group, supine STD RR and RMSSD showed higher variation, resulting in a lack of statistical significance between physiological perturbations *(Figure 4.1b and 4.1c)*.

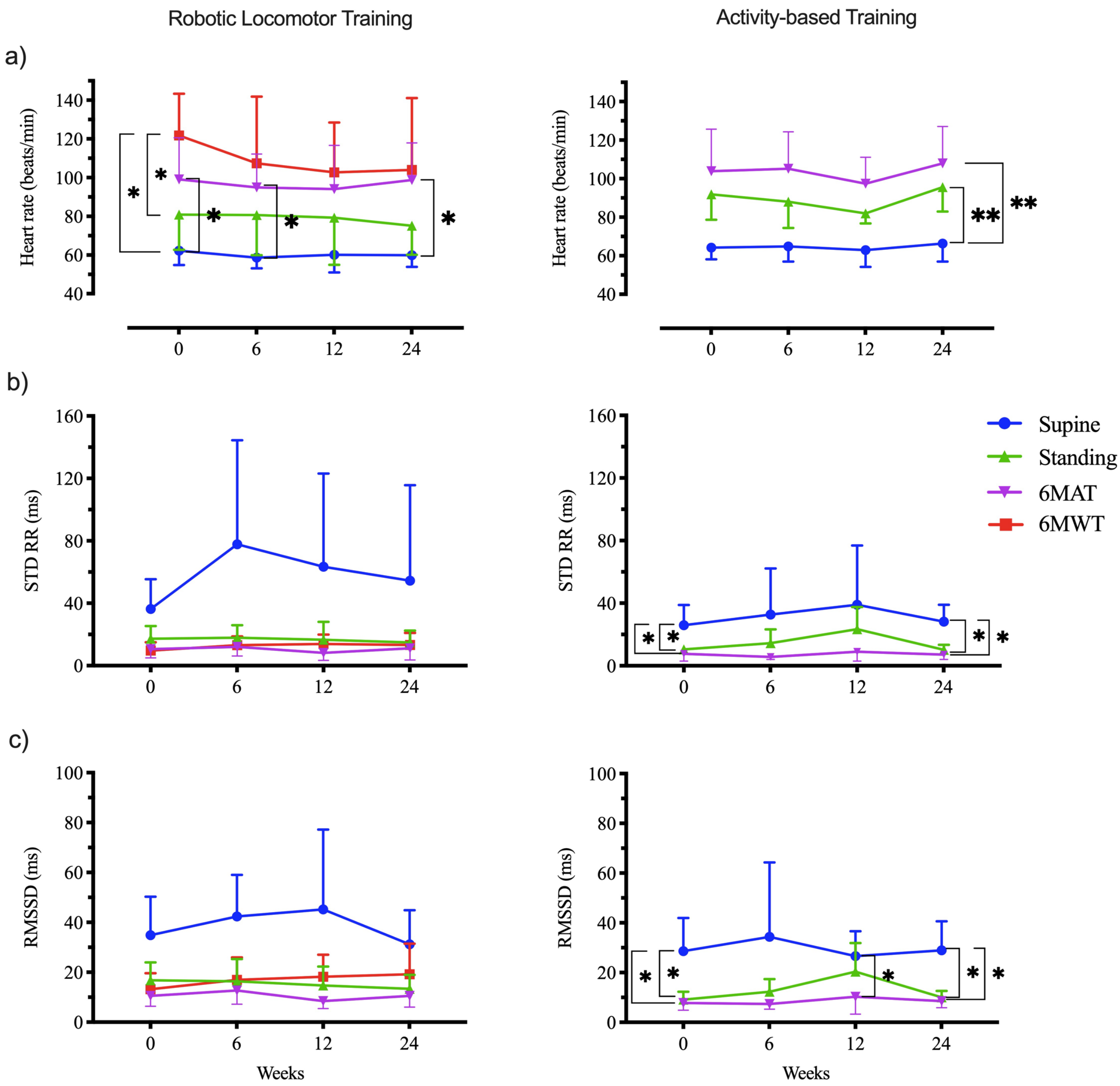


Figure 4.1: Comparison of heart rate and heart rate variability indices during supine, standing, 6-minute arm ergometry test and the 6-minute walk test within the robotic locomotor and activity-based training groups from baseline to 24-weeks. a) Heart rate; b) Standard Deviation R-R interval (STD RR); c) Root mean square of successive differences (RMSSD). Data presented as mean ± SD. * = $p < 0.05$ at single time point, ** = $p < 0.05$ at all time points throughout intervention.

4.3.4. Cardiovascular Efficiency:

During the 6MAT, mean heart rate and distance covered were not significantly different between groups or over time (*Table 4.3*). The THBI also showed no change between groups or over time.

Table 4.3: Mean heart rate, distance cycled, total heart beat index, post-test blood pressure and rating of perceived exertion from baseline to 24-weeks during the 6-minute arm ergometry test.

Variable	Time	RLT (n = 8)	ABT (n = 8)	p-value	Effect Size
Heart Rate (beats/min)	Baseline	103.87 ± 21.82	99.10 ± 21.52	0.99	0.22
	6-Weeks	105.13 ± 19.17	94.98 ± 17.19	0.74	0.56
	12-Weeks	97.37 ± 13.70	94.08 ± 22.56	0.99	0.18
	24-Weeks	107.97 ± 19.06	98.83 ± 19.06	0.84	0.48
Distance (m)	Baseline	1054 ± 662	1036 ± 606	0.99	0.03
	6-Weeks	990 ± 682	1094 ± 615	0.99	0.16
	12-Weeks	1098 ± 647	1165 ± 577	0.99	0.11
	24-Weeks	1110 ± 662	1185 ± 586	0.99	0.12
Total Heart Beat Index (beats/m)	Baseline	0.59 ± 0.59	0.64 ± 0.41	0.99	0.10
	6-Weeks	0.60 ± 0.57	0.57 ± 0.19	0.99	0.08
	12-Weeks	0.44 ± 0.31	0.50 ± 0.21	0.99	0.20
	24-Weeks	0.52 ± 0.45	0.47 ± 0.15	0.99	0.16
Systolic Blood Pressure (mmHg)	Baseline	129.38 ± 31.76	120.38 ± 22.39	0.95	0.33
	6-Weeks	125.13 ± 20.37	130.00 ± 15.63	0.98	0.27
	12-Weeks	124.13 ± 27.43	118.13 ± 23.45	0.98	0.23
	24-Weeks	122.75 ± 32.40	123.38 ± 25.23	0.99	0.02
Diastolic Blood Pressure (mmHg)	Baseline	75.13 ± 21.33	73.38 ± 12.55	0.99	0.10
	6-Weeks	71.75 ± 11.31	74.33 ± 13.77	0.99	0.21
	12-Weeks	72.75 ± 15.76	71.88 ± 10.95	0.99	0.06
	24-Weeks	69.13 ± 21.60	71.25 ± 10.95	0.99	0.12
Rating of Perceived Exertion (Borg)	Baseline	15.25 ± 2.87	14.88 ± 2.10	0.99	0.15
	6-Weeks	17.13 ± 3.09	14.67 ± 1.86	0.32	**0.96**
	12-Weeks	15.13 ± 3.40	13.63 ± 3.85	0.89	0.41
	24-Weeks	16.88 ± 2.17	13.88 ± 3.80	0.28	**0.97**

Data presented as mean ± SD. Bold represents large effect size.

The distance walked in the exoskeleton during the 6MWT significantly increased from baseline (68.3 ± 11.3m) to 24-weeks (109.9 ± 19.7m) ($p < 0.05$) *(Figure 4.2a)*. This was achieved with comparable RPE scores (*Figure 4.2b*) and a significant attenuation of heart rate from 121.8 ± 21.53 at baseline to 102.7 ± 25.8 at 12-weeks (*Table 4.2*). As a result, THBI significantly improved from 11.1 ± 2.6 at baseline to 7.5 ± 2.8 beats/meter walked within the first 6-weeks ($p < 0.02$) and was maintained thereafter *(Figure 4.2c)*.

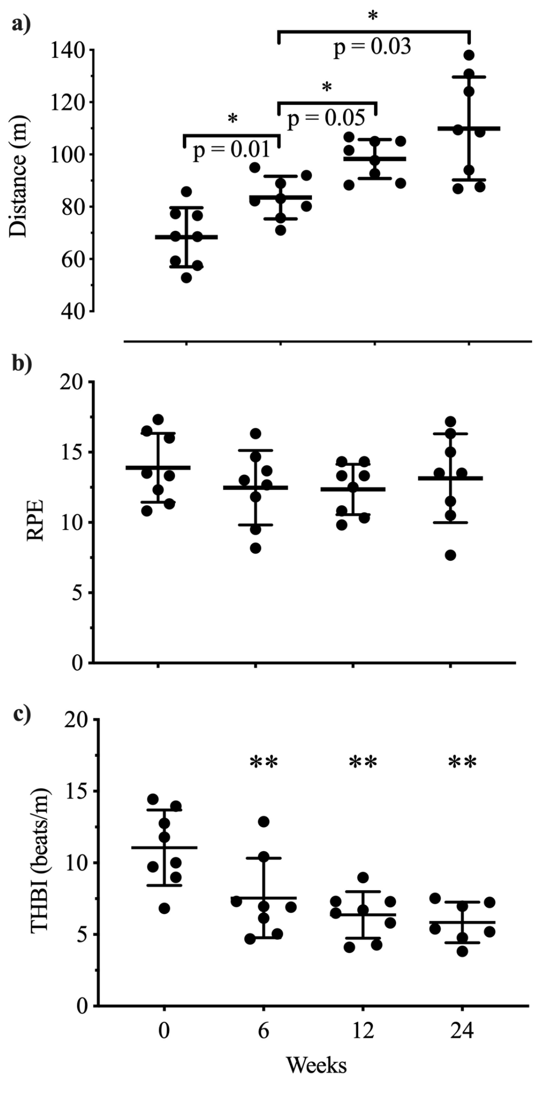


Figure 4.2: The a) Distance walked; b) Rating of Perceived Exertion (RPE) and; c) Total heart beat index (THBI) during the 6-minute walk test in the robotic locomotor training group from baseline to 24-weeks. Bars denote mean ± SD, dots denote individual participants. * = $p < 0.05$, ** = significantly different from baseline $p < 0.05$

4.4. Discussion:

The likelihood of developing cardiovascular dysfunction both at rest and during exercise is increased in individuals with a SCI above the T6 level[73,74]. This novel pilot study therefore aimed to describe the impact of 24-weeks of robotic locomotor and activity-based training on cardiovascular indices, during different physiological perturbations.

4.4.1. Heart Rate and Blood Pressure:

The first important finding showed that RLT may be more effective than ABT in improving cardiac responses to orthostatic stress, particularly over a longer intervention period of 24-weeks. Standing heart rate at 24-weeks was significantly lower in the RLT group (75.1 ± 15.0 beats/min) compared to the ABT group (95.6 ± 12.6 beats/min) (*Table 4.2*). A postural tachycardia during standing is typical of individuals with SCI who are not able to elevate their blood pressure due to associated autonomic dysfunction[104]. Lowered standing HR in the RLT group is hypothesised to have been caused by two mechanisms. Firstly, intensive high volume walking within the RLT group may increase lower limb muscle activity and tone[267]. Improved muscle tone would thus increase venous return and cardiac output, resulting in a lower heart rate required to maintain adequate cardiac output during orthostatic stress[268,269]. Secondly, improved cardiovascular conditioning was evident in the RLT group who experienced a high volume of aerobic training and standing time in comparison to the ABT group. Improvements in conditioning included a lowered resting heart rate and increased cardiovascular efficiency during the 6MWT. Aerobic exercise and prolonged standing, both major components of RLT, are known to improve neurohumoral blood pressure control in tetraplegic subjects, thereby possibly aiding in tolerance to orthostatic stress[104,267,268,270–272].

Differences in supine heart rate between RLT and ABT groups were evident within the early period of 6-weeks and the longer-term period of 24-weeks, resulting in large effect size estimates (>0.8)[216]. Resting heart rate may serve as a predictor of cardiovascular dysfunction in the SCI population[273,274]. Blood tends to pool in the lower extremities of individuals with SCI, resulting in compensatory increases in heart rate[275]. Therefore, maintenance of healthy supine heart rates and lower heart rates during standing over a longer 24-week period are indicative of improved cardiovascular functioning in the RLT group.

Brachial blood pressure did not change over the intervention but was elevated in comparison to similar studies[276,277]. Goh et al. (2018) reported a day-time systolic average of 114.8 ± 2.6mmHg and diastolic average of 68.2 ± 1.9mmHg within a cohort of 27 persons with incomplete tetraplegia[278]. Within our study, at baseline and across all participants, average resting systolic and diastolic brachial pressures were 132.3 ± 8.3mmHg and 81.6 ± 1.6mmHg respectively (*Table 4.1*). Elevated blood pressure measurements may be explained by a lack of prior engagement in physical activity as well the incomplete nature of our sample's injuries, allowing varying degrees of sympathetic innervation and blood pressure maintenance[75]. The average ABPI across both groups was relatively low (0.86 ± 0.15) in comparison to other studies[279,280], with Grew et al. (2000) demonstrating an average ABPI of 1.08 ± 0.08. This difference is likely due to the elevated brachial systolic blood pressures recorded, particularly in the RLT group, which would decrease the ABPI and explain the large effect sizes at baseline and 24-weeks (*Table 4.1*).

4.4.2. Heart Rate Variability:

Walking within an exoskeleton provides a unique physiological perturbation[94]. The stimulus of standing was, however, comparable to exoskeleton walking during a 6MWT when evaluating HRV metrics as both physiological perturbations increased sympathetic drive to the heart. Postural changes from supine to standing cause physiological unloading of the baroreceptors, resulting in withdrawal of vagal activity and sympathetic activation of the sinoatrial node[78]. This adaptation however relies on adequate sympathetic activation and functioning of the baroreflex, which may be impaired following cervical or high thoracic SCI[104]. Walking in the exoskeleton during the 6MWT elicited higher heart rates compared to standing, however, it did not further alter HRV metrics, evidenced by the similar STD RR and RMSSD values during standing and the 6MWT perturbations (*Figure 4.1b and c*). Thus, standing and RLT result in similar levels of vagal withdrawal and/or sympathetic activation and may provide a comparable stimulus to the parasympathetic nervous system.

At rest, the parasympathetic nervous system would be dominant[104], resulting in supine HRV values (STD RR and RMSSD) being greater than standing, 6MAT and 6MWT values within both groups. Due to high variability, these differences only reached a level of significance ($p < 0.05$) in the ABT group.

4.4.3. Cardiovascular Efficiency:

Cardiovascular efficiency of walking within the RLT group improved over the course of the intervention, particularly after 6-weeks. Participants were able to consistently walk further distances at lower heart rates throughout the 24-week intervention (*Figure 4.2c*). The distance walked in the 6MWT at baseline was similar to previous studies[109,281], but did show greater improvements over the longer intervention period. The mean distance walked from baseline to 24-weeks increased by 41.6 ± 9.8m whereas other studies showed a mean increase of only 26.7 ± 7.0m[49,57,109,282,283]. Previous interventions were unable to demonstrate changes in heart rate during RLT[93,96,282,284], however, in this study mean heart rate during the 6MWT lowered from baseline to 12-weeks ($p < 0.05$) and was maintained at 24-weeks (*Table 4.2*). The improved walking efficiency shown may be attributed to a learning effect with the exoskeleton, which has previously been demonstrated by Kozlowski et al. (2015)[66], and secondly through improved cardiovascular fitness as a result of the aerobic training of RLT[281].

Cardiovascular efficiency, however, did not change between groups or over time during the 6MAT. Test-retest reliability and validity of the 6MAT has been demonstrated[195], however the 6MAT test may not be sufficiently responsive to detect changes in aerobic capacity in our cohort. This may be due to the test's fixed RPM and wattage protocol which produced similar heart rate, distance and RPE values at all time points.

4.5. Limitations:

A number of limitations were present in this study. Firstly, the frequency domain components of HRV were affected by the presence of outliers and excluded from the analysis. Outliers were in part caused by noise generated from movement of the Faros HRV device on the participants' chest. Secondly, autonomic dysreflexia could have contributed to the high variability. Common causes of autonomic dysreflexia include urinary tract infections, pressure to skin and joint pain/discomfort[285], factors which were present within the testing protocols. Lastly, due to a small sample size and low power, statistical comparisons between groups should be interpreted with caution and no claims made regarding treatment efficacy. In this pilot study, we aimed to find clinical significance with large effect sizes that advocate for a larger RCT.

4.6. Conclusion:

This study offers novel insights into the effect of RLT and ABT on cardiovascular responses in a homogenous group of individuals with SCI. This pilot study was able to highlight meaningful clinical changes in cardiovascular indices during RLT as early as 6-weeks and up to 24-weeks of rehabilitation. The findings describe how RLT lowered standing heart rate and improved cardiac responses to orthostatic stress. Secondly, the stimulus of standing achieved a comparable HRV response to a 6MWT in an exoskeleton. Thus, in the absence of access to RLT, standing may provide a comparable stimulus to the parasympathetic nervous system. Cardiovascular efficiency of walking within the RLT group improved over the course of the intervention, particularly during the first 6-weeks. Large effect sizes and significant differences between groups found in this pilot study support the clinical effectiveness of RLT and ABT for changing cardiovascular indices over a 24-week period. Therefore, a larger sample sized RCT over long period is warranted.

The conclusion of Chapter 4 marks a transitioning point within this dissertation. As we move to Chapters 5-7, we start to explore the psychological effects of participating in a SCI trial. Chapters 5 and Appendix 5 are quantitative in nature whilst Chapter 6 provides qualitative insight. Exercise science is often focused upon objective physiological findings, with a reluctance towards the 'softer science' of qualitative research[286]. The use of both quantitative and qualitative methods, however, brings strength to a study design and provides a richer understanding of participants[215].

CHAPTER 5

Perceived quality of life and the role of psychological resources in individuals with SCI undertaking a 24-week exercise-based intervention.

5.1. Introduction:

The prevalence of psychosocial disturbances such as major depression, anxiety, post-traumatic stress and suicide is higher within individuals with SCI compared to the general population[124,157,184,287]. Although individuals with SCI face these psychosocial challenges, paradoxically, many report high levels of quality of life (QoL). Psychological resources may support high perceptions of QoL[130–133]. Psychological resources are inner, health protecting or health promoting characteristics of a person[288,289]. They include factors such as resilience, self-efficacy and post-traumatic growth, which can have a buffering effect on negative mood states[290,291]. Self-efficacy and post-traumatic growth are prominent contributors to resilience, with all three being associated with stronger mental health and higher QoL post SCI[136,292–295].

Despite the presence of psychological resources, careful communication regarding possible unrealistic expectations of individuals entering a rehabilitation programme is vital. Large discrepancies can exist between patient's expectations of recovery versus that of their medical team[296]. Unmet expectations (particularly with the use of novel technology such as an exoskeleton) may create feelings of despair, potentially triggering mood disturbances[151,297].

With the risk of unmet expectations in samples that otherwise have little or no access to care, on-going monitoring of participants' mood is important[15]. This monitoring is largely absent in SCI research studies, but crucially allows for early identification of individual mood disturbances with support structures on hand[63]. Although put in place to guard against harm, monitoring may also share insight into possible changes experienced throughout an intervention[220,298]. Changes in psychological resources such as resilience, self-efficacy and post-traumatic growth in individuals participating in a SCI trial are unclear[136,299]. Researchers generally prioritise physiological outcome measures during exercise-based SCI trials[300]. Therefore, this chapter will provide novel insights into the often-overlooked psychological state of the participants partaking in this pilot randomised control study.

5.1.1 Aim:

The aim of the present chapter was to a) screen and monitor psychosocial factors in individuals with SCI engaging in a clinical trial, b) compare mean scores from this trial to similar cohorts in the literature and, c) describe these changes over a 24-week period within two different interventions, robotic locomotor training (RLT) and activity-based training (ABT). We hypothesized that: a) unmet expectations may be associated with markers of mood disturbances in some participants and, b) positive psychosocial changes may be experienced by some participants as a result of exposure to social support and increased physical activity.

5.2. Methods:

5.2.1. Participants & Procedures:

The recruitment of participants, interventions and outcome measures are discussed in detail in Chapter 2 of this dissertation. Participant characteristics are summarized in Table 3.1 – Chapter 3. A brief repetition of the methods pertaining to the outcome measures of this chapter is provided below.

5.2.2. Questionnaires:

Psychometric questionnaires (*Appendix 6*) were completed at four time points during the intervention: baseline, 6, 12, and 24-weeks. At baseline, researchers explained and were on hand to assist participants in completing paper versions of questionnaires. Questionnaires were then adapted into a *Google Docs* format with further time-points being completed electronically. Outcomes of interest included: quality of life (SCI QoL-BDS)[189], resilience (CD-RISC 25)[190], self-efficacy (MSES)[191], post-traumatic growth (PTGI)[134], depression (BDI)[193], anxiety (SAI)[194] and expectations of recovery (VAS-Expectation).

5.2.3 Statistical Analysis:

Comprehensive methods of the statistical analysis are contained in Chapter 2. Descriptive statistics were computed to allow comparison to similar cohorts in the literature. Outcome measures were analysed using effect sizes to provide insight into treatment effects within a small sample[216]. Effect sizes, however, do not necessarily equate to clinically meaningful effects[301,302]. For this reason, Reliable and Clinically Significant Change (RCSC) were also calculated according to the methods set out by Jacobson & Traux (1991) and Jacobson et al. (1999)[303,304].

RCSC was calculated on changes in individual participant scores from baseline to 24-weeks using reference studies for each psychometric measure[134,190,194,202,205,305]. RCSC is achieved when the criteria for both reliable change (RC) and clinical significance (CS) is met. Participant's scores were classified as undergoing a statistically reliable change (RC) if the Reliable Change Index (RCI) exceeded 1.96, denoting a change of larger than two standard deviations[303]. The RCI evaluates the magnitude of change to an outcome measure while controlling for the imprecision associated with that measure, in order to reliably detect a clinically significant change[303,306]. Clinically significant indices attempt to reflect to what extent the magnitude of change observed in the outcome measures translates to a practical significance for the participant[302]. Clinical significance (CS) was determined if the participant's 24-week score moved across cut-off point C as described by Jacobson et al. (1999)[304]. Cut-off point C is the most appropriate and preferred cut-off point to use when appropriate normative data is available for the specific outcome measure. The cut-off is used to evaluate whether a participant's post-treatment scores on the specific outcome measure are similar to those of a normative sample with pre-specified cut-off scores.

When the criteria for only RC is met, a participant's functioning on the specific outcome measure is classified as "improved but not recovered". However, if only the criteria for CS is achieved, a participant's functioning is seen as "unclassified", as it is unclear whether or not the magnitude of change in their scores would be due to the imprecision associated with the specific outcome measure[303,304,306].

The response rate was 100% on all questionnaires. Mean psychometric scores for one participant (participant X) were compared to the group mean using t-tests. One participant's post-traumatic growth inventory (PTGI) responses were excluded due to misinterpretation of the scale's instructions.

5.3. Results:

Table 5.1. Psychometric questionnaire results of the robotic locomotor training (RLT) and activity-based groups (ABT) over the intervention.

Variable	Time	RLT (n = 8)	ABT (n = 8)	p-value	Effect Size
Quality of Life					
(SCI QoL-BDS)	Baseline	6.75 ± 1.23	6.75 ± 2.17	0.99	0.00
	6-Weeks	7.33 ± 0.80	7.08 ± 2.05	0.99	0.16
	12-Weeks	7.29 ± 1.06	7.17 ± 1.80	0.99	0.09
	24-Weeks	8.50 ± 1.38	7.46 ± 1.79	0.62	0.65
Resilience					
(CD-RISC 25)	Baseline	87.00 ± 10.23	80.88 ± 17.99	0.89	0.42
	6-Weeks	88.25 ± 13.26	75.38 ± 19.92	0.49	0.76
	12-Weeks	86.25 ± 15.67	79.50 ± 20.16	0.92	0.37
	24-Weeks	87.13 ± 11.95	77.75 ± 19.23	0.71	0.59
Self-efficacy					
(MSES)	Baseline	100.25 ± 11.84	96.25 ± 12.87	0.95	0.32
	6-Weeks	100.50 ± 8.86	96.63 ± 10.20	0.90	0.41
	12-Weeks	100.13 ± 10.43	93.38 ± 12.06	0.69	0.60
	24-Weeks	102.50 ± 10.03	96.13 ± 14.05	0.78	0.52
Post-traumatic growth					
(PTGI)	Baseline	79.88 ± 20.30	72.38 ± 23.15	0.94	0.34
	6-Weeks	91.75 ± 10.75	69.75 ± 30.41	0.30	**0.96**
	12-Weeks	86.63 ± 18.67	67.75 ± 31.48	0.53	0.73
	24-Weeks	86.25 ± 17.16	71.50 ± 31.30	0.71	0.58
Depression					
(BDI)	Baseline	8.75 ± 7.12	10.13 ± 8.69	0.99	0.17
	6-Weeks	6.75 ± 4.50	10.25 ± 9.60	0.85	0.46
	12-Weeks	6.88 ± 5.46	9.38 ± 12.18	0.98	0.26
	24-Weeks	5.50 ± 3.55	9.88 ± 11.26	0.79	0.52
State Anxiety					
(SAI)	Baseline	47.13 ± 7.02	46.38 ± 5.73	0.99	0.12
	6-Weeks	48.25 ± 4.40	44.38 ± 5.13	0.42	**0.81**
	12-Weeks	44.75 ± 6.65	45.75 ± 3.62	0.99	0.19
	24-Weeks	48.38 ± 5.32	45.00 ± 4.93	0.60	0.66

Data shown as mean ± SD. Measurements taken at baseline, 6, 12 and 24-week time periods. Large effect sizes are highlighted in bold

No time, group or interaction effects were evident in the psychometric scales administered, except for perceptions of QoL which showed a significant improvement over time in the RLT group ($p = 0.02$) (*Table 5.1*). The mean scores across all time points for the RLT and ABT groups combined were, SCI QoL-BDS: 7.32 ± 1.60, CD-RISC 25: 82.77 ± 16.20, MSES: 98.22 ± 11.13, PTGI: 82.15 ± 19.15, BDI: 8.44 ± 8.05, SAI: 46.25 ± 5.34. Over the course of the intervention, depression (Beck Depression Inventory - BDI) scores decreased in 56% (9/16), remained stable in 19% (3/16) and deteriorated in 25% (4/16) of participants.

The ABT group showed higher variation than the RLT group in all scales, except the State Anxiety Inventory. Increased variation in the ABT group was largely caused by a single participant (X). In comparison to the mean results of the ABT group, Participant X's mean score was significantly ($p < 0.05$) lower in the SCI QoL-BDS: 2.91 ± 0.68, CD-RISC 25: 39.5 ± 4.66, MSES: 68.75 ± 5.12, PTGI: 36.25 ± 10.90 and higher in the BDI: 33.5 ± 4.43 – *Figure 5.1*. The temporary removal of participant X from the analysis did not alter the significance of the between-group analysis.

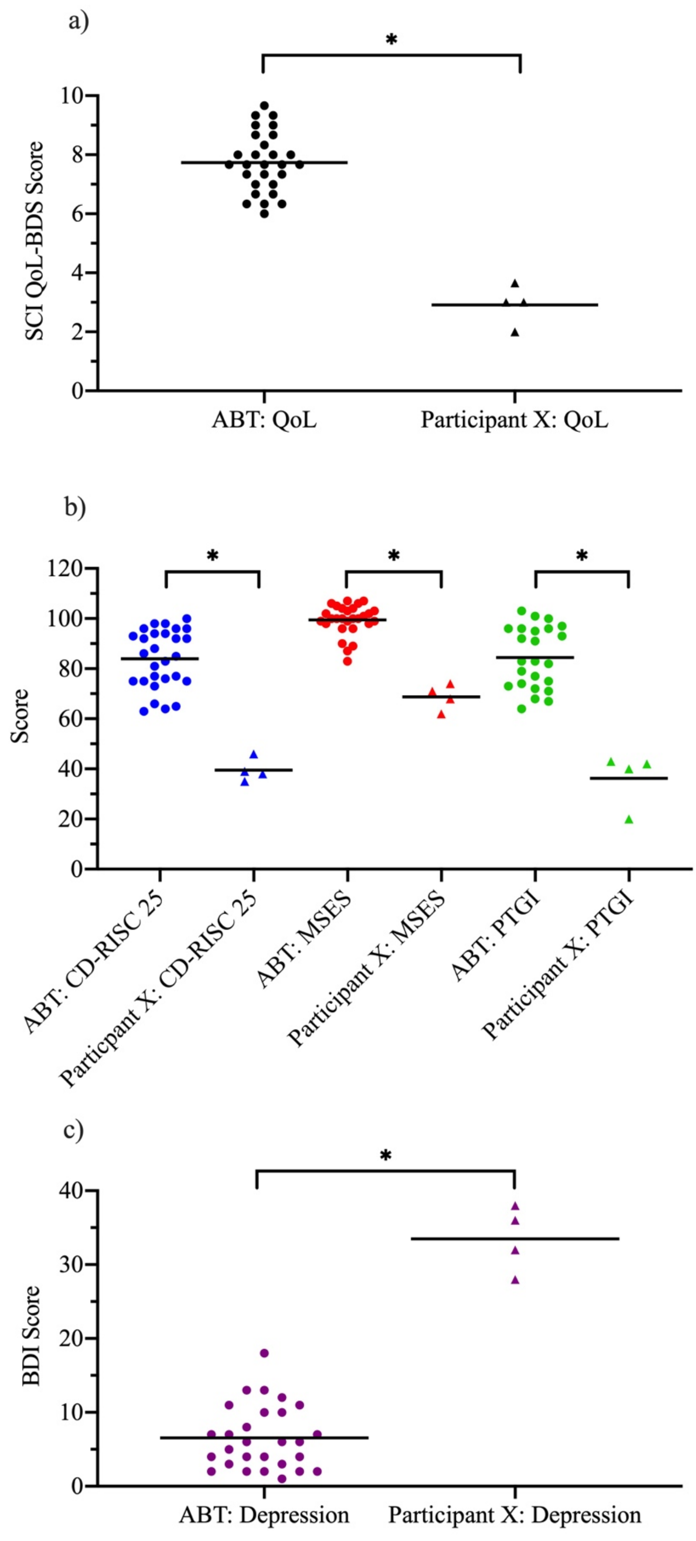


Figure 5.1: Scatterplot of quality of life (SCI Qol-BDS), resilience (CD-RISC 25), self-efficacy (MSES), post-traumatic growth (PTGI) and depression (BDI) within the ABT group and participant X across all time points (baseline, 6, 12 and 24-weeks). Horizontal bar denotes the mean, dots denote individual participants. * $p < 0.05$

According to the methods of Jacobson & Traux (1991)[303], statistically reliable improvements in individual scores from baseline to 24-weeks across all psychometric measures were observed twelve times in the RLT group and two times in the ABT group. Statistically reliable deteriorations were observed 2 times in both the RLT and ABT groups (*Figure 5.2a*). According to the methods of Jacobson et al. (1999)[304], clinically significant improvements in individual scores from baseline to 24-weeks across all psychometric measures were observed eight times in the RLT group and five times in the ABT group. Clinically significant deteriorations were observed seven times in the RLT group and three times in the ABT group (*Figure 5.2b*). Changes that were both statistically reliable and clinically significant in the RLT group included one case of deterioration in markers of both anxiety and self-efficacy each, one case of improvement in markers of post-traumatic growth, and two cases each for improvements in markers of depression, self-efficacy and quality of life. Changes that were both statistically and clinically significant in the ABT group included one case of deterioration in markers of both depression and resilience.

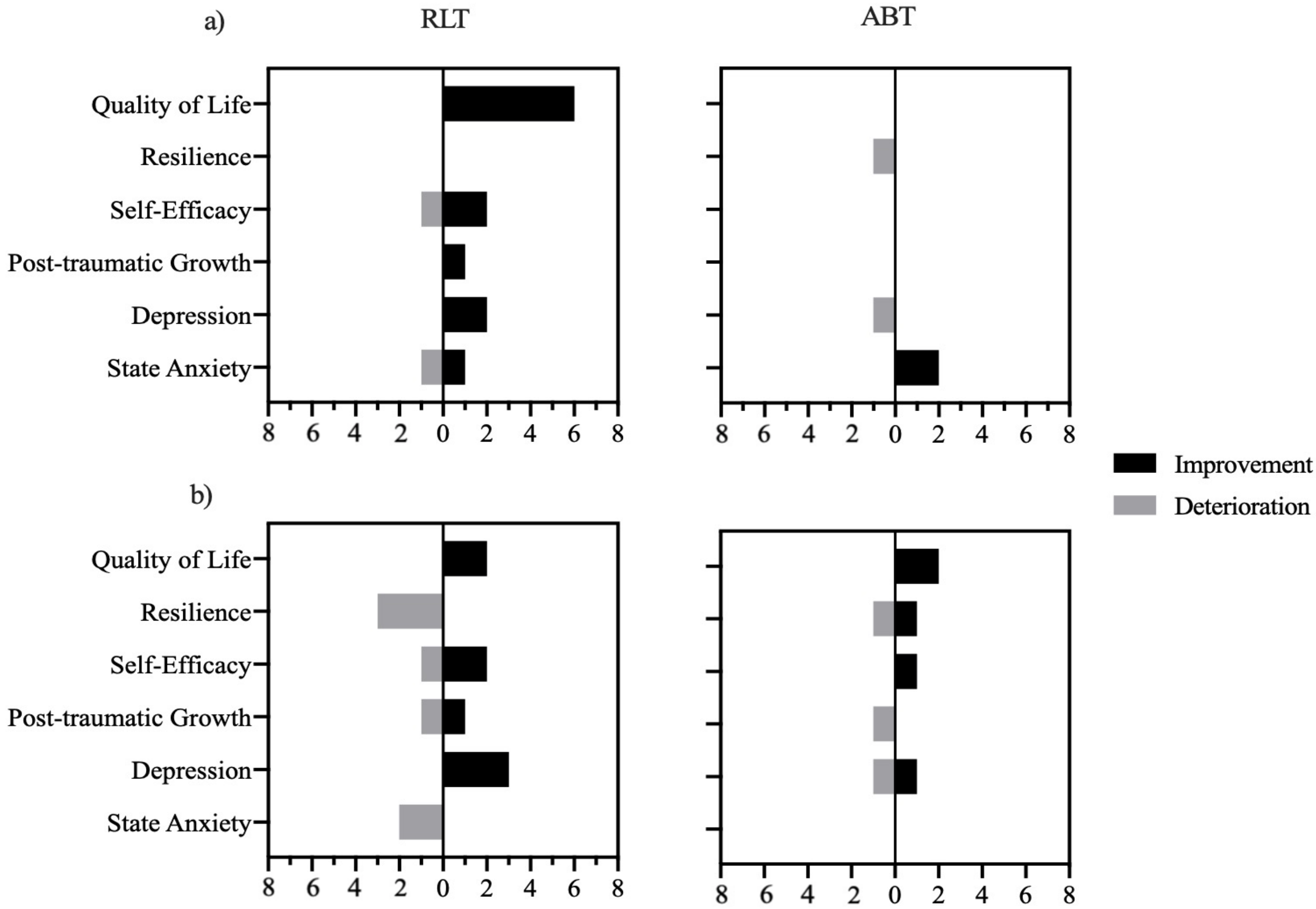


Figure 5.2: Number of participants demonstrating a) Statistically reliable change and b) Clinically significant change in quality of life (SCI Qol-BDS), resilience (CD-RISC 25), self-efficacy (MSES), post-traumatic growth (PTGI), depression (BDI) and state anxiety (SAI) within the RLT and ABT groups from baseline to 24-weeks.

5.4. Discussion:

The purpose of this chapter was to evaluate the hypothesis that, a) unmet expectations may be associated with markers of mood disturbances in participants engaging in a SCI clinical trial, and b) positive psychosocial changes may be experienced by participants as a result of exposure to extensive medical care, social support and increased physical activity. The findings of the study, which will be discussed further below, demonstrated stable mood which was evident through the psychometric scores of our sample. Psychometric scores were favourable when compared to similar samples, except for the State Anxiety Inventory. Individual psychometric responses to the intervention, analysed for statistical reliability and clinical significance, showed similar numbers of improvement and deterioration in the ABT group whilst a greater disposition towards improvement was seen in the RLT group. Engagement in an RLT programme may thus improve subjective psychological well-being in comparison to other exercise-based interventions. Significant markers of mood and psychosocial disturbances were identified and monitored in one participant (X), which did not improve during the intervention.

The results of the psychometric scales used suggest that the participants within this study, regardless of their group allocation, possessed high levels of psychological resources. The mean CD-RISC 25 score of 82.77 ± 16.20 was comparable to the 82.57 ± 10.61 reported by White et al. (2010) but higher than scores of acute patients in numerous studies[133,204,295,307]. Mean MSES score of 98.22 ± 11.13 was elevated compared to the 84.4 ± 18.9 reported by Middleton et al. (2016)[205] and other SCI samples [7,131,205,307–309]. Mean PTGI score of 82.15 ± 19.15 was higher than the 60.83 ± 26.48 reported by Zarin et al. (2017)[310] and 52.5 ± 28.5 within a sample of hospitalised tetraplegics[295]. Mean BDI score of 8.44 ± 8.05 was lower than the 23.73 ± 10.47 reported in a sample of acute SCI[210]. The mean SCI QoL-BDS of 7.32 ± 1.60 was higher than the 6.6 ± 1.7 reported by Post et al. (2016) and 6.9 ± 1.9 reported by New et al. (2019)[202,311].

These favourable results support the hypothesis that, despite trauma, individuals with SCI often possess psychological resources that support high perceptions of quality of life[132]. Uniquely, SAI mean scores of 46.25 ± 5.34 were higher in this study compared to others in the literature.

Mean SAI scores obtained by Rintala et al. (2005) from a telephonic survey of 165 male US veterans with varying completeness of injury was 38 ± 16.3, whilst Harper et al. (2014) demonstrated mean scores of 34.9 ± 19.1 within a sample of 40 Columbian individuals with varying injury levels[214,312]. A systematic review by Naidoo et al. (2020) elaborated on the research burden (i.e., the psychological, physical, and financial burdens) placed on patients through their participation in a RCT[313]. Feelings of anxiety were reported when participants felt they were 'guinea pigs', as well as during the randomization phase, particularly if allocated to a control or placebo group. Trial closure and follow-up also served as an additional source of stress and anxiety. 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[15,314].

The stability of scores across psychometric measures offers support for hedonic adaptation, whereby an individual's mood state fluctuates around a biologically determined set-point[315]. A lack of statistically significant ($p < 0.05$) findings between groups or over time may appear as a null finding, however, in a study with the possibility of unrealistic expectations causing mood disturbances, this lack of change is reassuring. Individual fluctuations in psychometric measures were analysed in more detail and quantified using statistically reliable and clinically significant change indices[303,304]. Notably, seven improvements that were both statistically reliable and clinically significant (one observation of improvement in markers of post-traumatic growth, and two observations each for improvements in markers of depression, self-efficacy and quality of life) were seen in the RLT group. In contrast, no observations of improvements that were both statistically reliable and clinically significant were seen in the ABT group. The novelty of and improved psycho-emotional wellness associated with walking in an exoskeleton likely contributed to the individual improvements seen in the RLT group[40,63].

The study's individual monitoring was successful in identifying participant X, whose baseline psychosocial indices were of concern. Identification of markers of negative mood states in participants is of utmost importance considering suicide is the leading cause of death in individuals with SCI younger than 55 years, with 75% of suicides occurring within 5 years of injury[117]. The study's psychologists deemed the benefit of participating in the trial to exceed the risks of further deterioration in mood, and hence participant X was included in the study. Hedonic adaptation was once again evident as participant X's indices were poor at initiation of the study and remained poor throughout. The lack of improvement was, however expected, as the intervention had no targeted psychological component. One-on-one sessions with a clinical psychologist, as part of the monitoring programme, were able to ensure participant X completed the intervention without a deterioration in mood. The participant continued with management of their mood externally once completing the study.

5.5. Limitations:

The study's sample size did not provide sufficient power to perform inferential statistics. A sample size calculation was performed using the BDI data to determine the number of participants required to show a statistically significant improvement in BDI scores over the intervention. At a power level of 0.8 and alpha = 0.05, 69 participants would be required in each group. A large sample size was beyond the financial and human resources available for this project and dissertation, thus a randomised pilot was conducted to support the running of a full RCT.

This study was solely reliant on subjective self-reported measures. Self-report questionnaires possess numerous limitations including bias and distortions within responses. These limitations may affect the reliability, validity and generalisability of results[316]. By using psychometrics, this study also assumed that complex psychological attributes are quantitative[317]. The inclusion of a qualitative analysis would provide a more robust understanding of participants, hence this has been included in Chapter 6.

5.6. Conclusion:

Despite experiencing significant trauma, participants with SCI possessed markers of psychological resources including resilience, self-efficacy and post-traumatic growth which contributed to high perceptions of quality of life. Statistically reliable and clinically significant improvements in individual scores were seen in the RLT group but not in the ABT group, demonstrating the potential positive impact the use of an exoskeleton may have on subjective psychological well-being. Monitoring of participants' mood and the potential negative effect of unrealistic expectations successfully identified one participant (X) deemed at risk. Participant X demonstrated signs of hedonic adaptation, successfully completing the intervention but neither improving nor deteriorating in psychosocial markers throughout the trial.

CHAPTER 6

"I was like intoxicated with this positivity": the politics of hope amongst participants in a trial of a novel spinal cord injury rehabilitation technology in South Africa.

Certain components of the present chapter have been published in *Disability & Rehabilitation: Assistive Technology* (2020) – Evans RW, Bantjes J, Shackleton CL, West S, Derman W, Albertus Y, Swartz L. "I was like intoxicated with this positivity": the politics of hope amongst participants in a trial of a novel spinal cord injury rehabilitation technology in South Africa. *Disability and Rehabilitation: Assistive Technology*. 2020 Sep 3:1-7. DOI: 10.1080/17483107.2020.1815086

6.1. Introduction:

The previous chapter of this dissertation highlighted that positive psychosocial changes may be experienced by participants as a result of exposure to social support and increased physical activity. The current chapter tries to further understand the expectations and feelings of hope in the participants throughout the intervention period.

The recovery process after SCI involves a significant degree of social interaction with medical professionals, family and other patients. Beyond treatment protocols, rehabilitation outcomes are affected by people's attitudes, thoughts and motivation to engage[318]. The positivist research paradigm, which places emphasis on quantitative and objective data collection, is often unable to describe these social factors[319]. Qualitative research, through an ontological perspective, plays a pivotal role in helping researchers and clinicians to better understand some of the most complex topics in the field, including practitioner-client interaction and the subjective lived experience of disability[319,320].

The interest in and use of qualitative research has seen exponential growth in the last 20 years. This growth is in part fueled by funding bodies that have more readily acknowledged the value of mixed-method approaches[319]. Many types of qualitative research exist, with thematic analysis providing one of the most easily accessible and valuable tools to identify, analyse and report on patterns/themes within data[218]. These tools hold promise for the future, where researchers can look beyond the black and white of traditional medical research and into the grey of a patient-centred understanding of the treatment provided[321].

Much of the SCI-based qualitative psychological literature focuses on multiple trauma and adverse psychological sequelae. More recently, there is increasing interest not only in adverse sequelae of life-changing events but also on salutogenic issues such as posttraumatic growth[125,126]. Research questions have evolved over time that recognize the opportunity for growth and positive outcomes associated with trauma[134]. Hope is an integral part of the positive psychology paradigm, with Snyder et al. (1991) defining hope as the belief that one can find pathways to desired goals and have the agency to use those pathways [138]. Hope has been widely studied within the SCI population[144–147].

Hope is an especially interesting issue to explore in the context of new technologies and treatments for any condition, including SCI. New technologies, especially those which promise to offer novel solutions to intractable problems, may be associated with a great deal of hope and optimism, some of which may be well placed but some unrealistic[164,297,322,323]. Just as a pathology approach to adjusting to sequelae of SCI may overlook positive change and post-traumatic growth, it is important within a positive psychology framework to consider the potential problem of false hope. As Jha (2018) notes, "The demarcating line between offering over-optimistic and truthful hope is rather thin"(p. 1)[177].

With these considerations in mind we explore the experiences of a group of participants with SCI in South Africa given the opportunity to be part of a trial of a novel robotic technology. There is an important further contextual factor to consider in relation to this trial. Not only is the technology new, and currently expensive, the trial 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[15,27,231,324]. For most people who survive a SCI in these contexts, there may be some immediate acute care, but it is not uncommon for there to be no rehabilitative follow-up, for a range of reasons including overstretched health systems and unavailability of affordable accessible transport[15,253]. For a person with a SCI in South Africa to be part of a trial (even in a control group which does not use new technology like an exoskeleton) is unusual, and part of what becomes of interest here, apart from the new technology, is access to care which is not universally available, which may in itself have psychological meaning for participants[258].

6.2. Aims:

The aim of this qualitative chapter is to document a group of participants' (n=16) lived experience of participating in a pilot randomised control trial of two exercise-based interventions for individuals with SCI in Cape Town, South Africa. Detailed methods relating to participant recruitment, the rehabilitation interventions and data collection are contained in Chapter 2. Additional detail of the qualitative methods is provided below.

6.3. Methods

6.3.1 Data Collection:

All interviews were conducted by clinical psychologists at two time points, before participants started their respective intervention and six-months later after completing the intervention. Interviews lasted on average approximately 45-minutes. 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 as a result of the intervention or the interviews, or if they exhibited any signs of psychopathology. Pseudonyms have been used to protect participants' privacy.

6.3.2. Data Analysis:

Interviews were audio-recorded and transcribed verbatim. After reading and re-reading the transcripts, Thematic Analysis was performed where text was coded according to broad categories of meaning[218]. During a second round of coding, broad categories were refined into a detailed coding structure and categories. Categories were grouped into themes with all quotes being exclusive to one theme. The results pertaining to the experience of the exoskeleton are based on eight of the participants as the remaining eight in the ABT group had not yet used the device at the time of second interviewing.

The following strategies were used to improve the trustworthiness and credibility of the findings[325]: a member of the research team 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 subsample of interviews.

6.4. Results:

Thematic analysis identified four superordinate themes, namely: 1) participants' experience of their SCIs and life before entering the research programme, 2) reactions to entering and experiencing the research programme, 3) the complexity of hope, and 4) expectations and experience of the exoskeleton itself.

6.4.1. The experience of the SCI and life before entering the research study

All participants' injuries were traumatic in nature. The majority were able to recall vivid details of their accident, years after it had occurred:

> *James: "I was conscious through everything. You know when I went through the sun roof, I knew what was happening, I felt how I fell on my head, I heard my neck snap, it sounds like a stick, like a dry twig type of thing, everything dead immediately. So I knew exactly what was going on."*

Some participants expressed difficulty with sleeping or had experienced difficulty in the past due to flashbacks of their accidents:

> *William: "It brought back everything at once, it wasn't like piece by piece, it just hit me all at once. And I think for like two nights straight I struggled to sleep. I still kind of get nightmares sometimes now, but they are not as bad as they used to be. Like I always get put back in that seat because, I was sitting there for about half an hour before someone found me… Um, ja, I sometimes wake up, with a fright, like a scare. Because some nights I dream I am back sitting in that car"*

Most participants were prescribed anti-depressants after their injuries with some still remaining on their prescription:

Junior: "… I am still on it [anti-depressant]. From the day I broke my neck, I did go off of it for like a year, but I feel like I got more angry and irritable without it, than with it."

Participants described feelings of depression and anxiety. They spoke of "struggling" and "battling" against these emotions and how these feelings eroded their hope and optimism.

Mpho: "All of us have got this enemy from within, there's always this little voice inside you."

Mateo: "I find when I am alone, and I am sure all the guys are alone, just thinking to yourself, and then there is a mind wall, there, then it's up to you really. Am I going to slip backwards and get upset about things or, so I start thinking about the future and start getting excited about things."

In the acute setting, the prognosis of their recovery provided by medical professionals was often seen as pessimistic, with some participants feeling resentful at being given a poor prognosis:

Mpho: "I've been through hell, [laughs] I really have been through hell, this four years of my life was like, I really started to believe the doctors."

A lack of independence created frustration, which was a key source of negative emotions such as irritability and depression:

James: "I mean everybody gets depression now and then, you do get upset because you can't do certain things, you try to explain to somebody how to do something, and they just don't get it or they don't do the way you want it done."

Many participants were open about their experiences of suicidal thoughts:

Liam: "To be honest I have often, often, often thought I have had enough, I am going to take myself out. Um, my mother-in-law, told me don't ever think about something like that, just think what it would do to [daughter's name], and that's the only thing that's sort of, often has kept me here."

6.4.2. Reactions to entering and experiencing the research programme

Participation in this intensive and well-funded programme, whether in the RLT or the ABT group, was an unusual experience which was markedly different from their previous experience of rehabilitation. Participants explicitly expressed gratitude for being included in the intervention. As Ethan and Calvin put it:

Ethan: "I don't know of anyone who would have given me six months of three, or thrice-a-week, exercise rehabilitation, physical rehabilitation. So, I'm immensely grateful for that."

Calvin: "Well the programme is a very good thing as quite a lot of people cannot pay for this kind of a programme, to get involved in a way, it is something which everybody needs, because there are a lot of people who cannot afford to pay for it."

Participants also valued access to transport, which had been provided to facilitate their getting to and from the intervention. As Samuel noted, even if he could use public transport, it was too dangerous:

> *Samuel: "But it is too dangerous to take the train. What am I going to do if someone grabs my bag? There is not much I can do, is there?"*

The sense of being part of a group whose needs were being acknowledged and catered for helped engender an optimistic and grateful attitude:

> *Mpho: "And when I came in here as well. 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."*

For some participants, participating in the programme accorded with their pre-existing hope that they would improve in function and even, for some, that they would walk again. All participants had incomplete tetraplegia, which carried the possibility of an improved prognosis for a return of function. The open-ended nature of their diagnosis fuelled the drive to improve. They expressed motivation to pursue physical and emotional recovery, despite multiple years passing since their injuries:

> *James: "I made the decision, you know what you are going to stay in here and lead a comfortable life, or you can try and better yourself, but it is going to be very difficult, fortunately, fortunately I took the difficult road."*

> *Mateo: "I know it [walking] is going to happen, it is really just up to me. Especially with myself and my physicality and my, like I can move and I can feel a lot compared to other guys, I've got different advantages to what they have…"*

Prior to joining the programme, especially given transport challenges, most participants had been socially isolated. Simply meeting and being in regular contact with others with SCI was experienced as beneficial:

> *Mpho: "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, camaraderie, that peer-support and understanding."*

Seeing improvements in physical functioning during the intervention, regardless of whether in the RLT or ABT group, provided further motivation to attain greater goals. This was a source of excitement and optimism to participants:

> *Corey: "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 and stuff, then anything is possible, it's like, yes I was like watching movies and stuff like this, but now my life is like a reality."*

6.4.3. The complexity of hope

Participants universally shared hope for recovery, and many were focused on the possibility of regaining the ability to walk:

> *Siya: "I will stand up and walk, that's my greatest expectation. And it's, the science is there. There is some science. I will not, get off the programme until I walk. Laughs. I hope so."*

It seemed that to some participants the wish to walk, even where the clinical evidence suggested that this was very unlikely and had been communicated as such to them, was non-negotiable:

> *Mateo: "I know I will walk, I know I will, I expect to walk in five years, it has to happen."*

Other participants expressed the need to be more realistic:

> *Lucas: "Some people believe in faith, they can just get up and walk. Belief and faith is part of it, but you need to be realistic, you can't just get better after six months, because depending on the injury you might get better, but this is not going to be a miracle cure."*

> *Ethan: "You know, the thing is, because I have also been paralysed and in a wheelchair for ten years, I also know that there isn't some miracle cure to spinal cord injuries."*

6.4.4. Expectations and experience of the exoskeleton itself

Participants were interviewed both before and after using the exoskeleton. The differing time points provided insight into initial expectations in comparison to the actual experience of utilising the exoskeleton as a rehabilitative tool. Within the context of a middle-income country where there is limited access to rehabilitation, the prospect of an exoskeleton was met with considerable curiosity, regardless of which group the participants would be randomised into:

> *Mohammad: "When they advertised, they said the suit and I was thinking, great there's my opportunity now, to see what the suit can do and how it's going to benefit me."*

Exoskeletons have received considerable media coverage within the SCI community, potentially influencing the participants' views of the device, and raising expectations. Some participants were clear on the need to have realistic expectations:

> *Ethan: I don't want to try it out because it's a suit, I want to try it, really try it out because of my hips. I really feel my hips and my legs need that walking rotation, it's not because it's a suit that comes from Germany and everyone thinks it's so fantastic."*

Participants were long-term wheelchair users, the majority of whom had not been able to stand or take any steps for several years. Those who did have the experience of using the exoskeleton, experienced strong emotions, including exhilaration:

> *Mateo: "Exhilarating, there's the word. It is really exciting, it's emotional. A couple of times I mean I actually was walking, like I got emotional, just knowing I am walking*

> *again, it triggers it again, in your mind, you are actually doing this, and, as I say a couple of times, I got tearful, emotional, I am actually doing this, I was actually doing this. I am actually doing this."*

However, participants also spoke of feeling vulnerable while in the exoskeleton. They said being upright and out of a wheelchair was frightening and was associated with a fear of falling.

> *Jacob: "Um, what's the correct word? Fear? I was kind of scared, but also just, it's normal because somewhere in the back of my mind I still remember but it's like standing on the edge of a building looking down, if I were to describe it. Just a pit in your stomach, like wow ok, step back."*

Participants perceived several benefits of the exoskeleton, including improvements in muscle strength, spasticity, breathing, posture, mood, circulation and bowel function.

> *Corey: "The suit is also like helping with spasms and stuff, it's less spasms that you have, and it brings such amazing [benefits]to my health man, and so like the breathing stuff and she push me longer on distance and all that stuff because of the blood flowing and all. Because if you sit like this, all your organs is like this, but if you stand up then everything falls in place and you can like breathe and stuff, and so it's for me like a, it so a good thing that they invent. Whoever invent that thing … it's a cool thing man to for people like us in wheelchairs and … to have that moment … and see the other guys with the glints in their eyes and how they are liking it."*

6.5. Discussion:

All participants had experienced acute trauma as well as ongoing physical challenges in addition to social isolation and a lack of access to rehabilitation. For all of them, therefore, the mere participation in the trial offered a range of benefits far beyond the actual treatments offered. These included attention from a dedicated health care team, easy and regular access to services, and the sense of being part of a community of people with similar challenges. In this context, participants expressed gratitude for being in the study, and hope both for what this intervention could do and for the future.

The issue of hope in this context is, however, a complex one. First, from a clinical perspective it is not likely that the majority of these participants will walk again, but to many participants this belief in the possibility of walking seemed to be psychologically important and provided impetus and motivation to participate in the intervention. This creates something of a dilemma for a research team, especially as it has been established in related fields that reassurance and promises of recovery may be helpful in the short-term. However, unrealistic reassurance and lack of challenge to unrealistic expectations may be associated with disappointment and poorer long-term outcomes[326]. For clinicians, the path between supporting positive emotions (which may lead to positive outcomes) on the one hand, and confronting unrealistic hope (which may lead to negative outcomes) may be difficult. This difficulty is intensified when there is a commitment from the research team to engage participants as fully as possible within an intervention programme which requires considerable effort from participants. These issues take on particular salience in a context where a new technology may be associated with increased unrealistic optimism, and in a low-resourced context where, as our participant Ethan put it, “it’s a suit that comes from Germany and everyone thinks it’s so fantastic” – a reference to a widespread belief that technologies developed in high-income countries are invariably superior to what is generally available in countries with fewer resources. This belief may not always be well placed, with some technologies and assistive devices developed in wealthier countries being of limited use in low-income environments[327].

This does of course raise important ethical questions about a study such as ours and interventions of this nature. It was clear that part of the appeal of participation in this study was its provision of opportunities and infrastructure not available to our participants in the usual course of events. There is considerable debate in the literature as to whether studies which offer technologies and treatments which cannot be contextually sustained after the studies have been completed may in effect violate the rights of participants by offering and then withdrawing care[328,329]. In our study, the research team did everything possible to be honest with participants and not to promise more than could be delivered, but this does not absolve us from considering this question. In terms of follow-up after the end of the study itself, we provided a 12-week post-trial care period with the major goal being reintegration into the community. Provision was made for continued (income-level graded) subsidised access to physical rehabilitation and free psychological support after the study.

In some ways, the dilemmas associated with allowing for optimism and hope versus guarding against false hope are mirrored in the experiences of the exoskeleton itself. Participants expressed both wonder and exhilaration at use of the new technology, as well as fear of falling and further injury, an issue which had to be sensitively managed by the biokineticists on the project. There is very little research documenting the experience of using an exoskeleton, and though our study does go some way to filling the research gap, there is clearly much more data that needs to be collected on this issue.

Overall, our participants experienced benefits from both forms of intervention. Across the two interventions, though, was a context of care to which participants, sadly, were not accustomed. It is important that we follow up these particular participants in the contexts of their lives after the interventions were complete. It is also crucial that we and others in the field work to improve access to appropriate services for an often-neglected group of people who have experienced both acute trauma and the ongoing challenges of social isolation and lack of access to the best possible care.

CHAPTER 7

Clinical Insights & Conclusions

7.1. Introduction:

Barriers and delays are often present in the translation of scientific research into clinical practice. It has been reported that only 14% of scientific evidence is implemented into clinical practice and it takes, on average, 17 years for this to occur[330,331]. Fixsen et al. (2005) describes the various steps of knowledge translation. The first is passive in nature, called 'letting it happen', where research findings are written-up and published, allowing for diffusion into clinical practice. In the case of this SCI trial, this first step has been taken through the dissertation write-up and the publications/conference proceedings produced. The second step of knowledge translation is called 'helping it happen', which involves the provision of toolkits that aid in the efficient dissemination of research results[332]. One toolkit is the use of infographics, which are increasing in popularity due to their ability to convey complex research findings into an easily understood format[333]. In a *British Journal of Sports Medicine* editorial by Scott et al. (2016), the use of infographics was advocated for, with the authors suggesting that it would be beneficial if every research paper produced an accompanying infographic[334].

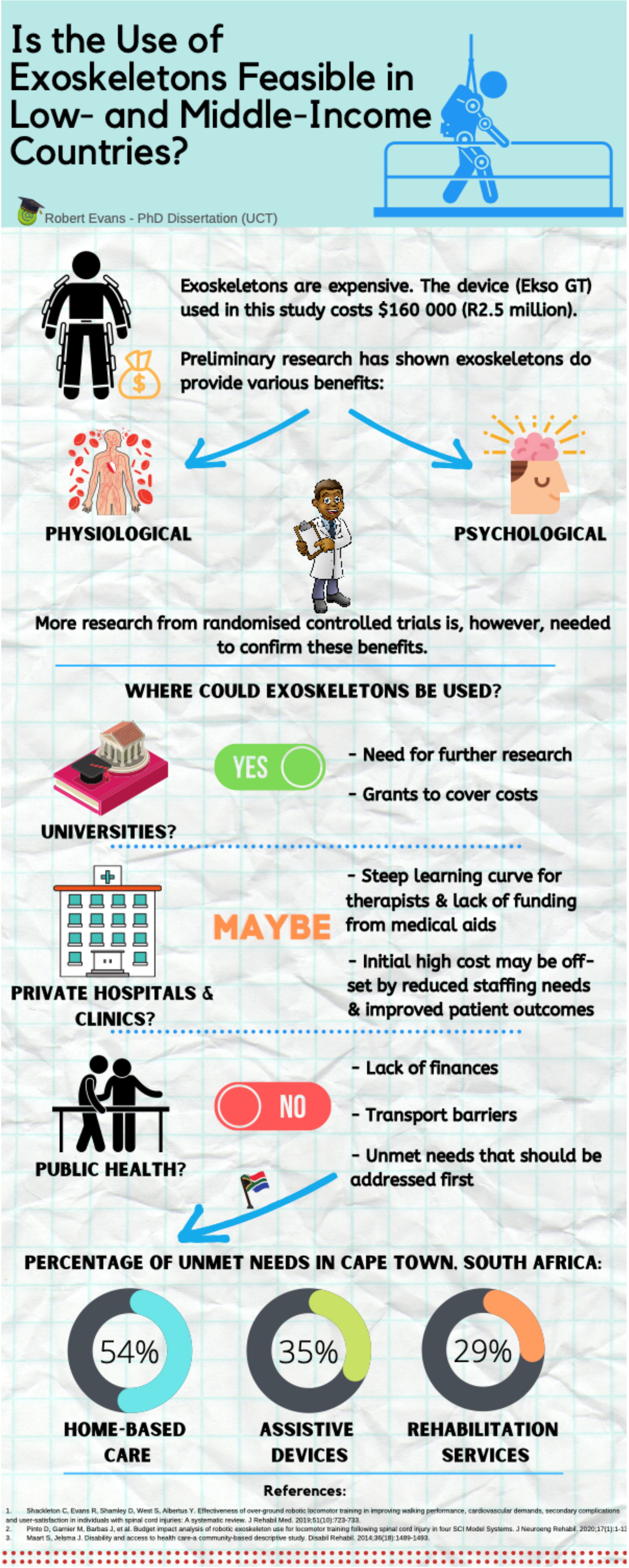
This chapter serves to help bridge the gap between scientific research and clinical practice, using the findings from this dissertation to provide recommendations for clinicians working with individuals with SCI. Below are the key clinical questions, which have risen from this dissertation and the current literature, summarised in the form of infographics.

7.2. Question 1:

Is the use of exoskeletons feasible in low- and middle-income countries?

Rehabilitation facilities in low- and middle-income countries strive to provide optimal care with limited resources[15]. Investing in new technologies such as an exoskeleton may improve patient outcomes, but could also compromise the financial sustainability of a facility[68]. A significant body of quasi-experimental research supports various physiological and psychological benefits to Robotic Locomotor Training, however, evidence from randomised controlled trials is limited[63]. With inconclusive efficacy, the cost-effectiveness of exoskeletons is yet to be established. Based on the experiences of this dissertation, the use of exoskeletons in low- and middle-income countries is currently limited to research settings and a minority of well-funded private institutions. The public health sector faces numerous challenges that need to be prioritized first before exoskeletons could potentially be introduced into standard of care practices[230].

The content of this infographic is based on Chapter 1 and 3 of this dissertation, with certain components being published in the *Journal of Rehabilitation Medicine*[63]. DOI: 10.2340/16501977-2601.


Is the Use of Exoskeletons Feasible in Low- and Middle-Income Countries?
Robert Evans - PhD Dissertation (UCT)
Exoskeletons are expensive. The device (Ekso GT) used in this study costs $160 000 (R2.5 million).
Preliminary research has shown exoskeletons do provide various benefits:
PHYSIOLOGICAL
PSYCHOLOGICAL
More research from randomised controlled trials is, however, needed to confirm these benefits.
WHERE COULD EXOSKELETONS BE USED?
UNIVERSITIES?
YES
- Need for further research
- Grants to cover costs
PRIVATE HOSPITALS & CLINICS?
MAYBE
- Steep learning curve for therapists & lack of funding from medical aids
- Initial high cost may be off-set by reduced staffing needs & improved patient outcomes
PUBLIC HEALTH?
NO
- Lack of finances
- Transport barriers
- Unmet needs that should be addressed first
PERCENTAGE OF UNMET NEEDS IN CAPE TOWN, SOUTH AFRICA:
54%
HOME-BASED CARE
35%
ASSISTIVE DEVICES
29%
REHABILITATION SERVICES
References:
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7.3. Question 2:

Can Robotic Locomotor Training improve fitness and cardiovascular health?

The beneficial effects of physical activity on cardiovascular function in individuals with SCI has been widely established[99]. Robotic Locomotor Training (RLT) provides a comparable stimulus to moderate-intensity exercise[94], however, novel benefits attributable to RLT are unclear[63]. Exercise performed whilst standing provides additional intensity to individuals with SCI due to the orthostatic stress involved[104]. Within this dissertation, cardiovascular benefits that were novel to the RLT group included, a lowering of resting heart rate, as well as a lowering of standing heart rate, which is indicative of improved orthostatic tolerance[268]. The cardiovascular benefits of RLT appear to plateau as the user's body adapts to the stimulus. This adaptation occurs through a learning effect as well as an increase in aerobic capacity[66]. Physical activity, regardless of the modality used, requires progressive increments in volume and intensity to generate physiological adaptation and improvements in cardiovascular function[335].

The content of this infographic is based on Chapter 4 of this dissertation, with certain components being published in the *Archives of Physical Medicine and Rehabilitation* (In Press).

Can Robotic Locomotor Training Improve Fitness and Cardiovascular Health?

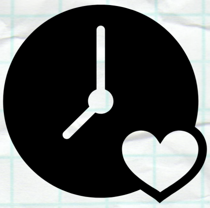
Robert Evans - PhD Dissertation (UCT)

LIKELY

Robotic locomotor training (RLT) has been shown to provide the same stimulus as moderate-intensity exercise. Improvements in cardiovascular function in this study were shown via:

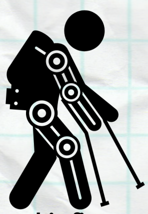
Lowered resting heart rate

Improved orthostatic tolerance (dizziness)



The cardiovascular benefits of RLT may plateau relatively quickly as the user adapts to the stimulus of walking. This plateau could possibly be caused by:

A learning effect that improves biomechanical efficiency



Improved aerobic fitness through regular robotic walking sessions

Long-term cardiovascular benefits can be achieved by increasing the volume and intensity of training. Progressive aerobic and resistance exercise that incorporates standing is key, whether the modality of an exoskeleton is used or not.

References:

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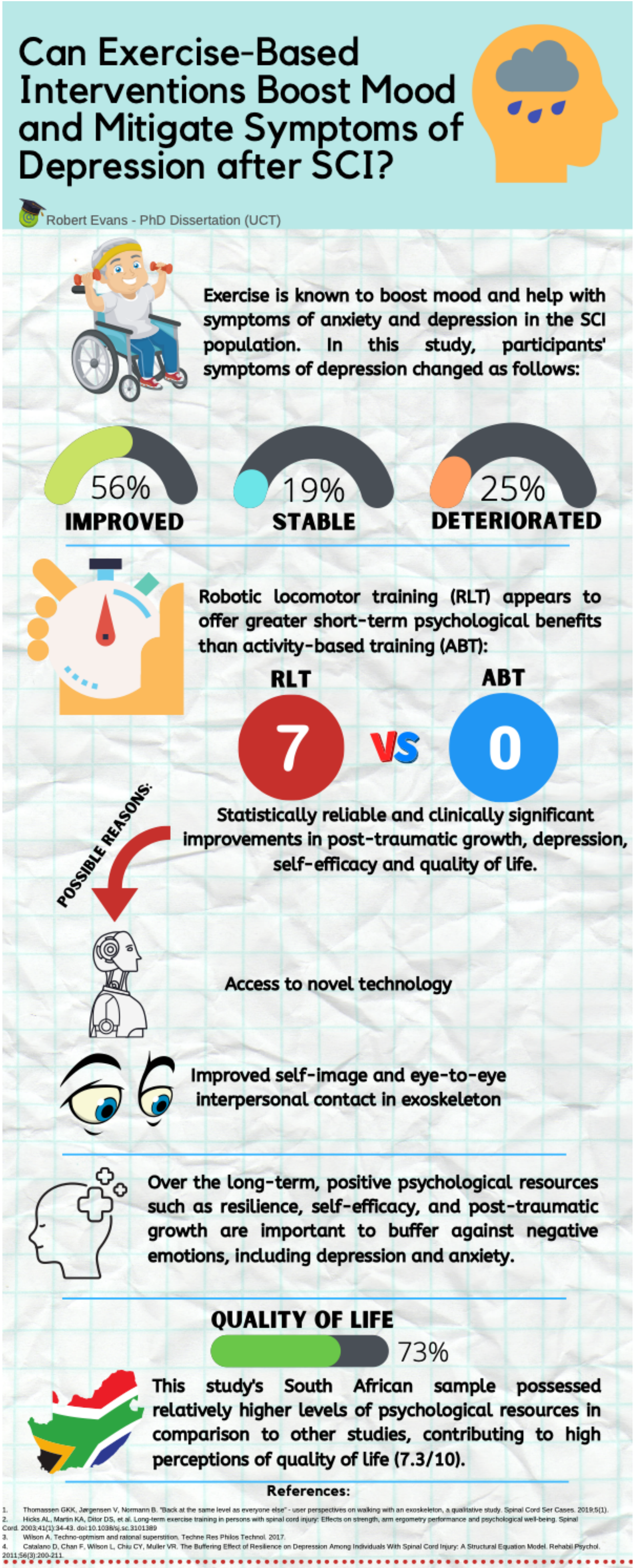
7.4. Question 3:

Can exercise-based interventions boost mood and mitigate depression after SCI?

Exercise provides a potent stimulus to aid in managing symptoms of anxiety and depression, both in the general and SCI population[162]. This finding is mirrored somewhat in the results of this dissertation, where the majority of participants (56%) demonstrated improvements in symptoms of depression. It is, however, important to recognize the unique responses of each individual, particularly the 25% of participants whose symptoms of depression deteriorated during the intervention. In this dissertation, Robotic Locomotor Training appears to provide greater short-term psychological benefits than Activity-based Training. This may be due to access to a novel technology as well as the unique attributes of improved self-image and eye-to-eye interpersonal communication provided by an exoskeleton[41]. Beyond the short-term use of an exoskeleton, psychological resources, which were high within this dissertation's sample, aid in maintaining high perceptions of quality of life.

The content of this infographic is based on Chapter 5 of this dissertation.


Can Exercise-Based Interventions Boost Mood and Mitigate Symptoms of Depression after SCI?
Robert Evans - PhD Dissertation (UCT)
Exercise is known to boost mood and help with symptoms of anxiety and depression in the SCI population. In this study, participants' symptoms of depression changed as follows:
56%
IMPROVED
19%
STABLE
25%
DETERIORATED
Robotic locomotor training (RLT) appears to offer greater short-term psychological benefits than activity-based training (ABT):
RLT
ABT
7
VS
0
Statistically reliable and clinically significant improvements in post-traumatic growth, depression, self-efficacy and quality of life.
POSSIBLE REASONS:
Access to novel technology
Improved self-image and eye-to-eye interpersonal contact in exoskeleton
Over the long-term, positive psychological resources such as resilience, self-efficacy, and post-traumatic growth are important to buffer against negative emotions, including depression and anxiety.
QUALITY OF LIFE
73%
This study's South African sample possessed relatively higher levels of psychological resources in comparison to other studies, contributing to high perceptions of quality of life (7.3/10).
References:
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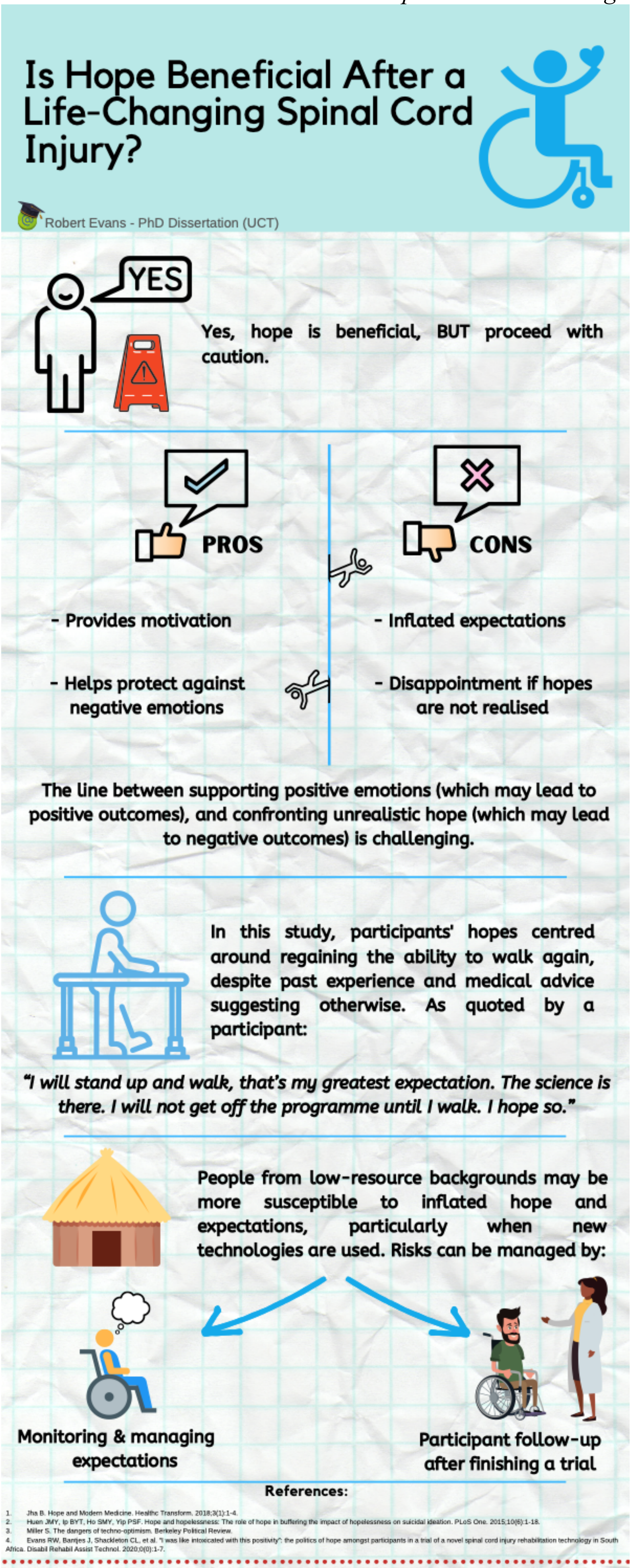
7.5. Question 4:

Is hope beneficial after a life-changing spinal cord injury?

Hope can be a controversial topic following a SCI. It is a part of human nature to hope for better outcomes after a life-changing injury[177]. This hope can serve as a source of motivation and support, but can also lead to unrealistic expectations and disappointment[146]. Within this dissertation, participant's hopes centered around regaining the ability to walk. Managing such hope is challenging for the clinician. It is important to not give unrealistic hope to an individual; however, it is equally important to not diminish intrinsic hope[168]. Individuals from low resource environments may be more susceptible to inflated expectations during novel interventions[164]. Monitoring of expectations both before and during an intervention is important, as well as follow-up once returning to the community.

The content of this infographic is based on Chapter 6 and Appendix 5 of this dissertation, with certain components being published in *Disability and Rehabilitation: Assistive Technology*[168]. DOI: 10.1080/17483107.2020.1815086


Is Hope Beneficial After a Life-Changing Spinal Cord Injury?
Robert Evans - PhD Dissertation (UCT)
YES
Yes, hope is beneficial, BUT proceed with caution.
PROS
CONS
- Provides motivation
- Inflated expectations
- Helps protect against negative emotions
- Disappointment if hopes are not realised
The line between supporting positive emotions (which may lead to positive outcomes), and confronting unrealistic hope (which may lead to negative outcomes) is challenging.
In this study, participants' hopes centred around regaining the ability to walk again, despite past experience and medical advice suggesting otherwise. As quoted by a participant:
"I will stand up and walk, that's my greatest expectation. The science is there. I will not get off the programme until I walk. I hope so."
People from low-resource backgrounds may be more susceptible to inflated hope and expectations, particularly when new technologies are used. Risks can be managed by:
Monitoring & managing expectations
Participant follow-up after finishing a trial
References:
1. Jha B. Hope and Modern Medicine. Healthc Transform. 2018;3(1):1-4.
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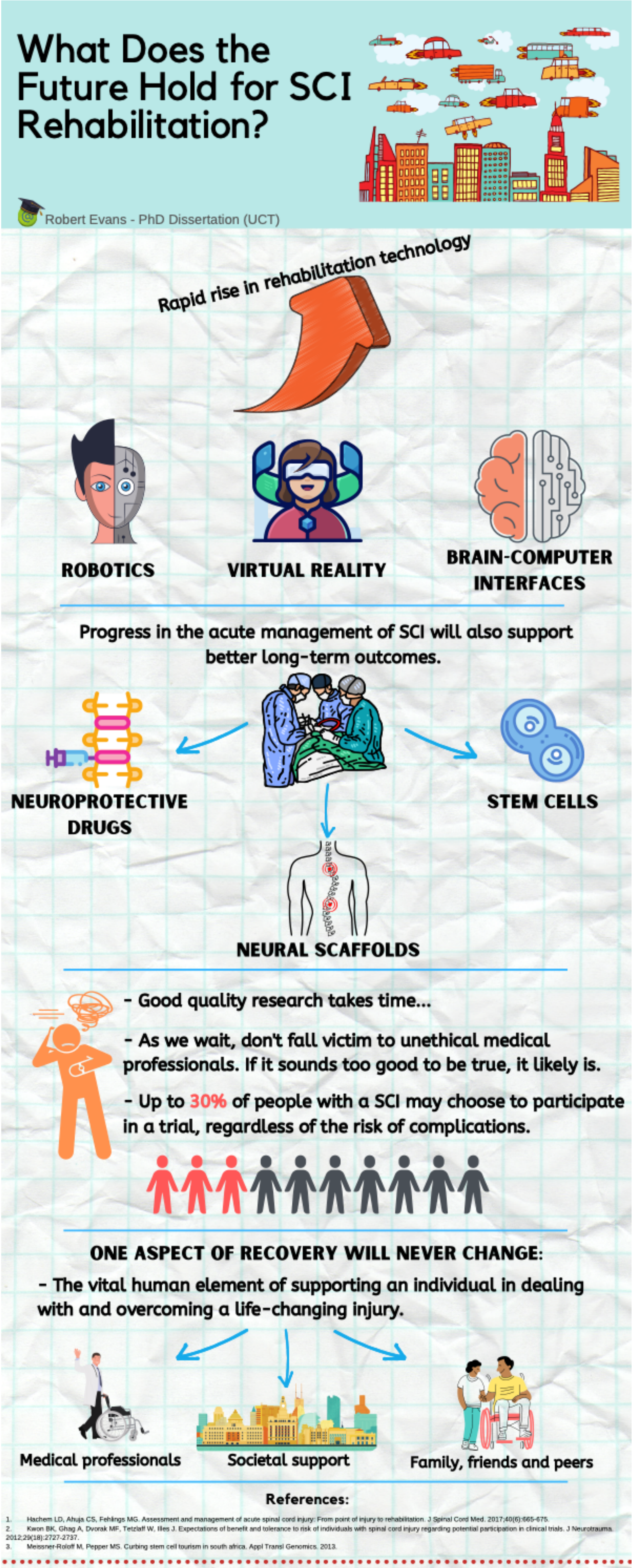
7.6. Question 5:

What does the future hold for SCI rehabilitation?

Significant progress in the rehabilitation of individuals with SCI has been made since Sir Ludwig Guttman brought about a paradigm shift in the 1940's. This shift improved the prevention and treatment of SCI related secondary complications, as well as introducing active rehabilitation and community reintegration[13]. Technology and modern medicine now play an integral role in improving the future of SCI treatment and rehabilitation. New rehabilitation modalities that have the potential to improve functional outcomes are being developed and introduced into the clinical setting. These modalities include robotics, virtual reality and brain-computer interfaces[23–25]. Preservation and regeneration of the injured spinal cord is also being targeted through procedures such as neural scaffolds, stem cells and neuroprotective drugs[6,22]. With these new possibilities and largely unknown efficacies, people with a SCI may be vulnerable to opting for unproven therapies at high costs[156,336]. The emotional aspect of dealing with a SCI will always be dependent on a strong support system both from family, friends and peers, as well as medical professionals[145].

The content of this infographic is based on Chapter 1 of this dissertation.


What Does the Future Hold for SCI Rehabilitation?
Robert Evans - PhD Dissertation (UCT)
Rapid rise in rehabilitation technology
ROBOTICS
VIRTUAL REALITY
BRAIN-COMPUTER INTERFACES
Progress in the acute management of SCI will also support better long-term outcomes.
NEUROPROTECTIVE DRUGS
STEM CELLS
NEURAL SCAFFOLDS
- Good quality research takes time...
- As we wait, don't fall victim to unethical medical professionals. If it sounds too good to be true, it likely is.
- Up to 30% of people with a SCI may choose to participate in a trial, regardless of the risk of complications.
ONE ASPECT OF RECOVERY WILL NEVER CHANGE:
- The vital human element of supporting an individual in dealing with and overcoming a life-changing injury.
Medical professionals
Societal support
Family, friends and peers
References:
1. Hachem LD, Ahuja CS, Fehlings MG. Assessment and management of acute spinal cord injury: From point of injury to rehabilitation. J Spinal Cord Med. 2017;40(6):665-675.
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7.7. Limitations of this Dissertation

In addition to the limitations discussed within each chapter, it is important to note that this dissertation is based upon a pilot study. Due to the nature of the study, the results discussed do not claim to report on the efficacy of different rehabilitation protocols, but should rather be interpreted as 'potential effectiveness'. The small sample size reduced the power to identify between-group changes. The lack of a sedentary control group, due to ethical considerations, created further difficulty in detecting differences between two exercise-based interventions.

Pilot and feasibility studies are synonymous with each other and play a crucial role in informing the design of future RCTs[337]. The research process and management of this pilot trial were deemed feasible to allow for a full-scale RCT, however, financial budgeting focusing on high costs for transport and human resources are needed to support an expansion of the trial. Follow-up assessment to evaluate participants' physical and psychological wellness once returning to their communities would add more insight, and a follow-up study is therefore planned.

7.8. Conclusion

A spinal cord injury is life-altering, creating a multitude of physical and psychological challenges. These challenges may be amplified by a lack of resources in low- and middle-income countries. Robotic Locomotor Training (RLT) is a novel rehabilitation modality which could enhance recovery following a SCI, however, the systemic effects of RLT are not yet adequately documented through large-scale trials. This pilot randomised control trial demonstrated that multiple challenges are present, particularly limited human and financial resources, when conducting a SCI trial in South Africa. Despite these challenges, the trial was successfully conducted. Exposure to the two exercise-based interventions, RLT and ABT, had notable cardiovascular and psychological effects on participants. The numerous significant findings from this pilot trial advocate for a full-scale RCT. Limitations in human and financial resources would, however, need to be overcome in order to support a large-scale RCT.

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APPENDIX

Appendix 1: Full schedule of variables collected during the 24-week rehabilitation intervention

	Screening	**Baseline**	**4 Weeks**	**6 Weeks**	**8 Weeks**	**12 Weeks**	**16 Weeks**	**20 Weeks**	**24 Weeks**
Informed Consent	X								X
Anthropometry	X								
ISNCSCI[1]	X								X
DEXA[2]	X								X
Bio, Physio, Doctor Screening[3]	X								
Psychological Interviews (Qualitative)	X		X		X	X	X	X	X
Psychometric Questionnaires[4]		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[5]		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[6]		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[7]		X		X		X			X

1. *ISNCSCI = International Standards for Neurological Classification of Spinal Cord Injury.*
2. *DEXA = Dual-Energy X-Ray Absorptiometry.*
3. *Bio = biokineticist, Physio = physiotherapist, Doctor = physician specialising in SCI. All three groups involved in final screening of participants and confirming inclusion and exclusion criteria.*
4. *Psychometric Questionnaires = CD RISC-25[190], Moorong Self-Efficacy Scale[191], Post-Traumatic Growth Inventory[192], Beck Depression Inventory[193], State-Trait Anxiety Inventor y[194].*
5. *6-minute walk test (6MWT) is exclusive to participants in the RLT group.*
6. *SCI-FAI = Spinal Cord Injury Functional Ambulation Index.*
7. *PARA-SCI = Physical Activity Recall Assessment for People with Spinal Cord Injury.*

Appendix 2: Ethical Approval

UNIVERSITY OF CAPE TOWN
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13 October 2016

HREC REF: 384/2016

Dr Y Albertus
Sport Science Institute
Human Biology

Dear Dr Albertus

PROJECT TITLE: THE EFFECT OF A ROBOTIC WALKING AND EXERCISE ACTIVITY-BASED REHABILITATION ON MUSCLE ACTIVITY, HEALTH-RELATED BENEFITS, FUNCTIONAL CAPACITY AND PSYCHOLOGICAL WELL-BEING IN INDIVIDUALS WITH SPINAL CORD INJURY (SCI) (PhD candidate- Mr R Evans)

Thank you for submitting your response to the Faculty of Health Sciences Human Research Ethics Committee received on 27 September 2016.

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 30th October 2017.

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 before the research may occur.

The HREC acknowledge that the student, Robert Evans 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

HREC 384/2016

Appendix 3: Informed consent

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

PRE-SCREENING
INFORMED CONSENT

<u>Research Project:</u>

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 eg. 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?

<u>In order to participate in this study,</u>

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 program 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 program.

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 a 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 BENFITS 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:

Primary Investigator (Supervisor)
Dr Yumna Albertus
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Phone: (021) 650 4560

Student Investigator
Robert Evans
Email: RobertEvansSA@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)

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

EXERCISE-BASED REHABILITATION PROGRAM 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 eg. 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 program. 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 program 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 program.

5) WHAT EXERCISE REHABILITATION WILL I NEED TO COMPLETE?

We have randomised you to perform the exercise-based rehabilitation program.

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

The activity-based rehabilitation program 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 program 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 12 and week 24 of your rehabilitation program. 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. 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 (DEXA) [20 minutes]

Your hip X-ray will be performed before and after your 24-week rehabilitation program. 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 hand held 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 program. 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 program 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, 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 program. I will be free to ask any questions about the equipment used.
2. **Rehabilitation program:** 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 program will be exercise-based activity.
3. **Testing procedures:** I understand that I will be need 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 program - the details of which have been explained to me.
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
Email: RobertEvansSA@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)

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)
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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 PROGRAM 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 eg. 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 program. 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 program 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 program.

5) WHAT EXERCISE REHABILITATION WILL I NEED TO COMPLETE?

We have randomised you to perform the robotic suit rehabilitation program.

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 program 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 12 and week 24 of your rehabilitation program. 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 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 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 program. 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 hand held 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 program. 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 program 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, 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 program. I will be free to ask any questions about the equipment used.
2) **Rehabilitation program:** 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 program will involve walking in a robotic suit.
3) **Testing procedures:** I understand that I will be need 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 program - the details of which have been explained to me.
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
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Student Investigator
Robert Evans
Email:
RobertEvansSA@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
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Prof. Marc Blockman
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Appendix 4: Therapy & Beyond Rehabilitation Programme

The programme is not linear in design but rather recursive, where progression is back and forth as needed, throughout the stages.

Stage I – *Prehabilitation*: The goal of Stage I is to prepare the participant for the intensive rehabilitation program 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.

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 fibers improves. This stage requires intense concentration from the participant to cognitively re-connect with the neurons that activate muscular contractions

***Stage III – Posture & Joint Stability*:** The body cannot move effectively through single muscle contractions, it must function as a kinetic chain. Correct posture and joint 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 stability in 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 independently weight bear.

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 function are of key importance.

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 their legs and arms, but do not have the strength, balance, proprioception, 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.

Stage VI – *Gait Training*: The objective of Stage VI is to provide advanced functional gait training for individuals 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 program in Stage VI 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 sport

Appendix 5: The development and piloting of a novel expectation visual analogue scale (VAS-Expectation) for use with spinal cord injured persons.

Introduction:

Chapter 5's psychometric findings were predominantly stable throughout the intervention. This finding is positive when considering the concern for mood disturbances, however, it also highlights a potential lack of sensitivity to detect differences between groups or over time. Within this appendix we explore the sensitivity and potential value of a novel scale to detect differences in participants expectations of physical function when entering a trial.

Individuals with a SCI may be considered to be physically and emotionally more vulnerable than the general population[338,339]. This statement and term of vulnerability is, however, met with opposition from some disability activists[340,341]. Ableism is a social bias generated from a set of beliefs that sees individuals with disabilities as 'other' and a diminished state of being human[342]. Labelling persons with a disability as vulnerable can be construed as a form of ableism, viewing the disabled as 'weaker than' or 'less capable' than their able bodied counterparts[343]. It is, however, undeniable that after a SCI most individuals will experience feelings of uncertainty, vulnerability and dependence[158,344]. Hope becomes an important factor to buffer against these emotions[154]. Experimental trials investigating new SCI treatments or rehabilitation modalities can provide hope within the SCI community[323,345]. These experimental trials currently include treatments such as stem cells, epidural electrical stimulation as well as rehabilitation modalities such as robotic exoskeletons[63,346].

Clinical interventions have the potential to improve mental health if favourable outcomes are experienced, however, they equally pose the threat of worsening mental health if expectations are not met[160]. This is particularly salient in the SCI population who have an increased prevalence of mood and anxiety disturbances compared to the general population[157]. Screening and monitoring of the psycho-social health of participants engaging in an SCI trial is thus important.

Psychometric questionnaires serve as a useful tool to quantify various psycho-social characteristics. They are generally used on large samples in order to gain enough power to be reliable and valid in their description of the sample[347,348]. Their utilisation on smaller clinical samples and sensitivity to identify small changes in individual psycho-social health can however be limited[349]. In these instances, visual analogue scales (VAS) provide a time efficient and potentially more sensitive alternative to psychometric questionnaires[350,351].

Time is restricted within the rehabilitation setting and prioritisation of resources fundamental to optimizing the care of patients[352]. Clinicians carry significant administrative burden behind the scenes of their patient contact time[353]. To avoid adding to this burden, the relative quick use of a VAS to gain insight into the psycho-social state of individuals holds value. The value of an instrument is evaluated through multiple constructs, one of which is the responsiveness of the instrument[354]. Responsiveness is an important component of an instrument's validation process and refers to its ability to detect changes in participant's responses to therapeutic interventions[355].

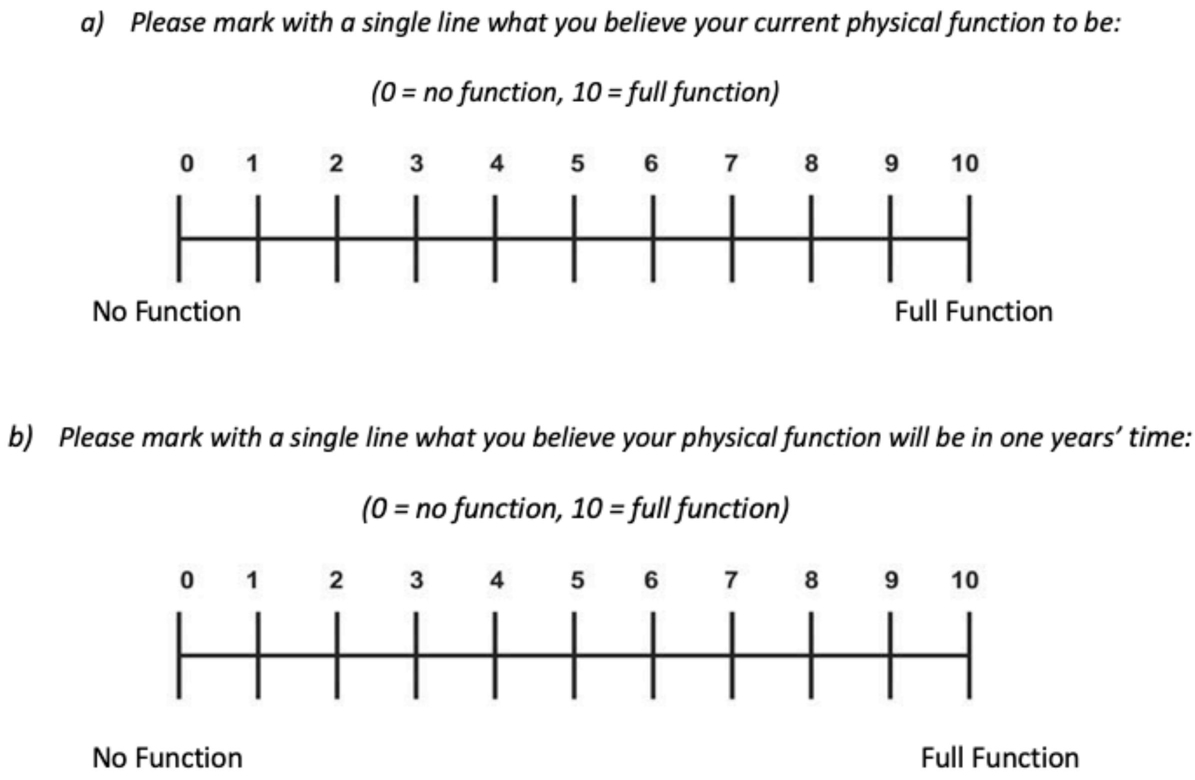
The aim of this appendix was thus to develop, pilot and assess the responsiveness of a new scale, the Expectation Visual Analogue Scale (VAS-Expectation). The scale was piloted in order to; 1) assist in initial individual screening for potentially harmful unrealistic expectations upon entering a clinical trial and, 2) describe the changes in these expectations in two intervention groups over the course of the trial.

Methods:

Detailed methods relating to participant recruitment, the rehabilitation interventions and data collection are contained in Chapter 2. Additional detail of the methods relating to this appendix is provided below.

Expectation Visual Analogue Scale (VAS-Expectation)

The VAS-Expectation (*Appendix Figure 1.1*) contained two ratings: 1) Current perceived physical function, and 2) Perceived physical function in one-year. Each rating is scored on a separate 100mm numeric VAS (0-10), with 0 representing no function and 10 representing full function. The participant is asked to mark a vertical line on the VAS that best represents their perceptions. Rating 1 is subtracted from rating 2 with the difference calculated providing an Expectation Score. This Expectation Score is representative of the individuals anticipated (positive) gain or (negative) loss of physical function in the coming year. Participants completed the VAS-Expectation at baseline, 6, 12 and 24-week time periods.



Appendix Figure 1.1: Expectation Visual Analogue Scale (VAS-Expectation) for a) current and b) future physical function (one years' time).

Data Analysis:

Data were analysed using statistical software (Statistica 13, Statsoft Inc. Tulsa. Oklahoma, USA & Prism 8, GraphPad, California, USA). Significance was accepted at a p value of < 0.05. Normality was assessed using Shapiro-Wilks tests. Two-way repeated measures analysis of variance (ANOVA) were used to evaluate changes between groups and over time in VAS-Expectation scores. Sphericity was not assumed when conducting the ANOVAs and hence p-values were adjusted according to the Greenhouse-Geisser correction. 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[216].

Responsiveness and sensitivity to change were estimated via the standardised response mean (SRM). SRM was calculated by dividing the mean change from baseline to 24-weeks by the standard deviation of the change[356] . In order to avoid over- or underestimation of the SRM, as suggested by Middel & van Sonderen (2002), the SRM was adjusted in relation to the correlation coefficient (r) between baseline and 24-week scores[357]. The SRM does not deviate when r = 0.5, however, underestimation can occur if r > 0.5 and overestimation can occur if r < 0.5. After adjustment, the SRM may be interpreted in the same manner as Cohen's d where 0.2-0.5, 0.5-0.8 and >0.8 represent small, medium and large effects, respectively[216]. The formula used for adjustment was[357]:

$$Adjusted\ SRM = \frac{\mathrm{SRM}\ /\ \sqrt{2}}{\sqrt{1-r}}$$

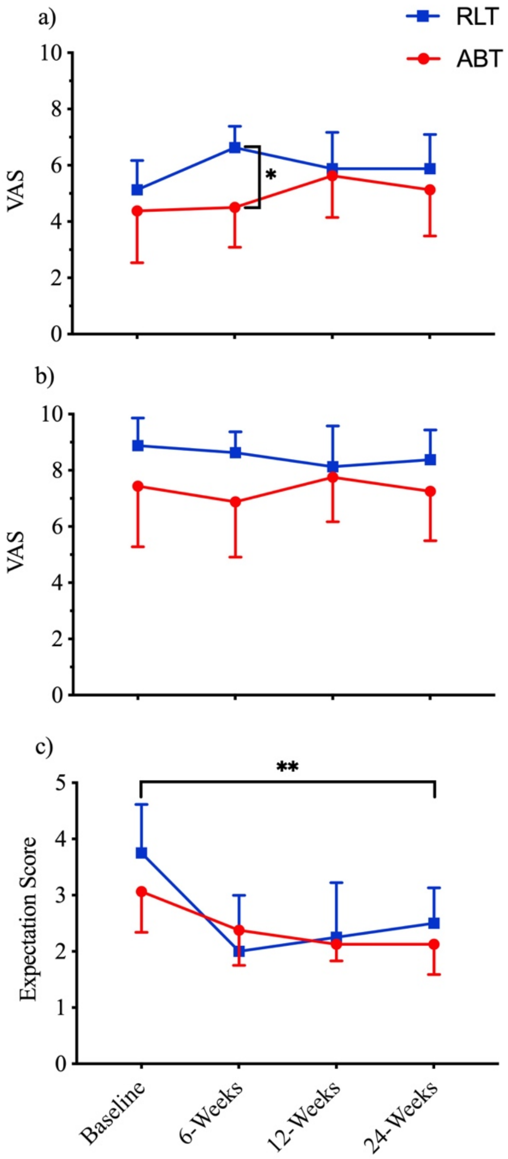
Results:

Responsiveness of the VAS-Expectation scale, evaluated through the SRM, demonstrated small effect sizes for the two subscales of a) current perceived function (SRM = 0.37) and b) perceived function in one-years' time (SRM = 0.29). The expectation score (one year minus current) demonstrated a medium effect size (SRM = 0.64) – Appendix *Table 1.1*.

Appendix Table 1.1. VAS-Expectation scores within the robotic locomotor training (RLT) and activity-based groups (ABT) across baseline, 6, 12 and 24-week time periods.

Variable	Time	RLT (n = 8)	ABT (n = 8)	Combined (n = 16)	SRM	p-value	Effect Size
Perceived physical function – current (VAS)	Baseline	5.13 ± 1.25	4.38 ± 2.20	4.75 ± 1.77		0.89	0.42
	6-Weeks	6.63 ± 0.92	4.50 ± 1.69	5.56 ± 1.71		0.04*	**1.56**
	12-Weeks	5.88 ± 1.55	5.63 ± 1.77	5.75 ± 1.61		0.99	0.15
	24-Weeks	5.88 ± 1.46	5.13 ± 1.96	5.50 ± 1.71	0.37	0.87	0.43
Perceived physical function – one year (VAS)	Baseline	8.88 ± 0.99	7.44 ± 2.16	8.16 ± 1.79		0.40	**0.86**
	6-Weeks	8.63 ± 0.74	6.88 ± 1.96	7.75 ± 1.69		0.16	**1.18**
	12-Weeks	8.13 ± 1.46	7.75 ± 1.58	7.94 ± 1.48		0.98	0.25
	24-Weeks	8.38 ± 1.06	7.25 ± 1.75	7.81 ± 1.51	0.29	0.47	0.78
Expectation Score (one year minus current VAS)	Baseline	3.75 ± 1.04	3.06 ± 0.86	3.41 ± 0.99		0.52	0.72
	6-Weeks	2.00 ± 1.20	2.38 ± 0.74	2.19 ± 0.98		0.91	0.38
	12-Weeks	2.25 ± 1.16	2.13 ± 0.35	2.19 ± 0.83		0.99	0.14
	24-Weeks	2.50 ± 0.76	2.13 ± 0.64	2.31 ± 0.70	0.64	0.76	0.53

Data shown as mean ± SD. ABT = activity-based training, RLT = robotic locomotor training. SRM = standardized response mean - adjusted according to r (Pearson correlation coefficient). p-value and effect size relate to difference between RLT and ABT at each time point. * $p \leq 0.05$. Bold represents large effect size.



Appendix Figure 1.2: a) Current perceived physical function b) One-year perceived physical function and c) Expectation score (one year minus current) of the RLT and ABT groups across baseline, 6, 12 and 24-week time periods. Bars denote mean ± SD. ABT = activity-based training, RLT = robotic locomotor training. *RLT > ABT; ** Time effect across RLT and ABT groups; $p < 0.05$.

Perceived physical function: current (*Appendix Figure 1.2a*) approached significance in both the time ($p = 0.07$) and time by group interaction ($p = 0.09$). At 6-weeks, perceived physical function: current (*Figure 7.2a*) RLT values (6.63 ± 0.92) were significantly higher ($p = 0.04$) than the ABT group (4.50 ± 1.69). Large effect sizes indicated that perceived physical function: one-year (*Appendix Figure 1.2b*) was higher in the RLT group at baseline (ES = 0.86) and 6-weeks (ES = 1.18). Perceived physical function: one-year (*Appendix Figure 1.2b*) approached significance in the group factor ($p = 0.10$). Expectation Scores (*Appendix Figure 1.2c*) significantly lowered over time ($p < 0.01$).

Discussion:

The main finding of this appendix is that the the VAS-Expectation is sensitive enough to detect differences over time and between RLT and ABT intervention groups, where RLT may elevate perceptions of physical function after 6-weeks.

The conceptualisation and piloting of the VAS-Expectation scale was inspired by the need for clinicians to, quickly and easily, gain insight into a participant's state of either optimism or pessimism about their recovery. Hope for recovery, based on Snyder's (1991) model, is a crucial motivating force driving the rehabilitation process[138]. Numerous studies have demonstrated high levels of hope and optimism in persons with SCI[144–147]. These observations of high hope are reinforced within this study whereby participants had raised expectations at the start of the study, with a baseline mean Expectation Score of 3.41 ± 0.99 across both groups. This score translates to an expectation from participants that their physical functioning would improve by 72% in one years' time.

Prior to the study, participants had experienced traumatic injuries, social isolation and a lack of access to rehabilitation[229]. These factors would, in combination with inherent hopefulness, raise the perceived benefit the interventions would offer[323]. Interestingly, at no point did expectations of recovery drop below a score of two, illustrating an enduring optimism bias amongst participants[358]. Initial high expectations were, however, lowered after 6-weeks with a mean Expectation Score across both groups of 2.19 ± 0.98, contributing to a significant time effect across the intervention ($p < 0.01$). The downward adjustment and rationalisation of participants' expectations may represent a confrontation with inflated hope caused by the novelty of the interventions and a movement towards more grounded optimism[177]. This rationalisation occurred without discussion and influence from the research team, however, future studies may need to address inflated expectations if they are identified as outliers within the sample.

The use of the Ekso GT exoskeleton within this study was novel to participants who had little access to outpatient care[15]. The introduction of new technology has the potential to create 'techno-optimism' where beliefs of a technology's efficacy may supersede available scientific evidence[164]. After 6-weeks, the RLT group using the exoskeleton, provided significantly ($p = 0.04$) higher scores for current perceived physical function (6.63 ± 0.92) compared to the ABT group (4.50 ± 1.69). This difference may in part be due to techno-optimism but is also likely a valid observation of how the act of therapeutic walking, after multiple years of being a wheelchair user, has the ability to improve perceptions of physical function[40].

The numerous findings relating to the VAS-Expectation scale discussed above are in contrast to Chapter 5's psychometric findings; which were largely stable and not sensitive to change over the course of the intervention. The ability of the VAS-Expectation to demonstrate a moderate expectation score SRM of 0.64 and detect differences both between groups and over time provides support for its sensitivity[357].

Limitations:

The responsiveness or sensitivity to change of the VAS-Expectation evaluated provides insight into a single psychometric property. The VAS-Expectation shows potential within this sample, however, the reliability and validity of the tool needs to be studied in much greater depth in order to determine the appropriateness of its use. A small sample size also limits the inferences that can be made from the significant results found.

Conclusion

In conclusion, this appendix introduces a basic tool (VAS-Expectation) for SCI research and clinical use. Within our sample, initial high expectations were lowered over the course of the intervention and the novel use of an exoskeleton temporarily increased perceptions of current physical function. Responsiveness of the VAS-Expectation is evident, however, further reliability and validity testing is required.

Appendix 6: Psychometric Questionnaires

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

Connor-Davidson Resilience Scale:

		not true at all (0)	rarely true (1)	sometimes true (2)	often true (3)	true nearly all the time (4)
1.	I am able to adapt when changes occur.	☐	☐	☐	☐	☐
2.	I have at least one close and secure relationship that helps me when I am stressed.	☐	☐	☐	☐	☐
3.	When there are no clear solutions to my problems, sometimes fate or God can help.	☐	☐	☐	☐	☐
4.	I can deal with whatever comes my way.	☐	☐	☐	☐	☐
5.	Past successes give me confidence in dealing with new challenges and difficulties.	☐	☐	☐	☐	☐
6.	I try to see the humorous side of things when I am faced with problems.	☐	☐	☐	☐	☐
7.	Having to cope with stress can make me stronger.	☐	☐	☐	☐	☐
8.	I tend to bounce back after illness, injury, or other hardships.	☐	☐	☐	☐	☐
9.	Good or bad, I believe that most things happen for a reason.	☐	☐	☐	☐	☐
10.	I give my best effort no matter what the outcome may be.	☐	☐	☐	☐	☐
11.	I believe I can achieve my goals, even if there are obstacles.	☐	☐	☐	☐	☐
12.	Even when things look hopeless, I don't give up.	☐	☐	☐	☐	☐
13.	During times of stress/crisis, I know where to turn for help.	☐	☐	☐	☐	☐
14.	Under pressure, I stay focused and think clearly.	☐	☐	☐	☐	☐
15.	I prefer to take the lead in solving problems rather than letting others make all the decisions.	☐	☐	☐	☐	☐
16.	I am not easily discouraged by failure.	☐	☐	☐	☐	☐
17.	I think of myself as a strong person when dealing with life's challenges and difficulties.	☐	☐	☐	☐	☐
18.	I can make unpopular or difficult decisions that affect other people, if it is necessary.	☐	☐	☐	☐	☐
19.	I am able to handle unpleasant or painful feelings like sadness, fear, and anger.	☐	☐	☐	☐	☐
20.	In dealing with life's problems, sometimes you have to act on a hunch without knowing why.	☐	☐	☐	☐	☐
21.	I have a strong sense of purpose in life.	☐	☐	☐	☐	☐
22.	I feel in control of my life.	☐	☐	☐	☐	☐
23.	I like challenges.	☐	☐	☐	☐	☐
24.	I work to attain my goals no matter what roadblocks I encounter along the way.	☐	☐	☐	☐	☐
25.	I take pride in my achievements.	☐	☐	☐	☐	☐

Moorong Self-Efficacy Scale:

Items Composing the Moorong Self-Efficacy Scale

1. I can maintain my personal hygiene with or without help.
2. I can avoid having bowel accidents.
3. I can participate as an active member of the household.
4. I can maintain relationships in my family.
5. I can get out of my house whenever I need to.
6. I can have a satisfying sexual relationship.
7. I can enjoy spending time with my friends.
8. I can find hobbies and leisure pursuits that interest me.
9. I can maintain contact with people who are important to me.
10. I can deal with unexpected problems that come up in life.
11. I can imagine being able to work at some time in the future.
12. I can accomplish most things I set out to do.
13. When trying to learn something new, I will persist until I am successful.
14. When I see someone I would like to meet, I am able to make the first contact.
15. I can maintain good health and well-being.
16. I can imagine having a fulfilling lifestyle in the future.

Post-Traumatic Growth Inventory:

Listed below are 21 areas that are sometimes reported to have changed after traumatic events. Please mark the appropriate box beside each description indicating how much you feel you have experienced change in the area described. The 0 to 5 scale is as follows:

0 = I did not experience this change as a result of my crisis
1 = I experienced this change to a very small degree
2 = a small degree
3 = a moderate degree
4 = a great degree
5 = a very great degree as a result of my crisis

	possible areas of growth and change	*0*	*1*	*2*	*3*	*4*	*5*
a.	my priorities about what is important in life						
b.	an appreciation for the value of my own life						
c.	I developed new interests						
d.	a feeling of self-reliance						
e.	a better understanding of spiritual matters						
f.	knowing that I can count on people in times of trouble						
g.	I established a new path for my life						
h.	a sense of closeness with others						
i.	a willingness to express my emotions						
j.	knowing I can handle difficulties						
k.	I'm able to do better things with my life						
l.	being able to accept the way things work out						
m.	appreciating each day						
n.	new opportunities are available which wouldn't have been otherwise						
o.	having compassion for others						
p.	putting effort into my relationships						
q.	I'm more likely to try to change things which need changing						
r.	I have a stronger religious faith						
s.	I discovered that I am stronger than I thought I was						
t.	I learned a great deal about how wonderful people are						
u.	I accept needing others						

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

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