The effects of robot assisted gait training on temporal-spatial characteristics of people with spinal cord injuries: A systematic review

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Context: Robotic assisted gait training (RAGT) technology can be used as a rehabilitation tool or as an assistive device for spinal cord injured (SCI) individuals. Its impact on upright stepping characteristics of SCI individuals using treadmill or overground robotic exoskeleton systems has yet to be established.

Objective: To systematically review the literature and identify if overground or treadmill based RAGT use in SCI individuals elicited differences in temporal-spatial characteristics and functional outcome measures.

Methods: A systematic search of the literature investigating overground and treadmill RAGT in SCIs was undertaken excluding case-studies and case-series. Studies were included if the primary outcomes were temporal-spatial gait parameters. Study inclusion and methodological quality were assessed and determined independently by two reviewers. Methodological quality was assessed using a validated scoring system for randomised and non-randomised trials.

Results: Twelve studies met all inclusion criteria. Participant numbers ranged from 5-130 with injury levels from C2 to T12, American Spinal Injuries Association A-D. Three studies used overground RAGT systems and the remaining nine focused on treadmill based RAGT systems. Primary outcome measures were walking speed and walking distance. The use of treadmill or overground based RAGT did not result in an increase in walking speed beyond that of conventional gait training and no studies reviewed enabled a large enough improvement to facilitate community ambulation.

Conclusion: The use of RAGT in SCI individuals has the potential to benefit upright locomotion of SCI individuals. Its use should not replace other therapies but be incorporated into a multi-modality rehabilitation approach.

Keywords: spinal cord injury, robot assisted gait training, overground gait, treadmill gait, temporal-spatial characteristics.

Subject classification codes: 130.160 Physical Medicine and Rehabilitation / Locomotor Training

Introduction

An estimated 500,000 spinal cord injuries (SCIs) occur worldwide every year.[1] The most life-impacting result of a spinal cord injury is paralysis or mobility impairment.[2-5] In most cases of SCI, the subsequent requirement of a wheelchair enforces the user to adopt a seated position from which activities of daily living, social interaction and mobility are undertaken.[6, 7] A number of SCI comorbidities are negatively impacted by a continuously seated posture and a less active lifestyle; reduced bone mineral density,[8, 9] increased chance of pressure sores,[10] reduced respiratory capacity,[6, 10] increased risk of coronary heart disease[11] and bladder and bowel dysfunction.[12] These sequelae, along with a reduced capacity for mobility, have a direct impact on the quality of life of SCI individuals.[13, 14] There is currently no treatment that can completely restore motor and or sensory function after an SCI.[15] The primary goal of rehabilitation must therefore be to improve the quality of life for SCI individuals by attenuating the deleterious consequences of the associated comorbidities.[16]

Upright mobility may have a beneficial effect on a number of SCI comorbidities, including those listed above,[13, 17] therefore upright locomotor training can be an effective component of physical rehabilitation for patients with a number of neurological injuries and disorders (including stroke, multiple sclerosis, cerebral palsy and SCI).[18] In incomplete spinal cord injured (iSCI) individuals, locomotor training has the potential to facilitate improved functional ambulation by driving neural plasticity at the spinal level, through afferent feedback to central pattern generators.[19] Although voluntary movement below the level of lesion in complete spinal cord injured (cSCI) individuals cannot be recovered, the negative effects of being chair- or bed-bound are temporarily reduced through upright stepping.[19] There are currently a number of locomotor training methods available to SCI individuals; these include body weight support treadmill training or overground gait training[20] with either manual assistance from therapists, functional electrical stimulation, robotic assisted gait training (RAGT) or a combination of these to facilitate stepping.[3, 7, 15, 21-23] A number of RAGT systems have been developed, both treadmill-based and overground.[24]

Limited information is available regarding physiotherapeutic gait improvement programmes[25] and the prescription of RAGT in SCI rehabilitation in the UK. The clinical guidelines provided by the UK's National Spinal Cord Injury Strategy Board and the National Health Service (NHS) Clinical Advisory Group only detail care from pre-admission to acute rehabilitation (2010). Other guidelines provided by various clinical bodies advise on pressure ulcer management,[26] movement and handling of individuals with SCI[27] and guidance on standing post SCI.[27] Information linked directly to the use of RAGT is limited to NICE medtech innovation briefings (MIB93)[28] and in the NICE clinical guidelines for stroke rehabilitation in adults (CG162) where electromechanical gait training is advised as part of research studies.[29] In conjunction with the limited information available from formal guidelines, there is no consensus among practitioners and clinical researchers regarding the efficacy of RAGT[2] and which types of RAGT system are most beneficial for the user. Thus it is difficult to determine which systems will provide the most appropriate treatment for each individual based on their clinical need and associated comorbidities.

A number of different RAGT systems have become commercially available and others are in development. The choice of system is often governed by availability, with the main considerations centred around user safety and the users' current capacity. Although these considerations are of the utmost importance, the potential exists for different types of RAGT systems to be more appropriate for use with specific populations due to the nature of an individuals' injury and the clinical goals of the locomotor training. Therefore, the aim of the current systematic review was to identify if overground and treadmill-based RAGT systems produced different upright stepping characteristics in SCI populations. It is acknowledged that most facilities will only possess a single RAGT system but will treat a broad spectrum of patients. Rehabilitation centres and healthcare professionals need evidence-based information to make the most suitable choice when purchasing rehabilitation equipment. A secondary aim was to identify any differences in the use of RAGT systems for cSCI and iSCI populations. The final aim was to identify if an overground or treadmill-based RAGT system resulted in greater improvements in functional gait outcome measures in SCI individuals.

Overground RAGT requires balance and postural control to facilitate ambulation unlike treadmill-based RAGT systems where individuals can rely on the body weight support component of the system to facilitate standing.[21] Based on this principle, the primary hypothesis of this review was that overground RAGT systems would facilitate the appearance of more natural upright stepping in SCI individuals than treadmill-based RAGT systems. The secondary hypothesis was that overground systems would be most effective in a rehabilitation environment for iSCI individuals based on the training principles of specificity, repartition and problem solving in motor learning[2, 30, 31] and that cSCI individuals would receive the same benefits from both overground and treadmill-based RAGT. The final hypothesis was that overground RAGT training would result in improvements in functional gait outcome measures including greater distance walked in the six-minute walk test (6MWT) and faster times in the ten meter walk test (10MWT).

Methods

A systematic computer-based search of the literature was conducted to identify studies using RAGT devices with SCI populations. Titles and abstracts were screened by two independent reviewers using pre-defined inclusion and exclusion criteria. Quality assessment of the included papers and data extraction were completed by the same independent researchers. Upright stepping parameters were identified as walking speed, step length, cadence, stride width, toe clearance height, duration of gait cycle, duration of stance phase and duration of swing phase.[32, 33]

Search Strategy

A search of the literature was performed for the period of January 1990 to May 2015 in the following databases: PubMed (Medline), Web of Science (Thomson Reuters), Physiotherapy Evidence Database (PEDro, Centre of Evidence-Based Physiotherapy) and the Cochrane Library (Cochrane Controlled Trials Register, Wiley Online Library). A manual search of reference lists of relevant reviews and included studies was also conducted by the same single reviewer. The search strategy was devised using the PICO (Population, Intervention, Comparison and Outcome) methodology.[34] This methodology allows the search strategy to be formulated by identifying search terms under one of the four headings listed (Table 1). Key words and phrases were combined from the four categories using Boolean operators (AND, OR, NOT) to search each database; MeSH (Medical Subject Headings) terms were used to search PubMed and the Cochrane Library. Using the inclusion/exclusion criteria, two researchers completed an independent screen of the collated publications to identify eligible papers based on their titles, key words and abstracts. A consensus method was used to agree the preliminarily accepted studies[35]; full-text copies of papers were obtained and reviewed independently against the inclusion and exclusion criteria by the same two researchers.

Table 1. Search terms and phrases associated with each variable of the PICO methodology used in the search strategy. The Boolean operator OR was used between terms in each column and the term AND was used between columns.

Population	Intervention	Comparison	Outcome
Spinal cord injury / injuries	Lower extremity gait	Treadmill	Walking
Spinal fractures	lower limb gait	Overground	Unaided gait / walking
SCI	gait ataxia	Complete SCI	Gait / walking endurance
Paraplegia / paraplegic	Lower extremity robotics	Incomplete SCI	Temporal-spatial parameters: Speed / velocity Cadence / step rate Step / stride length
Quadriplegia / Quadriplegic	lower limb robotics	Physical therapy	Robotic assisted independence
Paralysis	Motorised / robotic rehabilitation	Gait training	Reduced impairment to body function
	Motorised / robotic physical rehabilitation		Self-reported quality of Life
	Motorised / robotic medicine		Spasticity
	Motorised / robotic gait		ROM / range of motion
			FIM / functional independence measure

Inclusion and exclusion criteria

The inclusion/exclusion criteria was formulated using the same PICO methodology.[34]

Inclusion

Studies were included if:

- The population consisted of adult (18+ years) human participants with at least one group of SCI individuals (cervical, thoracic or lumbar). Studies with SCI individuals with either complete or incomplete lesions with an A – D American Spinal Injury Association (AISA) Impairment Score[4] were accepted.
- They used any overground or treadmill-based robotic locomotor training system with a primary focus on gait function in or out of the assistive device.

- Comparisons were made between: conventional therapies and robotic locomotor systems, overground systems and treadmill-based systems or, cSCI populations and iSCI populations.
- Temporal-spatial gait parameters were reported. Studies may also have included variables related to quality of life, social participation, range of motion, balance, spasticity, kinematics and/or kinetics and subjective independence measures.

All forms of study design were included apart from case reports or case series in order to maximise the data available.

Exclusion

Studies were specifically excluded if:

- The focus was on populations of stroke or hemiplegia patients or if comparisons were made between any populations other than able-bodied and SCI individuals.
- They used only body weight support systems or orthotics with no robotic limb driving component or used functional electric stimulation in conjunction with RAGT.
- The primary outcome measure was cardio respiratory or related to bone mineral density.

Data Extraction

Data were extracted from each study under seven categories by the lead researcher, reference information, study design, population, intervention, comparison groups, outcome measures and results. Reference data included the year of publication, country of origin and the journal name. Population was inclusive of participant sex, mean age, injury level, American Spinal Injury Association Impairment Scale classification (AIS), time since injury, sample size, sample drop out and sample size using RAGT. Intervention recorded the device(s) used, session duration and frequency and training walking speed. Comparison groups detailed which comparisons were made by each study; either population to population, intervention types or both. The primary outcomes extracted from each study were walking speed, temporal-spatial parameters and functional walking test data. Secondary outcomes were the Functional Independence Measure-Locomotor section (FIM–L),[36] Lower Extremity Motor Score (LEMS)[37] and the Walking Index for Spinal Cord Injury (II) (WISCI-II).[38]

Quality Assessment

Each study was evaluated using a checklist devised to assess the methodological quality of randomised and non-randomised studies.[39] The checklist comprised of 27 questions over five sections: reporting, external validity, internal validity - bias, internal validity – confounding and power. Each question was scored out of one except questions five and 27 which were scored out of two and five respectively, with a maximum score of 32 possible. The higher the score the higher the quality of the study. Each study was assessed independently by two researchers and discrepancies were resolved by discussion.

Results

Search Results

The initial search returned 3252 studies (PubMed 1843, Web of Knowledge 1314, Physiotherapy Evidence Database 0 and Cochrane Library 95). Duplicate studies (396) were removed leaving 2856 papers for the first stage of review. After the initial review process based on title, keywords and abstracts 25 studies remained. A single study was identified in manual searches of the reference sections of pertinent studies. Full text copies of the remaining 25 studies were obtained for evaluation against the full inclusion exclusion criteria (Figure 1). Three of the studies were identified to have been based on the same cohort with one of the studies published prior to study completion as a preliminary report; this study was excluded from this review. The remaining two studies were included as they focused on different aspects of gait and upright stepping using the same participant cohort. A total of twelve studies were included in the final analysis.

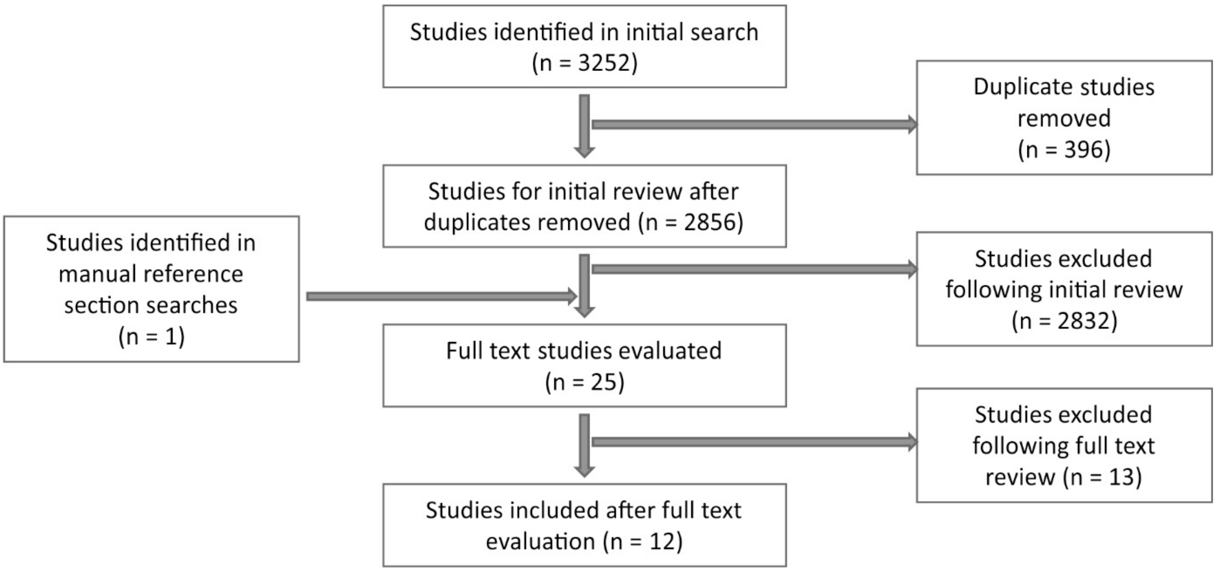

Figure 1. Search methodology and results PRISMA flowchart.

Included studies

Descriptive data of the included studies are reported in Table 2. There was a sum of 521 participants; 505 participants were SCI individuals and the remaining 16 were able-bodied individuals. The number of participants recruited ranged from five[40] to 130.[41] Eight of the studies included participants with American Spinal Injury Association (ASIA) scores C and D.[21, 41-47] Hornby *et al*.[45] also included SCI individuals with ASIA B and Benito-Penalva *et al*.[41] included participants with ASIA A and B. The remaining three studies only included participants with ASIA levels A – B.[40, 48, 49] The injury level of participants recruited ranged from C1 to L3 although one study did not report the injury levels included.[41]

Table 2. Study characteristics and population data for included studies.

			Population								
Study	Study type	Country of origin	Sample size (N)	RAGT users (N)	Non-RAGT users / Controls (N)	Drop out (N)	Sex	Mean age (Years)	ASIA	Injury level	TSI (years)
Alcobendas-Maestro (2012)	RCT	Spain	80	40	(40) SCI	5	M / F	47	C-D	C2-T12	0.25 - 0.5
Arazpour (2013)	CT Cross-over	Iran	5	5	(5) SCI	0	M / F	27	A-B	T6-T12	0.75 - 4.25
Arazpour (2014)	CT	Iran	7	7	(3) AB	0	M / F	28	A-B	T6-T12	0.75 - 4.25
Benito-Penalva (2012)	Longitudinal	Spain	130	46	(84) SCI	25	M / F	45	A-D	NR	NR
Esclarin (2014)	Randomised Open Control	Spain	88	44	(44) SCI	5	M / F	42	C-D	C2-L3	0.3 - 0.4
Nooijen (2009)	RCT	USA	85	12	(39) SCI (10) AB	24	M / F	38	C-D	C3-T10	>1
Field-Fote (2011)	RCT	USA	74	15	(59) SCI	10	M / F	41	C-D	C3-T10	>1
Fineberg (2013)	Cross Sectional	USA	9	6	(3) AB	0	M / F	44	A-B	T1-T11	6.25
Hornby (2005)	RCT	USA	35	10	(25) SCI	5	NR	NR	B-D	T10 ↑	<1
Labruyère (2014)	Randomised Cross-over	Switzerland	9	9	(9) SCI	1	M / F	59	C-D	C4-T11	>1
Nui (2014)	CT	USA	40	20	(20) SCI	0	M /F	46	B-D	T10 ↑	8.2
Varoqui (2014)	CT	USA	30	15	(15) SCI	0	M / F	48	C-D	T10 ↑	9.9

AB = Able-Bodied, ASIA = American Spinal Injury Association, CT = Controlled Trial, NA = Not applicable, NR = Not Reported, RCT = Randomised Controlled Trial, SCI = Spinal cord injury, TSI = Time since injury.

Excluded studies

Thirteen studies were excluded from this review based on the full text review process. Eight of the excluded studies were case series and three studies had no temporal spatial parameters reported. One study was excluded as no RAGT system was used and another was only a preliminary report of the work by Field-Fote and Roach[44] and Nooijen *et al*.[7]

Quality assessment

A quality assessment tool designed to evaluate randomised and non-randomised trials was used to assess study quality for this review as few randomised control trials have been completed in this subject area and none were identified using overground RAGT systems. The twelve studies included in the current review were independently quality assessed by both reviewers; after the initial review process differences in quality assessment scores were discussed and a consensus was reached. Table 3 presents the results of this assessment and overall scores for each study. The median total score for the 11 studies was 24 out of 32. The larger randomised controlled trials received the higher scores. The study by Esclarín-Ruz *et al*.[43] received the highest score of 25 and the lowest score of 13 was attributed to the study by Hornby *et al*.[45] The majority of studies performed poorly in reporting adverse events and in all three questions related to external validity. The three overground RAGT studies scored poorly in internal validity-confounding and power relative to the other studies.

Table 3. Methodological quality assessment scoring using an assessment tool for randomised and non-randomised trials (Downs & Black, 1998).

Study	Reporting										External Validity			Internal Validity - Bias							Internal Validity - Confounding						Power	Total Score
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	
	Hypothesis / Aims	Outcomes	Patient Information	Interventions	Principle confounders	Findings	Variability Estimates	Adverse Events	Withdrawals	Exact Probability	Represents Population Asked	Represents Population Included	Represents Facilities	Participant Blinding	Researcher Blinding	Data Dredging Clear	Follow up Adjustments	Appropriate Statistics	Intervention Compliance	Validity & Reliability	Participant Groups From Same Population	Recruitment Groups & Time Periods	Randomisation	Hidden Randomisation	Confounding Adjustment	Withdrawal Accounted for	Power	
Alcobendas -Maestro (2012)	**1**	**1**	**1**	**1**	**1x**	**0**	**0**	**0**	**1**	**1**	**1**	**1**	**0**	**0**	**1**	**0**	**1**	**1**	**1**	**1**	**1**	**1**	**1**	**0**	**1**	**0**	**5**	**23**
Arazpour (2013)	1	1	1	1	1x	1	1	0	1	1	0	0	0	0	0	0	1	1	1	0	0	1	0	0	1	1	3	18
Arazpour (2014)	**1**	**1**	**1**	**1**	**0**	**1**	**0**	**0**	**1**	**1**	**0**	**0**	**0**	**0**	**0**	**0**	**1**	**1**	**1**	**1**	**1**	**0**	**0**	**0**	**0**	**1**	**2**	**15**
Benito-Penalva (2012)	1	1	0	1	1x	1	1	0	0	1	1	1	0	0	0	0	1	1	1	1	1	1	1	0	1	0	5	22
Esclarin (2014)	**1**	**1**	**1**	**1**	**2**	**1**	**1**	**0**	**0**	**1**	**1**	**1**	**0**	**0**	**1**	**0**	**0**	**1**	**1**	**1**	**1**	**1**	**1**	**0**	**1**	**1**	**5**	**25**
Nooijen (2009)	1	1	1	1	2	1	0	1	0	1	0	0	0	0	0	0	1	1	1	1	1	1	1	0	1	1	5	23
Field-Fote (2011)	**1**	**1**	**1**	**1**	**0**	**1**	**1**	**1**	**1**	**1**	**0**	**0**	**0**	**0**	**0**	**0**	**1**	**1**	**1**	**1**	**1**	**1**	**1**	**0**	**1**	**1**	**5**	**23**
Fineberg (2013)	1	1	1	1	0	1	1	0	1	0	0	0	0	0	0	1	0	1	1	1	1	0	0	0	0	1	2	15
Hornby (2005)	**0**	**1**	**0**	**1**	**0**	**0**	**0**	**0**	**0**	**1**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**1**	**1**	**1**	**1**	**1**	**0**	**0**	**0**	**5**	**13**
Labruyèrel (2014)	1	1	1	1	2	1	1	0	0	1	0	0	0	0	1	0	0	1	1	1	1	1	1	0	0	0	3	19
Nui (2014)	**1**	**1**	**1**	**1**	**2**	**1**	**1**	**0**	**0**	**1**	**0**	**0**	**0**	**0**	**0**	**1**	**1**	**1**	**1**	**1**	**1**	**1**	**1**	**0**	**1**	**1**	**5**	**24**
Varoqui (2014)	1	1	1	1	2	1	1	0	0	1	0	0	0	0	0	1	1	1	1	1	1	1	1	0	1	1	5	24

1 = Yes, item addressed appropriately, 0 = No, item not addressed or unable to determine. Q5 1x = Partially addressed, 2 = item addressed appropriately

Interventions

Table 4 presents intervention information. Only three of the studies included in this review examined overground RAGT systems , one used the ReWalk^{TM} (ARGO Medical Technologies Ltd., Yokneam, Israel)[49] a commercially available overground RAGT system and two used a custom-built powered gait orthosis.[40, 48] Nine of the studies included in this review used the Lokomat® (Hocoma AG, Volketswil, Switzerland), a commercially available treadmill-based RAGT system. The number of sessions each participant received using the RAGT system ranged from 11 to 60 across four to 24 weeks (Table 4). Walking speeds of the RAGT systems were set relative to the participant's capacity in eight of the twelve included studies. Two of the studies selected specific speeds, 1.5 and 2.0 km/h,[41, 45] and one of the studies did not report training speed. Population and intervention comparisons were made across the different studies, three studies compared RAGT use in SCI individuals to able-bodied controls[7, 48, 49] and two of these studies investigated overground RAGT systems. No studies were found that reported a direct comparison between overground RAGT and treadmill-based RAGT systems.

Table 4. Intervention data for included studies, detailing RAGT device used, outcome measures and training protocol parameters.

Study	Device	Total Number of session	Duration (weeks)	Training Speed	Control - Comparison Group	Outcome Measures
Alcobendas-Maestro (2012)	Lokomat®	40	8	NR	SCI - OGT	10mWT, 6MinWT, FIM-L, WISCI II, LEMS,
Arazpour (2013)	PGO	24	8	Patient centred	SCI - HKAFO SCI - IRGO	Speed recorded during testing, distance walked without stopping
Arazpour (2014)	PGO	30	6	Patient centred	AB control	Speed recorded during testing, step length, cadence, Joint ROM
Benito-Penalva (2012)	Lokomat®	40	8	1.5 km/h	SCI - Gait Trainer	10mWT, WISCI II, LEMS
Esclarin (2014)	Lokomat®	40	8	Patient centred	SCI - OGT	10mWT, 6MinWT, FIM-L, WISCI II, LEMS
Nooijen (2009)	Lokomat®	50	12	As fast as possible	SCI - TM+PT SCI - TM+ES SCI - OGT +ES AB control	Cadence, step length, stride length, symmetry index, intra-limb coordination, timing of knee extension onset
Field-Fote (2011)	Lokomat®	60	12	As fast as possible	SCI - TM+PT SCI - TM+ES SCI - OGT +ES	10mWT, 2MinWT, LEMS
Fineberg (2013)	ReWalk™	11-41	20-24	Patient centred	AB control	Speed recorded during testing, vGRF
Hornby (2005)	Lokomat®	24	8	2.0 km/h	SCI - TM BWS+PT SCI - BWS OGT	10mWT, 6MinWT, FIM-L, WISCI II, LEMS, TUG
Labruyère (2014)	Lokomat®	16	4	1-2 km/h	SCI - Strength training	10mWT, gait symmetry, WISCI II, LEMS, BBS
Nui (2014)	Lokomat®	12	4	1.5 – 3.4 km/h	SCI - Control group	10mWT, 6minWT, TUG, ankle MVC
Varoqui (2014)	Lokomat®	12	4	1.5 – 3.0 km/h	SCI - Control Group	10mWT, 6minWT, TUG, ankle ROM and ankle MVC

AB = Able-Bodied, BBS = Borg Balance Scale, BWS = body weight support, ES = electrical stimulation, FIM-L = Functional independence measure – Locomotor section, HKAFO = Hip knee ankle foot orthosis, IRGO = Isocentric reciprocating gait orthosis, LEMS = Lower Extremity Motor Score, MVC = Maximal Voluntary Contraction, NR = not reported, OGT = Overground Gait Training, PGO = Powered Gait Orthosis PT = Physiotherapist, ROM = Range of Motion, TM = treadmill, TUG = Timed Up and Go, WISCI II = Walking Index for Spinal Cord Injury, 10mWT = 10 meter timed walk test, 2minWT = 2 minute walk test, 6minWT = 6 minute walk test. Gait Trainer = a cable driven platform step simulating gait training device

Walking speed

Walking speed was recorded as an outcome measure in all of the studies and reported in eleven of the studies (speed and distance walked were reported in Field-Fote and Roach[44] but not in Nooijen *et al*.[7] as the two studies reported different aspects of the same data set). Eight studies provided walking speed based on the 10mWT; each of these reported walking speed pre- and post-intervention and demonstrated an increase in speed irrespective of the intervention method (Table 5). Hornby *et al*.[45] did not find any significant differences between interventions in speed and did not report any values. The three studies that focused on overground RAGT systems recorded speed during their respective data collection procedures and not as part of a standardised test.

Table 5. Average walking speed for treadmill and overground RAGT and control groups.

Study (Treadmill RAGT)	Walking Speed (m/s)					
	RAGT			Control		
	Pre	Post	Diff	Pre	Post	Diff
Alcobendas-Maestro (2012)	0.3*	0.4*	0.1	0.3*	0.3*	0.0
Benito-Penalva (2012)	0.06	0.25	0.19	0.09	0.28	0.18
Esclarin (2014)	0.36	0.47	0.11	0.32	0.42	0.10
Field-Fote (2011)	0.17	0.18	0.01	0.18	0.24	0.06
Labruyère (2014)	0.62	0.66	0.04	0.58	0.64	0.06
Nui (2014)	0.48	0.56	0.08	0.53	NR	NA
Varoqui (2014)	0.56	0.64	0.08	0.56	NR	NA
Hornby (2005)	No significant differences between groups (data NR)					
Study (Overground RAGT)	**SCI**			**Control**		
Arazpour (2013)	RAGT	0.35		HKAFO IRGO	0.23 0.25	
Arazpour (2014)	SCI RAGT	0.40		AB Control AB RAGT	1.22 0.87	
Fineberg (2013)	Min assist No assist	0.16 0.31		AB Control	1.36	

AB = Able-Bodied, HKAFO = Hip knee ankle foot orthosis, IRGO = Isocentric reciprocating gait orthosis, NA = Not applicable, NR = Not Reported, Min = Minimum.

** Only reported to 1 decimal place.*

The values reported are averages for all participants associated with each group irrespective of completeness or level of injury.

The average walking speeds reported by Arazpour *et al*.[40, 47] for the SCI individuals using the overground RAGT system were greater than either SCI group in the study by Fineberg *et al*.[49] The average post-intervention walking speed reported for cSCI individuals only in the study by Benito-Penalva *et al*.[41] was 0.207 m/s; this was slower than the participants who walked without assistance in all three overground RAGT studies. It was however faster than the ReWalk walking speed for the group requiring minimal assistance.[49] Further comparison is difficult as time since injury and injury level were not reported by Benito-Penalva *et al*.[41]

Walking distance

Walking distance was reported by seven of the 12 studies (Table 6). Hornby *et al*.[45] reported that no significant difference existed between groups but did not provide any data to support this claim. Two of the remaining studies showed a significant increase in walking distance after RAGT-use compared to traditional overground gait training ($p < 0.05$ and $p = 0.047$,[42, 43] respectively, and two of the studies showed no significant between-group differences.[46, 47] Field-Fote and Roach[44] recorded the distance walked over a two-minute time period and found that non-RAGT overground gait training produced a significant improvement in walking distance whereas RAGT use did not. Walking distance was only reported by a single study for overground RAGT systems; cSCI participants using the overground RAGT were able to walk approximately a third further (120 meters) when compared to using a non-powered reciprocating gait orthosis (90 – 96 meters).[40]

Table 6. Walking distances from studies reporting distance of treadmill or overground RAGT groups and control groups.

Study	Walking Distance (m)					
	RAGT			Control		
	Pre	Post	Diff	Pre	Post	Diff
Alcobendas-Maestro (2012)	110.1	169.4	59.3	82.3	91.3	9.0
Esclarin (2014)	102.5	172.51	70.01	93.8	132.52	38.72
Field-Fote & Roach (2011)	16.8	17.9	1.2	22.2	28.6	6.4
Nui (2014)	160.84	165.20	4.36	163.22	NR	NA
Varoqui (2014)	206.96	208.87	1.91	205.6	NR	NA
Hornby (2005)	No significant differences between groups (data NR)					
Study (Overground RAGT)	SCI			Control		
Arazpour (2013)	RAGT	120		HKAFO IRGO	90.2 96.4	

Diff = Difference, HKAFO = Hip knee ankle foot orthosis, IRGO = Isocentric reciprocating gait orthosis, NA = Not applicable, NR = Not Reported.

Stepping characteristics

Three studies measured temporal-spatial parameters other than walking speed (Table 7). Cadence and step length were reported by two studies[7, 48] and symmetry was reported by Nooijen *et al*.[7] and Labruyere and van Hedel.[21] Arazpour *et al*.[48] reported average cadence and step length for each group identifying a reduced cadence and step length compared to able-bodied normal walking. Furthermore, they demonstrated that step length was restricted by the RAGT system but that cadence was controlled by the individual as able-bodied individuals using the RAGT had an increased cadence compared to normal walking (Table 7). Nooijen *et al*.[7] did not report values for cadence and step length but provided the average differences for pre- and post-intervention. However the results in Table 7 suggest that the treadmill-based RAGT system was less effective at maximising stepping characteristics than the other interventions used. Nooijen *et al*.[7] identified significantly reduced cadence for SCI individuals pre- and post-training and a significantly shorter step length was identified for the weaker leg pre-training, which was consistent with the study by Arazpour *et al*.[48] No significant differences were identified between pre- and post-training interventions in either study reporting symmetry data[7, 21] (Table 7).

Table 7. Stepping characteristics of SCI and able-bodied controls from those studies reporting temporal-spatial data other than walking speed.

Study	Stepping Characteristics		
	Cadence (steps/min)		
Arazpour (2014)	SCI RAGT	49	
	AB Control	90	
	AB RAGT	106	
	Cadence (steps/min) pre-post intervention difference		
Nooijen (2009)	RAGT	↑1.5	AB vs SCI
	TM+PT	↑2.3	SCI took significantly less steps both pre- and post-training
	TM+ES	↑3.9	
	OGT +ES	↑5.0	
	Step Length (cm)		
Arazpour (2014)	SCI RAGT	44.15	
	AB Control	62.66	
	AB RAGT	49.00	
	Step Length (cm) pre-post intervention difference		
Nooijen (2009)	RAGT	≤0.01	AB vs SCI
	TM+PT	↑2.3	SCI took significantly shorter steps with the weaker leg pre-training in RAGT group. Post-training weaker and pre- and post- with stronger (e.g., no significant differences).
	TM+ES	↑3.9	
	OGT +ES	↑5.0	
	Symmetry Index pre-post intervention difference		
Labruyère (2014)	RAGT	↑0.02 (pre 0.91 post 0.93)	
	ST	↑0.03 (pre 0.93 post 0.96)	
	6-month Follow Up	0.92	
Nooijen (2009)	No significant difference identified pre- and post-training $p > 0.05$		AB vs SCI SCI symmetry significantly lower pre-training. Post-training no significant difference

ES = Electrical Stimulation, OGT = Overground Gait Training, PT = Physiotherapist, ST = strength training, TM = Treadmill, ↑= increase.

Functional gait measures

Table 8 presents the results of the functional measures used in each study to assess physical improvement and gait quality. The LEMS was reported by six studies and all demonstrated an increase in score post-training irrespective of the intervention type. The WISCI-II was reported by five studies producing similar findings to the LEMS. All studies showed an increase in WISCI-II score post-intervention. The results for these two measures provided by Labruyère & van Hedel[21] did not show the marked improvents seen in the other studies. This is most likely due to the higher scores achieved prior to intervention; the pre intervention scores reported by Labruyère & van Hedel[21] are greater than the majority of scores reported by the other studies post intervention. Only three studies used the FIM-L; all three demonstrated an improvement post-intervention. No functional measures were used by any of the studies that used an overground RAGT system.

Table 8. Change in functional outcome measure scores reported by treadmill-based RAGT studies.

Study	LEMS		WISCI-II		FIM-L	
	RAGT	Control	RAGT	Control	RAGT	Control
Alcobendas-Maestro (2012)	↑7	↑5	↑12	↑5	↑6	↑3
Benito-Penalva (2012)	↑7.1	↑9.3	↑5.3	↑5.1	NM	
Esclarin (2014)	↑7.2	↑3.9	↑7.0	↑6.0	↑3.4	↑2.9
Field-Fote (2011)	↑1.2	↑1.4	NM		NM	
Hornby (2005)	Significant increase for all modalities (data NR)		Significant increase for all modalities (data NR)		Significant increase for all modalities (data NR)	
Labruyère (2014)	↑0.7	↑1.0	↑0.8	↑0.4	NM	

FIM-L = Functional Independence Measure – Locomotor section, LEMS = lower extremity motor score, NM = not measured, WISCI-II = Walking Index for Spinal Cord Injury, ↑= increase.

Discussion

The primary aim of this review was to identify if overground or treadmill-based RAGT systems produced different upright stepping characteristics in SCI individuals. The limited number of studies included in this review, that focused on the use of overground RAGT systems, and the low quality scores of said studies, highlight that the evidence related to the use of overground RAGT is limited. A recent systematic review into gait speed in overground RAGT use only identified a total of 106 independent studies of which 15 were deemed eligible for inclusion but none of these were randomised controlled trials.[50] A larger body of evidence on the use of treadmill-based RAGT systems was available, however comparisons across studies were still limited due to the differences in participant demographics and training protocols. The single temporal-spatial parameter reported by all of the studies included in the current review was walking speed and even this was measured using different methods. The treadmill-based RAGT studies all measured walking speed using a 10mWT whereas the overground based studies all measured walking speed over different distances. Further temporal-spatial characteristics were only reported by three of the included studies limiting the conclusions that could be drawn on the effectiveness of the different RAGT devices to improve stepping characteristics. As a result of these limitations it is not possible to accept or reject the primary hypothesis about whether overground RAGT systems encourage the appearance of a more stereotypical upright stepping pattern compared to treadmill-based RAGT systems.

The secondary aims of this review were to identify any differences in the use of RAGT systems with respect to the completeness of injury and to identify if any differences were evident between treadmill and overground RAGT systems relative to functional outcome measures post-training. Research into the use of treadmill-based RAGT is predominantly focused on the iSCI populations and no studies using overground RAGT based systems were identified by this review that recruited iSCI individuals. The novel concept that overground RAGT systems have been designed as functional mobility aids for everyday use[51] has dominated the scope of the research into these devices rather than their capacity in rehabilitative therapy. As such research has tended to focus on safety and functional capacity of the device[3, 52] rather than the potential for rehabilitation. More research investigating the use of RAGT systems in iSCI vs cSCI is warranted.

Temporal-spatial characteristics

Walking speed as an indicator of walking capacity in populations with mobility deficits has been well documented.[53-55] Standardised methods of assessment such as the 10mWT have been developed, their level of reliability and validity must be reported according the specific clinical population. Validity and reliability data are available for different populations including SCI.[54, 56, 57] The larger and higher scoring methodological studies included in this review (predominantly those focusing on treadmill RAGT systems) used the 10mWT as an outcome measure for walking speed. Four of the studies found no significant difference in walking speed between the RAGT training interventions and the more conventional training methods.[41-43, 45] However, Field-Fote and Roach[44] and Labruyère and van Hedel[21] found the RAGT to be less effective than the alternative methods. This suggests that the use of treadmill-based RAGT is no better than conventional gait training methods to improve walking speed. Two studies compared treadmill RAGT use to control groups with no intervention. Varoqui *et al*.[47] found the use of treadmill RAGT training to have a significant impact on walking speed with an increase of 0.08 m/s (Table 5) equivalent to 13.4%. Although Nui *et al*.[46] showed an overall improvement in walking speed, they explicitly differentiated between individuals with high and low walking capacity and advocated the use of RAGT in individuals with a higher functional capacity. This approach to identifying patients based on high or low walking capacity would exclude the use of treadmill RAGT in cSCI populations.

The 10mWT completed in the treadmill RAGT studies was always carried out overground and without the aid of robotic devices, however individuals were able to use orthotics and walking aids (i.e. elbow crutches) to facilitate ambulation. Conversely, the overground RAGT studies always measured walking speed with the device. Arazpour *et al*.[48] calculated the average speed of five trials over a six-meter walkway. Fineberg *et al*.[49] calculated walking speed for each individual once participants were capable of ambulating ten meters using the RAGT system without pausing and Arazpour *et al*.[40] measured walking speed around a 40-meter rectangular walkway. All of the SCI participants had complete injuries and would not have been able to ambulate without some form of mechanical assistance. The principles of motor learning may have played a substantial role in the outcome of these results.[19] Participants in the treadmill-based studies may not have performed as well in an overground walking test due to task specificity.

Categories of functional ambulation post-SCI have been identified, with specific walking speeds used to define thresholds for each.[53] The SCI participants not requiring assistance in the overground RAGT studies achieved average speeds between 0.31 - 0.4 m/s (Table 5). These speeds were below the threshold of 0.44 m/s that differentiates someone who can ambulate outdoors with aid from someone who can walk indoors but is dependent upon a wheelchair outdoors. Only four of the studies using treadmill-based

RAGT systems reported speeds that were above this threshold post intervention, however the initial average walking speed for three of these four studies was already faster than 0.44 m/s (Table 5). Although faster walking speed was identified by most of the studies included in this review, no rehabilitation modality enabled a large enough improvement to facilitate community ambulation in participants below the 0.44 m/s threshold.

This review identified limited evidence of other stepping characteristics reported during and post-RAGT use in SCI individuals. The nature of the overground RAGT systems and the requirement for the user to shift their own body weight in order to initiate and or control ambulation can impact stepping characteristics such as step length, cadence, stance and swing time.[3, 52] The body weight support component and passive, cyclic, predefined movements produced by a treadmill-based RAGT system using a trajectory control strategy[51] will eliminate natural variation in stepping characteristics.[58, 59] Field-Fote and Roach[44] found that the use of the treadmill-based RAGT system was the only modality they tested not to show an increase in walking speed post-training and similarly Nooijen *et al*.[7] found that the RAGT group showed the least improvement in cadence and step length. Field-Fote and Roach[44] suggested that training should potentially focus on repetitive step initiation rather than taking advantage of afferent activation of the spinal locomotor centres being triggered by the continuous movement of the treadmill belt. Although overground RAGT still uses a trajectory control strategy to move the lower limbs, balance and postural control of the upper body are needed to maintain smooth ambulation. This suggests that the use of overground RAGT, in conjunction with other rehabilitative modalities, such as strength training may be an effective strategy for gait rehabilitation in iSCI individuals.

Functional outcomes

Six treadmill-based RAGT studies reported distance walked as a functional outcome; only one overground RAGT study reported walking distance. Alcobendas-Maestro *et al.*[42] and Esclarin *et al*.[43] both found treadmill RAGT training produced larger improvements in walking distance than conventional overground gait training. The remaining four studies did not find treadmill RAGT to elicit any increase in walking distance (Table 6). Field-Fote and Roach[44] used a two-minute walk test, instead of the six-minute test used by the other studies. Consequently, direct comparisons were not possible as fatigue may have had an effect. Mechanical or reciprocating gait orthoses have been designed to enable paraplegic individuals to ambulate. In some cases, without their assistance, walking would not be possible; however, they have been shown to produce an inefficient gait with high energy costs.[60] The use of overground RAGT systems can significantly reduce the energy costs of walking for the SCI population resulting in an increase in walking distance and ambulation time.[40]

None of the overground RAGT based studies provided data on any other functional outcome measures. A number of the treadmill-based RAGT studies provided results from functional outcome measures that demonstrated an increase in capacity irrespective of rehabilitation modality (Table 8). Although balance is an important component of walking, only one study included in this systematic review presented data from a clinical balance measure, Berg balance scale.[21] They identified no significant differences in balance between treadmill RAGT and strength training. The body weight support component of treadmill RAGT prevents the possibility of individuals falling, thus minimising the requirement of balance control,[21] unlike in overground RAGT where balance is constantly required to initiate and maintain stepping.

Clinical implication

The general consensus from this systematic review is that the use of RAGT, in any form, can be positive for both cSCI and iSCI individuals as long as it is not used as the sole rehabilitation method. The secondary hypotheses can therefore be partially accepted as cSCI individuals will receive the same benefits in terms of gait training from both system types and RAGT can be part of a rehabilitation programme leading to improved functional gait outcomes. Evidence suggests that specificity is one of the most important factors of gait training. Both the highest and lowest scoring studies in this review identified the potential benefits of the stimulation of central pattern generators in the spinal locomotor centres that can lead to positive neural plastic changes.[43, 45] Esclarín-Ruz *et al.*,[43] Alcobendas-Maestro *et al.*,[42] and Labruyère and van Hedel[21] also identified strength increases as one of the key contributors to improved gait in iSCI individuals.

Passive movement has been identified as a potential limitation for RAGT both by a number of studies included[7, 21, 44] and excluded from this review.[22, 59, 61] Adaptive programmes providing resistance to movement at specific phases of the gait cycle are now possible in treadmill-based RAGT systems.[61, 62] This development encourages patient engagement during rehabilitation and has the potential to introduce task variability, facilitating motor learning.[21, 22, 58]

The practical implications of the different types of RAGT systems have been acknowledged from two perspectives which may be relevant to clinicians. Field-Fote and Roach[44] suggested that overground walking was potentially a more cost effective and appropriate intervention as the equipment was cheaper than a RAGT system. However the use of RAGT reduces the number of staff required to train a single patient, limits the physical exertion by therapists, and allows for longer and more intense training sessions.[45]

Strengths and limitations

The strengths of this systematic literature review include identifying and evaluating studies related to RAGT use in SCI populations and providing an up to date overview of the current literature. The use of a methodological assessment tool has enabled study quality to be quantified, thereby identifying research strengths and areas of good practice such as the use of valid and reliable data collection tools, excellent intervention compliance and clear outcome reporting. Furthermore, the identification of areas of poor practice, with associated limitations, have been highlighted, focusing on the reporting of adverse events and external validity, specifically associated with the representation of the entire population. The limitations of this review are predominantly related to the small number of research studies in this field, the varied outcome measures used by researchers working with SCI populations and the number of papers excluded based on the lack of temporal-spatial data. As such it was difficult to answer fully some of the aims presented at the start of this review. Finally, overground RAGT studies appear to be in their infancy and more research needs to be undertaken relative to their capacity as rehabilitative devices.

Conclusion

The evidence discussed above suggests that RAGT has the potential to provide SCI individuals with benefits related to upright locomotion. However, there is no consensus about which systems are most effective for particular patient groups based on temporal-spatial characteristics alone. The use of RAGT in SCI rehabilitation appears to have a number of positive effects beyond the scope of this review, but the most important and clinically meaningful finding is that RAGT should be used as part of a multi-modality rehabilitation approach and not as a replacement for other therapies.

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References

1. World Health O. Spinal Cord Injury Fact Sheet No384. 2013.

2. Field-Fote EC, Lindley SD, Sherman AL. Locomotor training approaches for individuals with spinal cord injury: a preliminary report of walking-related outcomes. Journal of neurologic physical therapy : J Neurol Phys Ther 2005;29(3):127-37.

3. Zeilig G, Weingarden H, Zwecker M, Dudkiewicz I, Bloch A, Esquenazi A. Safety and tolerance of the ReWalk™ exoskeleton suit for ambulation by people with complete spinal cord injury: a pilot study. J Spinal Cord Med 2012;35(2):96-101.

4. Kirshblum SC, Burns SP, Biering-Sorensen F, Donovan W, Graves DE, Jha A, *et al*. International standards for neurological classification of spinal cord injury (revised 2011). J Spinal Cord Med 2011;34(6):535-46.

5. DeSanto-Madeya S. Adaptation to spinal cord injury for families post-injury. Nursing Science Quarterly 2009;22(1):57-66.

6. Minkel JL. Seating and mobility considerations for people with spinal cord injury. Physical Therapy 2000;80(7):701-9.

7. Nooijen CFJ, ter Hoeve N, Field-Fote EC. Gait quality is improved by locomotor training in individuals with SCI regardless of training approach. J Neuroeng Rehabil 2009;6(1):36-.

8. Bauman WA, Schwartz E, Song ISY, Kirshblum S, Cirnigliaro C, Morrison N, *et al*. Dual-energy X-ray absorptiometry overestimates bone mineral density of the lumbar spine in persons with spinal cord injury. Spinal Cord 2009;47(8):628-33.

9. Edwards WB, Schnitzer TJ, Troy KL. The mechanical consequence of actual bone loss and simulated bone recovery in acute spinal cord injury. Bone 2014;60:141-7.

10. Vette AH, Masani K, Wu N, Popovic MR. Multidirectional quantification of trunk stiffness and damping during unloaded natural sitting. Med Eng & Phys 2014;36(1):102-9.

11. Bauman WA, Spungen AM. Coronary heart disease in individuals with spinal cord injury: assessment of risk factors. Spinal Cord 2008;46(7):466-76.

12. Benevento BT, Sipski ML. Neurogenic Bladder, Neurogenic bowel, and sexual dysfunction in people with spinal cord injury. Physical Therapy 2002;82(6):601-12.

13. Swinnen E, Duerinck S, Bayeyens J, Meeusen R, Kerckhofs E. Effectiveness of robot-assisted gait training in persons with spinal cord injury: a systematic review. Journal of Rehabilitation Medicine 2010. p. 520-6.

14. Song H-Y. Modeling social reintegration in persons with spinal cord injury. Disability and Rehabilitation 2005;27(3):131-41.

15. Thuret S, Moon LDF, Gage FH. Therapeutic interventions after spinal cord injury. Nat Rev. Neurosci 2006;7(8):628-43.

16. Gómara-Toldrà N, Sliwinski M, Dijkers MP. Physical therapy after spinal cord injury: a systematic review of treatments focused on participation. J Spinal Cord Med 2014;37(4):371-9.

17. Mikolajewska E, Mikolajewski D. Exoskeletons in neurological diseases – current and potential future applications. Adv Clin and Exp Med 2011;20(2):227-33.

18. Swinnen E, Baeyens J-P, Knaepen K, Michielsen M, Clijsen R, Beckwée D, *et al*. Robot-assisted walking with the Lokomat: the influence of different levels of guidance force on thorax and pelvis kinematics. Clin Biomech 2015;30(3):254-9.

19. Hubli M, Dietz V. The physiological basis of neurorehabilitation - locomotor training after spinal cord injury. J Neuroeng Rehabil 2013;10(1):5-.

20. Dobkin B, Apple D, Barbeau H, Basso M, Behrman A, Deforge D, *et al*. Weight-supported treadmill vs over-ground training for walking after acute incomplete SCI. Neurology 2006;66(4):484-93.

21. Labruyère R, van Hedel HJA. Strength training versus robot-assisted gait training after incomplete spinal cord injury: a randomized pilot study in patients depending on walking assistance. J Neuroeng Rehabil 2014;11(1):4-.

22. Ramanujam A, Cirnigliaro CM, Garbarini E, Asselin P, Pilkar R, Forrest GF. Neuromechanical adaptations during a robotic powered exoskeleton assisted walking session. J Spinal Cord Med 2017:1-11.

23. Ramanujam A, Spungen A, Asselin P, Garbarini E, Augustine J, Canton S, *et al*. Training response to longitudinal powered exoskeleton training for SCI. Wearable Robotics: Challenges and Trends. Switzerland: Springer; 2017; 361-6.

24. Díaz I, Gil JJ, Sánchez E, Gil JJ, nchez E. Lower-limb robotic rehabilitation: literature review and challenges. Journal of Robotics 2011;1-11.

25. van Hedel HJA, Dietz V. Rehabilitation of locomotion after spinal cord injury. Restor Neurol Neurosci 2010;28(1):123-34.

26. NICE. Pressure ulcers: the management of pressure ulcers in primary and secondary care. 2014.

27. Spinal Cord Injury Centre Physiotherapy Lead C. Clinical guideline for standing adults following spinal cord injury. 2013.

28. NICE. Ekso exoskeleton for rehabilitation in people with neurological weakness or paralysis. 2017.

29. NICE. Stroke rehabilitation in adults. 2013.

30. Hornby G, Straube D, Kinnaird C, Holleran C, Echauz A, Rodriguez K, *et al*. Importance of specificity, amount, and intensity of locomotor training to improve ambulatory function in patients poststroke. Top Stroke Rehabil 2011;18(4):293-307.

31. Levin MF, Weiss PL, Keshner EA. Emergence of virtual reality as a tool for upper limb rehabilitation: incorporation of motor control and motor learning principles. Physical Therapy 2015;95(3):415-25.

32. Kirtley C. Clinical Gait Analysis Theory and Practice. Churchill Livingstone: Elsevier; 2006.

33. König N, Singh NB, von Beckerath J, Janke L, Taylor WR. Is gait variability reliable? An assessment of spatio-temporal parameters of gait variability during continuous overground walking. Gait & Posture 2014;39(1):615-7.

34. Boland A, Cherry MG, Dickinson R. Doing a systematic review a student guide. London: Sage; 2014.

35. van Tulder M, Furlan A, Bombardier C, Bouter L. Updated method guidelines for systematic reviews in the Cochrane Collaboration Back Review Group. Spine 2003;28(12):1290-9.

36. Stineman MG, Escarce JJ, Goin JE, Hamilton BB, Granger CV, Williams SV. A case-mix classification system for medical rehabilitation. Medical Care 1994;32(4):366-79.

37. Steeves JD, Lammertse D, Curt A, Fawcett JW, Tuszynski MH, Ditunno JF, *et al*. Guidelines for the conduct of clinical trials for spinal cord injury (SCI) as developed by the ICCP panel: clinical trial outcome measures. Spinal Cord 2007;45(3):206-21.

38. Dittuno PL, Dittuno Jr JF. Walking index for spinal cord injury (WISCI II): scale revision. Spinal Cord 2001;39(12):654-6.

39. Downs SH, Black N. The feasibility of creating a checklist for the assessment of the methodological quality both of randomised and non-randomised studies of health care interventions. Journal of Epidemiology & Community Health 1998;52(6):377-84.

40. Arazpour M, Bani MA, Hutchins SW, Jones RK. The physiological cost index of walking with mechanical and powered gait orthosis in patients with spinal cord injury. Spinal Cord 2013;51(5):356-9.

41. Benito-Penalva J, Edwards DJ, Opisso E, Cortes M, Lopez-Blazquez R, Murillo N, *et al*. Gait training in human spinal cord injury using electromechanical systems: effect of device type and patient characteristics. Arch Phys Med Rehabil 2012;93(3):404-12.

42. Alcobendas-Maestro M, Esclarín-Ruz A, Casado-López RM, Muñoz-González A, Pérez-Mateos G, González-Valdizán E, *et al*. Lokomat robotic-assisted versus overground training within 3 to 6 months of incomplete spinal cord lesion. Neurorehabilitation and Neural Repair 2012;26(9):1058-63.

43. Esclarín-Ruz A, Alcobendas-Maestro M, Casado-Lopez R, Perez-Mateos G, Florido-Sanchez MA, Gonzalez-Valdizan E, *et al*. A comparison of robotic walking therapy and conventional walking therapy in individuals with upper versus lower motor neuron lesions: a randomized controlled trial. Arch Phys Med Rehabil 2014;95(6):1023-31.

44. Field-Fote EC, Roach KE. Influence of a locomotor training approach on walking speed and distance in people with chronic spinal cord injury: a randomized clinical trial. Physical Therapy 2011;91(1):48-60.

45. Hornby G, Campbell D, Zemon D, Kahn J. Clinical and quantitative evaluation of robotic-assisted treadmill walking to retrain ambulation after spinal cord injury. Top Spinal Cord Injury Rehabil 2005;11(2):1-17.

46. Niu X, Varoqui D, Kindig M, Mirbagheri M. Prediction of gait recovery in spinal cord injured individuals trained with robotic gait orthosis. Top Spinal Cord Injury Rehabil 2014;11(42).

47. Varoqui D, Niu X, Mirbagheri MM. Ankle voluntary movement enhancement following robotic-assisted locomotor training in spinal cord injury. J Neuroeng Rehabil 2014;11(46).

48. Arazpour M, Mehrpour SR, Bani MA, Hutchins SW, Bahramizadeh M, Rahgozar M. Comparison of gait between healthy participants and persons with spinal cord injury when using a powered gait orthosis-a pilot study. Spinal Cord 2014;52(1):44-8.

49. Fineberg DB, Asselin P, Harel NY, Agranova-Breyter I, Kornfeld SD, Bauman WA, *et al*. Vertical ground reaction force-based analysis of powered exoskeleton-assisted walking in persons with motor-complete paraplegia. J Spinal Cord Med 2013;36(4):313-321.

50. Louie DR, Eng JJ, Lam T, Spinal Cord Injury Research Evidence Research Team SCIRER. Gait speed using powered robotic exoskeletons after spinal cord injury: a systematic review and correlational study. J Neuroeng Rehabil 2015;12:82-.

51. Chen G, Chan CK, Guo Z, Yu H. A review of lower extremity assistive robotic exoskeletons in rehabilitation therapy. Crit Rev Biomed Eng. 2013;41(4-5):343-63.

52. Esquenazi A, Talaty M, Packel A, Saulino M. The ReWalk powered exoskeleton to restore ambulatory function to individuals with thoracic-level motor-complete spinal cord injury. American Journal of Physical Medicine & Rehabilitation / Association of Academic Physiatrists. 2012;91(11):911-21.

53. van Hedel HJA. Gait speed in relation to categories of functional ambulation after spinal cord injury. Neurorehabil Neural Repair 2008;23(4):343-50.

54. Schmid A, Duncan PW, Studenski S, Lai SM, Richards L, Perera S, *et al*. Improvements in speed-based gait classifications are meaningful. Stroke 2007;38(7).

55. Fritz S, Lusardi M. White paper: "walking speed: the sixth vital". J Geriatr Phys Ther 2009;32(2):46-9.

56. Lam T, Noonan VK, Eng JJ. A systematic review of functional ambulation outcome measures in spinal cord injury. Spinal Cord 2008;46(4):246-54.

57. Bohannon RW. Comfortable and maximum walking speed of adults aged 20-79 years: reference values and determinants. Age and Ageing 1997;26(1):15-9.

58. Hidler J, Wisman W, Neckel N. Kinematic trajectories while walking within the Lokomat robotic gait-orthosis. Clin Biomech 2008;23(10):1251-9.

59. Fleerkotte BM, Koopman B, Buurke JH, van Asseldonk EHF, van der Kooij H, Rietman JS. The effect of impedance-controlled robotic gait training on walking ability and quality in individuals with chronic incomplete spinal cord injury: an explorative study. J Neuroeng Rehabil 2014;11(1):26-.

60. Massucci M, Brunetti G, Piperno R, Betti L, Franceschini M. Walking with the advanced reciprocating gait orthosis (ARGO) in thoracic paraplegic patients: energy expenditure and cardiorespiratory performance. Spinal Cord 1998;36(4):223-7.

61. Lam T, Pauhl K, Krassioukov A, Eng JJ. Using robot-applied resistance to augment body-weight–supported treadmill training in an individual with incomplete spinal cord injury. Physical Therapy 2011;91(1):143-51.

62. Duschau-Wicke A, von Zitzewitz J, Caprez A, Lunenburger L, Riener R. Path Control: A method for patient-cooperative robot-aided gait rehabilitation. IEEE Trans Neural Syst Rehabil Eng 2010;18(1):38-48.