

Sitting and Standing Balance Following Spinal Cord Injury

Janelle Unger, PhD Carlos L. Cano Herrera, PhD Tyra Chu, BKin, MPT Frances Fan, BKin (Student) Elsa Sun, BKin (Student) Amrit Dhaliwal, BSc (PT) Janice Eng, PhD

Our Partners:







Vancouver CoastalHealth Research Institute





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Key Points

1.1 Sitting Balance

Sitting balance is a significant component of independent daily living for people with SCI, especially those with cervical level injuries or those with complete injuries at the thoracic/lumbar level (Lei et al. 2023). It may be especially important to consider sitting balance in people with SCI as they may have limited trunk control, and otherwise simple daily tasks, like reaching for something, moves the person's center of gravity, and they may lose their balance, and put them at risk for falls. Dressing, wheelchair handling, transfers, sitting on the edge of or across surfaces, and toileting all require a combination of static and dynamic postural control involving the trunk (Lee & Lee 2021; Tak et al. 2015). Therefore, the rehabilitation of sitting balance is beneficial for enhancing quality of life after SCI.

1.1.1 Evidence of Virtual Reality (VR)

Virtual reality (VR) balance training produces improvements in sitting balance in people with both acute and chronic SCI.

1.1.2 Evidence of Exercise and Activity-Based Therapy (ABT)

Various exercise interventions (i.e., wheelchair skills training program, unsupported sitting, seated Tai Chi, arm crank or kayak ergometry, Spinal Mobility, and activity-based therapy [ABT]) can be used to improve sitting balance in people with subacute and chronic SCI.

Evidence is lacking about the optimal dosage and length of intervention for improving sitting balance in people with acute or chronic SCI.

1.1.3 Evidence of Body-Weight Supported Locomotor Training (BWSLT)

Studies with strong evidence show that different body-weight supported locomotor training (BWSLT) methods do not improve sitting balance in people with chronic SCI.

Only preliminary recommendations can be made from the results of lower-quality and smaller studies assessing exoskeleton training methods for sitting balance in people with chronic SCI.

1.1.4 Evidence of Electrical Stimulation

Electrical stimulation plus balance training can be used to facilitate trunk stability for seated dynamic postural control in people with spinal cord injury (SCI), though a virtual reality program plus balance training provided superior results.

In people with acute SCI, electrical stimulation can improve dynamic trunk stability more so in motor incomplete tetraplegia than motor complete tetraplegia.

In people with chronic SCI, a combination of electrical stimulation and therapeutic exercise can improve sitting balance outcomes.

1.2 Standing Balance

Up to 75 % of individuals with incomplete SCI experience falls while standing and frequent losses of balance post-rehabilitation (<u>Arora et al. 2020</u>; <u>Brotherton et al. 2007</u>). Moreover, falls are among the most common cause of SCI in persons > 60 years old (<u>Dohle & Reding 2011</u>), so standing balance training may be particularly important for the safety of older people and people with incomplete SCI.

1.2.1 Evidence of Virtual Reality (VR)

VR training is an effective strategy to improve walking and standing balance performance in patients with incomplete SCI, and may afford further benefits compared with the same training interventions without the VR biofeedback.

Electromyography (EMG) Biofeedback, visual feedback, or visuotemporal cue feedback adding to standing, stepping or body-weight supported treadmill training (BWSTT) protocols may improve gait, balance, and lower limb muscle strength in incomplete SCI and chronic SCI.

1.2.2 Evidence of Non-Body-Weight Supported Training

A number of balance training interventions can improve standing balance in people with SCI. Perturbation-based balance training, conventional intensive balance training, task-specific (stepping) and impairment-based training, walking training over different surfaces, rebound therapy, overground multi-modal locomotor training, or community-based ambulation training may result in improvements, mainly in standing balance and balance confidence.

High-intensity locomotor (70%-85% HR_{max}) and resistance (isometric contractions of maximum volitional effort) training programs seem to be safe in patients with SCI; however, the effectiveness for improving standing balance is contradictory. Larger randomized controlled trials (RCTs) are necessary.

Studies assessing non-body-weight supported treadmill training or overground training programs in people with acute and/or complete SCI have been inconclusive or trials were of lower quality.

1.2.3 Evidence of Body-Weight Supported Treadmill Training (BWSTT)

Though typically body-weight support treadmill training improves walking safety, and does not effectively test standing balance, many studies assessing walking have also included secondary outcomes measuring standing balance (e.g., the Timed Up and Go test).

Evidence to date shows that BWSTT has similar effects on standing balance and functional independence outcomes as overground mobility training of similar intensity.

1.2.4 Evidence of Wearable Powered Exoskeletons

Even though wearable exoskeleton-assisted gait training has been studied to improve gait performance, some studies have measured standing balance in patients with SCI, though there is little consensus regarding training regimens and exoskeleton models used. There is insufficient evidence regarding whether wearable exoskeleton-assisted training provides better walking function, balance performance, or energy expenditure outcomes, compared with other approaches (such as robotic-assisted gait training [RAGT] with Lokomat or knee ankle foot orthoses [KAFOs]) in patients with SCI.

Powered Exoskeleton use may be cumbersome, not available for home use, have a high cost, and participants may experience adverse events.

1.2.5 Evidence of Neuromodulation

1.2.5.1 Evidence of Functional Electrical Stimulation (FES)

Some RCTs involving BWSTT coupled with functional electrical stimulation (FES) or FES-cycling have shown improvements in standing balance outcomes or functional independence, and some have not.

1.2.5.2 Evidence of Transcranial Direct Current Stimulation (tDCS)

Concurrent application of transcranial direct current stimulation (tDCS) did not further enhance the effects on walking, balance, and strength outcomes of motor skill training, overground walking training, or BWSTT in patients with motorincomplete SCI.

1.2.5.3 Evidence of Repetitive Transcranial Magnetic Stimulation (rTMS) (and Other Approaches)

Repetitive transcranial magnetic stimulation (rTMS) and non-invasive brain stimulation (NIBS) combined with locomotor or exercise training do not seem to provide more benefits in standing balance and walking function than exercise alone in patients with SCI; however, they may provide positive effects on lower limb strength.

1.3 Gaps in the Literature

- Many studies we found tested balance as a secondary outcome with walking as the primary outcome; specifically, studying balance function as a primary outcome in SCI should improve data available, and in turn, clinical recommendations.
- Most studies we found testing balance in SCI, even high-quality RCTs, have fewer than 20 people per condition; authors of recent systematic reviews have stated that more well-designed and appropriately powered RCTs testing balance function are needed (<u>Benn et al. 2025</u>; <u>Walia et al. 2023</u>).
- Most studies on balance in people with SCI include people with incomplete injuries and at the chronic phase of SCI; more studies including people at the acute phase of injury and/or complete SCI would provide results more representative of the general SCI population.

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1 Executive Summary

1.1 Balance Definition and Components

Balance, defined as the ability to maintain or recover the centre of mass within the base of support; is important for activities of daily living, general mobility, and prevention of falls (<u>Maki & Mcllroy 2006</u>). Physiologically, balance is not a singular ability, but rather the ability of various systems to work together. The Systems Framework of Postural Control, first described by Horak (<u>2006</u>), is a comprehensive approach describing the components of balance to guide assessment and treatment. The 10 components of balance include:

- 1) Functional stability limits,
- 2) underlying motor systems,
- 3) static stability,
- 4) verticality,
- 5) reactive postural control,
- 6) anticipatory postural control,
- 7) dynamic stability,
- 8) sensory integration,
- 9) cognitive influences,
- 10) balance confidence.

Musselman et al. (2022) reported that all 10 components of balance are impaired to varying degrees in people with SCI. Functional stability limits, underlying motor systems, sensory integration, static stability, reactive postural control, cognitive influences, and balance confidence are all impacted more greatly by SCI, while the effect on verticality is minimal. The severity of impact for some components, like dynamic stability and anticipatory postural control is variable and likely depends on the severity of injury. When assessing balance, it is important for healthcare professionals to consider all 10 components, as impairments in any one of them can impact overall performance. To optimize treatment, interventions should then be tailored to each individual's needs based on which components are most greatly impacted.

1.2 Measuring Balance

Assessment of balance function in clinical settings can be performed using biomechanical instruments or clinical assessment tools (<u>Arsh et al. 2021</u>). Many research studies will use instrumented assessments like inertial measurement units, force plates, or motion capture systems, allowing for greater sensitivity in balance assessment; however, they are often costly and not widely available in clinical settings (<u>Arora et al. 2020</u>; <u>Musselman et al. 2022</u>). Until more accessible and affordable options become available, it is best for clinicians to focus on using validated clinical outcome measures (<u>Arora et al. 2020</u>).

Arsh et al. (2021) systematically reviewed articles reporting the validity and reliability of diagnostic tests used to assess balance function in patients with SCI. The following 10 clinical instruments were reported: Functional Reach Test (FRT), Berg Balance Scale (BBS), Mini-

Balance Evaluation Systems Test (Mini-BESTest), Function in Sitting Test (FIST), T-Shirt Test, Motor Assessment Scale item 3, Sitting Balance Score, Five Times Sit to Stand Test (FTSTS), Tinetti scale, and Sitting Balance Measure. The Timed Up and Go (<u>TUG</u>) Test was included as a balance measure in Hosseinzadeh et al. (<u>2024</u>), who aimed to test the psychometric properties (reliability and validity) of outcome measures used to assess walking and balance in people with SCI.

1.3 Sitting Balance

Sitting balance is a significant component of independent daily living for people with SCI, especially those with cervical level injuries or those with complete injuries at the thoracic/lumbar level (Lei et al. 2023). It is especially important to consider sitting balance in people with SCI as they may have limited trunk control, and an otherwise simple daily task, like reaching for something, moves the person's center of gravity, and they may lose their balance putting them at risk for falls. Dressing, wheelchair handling, transfers, sitting on the edge of or across surfaces, and toileting all require a combination of static and dynamic postural control involving the trunk (Lee & Lee 2021; Tak et al. 2015). Therefore, the rehabilitation of sitting balance is beneficial for enhancing quality of life after SCI.

It has been shown in individuals with motor-complete thoracic SCI that dressing or reaching while sitting with reduced thigh support provides more challenges in the dynamic sitting balance (postural control measured by the center of pressure parameters) than sitting with more thigh support (<u>Ilha et al. 2020</u>). Also, it has been shown that participants with cervical SCI are more reliant on visual and vestibular systems for sitting balance while depending less on proprioception and muscle control compared to controls (because they may not have control on these functions to maintain balance); showing that this strategy is ineffective in maintaining postural stability during unsupported sitting (<u>Lei et al. 2023</u>). Consequently, emphasizing the importance of proprioception and muscle control for seated postural stability and/or training during unsupported sitting to improve sitting balance is important in people with upper SCI (<u>Ilha et al. 2020</u>; <u>Lei et al. 2023</u>).

1.3.1 What Management Options are There for Sitting Balance Following Spinal Cord Injury (SCI)?

• Virtual reality (VR):

In recent years, technological advances such as VR have been introduced in the field of SCI rehabilitation and are being used as a therapeutic tool (<u>Abou et al. 2020</u>). The addition of VR to different seated exercise interventions provides significant improvements in sitting balance function for people with SCI compared with real world-task specific balance or standard rehabilitation (<u>Abou et al. 2020</u>; <u>Wang et al. 2024</u>).

• Exercise and Activity-Based Therapy (ABT):

Exercise interventions that have been tested on balance in people with SCI include: wheelchair skills training programs, therapeutic exercise in unsupported sitting, seated/wheelchair Tai Chi, arm crank ergometry, kayak ergometry, Spinal Mobility, and ABT.

RCTs in sitting balance for people with SCI were shown for wheelchair skills training programs and for seated Tai Chi programs, when compared to conventional physical therapy (<u>Nam et al.</u> 2023; <u>Qi et al. 2018</u>). Other studies of lower quality also showed positive results on sitting balance for arm crank ergometry, a Spinal Mobility program (comprising resistance exercises, aerobic conditioning, trunk stability and health education), and ABT (<u>Williams et al. 2020</u>; <u>Sliwinski et al. 2020</u>; <u>de Oliveira et al. 2023</u>; <u>de Oliveira et al. 2019</u>; <u>Larson 2022</u>).

One RCT on task-specific sitting balance showed no difference between it and standard rehabilitation, though it is likely that the 6-week training program was too short to show treatment effects (<u>Harvey et al. 2011</u>).

• Body-weight supported locomotor training (BWSLT):

The main aim of BWSLT is the improvement of walking and/or standing balance functions, but some studies included sitting balance as a secondary outcome.

Results are generally mixed or insignificant; some smaller studies showed that BWSLT report positive effects in sitting balance and/or trunk muscle strength, but RCTs in this area show no differences between BWSLT and standard rehabilitation (<u>Khan et al. 2019b; Tsai et al. 2021;</u> Okawara et al. 2022; Piira et al. 2019a; Piira et al. 2019b; Martinez et al. 2018).

• Electrical Stimulation:

Though not yet definitive, it seems that different electrical stimulation approaches (e.g., electromyography triggered electrical stimulation [EMG-ES] and functional electrical stimulation [FES]), paired with an exercise program especially focusing on trunk muscles, are beneficial in improving sitting balance function in people with complete and/or incomplete SCI. (Bayraktar et al. 2024; Bergmann et al. 2019).

1.4 Standing Balance

Up to 75% of individuals with incomplete SCI experience falls while standing and frequent losses of balance post-rehabilitation (<u>Arora et al. 2020</u>; <u>Brotherton et al. 2007</u>). Moreover, falls are among the most common causes of SCI in persons > 60 years old (<u>Dohle & Reding 2011</u>).

1.4.1 What Management Options are There for Standing Balance Following Spinal Cord Injury (SCI)?

• VR:

In participants with chronic SCI, VR (including electromyography [EMG] biofeedback or visuotemporal cues) provides higher benefits in standing balance than usual care or

interventions without the VR/biofeedback addition (<u>An & Park 2022</u>; <u>Amatachaya et al. 2023</u>; <u>Nithiatthawanon et al. 2020</u>; <u>Pramodhyakul et al. 2016</u>).

Participants with acute SCI have been less studied than those with chronic SCI, and the only study of high quality has shown no differences between VR training and conventional therapy (<u>Sengupta et al. 2020</u>).

• Non-Body-Weight Supported Training:

Overground walking training has the advantages of being inexpensive, more closely resembling daily life, and likely to achieve a patient's full engagement, encouraging voluntary movements compared to walking on a treadmill (Yu et al. 2019).

High-quality studies have found significant improvements in standing balance in people with SCI by using intensive balance training/perturbation-based balance training (<u>Unger et al. 2021</u>), task-specific stepping practice (<u>Lotter et al. 2020</u>), walking training program on a track with different surfaces (<u>Amatachaya et al. 2021</u>), rebound therapy (<u>Sadeghi et al. 2019</u>), and lower limb resistance training programs at maximum intensity (<u>Jayaraman et al. 2013</u>).

On the other hand, an RCT assessing 24 weeks of ABT did not provide significant improvements in standing balance in comparison with a control intervention (Jones et al. 2014a).

One high-quality study found no differences in standing balance improvements when comparing high-intensity (70%-85% HR_{max}) locomotor training to low-intensity (50%-65% HR_{max}) locomotor training (<u>Brazg et al. 2017</u>).

• Body-weight supported treadmill training (BWSTT):

BWSTT is the intervention more extensively studied in participants with SCI for improving standing balance function; we found 38 studies with a total sample size of 1815 participants.

High-quality studies on participants with acute SCI have shown that BWSTT has similar effects to conventional rehabilitation, consisting of an equivalent amount of overground mobility practice for standing balance (Dobkin et al. 2006; Midik et al. 2020; Shin et al. 2014). For participants with chronic SCI, the higher quality studies have also shown that different BWSTT approaches (e.g., robotic-assisted gait training [RAGT] with Lokomat, BWSLT with manual assistance, or BWSTT with assistance using a cable-driven robotic device) provide similar improvements in standing balance function than other non-body-weight supported training (e.g., usual care, overground 'precision' skilled walking training, strength training, or BWSTT with no assistance) (Labruyere & van Hedel 2014; Piira et al. 2019a; Piira et al. 2019b; Yang et al. 2014; Wu et al. 2018).

Because of the limited motor control and balance functioning recruited, BWSTT is likely not the ideal approach for improving standing balance in people with SCI.

• Wearable exoskeletons:

The number of studies on wearable exoskeletons during the past 10 years has seen a rapid increase; we found 17 studies including 270 participants with SCI assessing the training effect of wearable exoskeletons on standing balance.

Studies of high quality show that wearable exoskeleton-assisted training does not provide higher improvements in standing balance compared with other interventions (such as BWSTT or training regimens using knee ankle foot orthoses [KAFOs]) (<u>Edwards et al. 2022; Rodríguez-Fernández et al. 2022; Chang et al. 2018</u>).

These results, plus the fact of high heterogeneity in training dosage or models in exoskeletons, the numerous adverse events (AEs) reported, or high cost, among others, should be taken into account when providing research-clinical recommendations.

- Neuromodulation:
 - FES: Five studies, including 178 participants with chronic SCI, show that FES-cycling and FES-assisted BWSTT do not provide greater benefits in standing balance versus the same interventions without FES (<u>Galea et al. 2018</u>; <u>Kapadia et al. 2014</u>).
 - Transcranial direct current stimulation (tDCS): Four studies, including 118
 participants with chronic SCI, show that the addition of tDCS to different exercise
 interventions (e.g., gait retraining, motor skill training) provides no differences in
 standing balance when compared to the same exercise interventions paired with sham
 stimulation. (Simis et al. 2021; Raithatha et al. 2016; Evans et al. 2022; Klamruen et al.
 2024).
 - Repetitive transcranial magnetic stimulation (rTMS): Three studies, including 77 participants with acute/subacute motor incomplete SCI, found that rTMS before exercise training does not provide additional improvements when compared to exercise training plus sham stimulation (Krogh et al. 2021; Benito et al. 2012; Naro et al. 2022).

1.5 Gaps in the Literature

- Many studies we found tested balance as a secondary outcome with walking as the primary outcome; specifically studying balance function as a primary outcome in SCI should improve data available, and in turn, clinical recommendations.
- Most studies we found testing balance in SCI, even high-quality RCTs, have fewer than 20 people per condition; authors of recent systematic reviews have stated that more well-designed and appropriately powered RCTs testing balance function are needed (<u>Benn et al. 2025; Walia et al. 2023</u>).
- Most studies on balance in people with SCI include people with incomplete injuries and at the chronic phase of SCI; more studies including people at the acute phase of injury and/or complete SCI would provide results more representative of the general SCI population.

2 Introduction

Balance, defined as the ability to maintain or recover the centre of mass within the base of support; is important for activities of daily living, general mobility, and prevention of falls (<u>Maki & Mcllroy 2006</u>). Physiologically, balance is not a singular ability, but rather the ability of various systems to work together. The Systems Framework of Postural Control, first described by Horak (<u>2006</u>), is a comprehensive approach describing the components of balance to guide assessment and treatment. The 10 components of balance include:

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- 6) anticipatory postural control,
- 7) dynamic stability,
- 8) sensory integration,
- 9) cognitive influences,
- 10) balance confidence.

Musselman et al. (2022) reported that all 10 components of balance are impaired to varying degrees in people with SCI. Functional stability limits, underlying motor systems, sensory integration, static stability, reactive postural control, cognitive influences, and balance confidence are all impacted more greatly by SCI, while the effect on verticality is minimal. The severity of impact for some components, like dynamic stability and anticipatory postural control are variable and likely depend on the severity of injury. When assessing balance, it is important for healthcare professionals to consider all 10 components, as impairments in any one of them can impact overall performance. To optimize treatment, interventions should then be tailored to each individual's needs based on which components are most greatly impacted.

2.1 Measuring Balance

Assessment of balance function in clinical settings can be performed using biomechanical instruments or clinical assessment tools (Arsh et al. 2021). A systematic review by Arora et al. (2020) found that there are clinical assessments that can be used to measure all components of balance following SCI; however, many research studies will also use instrumented assessments, such as inertial measurement units, force plates, or motion capture systems. Using such technologies allows for greater sensitivity in balance assessment, as variables such as sway, velocity, or force production can be evaluated; however, they are often costly and not widely available (Arora et al. 2020; Musselman et al. 2022). Therefore, instrumented assessments are valuable in research to gain a greater understanding of the impact SCI has on balance, but are less clinically feasible. Until more accessible and affordable options become available, it may be best for clinicians to focus on using validated clinical outcome measures (Arora et al. 2020):

	salance Outcome Measures and the items They Measure					
	Balance Scales Evaluating Sitting Balance					
	Sitting alone	Sitting and other tasks	Standing only	Standing and other tasks	Walking and other tasks	Transfer tasks
<u>mFRT</u>	Х					
Test Table Test	Х					
Motor Assessment Scale	Х					
Sitting Balance Score	Х					
Sway Meter	Х		Х			
Clinical Test of Sensory Organization and Balance	Х					
T-Shirt Test	Х					
Seated Reaction to Perturbation	Х					
Berg Balance Score		Х		Х		
ABLE		Х		Х	Х	
Tinetti		Х		Х	Х	
Balance CAT		Х		Х		
Standing FRT			Х			
Traditional Romberg			Х			
Timed Standing			Х			
Timed Tandem Stance			Х			
Mini-BESTest				Х	Х	
CB&M				Х	Х	
DGI					Х	
Walking Romberg					Х	
Obstacle Clearance Test					Х	
Five Times Sit to Stand						Х

Table 1. Balance Outcome Measures and the Items They Measure

Balance ability during some transfer activities, such as lateral seated transfers, sit-to-stand and/or stand-to-sit are assessed as part of the <u>BBS</u>, Activity-based Balance Level (ABLE), Tinetti, Mini-Balance Evaluation Systems Test (mini-BESTest), and Balance Computerized Adaptive Test (Balance CAT). Arsh et al. (2021) focused on systematically reviewing articles reporting the validity and reliability of diagnostic tests used to assess balance function in patients with SCI. The following 10 clinical instruments were reported: Functional Reach Test (FRT), Berg Balance Scale (BBS), Mini-Balance Evaluation Systems Test (Mini-BESTest), Function in Sitting Test (FIST), T-Shirt Test, Motor Assessment Scale item 3, Sitting Balance Score, 5 Times Sit-to-Stand Test, Tinetti scale, and Sitting Balance Measure. On the other hand, the Timed Up and Go (TUG) Test was included as a balance measure in Hosseinzadeh et al. (2024), which aimed to test the psychometric properties (reliability and validity) of outcome measures used to assess walking and balance in people with SCI.

2.2 Training Balance

There has been a great deal of focus on the effectiveness of gait training in SCI rehabilitation research (Mehrholz et al. 2012; Van Hedel & Dietz 2010; Wessels et al. 2010), but there has been relatively little attention on the impact of interventions specifically targeting balance outcomes. Most persons with incomplete SCI have the potential to recover some degree of mobility and many functional activities of daily living through rehabilitation (McKinley et al. 1999). Proper balance control is important not only for mobility and ambulation but also for performing important daily home activities in sitting and standing, such as dressing, eating, cooking, toileting, and safe transfers (Huxham et al. 2001). In recent years, and with the rapid development in technology (e.g., exoskeletons, virtual reality [VR], neuromodulation), there has been more data available about sitting and/or standing balance outcomes following gait training, neuromodulation interventions, or VR-based training, as well as specific sitting or standing balance interventions in people with SCI.

3 Sitting Balance

Sitting balance is a significant component of independent daily living for people with SCI, especially those with cervical level injuries or those with complete injuries at the thoracic/lumbar level, due to limited motor control through the hips, pelvis, and spinal extensors (Lei et al. 2023). It may be especially important to consider sitting balance in people with SCI as they may have limited trunk control, and otherwise simple daily tasks, like reaching for something, moves the person's center of gravity, and they may lose their balance putting them at risk for falls. Dressing, wheelchair handling, transfers, sitting on the edge of or across surfaces, and toileting all require a combination of static and dynamic postural control involving the trunk (Lee & Lee 2021; Tak et al. 2015). Therefore, the rehabilitation of sitting balance is beneficial for enhancing quality of life after SCI.

Numerous studies have investigated sitting balance training in rehabilitation after SCI. Research has investigated both unsupported sitting exercises and BWSTT on sitting balance outcomes. In

addition, the use of VR or electrical stimulation as a therapeutic modality have led to favourable outcomes in sitting balance.

Multiple outcome measures were utilized in these studies to assess sitting balance. A systematic review by Arora and colleagues (2020) identified the modified functional reach test (mFRT) as the most used balance scale of those that evaluated sitting balance alone for people with an incomplete injury. The Berg Balance Scale (BBS) also assesses sitting balance alongside items evaluating balance with other tasks.

Falls are common among individuals living with SCI, even if they do not ambulate (<u>Abou & Rice</u> 2022). A recent review estimated that approximately 69% of non-ambulatory individuals with SCI experience at least one fall in a period of 6-12 months (<u>Khan et al. 2019a</u>). More recently, it has been reported that a shorter time since injury, higher mobility level (Spinal Cord Independence Measure version III [SCIM-III]), and lower FIST score represent significant risk indicators for falls in 59 wheelchair users with SCI (<u>Abou & Rice 2022</u>; <u>Abou & Rice 2024</u>). It should be noted that none of the studies included in this section (sitting balance) included fall data as an outcome measure. Future studies assessing different types of interventions and identifying the risk predictors for falls will be of interest.

It has been shown in individuals with motor-complete thoracic SCI that reaching forward while sitting with reduced thigh support provides more challenges in the dynamic sitting balance (postural control measured by the center of pressure parameters) than sitting with more thigh support (Ilha et al. 2020). Also, it has been shown that participants with cervical SCI are more reliant on visual and vestibular systems for sitting balance while depending less on proprioception and muscle control compared to controls (because they may not have control on these functions to maintain balance); showing that this strategy is ineffective in maintaining postural stability during unsupported sitting (Lei et al. 2023). Consequently, emphasizing the importance of proprioception and muscle control for seated postural stability and/or training during unsupported sitting to improve sitting balance is important in people with upper SCI (Ilha et al. 2020; Lei et al. 2023).

3.1 Virtual Reality (VR) for Sitting Balance

In recent years, technological advances such as VR have been introduced in the field of SCI rehabilitation and are being used as a therapeutic tool (Abou et al. 2020). VR is a computerbased technology that allows users to interact in a computer-generated environment, allowing the practice of rehabilitation exercises in a safe, standardized, reproducible, and controlled environment (Abou et al. 2020). VR comprises two types of systems according to the immersion level: (i) semi-immersive or non-immersive systems, and (ii) immersive systems (De Miguel-Rubio et al. 2020). Semi-immersive and non-immersive systems use a screen to display the environment with a low level of immersion (e.g., commercial videogame consoles), and immersive systems can incorporate other devices (e.g. gloves, exoskeletons, etc.) to provide sensory inputs to the patient (e.g., VR caves, large-screen projections, and head-mounted displays) (De Miguel-Rubio et al. 2020; Henderson et al. 2007). The use of VR therapy can be considered an additional therapeutic tool that helps practitioners provide external feedback to their patients about their performance and increase their motivation in adhering to intensive and repetitive exercise training (<u>Levin et al. 2015</u>); and may be considered in either an acute or chronic phase of SCI treatment (<u>Ionite et al. 2022</u>; <u>Leemhuis et al. 2021</u>).

Biofeedback may be defined as a process that enables an individual to learn how to change physiological activity for the purpose of improving health and performance (<u>Schwartz 2010</u>). Precise instruments measure physiological activity and rapidly and accurately "feedback" information to the user (<u>Schwartz 2010</u>). The presentation of this information—often in conjunction with changes in thinking, emotions, and behavior—supports desired physiological changes (<u>Schwartz 2010</u>), specifically gait movements and balance in this chapter. Biofeedback techniques in publications include those based on electromyography (EMG) recordings of muscle activation or position or force sensors that provide feedback on joint motion or functional attributes such as weight-shifting.

Authors Year; Country Date included in the review Number of articles Level of Evidence Type of Study AMSTAR Score	Method Databases Outcomes Measures		Conclusions
<u>Wang et al. (2024)</u> China	Methods: The study aimed to describe and calculate the effect sizes of virtual reality (VR) intervention on the functional	1.	There was no significant difference in TUG scores (seconds) of patients before and after training (MD=1.98, 95% Cl: -0.72 to4.69, <i>P</i> =.15).
Reviewed published articles up to October 2023	performance of SCI. Databases: PubMed, Embase, Web of Science, and Cochrane Library.	2.	There was a significant difference in the stability LOS test scores before and after training (SMD=1.75, 95% CI: 0.99 to 2.52, P<.01).
N=16 were included in the systematic review and 9 were in the meta-	Outcome Measures: Motor function and balance function (extremity motor score, box and block test, 10WMT, timed up and	3.	There was a significant difference in the BBS scores before and after training (MD=4.22, 95% CI: 1.78 to 6.66, P<.01).
analysis Level of evidence: Eight-item Quality Assessment Tool	go test [TUG], manual muscle strength assessment, BBS, and limit of stability [LOS] testing) and activities of daily living (Barthel Index).	4.	VR positively impacted movement and balance function in participants with SCI.
Type of study: 5 RCT and 4 non- RCTs			

Table 2. Systematic Reviews Assessing Virtual Reality (VR) (Monitoring Biofeedback) for Balance Outcomes in Patients With SCI

AMSTAR: 8			
Abou et al. (2020); USA Reviewed published articles up to September 2019 N=10 in the systematic review and 6 in the meta- analysis Level of evidence: Cochrane Risk of Bias Tool for RCTs and Quality Assessment Tool for pre-post studies with no control group Type of study: 3 RCTs 7 pre-post trials AMSTAR: 8	Method: The main objective of this systematic review and meta- analysis was to evaluate and synthesize the effects of VR therapy on gait and balance rehabilitation among people with SCI. Database: PubMed, Web of Science, Scopus, SportDiscus, and CINHAL. Outcome Measures: Sitting balance (T-shirt test and the modified functional reach test [mFRT]); static sitting balance (Trunk Recovery Scale item D and sway distance and velocity); dynamic sitting balance assessment (Trunk Recovery Scale item E); standing balance assessment (BBS, the activities- specific balance confidence scale [ABC scale], the LOS, the Romberg Index, the parameters of the center of pressure [CoP], the forward functional reach test and lateral functional reach test; and gait outcomes (WISCI II, IOMWT, TUG, 2MWT, spatiotemporal gait parameters, 6MWT, and gait speed).	1. 2. 3.	 A total of 149 participants from the 10 studies were included. Five studies used only VR therapy and the other studies used a combination of VR therapy with balance or coordination training. Methodological quality: a. Two of the three RCTs included in this review presented a low risk of bias and the third was rated as high risk of bias (and was not included in the meta-analysis). b. Four out of the seven pre-post studies included in this review presented as fair overall good quality and three studies were rated as fair overall quality (and were not included in the meta-analysis). Effects of VR therapy assessed by meta-analysis (n=6 studies): a. VR therapy with conventional balance rehabilitation was more effective in improving sitting balance compared with conventional sitting balance rehabilitation for the two meta-analyses (T-shirt test and mFRT) showed a statistically significant between-group difference (SMD=1.65; 95% CI 1.21-2.09; p<.01).
<u>De Miguel-Rubio et</u> <u>al. (2020);</u> Spain	Method: To analyze the effectiveness of VR systems to recover balance in patients with SCI.	1.	A total of 188 participants [comparison group, n=57; intervention group, n=131] took part in the different studies.
Reviewed published articles up to December 2019	Database: Embase, Web of Science, CINAHL, Scopus, Medline, PEDro, PubMed, and the Cochrane Central Register of Controlled Trials.	2.	The methodological quality of the RCTs included in this review was generally good (average total PEDro score = 6.3, range 4-8). Regarding the intervention protocols,
N=12 studies were included in the systematic review	Outcome Measures: Sitting balance and standing balance.		all the studies analyzed the effects of VR interventions through different technological devices compared to conventional physical therapy.

and 2 in the meta- analysis	4.	The results of the systematic reviews showed that all the studies got positive results on balance recovery for VR interventions.
Cochrane Collaboration tool, SCIRE system and the PEDro scale	5.	The overall results of the meta- analysis (n=2) of VR intervention in SCI patients using the mFRT and t-shirt test were favorable.
Type of study:		
3 RCTs		
9 cross-sectional studies and case- series studies		
AMSTAR: 8		

Table 3. Virtual Reality (VR) for Sitting Balance

Author Year Country Research Design Score Total Sample Size	Methods	Outcomes
	Acute SCI (<1 year)	
<u>Khurana et al.</u> (2017); India RCT <u>PEDro=8</u> Level 1 N=30	 Population: 30 participants with traumatic SCI and with the ability to sit unsupported for at least 10 s and had a minimum of active 90° of shoulder flexion; 28 males and 2 females; mean age 29.6 years; level of injury T6 (n=3), T7 (n=5), T8 (n=9), T9 (n=4), T10 (n=3), T11 (n=2), T12 (n=3); AIS A or B; and time since injury < 6 months. Treatment: All the participants received conventional physical therapy sessions; and were randomly allocated to either of 2 groups which consisted of balance training interventions, performed for 45 min a day, 5 times a week for 4 weeks, and with a progression of the difficulty level of exercises: 	 Overall, participants who received VR game-based balance training showed better improvement on the mFRT and the t-shirt test as compared to participants who received real-world task-specific balance training. The mFRT scores showed a significant change for time (p=0.001) and Time x Group (p=0.001) but no significant change for group effect (p=0.057).
	 Participants in group A (n=15) underwent VR game-based balance training in 3 environments (used to challenge movements and positions 	 The t-shirt test scores showed a significant change for group effect (p=0.05), but no significant change for time (p=0.14)

	 of various body segments to train the sitting balance). Participants in group B (n=15) underwent real-world task-specific balance training in an unsupported sitting position. Outcome Measures: mFRT and t-shirt test were assessed at the beginning and at the end of the intervention. 	and Time x Group (p=0.99).
Goel et al. (2023); India RCT PEDro=6 Level 1 N=18	 Population: 18 participants with SCI and AIS B, C, or D: VR + CPT Group (n=9): 8M, 1F; mean age: 39.11 years; and mean time since injury: 7.56 months FES + CPT Group (n=9): 7M, 2F; mean age: 41.89 years; and mean time since injury: 6.89 months Treatment: Eligible participants were randomized into the VR group and FES group; both groups received conventional physical therapy (CPT) treatment as well. Each participant was exposed to 45-min session of VR or FES along with the CPT session of 30 min, conducting five sessions per week for 4 consecutive weeks: VR training: Immersive type of VR, with games focused on trunk movements while the participant was in sitting position. Functional Electrical Stimulation: FES was used to induce muscle contraction in erector spinae and rectus abdominis in the thoraco-lumbar area, bilaterally on the motor points. Participants were in sitting position with back unsupported and, hands crossed and kept on shoulders or while performing reach outs. Three phases in the FES program used were as follows: first warmup, followed by work phase, and lastly recovery phase in simultaneous mode was used. The pulse frequency for warmup and recovery was set to 3 Hz. Both of these phases last for 5 min. The duration of the work phase was 30 min with a frequency set to 18 Hz. The intensity of the current was individually elevated to a level at which visibly strong 	 mFRT: Within-group analysis reported statistically significant improvement (p=0.001) in VR + CPT group as well as in FES + CPT Group. Between-group analysis revealed that trunk stability was more significantly improved in VR + CPT group as compared to FES + CPT group (p=0.003) with a 95% CI of 1.52–6.07. The calculated mean change between both the groups of 4.79 cm was more than the previously established MCID value with a large effect size (1.67), thus indicating clinical improvement. FIST: Statistically significant result has been calculated in VR + CPT group (P=0.01) as well as in FES + CPT group (P=0.01). Between-group analysis revealed significant differences proving VR is a more effective treatment than FES (P=0.002) within the calculated range of -2-13 points. Clinical significance was reported with calculated changes in scores (7 points) being more than MDC of the scale and medium effect size (0.72) for both the groups.

	contraction is obtained, but he/she having no unpleasant sensation. Muscles were activated simultaneously to generate co- activation and, therefore, to stiffen the trunk.	3.	SCIM-III: For all domains, there was statistically significant improvement in the VR + CPT group (P=0.01) and the FES + CPT group (P=0.01).
	Conventional Physical Therapy consisted of 2 sets of 12 repetitions of each range of motion exercises for both upper and lower limbs and mat exercises like rolling, long sitting and kneeling (2 repetitions with 5 min hold each). Outcome Measures: mFRT, function in	4.	The VR + CPT group had greater improvements than the other group, with a in self-care, mobility, and total scores, P=.006, 0.004, and 0.006 respectively,
	sitting test (FIST) (both static and dynamic components were evaluated), and SCIM-III were assessed at baseline, 2 and 4 weeks after intervention.		but non-significant in respiration and sphincter management with scores ranging from 1 to 19.
		5.	In both groups, no significant difference was noted in terms of the level of independence clinically as median changes in total scores (8 points) were less than the established MCID.
		6.	Side effects: The headset was found to be a little heavy, which was troublesome to some participants. Fear of fall initially after wearing the headgear and starting the game was felt by the participants. No other known harms of side effects were reported in general.
<u>Sengupta et al.</u> (2020); India Prospective	Population: 33 patients with SCI, neurological level of injury C5 or below and ability to abduct both shoulder at >90°; 27 males and 6 females; mean age 29.25 years; level of injury cervical (n=11), upper dorsal (n=10) and lower dorsal (n=12); AIS A (n=10), AIS B (n=8), AIS C (n=8), and AIS D (n=7); and mean time since injury < 6 months.	1.	No statistically significant differences between the groups in the scores of pre- and post-therapy were observed.
control trial Level 2 N=33	Treatment: Conventional therapy with individualized exercise program was provided to all participants. Additionally, participants were divided in two groups:		
	 VR training group (n=25): Participants performed VR training 5 days a week for 3 weeks with sessions lasting 30 		

	 min. All the games selected focused on static and dynamic balance and were played either while sitting or standing depending on the functional ability of the participant. The level of difficulty was gradually upgraded based on their performance. Control group (n=12 matched controls). Outcome Measures: BBS, balance section of the Tinetti Performance-Oriented Mobility Assessment (POMA-B), and Functional Reach Score (seated) were assessed pre and post intervention.		
	Chronic SCI (>1 year)		
Nair et al. (2022); India RCT PEDro=6 Level 1 N=21	 Population: 21 participants with SCI, the ability to sit unsupported for 30 s, and the ability to raise their hands to the head without losing balance. Group A (n=10): Mean (SD) age: 30.1 (8.37) years; 7M, 3F; level of injury: TIO-TI2 (n=4), LI-L4 (n=6); and mean (SD) time since injury: 2.45 (0.71) years Group B (n=11): Mean (SD) age: 32.45 (7) years; 6M, 5F; level of injury: TIO-TI2 (n=6), LI-L4 (n=5); and mean (SD) time since injury: 2.35 (0.96) years Treatment: Treatment Intervention was set for four weeks. Both groups received their routine therapy (exercise program focusing on strengthening, mobility, postural stability, and skill training) on six days of the week for 45 min. In addition, for three days per week, participants were assigned into one of the two groups: Group B (n=11): Received 30 min of VR training in the seated position using Xbox Kinect. Group A (n=10): Received 30 min of conventional therapy focused on training sitting balance. 	1.	For the mFRT, the within- group analysis showed that both groups showed significant difference post the intervention (P<0.05) in all the reach distances. On comparison between the two groups, it was seen that Group B showed significant improvement in all the reach distances.
<u>Lee & Lee (2021);</u> Korea	Population: 20 participants with chronic incomplete paraplegia and with capacity to maintain an independent sitting position for	1.	Both groups showed a statistically significant increase in post-

RCT PEDro=5 Level 2 N=20	more than 30 s; 13 males and 7 females; mean age 54.4 years; level of injury thoracic (n=21) and lumbar (n=9); AIS C (n=13) and AIS D (n=7); and mean time since injury 25.2 months. Treatment: Both groups received general	2.	treatment Force Sensitive Application and LOS scores as compared to the pre-treatment scores (p<0.05). Between-groups
	occupational therapy consisting of five 30- min sessions per week for 8 weeks. Participants were randomly allocated to one of two groups:		comparison showed a statistically significant increase in scores of all assessments in the
	 VR therapy group (n=10): Participants received 30 min of VR balance training on a sitting position with an individualization of the difficulty level. 		experimental group as compared to the control group (p<0.05).
	 Control group (n=10): Participants received 30 min of general rehabilitation (comprised for improving sitting balance). 		
	Outcome Measures: Sitting balance ability (measured by Force Sensitive Application) and LOS was assessed pre and post treatment.		
	Population: 11 participants with a SCI lower than TI and have passed the early subacute phase; 7 males and 4 females; mean (± SD) age 42.36 (± 12.90) years; AIS A (n=6), AIS C (n=3) and AIS D (n=2).	1.	No statistically significant differences were found between groups after the intervention in SCIM-III and mFRT.
<u>Manzanares et al.</u> (2021); Spain	Treatment: All participants in both groups performed the hospital rehabilitation protocol consisting of 2h per day of physiotherapeutic exercise, strengthening and mobility work, 5 days a week.	2.	Within group pre-post analyses showed significant improvement for mobility variable of the SCIM (p=0.036) for
RCT <u>PEDro=4</u> Level 2 N=11	In addition, participants were randomly assigned to control (n=5) or experimental (n=6) group. The experimental group underwent semi-immersive VR navigation therapy (virtual sailing in a sitting position) for 30–40 min per day, 3 times per week for 6 weeks.	3.	experimental group Within-group pre-post analyses showed that only the experimental group improved in the mFRT (p=.011).
	Outcome Measures: SCIM-III and mFRT were assessed one week before the start of the experimental phase and one day after the last session.		
<u>Tak et al. (2015)</u> ; South Korea RCT <u>PEDro=7</u> Level 1	Population: 26 participants with SCI and the ability to sit for more than 30 s independently; 20 males and 6 females; mean age 46.3 years; injury level cervical (n=9) and thoracic (n=17); AIS A (n=20) and AIS B (n=6); mean time since injury 22.0 months.	1.	Significant improvements in static balance parameters (anterior- posterior sway distance and velocity; medial- lateral sway distance and

N=26	 Treatment: All participants underwent conventional rehabilitation, consisting of a daily 3-hour physical and occupational therapy session, including stretching, strengthening, and functional training with sitting balance training, transfer to toilet, and positioning according to an individualized exercise schedule (5 days a week for 6 weeks). Additionally, participants were assigned to either a: VR training (n=13): Patients underwent a 30-min VR training program, using a Nintendo Wii, 3 times a week for 6 weeks, while sitting. According to the game selected, the patient may do balance training by using the arms and trunk, and can identify the correct motion through an avatar and feedback on the screen. Control group (n=13). Outcome Measures: Static balance ability, postural sway (PS) distance, and velocity were evaluated with the participants seated on a chair and asked to stare at the 10-cm diameter target placed 3 m away (by using a forceplate); and dynamic balance ability was assessed using the mFRT and T-shirt test. 	2. 3. 4.	velocity; and total sway distance and velocity) were found in patients who received VR training (p<.05). The VR group showed significant improvement compared to the control group, only for anterior- posterior sway distance and velocity (p<0.05), and total sway distance and velocity (p<0.05). Dynamic balance significantly improved in the VR group compared with that in the control group (p<0.05). The mFRT scores were significantly better for left (25%), front (39%), and right (43%). The T-shirt test time after intervention was shorter (23%) than the pre-test time in the VR group.
	forceplate); and dynamic balance ability was assessed using the mFRT and T-shirt test. Assessments were conducted at the beginning and at the end of treatment.		time in the VR group.

Discussion

A meta-analysis by Abou et al. (2020) included 6 studies, and found that the effects of virtual reality (VR) therapy with conventional balance rehabilitation were more effective in improving sitting balance compared to conventional sitting balance rehabilitation only. The combination of the two meta-analyses (T-shirt test and mFRT) showed a statistically significant between-group difference (SMD=1.65; 95% CI 1.21-2.09; p<.01) (Abou et al. 2020). Similarly, a recent systematic review and meta-analysis by Wang et al. (2024), included 16 studies, and supports VR therapy to be beneficial for standing balance in patients with SCI. There were significant differences in BBS (MD = 4.22, 95% CI: 1.78 to 6.66, P < .01) and limit of stability (LOS) (SMD = 1.75, 95% CI: 0.99 to 2.52, P < .01) (Wang et al. 2024). However, it is important to note that frontal plane balance improved while sagittal plane balance did not improve significantly, potentially due to the VR exercises given to participants (Wang et al. 2024).

Khurana et al. (2017) is a high-quality RCT which studied the inclusion of VR in a balance training intervention in acute SCI. Khurana et al. (2017) found that participants who received VR training showed improvement in sitting balance (especially on the t-shirt test) and functional independence (self-care components of the SCIM-III) compared to those who received real-

world task-specific balance training. Goel et al. (2023) compared the effects of participants either receiving VR training or functional electrical stimulation (FES) on trunk muscles on static and dynamic sitting balance; it was shown that sitting balance improved in both groups; however, the group that performed VR training showed more significant and clinically relevant results than the group receiving FES. In addition, the VR group outperformed the FES training group in terms of functional independence (SCIM-III scores; p=0.001), though neither group reached clinically significant difference scores (Goel et al. 2023).

There were four other RCTs that investigated the inclusion of VR balance training to usual rehabilitation protocols in patients with chronic paraplegia on sitting balance (Lee & Lee 2021; <u>Manzanares et al. 2021; Tak et al. 2015; Nair et al. 2022</u>). In three of the four RCTs (Lee & Lee 2021; <u>Tak et al. 2015; Nair et al. 2022</u>), there are significantly larger improvements in sitting balance in the VR experimental groups.

Two other studies (<u>Manzanares et al. 2021</u>; <u>Sengupta et al. 2020</u>) found no differences between groups who received additional balance training versus those who did not. It is possible that no differences were found because the studies were small and of short duration.

Conclusions

There is level 1 evidence (from 1 RCT: <u>Goel et al. 2023</u>) that a VR training program along with conventional physical therapy provides significant and more clinically relevant improvements in both static and dynamic sitting balance than a training program involving FES for the trunk muscles along with conventional physical therapy in participants with acute (mean time since injury < 8 months) and complete (AIS B, C, or D) SCI.

There is level 1 evidence (from 1 RCT: <u>Khurana et al. 2017</u>) that VR game-based balance training provides higher improvements in sitting balance (mFRT and t-shirt test) and on self-care components of the SCIM-III compared with real-world task-specific balance training in patients with paraplegia and acute SCI.

There is level 2 evidence (from 1 prospective control trial: <u>Sengupta et al. 2020</u>) that VR training added to routine conventional therapy, in comparison with only conventional therapy, does not provide improvements in sitting balance in patients with acute SCI.

There is level 1 and 2 evidence (from 2 RCTs: <u>Tak et al. 2015</u>; <u>Lee & Lee 2021</u>) that adding seated VR training to standard rehabilitation provides significant improvements in static and dynamic sitting balance versus standard rehabilitation alone in patients with chronic SCI.

There is level 1 evidence (from 1 RCT: <u>Nair et al. 2022</u>) that VR training in sitting position, along with routine therapy, provides larger improvements in sitting balance (mFRT) than conventional therapy focused on training sitting balance, along with the same routine therapy for people with chronic SCI.

There is level 2 evidence (from 1 RCT: <u>Manzanares et al. 2021</u>) that VR balance training can provide statistically significant gains in balance (as measured by the mFRT) and in mobility (as measured by SCIM-III).

Key Points

VR balance training produces improvements in sitting balance in people with both acute and chronic SCI.

3.2 Exercise and Activity-Based Therapy (ABT) for Sitting Balance

The effects on sitting balance in people with SCI have been investigated by several studies carrying out different exercise interventions.

Author Year Country Research Design Score Total Sample Size	Methods	Outcome
Nam et al. (2023); Republic of Korea RCT PEDro=4 Level 2 N=24	 Population: 24 participants with tetraplegia who were using a manual wheelchair for independent mobility. Wheelchair skills training program Group (n=12): Mean (SD) age: 36.02 (7.16) years; 9M, 3F; injury level: C5-C6 (n=7), C7-T1 (n=5); AIS: AIS B (n=6), AIS C (n=6); and mean (SD) time since injury: 34.92 (8.35) months Control Group (n=12): Mean (SD) age: 35.81 (4.51) years; 8M, 4F; injury level: C5-C6 (n=6), C7-T1 (n=6); AIS: AIS B (n=5), AIS C (n=7); and mean (SD) time since injury: 36.41 (9.19) months Treatment: Both groups underwent an 8-week intervention consisting of three 1 h sessions per week, including warm-up, training programs, and cool-down activities. Participants were assigned to: The wheelchair skills training program involved various wheelchair-related tasks, such as wheelchair propulsion, navigating obstacles, and transferring to and from a wheelchair. 	 A significant increase in ABLE scores was observed in the wheelchair skills training program group across all intervention periods (baseline to 4 weeks, 4 to 8 weeks, and baseline to 8 weeks) (p<0.05). However, no significant changes were observed in the control group at any intervention period (p>0.05). The wheelchair skills training program group demonstrated significantly higher changes in ABLE scores, compared to the control group in the baseline to 4 weeks and baseline to 8 weeks periods.

Table 4. Exercise and Activity-Based Therapy (ABT) for Sitting Balance

	 The control group underwent conventional physical therapy concurrently with the training group. Conventional physical therapy included upper extremity strengthening and endurance exercises on an arm ergometer, as well as aerobic exercise with indoor track cycling. Conventional physical therapy was performed at 70% maximum heart rate intensity (or a Borg rating of 3–4). Outcome Measures: Activity-based Balance Level (ABLE), pulmonary 	
	function, and Wheelchair Skills Test (version 4.1) were assessed at baseline and at the end of the intervention.	
Qi et al. (2018); China RCT <u>PEDro=5</u> Level 2 N=40	 Population: 40 participants with SCI, right-handed, and able to maintain a sitting posture for more than 30 min in a wheelchair. Wheelchair Tai Chi (WCTC) group (n=20): Mean (SD) age: 38.3 (10.24) years; 15M, 5F; injury level: C6-TI (n=3), T2-T5 (n=5), T6-TI2 (n=8), and below L1 (n=4); AIS: AIS B (n=2), AIS C (n=3), and AIS D (n=8); and mean (SD) time since injury: 5.61 (3.76) months Control group (n=20): Mean (SD) age: 43.05 (11.80) years; 16M, 4F; Injury level: C6-TI (n=4), T2-T5 (n=6), T6-TI2 (n=7), and below L1 (n=3); AIS: AIS B (n=2), AIS C (n=2), and AIS D (n=8); and mean (SD) time since injury: 5.11 (3.94) months Treatment: All participants in both 	 Compared with the control group, static sitting balance, left handgrip strength, and the psychological domain of quality of life improved significantly in the WCTC group (time by group interaction, p<0.05).
	groups were undergoing individual standard rehabilitation according to each patient's condition (consisted of personalized rehabilitation education, teaching mobility and transfer skills, preventing injury progression, handling spasticity, managing secondary complications, and helping patients to become more independent).	

	 Participants in the control group only received the standard rehabilitation intervention. The WCTC intervention involved a 30-min session, two sessions per day, and five days per week for a total of six weeks. The program consisted of three parts: a 5-min warm-up session, WCTC movements that encompassed 16 easy-to-learn and easy-to-perform forms, and a 5-min cool-down session. 	
	Outcome Measures: Muscle strength (trunk muscles and hand dynamometry), static sitting balance (the total displacement of center of pressure in the anteroposterior (COP _{AP}) and mediolateral (COP _{ML}) directions were collected), and quality of life (WHOQOL-BREF) were collected at baseline and after the intervention period.	
Harvey et al. (2011); Australia/Bangledesh RCT PEDro=8 Level 1 N=32	Population: 32 participants - 30 males and 2 females; motor level TI – L1; 29 AIS A, 2 AIS B, 1 AIS C; age range= 24- 31y; years post injury= 8-17 weeks Treatment: In the control group, participants received 6 weeks standard inpatient rehabilitation. In the experimental group, participants received 6 weeks standard inpatient rehabilitation + 3 additional 30-min sessions/wk of 84 task specific exercises with 3 levels of difficulty (252 exercises) in unsupported sitting. Outcome Measures: Maximal Lean Test (Maximal Balance Range), Maximal Sideward Reach Test, Performance Item of the Canadian Occupational Performance Measure (COPM)	 The mean between-group differences for the Maximal Lean Test, Maximal Sideward Reach Test and the Performance Item of the COPM were –20 mm, 5% arm length, and 0.5 points respectively.
<u>Boswell-Ruys et al.</u> <u>(2010);</u> Australia RCT	Population: 30 participants- 25 males and 5 females; 25 AIS A, 15 AIS B; level of injury: TI-12; mean age=45y; mean years post injury= 14.5y.	 The between-group MD for the maximal balance range was 64mm (p=0.006).
PEDro=8 Level 1	Treatment: Participants in the experimental group received 1hr of 84 task specific exercises with 3 grades of difficulty in an unsupported sitting 3	

N=30	times a week for 6 weeks. The control group did not receive any intervention. Outcome Measures: Primary measures were: Upper Body Sway Test, Maximal Balance Range Test; Secondary measures were: Alternating Reach test (supported and unsupported), Seated Reach Test 45°to right, Coordinated Stability Test (Version A), Upper Body Sway Test (lateral and antero-posterior components).	
Tsang et al. (2015); Hong Kong Prospective controlled trial Level 2 N=11	 Population: 19 wheelchair users with SCI, assigned to: Control group (n=8): Mean (SD) age: 46.2 (11.8) years; 7M, 1F; injury level: C6-TI (n=3), T2-T7 (n=2), and T8-L1 (n=1); AIS: AIS B (n=6), AIS C (n=0), AIS D (n=2); and mean (SD) time since injury: 17.3 (7.8) years Sitting Tai Chi Group (n=11): Mean (SD) age: 49.1 (10.3) years; 4M, 7F; injury level: C6-TI (n=6), T2-T7 (n=1), and T8-L1 (n=4); AIS: AIS B (n=5), AIS C (n=3), AIS D (n=3); and mean (SD) time since injury: 14.7 (13.7) years Treatment: Participants participated in either Tai Chi intervention or control group activities according to their preferences: The Tai Chi Intervention. The sitting Tai Chi intervention involved two 90-minute sessions, 2 times per week for 12 weeks. A 12-form sitting version of Yang's Tai Chi style was designed for the experiment. Each session included a 5-minute warm-up and 5-minute cool- down with rests as necessary. The whole 12 forms required approximately 3 minutes to complete and it took 6 lessons for the participants to learn the whole sitting Tai Chi routine. The participants spent the rest of the training sessions in polishing the forms and engaging in sitting balance training. The participants 	 No adverse events (AEs) and complications (e.g., dizziness) were reported during the training period. Changes in the Limits of Stability: A significant time by group interaction effect (p = 0.042; effect size = 0.263) was found in the reaction time. Paired <i>t</i>-tests revealed that only the sitting Tai Chi group had significantly better reaction time performance (p = 0.025) after three months of training. No significant change was found in the control group over time (<i>P</i> = 0.469). A significant time by group interaction (p = 0.016; effect size = 0.349) was found in the average maximum excursion. Only the sitting Tai Chi group achieved an improvement in the CoP distance travelled (p = 0.006) after three months of training. No significant change was found in the control group (p = 0.613). A significant time by group interaction (p = 0.025; effect size = 0.310) was found in the average directional control. The sitting Tai Chi trainees showed a

	 were encouraged to also practice at home for 90 minutes each week. Participants in the control group were involved in educational talks and social activities of equivalent duration and frequency. Outcome Measures: Sitting balance control (involving the limits of stability test and a sequential weight shifting test in the participant's own wheelchair), handgrip strength, and quality of life (WHOQOL-BREF) were conducted at baseline and post- intervention. 	 significant improvement (p = 0.047) after three months of training while there was no significant change in the control group (p = 0.076) over time. Changes in Sequential Weight Shifting Performance: The total time to complete the sequential weight shifting test showed a significant time by group interaction (p = 0.035; effect size = 0.281). Paired <i>t</i>-tests showed that only the Tai Chi group showed a significant average improvement (p= 0.012) after the three months of training. No significant change was found in the control group (p = 0.399). Between-group comparisons demonstrated that the difference between the two groups was statistically significant after the intervention (p = 0.001). A significant time by group interaction (p = 0.033; effect size = 0.286) was also found in
		terms of directional control, but there was no significant change in either group after the three-month intervention.
	Population: 12 participants - 9 males and 3 females; 11 AIS A, 1 AIS B; level of injury: T6-12. mean age= 40.86y.	 There was an increase in the mFRT distance in the experimental group.
<u>Kim et al. (2010);</u> Korea Prospective Controlled Trial	Treatment: The control group received conventional PT. The experimental group received conventional PT and goal-oriented	2. The experimental group showed a decrease in sway area with both opened and closed eyes after training.
Level 2 N=12	Level 2 training on a rocker board. The patients sat on a stable surface with	3. The experimental group showed a significant difference before and after training compared to the control, as shown by MFRT distance and swaying area.

	Outcome Measures: mFRT, sway area and sway velocity using the Balance Performance Monitor.	
	Population: 13 participants with SCI and a minimum total score of 2 points on the Modified Rivermead Mobility Index; mean (SD) age: 32.1 (12.4) years; 9M, 4F; injury level: C3-L1; AIS: AIS A (n=6), AIS B (n=5), AIS C (n=1), and AIS D (n=1); and mean (SD) time since injury: 46.5 (65.9) months	 There was an increase of 9% in the standardized reach distance (95% CI 2–16) for sitting balance.
de Oliveira et al. (2023); Australia Case series Level 4 N=13	Treatment: Participants received the activity-based therapy (ABT) Program. Exercise programs were individually tailored according to the person's goals and functional abilities. The intervention involved three key elements: (i) task-specific training, (ii) weight-bearing tasks and (iii) whole-body muscle strengthening. This approach included training in different positions such as sitting on the edge of the bed, 4-point kneeling, kneeling, standing with partial or full body-weight, body-weight supported treadmill training (BWSTT), active-assisted exercises, resistance training, neuromuscular electrical stimulation and balance and coordination tasks. All exercises were performed out of the wheelchair, incorporating whole-body movements. Participants were encouraged to perform all exercises to their maximum capacity with 1 to 5 min for recovery, if required, between exercises. The length of intervention varied from 4 to 24 weeks with a frequency of 2 to 4 times per week. Each session was 2 h long.	
	Outcome Measures: Seated Reach Distance test (SRD) was assessed at baseline (during the multiple-baseline 4-week period, weekly), at the start and end of the intervention period, at 2-week intervals during the intervention period, and at 8-week follow-up.	
<u>Larson (2022);</u> USA	 Population: 23 participants were included into three groups: OMA (Olfactory mucosa autografts) Group (n=7): Mean (SD) 	 ABT (average dose: 7 hours per week over 4.6 months) appeared to promote improvements in sitting

Prospective controlled trial Level 2 N=23	age: 30.3 (9.1) years; 7M, OF; level of injury: C4-T4; AIS: A (n=5), B (n=1), C (n=1), D (n=0); tetraplegia (n 6), paraplegia (n=1); mean (SD) time since injury: 2.9 (1.9) years		strength in four directions (0.6-0.8 kg per month) and dynamic balance in four of five directions (0.7-1.3 cm per month).
	 MC (matched controls) Group (n=6): Mean (SD) age: 28.4 (10.5) years; 6M, 0F; level of injury: C4-T5; AIS: A (n=4), B (n=1), C (n=1), D (n=0); tetraplegia (n=5), paraplegia (n=1); and mean (SD) time since injury: 5.0 (6.2) years 	2.	Individuals who had undergone an OMA had similar, but not greater, improvements in static and dynamic balance when compared with those who had ABT alone.
	 Other group (n=10): Mean (SD) age: 30.9 (10.8) years; 7M, 3F; level of injury: C6-T11 & cauda equina; AIS: A (n=5), B (n=0), C (n=3), D/cauda equina (n=1/1); tetraplegia (n=2), paraplegia (n=8); mean (SD) time since injury: 6.8 (8.4) years 		
	Treatment: All participants participated in an outpatient and individualized ABT program with a minimum dose of three to five 3-hour sessions per week over 3 to 6 months. The ABT program included 1 hour each of (a) pre-gait (e.g., weight bearing in multiple positions, posture and balance training, crawling, and standing pre-gait activities) and/or gait training (e.g., BWSTT and overground gait training), (b) intense exercise (e.g., repetitive neuromuscular facilitation, mat mobility, strengthening and endurance exercises, WBV, biofeedback, virtual gaming, and/or musculoskeletal interventions), and (c) FES cycling and/or dynamic standing frame activities. * Participants in the OMA group underwent the OMA procedure (mean time since OMA = 3.7 ± 3.9 months)		
	Outcome Measures: handheld dynamometer (peak force), measuring sitting strength – static balance, and the multi-directional reach test in sitting position measuring dynamic balance were assessed at initial examination, every 30 days, and at discharge from the ABT program.		

Williams et al. (2020); Canada Pre-post Level 4 N=14	Population: 14 participants with chronic SCI, been able to use an arm crank ergometer and with the ability to maintain an unsupported seated posture for at least 1 min; 8 males and 6 females; mean (± SD) age 44.3 (± 10.4) years; level of injury C4 (n=1), C5 (n=2), C6 (n=1), C7 (n=1), T4 (n=3), T5 (n=1), T11 (n=1), and T12 (n=3); AIS A (n=6), AIS B (n=5), AIS C (n=2), and AIS D (n=1); and mean (± SD) time since injury 21.7 (± 13.0) years. Treatment: Participants took part in a 5-week arm crank ergometry training program, which was delivered as a group "spin" 60 min class. Classes were held 3×/week and were standardized following an interval training routine with varying bouts that manipulated resistance, cadence, and/or sitting condition. Approximately 30% of the 40-min arm crank ergometry workout consisted of sitting in unsupported posture. Outcome Measures: Seated balance control with participants seated on an elevated force plate (static balance [root mean square distance and root mean square velocity from the center of pressure trajectory; and the confidence ellipse area [AREA-CE]], and dynamic balance [LOS in eight cardinal directions]) were assessed within two weeks of the start and end	1. 2. 3.	12 participants are reported for all outcomes. After training, there were no significant improvements in any of the static balance measures during the eyes open condition; however, in the eyes closed condition, there was a significant improvement in root mean square velocity (p=.013) and AREA-CE (p=.047); and a trend toward significance in root mean square distance (p=.074) after training. There were no significant improvements in LOS distance from pre- (387.5 mm ± 176.3 mm) to post-training (408.4 mm ± 205.2 mm) (p=.241).
	within two weeks of the start and end of the intervention.		
Sliwinski et al. (2020); USA Case series Level 4 N=19	 Population: 19 participants with SCI; level of injury C2-L5; complete injury (n=6), incomplete injury (n=10) and unknown (n=3); and mean time since injury 8.6 years. Treatment: Participants received Spinal Mobility program, which consisted in an 8-week community exercise program once a week in a community center setting for 4 hours and included a four-station circuit of resistance exercises, aerobic conditioning, trunk stability, and health education. 	1.	The paired t-test for the mFRT demonstrated a statistically significant (p<0.001) improvement of 5 cm from 27.1 cm (± 16.7) to 32.1 cm (± 17.6) for participants at the conclusion of the intervention.

	Outcome Measures: mFRT was assessed at baseline and post-intervention.		
	Population: 91 participants with non- progressive SCI; 65 males and 26 females; mean age (± SD) 35.3 (± 17.9) years; tetraplegia (n=49) and paraplegia (n=42); AIS A (n=31), AIS B (n=36), AIS C (n=15) and AIS D (n=9); and mean (± SD) time since injury 43.1 (± 51.4) months.		There was a significant improvement over 12 months in overall mobility (p=.000), showing a change score in the Modified Rivermead Mobility Index of 2 points (95% Cl: 1 - 2.3).
<u>De Oliveira et al.</u> (2019); Australia Case series Level 4 N=91	Treatment: During 3 to 12 months, participants received ABT 1 to 4 times per week for 2-h sessions, which consisted in an exercise program individually tailored. The intervention involved three key elements (e.g., task- specific training, weight-bearing tasks and whole-body muscle strengthening) and involved training in different positions. Participants were encouraged to perform all modalities of exercise to their maximum capacity. Outcome Measures: General mobility	3.	There was a significant improvement over 12 months in sitting balance (p=.000), showing a change of 0.2 in the SRD (95% CI: 0.1-0.22). There were no interaction effects between time and the neurological level of injury, AIS score, or duration post- injury for most outcomes.
	(The Modified Rivermead Mobility Index) and balance in sitting (the seated reach distance [SRD]) were measured at baseline, 3-, 6-, 9-, and 12- month.		
<u>Bjerkefors et al.</u> (2007);	Population: 10 participants - 7 males and 3 females; 7 AIS A, 2 AIS B, 1 AIS C; level of injury between T3-12; mean age= 37.6 ± 12y; median years post- injury= 11.5y. Treatment: Participants paddled a modified kayak ergometer for 60 min		Anterior-posterior angular and linear and twisting angular during lateral translations for all kinematic responses were significantly decreased except II for anterior-posterior angular.
Sweden Pre-post Level 4 N=10	3 times a week for 10 weeks. Outcome Measures: anterior- posterior, medio-lateral angular and linear and twisting displacements on support surface translations – forward, backward and lateral; Kinematic Responses include: I-onset of acceleration (unpredictable), II- constant velocity, III-deceleration (predictable), IV-end of deceleration.	3.	Medio-lateral angular displacements during lateral translations-significant decrease for kinematic response IV. Medio-lateral linear displacement during lateral translations-no significant effects for all kinematic responses.
<u>Bjerkefors &</u> <u>Thorstensson (2006)</u> ; Sweden	Population: 10 participants - 7 males and 3 females; 7 AIS A, 2 AIS B, 1 AIS C; level of injury between T3-12; mean		Sit and reach tests significantly increased from

Pre-post Level 4	age= 37.6 ± 12y; median years post- injury= 11.5y.		3.5cm at baseline to 5.8cm at the end of 10 weeks.
N=10	Treatment: Participants paddled a modified kayak ergometer for 60 min 3 times a week for 10 weeks.		
	Outcome Measures: Sit and reach tests.		
	Population: Experimental group: 12 participants - 9 males and 3 females; chronic SCI; 6 AIS A, 5 AIS B, 1 AIS C; level of injury: T2-11; mean age=40y; median years post-injury= 17y;	1.	Small effects in all 3 variables except on the median frequency in the sagittal plane (opposite to becoming normal).
<u>Grigorenko et al.</u> <u>2004</u> ; Sweden	Control group: 12 people without SCI who did not train.	2.	Before training and comparing to the control group, all variables differed.
	Treatment: Participants were involved in 2-3 modified kayak sessions on open water per week for 8 weeks.	3.	•
Pre-post Level 4 N=24	Outcome Measures: sitting quietly on a force plate-standard deviation (SD), median velocity, median frequency.	4.	Kayak training did not create significant sagittal or frontal CoP displacement with peoples with SCI.
		5.	9 of 12 participants with SCI stated that they had noted improvements in balance control in their wheelchair directly after their period of training.

Discussion

There were 12 studies that investigated the effects of various interventions (i.e., wheelchair skills training program, therapeutic exercise in unsupported sitting, seated/wheelchair Tai Chi, arm crank ergometry, kayak ergometry, Spinal Mobility, and activity-based therapy [ABT]) on sitting balance. Most of the participants had motor complete SCI (n=332, AIS A=113, AIS B=101, AIS C=47, AIS D=33).

After eight weeks of wheelchair skills training (<u>Nam et al. 2023</u>), in addition to conventional physical therapy, the wheelchair skills training program group demonstrated significantly larger increases in sitting balance. It should be noted that a significant relationship between maximal inspiratory pressure and balance, which appeared to be stronger in individuals with poor functional sitting balance, has been shown (<u>Palermo et al. 2022</u>). Considering the relationships between sitting balance and respiratory function, future research should focus on the effect of SCI-based breathing interventions on functional sitting balance.

One high-quality RCT examined the effect of an additional three weeks of task-specific exercises on sitting balance in people with acute SCI following six weeks of standard inpatient rehabilitation consisting of practice of activities of daily living (<u>Harvey et al. 2011</u>). Despite receiving more training sessions, there was no additional benefit for the experimental group

compared to the control group on functional outcomes of sitting balance, possibly due to the short period of balance training. In a similar study measuring unsupported sitting, Boswell-Ruys et al. (2010) found overall improvements in both the training and control groups, though no significant differences between groups on upper body sway or T-shirt tests. In a small RCT, Kim et al. (2010) found that exercise training on an unstable surface (with both eyes open and eyes closed) significantly improved people's performance on the mFRT and reduced swaying.

We found two studies assessing the effects of Tai Chi programs in people with SCI. Qi et al. (2018), found that the experimental group had significant improvements in static sitting balance and the psychological domain of quality of life. Similarly, Tsang et al. (2015) found that participants in the Tai Chi group improved their directional control and seated stability.

Three case series studies and one prospective controlled trial assessed sitting balance in participants with chronic SCI using similar therapeutic interventions (Spinal Mobility program and ABT) (de Oliveira et al. 2023; de Oliveira et al. 2019; Sliwinski et al. 2020; Larson 2022). The Spinal Mobility program comprised resistance exercises, aerobic conditioning, trunk stability, and health education for eight weeks and once a week (Sliwinski et al. 2020); meanwhile, ABT comprised task-specific training, weight-bearing tasks and whole-body muscle strengthening for 1 to 12 months and 1 to 4 times per week (de Oliveira et al. 2023; de Oliveira et al. 2019). Overall, significant improvements in sitting balance (mFRT, multi-directional reach test, seated reach test), sitting strength (peak force measured by a handheld dynamometer), functional independence (SCIM) or general mobility (Modified Rivermead Mobility Index) were shown after the intervention periods; however, the wide variance in the dosage in these studies makes difficult to extrapolate the results (de Oliveira et al. 2023; de Oliveira et al. 2019; Sliwinski et al. 2020; Larson 2022).

Sitting balance significantly improved with kayak ergometer training with substantial transfer effects to functional tests in the wheelchair (<u>Bjerkefors & Thorstensson 2006</u>; <u>Bjerkefors et al.</u> 2007). However, Williams et al. (2020) found that patients with SCI who enrolled in arm ergometry training improved on only some elements of static balance control, and none of the dynamic balance scores. Another study found that participants with SCI improved sagittal and frontal center of pressure (CoP) displacement after an 8-week open water kayak training program (<u>Grigorenko et al. 2004</u>).

Conclusions

There is level 1 evidence (from 1 RCT: <u>Harvey et al. 2011</u>) that the addition of task-specific sitting balance exercises, for three 30-min sessions per week, to a six-week standard inpatient rehabilitation period, resulted in no difference in balance outcomes in comparison with the standard inpatient rehabilitation period in participants with acute SCI.

There is level 1 evidence (from 1 RCT: <u>Boswell-Ruys et al. 2010</u>) that task-specific sitting balance exercises in participants with chronic SCI, three times a week for six weeks, provide significant improvements in maximal sitting balance range in comparison with no intervention.

There is level 2 evidence (from 1 RCT: <u>Nam et al. 2023</u>) that a wheelchair skills training program for eight weeks, along with conventional physical therapy, provides significant and larger

improvements in sitting balance (measured by the ABLE) compared with only conventional physical therapy in manual wheelchair users with chronic tetraplegia.

There is level 2 evidence (from 1 RCT: <u>Qi et al. 2018</u>; and from 1 prospective controlled trial: <u>Tsang et al. 2015</u>) that seated Tai Chi training programs provide significant improvements in sitting balance (kinematic) outcomes in wheelchair users with subacute and chronic SCI.

There is level 4 evidence (from 1 pre-post study: <u>Williams et al. 2020</u>) that a 5-week arm crank ergometry training program provides improvements in some elements of static balance in patients with chronic SCI.

There is level 4 evidence (from 1 pre-post study: <u>Sliwinski et al. 2020</u>) that a Spinal Mobility program (comprising resistance exercises, aerobic conditioning, trunk stability and health education) improves sitting balance in patients with chronic SCI.

There is level 4 evidence (from 2 case series: <u>de Oliveira et al. 2023</u>; <u>de Oliveira et al. 2019</u>) that ABT improves sitting balance (seated reach distance), seated postural control (seated reach test), functional independence (SCIM) and mobility (Modified Rivermead Mobility Index); especially in earlier phases of ABT exposure, in patients with chronic SCI.

Key Points

Various exercise interventions (i.e., wheelchair skills training program, unsupported sitting, seated Tai Chi, arm crank or kayak ergometry, Spinal Mobility, and ABT) can be used to improve sitting balance in people with subacute and chronic SCI.

Evidence is lacking about the optimal dosage and length of intervention for improving sitting balance in people with acute or chronic SCI.

3.3 Body-Weight Supported Locomotor Training (BWSLT) for Sitting Balance

There are different body-weight supported locomotor training (BWSLT) modalities that have been studied to determine the effects on sitting balance and trunk function in patients with SCI. However, these interventions have been extensively studied regarding their effects on standing balance and/or walking function (see section 4).

Author Year Country Research Design Score Total Sample Size	Methods	Outcome
<u>Piira et al. (2019a);</u> Norway	Population: 20 participants with chronic and motor incomplete SCI; 15 males and 5 females; mean age 50 years; level of injury	 There was no significant difference in change between the groups for

Table 5. Body-Weight Supported Locomotor Training (BWSLT) for Sitting Balance

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RCT PEDro=7	cervical (n=8), thoracic (n=8) and lumbar (n=4); AIS C (n=6) and AIS D (n=14); and		mFRT, 6.6 cm (–5.4, 18.5), p=0.26.
Level 1	median time since injury 4 years.	2.	The training intervention
N=20	Treatment: Participants were randomly divided in two groups:		was well tolerated with no AEs, and there were only
	 Control group (n=10): Participants received usual care (which might include overground walking). 		minor side-effects, such as superficial abrasions, which did not interfere
	 Intervention group (n=10): A treadmill with body-weight supported system was used for 60 days training, with 2 daily sessions of body-weight supported locomotor training (BWSLT) with manual assistance for a total of 90 min per day, 5 days per week for 3 4-weeks periods; with the aim of reducing the body-weight support (BWS) to <40% and/or increase walking speed towards normal (3–5 km/h). BWSLT also included overground training. The participants performed home exercises between the training periods. Outcome Measures: 10MWT, 6MWT, LEMS, 		with the regular training program.
	BBS, and mFRT were assessed at baseline and 2–4 weeks after the program.		
	Population: 24 participants wheelchair- dependents with or without some walking function and with chronic incomplete SCI; 9 males and 15 females; mean age 50.5 years; level of injury cervical (n=10), thoracic (n=9); and mean time since injury 18 years.	1.	There was a statistically significant group difference in postural control (mFRT), which declined 8.6 cm more in the intervention
<u>Piira et al. (2019b);</u>	Treatment: Participants were randomized to either intervention (n=7) or control group		compared with the control group.
Norway RCT PEDro=7 Level 1 N=24	 (n=12): Intervention participants received 60 days of robot-assisted locomotor training (with Lokomat®), with 3 training sessions per week over a period of 6 months. Each session included preparation (≈ 20–30 min), stepping on a treadmill (20–60 min) with BWS <40% of the participants's weight, and a few min of overground walking and/or exercises on the treadmill. 	2.	The intervention was well tolerated with no AEs, except for minor issues such as small leg abrasions.

	 Control participants received low- intensity usual care, 1–5 times per week. Outcome Measures: Full or partial recovery of walking function, 10MWT and 6MWT; LEMS; BBS; and mFRT were assessed within 30 days before randomization, and within 14–30 days after completion of the program. 		
	Population: 13 participants with chronic SCI; mean age: 37.2 years; 9 males, 3 females; traumatic (n=11) and non-traumatic (n=2); level of injury: TI-TI1; AIS A (n=1), AIS B (n=1), AIS C (n=7), and AIS D (n=3); and > 1 year of duration.	1.	Only 13 participants (of a planned 24) completed at least one intervention phase of the study, and 9 completed both phases of the study.
	Treatment: Each phase consisted of 48 sessions (three to five sessions per week) of one intervention followed by a washout period of at least 6 weeks.	2. 3.	There were no serious AEs during the study. No statistically significant
Martinez et al. (2018); USA RCT cross-over <u>PEDro=5</u> Level 2 N=13	 Sessions lasted 30 minutes not including setup, with 1–2 minute rest periods at least every 10 minutes. Exercise task difficulty was adjusted to achieve a desired range of RPE between 11 to 15 (out of 20). BWS for both interventions was provided by the overhead harness of the Lokomat system. BWS was set to 60% of body-weight initially, and then gradually reduced as tolerated. Several participants who reached independent weight support still wore the harness for safety. Treadmill exercise: Participants walked on a robotic-assisted treadmill (Lokomat) at initial speeds of 1–1.5 km/h. Speed was gradually increased as tolerated to a maximum of 3.2 km/h. The Lokomat's built-in guidance force (amount of assistance to reach a pre- 		differences between or within interventions were found for any balance outcome.
	defined gait kinematic pattern) was also gradually reduced as tolerated. Participants were reminded to swing their arms while walking.		
	 Multimodal exercise: Participants performed simultaneous balance and skilled upper extremity exercises. In addition to partial BWS, study personnel provided manual stabilization and perturbation as necessary. 		

	 Balance (subcortical) component: Participants' feet 		
	were placed on a semi- spherical balance platform (Bosu). Participants were instructed to keep the balance surface as stable as possible.		
	 Fine upper extremity (corticospinal) component: During balance exercise, participants performed a variety of skilled arm or hand manipulations, either unimanually or bimanually. All tasks were designed to require movements that engage corticospinal circuits. 		
	Outcome Measures: 'Sitting with back unsupported' subsection of the BBS and computerized posturography (sitting balance) were assessed at baseline and within one week of completing an intervention. A follow-up evaluation was planned for 6 weeks after intervention completion.		
	Population: 9 outpatients with chronic SCI; 6 males and 3 females; mean (\pm SD) age 37.8 (\pm 15.6) years; level of injury C5 (n=1), C6 (n=4), C7 (n=1), T1 (n=1), T11 (n=1), and T12 (n=1); AIS A (n=2), AIS B (n=3), AIS C (n=2) and AIS D (n=2); and mean (\pm SD) time since injury 51.1 (\pm 31.8) months.	1.	There were significant improvements in lateral (from 3.4 ± 2.8 to 6.9 ± 3.6 , P=0.002) and posterior (from 3.5 ± 2.9 to 6.9 ± 4.4 , P=0.044) trunk muscle strengths after 20 training
<u>Okawara et al.</u> <u>(2022)</u> ; Japan	Treatment: All participants underwent 20 BWSTT with the voluntary driven exoskeleton (using the hybrid assistive limb [HAL]) training sessions, which lasted 60 min and were performed 2-5 times a week.	2.	sessions relative to baseline. Anterior trunk muscle strength improved only in the AIS-D subgroup, and
Pre-post Level 4 N=9	Outcome Measures: Trunk muscle strength (defined as the ability to maintain a seated posture in four directions [anterior, posterior, left lateral and right lateral]; and		posterior trunk muscle strength improved in both the AIS-C and AIS-D subgroups.
	10MWT (only performed by 5 participants) were measured at baseline, and after 10 and 20 training sessions.	3.	Improvements in lateral trunk muscle strength showed a significant positive correlation with great gait speed (IOMWT) $(r_s = 1.00, P < 0.01).$
		4.	Older adult participants achieved greater improvement in trunk

			muscle strength than younger participants.
Tsai et al. (2021); USA Pre-post Level 4 N=8	 Population: 8 participants with chronic motor complete SCI who were using a wheelchair; 7 males and one female; median age 53 (37-64) years; level of injury TI (n=1), T2 (n=2), T4 (n=1), T7 (n=1), T8 (n=1), T9 (n=1), and T11 (n=1); AIS A (n=7) and AIS B (n=1); and median time since injury 3.5 (1.5-14) years. 7 participants without SCI (6 males and 1 female) joined in the study for seated balance tests only as a healthy comparative group. Treatment: Participants received supervised exoskeleton-assisted walking (EAW) training using a ReWalk including 3-4 sessions (4-6 h) per week (with a median of 30 [7-90] sessions within a median 111 [87-210] days) with the aim of reach an independent walking with the ReWalk and perform certain mobility skills. Each session included device donning and doffing, sit-to-stand and stand-to-sit, standing weight shifting balance skills, balancing with one crutch/walker timing, appropriate weight shifting during walking and stopping. Other mobility training was added when possible (e.g., turns, navigating to rest on a wall, and walking outdoor and up and down a ramp). Outcome Measures: Sitting balance* (sitting LOS using computerized dynamic posturography and mFRT) was evaluated pre and post training intervention. 	2.	The majority of participants had improvement in their computerized dynamic posturography seated balance tests after the intervention, with significant increases in total-direction endpoint excursion and maximal excursion (P=0.008 and 0.016 respectively). If the change in each direction is further explored, the participants demonstrated statistically non-significant improvements in endpoint excursion, maximal excursion, and directional control in most of the eight directions. These increases were toward the values measured in the healthy comparative group. After EAW training, mFRT results showed a slight increase but did not reach significant differences compared to before training.
<u>Okawara et al.</u> <u>(2020)</u> ; Japan Prospective controlled trial Level 2	Population: 20 participants with chronic SCI who had reached a plateau in recovery from paralysis symptoms; 15 males and 5 females; mean (± SD) age 43.3 (± 16.6) years; level of injury cervical (n=10), thoracic (n=9) and lumbar (n=1); AIS A (n=2), AIS B (n=4), AIS C (n=8) and AIS D (n=6); and mean (± SD) time since injury 80.4 (± 128.8) months.	1. 2.	There were no AEs. Participants in the low walking ability group showed little improvement in sitting balance.
N=20	Based on baseline WISCI II score, 8 participants were categorized into the low		

	walking ability group (n=8) and into the high walking ability group (n=12). Treatment: Participants underwent 20 sessions of BWSTT with voluntary driven exoskeleton (using the hybrid assistive limb [HAL]) (2–5 sessions per week [mean frequency 2.6 ± 1.1 sessions] with 60 min of duration) on a treadmill with 50% BWS. The velocity of the treadmill was individually set to the participant's comfortable walking speed, and there was no inclination. Outcomes Measures: The speed, distance,		
	and duration walked, and RPE were recorded in each session. WISCI II, 10MWT*, 2MWT, TUG, BBS, BBS in three categories (sitting balance, standing balance, and dynamic balance), and LEMS were evaluated at pre and post intervention. *No participants in the low group were able to complete the 10MWT at either time point.		
Khan et al. (2019b); Canada Pre-post Level 4 N=12	 Population: 12 participants with chronic, non-progressive SCI, using the wheelchair as the primary mode of mobility and able to use forearm crutches; mean (± SD) age 37.5 (± 13.7) years; level of injury C6 (n=2), C7 (n=1), T3 (n=2), T4 (n=2), T6 (n=1), T7 (n=2), T9 (n=1), T10 (n=1); AIS A (n=6), AIS B (n=2), AIS C (n=3) and AIS D (n=1); and mean (± SD) time since injury 7.7 (± 8.1) years. Treatment: Participants used the ReWalk 2.0 exoskeleton for training different activities (such as donning and doffing, sitto-stand, stand-to-sit, balancing in standing and walking) 4 days per week during 12 weeks of training. *Uninjured (i.e., control) participants were also recruited for comparison of some physiological measures. Outcome Measures: 10MWT during continuous walking in the ReWalk, 6MWT, LEMS, and sitting balance (for the LOS and for sway speed which were measured on a force platform) were evaluated before, during, immediately after, and at follow-up (2–3 months after training). 	1. 2. 3. 4.	10 participants completed the program and 9 of them were assessed at follow-up. AEs and technical issues included two falls (without no injuries sustained by the participants); skin abrasions; and some minor injuries in the trainer. ReWalk training improved the LOS in sitting between baseline and after training (p=0.02, mean change 4.5 ± 4.1 cm). Sway speed in sitting with eyes closed also improved significantly (p=0.03) for many participants.
<u>Chisholm et al.</u> <u>(2017);</u> Canada Case series	 Population: 3 participants with traumatic SCI: P1: 41 years of age, male, injury level: T3, AIS A, 23 years post injury. 	1.	Improved postural stability after training with Ekso compared to Lokomat during static balance tasks, indicated

		
Level 4 N=3	• P2: 42 years of age, male, injury level: C7, AIS B, 18 years post injury.	by reduced CoP root mean square distance
	• P1: 39 years of age, female, injury level: T4, AIS A, 25 years post injury.	and ellipse area, was shown. In addition, Ekso
	Treatment: An alternating treatment design with three intervention phases to compare the Ekso and Lokomat methods of robotic gait training was used. The two groups were Ekso-Lokomat-Ekso (P1 and P3) and Lokomat-Ekso-Lokomat (P2), with 10 training sessions in each intervention phase for a total of 30 sessions and no washout between intervention phases.	 training increased total distance of CoP movements during a dynamic balance task. Clinical measures of seated balance control: All participants slightly reduced their total time during the T-Shirt Test and increased their
	Participants performed up to 45 min of robotic-assisted gait training (RAGT) 3–4 times per week.	distance during the mFRT after Ekso training. There was a tendency for
	 Initial training with the Ekso™ consisted of sit-to-stand, standing balance, weight shifting, and stand- to-sit functions. Training focused on improving walking performance. 	greater time taken on the T-Shirt Test and shorter distance during the mFRT after Lokomat training as compared to Ekso
	 Gait training with the Lokomat robotic gait orthosis focused on increasing gait speed. Treadmill speed was set to the fastest speed that the patient could tolerate, and subsequently increased by increments of 0.1 km/h every 10 min. The level of BWS was adjusted to the minimum tolerated by the patient while ensuring appropriate stance phase kinematics. 	training.
	Outcome Measures: Seated (static and dynamic) balance control outcome measures (CoP, T-shirt test, and mFRT) were assessed at baseline and at the end of each intervention phase.	

Discussion

There were eight studies that investigated the effects of various BWSLT modalities (e.g., robotic-assisted gait training [RAGT] and walking training with an exoskeleton, BWSTT, or multimodal cortical and subcortical exercise with partial body support) on sitting balance and trunk function in patients with chronic SCI (<u>Chisholm et al. 2017; Khan et al. 2019b; Martinez et al. 2018; Piira et al. 2019a; Piira et al. 2019b; Okawara et al. 2022; Okawara et al. 2020; Tsai et al. 2021</u>). There were more participants with incomplete SCI than with complete SCI (n=109, AIS A [n=19], AIS B [n=12], AIS C [n=26] and AIS D [n=26]).

Overall, these studies expressed contradictory results. In one RCT, Piira et al. (2019a), sitting balance (assessed by mFRT) was improved with 60 days of BWSLT as much as in those receiving usual care (which included overground walking). However, another RCT by Piira et al. (2019b) found that sitting balance (assessed by mFRT) significantly decreased by 8.6 ± 2.17 cm after 6 months (3 training sessions per week) of robot-assisted locomotor training (with the use of Lokomat®), compared with usual care. Lastly, in the cross-over RCT by Martinez et al. (2018), sitting balance, as measured by "sitting with back unsupported" subsection of the BBS and computerized posturography, did not improve either in the group who received BWSTT, nor in the group who performed multimodal exercise.

The remaining four studies included patients with SCI who received a different number of sessions of BWSTT with Lokomat or different exoskeletons (e.g. hybrid assistive limb [HAL], $Ekso^{TM}$, or ReWalkTM) (Chisholm et al. 2017; Khan et al. 2019b; Okawara et al. 2020; Okawara et al. 2022; Tsai et al. 2021). Patients with chronic SCI showed promising results on trunk muscle strength (Okawara et al. 2022) and sitting balance (Chisholm et al. 2017; Khan et al. 2019; Okawara et al. 2020; Tsai et al. 2021). Surprisingly, the changes in anterior, posterior, and lateral trunk muscle strength showed significant positive correlations with age at baseline, indicating that older adult participants with chronic SCI experienced greater improvements than younger adults in trunk muscle strength following BWSTT with the voluntary driven exoskeleton (using the hybrid assistive limb [HAL]) (Okawara et al. 2022).

Conclusions

There is level 1 evidence (from 1 RCT: <u>Piira et al. 2019a</u>) that BWSLT with manual assistance does not provide more improvements than usual care in postural control in patients with motor incomplete and chronic SCI.

There is level 1 evidence (from 1 RCT: <u>Piira et al. 2019b</u>) that RAGT (with Lokomat®), compared to usual care, worsens the postural control (mFRT) in patients with chronic SCI.

There is level 2 evidence (from 1 RCT: <u>Martinez et al. 2018</u>) that neither BWSTT with Lokomat® nor multimodal exercise (simultaneous balance and skilled upper extremity exercises with partial body-weight support [BWS]) for 48 sessions did not provide improvements in sitting balance in people with chronic paraplegia.

There is level 4 evidence (from 2 pre-post studies: <u>Okawara et al. 2020</u>; <u>Okawara et al. 2022</u>) that BWSTT with the voluntary driven exoskeleton (using the hybrid assistive limb [HAL]) provides an improvement in trunk muscle strength, especially in an older adults subsample, and in sitting balance, in people with chronic SCI.

There is level 4 evidence (from 2 pre-post studies: <u>Khan et al. 2019b</u>; <u>Tsai et al. 2021</u>) that exoskeleton-assisted walking (EAW) training (with ReWalk[™]), consisting of different mobility skills, improves some sitting balance parameters (the control of trunk movement) in patients with chronic SCI.

Key Points

Studies with strong evidence show that different BWSLT training methods do not improve sitting balance in people with chronic SCI.

Only preliminary recommendations can be made from the results of lower-quality and smaller studies assessing exoskeleton training methods for sitting balance in people with chronic SCI.

3.4 Electrical Stimulation for Sitting Balance

FES utilizes short electric pulses through electrodes attached to the skin (<u>Goel et al. 2023</u>). Electrical stimulation pulses go through the skin to stimulate the nerves of muscles beneath the skin, and muscles contract as a result of the electrical stimulation. Specific to balance, FES targets upper motor neurons that help to improve trunk stability (<u>Bergmann et al. 2019</u>). Physiological changes in muscle tone brought about by FES will often remain after FES has stopped (<u>Senthilnathan et al. 2022</u>).

Author Year Country Research Design Score Total Sample Size	Methods	Outcome
<u>Goel et al. (2023);</u> India RCT <u>PEDro=6</u> Level 1 N=18	 Population: 18 participants with SCI and AIS B, C, or D: VR + CPT Group (n=9): 8M, 1F; mean age: 39.11 years; and mean time since injury: 7.56 months FES + CPT Group (n=9): 7M, 2F; mean age: 41.89 years; and mean time since injury: 6.89 months Treatment: Eligible participants were randomized into the VR group and FES group; both groups received conventional physical therapy (CPT) treatment as well. Each participant was exposed to 45-min session of VR or FES along with the CPT session of 30 min, conducting five sessions per week for 4 consecutive weeks: VR training: Immersive type of VR, with games focused on trunk 	 mFRT: Within-group analysis reported statistically significant improvement (p=0.001) in VR + CPT group as well as in FES + CPT Group. Between- group analysis revealed that trunk stability was more significantly improved in VR + CPT group as compared to FES + CPT group (p=0.003) with a 95% CI of 1.52–6.07. The calculated mean change between both the groups of 4.79 cm was more than the previously established MCID value with a large effect size (1.67), thus indicating clinical improvement.

Table 6. Electrical Stimulation for Sitting Balance

	 movements while the participant was in sitting position. Functional Electrical Stimulation: FES was used to induce muscle contraction in erector spinae and rectus abdominis in the thoraco-lumbar area, bilaterally on the motor points. Participants were in sitting position with back unsupported and, hands crossed and kept on shoulders or while performing reach outs. Three phases in the FES program used were as follows: first warmup, followed by work phase, and lastly recovery phase in simultaneous mode was used. The pulse frequency for warmup and recovery was set to 3 Hz. Both of these phases last for 5 min. The duration of the work phase was 30 min with a frequency set to 18 Hz. The intensity of the current was individually elevated to a level at which visibly strong contraction is 	2.	FIST: Statistically significant result has been calculated in VR + CPT group (p=0.01) as well as in FES + CPT group (p=0.01). Between- group analysis revealed significant differences proving VR is a more effective treatment than FES (p=0.002) within the calculated range of -2–13 points. Clinical significance was reported with calculated changes in scores (7 points) being more than MDC of the scale and medium effect size (0.72) for both the groups. SCIM-III: For all domains, there was statistically significant improvement in the VR + CPT group (p=0.01) and the FES + CPT group (p=0.01).
	 FES was used to induce muscle contraction in erector spinae and rectus abdominis in the thoracolumbar area, bilaterally on the motor points. Participants were in sitting position with back unsupported and, hands crossed and kept on shoulders or while performing reach outs. Three phases in the FES program used were as follows: first warmup, followed by work phase, and lastly recovery phase in simultaneous mode was used. The pulse frequency for warmup and recovery was set to 3 Hz. Both of these phases last for 5 min. The duration of the work phase was 30 min with a frequency set to 18 Hz. The intensity of the current was individually elevated to a level at which visibly strong contraction is obtained, but he/she having no unpleasant sensation. Muscles were activated simultaneously to generate co-activation and, therefore, to stiffen the trunk. CPT consisted of 2 sets of 12 repetitions of each range of motion exercises for both upper and lower limbs and mat exercises like rolling, long sitting and kneeling (2 repetitions with 5 min hold each). Outcome Measures: mFRT, FIST (both static and dynamic components were evaluated), and SCIM-III were assessed at baseline, 2 and 4 weeks after intervention. 	4.	as well as in FES + CPT group (p=0.01). Between- group analysis revealed significant differences proving VR is a more effective treatment than FES (p=0.002) within the calculated range of -2-13 points. Clinical significance was reported with calculated changes in scores (7 points) being more than MDC of the scale and medium effect size (0.72) for both the groups. SCIM-III: For all domains, there was statistically significant improvement in the VR + CPT group (p=0.01) and the FES + CPT group (p=0.01). The VR + CPT group was found to be more statistically significant than the other group, with a p=.006, 0.004, and 0.006 in self-care, mobility, and total scores, respectively, but non-significant in respiration and sphincter management. In both groups, no significant difference was noted in terms of the level of independence clinically as median changes in total scores (8 points) were less than the established MCID.
<u>Bayraktar et al.</u> <u>(2024);</u> Turkey RCT	 Population: 34 participants with complete (AIS A) SCI at least 3 months prior and able to sit unsupported in a wheelchair. Experimental group (n=17): Mean (SD) age: 34.8 (12.8) years; 6F, 11M; 	1.	Significant changes were observed in the experimental group's mFRT and trunk control test between the pre- and post-
PEDro=5 Level 2 N=34	injury level: T4-T7 (n=8), T8-T12 (n=9) Control group (n=17): Mean (SD) age: 39.5 (13.6) years; 4F, 13M; injury level: T4-T7 (n=8), T8-T12 (n=9)		assessment points (p<0.05). Similarly, in the control group, significant changes were observed (p<0.05).

 Treatment: Both groups underwent routine rehabilitation during hospitalization, including active or passive range of motion exercises, stretching and balance coordination exercises. Additionally, for three times a week for four weeks, participants were assigned into one of two groups: The control group received abdominal isometric strengthening exercises, applied three sets per session. The therapy provided to the control group was identical to that of the experimental group, with the exception of the stimulation. 	2.	The MD between groups for the mFRT area was 242.8 cm ² (95% Cl: 181.3–329.8; effect size 0.92; p<0.001) and 5.0 points for trunk control test (95% Cl: 3.9–6.0; effect size 0.98, p<0.001), favoring the experimental group.
 The experimental group received abdominal muscle stimulation for 10 min per session. Five minutes were allocated to bilateral rectus abdominis and 5-min to bilateral obliques externus, obliques internus and transversus abdominis muscles. To reduce muscle fatigue, the stimulation frequency was set at 25 Hz (low frequency) and to increase the number of stimulated muscle fibers, the stimulus duration was adjusted to 300 µs. The amplitude was increased to a maximum of 100 mA until a noticeable contraction was observed. The experimental group received electrical stimulation triggered by electromyography (EMG) activity during 10-s intervals. Each stimulation period, participants voluntarily flexed their head, inducing contraction in the abdominal muscles. The EMG device detected this contraction and delivered electrical stimulation. The experiment consisted of cycles of 10 s of stimulation followed by 10 s of rest, totaling 20 s per cycle, at a rate of three cycles per minute. *Electromyography triggered electrical stimulation (EMG-ES) is a method that uses a biofeedback-enabled electrical stimulation device to detect muscle 		

		1	
	contractions. The EMG signal triggers the muscle stimulation mode of the device.		
	Outcome Measures: mFRT, trunk control test, trunk muscles ultrasonographic muscle thickness measurement, and pulmonary function tests were assessed before and after the treatment.		
Bergmann et al. (2019); Estonia RCT (cross-over trial) <u>PEDro=5</u> Level 2 N=5 patients with SCI and 8 participants without SCI	 Population: 5 participants with tetraplegia; mean age (± SD) 39.2 (± 7.1) years; level of injury C5-C6; AIS B (n=4) and AIS C (n=1); and mean (± SD) time since injury 10.8 (± 30) years. 8 control group participants, whose gender and age were matched with participants with SCl' respective characteristics. Treatment: Participants with SCI were grouped in two groups (SCI_FES+TE and SCI_TE) and a cross-over design with a 7-month break was performed: Therapeutic exercise (TE) home program consisted of 8 different exercises (aimed at improving sitting balance and upper body posture) for 6 weeks, twice a week. Control group carried out only one round of therapy to collect reference data. FES: Erector spinae and rectus abdominis were stimulated simultaneously and bilaterally with a 4-channel FES device for 30-40 min. Outcome Measures: Dynamic sitting balance (LOS using a CONFORMat sensor) was assessed on the last therapy session of the first intervention period and the first 	1.	After six weeks of intervention, LOS of flexion increased 31.3% in SCI_FES+TE (p=0.465) but decreased by 12.1% in SCI_TE (p=0.345); LOS of lateral flexion right increased 5.0% in SCI_FES+TE (p=0.686) and 2.7% in SCI_TE (p=0.465) with no statistically significant difference between the 3 study groups post-intervention (p=0.054); and LOS of lateral flexion left increased 20.1% in SCI_FES+TE (p=0.686) and 21.3% in SCI_TE (p=0.500) with no significant differences between groups (p=0.116) after the intervention. After the seven-month break period, LOS of flexion decreased by 31.9% (p=0.138), LOS of lateral flexion right decreased by 27.3% (p=0.225), and LOS of lateral flexion left decreased
	therapy session of the second intervention period after a seven-month break.		by 46.4% (p=0.043).
<u>Tharu et al. (2023);</u> China Pre-post Level 4	Population: 5 participants with complete (AIS A) and chronic SCI and with impaired trunk and sitting function; 2 males and 3 females; mean (± SD) age 42.0 (± 13.7) years; level of injury C4 (n=1), C5 (n=2), C6 (n=1), and C7 (n=1); and mean (± SD) time since injury 9.3 (± 7.4) years. Treatment: Participants underwent two phases of treatment (each lasting for 12	1.	Compared to baseline, the overall forward reach distance significantly increased after TSCS+TSR (p=0.026), and further slightly raised during TSR (p=0.024), which was maintained throughout the follow-up period (p=0.026).
N=5	weeks [TSCS + task-specific rehabilitation followed by task-specific rehabilitation alone]). Participants attended one to three sessions per week.	2.	The overall mean trunk control test and mean FIST scores significantly increased after TSCS+TSR administration, increased

	 Task-specific rehabilitation (TSR) consisted in the training in a variety of positions, ranging from sitting in a wheelchair to lying on a bed or a floor mat. For transcutaneous electrical spinal cord stimulation (TSCS) + TSR treatment, the participant was asked to perform various task- specific exercises for 45–60 min each session. TSCS were applied with two stimulation electrodes attached between TII–TI2 and L1–L2. Outcome Measures: mFRT; static and dynamic balance (by trunk control test; functional sitting balance (by FIST); and ISNCSCI motor levels were assessed at baseline; at 6, 12, 18 and 24 weeks; and at 6 weeks follow-up. 	further during TSR, and showed a slight reduction at the follow-up period. All these values were significantly greater than the baseline values (p<0.01). However, there was no significant difference between TSCS+TSR and TSR, between TSCS+TSR and follow-up, or between TSR and follow-up.
Tefertiller et al. (2022); USA Pre-post Level 4 N=50	 Population: 50 participants with cervical SCI receiving outpatient therapy; mean (± SD) age 34.1 (± 16.7) years; level of injury CI (n=3), C2 (n=2), C3 (n=6), C4 (n=21), C5 (n=7), C6 (n=9), and C7 (n=2); AIS A (n=5), AIS B (n=8), AIS C (n=23), and AIS D (n=14); and mean (± SD) time since injury 5.4 (± 2.4) months. Treatment: Upper extremity training sessions were performed for 1.5 hours/day, 5 days/week for a minimum of 40 sessions and consisted of 3 components: 60 min of functional task-specific practice in combination with wide pulse/high frequency FES (WPHF-FES) to the trunk and upper extremities. 15 min of functional training without WPHF-FES. Home integration training. The Sage System (pulse width available of 500 µs) (n=f) and XciteÔ system (pulse width available of 1000 µs) (n=15) were used to stimulate the muscle groups. Outcome Measures: Trunk stability (mFRT) was assessed at baseline and at outpatient therapy discharge. 	 The mFRT effect size was moderate to large as the mean improvement (13.6 cm) was greater than established MDC (5.16 cm). After adjusting for completeness of injury; the motor incomplete group experienced a moderate to large effect size for mFRT (15.6 cm, p<.001); and the motor complete group experienced non-significant improvement in changes in mFRT (6.5, p=.074). After adjusting by treatment pulse width, significant results for mFRT remained robust across all analyses. However, the 1000 µs group showed more changes in the mFRT scores than the 500 µs group (23.4 cm vs. 10.0 cm).

	Population: 11 wheelchair rugby athletes with tetraplegia; 10 males and one female; mean age 41.6 years; level of injury C4 (n=2), C4-C5 (n=2), C5-C6 (n=1), C6 (n=4) and C7 (n=2); and mean time since injury 17.5 years.	1.	Total reaching with electrical stimulation was significantly (p=0.03) higher (9%, large effect size) compared with the non-
<u>Kouwijzer et al.</u>	Treatment: A single session of electrical stimulation was applied on the rectus		electrical stimulation condition.
<u>(2022)</u> ;	abdominis, obliquus externus abdominis	2.	Of the individual reaching
The Netherlands	and erector spinae muscle simultaneously		directions, the diagonal
Post-test	to create co-contraction.		direction with dominant
Level 4	Outcome Measures: Trunk stability (n=9) (reaching task [the participant sat in his/her		arm was the only task that scored significantly (p=0.04)
N=11	own daily wheelchair without any strappings with the purpose of to push away a tube as far as possible in a forward, lateral and diagonal direction]) was measured and compared between the electrical stimulation and non-electrical stimulation condition.		higher with electrical stimulation (33%, medium effect size) compared with the non-electrical stimulation condition.

Discussion

Goel et al. (2023) compared the effects of participants either receiving FES on trunk muscles or VR training on static and dynamic sitting balance; it was shown that sitting balance improved in both groups; however, the group who performed VR training showed more significant and clinically relevant results than the group receiving FES (Goel et al. 2023). In addition, the VR group outperformed the FES training group in terms of functional independence (SCIM-III scores; p=.001), though neither group reached clinically significant difference scores (Goel et al. 2023).

Recently, one randomized controlled trial (RCT) assessed the effects of a specific type of electrical stimulation called electromyography triggered electrical stimulation (EMG-ES) (<u>Bayraktar et al. 2024</u>). After four weeks of training, both groups showed improvements in sitting balance outcomes; however, the group who received EMG-ES showed significant improvements compared to the control groups on modified functional reach test (mFRT) and trunk control test scores (p<0.001; effect sizes 0.92, 0.98) (<u>Bayraktar et al. 2024</u>).

One cross-over RCT compared the effects on dynamic sitting balance of participants receiving FES (on erector spinae and rectus abdominis) plus therapeutic exercise (aimed at improving sitting balance and upper body posture) for 6 weeks, twice a week; and participants performing only the exercise (Bergmann et al. 2019). Most of the dynamic sitting balance parameters improved in both groups with no significant differences between groups (Bergmann et al. 2019).

In a pre-post study on FES and trunk stability/reach, Tefertiller et al. (2022) grouped participants with SCI into motor incomplete or motor complete and in those who received wide pulse/high frequency-FES (WPHF-FES) pulse width of 500 μ s or 1000 μ s (Tefertiller et al. 2022). Only the motor incomplete group experienced statistically significant and clinically meaningful improvements for mFRT (15.6 cm); regarding the pulse width, the 1000 μ s group showed larger mFRT change scores (23.4 cm vs. 10.0 cm).

One small pre-post study (N=5) included five patients with motor complete tetraplegia who underwent a task-specific rehabilitation (TSR) intervention with the application of transcutaneous electrical spinal cord stimulation (TSCS) simultaneously at T11 and L1 spinal levels for 12 weeks, followed by the same intervention (but without TSCS) for another 12 weeks (<u>Tharu et al. 2023</u>). Dynamic and static sitting balance (as measured by mFRT, trunk control test and FIST) were assessed at baseline, after the combined intervention (TSCS + TSR), after the intervention alone (TSR) and at 6 weeks follow-up (<u>Tharu et al. 2023</u>). Compared to baseline, dynamic and static sitting balance (as measured by mFRT, trunk control test, and FIST) were shown after the combined intervention and were maintained throughout the follow-up periods (<u>Tharu et al. 2023</u>).

Conclusions

There is level 1 evidence (from 1 RCT: <u>Goel et al. 2023</u>) that a VR training program along with conventional physical therapy provides significant and more clinically relevant improvements in both static and dynamic sitting balance than a training program involving FES for the trunk muscles along with conventional physical therapy in participants with acute (mean time since injury < 8 months) and complete (AIS B, C, or D) SCI.

There is level 2 evidence (from 1 RCT: <u>Bayraktar et al. 2024</u>) that a 4-week training program using EMG-ES for abdominal muscles provides significant improvements in sitting balance (mFRT and trunk control test) compared with an abdominal isometric strengthening exercise program (without stimulation) in participants with complete (AIS A) SCI who continued with their routine rehabilitation program (active or passive range of motion exercises, stretching, and balance coordination exercises).

There is level 2 evidence (from 1 RCT: <u>Bergmann et al. 2019</u>) that the combination of a therapeutic exercise program and FES on trunk muscles for 6 weeks, compared with therapeutic exercise only, provides an improvement in the dynamic sitting balance in patients with chronic tetraplegia.

There is level 4 evidence (from 1 pre-post study: <u>Tharu et al. 2023</u>) that 12 weeks of TSR and the simultaneous application of TSCS at T11 and L1 spinal levels provide significant improvements in dynamic and static sitting balance, and these improvements were maintained at 6 weeks follow-up.

There is level 4 evidence (from 1 pre-post study: <u>Tefertiller et al. 2022</u>) that upper extremity training sessions (consisting of 60 min of functional task-specific practice in combination with WPHF-FES to the trunk and upper extremities, on 15 min of functional training without WPHF-FES, and on home integration training) improve the trunk stability (mFRT) only in patients with acute motor incomplete tetraplegia (and not in acute motor complete tetraplegia).

Key Points

Electrical stimulation plus balance training can be used to facilitate trunk stability for seated dynamic postural control in people with SCI, though a VR program plus balance training provided superior results.

In people with acute SCI, electrical stimulation can improve dynamic trunk stability more so in motor incomplete tetraplegia than motor complete tetraplegia.

In people with chronic SCI, a combination of electrical stimulation and therapeutic exercise can improve sitting balance outcomes.

3.5 Sitting Balance Summary

Numerous studies have investigated the effects of different interventions on sitting balance function in people with SCI. These interventions have been grouped into electrical stimulation, exercise training, VR, and BWSLT. Although further studies are needed focusing on the sitting balance function in people with SCI, taking all the results from this review together and from a clinical perspective:

- VR consistently provided positive effects on sitting balance performance in people with SCI.
- Different exercise interventions provide the most positive effects on sitting balance and/or trunk strength for people with SCI.
- On the other hand, different body-weight supported training interventions generally do not provide significant effects on sitting balance function in people with SCI. Even though numerous studies in the area, the main/primary outcome measures of these interventions are usually walking and/or standing balance function (and not sitting balance). So, BWSLT does not seem to be an ideal intervention for improving sitting balance function.
- Different types of electrical stimulation added to exercise programs did not seem to add to the effects of the exercise programs re: sitting balance outcomes in people with SCI.
- Further high-powered studies with larger sample sizes, and where balance is studied as a primary outcome in studies, would be helpful to understand training effects and dosage of interventions in sitting balance.

4 Standing Balance

Up to 75% of individuals with incomplete SCI experience falls while standing and frequent losses of balance post-rehabilitation (<u>Arora et al. 2020</u>; <u>Brotherton et al. 2007</u>). Moreover, falls are among the most common cause of SCI in persons > 60 years old (<u>Dohle & Reding 2011</u>), so

standing balance training may be particularly important for the safety of older people and people with incomplete SCI.

There are several different interventions which focus on the recovery of standing balance in people with SCI. Some investigations have examined the effect of locomotor training on enhancing balance performance as a secondary measure, which could be justified as walking and standing balance outcome measures are highly correlated (Forrest et al. 2012). Several systematic reviews have been conducted to show the effects on balance due to technology-assisted rehabilitation (Lorusso et al. 2022), or due to the use of specific technologies such as RAGT with Lokomat (Alashram et al. 2021), overground powered lower limb exoskeletons (Tamburella et al. 2022), and VR (Abou et al. 2020) in patients with SCI. Overall, there is very low quality of evidence that walking interventions and upright balance training with visual feedback had clinically meaningful and significant pooled effects on improving standing balance control (Benn et al. 2025).

There are many different outcome measures used in the studies included below assessing standing balance; however, the systematic reviews of Arsh et al. (2021) and Arora et al. (2020) showed that the FRT, <u>BBS</u>, and Mini-BESTest are the most studied tests and appear to be valid and reliable clinical instruments assessing balance function in patients with SCI. Another systematic review suggested the Mini-BESTest is a reliable tool for assessing standing balance in people with SCI (<u>Hosseinzadeh et al. 2024</u>).

Authors Year; Country Date included in the review Number of articles Level of Evidence Type of Study AMSTAR Score	Method Databases Outcomes Measures		Conclusions
<u>Benn et al. (2025);</u> Canada	Method: This systematic review and meta-analysis aimed to describe and compare the efficacy and dosage of	1.	Methodological quality of the included studies: Of the included studies, 12 (46%) were deemed to have good (i.e., modified D&B Checklist score >19)
Reviewed published articles up to June 2023	interventions targeting upright balance control, balance confidence, and falls for adults with motor-incomplete SCI/D.		methodological quality, while the remaining studies (n=14, 54%) were deemed to have moderate (i.e., modified D&B Checklist score=11-19)
N=26	Database: APA PsycINFO (Ovid), CINAHL, Embase (Ovid), Emcare Nursing (Ovid), Web of Science	2.	quality. Study participants and setting: A total of 500 participants participated in the studies, with sample sizes of individual

Table 7. Systematic Reviews Assessing Different Strategies and/or Balance Interventions for Standing Balance Outcomes in Patients With SCI

Level of evidence:	Core Collection, and Medline ALL (Ovid).		studies ranging from 4-95 participants. The time since injury ranged from 1-37
Modified Downs and Black (D&B) tool	 Outcome Measures: Standing balance control: BBS, kinetic variables measured via force plates, 		years, and the neurologic level of injury ranged from C1 to L3. More participants were rated AIS D (n=266) than AIS C (n=110).
Type of study: 14 pre-post 8 RCT 4 cross-over	Five Times Sit to Stand Test (FTSTS), Mini-BESTest, Community Balance and Mobility scale, Functional Reach Test, and Tinetti Scale.	3.	The interventions studied were: BWSTT (n=5), VR combined with standing balance activities (n=6), robotic BWSTT (n=2), robotic resistance treadmill training (n=2), VFT (n=2), stepping training (n=2), stepping training + visual feedback balance training (VFBT) (n=1),
AMSTAR: 7	 Balance confidence: ABC scale and Falls Efficacy Scale - International (FES-I). Occurrence of falls. 		perturbation-based balance training (VFDF) (n=n), perturbation-based balance training (n=1), FES + VFT (n=1), underwater treadmill training (UTT) (n=1), walking training on a walking track with differing surfaces (n=1), skill training (n=1), and community-specific ambulation training in various community locations (n=1).
		4.	Dosage: The included interventions ranged from 4-20 weeks in length, at a frequency of 2-15 sessions/week, and 0.37-1.5 hours per session; resulting in a total of 5.4-180 hours of therapy and 12- 180 sessions. The results of the meta- regressions indicated that total dosage did not predict outcomes on the BBS (P=0.34) or ABC Scale (P=0.81).
		5.	AEs: Minor AEs (increased tone and spasticity with robotic resistance treadmill training, a controlled fall in Perturbation-based Balance Training, minor skin abrasions in BWSTT and robotic BWSTT, falls and ankle soreness in task-specific training, fatigue and muscle soreness with stepping training, and neuropathic and musculoskeletal pain within VR were reported in 8 (30.77%) of the included studies, and no serious AEs were reported.
		6.	Pooled effects:
			a. For upright balance control as measured with the BBS, there was a significant pooled effect, meaning upright balance control improved with balance interventions (Hedge's g=.51; 95% Cl, .3666; l ² =.60). When

the effect was examined by category of balance intervention, the pooled effects were significant for walking interventions (Hedge's g=.55; 95% Cl, .2982; l ² =.63) and upright balance with visual feedback interventions (Hedge's g=.57; 95% Cl, .1797; l ² =.63), but not for conventional physiotherapy (Hedge's g=.42; 95% Cl, .12 to .97; l ² =.62).
 b. Similarly, when the FTSTS score was examined as a measure of upright balance control, there was a significant pooled effect (Hedge's g= .73; 95% CI, 1.18 to .27; I²=.99), with all studies that used this measure evaluating walking interventions.
 c. There was a significant pooled effect for balance confidence as measured with the ABC Scale, meaning balance confidence improved with balance interventions (Hedge's g=.40; 95% CI, .1367; I²=.56). In this case, only walking interventions showed significant pooled effects (Hedge's g=.22; 95% CI, .0242; I²=.00) and not interventions targeting upright balance with visual feedback (Hedge's g=.38; 95% CI, .22 to .98; I²=.79).
 d. There was no significant pooled effect on the number of fallers (Hedge's g=.97; 95% CI, 6.32 to 8.27; l²=.98), with the studies included in this analysis focused on walking interventions.
7. Evaluation of the certainty of the evidence:
a. The quality of the evidence suggesting that walking-specific interventions and interventions focused on upright balance with visual feedback improve upright balance control, as measured with the BBS, is "very low. Similarly, the quality of the evidence suggesting conventional physiotherapy does

			 not affect upright balance control was deemed "very low." b. For the outcome of balance confidence, there was "low" quality evidence suggesting walking-specific interventions improve confidence and "very low" quality evidence suggesting the opposite for interventions with visual feedback. c. "Very low" quality evidence suggested walking-specific
			interventions do not affect falls.
Walia et al. (2023); India Reviewed published articles up to March 2021 N=14 Level of evidence: PEDro scale for RCT and modified checklist of the Downs and Black tool for non-RCT	Method: This systematic review and meta-analysis aimed to assess the methodological quality and effectiveness of various rehabilitation interventions offered for improving standing balance in individuals with incomplete SCI. Database: SCOPUS, PEDro, PUBMED, and Web of Science. Outcome Measures: BBS, Tinetti test, TUG, normalized jerk and root mean of sway, postural sway length as measured by a forceplate, and static and dynamic stability test using Stabilan-01 stabiloplatforms, forward functional reach test, and lateral functional reach test.	1.	 Participant characteristics: a. RCT: The pooled sample of studies included a total of 222 individuals with iSCI. Injury level: Cervical (59%), thoracic (29.7%), and lumbar (8,56%). AIS: AIS C (20.7%) and AIS D (53.6%). b. Non-RCT: The pooled sample of studies included a total of 967 individuals with iSCI. Injury level: Cervical (71%), thoracic (26.5%), and lumbar (1%). AIS: AIS C (30.5%) and AIS D (69.3%). Quality of trials: a. RCT: The average PEDro score for all trials was 7/10 (good quality). b. Non-RCT: The average modified Downs and Black score for the trials was 6/9 (moderate quality).
Type of study:		3.	
10 RCTs 8 pre-post 4 prospective observational cohort study			 a. The pooled SMD for controlled and uncontrolled trials of body-weight supported training interventions was -0.26 (95% Cl, -0.70 to 0.18; p=.25) and 0.46 (95% Cl, 0.33 to 0.59; p<.001), respectively.
1 cross-over study 1 prospective study 1 quasi- experimental AMSTAR: 6			 b. The pooled effect size of-0.98 (95% Cl, -1.93 to -0.03; p=.04) indicated significant improvements in balance after a combination of body-weight supported training and stimulation. c. Pre-post studies analyzing the effect of VR training interventions on BBS scores in individuals with iSCI

		1	
			reported a MD of 4.22 (95% Cl, 1.78 to 6.66; p=.0007).
			d. Small effect sizes were seen in pre- post studies of VR+stimulation and aerobic exercise training interventions indicating no significant improvements after training on standing balance measures.
	Method: The aim of this review	1.	Most of the studies reached a
Italy	was to explore the technology- assisted strategies to assess and rehabilitate balance function in people with SCI.		"moderate" quality score (D&B score: 13.8 ± 2.14), while the remaining 4 studies were classified as "poor" (D&B score: 8.75 ± 1.5).
published articles	Database: MEDLINE, Embase, Scopus, Cochrane Library and IEEE Xplore.	2.	327 participants (n=270 persons with SCI) were enrolled in the selected studies.
	Outcome Measures: In the 15	3.	The technological devices used for
N=19 (n=15 focused on technology- assisted rehabilitation)	studies based on technology- assisted rehabilitation device effects on balance (most of these studies considered the balance rehabilitation as a side effect of gait training) were analyzed by means of clinical scales (N=11)		balance rehabilitation were grouped into three main categories: Treadmill- Based Devices (no guidance, pelvis guidance, hip-knee guidance and lower-leg guidance), Over Ground Devices (hip-knee guidance: Ekso and ReWalk) and Tilt Table Devices.
evidence:	(BBS, TUG, the mFRT, the functional reach test (FRT), the ABC scale, the T-shirt test and the Tinetti scale), instrumental	4.	The training protocols (number of sessions, frequency and duration) were heterogeneous and sometimes not reported.
	assessment (N=7) (body's Centre of Mass and CoP), or both clinical	5.	Five studies reported AEs during training and showed that skins
Type of study:	and instrumental assessments for balance analysis.		abrasions, pain and various levels of
2 RCTs			ulceration were the most frequent; with no serious AEs reported.
3 cohort studies		6.	Six studies did not report significant
2 cross-over trial 1 descriptive study			changes in any balance outcome addressed (N=1: Over Ground Devices and Treadmill-Based Devices; N=3:
1 case series study			Treadmill-Based Devices hip-knee
1 Non-RCT			guidance; N=2: Over Ground Devices knee guidance).
5 case reports		7.	The significant changes were:
l correlational study			a. For each one of the different Treadmill-Based Devices categories
2 cross sectional studies			at least one study with significant changes due to training was
1 not reported			identified.

AMSTAR: 4		Device signific in the c c. For the (Erigo c BBS wa	ining with Over Ground s allowed statistically cant effects on balance only case of hip-knee guidance. e Tilt Table Devices category device), the improvement in as statistically significant in s with post-acute SCI.
Tamburella et al. (2022); ItalyReviewed published articles up to December 2020N=41Level of evidence: Downs and Black (D&B) toolType of study: RCTs of parallel- group or cross- over design and n-RCTs (such as cohort studies,	 Method: The aim of this systematic review was to explore the current state of the art of the overground lower limb exoskeletons its effects on walking and on secondary health conditions in people with SCI. Database: MED-LINE, Embase, Scopus, Web of Science and Cochrane Library (Cochrane Central Register of Controlled Trials). Outcome Measures: Walking domain (N=27) (e.g., 10MWT, 2MWT 6MWT, kinematics, WISCI II); balance (N=5) (e.g., TUG); muscle strength (N=6) (e.g., LEMS); activities of daily living (N=5) (e.g., FIM, SCIM, Barthel Index). 	"poor" or " A total san analyzed. Different e n=20; ReW n=2; and R Thirteen s during tra lesions as The averag across the and for ses per week studies ince Effects on a. All exos a posit perform time si b. Other o propos	pgical quality was reflected as moderate". nple of 566 participants was exoskeletons devices (Ekso, /alk, n=14; Indego, n=4; HAL, eex, n=2) were analyzed. tudies reported different AEs ining, showing the skin the most frequent AEs. ge total number of sessions studies ranged from 1 to 55; ssion frequency, 3 sessions were performed in 42% of the cluded. balance domain (n=12): skeletons trainings reported ive trend in TUG (n=8) mance regardless of AIS and nce injury. different indexes were sed by single studies to s balance domain (n=3) and
case–control, case series and pilot studies) AMSTAR: 8		results improv	indicated significant early ements, which were not ined at follow-up.

4.1 Virtual Reality (VR) for Standing Balance

Table 8. Systematic Reviews Assessing Virtual Reality (VR) (some including Biofeedback Techniques) for Standing Balance

Authors Year; Country Date included in	Method Databases	Conclusions
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the review Number of articles Level of Evidence Type of Study AMSTAR Score	Outcome Measures			
Abou et al. (2020); USA Reviewed published articles up to September 2019 N=10 in the systematic review and 6 in the meta- analysis Level of evidence: Cochrane Risk of Bias Tool for RCTs and Quality Assessment Tool for pre-post studies with no control group Type of study: 3 RCTs 7 pre-post trials AMSTAR: 8	Method: The main objective of this systematic review and meta- analysis was to evaluate and synthesize the effects of VR therapy on gait and balance rehabilitation among people with SCI. Database: PubMed, Web of Science, Scopus, SportDiscus, and CINAHL. Outcome Measures: Sitting balance (T-shirt test and the mFRT); static sitting balance (Trunk Recovery Scale item D and sway distance and velocity); dynamic sitting balance assessment (Trunk Recovery Scale item E); standing balance assessment (BBS, the ABC scale, the LOS, the Romberg Index, the parameters of the CoP, the forward functional reach test and lateral functional reach test; and gait outcomes (WISCI II, 10MWT, TUG, 2MWT, spatiotemporal gait parameters, 6MWT, and gait speed).	1. 2. 3.	in Fi ^t th of cc M a. b. Ef m	total of 149 participants were cluded. ve studies used only VR therapy and e other studies used a combination VR therapy with balance or bordination training. ethodological quality: Two of the three RCTs included in this review presented a low risk of bias and the third was rated as high risk of bias (and was not included in the meta-analysis). Four out of the seven pre-post studies included in this review presented an overall good quality and three studies were rated as fair overall quality (and were not included in the meta-analysis). fects of VR therapy assessed by eta-analysis (n=6): After completion of VR therapy, standing balance significantly improved compared with baseline. The analysis of the BBS scale showed a statistically significant within-group difference (MD=4.22; 95% CI 1.78-6.66; P<.01) and the analysis of the ABC scale showed a statistically significant within- group difference (MD = 8.53; 95% CI 2.52- 14.53; P<.01).

Table 9. Virtual Reality (VR) and/or Biofeedback for Standing Balance

Author Year Country Research Design Score Total Sample Size	Methods	Outcome
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	Virtual Reality/Biofeedback				
An & Park (2022); Republic of Korea RCT PEDro=7 Level 1 N=40	 Population: 40 participants with tetraplegia and incomplete SCI; 23 males and 17 females; mean age 42.6 years; level of injury C5-7 (n=40); AIS C (n=17) and AIS D (n=23); and time since injury > 1 year. Treatment: Participants were randomly divided into two groups and received 12 sessions of a 30 min therapy three days/week for four weeks in their homes: Participants in the experimental group (n=20) underwent rehabilitation while sitting in a wheelchair, performing a virtual soccer game. Participants in the control group (n=20) underwent a similar rehabilitation intervention but without the VR content. Outcome Measures: Stability and balance control during a pattern of FTSTS movements (by the chair stand test); the risk of falls (by the TUG test); and walking speed (by 10MWT) were assessed before and after the intervention protocol. 	 Within-group improvements were significant in both groups (p<0.02). a. Chair stand test times had an effect size (Cohen's d=0.71), classified as large. b. 10MWT had an effect size (Cohen's d=0.61), classified as medium. c. TUG test time had an effect size (Cohen's d= 0.42), classified as medium. There were significant differences between groups at the end of the intervention, favouring the experimental group for chair stand test time (p=0.03), for 10MWT (p=0.03), and for TUG test (p=0.04). 			
Sengupta et al. (2020); India Prospective control trial Level 2 N=33	 Population: 33 patients with SCI, neurological level of injury C5 or below and ability to abduct both shoulder at >90°; 27 males and 6 females; mean age 29.25 years; level of injury cervical (n=11), upper dorsal (n=10) and lower dorsal (n=12); AIS A (n=10), AIS B (n=8), AIS C (n=8), and AIS D (n=7); and mean time since injury < 6 months. Treatment: Routine conventional therapy, consisting of individualized exercise program, was provided to all participants. Additionally, participants were divided into two groups: VR training group (n=25): Participants performed VR training 5 days a week for 3 consecutive weeks with sessions lasting 30 min. All the games selected focused on static and dynamic balance and were played either while sitting or 	 No major AEs were reported by participants in either group. No statistically significant difference between groups in the scores of all the outcome measures at pre- and post- therapy (the main effect in both groups) was observed. 			

	 standing depending on the functional ability of the participant. The level of difficulty was gradually upgraded based on their performance. Control group (n=12 matched controls). Outcome Measures: BBS, balance section of the Tinetti Performance-Oriented Mobility Assessment (POMA-B), and Functional Reach Score (seated) were assessed pre and post intervention. 	
D'Addio et al. (2014); Italy Prospective controlled trial Level 2 N=30	 Population: 30 participants with SCI; mean (SD) age: 43 (18.7) years; and AIS C-D. Treatment: All participants joined in a 12-week training protocol (3 sessions per week) and were assigned randomly to one of the following two groups: Control group (n=15), receiving standard rehabilitation protocol (SRP) for balance training alone. The SRP refers to a combination of active/passive lower and upper limb stretching, exercises to increase strength and improve posture. Sessions lasted 60 minutes. Study group (n=15), received in addition to the SRP session, a Nintendo Wii Fit balance training (four games), along with its balance board. Outcome Measures: BBS and posturography testing (which consists of two randomized tests, each of 60 seconds: standing on a firm surface with eyes open and eyes closed; in this way has been possible to estimate the Romberg Index) were assessed at the first visit and at discharge. 	 Both groups showed significant (p<0.04) improvements in BBS and posturography balance measures between pre- and post-intervention. Additionally, all participants related to the study group showed a greater (p<0.02) improvement at discharge than those in the control group as shown by the higher scores obtained in clinical scales and in different kinematic indices.
Villiger et al. (2015); Switzerland Prospective controlled trial Level 2 N=23	Population : 9 participants with SCI - 5 males and 4 females; incomplete SCI; all AIS D; Lesion level between C4 to TI2; mean age= 55.1 ± 15.8y; years post injury= 1- 5y; 14 healthy persons were in the control group - 8 males and 7 females; mean age= 47.1 ± 14.4y.	 The intense VR-augmented training of limb control improved significantly balance, walking speed, ambulation, and muscle strength in patients.

	Treatment : Patients underwent 4 weeks of intensive VR-augmented lower limb training. The patients with iSCI were trained with the VR movement tasks 16–20 times during the 4 weeks (4–5 × 45 min. per week). The training used a VR- augmented therapy system for lower limbs combining action observation, imagination and execution. Before and after the training period a structural volumetric 3D MRI data set was acquired in patients. Retention of the performance improvements was assessed in a 3–4 months follow-up session. Outcome Measures: 10MWT, BBS, LEMS, and SCIM mobility.	2. Retention of clinical improvements was confirmed by the 3–4 months follow-up.
Shin et al. (2021); Korea Pre-post Level 4 N=13	 Population: 13 participants with SCI; 8 males and 5 females; median (range) age 52 (19-85) years; tetraplegia (n=11) and paraplegia (n=2); AIS C (n=1) and AIS D (n=12); and median (range) time since injury 48 (19-139) days. Participants were subgrouped according to the initial proprioception status: Normal group (n=6): Participants with grade 2 of proprioception of the ankle and knee. Abnormal group (n=7): Participants with grade 0 or 1 of proprioception of the ankle and knee. Treatment: Participants received RAGT with Morning Walk® with visual feedback (through a VR screen), so the participants could have the experience of walking through a park or the forest according to the gait speed. RAGT were performed for 30 min in the ground-level (starting with a cadence of 30 steps/min, a step length of 30 cm, and 20% BWS; and an estimated progression for each participant). In addition, one hour of conventional physiotherapy (consisting in sitting and standing balance training, sit- to-stand training, and strengthening exercises) were performed 5 times per week for 4 weeks. 	 After the intervention, the patient with paraplegia AIS C improved to AIS D. After the intervention, BBS, 10MWT, 6MWT, LEMS, and WISCI II significantly improved (p<0.003). Based on the subgroup analysis of the initial proprioception status: The normal group showed a significant improvement on the BBS, 10MWT, 6MWT and WISCI II (p≤0.028); however, LEMS did not show a significant improvement (p=0.068). In the abnormal group, BBS, 10MWT, 6MWT, LEMS, and WISCI II were significantly improved (p≤0.028). In the between-group comparisons, only the WISCI II showed a statistically significant difference (p=0.037); with an improvement favouring the normal group.

	the ISNCSCI at the ankle and knee), BBS, and WISCI II were assessed within 48 h before and after the intervention.		
	Population: 15 participants with incomplete and chronic SCI who could walk independently for 2 min without assistance; 11 males and 4 females; mean (± SD) age 59 (± 12) years; AIS level C (n=2) and D (n=13); and mean (± SD) time since injury 42 (± 48) months.	1.	Patients' balance confidence significantly increased after GRAIL training (76 ± 18), compared to baseline (69 ± 18) (p=0.001); however, there was no significant difference between post and follow-up
	Treatment: Individualized VR gait training on the GRAIL for 12 1-h training sessions spread over a 6-week period.		measurement.
Van Dijsseldonk et al. (2018); Netherlands Pre-post Level N=15	The GRAIL consisted of an instrumented dual belt treadmill with two embedded force plates and an eight-camera motion capture system. The platform was able to move in several directions to generate mechanical perturbations. In front of the treadmill, VR environments were projected on a 180° semi-cylindrical screen. Reflective markers were adhered to the patients to interact with the virtual environment and to capture kinematic data. The GRAIL system was controlled, and the visual information was matched to the treadmill speed. During the GRAIL training multiple applications (categorized in three themes; "gait adaptability", "walking ⁺ ", and "balance in stance") were performed in an individualized nattorn		
	individualized pattern. Outcome Measures: 2MWT on the GRAIL; spatiotemporal parameters (walking speed, stride length, step width, and stride frequency); gait stability measures (dynamic stability margin, extrapolated center of mass relative to the center of pressure in anterior-posterior and medial- lateral, center of mass relative to the center of pressure in anterior-posterior and medial-lateral); and balance confidence (ABC scale) were assessed at baseline (at the 2 nd and the 3 rd sessions), at the last training session (post measurement), and at 6 months after the last training session (follow-up measurement).		

An & Park (2018); Republic of Korea Pre-post Level 4 N=10	 Population: 10 participants with chronic SCI; 6 males and 4 females; mean (± SD) age 44.20 (± 8.66) years; level of injury C2 (n=1), C4 (n=3), C6 (n=2), C7 (n=2), and TI (n=1); AIS level C (n=4) and D (n=6); and mean (± SD) time since injury 19.20 (± 3.93) months. Treatment: Participants underwent semi-immersive VR therapy (using an Interactive Rehabilitation Exercise [IREX] 30 min per day, 3 times a week for 6 weeks. Six programs were included: "soccer", "conveyor", "volleyball", "formula racer", "airborne", and "snowboard". Each program was performed for 4 min with a 1-min break between programs. Outcome Measures: Standing balance function (limit of stability and BBS) and upright mobility function (TUG, ABC scale and WISCI II) were assessed before and after the intervention. 	1. 2. 3. 4.	There were no AEs during the semi-immersive VR therapy. The WISCI II score after intervention showed significant improvement from 16.30 to 17.90 (p<0.05). On the computerized standing balance test, overall limit of stability score was significantly increased from pre- to post-intervention (32.00 to 46.40, respectively; P<0.01); however, forward and backward directional limit of stability scores did not differ significantly after therapy. The BBS score was significantly increased post-intervention (35.70 to 40.10, respectively; p<0.01). The TUG time was significantly decreased (19.35 to 17.14, respectively; p<0.05), while the ABC scale score was significantly increased (67.90
Villiger et al. (2017); Switzerland Pre-post Level 4 N=11	 Population: 11 participants with motor- incomplete SCI and able to sit in a chair without assistive and supporting systems; mean (± SD) age 60 (± 10.2) years; level of injury C4 (n=1), C5 (n=3), C7 (n=2), T4 (n=1), T9 (n=1), T12 (n=2), and L3 (n=1); AIS C (n=1) and AIS D (n=10); and mean time since injury 7.6 years. Treatment: All participants were trained at home on the VR tasks over a period of 4 weeks, with 16–20 sessions of 30–45 min each, and with the mobile prototype of the YouKicker system. Around 500 repetitions of ankle movements and 100 knee movements with each leg were performed through different blocks by a typical patient during a training session. Outcome Measures: LEMS, BBS, TUG, 10MWT, 6MWT, SCIM-III, and WISCI II were tested 4 weeks before treatment (pre- baseline), directly before treatment (baseline), after finishing the training program (post-assessment), and 2-3 	1. 2.	to 76.85, respectively; p<0.05). None of the participants had any pain while playing the games or after the sessions. At post-assessment, significant increases in comparison with the averaged pre-baseline and baseline were found in balance (BBS, p=0.008) and functional mobility (TUG, p=0.005). However, there were no significant effects on SCIM- III mobility (p=0.018). At follow-up assessment, a significant increase in comparison with the averaged pre-baseline and baseline was found in functional mobility (TUG, p=0.005), but no significant changes were found in balance (BBS, p=0.28) and SCIM-III mobility (p=0.026]).

	months after the treatment program (follow-up).			
<u>Villiger et al.</u> (2013); Switzerland Pre-post Level 4 N=14	 Population: 14 participants - 9 males and 5 females; chronic SCI; 2 AIS C and 12 AIS D; level of injury: C4-T12. mean age= 53y; median years post-injury= 4y. Treatment: Participants received 4-5 45-min sessions of intensive VR augmented training sessions per week for a total of 16-20 sessions. Outcome Measures: BBS, 10MWT and WISCI II. 	1.	Significant improvements in 10MWT, BBS and WISCI II were shown after intervention.	
Wall et al. (2015); USA Pre-post Level 4 N=5	 Population: 5 participants with incomplete (AIS D) SCI; WISCI II score>6; able to tolerate static standing for at least five minutes at a time with no greater than minimal assistance; 5 males; mean age: 58.6 years; injury level: C4 (n=1), C5 (n=1), C6 (n=2), L1 (n=1); and mean time since injury: 7.6 years. Treatment: The sessions consisted of multiple games from an off the shelf VR training system (Nintendo Wii Fit) to promote weight shifting, stability, balance, and coordination. Games were randomly varied throughout each session. Each session was one hour, two times per week for seven weeks. Outcome Measures: TUG test, the forward functional reach test, and the lateral functional reach test were assessed one time per week for three weeks (pre- testing), within one week after the end of the training period, and at four weeks after the last intervention session. 	2.	There was a significant increase from pre- intervention to post- intervention on gait speed (p= 0.001, d=0.35), forward functional reach test (p<0.001, d=1.12), and lateral functional reach test (p< 0.001, d=0.88). However, there was no change for the TUG (p=0.25, d=-0.04). Survey reports suggested improvements in balance, endurance, and mobility with daily tasks at home.	
	Other Biofeedback Approaches			
<u>Amatachaya et al.</u> (2023); Thailand RCT <u>PEDro=6</u> Level 1 N=44	 Population: 44 ambulatory individuals with chronic SCI and with the ability of independent walking with or without a walking device over a distance of at least 15m: Control group (n=22): Mean (SD) age: 53.3 (12.1) years; 15M, 7F; AIS: AIS C (n=8) and AIS D (n=14); level of 	1.	Mobility outcomes: a. After the training programs, participants demonstrated significant improvement in all mobility outcomes at week two and week four (within-group analysis) (p<0.05). The mobility	

	 injury: Tetraplegia (n=5) and paraplegia (n=17); and mean (SD) time since injury: 57.6 (34.7) months Experimental group (n=22): Mean (SD) age: 51.2 (14.9) years; 18M, 4F; AIS: AIS C (n=10) and AIS D (n=12); Level of injury: Tetraplegia (n=8) and paraplegia (n=14); and mean (SD) time since injury: 51.7 (31.4) months Treatment: Participants were assigned to the control intervention group (i.e., bodyweight shifting and lower limb loading training without augmented loading feedback) or the experimental intervention group (i.e., body-weight shifting and lower limb loading training with augmented loading feedback) or the experimental intervention group (i.e., body-weight shifting and lower limb loading training with augmented loading feedback) for 30min/day, 5days/week, over 4weeks. Control intervention program (n=22): The participants in this group engaged in stepping training while in a step-standing position, for each leg continuously, as long as they could without fatigue, for 10min/leg. They were then trained to walk on a smooth, flat, and firm surface for 10min. Experimental intervention group (n=22): The participants were trained using the same protocols as those used in the control intervention group; however, in this group, external augmented loading feedback was also obtained using a visual weight-taking machine. Outcome Measures: Incidence of falls was measured 6 months before the start of the intervention. Mobility outcomes (TUG test, 10MWT, FTSST, and 6MWT) were assessed at baseline, at week two and week four, and after 6 months follow-up. 	2.	outcomes of participants in the experimental intervention group also showed significant improvement at six-month follow-up. b. When adjusted for the baseline data, the mobility improvement of participants in the experimental intervention group at week two and week four was significantly greater than that of the participants in the control intervention group (p<0.05). However, this difference was not found at six months after the training programs. Fall data: During the six months after the training, there were nine participants who fell in the control intervention group and four participants who fell in the experimental intervention group. The number of faller participants was significantly different between the groups (p=0.044).
<u>Nithiatthawanon</u> <u>et al. (2020);</u> Thailand RCT cross-over <u>PEDro=6</u>	Population: 30 community-dwelling participants with SCI who had the ability to walk independently, with or without a walking device, over at least 17 m (FIM Locomotor Score of 5–7); 22 males and 8 females; mean age (± SD) 53.2 (± 11.8) years;	1.	Both training programs significantly improved all the outcome measures, excepting the TUG and lower limb loading of the less-affected leg, where improvement was

Level 1 N=30	 level of injury paraplegia (n=20) and tetraplegia (n=10); AIS C (n=12) and AIS D (n=18); and mean (± SD) time since injury 71.9 (± 74.5) months. Treatment: All participants involved in a single control and a single experimental session with a 2-week washout period between them: Control intervention session, consisting of: Bodyweight shifting and lower limb loading training during stepping (forward and backward) without external feedback for 10 min for each leg. Overground walking training with an emphasis on lower limb loading, with or without a walking device, according to their ability for 10 min. Experimental intervention session: The participants were trained using the same protocols as those of the control intervention program but with visual feedback relating to the amount of lower limb loading of the stance leg from a visual weighttaking machine to alert the participants and the therapist of the adequate amount of lower limb (at least 80% of the participant's bodyweight). 	found only after the experimental intervention. 2. The improvement after the experimental intervention program was significantly greater than that following the control intervention program for all the outcome measures (p<0.05): a. The mean (95% Cl) between-group differences for the TUG = 1.9 [0.6–3.3] s.
<u>Cheung et al.</u> (2019); China RCT <u>PEDro=8</u> Level 1 N=16	Population: 16 participants with incomplete SCI and able to perform BWSTT; 11 males and 5 females; mean age 54.3 ± 9.6 years; level of injury C1-L2; AIS C (n=11) and AIS D (n=5); and mean time since injury 13.7 ± 7.4 months. Treatment: All participants received, twice a week, one hour of standard	 No AE or discomfort was reported by participants. Significant (p<0.025) improvements in BWSTT group in the mobility sub- score of SCIM-III and bilateral symmetry were shown, but none of these outcome

	 physiotherapy program, including limbs mobilization and strengthening, trunk stabilization, wheelchair maneuver training and overground walking training. Additionally, 3 times per week, for 8 weeks, participants were randomly allocated to: 30 min of BWSTT with Lokomat system, at comfortable walking speed, with assist-as-needed guidance force, and 40% of BWS. Additionally, EMG-biofeedback system was applied to the bilateral vastus lateralis and audio feedback was generated if the muscle activation was less than 30% of maximal recruitment to encourage active participation during the stance phase of the gait cycle. Control group: Participants received passive lower limb mobilization training by using lower limb active-passive exerciser. Outcome Measures: WISCI II, SCIM-III, LEMS, Lower limb-force (L-force) function in Lokomat system, and quality of gait pattern (by gait analysis system) (walking speed, heel-heel base support, bilateral stance duration and bilateral symmetry [ratio of stride length of two legs]) were collected within 1 week after the completion of the 8 weeks program. 	measures were found to be improved in control group. 3. No significant time x group interaction was found in other outcomes with no significant between group difference (p>0.05).
Pramodhyakul et al. (2016); Thailand RCT PEDro=5 Level 2 N=32	 Population: 32 participants - 26 males and 10 females; incomplete SCI; 26 AIS D and 10 AIS C; mean age= 41.69 ± 10.90y; months post injury= 35.00 ± 24.40 months. Treatment: Participants were randomly assigned to the experimental or control groups using stage of injury, severity of SCI, and baseline walking ability as criteria for group arrangement (16 participants per group). The participants were trained to walk over level ground at their fastest safe speed with or without a visuotemporal cue, 30 min/day, for 5 consecutive days. Outcome Measures: 10MWT, 6MWT, TUG test and FTSTS. 	 The participants demonstrated significant improvement in all functional tests after the 5 days of training. The improvement in the group trained using the visuotemporal cue was significantly better than that trained without using the cue.

Tamburella et al. (2013); Italy Prospective controlled trial Level 2 N=12	Population: 12 participants with SCI; 6 in the vBFB group and 6 in control group. vBFB group: mean (SD) age: 52 (11.74); 3M 3F. Control group: mean (SD) age: 53.5 (13.21); 3M 3F. Treatment: 2 groups: vBFB and Rehab group (control). vFBF and control groups underwent 8 wks of rehab 5 times/wk (control: 60 min devoted to Rehab; vBFB: 40 min of rehab plus 20 of vBFB). Outcome Measures: BBS; WISCI; 6MWT; 10MWT; TUG; balance performance and kinematic spatio-temporal gait parameters. *vBFB (visual biofeedback task-specific balance training).	 Only the vBFB group experienced a significant improvement in balance: BBS: 26 (10.69) at baseline to 41 (7.8) at end of intervention. TUG: 21.70 (10.7) s at baseline to 15.22 (6.14) s at end of intervention The improvement in balance for the vBFB group was maintained at follow-up examinations. vBFB participants experienced greater improvements than control participants for TUG, BBS, and for all balance indices, except for the center of pressure mean velocity with eyes closed.
Houston et al. (2020; 2021) Canada Pre-post Level 4 N=5	 Population: 5 participants with chronic incomplete SCI; 1 male and 4 females; age range 55-68 years; level of injury CI (n=1), C3 (n=1), C5 (n=1), T6 (n=1) and TIO (n=1); AIS C (n=3) and AIS D (n=2); and mean time since injury 46.8 months. Treatment: Participants completed three Ih training sessions per week for 4 weeks consisting of FES applied bilaterally to the ankle plantarflexors and dorsiflexors while they performed visual feedback balance training (VFBT) exercises. A closed-loop FES system was used in which the CoP was continually monitored and the level of electrical current administered was automatically adjusted. Outcome Measures: Outcome measures were collected before beginning the intervention, after completion of training, and 4 and 8 weeks after the intervention: Clinical assessment: BBS, Mini-BESTest and ABC scale. Biomechanical assessment: Static balance test (in standing) (measuring postural sway through calculation of CoP velocity and the root-mean-square of the CoP displacement in both anterior-posterior and medio-lateral 	 Improvements were seen for four of the five participants on at least one of the clinical scales following completion of the training intervention. All participants showed greater maximal CoP excursion area during the LOS test after the training intervention, whereas only one participant demonstrated a reduction in PS. Regarding the semi- structured interviews, risk of falling was perceived as slightly reduced or unchanged, but participants felt that their balance confidence had increased. No training-related AEs were reported.

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	directions) and dynamic balance test (in standing) (evaluating the LOS).		
	Semi-structured interviews were conducted after completion of the balance training intervention and 8-weeks post- training to understand participants' experiences.		
	Population: 6 participants- 5 males and 1 female; chronic SCI; 4 AIS C and 2 AIS D; level of injury: C4-T12; mean age= 41y; median years post-injury= 7y	1.	All participants showed substantial improvements in the scores, which varied between 236±94 and 130±14%
<u>Sayenko et al.</u> (2010); Canada, Japan Pre-post Level 4 N=6	Treatment: Patients participated in 3 60- min visual feedback training sessions, for a total number of 12 sessions. During training, participants stood on a force platform and were asked to shift their CoP in the indicated directions as represented by a cursor on the monitor.		of the initial values for different exercises.
		2.	Improvements were all statistically significant for both eyes open and closed except mean velocity in the medial/lateral direction.
	Outcome Measures: Static standing eyes open and closed as measured by CoP displacement; Dynamic standing as measured by voluntary CoP displacement.	3.	The balance performance during training-irrelevant tasks was significantly improved: for example, the area inside the stability zone after the training reached 221±86% of the pre-training values.

Discussion

A meta-analysis by Abou et al. (2020), including six studies and 108 patients with SCI, found that after completion of VR therapy, standing balance significantly improved compared with baseline. The analysis of the BBS scale showed a statistically significant within-group difference (MD=4.22; 95% CI 1.78-6.66; p<.01) and the analysis of the activities-specific balance confidence (ABC) scale showed a statistically significant within-group difference (MD=8.53; 95% CI 2.52-14.53; p<.01) (Abou et al. 2020). Other systematic reviews have also shown promising effects in standing balance in people with SCI (Alashram et al. 2020; de Araújo et al. 2020; De Miguel-Rubio et al. 2020); however, there is a strong need for further well-designed RCTs investigating the effect of VR therapy on different mobility outcomes among persons with SCI and providing information about VR long-term effects in order to develop robust guidelines (Abou et al. 2020; Yeo et al. 2019).

There are two studies which assessed the effects of performing a VR training program on participants with acute SCI. The prospective control trial of Sengupta et al. (2020) assessed the inclusion of VR training focused on static and dynamic balance in patients with acute (less than 6 months since injury) paraplegia (n=11) and tetraplegia (n=21), and with motor complete (n=18) or motor incomplete (n=22) SCI. After 3 weeks, with five sessions per week, of routine

conventional therapy and VR training sessions (in sitting or standing depending on each participant's functional ability), participants did not show any significant differences with respect to the control group (only physical therapy sessions) for standing balance (BBS and balance section of POMA-B) (Sengupta et al. 2020). Conversely, the pre-post study of Shin et al. (2021) assessed if 30 min of BWSTT plus one hour of conventional physiotherapy, five times per week, had effects on standing balance in 13 patients with acute tetraplegia (n=11) or paraplegia (n=2) (mean time since injury 48 [19-139] days). BWSTT was performed with the Morning Walk®, which is an end-effector type robot and the first gait training robot using a saddle for weight support, and with visual feedback through a VR screen, so participants could have the experience of walking through a park or forest according to the gait speed (Shin et al. 2021). After 4 weeks of intervention, standing balance (BBS), gait speed (10MWT), gait endurance (6MWT), muscle strength (LEMS) and walking ability (WISCI II) showed significant improvements; and one patient with paraplegia AIS C improved to AIS D (Shin et al. 2021).

Several studies have been conducted in patients with chronic SCI who performed different training programs using VR (An & Park 2018, 2022; D'Addio et al. 2014; van Dijsseldonk et al. 2018; Villiger et al. 2013, 2015, 2017; Wall et al. 2015), or standing or BWSTT training programs coupled with different biofeedback approaches (Amatachaya et al. 2023; Cheung et al. 2019; Houston et al. 2020, 2021; Nithiatthawanon et al. 2020; Pramodhyak et al. 2016; Sayenko et al. 2010; Tamburella et al. 2013); showing overall benefits in standing balance outcome measures.

For VR, the most recent RCT was conducted by An and Park (2022), which included 40 patients with tetraplegia. Similar to a rehabilitation intervention, the VR intervention consisted of 12 sessions of performing a virtual soccer game while sitting in a wheelchair for 30 minutes three times a week (An & Park 2022). At the end of the intervention, both groups showed improvements in walking speed (10MWT) and standing balance (TUG and FTSTS), but the experimental group had significantly better results than the control group (An & Park 2022). The prospective controlled trial of D'Addio et al. (2014) included 30 participants with incomplete and chronic SCI who received a standard rehabilitation protocol for balance training. Participants in the experimental group (n=15) received, in addition, a Nintendo Wii Fit balance training, along with its balance board (D'Addio et al. 2014). After 12 weeks of training, both groups showed improvements in standing balance (BBS and posturography testing); however, the experimental group showed significantly higher scores (D'Addio et al. 2014).

For other biofeedback approaches, the cross-over RCT of Nithiatthawanon et al. (2020) included 30 participants with SCI (10 participants with tetraplegia and 20 with paraplegia) and the ability to walk independently. The aim of the study was to compare the immediate benefits of adding (or not adding) visual feedback relating to the amount of lower limb loading on the stance leg to alert the participants and the therapist of the adequate load (at least 80% of the participant's body weight) during a single 20 min-session comprising body-weight shifting and lower limb loading during stepping and overground walking training (Nithiatthawanon et al. 2020). It was shown that the TUG test and maximal lower limb loading of the less affected leg were improved only in the experimental group; although 10MWT, FTSST and maximal lower limb loading of the most affected leg improved similarly in both groups (Nithiatthawanon et al. 2020). Based on these results, the recent RCT of Amatachaya et al. (2023) carried out the same study protocol but over four weeks (30 min/day, 5 days/week) in participants with incomplete

and chronic SCI. At the end of the intervention, the mobility improvement of participants in the experimental intervention group was significantly greater than that of the participants in the control intervention group (p<0.05); however, this difference was not found at six months after the training programs (Amatachaya et al. 2023). In addition, during the six months after the training, the number of participants with falls was significantly lower in the experimental group than in the control group (Amatachaya et al. 2023). The RCT of Pramodhyak et al. (2016) included 32 participants with incomplete and chronic SCI who performed an overground walking training protocol at their fastest safe speed with or without a visuotemporal cue for five consecutive days. After the training protocol, the improvements in standing balance (TUG, FTSTS) were significantly higher in the group receiving the visuotemporal cue (Pramodhyak et al. 2016). The RCT of Cheung et al. (2019) included 16 participants with incomplete SCI who received, apart from standard physiotherapy, BWSTT three times per week during eight weeks (active group) or passive lower limb mobilization training (control group). BWSTT was performed with the Lokomat system, EMG biofeedback system was applied to the bilateral vastus lateralis, and audio feedback was generated if the muscle activation was less than 30% of maximal recruitment to encourage active participation during the stance phase of the gait cycle (Cheung et al. 2019). It should be noted that a significant time x group interaction was found only in the active group in WISCI II and mobility sub-score of SCIM-III, but not in the walking speed (Cheung et al. 2019).

Conclusions

Acute SCI (<1 year)

There is level 2 evidence (from 1 prospective control trial: <u>Sengupta et al. 2020</u>) that VR training added to routine conventional therapy, in comparison with only conventional therapy, does not provide better improvements in standing balance in patients with acute SCI.

There is level 4 evidence (from 1 pre-post study: <u>Shin et al. 2021</u>) that RAGT (with Morning Walk®) with visual feedback and conventional physiotherapy provides improvements in standing balance (BBS), gait speed (10MWT), gait endurance (6MWT), muscle strength (LEMS) and walking ability (WISCI II) in patients with acute (mean time since injury 48 days) motor incomplete SCI.

Chronic SCI (>1 year)

There is level 1 evidence (from 1 RCT: <u>An & Park 2022</u>) that a VR intervention, consisting of a virtual soccer game performed while sitting in a wheelchair, provides better improvements in walking speed (10MWT) and standing balance (FTSTS and TUG), than a similar rehabilitation intervention without the VR component in patients with chronic motor incomplete SCI and tetraplegia.

There is level 2 evidence (from 1 prospective controlled trial: <u>D'Addio et al. 2014</u>) that the addition of a Nintendo Wii Fit balance training to a standard rehabilitation protocol for balance training for 12 weeks provides significantly higher improvements in standing balance (BBS and posturography) in participants with chronic and incomplete SCI.

There is level 1 evidence (from 2 cross-over RCTs: <u>Amatachaya et al. 2023</u>; <u>Nithiatthawanon et al. 2020</u>) that adding visual feedback relating to the amount of lower limb loading during bodyweight shifting, stepping, and overground walking training provides improvements on the TUG test, FTSTS, and number of fallers in participants with chronic SCI.

There is level 1 evidence (from 1 RCT: <u>Cheung et al. 2019</u>) that BWSTT (performed with the Lokomat system and an EMG biofeedback system to encourage active participation during the stance phase of the gait cycle) during 8 weeks provides a significant time x group interaction in WISCI II and mobility sub-score of SCIM-III (but not in walking speed), in comparison with a passive lower limb mobilization training in participants with incomplete SCI.

There is level 2 evidence (from 1 RCT: <u>Pramodhyak et al. 2016</u>) that an overground walking training protocol for five consecutive days at the fastest safe speed with a visuotemporal cue provides significantly higher improvements in standing balance (TUG, FTSTS) than the same protocol without the cue in people with chronic and incomplete SCI.

There is level 4 evidence (from several pre-post studies) that different VR training protocols provide significant improvements in standing balance in people with chronic and incomplete SCI.

Key Points

VR training is an effective strategy to improve walking and standing balance performance in patients with acute or chronic and incomplete SCI, and may afford further benefits compared with the same training interventions without the VR biofeedback.

EMG Biofeedback, visual feedback, or visuotemporal cue feedback added to standing, stepping or BWSTT protocols may improve gait, balance, and lower limb muscle strength in incomplete SCI and chronic SCI.

4.2 Non-Body-Weight Supported Training for Standing Balance

Overground walking training does not require expensive devices and more closely resembles natural walking conditions in daily life, and it is likely to achieve a patient's full engagement, encouraging voluntary movements compared to walking on a treadmill (Yu et al. 2019). Overground training is usually implemented when there is improved neuromuscular capacity and a readiness to learn overground skills to use in the home and community. Though overground training is often used as a control group for other types of treatment (e.g., treadmill training), some studies have assessed a progressive approach to overground training, that is varying intensities, intervals, and/or incorporating perturbations to measure balance.

Table 10. Non-Body-Weight Support	ed Training and Standing Balance
Table 10: Non Dody Weight Support	

Author Year Country Score Research Design Total Sample Size	Methods		Outcome
	Population: 21 participants with chronic motor incomplete SCI; 7 males and 13 females; mean (\pm SD) age 56.9 (\pm 14.4) years; level of injury cervical (n=10), thoracic (n=8) and lumbar (n=2); AIS C and D (n=n/a); and mean (\pm SD) time since injury 90.4 (\pm 109.7) months.	1.	Six Conventional Intensive Balance Training and seven Perturbation-based Balance Training participants were able to progress to spending time outside of the harness during training.
	Treatment: Participants were randomized into Perturbation-based Balance Training group (n=10) or Conventional Intensive Balance Training group (n=11) for 1 hour, three times per week for 8 weeks. Both groups received a balance training which comprised on individualized, challenging static and dynamic balance tasks. The	2.	Participants in the Perturbation-based Balance Training group experienced more single step responses (p=0.01) and multi-step (p=0.03) but not fall responses (p=0.41) during training.
<u>Unger et al.</u> (2021); Canada RCT	Perturbation-based Balance Training group also experienced manual pushes and pulls from one member of the research team. Outcome Measures: Reactive balance by stimulating a forward fall (measured by	3.	For Lean-and-Release test, there were improvements in reactive stepping ability (p=0.049). There were no differences in reactive stepping ability between groups.
PEDro=8 Level 1 N=21	the behavioral response and foot contact time during the Lean-and-Release test); Mini-BESTest; Community Balance and Mobility Scale (CB&M) (only 13 participants [Perturbation-based Balance Training n=7, Conventional Intensive Balance Training		There was a significant effect of time (p<0.01), but no group or interaction effects for Mini- BESTest, CB&M, FES-I, and ABC Scale changes.
	n=6] were able to complete the CB&M); lower extremity manual muscle testing of 12 muscles groups bilaterally (hip flexors, extensors, adductors, abductors, internal rotators, external rotators, knee flexors and extensors, ankle dorsiflexors and plantarflexors, invertors, and evertors); gait parameters (step length, walking speed, cadence, and double support percentage) during two passes of the walkway at a self- selected speed using a gait aid if	Э.	There were improvements from baseline to 4-week (p<0.05) and baseline to 8- week (p<0.05) but not between the 4- week and 8- week scores. There were no differences between groups with respect to the proportion of participants who exceeded the MDC (p=0.12).
	necessary; balance confidence (ABC Scale); and fall concern (FES-I) were assessed at baseline (x 2), at midpoint (4- week), at final of treatment (8-week), at 3 months post-training follow-up and at 6	6.	At the 3-month assessment all participants retained their gains as demonstrated by significant effects of time on the Lean-and-Release test

	months post-training follow-up. During the 6-month follow-up period the number of falls experienced by participants were tracked by conducting a fall survey.	7.	behavioral response (p=0.03), Mini-BESTest (p=0.01), and FES-I (p=0.01), but not on the ABC Scale (p>0.05). There was one AE: A controlled fall during a training perturbation occurred for a Perturbation- based Balance Training participant who was practicing activities outside of the harness without resulting in any injury.
	Population: 54 ambulatory persons with SCI, with the ability of independent walking over at least 17 m with or without assistive devices (or a FIM locomotor score of 5-7); 36 males and 18 females; mean (±	1.	All participants in the experimental group could safely walk over a walking track with different surfaces without any AEs.
	SD) age 51.7 (± 15.4) years; paraplegia (n=34) and tetraplegia (n=20); AIS C (n=15) and D (n=39); and mean (± SD) time since injury 88.3 (± 79.6) months. Treatment: Participants were randomly stratified into:	2.	Only the participants in the experimental group showed significant improvements after 2- and 4-week training for the 10MWT, 6MWT, TUG, and FTSST (p<0.001).
<u>Amatachaya et</u> <u>al. (2021);</u> Thailand RCT	 Participants in the control group (n=26) performed an overground walking training over a hard flat, and smooth surface. Participants in the experimental 	3.	There were no significant differences after 6 months follow-up compared with at baseline for both training programs.
<u>PEDro=6</u> Level 1 N=54	group (n=28) performed a walking training on a walking track (10m long) with different surfaces (walking track with different surfaces consisted of artificial pebbled, grass, and soft areas).	4.	During 6-month follow-up, 5 (9 falls in total) participants in the experimental group and 12 (39 falls in total) in the control group experienced falls, with a relative risk of 0.39
	Training program was performed for 30 min/d, 5 d/wk over 4 weeks; and participants walked at their usual speed without fatigue.		for participants in the experimental group as compared to those in the control group.
	Outcomes Measures: 10MWT, TUG, FTSST, 6MWT, and fall data were assessed at baseline, after 2- and 4-week training, and at 6 months follow-up.		
Lotter et al. (2020); USA RCT <u>PEDro=6</u>	Population: 16 participants with motor incomplete SCI and the ability to walk overground at self-selected speeds <1.0 m/s without physical assistance but with devices and bracing below the knee as needed; 10 males and 6 females; mean age 48.5 years; injury level C1-C4 (n=6), C5-	1.	Task-specific training group had significant higher stepping parameters and average peak heart rate reserve during the training; however, average number of sessions completed, and

	C(p-4) and $T(T(p-4))$ and mean time		average and maximum DDF-
Level 1 N=16	C8 (n=4) and TI-TIO (n=6); and mean time since injury 4.1 years.		average and maximum RPEs were similar between groups.
	Treatment: Participants were randomized to receive up to 20 sessions of either task- specific or impairment-based training (both of 40 min sessions) over less than 6 weeks followed by the alternate training	2.	For BBS, there were no differences of time x training group-interactions, but there was a significant time effect.
	paradigm, with a break of at least 4 weeks between interventions:	3.	Significantly greater gains in ABC but not in PROMIS- Mobility score were observed
	 Task-specific training consisted of stepping practice in variable contexts (i.e., speed-dependent 		following task-specific vs. impairment-based training (10 ± 11 vs. 1.8 ± 11, p=.02).
	treadmill training, skill-dependent treadmill training, overground training, and stair climbing) within 1-hour sessions.	4.	There were no serious AEs during training intervention; however, between-group analysis revealed significantly
	 Impairment-based training consisted of non-walking interventions, including strengthening, balance tasks, aerobic conditioning and practice of transfers to improve lower extremity and trunk strength and coordination. 		greater cumulative incidence of minor AEs during task- specific (n=23) vs. impairment-based training (n=8), p<.01; with specific differences included greater number of falls (p=.03).
	A primary intent of both strategies was to achieve high cardiovascular intensities (e.g., 70%-80% heart rate reserve and RPE >14).		
	Outcome measures: Fastest speed over short distances, peak treadmill speed, self- selected speed, 6MWT, BBS, FTSTS, ABC scale, PROMIS-Mobility score, LEMS, and incidence of AEs were assessed prior to and following each training protocol.		
<u>Brazg et al.</u> <u>(2017)</u> ; USA RCT cross-over	Population: 15 participants with a chronic motor incomplete SCI at neurological injury level of TIO or above; 11 males and 4 females; mean (± SD) age 49 (± 8.1) years; injury level high cervical (C1-C4) (n=4), low cervical (C5-C8) (n=6), and thoracic (TI-TIO) (n=5); AIS C or D (n=15); and mean (± SD) time since injury 7.7 (± 7.9) years.	1. 2.	No significant AEs were noted. The average number of sessions completed and number of steps within sessions were not significantly different between groups.
PEDro=6 Level 1 N=15	Treatment: Participants were randomized to receive sessions of either a high- or low- intensity locomotor training over 4 to 6 weeks, followed by a 4-week wash-out.	3.	No significant main or interaction effects were observed for BBS scores.
	Both high- and low-intensity locomotor training consisted of up to 20 one-hour sessions at a frequency of 3 to 5 days/week over ≤ 6 weeks. The goals of sessions were		

	to achieve 40 min of stepping practice while maintaining the desired HRs or RPEs (high-intensity training [70%-85% HR _{max} , 15 to 17 {"hard" to "very hard"}] vs. low-intensity training [50%-65% HR _{max} , 11 to 13 {below "somewhat hard"}]). Each session was composed of 4 different stepping tasks practiced over ~10 min per session, including speed-dependent treadmill training, skill-dependent treadmill training, overground training, and stair climbing. Outcome Measures: 6MWT, peak treadmill speed, walking speed over short distances at self-selected speeds and fastest-possible speeds, BBS, and LEMS were assessed prior to and following each 4- to 6-week training paradigm.		
<u>Jones et al.</u> (2014a); USA RCT PEDro=5 Level 2 N=38	 Population: 38 participants - 27 males and 11 females; chronic, motor incomplete SCI; AIS C or D; age range= 22-63y; years post injury= >12 months. Treatment: A total of 9h/wk of ABT for 24 weeks including developmental sequencing; resistance training; repetitive, patterned motor activity; and task-specific locomotor training. Algorithms were used to guide group allocation, FES utilization, and locomotor training progression. Outcome Measures: Neurologic function (ISNCSCI), 10MWT, 6MWT, and TUG test, community participation (SCIM-III, and Reintegration to Normal Living Index), metabolic function (weight, body mass index, and Quantitative Insulin Sensitivity Check). 	1. 2.	Average time for completing the TUG test was substantially (but not significantly) decreased for experimental (- 37.2s) versus control group (- 6.2s) participants. Significant improvements were noted on the modified SCI-FAI for participants in the experimental group. Scores improved by an average of 5±8.03 points compared with no gain for participants in the control group. The intervention had no immediate beneficial impact on SCIM-III and Reintegration to Normal Living Index).
Jones et al. (2014b); USA Secondary analysis of results from an RCT PEDro=5 N=38	 Population: 38 participants - 27 males and 11 females; chronic, motor incomplete SCI; AIS C or D; age range= 22-63y; years post injury= >12 months. Treatment: A total of 9h/wk of ABT for 24 weeks including developmental sequencing; resistance training; repetitive, patterned motor activity; and task-specific locomotor training. Algorithms were used to guide group allocation, FES utilization, and locomotor training progression. Outcome Measures: Walking speed and endurance (10MWT and 6MWT) and functional ambulation (TUG test). 	1.	On the basis of the most conservative estimate, 18%, 26%, and 32% of the participants demonstrated clinically significant improvements on the TUG test, the 10MWT, and the 6MWT, respectively. This secondary analysis identified likely responders to ABT on the basis of injury characteristics: AIS classification, time since

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		injury, and initial walking ability.
		 Training effects were the most clinically significant in AIS grade D participants with
		injuries <3 years in duration.
	Effect Sizes: Forest plot of standardized me calculated from pre- and post-intervention	
	Jones et al. 2014; Activity-Based	
	ISNCSCI Motor (UEMS+LEMS)	0.22 (-0.40,0.83) 0.38 (-0.24,0.99)
	ISNCSCI LEMS (LEMS)	0.41 (-0.21,1.03)
	SCI-FAI	0.19 (-0.43,0.80)
	10MWT	0.28 (-0.33,0.90)
	6MWT —	0.25 (-0_37,0.86)
	TUG	06 (-0.55,0.67)
	SCIM-III	0.37 (-0.25,0.99)
	RNL	
	-2 -1.5 -1 -0.5	0 0.5 1 1.5 2
	Favours Control SMD	9(95%C.I.) Favours Treatment
	Population: Five participants with chronic	1. The BBS of the maximal-
	SCI; 5 males; mean (SD) age: 50 (12) years old; injury level: C2 (n=1), C3 (n=1), C5 (n=1), C6 (n=1), T7 (n=1); AIS C (n=2) and AIS D (n=3); and mean time since injury: 211,2 months.	intensity resistance training condition showed a significant increase when compared with the conventional progressive resistance training condition
<u>Jayaraman et al.</u> <u>(2013);</u> USA	Treatment: Participants were randomly assigned to 4 weeks (12 sessions) of either maximal-intensity intermittent resistance training or conventional progressive resistance training (2-months washout). Targeted muscle groups included bilateral knee flexors/extensors and ankle dorsiflexors/plantarflexors.	 (p=0.05). 2. Conventional progressive resistance did not show any within-condition difference for BBS following training. However, with the maximal-intensity resistance training
RCT cross-over <u>PEDro=5</u> Level 2 N=5	 Maximal-Intensity Resistance Training: The protocol was conducted using an isokinetic dynamometer. Participants performed 3 sets of 10 repetitions of maximum volitional effort of isometric contractions, each repetition lasting 5 seconds with a 5-second rest between repeated maximum volitional efforts. A 2- minute rest period was given between each set of 10 repetitions. Verbal encouragement, asking the participants to give their maximal effort with every contraction and visual feedback through a 	condition, BBS showed significant increases in the balance scores (p=0.01).

	1	
	 computer screen showing their torque curves, was provided during the training. Conventional Progressive 	
	Resistance Training: The protocol was conducted using specific strength training machines designed for the targeted muscle groups. The exercise regimen was developed using the American College of Sports Medicine's general recommendations for physical rehabilitation interventions for individuals with neurological injuries. Participants began their first training session by performing up to 12 repetitions at 60% to 65% of their predetermined one-repetition maximum. After completing 3 sets of 10 to 12 repetitions, a 5% to 10% increase in weight was added for the next training session. Verbal encouragement and rest breaks between exercise sets were similar to the other training condition.	
	Outcome Measures: BBS was assessed 1 day before and 1 day after the training protocols.	
	Population: 16 participants with SCI; mean age 36.15 years; level of injury between TI and TI2; AIS A (n=6), AIS B (n=6), AIS C (n=2) and AIS D (n=2); and mean time since injury 5.15.	 Interactions were significant for all 6 variables except excursion of CoP in mediolateral plane and the path length of CoP in
<u>Sadeghi et al.</u> (2019); Iran RCT <u>PEDro=4</u> Level 2 N=16	Treatment: Participants were randomly assigned to rebound group (n=8) or control group (n=8). The rebound group received rebound therapy exercise (in a sitting or lying position) to increase their balance and stability using an appropriate trampoline. The exercise programs lasted 10 to 30 min (with a progression through the intervention period). Exercise durations were set at 5-min intervals (with heart rate reserve maintained at 50% to 70%) with 3- min rest periods 3 times per week over the 12 weeks. Outcome Measures: Standing stability	anteroposterior plane; meaning that the control group had no progress, whereas the rebound group made a significant improvement (e.g., the mean values of the center of pressure excursion in the antero-posterior plane were 37.8 [15.4] mm and 20.6 [8.4] mm before and after the exercise [p=0.05], respectively; or the velocity of center of pressure in antero-posterior was 39.6 [15.5] m/s before and 22.7 [14.9] mm/s after the
	parameters (i.e., excursion, velocity, and path length of the CoP in mediolateral	exercise [p=0.004]).

L			
	and anteroposterior plane) were assessed before and after the exercise intervention by force plate.		
	and incomplete SCI; 12 males and 3 females; mean (± SD) age 41.5 (± 16.9) years; level of injury cervical (n=10), thoracic (n=2) and lumbar (n=3); AIS C (n=12) and AIS D	1.	12/14 participants demonstrated increased BBS scores postintervention with a mean score improvement of 4.53 ± 4.09 (p<0.001). 9/14 participants had
	months. Treatment: The protocol consisted of 12 to 15 weeks of overground locomotor		improved SCI-FAI scores with a mean score increase of 2.47 ± 3.44 (p=0.01).
<u>Neville et al.</u> <u>(2019);</u> USA	training 2 times per week, which consisted of three, 4-week segments. For each training session, focus alternated between uniplanar and multiplanar movements. Each 90-min training session consisted of 5 training segments: joint mobility, volitional neuromuscular activation, task-	3.	None of the gait parameters (captured overground by a pressure-sensitive walkway [e.g., step length, step width, percent stance, and stance- to-swing time ratio]) achieved statistical significance.
Pre-post Level 4 N=15	isolation, task-integration, and activity rehearsal. Individualized rate of progression over the training period was tracked in-session and altered by varying movement complexity, resistance, velocity, and volume of the specific tasks. All exercises were performed under volitional control without the assistance of BWS harnesses, robotic devices, or electrical stimulation.	4.	Step length increased 3.7 cm (40.6-44.3 cm; p=0.55) and step width increased 1.8 cm (14.5-16.3 cm; p=.039); meanwhile percent stance time decreased 2.8% (76.8%- 74.0%; p=0.25) and stance-to- swing time ratio decreased 0.4 (3.5-3.1; p=0.33).
	Outcome Measures: BBS and the SCI-FAI were assessed for all participants at baseline and post-intervention. Spatiotemporal measures were collected from the last 7 participants who walked on a 6-meter pressure-sensitive walkway.		
	Population: 4 participants with chronic SCI and able to walk 10 m without physical assistance but with assistive devices and	1.	BBS scores increased 2.8 ± 0.96 from pre- to post- intervention.
<u>Holleran et al.</u> <u>(2018);</u> USA	bracing below the knee as needed; 3 males, 1 female; age range: 18-48 years; AIS C (n=2), AIS D (n=2); injury level: C5 (n=2), C7 (n=1), T3 (n=1); and duration post-injury (14-53 months).	2.	In the participants who attended follow-up testing (n=3), gains in BBS were not maintained at least 1 year following training, with scores
Pre-post Level 4 N=4	Treatment: Participants received up to 40 sessions at 3 to 5 times per week within 10 weeks. Each 1-hour session allowed up to 40 minutes of stepping training in variable contexts at high-intensity, with rest breaks as needed. Targeted training intensities were up to 85% of age-predicted maximum HR.		similar to pretraining assessments.

	• During the first 2 weeks (6-10	
	 During the first 2 weeks (6-10 sessions), only forward stepping on a motorized treadmill was performed to allow participants to accommodate to the large volumes of stepping at higher cardiovascular intensities. Minimal BWS and handrail support were provided only as needed. 	
	 Training over the remaining weeks was divided into 10-minute increments of speed-dependent treadmill training, skill-dependent treadmill training (e.g., stepping in different directions, applied perturbations to challenge various aspects of stepping in the form of obstacles and/or weights on the trunk or limbs, limiting use of upper extremities, or inclined surfaces), overground training, and stair climbing, while trying to maintain the targeted HR range. 	
	Outcome Measures: BBS was tested prior to (<i>pre</i>) and following (<i>post</i>) up to 40 training sessions, with follow-up assessments at least 1 year post training.	
DiPiro et al.	Population: 10 participants with chronic SCI; the ability to walk independently for a minimum of 10 m with or without an assistive device and a self-selected walking speed >0.1 and <1.15 m ⁻¹ ; 5 males and 5 females; mean (SD) age: 57.9 (9.3) years; AIS C (n=1) and AIS D (n=9); injury level: Cervical (n=9) and thoracic (n=1); and mean (SD) time since injury: 11.1 (9.6) years.	 Although trends toward improvement were seen in the BBS, there were not statistically significant (p=0.15) changes.
<u>(2016);</u> USA Pre-post Level 4 N=10	Treatment: Participants completed a 6- week (3 sessions per week; 20 min per session) non-task-specific, progressive aerobic exercise training program; performed on a NuStep T5xr recumbent cross-trainer. The selected exercise modality required bilateral reciprocal stepping against resistive forces and synchronized upper extremity movement; thus, a total-body workout was achieved.	
	The weekly sessions included two steady- state exercise sessions at the target intensity and one high-intensity interval training session.	

	The intervention was developed to meet the SCI guidelines for aerobic activity and prepare participants to reach the levels of aerobic exercise recommended by the American College of Sports Medicine and 2008 Physical Activity Guidelines for Americans.		
	Outcome Measures: BBS was assessed before and following the aerobic exercise training intervention.		
	Population: 4 participants with incomplete SCI (3M, 1F); 33-63 yrs old; 2 AIS C, 2 AIS D.	1.	All outcome measures indicated an improvement in lower limb function from
<u>Oh & Park (2013);</u> Korea Pre-post Level 4 N=4	Treatment: 4-week training program consisting of 4 stages with different community situations. In each stage, patients underwent 1 hr sessions of community-based ambulation training; 6 times/wk for a 4-week period. During the training period, the level of difficulty was increased weekly with progressive changes in environmental demands.		baseline to 4-wk follow-up, as well as from baseline to the 1- yr follow-up.
	Outcome Measures: 10MWT; 6MWT; community walk test, walking ability questionnaire, and ABC scale.		

Discussion

There were seven RCTs, one secondary analysis of an RCT, and four pre-post studies which assessed different non-body-weight supported training interventions on standing balance outcomes that have been carried out in patients with motor incomplete and chronic SCI. These included ABT, community-based ambulation training, task-specific training, impairment-based training, different stepping tasks, overground (locomotor and other exercises) training, overground perturbation training, resistance training for lower extremity muscle groups, aerobic exercise using a recumbent cross-trainer, or the application of visual feedback during different exercises; or training intensities (high vs. moderate).

In a high-quality RCT, Unger et al. (2021) included 20 patients (10 with paraplegia and 10 with tetraplegia) who were randomly allocated to perturbation-based balance training or conventional intensive balance training for one hour, three times per week for eight weeks. After the intervention, and at 3 and 6 months follow-up, reactive stepping ability, balance control (Mini-BESTest and Community Balance and Mobility Scale [CB&M]), balance confidence (ABC scale), fall concern (Falls Efficacy Scale – International [FES-I]), falls parameters (e.g., number of falls, time to first fall, or number of fallers), LEMS, and gait parameters (walking speed, step length, or cadence) improved across both groups, suggesting that repetitive exposure to challenging balance training can lead to improvements regardless of the inclusion of external perturbations (Unger et al. 2021). In a cross-over RCT, Lotter et al. (2020) found significantly greater gains in balance confidence (ABC scale) following task-

specific vs. impairment-based training, while BBS, Five Times Sit to Stand Test (FTSTS), or LEMS showed similar improvements in both groups. The authors suggested that, as training specificity may be an important component of rehabilitation interventions, therapists must educate patients on strategies to minimize the minor adverse events (AEs) shown in the trial (Lotter et al. 2020).

We found one RCT that included people with motor complete SCI. Sadeghi et al. (2019) included 16 patients with paraplegia, 12 with motor complete and four with motor incomplete SCI, who were randomly assigned to the rebound group (moderate intensity sitting or lying trampoline training) or a control group (Sadeghi et al. 2019). At the end of the intervention period (12 weeks), the rebound group achieved significant improvements in standing balance parameters (e.g., the mean values of the center of pressure excursion in the antero-posterior plane, or the velocity of center of pressure in antero-posterior), whereas the control group had no progress (Sadeghi et al. 2019).

In a pre-post study, Neville et al. (2019) assessed 10 patients with tetraplegia and five with paraplegia who performed an overground locomotor training protocol twice a week in five individualized training segments (joint mobility, volitional neuromuscular activation, task-isolation, task-integration, and activity rehearsal). At post-intervention (12 to 15 weeks), most of the participants demonstrated increased BBS scores with a mean score improvement of 4.53 ± 4.09 , and several showed an improvement in SCI-FAI with a mean score increase of 2.47 ± 3.44 (Neville et al. 2019).

Several other studies have indicated that overground training for people with motor-incomplete SCI benefits standing balance and walking capacity (<u>Oh & Park 2013</u>). Overground training has also been integrated with a wider variety of other exercises to provide more comprehensive therapy (<u>Jones et al. 2014a</u>; <u>Jones et al. 2014b</u>), and others have suggested the additive benefits of providing visuotemporal cues during walk training (<u>Pramodhyakul et al. 2016</u>).

In an RCT, Brazg et al. (2017) compared high (70%-85% HR_{max}) vs. low-intensity training (50%-65% HR_{max}) in people with chronic incomplete SCI. Significantly greater improvements in peak treadmill speed, peak velocity, and VO₂ peak-match were observed following high-intensity training, while changes in self-selected speeds and 6MWT approached significance, but LEMS or BBS did not change (Brazg et al. 2017).

Jayaraman et al. (2013) assessed the effects of resistance training intensity over four weeks of resistance training that targeted the bilateral knee flexor/extensor and ankle dorsiflexor/plantar flexor using an isokinetic dynamometer or specific strength training machines. For standing balance (measured by the BBS), only the group that trained at maximal intensity showed significant improvements; however, further studies should be carried out with a larger sample size to corroborate these results (Jayaraman et al. 2013).

Additionally, it should be noted that most of the overground locomotor training in ambulatory persons with incomplete SCI was performed over a flat, smooth, and firm surface, and this training condition is different from the irregular, unstable areas that patients encounter in their daily living after discharge (Amatachaya et al. 2021). In an RCT, Amatachaya et al. (2021) showed that a walking training program for four weeks (5 d/w) on a walking track with different surfaces (including artificial grass, pebbles, and soft areas), compared to overground walking

training provides better results on standing dynamic balance (TUG and FTSTS), walking speed (10MWT), walking distance (6MWT), and risk of falling during 6-month follow-up (<u>Amatachaya et al. 2021</u>). The same research study group showed that low cognitive-motor interference (as measured by dual-task obstacle crossing) is a strong predictor of fall risk over the next six months (unadjusted odds ratio = 7.07, p<0.002, power = 1.000) in people with chronic SCI (<u>Amatachaya et al. 2019</u>). Incorporating cognitive-motor interference as part of an assessment and treatment program may help to identify those at risk of future falls and promote functional ability and improvement in people with SCI (<u>Amatachaya et al. 2019</u>).

Conclusions

There is level 1 evidence (from 1 RCT: <u>Unger et al. 2021</u>) that perturbation-based balance training and conventional intensive balance training provide similar improvements in reactive stepping ability (behavioral response and foot contact time during the Lean-and-Release test), lower limb strength, gait parameters, balance control (Mini-BESTest and CB&M), balance confidence (ABC Scale), fall concern (FES-I), and on falls parameters (number of falls, number of fallers, or time to first fall); compared to conventional intensive balance training, in patients with chronic motor incomplete SCI.

There is level 1 evidence (from 1 RCT: Lotter et al. 2020) that task-specific training (consisting of stepping practice) provides more improvements in balance confidence (ABC Scale) and similar improvements in patient's ability to safely balance (BBS), compared with impairment-based training in patients with chronic motor incomplete SCI.

There is level 1 evidence (from 1 RCT: <u>Brazg et al. 2017</u>) that high-intensity (70%-85% HR_{max}) locomotor training does not provide significantly greater improvements in standing balance (BBS) compared to low-intensity (50%-65% HR_{max}) locomotor training in participants with chronic and motor incomplete SCI.

There is level 1 evidence (from 1 RCT: <u>Amatachaya et al. 2021</u>) that a walking training program for 4 weeks (5 d/w) on a walking track with different surfaces (including artificial grass, pebbles, and soft areas), compared to overground walking training yields better results on standing dynamic balance (TUG and FTSTS) and a lower risk of falling during 6-month follow-up in patients with chronic motor incomplete SCI.

There is level 2 evidence (from 1 RCT: <u>Sadeghi et al. 2019</u>) that rebound therapy could provide improvements in standing stability parameters (excursion, velocity, and path length of the CoP) in patients with chronic motor complete and incomplete SCI.

There is level 2 evidence (from 1 RCT: Jayaraman et al. 2013) that a 4-week lower limb resistance training program at maximal intensity (isometric contractions of maximum volitional effort) provides significant improvements in standing balance (BBS), meanwhile, a conventional resistance training program at moderate intensity (60%-65% of their one-repetition maximum) did not.

There is level 2 evidence (from 1 RCT: <u>Jones et al. 2014a</u>) that 24 weeks of ABT (which included developmental sequencing; resistance training; repetitive, patterned motor activity; and task-

specific locomotor training) did not provide significant improvements in standing balance (TUG) in comparison with a control intervention in patients with incomplete and chronic SCI.

There is level 4 evidence (from 1 pre-post study: <u>Neville et al. 2019</u>) that overground locomotor training (consisting of joint mobility, volitional neuromuscular activation, task-isolation, task-integration and activity rehearsal) for 12-15 weeks provides improvements in standing balance (BBS) and in functional walking ability (SCI-FAI) in patients with chronic motor incomplete SCI.

There is level 4 evidence (from 1 pre-post study: <u>DiPiro et al. 2016</u>) that a 6-week progressive aerobic program (which included two steady exercise sessions at the target intensity and one high-intensity interval training session) using a recumbent cross-trainer does not provide significant improvements in standing balance in people with chronic SCI.

There is level 4 evidence (from 1 pre-post study: <u>Oh & Park 2013</u>) that community-based ambulation training that is progressively challenging may result in long-lasting benefits in standing balance and walking ability in people with incomplete SCI.

Key Points

Perturbation-based balance training, conventional intensive balance training, taskspecific (stepping) and impairment-based training, walking training over different surfaces, rebound therapy, overground multi-modal locomotor training, or community-based ambulation training may result in improvements, mainly in standing balance and balance confidence.

Most promising results seem to be from perturbation-based and specific balance training.

High-intensity locomotor (70%-85% HR_{max}) and resistance (isometric contractions of maximum volitional effort) training programs seem to be safe in patients with SCI; however, the effectiveness for improving standing balance is contradictory. Larger RCTs are necessary.

4.3 Body-Weight Supported Treadmill Training (BWSTT) for Standing Balance

Table 11. Systematic Reviews Assessing BWSTT Strategies and/or Balance Interventions for Standing Balance Outcomes in Patients With SCI

Authors Year; Country Date included in the review Number of	Method Databases Outcomes Measures	Conclusions
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articles Level of Evidence Type of Study AMSTAR Score			
Alashram et al. (2021); Italy Reviewed published articles up to January 2021 N=16 Level of evidence: PEDro scale Type of study: 13 RCTs 2 clinical controlled trials 1 pilot study AMSTAR: 6	Method: The present systematic review aimed to provide an overview of the immediate and long-term effects of the Lokomat on various impairments following SCI, to determine the optimal treatment dosage, and to define who most likely would benefit from the intervention. Database: PubMed, SCOPUS, PEDro, REHABDATA, MEDLINE, EMBASE, and web of science. Outcome Measures: Walking speed (10MWT), walking distance (6MWT, 2MWT, SCI-Functional Ambulation Profile [SCI-FAP]), functional ambulation (TUG, Functional Ambulation Category [FAC]), walking capacity (SCI-FAP, 6MWT), balance (BBS, Figure Eight Test, FES-I), functional level (WISCI II, FIM-L, SCIM, SCIM-III – mobility section [SCIM-III-M], Ambulatory Motor Index), leg strength (LEMS), strength (maximum voluntary contraction [MVC]), and agility (Probe Reaction Time).	3.	 Quality of the included studies: a. The median score on the PEDro scale was 6 (ranged from 2 to 8). b. Overall, 6 studies met 8 criteria, 7 criteria (n=1), 6 criteria (n=2), 3 criteria (n=2), 4 criteria (n=2), 3 criteria (n=1), and 2 criteria (n=1) for low risk of bias. A total of 658 patients with incomplete SCI were included. The included studies did not demonstrate any AEs or uncomfortable issues following the Lokomat intervention. Effects on balance: One study reported a significant improvement in the BBS scores after Lokomat training compared with the control group; however, 2 studies did not show significant differences between groups in the BBS, the Figure Eight Test, and the FES-I scores. Effects on functional level and functional ambulation: a. TUG: Two studies showed significant improvements after the RAGT, while one study reported no significant differences between groups.
<u>Nam et al. (2017)</u> ; South Korea Reviewed published articles up to January 2016	Method: A systematic review and meta-analysis were performed to assess the effects of RAGT (using Lokomat) on improving walking- related functional outcomes according to time since injury in patients with incomplete SCI. Database: MEDLINE, EMBASE, SCOPUS, Web of Science, Cochrane Central Register of	1. 2.	Of the 502 participants, 263 in four studies were assessed at < 6 months post-injury and 209 in five studies were assessed at > 12 months post-injury, and the remaining 30 participants in one study (mean 6.3 months post- injury) did not belong to any group. The mean PEDro score of the studies was 5.7 (range, 3 to 8).

N=10 Level of evidence: PEDro score	Controlled Trials, the World Health Organization International Clinical Trials Registry Platform, and the clinical trials registry and database of the U.S. National Institutes of Health (ClinicalTrials.gov) were searched.	3.	RAGT vs. conventional overground gait training, 2 investigated RAGT vs. body- weight supported gait training, 2 investigated RAGT vs. non-gait-specific training (strength or bike), and finally, three trials compared RAGT with no
Type of study: RCTs of parallel- groups or cross- over trials AMSTAR: 8	Outcome measures: Walking speed (10MWT), walking distance (6MWT), leg strength (LEMS), level of functional mobility and independence (WISCI II), independence of gait (FIM-L), functional mobility and balance (TUG test), and spasticity (Modified Ashworth Score).	4.	 intervention. Effects on balance: a. No trial with acute participants measured recovery of balance. b. Significantly greater improvements in TUG were observed in the chronic RAGT groups compared to the no intervention groups (pooled MD = 9.25, 95% CI 2.76 to 15.73, P=0.005, I2=74%; three trials, 120 participants).

Table 12. Body-Weight Supported Treadmill Training (BWSTT) for Standing Balance

Author Year Country Score Research Design Total Sample Size	Methods	Outcome
	Acute SCI (< 1 year)	
<u>Midik et al. (2020);</u> Turkey	Population: 30 males with traumatic incomplete SCI and a LEMS of ³ 10; mean (range) age 36.6 (19-53) years; AIS C (n=16) and AIS D (n=14); injury level T12 (n=7) and L1-L3 (n=23); median time since injury for the RAGT and control groups was 5 and 24 months, respectively.	1. Both groups significantly (p<0.01) improved in SCIM-III, but without statistically differences between groups, except in the RAGT group which showed higher SCIM-III values at T3 in comparison with the control group (p=0.01).
RCT <u>PEDro=4</u> Level 2 N=30	Treatment: All patients received regular physiotherapy (consisting of range of motion exercises, strengthening exercises, body stabilization, self-care ability, and ground walking training) for 5 times a week for a total of 5 weeks. Participants were randomized into two groups:	
	 RAGT group (n=15): Received additional RAGT (using 	

	Lokomat) for 3 times a week (each session lasted 30 min) for a total of 5 weeks. Treadmill speed and BWS was increased individually. • Control group (n=15). Outcome Measures: SCIM-III, LEMS and WISCI II were assessed at baseline (t1), at the end of the treatment (t2), and at three months after the treatment (t3).		
Wirz et al. (2017); Switzerland, Germany, Spain and UK RCT <u>PEDro=6</u> Level 1 N=18	 Population: 18 participants with acute SCI and limited walking ability (WISCI II < 5); 16 males and 2 females; mean age 34.9 years; level of injury C4 to TI2; AIS B (n=9) and AIS C (n=9); and study inclusion was set at maximum of 60 days post-trauma. Treatment: Patients performed 3–5 days of training per week of RAGT using Lokomat for a period of 8 weeks. Patients were randomly allocated to one of two groups depending on the stablished walking time per training: Intervention group (n=9): More than 50 min. Control group (n=9): Maximum of 25 min. Outcome Measures: SCIM-III mobility subscore was assessed at baseline and at 8 weeks of training. 	1.	For the SCIM-III mobility subscore, both groups improved to a statistically significant level; however, changes in the intervention group (19.0 [4-29]) were markedly greater than in control group (5.0 [0-30]).
Shin et al. (2014); Seoul RCT PEDro=5 Level 2 N=53	 Population: 53 participants- 34 males and 19 females with incomplete SCI; 31 with cervical injuries and 22 with thoracic & lumbar injuries; 36 with traumatic SCI and 16 with non-traumatic SCI; mean age= 48.15 ± 11.14y; months post injury= 3.33 ± 2.02 months. Treatment: Patients were included in a prospective, randomized clinical trial by comparing RAGT to regular physiotherapy. The RAGT group received RAGT three sessions per week at duration of 40 min with regular physiotherapy in 4 weeks. 	1.	At the end of rehabilitation, both groups showed significant improvement in SCIM-III mobility subscore.

	 The conventional group underwent regular physiotherapy twice a day, 5 times a week. Outcome Measures: LEMS, ambulatory motor index, SCIM-III mobility section (SCIM-III mobility subscore), and WISCI II. 		
Tang et al. (2014); China and Japan RCT PEDro=4 Level 2 N=30	 Population: 30 male participants with incomplete SCI; mean (± SD) age 38.6 (± 7.6) years; AIS D (n=30); and time since injury 189 days. Treatment: Participants were randomly assigned to two groups: Lokomat group (n=15): Participants performed one session using Lokomat with an initial training speed of 1.5 km/h (and progressively raised to 1.8 km/h while maintaining gait quality), with a BWS initiated at 35%, and with a 70% guidance force. Ergo bike group (n=15): Participants were instructed to pedal at a pedaling rate of 45 rpm with a workload of 60 W during 40 min for the session. Outcome Measures: Probe Reaction Time and 10MWT were assessed at baseline and after the training. 	1.	The Probe Reaction Time decreased significantly in the Lokomat group; however, it didn't significantly decrease in the Ergo bike group. Post-intervention, the Lokomat group had a significantly shorter Probe Reaction Time than the Ergo bike group.
Dobkin et al. (2006); USA RCT <u>PEDro=7</u> Level 1 N=292 (enrolled) N=117 (analyzed)	 Population: 117 males and females; age 16-69 yrs; AIS B-D; <8 wks postinjury. Treatment: BWSTT vs. overground mobility training: 5x/wk, 9-12 wks, 30-45 min/session. Outcome Measures: BBS, FIM-L, walking speed, 6MWT, WISCI at 3 and 6 months. 	1.	AIS C & D participants with upper motor neuron in both groups improved in BBS scores, without statistical difference between groups.
<u>Shahin et al.</u> (2017); Egypt Prospective controlled trial Level 2	 Population: 40 participants with acute SCI (onset less than 6 month). RAGT group (n=20): Mean age 32.4 ± 11.8 years; AIS B-C; tetraplegia (n=3) and paraplegia (n=17); and mean 	1.	The BBS was significantly improved in both groups in week 12; however, there was no statistical changes between groups.

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N=40	injury duration 4.7 ± 4.6 months	
	 Conventional group (n=20): Mean age 32.7 ± 10.5 years; AIS B-C; tetraplegia (n=3) and paraplegia (n=17); and mean injury duration 3.7 ± 3.1 months 	
	Treatment: Participants were assigned into one of the following two groups:	
	 RAGT Group (n =20): Participants received RAGT (3 days per week) with the Lokomat system in addition to the rehabilitation program (2 days per week). Each session lasted for 60 minutes. The BWS was adjusted to the minimum without knee buckling or toe dragging. The walking speed was gradually increased up to 1.5 km/hr. 	
	 Conventional group (n=20): Participants received rehabilitation program only. Sessions were performed 30 minutes each, 5 sessions a week, included functional exercises according to the muscle grading, slow prolonged stretching of the spastic muscles, and strengthening exercises to the anti-spastic muscles. The conventional therapy included active or assisted active exercises. 	
	Outcome Measures: BBS was assessed before intervention (week 0) and at week 12 after treatment (week 12).	
<u>Schwartz et al.</u> (2011); Israel Case control Level 3 N=56	Population: 56 participants with SCI as a result of traumatic (57%) or non- traumatic causes; 37 males and 19 females; mean age 42.5 years; level of injury cervical (n=26), thoracic (n=16), and lumbar (n=14); AIS A (n=6), AIS B (n=7), AIS C (n=13), and AIS D (n=2); and mean time since injury 24 days.	 At the end of the rehabilitation period, both groups showed a significant improvement in ambulation ability according to FAC (Wilcoxon signed ranks test Z =-5.21, p<0.01), with no significant differences between groups.

	 Treatment: Participants in the intervention group were prospectively included and those in the control group were retrospectively matched. Intervention group (n=28): Participants received 30-min sessions of RAGT with Lokomat with individualized progression in speed and BWS, and 30-45 min of regular physiotherapy sessions; for 2-3 times a week and 12 weeks. Control group (n=28): Participants were treated by regular physiotherapy for 30-45 min five times a week using Bobath principles. Outcome Measures: FAC scale, SCIM, and WISCI II were assessed upon admission and upon discharge from the rehabilitation department. 	2.	Both groups improved significantly in their SCIM scores during the rehabilitation period, however the RAGT group improved significantly more in SCIM mobility scores than the controls (RAGT: 34±19 points to 64±17 points; Controls: 34±21 to 55±22; <i>F</i> _{1:54} =8.84, P=0.05).
<u>Harkema et al.</u> (2012); USA Pre-post Level 4 N=196	 Population: 196 participants (148 male, 48 female) with incomplete SCI; mean age 41±15 yrs; YPI- <1 yrs (n=101), 1-3 yrs (n=43), >3 yrs (n=52). Treatment: Locomotor training with three components: (1) 1 hour of step training in the BWS on a treadmill environment, followed by 30 min of (2) overground assessment and (3) community integration. Outcome Measures: BBS, 6MWT, and 10MWT. 	1. 2.	Scores on the BBS significantly improved by an average of 9.6 points. Increases were significant for patients with AIS grades C and D, and the amount of improvement was significantly different between these groups (rank-sum test, p<0.008). Of the 168 patients classified as at risk for falls at enrollment, 27% improved their scores to a value reflecting minimal risk for falls (11% AIS grade C, 37% AIS grade D).
	Chronic SCI (> 1 year)	7	The training intervention
<u>Piira et al. (2019a);</u> Norway RCT <u>PEDro=7</u> Level 1 N=20	Population: Participants with chronic and motor incomplete SCI; 15 males and 5 females; mean age 50 years; level of injury cervical (n=8), thoracic (n=8) and lumbar (n=4); AIS C (n=6) and AIS D (n=14); and median time since injury 4 years.	1. 2.	The training intervention was well tolerated with no AEs, and there were only minor side-effects, such as superficial abrasions, which did not interfere with the regular training program. In each group, 2 participants with AIS grade C were unable to walk

	 Treatment: Participants were randomly divided in two groups: Control group (n=10): Participants received usual care (which might include overground walking). Intervention group (n=10): A treadmill with body-weight supported system was used for 60 days training, with 2 daily sessions of BWSLT with manual assistance for a total of 90 min per day, 5 days per week for 3 4-weeks periods; with the aim of reducing the BWS to <40% and/or increase walking speed towards normal (3–5 km/h). BWSLT also included overground training. The participants performed home exercises between the training periods. Outcome Measures: 10MWT, distance walked with use of necessary walking aids (6MWT), LEMS, BBS, and mFRT were assessed at baseline and 2–4 weeks after 	3.	at baseline and did not gain independent walking post- intervention. Thus, only 7 participants in each group were available for post-intervention walking testing. There was no significant difference in change between the groups for BBS, –1.2 points 95% CI (–4.3, 1.9), <i>p</i> =0.42.
Piira et al. (2019b); Norway RCT <u>PEDro=7</u> Level 1 N=24	 program. Population: 24 participants wheelchair-dependents with or without some walking function and with chronic incomplete SCI; 9 males and 15 females; mean age 50.5 years; level of injury cervical (n=10), thoracic (n=9); and mean time since injury 18 years. Treatment: Participants were randomized to either intervention (n=7) or control group (n=12). Intervention participants received 60 days of robot-assisted locomotor training (with the use of Lokomat®), with 3 training sessions per week over a period of 6 months. Each session included preparation (≈ 20–30 min), stepping on a treadmill (20–60 min) with BWS <40% of the participants' initial 	1.	The intervention was well tolerated with no AEs, except for minor issues such as small leg abrasions. Both groups significantly improved the BBS after the intervention period (4.3 points for intervention participants [p=0.03] and 3.2 points for control group [p=0.04]) but changes were minimal between groups.

	weight, and a few minutes of	
	overground walking and/or exercises on the treadmill.	
	 Control participants received low-intensity usual care, usually 1–5 times per week. 	
	Outcome Measures: Full or partial recovery of walking function, walking speed and endurance (10MWT and 6MWT); LEMS; BBS; and mFRT were assessed within 30 days before randomization, and post-evaluation within 14–30 days after completion of the trial.	
	Population : 15 participants - 9 males and 6 females; chronic motor incomplete SCI; 5 AIS C and 10 AIS D; age range= 26-63y; years post injury> ly.	 Training was well tolerated by both groups, although participants in Loko-R tended to report higher levels of perceived exertion during training.
<u>Lam et al. (2014);</u>	Treatment : Participants were randomly allocated to BWSTT with Lokomat resistance (Loko-R group) or conventional Lokomat-assisted BWSTT (controls). Training sessions were 45 min, 3 times/wk for 3 months.	2. Participants in the Loko-R group performed significantly better in the SCI-FAP compared with controls at posttraining and in follow-up assessments.
Canada RCT	Outcome Measures: Skilled walking capacity (SCI-FAP), 10MWT, and 6MWT were measured at baseline,	
PEDro=8 Level 1	post=training, and 1 and 6 months follow up.	
PEDro=8	post=training, and 1 and 6 months follow up.	ed mean differences (SMD ± 95%C.I.) as ion data and pre-intervention to
PEDro=8 Level 1	post=training, and 1 and 6 months follow up. Effect Sizes: Forest plot of standardize calculated from pre- to post-interventi retention/follow-up data.	ion data and pre-intervention to Treadmill Training + Lokomat Resistance
PEDro=8 Level 1	post=training, and 1 and 6 months follow up. Effect Sizes: Forest plot of standardize calculated from pre- to post-interventi retention/follow-up data. Lam et al. 2014; Body Weight-Supported SCI-FAP (Pre->Post)	ion data and pre-intervention to
PEDro=8 Level 1	post=training, and 1 and 6 months follow up. Effect Sizes: Forest plot of standardize calculated from pre- to post-interventi retention/follow-up data. Lam et al. 2014; Body Weight-Supported	ion data and pre-intervention to Treadmill Training + Lokomat Resistance 0.27 (-0.85,1.40) 0.25 (+0.90,1.41)
PEDro=8 Level 1	post=training, and 1 and 6 months follow up. Effect Sizes: Forest plot of standardize calculated from pre- to post-interventi retention/follow-up data. Lam et al. 2014; Body Weight-Supported SCI-FAP (Pre->Post) SCI-FAP (Pre->Ret)	ion data and pre-intervention to Treadmill Training + Lokomat Resistance 0.27 (-0.85,1.40) 0.25 (+0.90,1.41)
PEDro=8 Level 1	post=training, and 1 and 6 months follow up. Effect Sizes: Forest plot of standardize calculated from pre- to post-interventi retention/follow-up data. Lam et al. 2014; Body Weight-Supported SCI-FAP (Pre->Post) SCI-FAP (Pre->Ret) -2 -1.5 -1 -0	ion data and pre-intervention to Treadmill Training + Lokomat Resistance 0.27 (-0.85,1.40) 0.25 (+0.90,1.41)

Level 1 N=35	1-hour sessions per week. The comprehensive physical therapy group is a structured rehab program individualized for each participant. The body-weight supported ambulation on a fixed track group consisted of body-weight supported ambulation on a fixed track. The BWSTT group involved body-weight supported ambulation on a treadmill. Outcome Measures: Tinetti scale, 10MWT, LEMS and total manual muscle test score (sum of upper
	extremity motor score and LEMS), and the motor domain component of the FIM measure.
	Effect Sizes: Forest plot of standardized mean differences (SMD ± 95%C.I.) as calculated from pre- and post-intervention data.
	Alexeeva et al. 2011; Body Weight Supported Treadmill Walking Speed Balance Score -2 -1.5 -1 -0.5 0 0.5 1 1.5 2 Favours Control SMD(95%C.I.) Favours Treatment
	Alexeeva et al. 2011; Body Weight Supported Track Walking Speed 0.03 (0.74,0.80) Balance Score 0.25 (-0.52,1.03)
	ASIA Motor Score -2 -1.5 -1 -0.5 0 0.5 1 1.5 2 Favours Control SMD(95%C.I.) Favours Treatment
<u>Wu et al. (2018);</u> USA RCT <u>PEDro=6</u> Level 1 N=14	 Population: 14 participants with incomplete SCI; 10 males, 4 females. Robotic group: Mean age: 48.4 years; level of injury C2-T7; AIS C (n=2) and AIS D (n=5); and mean time since injury: 5.8 years Treadmill only: Mean age: 48.1 years; level of injury C3-T10; AIS C (n=0) and AIS D (n=7); and mean time since injury: 9.4 years Treatment: Participants were randomly assigned to one of two

	 Robotic treadmill training (n=7): A custom-designed cable-driven robotic gait training system (CaLT) was used for providing a bilateral pelvis assistance load was applied to the pelvis from heel strike to mid-stance on the ipsilateral leg for facilitating weight shifting. The peak force was set at ~9% of body weight. In addition, an assistance load was applied to both legs from toe off to mid-swing to facilitate leg swing with magnitude of the force being determined using an adaptive control algorithm. 	
	 Treadmill only training (n=7): No assistance force was applied during treadmill training. 	
	Participants were fitted with an overhead harness that attached to a counterweight support system. BWS was provided as necessary for both groups to prohibit knee buckling or toe dragging during treadmill walking. Treadmill training speed was set at the participant's comfortable walking speed. Training was conducted 3 times/week for 6 weeks with the training time for each visit set to 45 minutes (i.e., 35 minutes of treadmill training and followed by 10 minutes of overground walking practice), excluding set up time. The targeted RPE was 12 to 16 (somewhat hard to hard levels).	
	Outcome Measures: BBS and ABC scale were assessed before, after 6 weeks of treadmill training, and 8 weeks after the cessation of treadmill training.	
Labruyere & van Hedel (2014);	Population : 9 participants- 5 males and 4 females; SCI ranging from C4 to T11; mean age= 59 ± 11y; months post injury= 50 ± 56m.	 There were no significant differences in changes in balance and fear of falling scores between the two interventions.
Switzerland RCT cross-over PEDro=6 Level 1	Treatment : Participants with a chronic iSCI were randomized to group 1 or 2. Group 1 received 16 sessions of RAGT (45 min each) within 4 weeks followed by 16	

N=9	sessions of strength training (45 min each) within 4 weeks. Group 2 received the same interventions in reversed order. Data were collected at baseline, between interventions after 4 weeks, directly after the interventions and at follow-up 6 months after the interventions. Pain was assessed repeatedly throughout the study. Outcome Measures: 10MWT at preferred and maximal speed,		
	walking speed under different conditions, balance (BBS and maximal mediolateral amplitude of the center of pressure movement over 30 s on a force plate), strength, FES-I.		
	Population : 22 participants; 16 males and 6 females; Level of injury between C2 and T12; mean age= 48 ± 13y; years post injury= 5.7 ± 10.5y.	1.	Both forms of training led to significant improvements in walking and confidence, though the changes in ABC scores were
<u>Yang et al. (2014);</u> Canada RCT PEDro=6 Level 1	Treatment: Twenty-two participants, ≥7 months post injury, were randomly allocated to start with Precision (precise, visually guided walking over obstacles) or Endurance Training (mass practice treadmill walking). Each phase of training was 5 times per week for 2 months, followed by a 2-month rest.		not significantly different in either the Precision group or the Endurance group (p=0.52).
N=22	Outcome Measures: Walking skills (SCI-FAP), walking speed (10MWT), walking distance (6MWT), walking ability (WISCI II), walking confidence (ABC scale), depression (Center for Epidemiologic Studies–Depression Scale), manual muscle strength of the lower extremities.		
Niu et al. (2014);	Population : 40 participants - 27 males and 13 females; spastic hypertonia in lower extremities.	1.	The baseline (i.e., pre-training) measures of MVC torque (dorsiflexion and plantarflexion
USA RCT PEDro=5 Level 2 N=40	Treatment : Each participant was assigned either to the control or intervention (Lokomat training) group according to a permuted block randomization design. All participants were injured within their cervical or upper thoracic (superior to TIO) vertebrae. Each participant received a one-hour training session		torques) could predict the differential treatment response, i.e., participants with high plantarflexion torque and dorsiflexion torque were more likely to have both high walking capacity and receive significant benefit from Lokomat training.

	three times per week for four consecutive weeks; as it took 15-20 mins to set up the participant, the gait training lasted up to 45 mins per session. Outcome Measures: 10MWT, 6MWT, TUG test, isometric torque resulting from MVC, Modified Ashworth Score, EMG, WISCI II.	2.	For TUG, the Growth Mixture Modeling analysis of joint groups found a beneficial training effect on participants with high walking capacity (P=0.05). Participants in Class 2 of the Lokomat group decreased their time at a rate of 0.41 s/week (p=0.02). Participants in Class 1 did not show significant benefit from the Lokomat training (p>0.05).
Wu et al. (2016); USA RCT PEDro=6 Level 1 N=14	Population: 14 participants with incomplete SCI; the ability to ambulate overground with/without assistive device as necessary, and with orthotics that do not cross the knee; walking with impaired walking function (self-selected walking speed < 1.0 m/s); mean age: 51.9 years; 10 males, 4 females; level of injury CI- TIO; AIS C (n=1) and AIS D (n=13); and time since injury: more than one year. Treatment: Participants were blocked by gait speed into slow (<0.5 m/s) or fast (<0.5 m/s) and randomly assigned to 1 of 2 groups of robotic treadmill training with resistance (n=7) or assistance (n=7) training. Training was performed 3 times per week for 6 weeks, with the training time for each visit set to 45 minutes (35 minutes of treadmill followed by 10 minutes of overground walking practice) as tolerated. For each training session, participants were fitted with an overhead harness attached to a counterweight support system. BWS was only provided in the instance that a counterweight was necessary to prohibit knee buckling or toe dragging during stepping. Treadmill speed was consistent with the participant's maximum comfortable walking speed, determined on the treadmill at the beginning of each training and was 12 to 16.	1.	Six participants in the resistance training group and six in the assistance training group completed all the 18 training sessions and three evaluation sessions. BBS and ABC scale had modest changes (all ns) after treadmill training for both the resistance and assistance training groups.

	* A custom-designed cable-driven robotic gait training system (CaLT) was used to provide controlled bilateral resistance or assistance load to the leg at the ankle of subjects during treadmill training. Outcome Measures: BBS and ABC scale were assessed before, after 6 weeks of treadmill training, and 8 weeks after the cessation of treadmill training.		
Wu et al. (2012); USA Repeated assessment with crossover PEDro=5 Level 2 N=10	 Population: 10 participants with chronic SCI (8M 2F); mean (SD) age: 47(7); mean (SD) DOI: 5.8(3.8) yrs; level of injury: C2-TI0. Treatment: Group 1: BWSTT with 4 wks assistance training, then 4 weeks resistance training. Group 2: BWSTT with 4 wks resistance training, then 4 wks assistance training. Resistance provided by a cable-driven robotic locomotor training system. Sessions were 45 min, 3x/wk x 8 weeks. Outcome Measures: Primary: self- selected and fast walking speed, 6MWT, BBS. Secondary: muscle strength tests, WISCI II, Physical SF- 36, ABC scale. 	1.	Mean BBS scores increased following resistance and assistance training, but there were no significant differences between these training conditions on the balance scores (P= .35), although BBS scores after resistance training were 2.7 times greater than those after assistance training. The Activities-specific Balance Confidence Scale score significantly increased from 34.0 7.8 to 39.5 7.3 (P= .02) and from 54.9% 18.5% to 70.4% 14.2% (P= .01), respectively, after robotic training.
Duffell et al. (2015); USA RCT PEDro=4 Level 2 N= 48	 Population: 26 individuals in locomotor treadmill training group- 19 males and 7 females; mean age= 46.6 ± 12.6y; years post injury= 9.3 ± 8.9y; 22 individuals in combined locomotor treadmill training and tizanidine group- 15 males and 7 females; mean age= 46.5 ± 11.9y; years post injury= 10.2 ± 10.4y; Level of injury 30 C and 15 T Treatment: Participants were randomly assigned into one of two intervention groups; locomotor treadmill training alone (n=26) or combined locomotor treadmill training and Tizanidine (n=22). Participants assigned to the combined locomotor treadmill training and Tizanidine group, were initially provided with Tizanidine alone for a period of 4 weeks, and results for that period have been 	1. 2.	 For TUG, there were no significant effects of either time point or group. Participants were classified in 2 ways: a. Based on achieving an improvement above the minimally important difference: Those who achieved the minimally important difference for the TUG had significantly longer times in the control (p=.04) and Lok (p=.04) groups. b. Using growth mixture modeling: For the TUG, significant improvements with time were also found for the Lok group in the higher-functioning class only (class 2, p<.05).

	presented elsewhere, together with the locomotor treadmill training group clinical outcomes. Outcome Measures: TUG, 10MWT, 6MWT, Modified Ashworth Score, Maximum voluntary isometric contractions, active range of motion, Peak isokinetic velocity were measured at 0, 1, 2 and 4 weeks from the start of locomotor treadmill training for both groups.	
Okawara et al. (2020); Japan Prospective controlled trial Level 2 N=20	Population: 20 participants with chronic SCI who had reached a plateau in recovery from paralysis symptoms; 15 males and 5 females; mean (± SD) age 43.3 (± 16.6) years; level of injury cervical (n=10), thoracic (n=9) and lumbar (n=1); AIS A (n=2), AIS B (n=4), AIS C (n=8) and AIS D (n=6); and mean (± SD) time since injury 80.4 (± 128.8) months. Based on baseline WISCI II score, 8 participants were categorized into the low walking ability group (n=8) and into the high walking ability group (n=12). Treatment: Participants underwent 20 sessions of BWSTT with voluntary driven exoskeleton (using the hybrid assistive limb [HAL]) (2–5 sessions per week [mean frequency 2.6 ± 1.1 sessions] with 60 min of duration) on a treadmill with 50% BWS. The velocity of the treadmill was individually set to the participant's comfortable walking speed, and there was no inclination. Outcomes Measures: The speed, distance, and duration walked, and RPE were recorded in each session. WISCI II, 10MWT*, 2MWT, TUG, BBS, BBS in three categories (sitting balance, standing balance, and dynamic balance), and LEMS were evaluated at pre and post intervention. *No participants in the low group were able to complete the 10MWT at either time point.	 There were no AEs. Overground walking ability without voluntary driven exoskeleton: In the high walking ability group, there was a significant improvement in TUG test (83.5 to 68.5 s, p=0.01) and BBS score (p=0.02).

Behrman et al. (2012); USA Prospective controlled trial Level 2 N=95	Population: 95 participants with SCI (75M, 20F); <1 yr (n=47), 1-3 yrs (n=24), ³ 3 yrs (n=24) since injury; level of injury: TII or above; Mean (SD) age: 43(17); median time since injury: 1 year; 31 AIS C, 64 AIS D. Treatment: At least 20 sessions of the NeuroRecovery Network Locomotor Training Program consisting of manual-facilitated body-weight supported standing and stepping on a treadmill and overground. Training consisted of 1hr of treadmill training, 30 min overground assessment, and 15-30 min of community reintegration. Frequency: 5 days/wk for ambulators, 4 days/wk for ambulators with pronounced assistance, 3 days/wk for independent walkers. Patients split into phases 1-3 depending on level of ability (higher ability = higher phase). Outcome Measures: ISNSCI AIS, BBS, 6MWT, 10MWT.	3.	For those who enrolled in phase 1 and were still classified phase 1 after NeuroRecovery Network training, no change was seen in BBS scores. For those who enrolled in phase 1 and were classified phase 2 after NeuroRecovery Network training, mean change scores were 1 for BBS. For those enrolled at Phase 1 and classified as Phase 3 after NeuroRecovery Network training, mean change scores were 38.5 for BBS. For those enrolled in Phase 2 and classified as Phase 2 after training, mean change scores were 7 for BBS. For those enrolled in Phase 2 and classified as Phase 3 after training, mean change scores were 7 for BBS.
Buehner et al. (2012); USA Prospective controlled trial Level 2 N=225	 Population: 225 participants with chronic incomplete SCI (167M, 58F); mean (SD) age=42.5 (15.9); Median DOI=2.45; 57 AIS C, 167 AIS D. Treatment: NeuroRecovery Network Locomotor Training Program. Training consisted of 1 hr of treadmill training, 30 min overground assessment, and 15-30 min of community reintegration. Frequency: 5 days/wk for non- ambulators, 4 days/wk for ambulators with pronounced assistance, 3 days/wk for independent walkers. Outcome Measures: LEMS, pinprick, light touch, 10MWT, 6MWT, BBS. 	1.	Significant gains in balance (43%) occurred after NeuroRecovery Network training regardless of initial AIS classification.
Lorenz et al. (2012); USA Longitudinal Level 2 N=337	 Population: 337 participants with SCI (255M, 82F); mean (SD) age: 40 (17); 99 AIS C, 238 AIS D. Treatment: At least 20 sessions of the NeuroRecovery Network Locomotor Training Program. Training consisted of 1hr of treadmill training, 30 min overground 	1. 2.	There was significant improvement on each outcome measure and significant attenuation of improvement over time. Patients varied significantly across groups defined by recovery status and AIS grade at enrollment with

	assessment, and 15-30 min of community reintegration. Frequency: 5 days/wk for non- ambulators, 4 days/wk for ambulators with pronounced assistance, 3 days/wk for independent walkers. Outcome Measures: BBS; 6MWT; 10MWT.	3.	respect to baseline performance and rates of change over time. Time since SCI was a significant determinant of the rate of recovery for all measures.
<u>Musselman et al.</u> (2009); Canada Prospective controlled trial Level 2 N=4	 Population: 2 male and 2 female participants, age 24-61, level of injury C5-L1, all AIS-C. Treatment: Initial 3 months BWSTT by all 4 patients. Patients 1, 2 received 3 months skills training, followed by 3 months BWSTT. Patients 3, 4 received the training in reverse order. Sessions were 1 hour long, 5 days a week for 3 months. Outcome Measures: BBS, Modified Emory Functional Ambulation Profile, 10MWT, 6MWT, ABC scale. 	1.	Improvement of Modified Emory Functional Ambulation Profile with skill training in all participants (average improvement 731.5); improvement also seen with BWSTT in 2 of 4 participants (- 1379 and -731 respectively); gains were maintained after training (statistical test for significant was not done). Minor improvements in BBS (9, 0, 10 and 5 points for participants 1, 2, 3 and 4 respectively), and no improvement for ABC.
Lin et al. 2022; USA Prospective controlled trial Level 2 N=15	 Population: 15 individuals with chronic incomplete SCI; 5 males and 10 females; mean age 46.5 years; injury level between C4-TIO; and mean time since injury 9.4 years. Treatment: Participants were tested on 2 separate days, with a one-week separation between the two testing conditions (pelvis perturbation with anodal transcutaneous spinal direct current stimulation vs. with sham). The order of the testing sequence was randomized across participants. On day 1, participants completed 3 continuous sessions of treadmill walking, which consisted of a 1 min of treadmill walking without pelvis perturbation or transcutaneous spinal direct current stimulation or transcutaneous spinal direct direct direct stimulation or transcutaneous spinal direct current stimulation or transcutaneous spinal direct current stimulation in the application of pelvic bilateral perturbation in the lateral directions (applied in 	1.	Participants demonstrated a smaller margin of stability during the late adaptation period for the anodal transcutaneous spinal direct current stimulation condition compared to sham (p=0.041), and this margin of stability intended to retain during the early post-adaptation period (p=0.05).

	 every step) paired with anodal transcutaneous spinal direct current stimulation, and 2 min of treadmill walking without the application of force perturbation and transcutaneous spinal direct current stimulation. On day 2, a protocol comparable to day 1 was used but only a sham stimulation was applied. The magnitude of peak perturbation force of each step was varied randomly within the range between 30 and 100% of the pre-determined force, which was set at 8–12% of body weight and was adjusted depending on participants' tolerance. transcutaneous spinal direct current stimulation was delivered with the anodal/sham electrode placed over the TIO-12 spinous process and the reference electrode placed above the right shoulder; and the current stimulation was set at 2.5 mA. Outcome measures: Lateral 	
	dynamic balance (assessed using the minimal margin of stability in the mediolateral direction) and electromyography of leg muscles (tibialis anterior, medial gastrocnemius, soleus, vastus medialis, rectus femoris, medial hamstring, adductor magnus, and hip abductor [gluteus medius]) from the weaker leg were assessed at baseline and post intervention.	
Lin et al. 2020; USA Prospective controlled trial Level 2 N=14	 Population: 14 individuals with chronic incomplete SCI; 11 males and 3 females; mean (± SD) age 53 (±13) years; injury level between C4-T10; and mean (±SD) time since injury 14 (±9) years. Treatment: A customized cable- driven robotic system was used to provide varied pelvis perturbation during treadmill walking. All participants were tested in two testing conditions (i.e., treadmill 	 Compared to treadmill training only, participants showed significant smaller margin of stability and double-leg support time after treadmill walking with pelvis perturbation.

walking with pelvis perturbation force and treadmill walking only), with more than 1-week interval inserted in between, and with a randomization across participants in the order of testing conditions. The treadmill speed was set at each participant's comfortable speed and was consistent for the two testing sessions. For each testing day, participants were instructed to walk on a 6-m gait mat at self-selected speeds.	
For the experimental condition, the next procedures were performed consecutively in the same order for each participant:	
 Baseline: Walking on a treadmill without pelvis perturbation for 1 min. 	
 Adaptation: A bilateral pelvis force was applied while walking on the treadmill for 10 min. 	
 Post-adaptation: The perturbation was removed, and participants walked on the treadmill for another 1 min. 	
 Re-adaptation: 5-min sitting break, followed by walking on the treadmill for another 10 min with the application of a bilateral pelvis force. 	
 Test the transfer effect from treadmill to overground walking: Walking on the gait mat immediately after treadmill walking. 	
• Test the retention of the training effect: Walking on the gait mat 10 min after the end of treadmill walking.	
For the control condition, the protocol was similar to the experimental condition, but no pelvis perturbation force was applied.	
Outcome measures: Margin of stability, weight shifting, step length,	

	step width, and double-leg support time were calculated.	
Lin et al. 2019; USA Pre-post Level 4 N=17	 Population: 17 individuals with chronic incomplete SCI; 12 males and 5 females; mean age 55.1 years; injury level between C4-T10; AIS B (n=1), AIS C (n=4) and AIS D (n=12); and mean time since injury 12.3 years. Treatment: A customized cable-driven robotic system was used to provide a controlled pelvis assistance force (set at 0 at the beginning and gradually increased at each step during the course of 10 minutes of walking [until the maximum magnitude of pelvis force 8~12% body weight was achieved]) while participants walked on a treadmill for one session. The intervention was performed consecutively in the following order for each participant: T1: Overground walking at each participant self-selected walking speed. T2, baseline (1 min): Walking on a treadmill with no force applied. T3, adaptation (10 min): Walking on a treadmill with force applied. T4, post-adaptation (1 min): Walking with no force applied. Seated break for 5 minutes and walking on the treadmill with force applied for another 10 minutes. T6, follow-up: Walking overground immediately after treadmill training. T6, follow-up: Walking. Treadmill speed was set at each participant's comfortable speed and remained the same throughout all 	 During treadmill walking, participants significantly improved weight shifting (i.e., center of mass lateral distance reduced from 0.16 ± 0.06 m to 0.12 ± 0.07 m, p=.012), and increased step length (from 0.35 ± 0.08 m to 0.37 ± 0.09 m, p=.037) on the stronger side when the force was applied, which were partially retained (i.e., center of mass distance was 0.14 ± 0.06, p=.019, and step length was 0.37 ± 0.09 m, p=.005) during the late post- adaptation period when the force was removed. In addition, weight shifting and step length on the weaker side during overground walking also improved (support base reduced from 0.13 ± 0.06 m to 0.12 ± 0.06 m, p=.042, and step length increased from 0.48 ± 0.12 m to 0.51 ± 0.09 m, p=.045) after treadmill training.

	testing sessions. BWS was provided as necessary. Outcome measures: Weight shifting, step length, margin of stability, and muscle activities (from 8 muscles, including tibialis anterior, medial gastrocnemius, soleus, vastus medialis, rectus femoris, medial hamstring, adductor magnus, and gluteus medius) of the weaker leg were used to quantify gait performance. The spatial-temporal gait parameters during overground walking were collected		
Covarrubias- Escudero et al. (2019); Chile Pre-post Level 4 N=34	Population: 17 healthy participants (13 males and 4 females; mean [± SD] age 37.5 [± 8.9] years) and 17 patients with chronic incomplete SCI (14 males and 3 females; mean [± SD] age 43.5 [± 3.7] years; level of injury cervical [n=11], thoracic [n=5] and lumbar [n=1]; AIS C [n=10] and AIS D [n=7]; and time since injury 19 [16-30] months). Treatment: The BWSTT program was distributed across 18 sessions over a 6-week period. Each session consisted of three 6-min series of locomotor treadmill training. Appropriated amount of BWS and treadmill speed were set individually. Outcome Measures: Standing balance test (ISway test with an accelerometer, a magnetometer, and a gyroscope) and WISCI II were assessed prior to and after the program. *Differences in standing balance between patients with SCI and healthy participants were established with the normalized jerk and root mean square, both computed during the ISway test.	1.	Despite achieving decreased normalized jerk values post- training (but not in ISway root mean square values), no changes in gait independence were found. An inverse correlation was found between the initial measures (p=0.020, r=0.564). However, no statistically significant correlation was observed between post- training normalized jerk values and WISCI II scores (p=0.526, r=0.151).
Jansen et al. (2017); Germany and USA Pre-post Level 4 N=21	Population: 21 participants with chronic SCI and some residual motor function of hip and knee extensor and flexor muscle groups; 15 males and 6 females; mean (± SD) age 44.8 (± 13.8) years; neurologic lesion level between C4 and L3 (paraplegia, n=18; tetraplegia, n=3); AIS A (n=10), AIS B	1. 2.	There was only temporary skin reddening at the site of the skin electrodes, leg cuffs, and shoes in four patients, but without causing an interruption of the training. TUG showed a significant improvement from baseline (53.29

	(n=1), AIS C (n=7) and AIS D (n=3); and mean (± SD) time since injury 6.5 (± 5.8) years. Treatment: All participants underwent BWSTT 5 times per week using the HAL robot suit exoskeleton for a 12-week period (5 sessions per week). Overall, each training session lasted approximately 90 min, divided into 30 min for preparation, 30 min of functional testing, and 30 min of HAL-BWSTT. During the intervention, training intensity was increased progressively by changing walking speed, time, and level of BWS, depending on each patient's abilities. Additionally, the training was supplemented by specific task exercises such as downhill/uphill/backwards walking and climbing stairs, using a mobile body-weight supported system. Outcome Measures: LEMS was assessed biweekly. 10MWT (gait speed, total time, and number of steps), 6MWT, TUG, and WISCI II were assessed without the exoskeleton at baseline, 6 weeks midtraining, and 12 weeks after training. The treadmill training performance parameters (walking		± 6.84 s) to midtraining (44.85 ± 6.54 s; p=0.002), from baseline to post-training (38.75 ± 5.70 s; p<0.001), and from 6 weeks to 12 weeks (p=0.007).
	distance, speed, and walking time) were recorded continuously.		
<u>Fleerkotte et al.</u> (2014); Netherlands Pre-post Level 4 N=10	 Population: 10 participants - 4 males and 6 females; motor incomplete chronic SCI; 1 AIS B, 5 AIS C, 4 AIS D; mean age= 48.75 ± 11.3y; months post injury= 46.75 ± 41.03 Treatment: Participants participated in an eight-week training program. Participants trained three times per week, for a maximum of 60 min per session. The training period was divided in two four-week periods, with one week scheduled for clinical tests in between During training 	1.	Participants experienced significant improvements in TUG (3.4 s, p=0.012) after eight weeks of training with LOPES. At the eight-week follow-up, participants retained the improvements measured at the end of the training period.
	tests in between. During training sessions, rest intervals were introduced if required by the participant or suggested by the therapist. The first training session was used to 1) fit the impedance-		

Sczesny-Kaiser et al. (2015); Germany Pre-post Level 4 N= 11	controlled robotic gait trainer (LOPES: Lower extremity Powered Exo Skeleton) to the participant, 2) let participants get used to walking in the device and 3) select their preferred walking speed. Outcome Measures: 10MWT, WISCI II, 6MWT, TUG test, LEMS, spatiotemporal, kinematics measures. Population : 11 participants - 7 males and 4 females; traumatic SCI with incomplete or complete paraplegia; mean age= 46.9 ± 2.7y; years post injury= 8.8 ± 2.1y. Treatment : Eleven SCI patients took part in HAL® assisted BWSTT for 3 months. Each patient was scheduled for a 30min training session 5 times a week for 12 weeks, as previously described by our group. Paired-pulse somatosensory evoked potentials were conducted before and after this training period, where the amplitude ratios (somatosensory evoked potential amplitude following double pulses - somatosensory evoked potentials amplitude following single pulses) were assessed and compared to eleven healthy control participants.	1.	After training, there was a significant improvement in TUG from 56.35 s ± 10.06 s to 38.65 s ± 7.2 s (p=0.01).
	Outcome Measures: 10MWT, 6MWT, TUG test, and LEMS.		
<u>Varoqui et al.</u> (2014); USA Post-test Level 4 N=30	Population: 30 participants; ambulatory chronic incomplete SCI; mean age= 50.80 ± 2.12y; years post injury= 11.80 ± 2.54y. Treatment: 15 participants with iSCI performed twelve 1-hour sessions of Lokomat training over the course of a month. The voluntary movement was qualified by measuring active range of motion, maximal velocity peak and trajectory smoothness for the spastic ankle during a movement from full plantar-flexion to full dorsi-flexion at the patient's maximum speed. Dorsi- and plantar- flexor muscle strength was quantified by isometric MVC. Clinical assessments were also performed	1.	For the training group, the TUG showed a significant reduction of 13.99 ± 3.53% in the time needed to perform the task (p<0.05). For the control group, there was no significant difference in TUG (p=0.45).

	using the TUG test, the 10MWT and the 6MWT. All evaluations were performed both before and after the training and were compared to a control group of fifteen patients with iSCI. Outcome Measures: Active range of motion, maximal velocity peak and trajectory smoothness from full plantar-flexion to full dorsi-flexion at patient's maximum speed, MVC, TUG test, 10MWT, 6MWT, Modified Ashworth Scale.		
Aach et al. (2014); Germany Pre-post Level 4 N=8	 Population: 6 males and 2 females; mean age 48 ± 9.43 years; years post injury= 97.2 ± 88.4 months; chronic stage of traumatic SCI; incomplete and complete SCI AIS A-D Treatment: The participants underwent a BWSTT five times per week using the HAL exoskeleton. Outcome Measures: Walking distance, speed, time, 10MWT, timed- up and go test (TUG test), 6MWT, the walking index for SCI II (WISCI II), AIS with the lower extremity motor score (LEMS), spinal spasticity (Ashworth scale), and the lower extremity circumferences. 	1. 2.	Significant improvements of HAL- associated walking time, distance, and speed were determined. Significant improvements were shown in the functional abilities without the exoskeleton for over- ground walking obtained in the 6MWT, TUG test, and the 10MWT, including an increase in the WISCI II score of three patients. Muscle strength (LEMS) increased in all patients accompanied by a gain of the lower limb circumferences.
<u>Knikou (2013);</u> USA Pre-post Level 4 N=14	 Population: 14 participants with chronic SCI (10M 4F); 21-55 yrs old; 0.5-11 yrs post-injury; 1 AIS A, 1 AIS B, 4 AIS C, 8 AIS D. Treatment: All participants received body-weight supported robot- assisted step training with a robotic exoskeleton system (Lokomat). Each participant was trained 1h/day, 5 days/wk. Outcome Measures: WISCI II; 6MWT; number of sit-to-stand repetitions completed within 30s; TUG; EMG measurements. 	3.	Body-weight supported robotic- assisted step training reorganized the soleus H-reflex in a functional manner during assisted stepping in people with clinically complete, motor incomplete and motor complete SCI. Training changed the amplitude and onset of muscle activity during stepping, decreased the step duration, and improved gait speed. For the AIS D group, TUG time non-significantly (p=0.11) decreased after body-weight supported training.
<u>Harkema et al.</u> (2012); USA Pre-post	Population : 196 participants (148 male, 48 female) with incomplete SCI; mean age 41±15 yrs; YPI- <1 yrs (n=101), 1-3 yrs (n=43), >3 yrs (n=52).	1. 2.	Scores on the BBS significantly improved by an average of 9.6 points. Increases were significant for patients with AIS grades C and D,

Level 4	Treatment: Locomotor training with		and the amount of improvement
N=196	three components: (1) 1 hour of step training in the BWS on a treadmill environment, followed by 30 min of (2) overground assessment and (3) community integration. Outcome Measures : BBS, 6MWT, and 10MWT.	3.	was significantly different between these groups (rank-sum test, p<0.008). Of the 168 patients classified as at risk for falls at enrollment, 27% improved their scores to a value reflecting minimal risk for falls (11% AIS grade C, 37% AIS grade D).
Yang et al. (2011); Canada Pre-post Level 4 N=19	 Population: 14 males, 5 females; mean age 44±13; >7 months post- injury (mean 5.8±8.9 years); AIS C or D. Treatment: 1 hour/day, 5 days/week of BWSTT until parameters did not progress for 2 weeks (minimum 10 weeks total, mean=18 weeks). Outcome Measures: 10MWT, WISCI II, LEMMT, BBS, EMG measurements (tibialis anterior, soleus, quadriceps, hamstrings), movement at the knee and ankles. 	2.	After training, 17/19 participants improved in duration of walking in a session (mean (SD) 15(11) min), 16/19 improved in treadmill speed (0.14(0.11) m/s), and 16/19 improved in their ability to support their own body weight (18-19%) decrease in BWS). 13 participants responded to the treatment; 9 showed improvements of >1 m/s (exceeding the smallest real difference in overground walking speed) and 4 showed improvements <1 m/s but greater WISCI II scores. BBS scores were not related to
Fritz et al. (2011); USA Pre-post Level 4 N=15	Population: 15 participants - 11 males and 4 females; incomplete chronic SCI; Lower functioning group: 10 participants - 8 males and 2 females; mean age= 38.5y; time since injury: 6.6y; AIS lower extremity score= 24; Higher functioning group: 5 participants - 3 males and 2 females; mean age= 50.4y; time since injury= 5.7y; AIS lower extremity score= 44. Treatment: Participants received intensive mobility training in activities that encouraged repetitive, task specific training of the lower extremities. Intensive mobility training combines BWSTT, balance exercises, muscle strengthening, coordination and range of motion in a massed intensive therapy. Sessions were 3 hours a day for 3-5 days per week for a total of 10 weeks. Outcome Measures: CAITPite (gait	1.	improvements in walking speed. Participants in the higher functioning iSCI group (BBS score ≥45 and gait speed ≥0.6m/s) spent more time in the intensive therapy on average than participants in the lower functioning ISCI group. Effect sizes were comparable for changes in balance and mobility assessments between the lower and higher functioning groups, with the largest effect sizes observed for the DGI.
	Outcome Measures: GAITRite (gait speed), BBS, Dynamic Gait Index		

	(DGI), 6MWT, Timed Go Walk (modified version of TUG), and SCI- FAI.		
<u>Hornby et al.</u> (2005);	Population: 2 males, 1 female; AIS C; 5 weeks/ 6 weeks/ 18 months post- injury.	 Balance results varied betwee the 3 participants suggesting generalizability. 	
USA Pre-post	Treatment: Therapist and Robotic- assisted, BWSTT (parameters varied between participants).		
Level 4 N=3	Outcome Measures: LEMS, FIM, WISCI II, 10MWT, 6MWT, TUG test, Functional Reach test, and modified sitting Functional Reach Test.		

Acute SCI (<1 year)

Eight studies have examined the effect of Lokomat-assisted or therapist-assisted BWSTT in people who had incurred an incomplete SCI <12 months prior (acute/subacute phase) (aggregate N=534) (Dobkin et al. 2006; Harkema et al. 2012; Midik et al. 2020; Schwartz et al. 2011; Shahin et al. 2017; Shin et al. 2014; Tang et al. 2014; Wirz et al. 2017) and one (Schwartz et al. 2011) in people who had incurred a complete SCI <12 months prior (acute/subacute phase) (N=6). Treatment time ranged from 90-300 min per week, and total treatment duration lasted between 4 and 12 weeks.

A good quality single-blind RCT (<u>Dobkin et al. 2006</u>) (n=117) showed no differences in effects between matched amounts of BWSTT with therapist assistance and overground mobility practice in incomplete SCI during inpatient rehabilitation for the locomotor score of the FIM, overground walking speed, or balance scores.

Although there is some evidence (from a case-control study) that the use of Lokomat-assisted BWSTTT in combination with conventional therapy provides better functional independence scores (SCIM) than conventional therapy alone in patients with acute SCI (Schwartz et al. 2011); there are other RCTs, case-control studies, and prospective controlled trials which showed similar improvements in standing balance (BBS), ambulation ability (Functional Ambulation Category), or functional independence (SCIM-III) for BWSTT plus conventional therapy and conventional therapy only (Midik et al. 2020; Schwartz et al. 2011; Shahin et al. 2017; Shin et al. 2014).

The effect of time of BWSTT sessions on mobility is a variable which has been studied in participants with SCI. The randomized, controlled, multicenter trial of Wirz et al. (2017) assessed the differences between a BWSTT intervention program using Lokomat with a 50-minute walking session versus a 25-minute walking session. After 8 weeks of intervention, both groups significantly improved the SCIM mobility subscore, but the intervention group improved more (without statistical analysis done between groups) than the control group (Wirz et al. 2017), suggesting that an intensive locomotor program could be feasible and beneficial in patients with acute SCI.

Chronic SCI (>1 year)

We found 11 RCTs (<u>Alexeeva et al. 2011; Duffell et al. 2015; Labruyere & van Hedel 2014; Lam et al. 2014; Niu et al. 2014; Piira et al. 2019a; Piira et al. 2019b; Wu et al. 2012; Wu et al. 2016; Wu et al. 2018; Yang et al. 2014), six prospective controlled trials (<u>Behrman et al. 2012; Buehner et al. 2012; Lorenz et al. 2012; Lin et al. 2020; Lin et al. 2022; Musselman et al. 2009</u>), and 13 prepost studies that altogether studied 1295 persons with complete and incomplete SCI, with chronicity ranging from 1 to 18 years post-injury. Treatment intensity ranged from 45 to 450 min per week, and treatment duration lasted between 3 and 18 weeks.</u>

In a recent systematic review and meta-analysis, Benn et al. (2025) included a total of 26 studies with 500 participants describing and comparing the efficacy and dosage of interventions targeting upright balance control, balance confidence, and falls for adults with motor-incomplete SCI. There was a significant pooled effect for improvement in upright balance control (measured by BBS: Hedge's g=.51; 95% CI, .36-.66; I²=.60; measured by FTSTS: Hedge's g=.73; 95% CI, 1.18 to .27; I^2 =.99) and balance confidence (measured by the ABC Scale: Hedge's g=.40; 95% CI, .13-.67; I²=.56) (Benn et al. 2025). The authors stated however, that the quality of the evidence of the included studies was low or very low; that there was a lack in those balance interventions targeting the cognitive strategies, static stability, and reactive postural control; and that there was no relationship between intervention dosage and balance-related outcomes (Benn et al. 2025). Similar results were found in the systematic review and meta-analysis completed by Walia et al. (2023), which included ten RCTs (n=222) and 15 pre-post trials (n=967) assessing people with incomplete SCI. Pooled SMD for controlled and uncontrolled trials of body-weight supported training interventions of -0.26 (95% CI, -0.70 to 0.18; p=0.25) and 0.46 (95% CI, 0.33 to 0.59; p<.001), respectively (Walia et al. 2023). The authors stated the need for further welldesigned and appropriately powered RCTs to evaluate specific features of training interventions to improve standing balance function in incomplete SCI (Walia et al. 2023).

Overall, most of the studies included showed some improvements in standing balance, in particular for groups with better baseline walking ability, whether locomotor training was provided with a treadmill or performed over ground, body-weight supported, or involved other variations on walk-based therapies (e.g., overground gait training with obstacles, robot-applied resistance). Two good-quality RCTs (Piira et al. 2019a; Piira et al. 2019b) used BWSLT (overground and on a treadmill) with manual assistance, and robot-assisted locomotor training (with the use of Lokomat®), respectively, in patients with motor incomplete SCI. Improvements in walking outcomes, standing balance, and strength were small and non-significant in the intervention groups, without differences between groups. An RCT by Niu et al. (2014) showed that Lokomat training in participants with low walking capacity at baseline did not show significant improvements, in contrast with participants with a high walking capacity who presented a consistent linear trend in time for both speed and functional balance (TUG) over the 4-week training period.

Longer periods of training on body-weight supported training also produced mixed results in balance outcomes for people with SCI. In an RCT, Alexeeva et al. (2011) included 35 participants with incomplete SCI who were randomly allocated to receive different ambulation therapy interventions. After 13 weeks of intervention, the physical therapy skill training and body-weight supported ambulation on a fixed track groups resulted in greater balance

improvements than body-weight supported ambulation on a treadmill (<u>Alexeeva et al. 2011</u>). Labruyere and van Hedel (<u>2014</u>) included 9 participants with incomplete SCI who received RAGT with Lokomat or strength training. After 16 sessions, there were no statistical differences between the interventions with respect to the changes in standing balance scores (measured by BBS) (<u>Labruyere & van Hedel 2014</u>). Other lower evidence (pre-post) studies showed contradictory results, as some provided significant improvements in balance outcomes (normalized jerk values [instrumented sway test], TUG, BBS) (<u>Covarrubias-Escudero et al.</u> <u>2019; Fritz et al. 2011; Varoqui et al. 2014</u>) and others did not (<u>Knikou et al. 2013</u>).

Alternative gait retraining therapies or modified approaches to BWSTT for chronic SCI are being introduced (Fleerkotte et al. 2014; Lam et al. 2014; Musselman et al. 2009; Wu et al. 2012; Wu et al. 2016; Wu et al. 2018; Yang et al. 2014). Musselman et al. (2009) and Yang et al. (2014) compared BWSTT with overground 'precision' skilled walking training. The skilled walking training consisted of task-specific practice (without WBS) of various gait tasks, such as stair climbing, obstacle crossing, and walking along sloped surfaces. Both training groups were comparable in improving standing balance (measured by the BBS and the ABC scale). Wu et al. (2012; 2016) demonstrated a new cable-driven robotic device to apply resistance against leg movements during BWSTT. Participants were randomized (in a cross-over design) to receive robotic resistance or BWSTT. Although there were no significant differences in outcomes between the two modalities (Wu et al. 2012; Wu et al. 2016), there was some indication that robotic resistance enabled greater gains in over ground walking speed and standing balance (BBS) in people who tended to have better initial ambulatory capacity (Wu et al. 2012). Wu et al. (2018) studied the same training program (assistive robotic BWSTT) and compared it with a BWSTT alone (no assistance), in the same way as in the previous studies, no changes were shown in standing balance as measured by the BBS or the ABC scale after 6 weeks of both training programs in people with incomplete SCI. The RCT of Duffell et al. (2015) compared the effects of a BWSTT intervention with Lokomat and a pharmacological drug for treating spasticity (Tizanidine). After four weeks, there were no significant effects between both groups in standing balance (TUG) (Duffell et al. 2015).

There were three studies which tried to assess the effects on balance (weight shifting) and gait (stepping) of the application of pelvis assistance (Lin et al. 2019), perturbation force (Lin et al. 2020), or perturbation force plus transcutaneous spinal direct current stimulation (Lin et al. 2022) during single sessions of treadmill walking with a customized cable-driven robotic system in people with chronic and incomplete SCI. Overall, the authors showed that applying pelvis assistance during treadmill walking may facilitate weight shifting and improve step length (which may partially transfer to overground walking) (Lin et al. 2019); that dynamic balance control capacity (calculated by margin of stability, weight shifting, and other spatiotemporal gait parameters) was improved after 10 min of treadmill walking paired with the application of a varied pelvis perturbation force (Lin et al. 2020); and that anodal transcutaneous spinal direct current stimulation may modulate motor adaptation to pelvis perturbation and facilitate learning of dynamic balance control (measured by the minimal margin of stability) (Lin et al. 2022). Despite these promising effects on dynamic balance and gait with meatics outcomes, more studies are needed using functional balance and gait outcomes (e.g., 6MWT, 10MWT, TUG, WISCI

and/or BBS), and with long-term training interventions, to confirm these promising results in people with chronic and incomplete SCI.

There is variability in studies we found in the percentage of bodyweight that supported each participant during BWSTT; ranging from ≤ 40% (Alexeeva et al. 2011; Labruyere & van Hedel 2014; Piira et al. 2019a; Piira et al. 2019b), 50% (Okawara et al. 2020), to 60% (Knikou 2013). In other cases, the BWS was set individually to provide as much support as necessary to prohibit knee buckling or toe drag during stepping, or adjusted to the minimum tolerated by the participant while ensuring appropriate stance phase kinematics (Covarrubias-Escudero et al. 2019; Lam et al. 2014; Musselman et al. 2009; Varoqui et al. 2014; Wu et al. 2012; Yang et al. 2011). All studies progressively decreased the amount of bodyweight supported depending on the participant's tolerance during the training period. As the authors are aware, there is no study published comparing the effects of different percentages of BWS on standing balance in patients with SCI. However, the RCT of El Semary and Daker (2019) compared 30% vs. 40% of BWS in patients with motor-incomplete SCI and paraplegia. After 6 weeks of BWSTT performed twice a week, walking speed, step length, stride length and cadence width (but not step width) were improved in both groups, but between-group comparisons revealed that there were highly significant changes in these parameters for the group who trained with a 40% of BWS (El Semary & Daker 2019).

Conclusions

Acute SCI (<1 year)

There is level 1 evidence (from 1 RCT: <u>Dobkin et al. 2006</u>) and level 2 evidence (from 2 RCTs: <u>Midik et al. 2020</u>; <u>Shin et al. 2014</u>; and from 1 prospective controlled trial: <u>Shahin et al. 2017</u>) that BWSTT has equivalent effects to conventional rehabilitation consisting of an equivalent amount of overground mobility practice for standing balance (BBS) and functional independence (SCIM) outcomes in patients with acute/sub-acute SCI.

There is level 1 evidence (from 1 RCT: <u>Wirz et al. 2017</u>) that intensive sessions (walking time per session > 50 min) of Lokomat-assisted BWSTT for 8 weeks were tolerable and could provide more improvement in SCIM mobility subscore than non-intensive Lokomat-assisted BWSTT sessions (walking time per session < 25 min) in patients with acute SCI.

There is level 3 evidence (from 1 case control study: <u>Schwartz et al. 2011</u>) that 12 weeks of BWSTTT with Lokomat in combination with conventional therapy provides significant and better functional independence scores (SCIM) than conventional therapy alone in patients with acute, complete and incomplete SCI.

Chronic SCI (>1 year)

There is level 1 evidence (from 1 RCT: <u>Alexeeva et al. 2011</u>) that physical therapy skill training and body-weight supported ambulation on a fixed track provides greater balance (Tinetti scale) improvements than body-weight supported ambulation on a treadmill in patients with chronic and incomplete SCI.

There is level 1 evidence (from 1 RCT: <u>Labruyere & van Hedel 2014</u>) that four weeks of a RAGT with Lokomat provides similar improvements in standing balance (BBS) as a strength training program in patients with incomplete and chronic SCI.

There is level 1 evidence (from 1 RCT: <u>Piira et al. 2019a</u>) that BWSLT with manual assistance does not provide more improvements than usual care in standing balance (BBS) in patients with chronic and motor incomplete SCI.

There is level 1 evidence (from 1 RCT: <u>Piira et al. 2019b</u>) that robot-assisted locomotor training (with Lokomat®), compared to usual care, does not provide better improvements in standing balance (BBS) in patients with chronic SCI.

There is level 1 (from 1 RCT: <u>Yang et al. 2014</u>) and level 2 evidence (from 1 prospective controlled trial: <u>Musselman et al. 2009</u>) that BWSTT or overground 'precision' skilled walking training provides similar improvements in standing balance (measured by the BBS and the ABC scale) in participants with chronic SCI.

There is level 1 evidence (from 1 RCT: <u>Wu et al. 2018</u>) that a 6-week BWSTT with assistance (using a cable-driven robotic device to provide bilateral pelvis assistance load) does not provide improvements in standing balance (BBS and ABC scale) in the same way that a BWSTT only (no assistance) in people with incomplete and chronic SCI.

There is level 2 evidence (from 2 cross-over RCTs: <u>Wu et al. 2012</u>; <u>Wu et al. 2016</u>) that a BWSTT with assistance or resistance (using a cable-driven robotic device to apply resistance against leg movements during BWSTT) provides similar effects after 6-8 weeks in standing balance (BBS and ABC scale) in people with incomplete and chronic SCI.

There is level 2 evidence (from 1 RCT: <u>Duffell et al. 2015</u>) that BWSTT (with Lokomat) or Tizanidine (a pharmacological drug for treating spasticity) does not provide significant improvement in standing balance (TUG) after four weeks of intervention in people with chronic SCI.

There is level 4 evidence (from 14 pre-test/post-test studies: <u>Behrman et al. 2012</u>; <u>Buehner et al.</u> 2012; <u>Covarrubias-Escudero et al. 2019</u>; <u>Fleerkotte et al. 2014</u>; <u>Fritz et al. 2011</u>; <u>Harkema et al.</u> 2012; <u>Lorenz et al. 2012</u>; <u>Varoqui et al. 2014</u>) that BWSTT (with different approaches) is effective for improving standing balance performance in people with chronic and incomplete SCI.

There is level 4 evidence (from 4 pre-post studies: <u>Aach et al. 2014</u>; <u>Jansen et al. 2017</u>; <u>Okawara et al. 2020</u>; <u>Sczesny-Kaiser et al. 2015</u>) that a BWSTT program using the HAL exoskeleton provides improvements in balance (TUG) in patients with complete or incomplete and chronic SCI.

Key Points

For patients less than 12 months post-SCI, BWSTT may have similar effects on standing balance and functional independence outcomes as overground mobility training of similar intensity. Longer durations of BWSTT sessions are encouraged, if possible, to provide improvements in the SCIM mobility subscore.

For patients with chronic incomplete SCI, body-weight supported gait training strategies can improve balance outcomes, though generally the results are mixed, and the BWS may improve safety but compromise balance improvement.

4.4 Wearable Powered Exoskeletons for Standing Balance

Newer generations of exoskeletons, known as overground exoskeletons, are designed with portable systems that allow the user to ambulate freely indoors and outdoors (<u>Yip et al. 2022</u>). Wearable exoskeletons or robotic orthoses are other terms that are used interchangeably for these robotic devices, which are wearable and operate in the close proximity of the joints of patients (<u>Jamwal et al. 2020</u>). Activation of these systems can be triggered by patients' voluntary movements or by a computer algorithm, depending on the patients' capabilities and the exoskeleton characteristics (<u>Rodriguez-Tapia et al. 2022</u>).

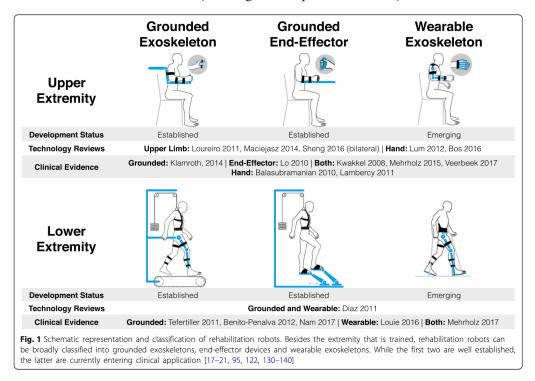


Figure 1. Schematic representation and classification of rehabilitation robots. From <u>Gassert & Dietz 2018</u>. Creative Commons license:

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Wearable powered exoskeletons differ from other RAGT systems because they offer new possibilities and key advantages in gait rehabilitation: first, wearable powered exoskeleton allows self-balancing, overground, gait training, with or without upper limb assistance; second, assistance during gait can be triggered voluntarily by the participant through muscle contraction and body movements; third, gait training, through TSR, can be performed in more ecological environments, promoting a more human-like gait pattern (including activation of trunk muscles during over ground or treadmill training); fourth, they are not limited to a laboratory or clinic setting, and users can wear them in community and home settings, providing opportunities to practice walking outside of a clinical environment; and finally, wearable powered exoskeletons enable walking with a lower energetic cost compared to other systems (Heinemann et al. 2020; Rodriguez-Tapia et al. 2022).

The number of studies on wearable exoskeletons during the past 10 years has seen a rapid increase, following the general tendency now towards rehabilitation robots (Esquenazi & Talaty 2019). The systematic review of Rodríguez-Fernández et al. (2021) identified 25 wearable lower-limb powered exoskeletons for overground training, without BWS, that have been tested for use with people who have gait disorders due to neuromuscular impairments (e.g., SCI, stroke, and other pathologies). From this number, only six have FDA approval and/or CE mark and are commercially available (i.e., Ekso, HAL, Indego, REX, ReWalk, and SMA) (Rodríguez-Fernández et al. 2021).

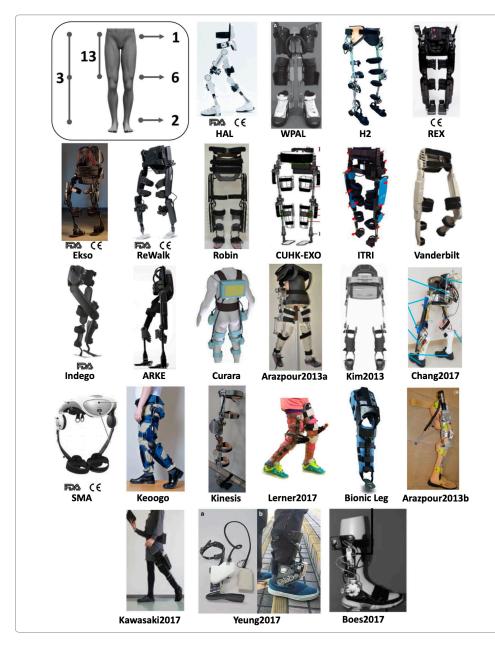


Figure 2. Exoskeletons included in the literature review of <u>Rodríguez-Fernández et al. 2021</u>. From <u>Rodríguez-Fernández et al. 2021</u>. Creative Commons license: <u>https://creativecommons.org/licenses/by/4.0/</u>. No changes have been made.

Currently, exoskeletons can be subdivided into assistive devices to be used in the community, such as the Indego Personal and Rewalk exoskeletons, or devices designed for rehabilitation with a therapeutic intent, such as the EksoNR and Indego Therapy exoskeletons (<u>Yip et al.</u> 2022). Nowadays, for patients with tetraplegia, FDA has approved three devices: Ekso® (allowed only for C7–T3 AIS D patients), Indego® (C7 or below) and Hal® (C4–L5 AIS C or D) (<u>Rodriguez-Tapia et al. 2022</u>). These three exoskeletons can be used after SCI if upper limb strength is enough to allow the use of assistive devices, such as crutches or walkers (<u>Rodriguez-</u>

Tapia et al. 2022). Other self-balancing wearable powered exoskeletons, like Atalante® or Rex®, allow ambulation without upper limb help or the use of an assistive device (Postol et al. 2021; Rodriguez-Tapia et al. 2022). Studies which assessed the effects on balance outcomes in trials after the use of these exoskeletons; as well as others such as the ABLE Exoskeleton, the AIDER (AssIstive DEvice for paRalyzed patient) powered robotic exoskeleton, the reWalk wearable lower limb powered exoskeleton, the Achilles exoskeleton, the ExoAtlet Medy®, the Erigo, and the H-MEX (Hyundai Medical Exoskeleton) have been included in the present section.

It could be necessary to know which patients would benefit the most from receiving exoskeleton training, as learning to use an exoskeleton is time-consuming, and the number of training sessions required to walk independently differs greatly between users (van Dijsseldonk et al. 2021). 20 participants with motor complete SCI received 24 training sessions in eight weeks with a ReWalk exoskeleton, and lesion level appeared to be an important predictor during the first four weeks of training, but did not influence participants' final skill level, while body mass index, age, and active lifestyle were predictors of exoskeleton skill performance toward the end of the training period (van Dijsseldonk et al. 2021).

Author Year Country Research Design Score Total Sample Size	Methods	Outcome
Rodríguez- Fernández et al. (2022); Spain RCT Cross-over PEDro=7 Level 1 N=10	 Population: 10 participants with chronic motor-complete SCI; 9 males and one female; mean (± SD) age 44.10 ± 5.93 years; level of injury T4 (n=3), T6 (n=1), T8 (n=2), T10 (n=1), T11 (n=2), and T12 (n=1); AIS A (n=8) and AIS B (n=2); and mean time since injury 10.5 years. Treatment: Participants were randomly assigned to one of two groups, depending on the device used for the training program: Knee ankle foot orthosis (KAFO). Knee-powered bilateral lower limb exoskeleton (i.e., the ABLE Exoskeleton). The training program consisted of 10 sessions (2 sessions per week, for 5 weeks) of 90-min duration: 8 overground gait training sessions (sessions 1 to 4 and 	 No serious AEs were reported during the study. The average level of assistance provided by the therapist to the participants was slightly (p>0.05) higher for the ABLE group compared to the KAFO group. No significant differences were found between the two groups for 6MWT, 10MWT, and TUG. Linear regression analysis between the outcome metrics of the standardized clinical tests and the level of injury revealed significant, strong correlations for the KAFO group. In contrast, correlations for the ABLE group were low to mild and not statistically significant.

Table 13. Wearable Powered Exoskeletons for Standing Balance

	(sessions 5 and 10). Participants spent a minimum of 30 min per training session doing sit-to-stand and stand-to-sit transitions, and standing and walking exercises using one of the two devices and the aid of a walker. There was a 2- week resting period between the final evaluation session and the first training session with the crossed-over device. Outcome Measures: TUG; 6MWT; 10MWT; and gait kinematics and spatiotemporal parameters (during 6MWT) were assessed at session 10.		
	Population: 25 patients with chronic motor incomplete SCI, with self-selected gait speed of <0.44 m/s, the ability to take at least one step, and be able to fit into the Ekso device; 18 males and 12 females; mean age 47.2 years; AIS C (n=9) and AIS D (n=21); level of injury C1-T10; and mean time since injury 6.8 years.	1.	There were 3 serious AEs (urinary tract infections unrelated to the device [n=2]) and one participant in the active group admitted to a hospital with lower extremity numbness and a urinary tract infection).
<u>Edwards et al.</u> (2022); USA RCT	 *45 participants were enrolled, of which 33 were randomized to the main study and 12 enrolled as run-in participants. Of the 33 randomized participants, 25 completed the assessments and training related to the primary endpoint analysis. Treatment: Over 12 weeks, participants were randomly assigned to one of three study arms: Ekso Robotic Intervention (n=9): 	2.	From the total sample of 45 participants*, AEs that were deemed "possibly" or "probably" related to the device or training include the following: 12 (8 Ekso, 4 Active) upper and lower extremity musculoskeletal issues; 4 (3 Ekso, 1 Active) neurological issues; 6 (5 Ekso, 1 Active) skin issues; and 1 (Ekso) visceral issue.
<u>PEDro=5</u> <u>L</u> evel 2 N=25	 Participants performed a 45 min session (standing/up and walking) in the Ekso device, 3 times per week; and if possible, overground training without BWS. Active Control (n=10): Each session comprising 45 min of BWSTT, and if possible, overground without BWS. 	3.	TUG test, self-selected gait speed, maximal gait speed, and median distance covered in the 6MWT following the intervention improved without reaching significant differences (p>0.05) for within group and between group comparisons.
	 Passive Control (n=6): Participants continued with daily activities as normal. Outcome Measures: Gait speed (10MWT); functional mobility and balance (TUG); endurance (6MWT); need of assistance and devices (WISCI II); and safety (AEs and serious AEs) were 	4.	Most participants in both the Ekso group and the Active Control group showed no change in type of assistive device used outside the clinic throughout the duration of the protocol; with no changes observed in the Passive Control group.

weeks), at the end of the intervention (12 weeks), and at 12 weeks post-intervention. Population: 7 participants with SCI and abled to independently stand for 2 min with or without an assistive device. Exoskeleton-assisted gait training Group (n=4): Mean (SD) age: 56 (17) years; 1 female, 3 males; injury level: C4 (n=1), C7 (n=1), T12 (n=2); AIS: AIS C (n=1), AIS D (n=3); mean (SD) time since injury of 15 (14) years Conventional physical therapy (CPT) Group (n=3): Mean (SD) age: 60 (2) years; 1 female, 2 males; injury level: C5 (n=1), T12 (n=2); AIS: AIS C (n=1), AIS D (n=3); mean (SD) time since injury of 7 (3) years Chang et al, [2018]; USA RCT Exoskeleton-assisted gait training group (n=4): Participants donned the Ekso exoskeleton and participated in individualized treatment sessions that included treatment sessions. CPT group (n=3): Participants Exoskeleton for 3 weeks with a total of 15 sessions. CPT group (n=3): Participants for eceived physical therapy designed to facilitate gait improvement. This included individualized treatment sessions consisting of stretching, strengther long, altone training, standing, sit o stand, stair, and gait training session lasted 60 min, and the 				
abled to independently stand for 2 min with or without an assistive device.statistically significant reduction in TUG time (CPT group: MD -16, 95% CI=-26, -0.6); Exoskeleton-assisted gait training group: MD - 15.43, 95% CI=(-47.5, 16.6) between pre- and post-assessments.Chang et al. (2D18) USA RCTConventional physical therapy (CPT) Group (n=3); Mean (SD) age: 60 (2) years; 1 female, 2 males; injury level: CS (n=1), AIS D (n=2); mean (SD) time since injury of 7 (3) yearsStatistically yightificant reduction in TUG time (CPT group: MD -15.43, 95% CI=(-47.5, 16.6) between pre- and post-assessments.Chang et al. (2D18) USA RCTTreatment: Participants were randomized into two groups: 		weeks), and at 12 weeks post-		
sessions with 5 days per week for 3 weeks.	(2018); USA RCT <u>PEDro=5</u> Level 2	 intervention. Population: 7 participants with SCI and abled to independently stand for 2 min with or without an assistive device. Exoskeleton-assisted gait training Group (n=4): Mean (SD) age: 56 (17) years; 1 female, 3 males; injury level: C4 (n=1), C7 (n=1), T12 (n=2); AIS: AIS C (n=1), AIS D (n=3); mean (SD) time since injury of 15 (14) years Conventional physical therapy (CPT) Group (n=3): Mean (SD) age: 60 (2) years; 1 female, 2 males; injury level: C5 (n=1), T12 (n=2); AIS: AIS C (n=1), AIS D (n=2); mean (SD) time since injury of 7 (3) years Treatment: Participants were randomized into two groups: Exoskeleton-assisted gait training group (n=4): Participants donned the Ekso exoskeleton and participated in individualized treatment sessions that included sit to stand, static and dynamic standing balance, weight shifting, walking, turning, and stand to sit. Each training was held 5 days per week for 3 weeks with a total of 15 sessions. CPT group (n=3): Participants received physical therapy designed to facilitate gait improvement. This included individualized treatment sessions with a total of 15 session lasted 60 min, and the training. Each training session lasted 60 min, and the training was held for a total of 15 session swith 5 days per week for 	1.	statistically significant reduction in TUG time (CPT group: MD -1.6, 95% CI=-2.6, -0.6); Exoskeleton-assisted gait training group: MD - 15.43, 95% CI=(-47.5, 16.6)) between pre-

	Outcome Measures: TUG test was assessed at baseline and at post-intervention.	
Tamburella et al. (2020b); Italy Prospective controlled trial Level 2 N=8	 Population: 8 participants with incomplete SCI and the ability to walk overground (with aids if necessary); 6 males and 2 females; mean age 53.5 years; injury level C6 (n=1), C7 (n=2), T5 (n=1), T10 (n=2), and T11 (n=1); AIS D (n=8); and mean (± SD) time since injury 18.3 (± 13.5) months for experimental group and 21.6 (± 11.1) months for control group. Treatment: All participants performed 10 sessions of 40-min gait training 3 times per week with the main goal of improving comfortable gait speed. Each training session was composed by few min of preparation (performing ankle or knee movements), followed by standing balance exercises, and by a specific walking training. Participants were divided into two groups: Experimental group (n=4, prospective enrollment): Participants used the NeuroMuscular Controller- controlled Achilles ankle exoskeleton (developed to assists plantar/dorsiflexion during walking). Control group (n=4, case-control matched): Participants didn't use the Achilles exoskeleton. Outcome Measures: Motion outcome measures (spatio-temporal parameters [speed, step length and width, gait cycle time and stance phase percentage] and ground reaction forces [GRFs]) were assessed by using four force plates; clinical outcome measures (6MWT*, 6- min gait speed, fatigue, muscle force [assessed by manual muscle testing of hip, knee and ankle joints], and dynamic balance [assessed by BBS]) were 	 After the intervention, no statistical differences were found for any analyzed variables between groups (p>0.05). Comparing after training vs. baseline data: At baseline, experimental participants were unable to complete the 6MWT without the support of the Achilles and was easily completed with the Achilles at the end of training; meanwhile only two participants in the control group showed improvements in 6MWT. For BBS, there was no statistically significant modifications in both groups.
	*6MWT was assessed with and without Achilles for the experimental group, and	

	only in free walking condition for control group.		
Jang et al. (2022); Korea Pre-post Level 4 N=4	Population: 4 participants with gait disturbance because of spinal root dysfunction (patients with previously neurologic deficit after brain or spinal cord disorders were excluded from the study). Mean age: 56.25 years 3M, 1F Causative nerve dysfunction: Right L5 (n=2) and cauda equina (n=2) Duration of weakness: 1 month (n=2), 26 (n=1), and 38 (n=1) months. *All participants had undergone spine surgery for spinal stenosis caused the neurologic deficit and intervention started one week after surgery. Treatment: Overground exoskeleton- assisted gait training protocol with ExoAtlet Medy® was scheduled for 4 or 8 weeks and 2-3 sessions per week. The duration of each session was 60 minutes. Training protocol included sit-to-stand, static standing balance, dynamic standing balance weight shifting, stepping, pivot turns and free walking. Outcome Measures: Muscle atrophy (calf circumference), vital sign (heart rate/blood pressure /peak flow), 6-meter walking test, TUG test, BBS, and modified geriatric depression scale were assessed before (TI) and at the end (T2) of the intervention. * The clinical results were not analyzed statistically because of the small sample size.	1.	All participants showed positive changes in gait performance, balance, proximal muscle strength, psychologic state and satisfaction of rehabilitation. 3 participants demonstrated the improvement of TUG test and BBS scores.
<u>Kerdraon et al.</u> (2021); France & USA Pre–post Level 4 N=11	Population: 12 participants with chronic complete (AIS A) SCI and able to wear the Atalante exoskeleton; 10 males and 2 females; mean age (± SD) 22.9 (± 9.3); injury level T5 (n=2), T6 (n=4), T8 (n=1), T10 (n=2), T11 (n=1), and T12 (n=2); and mean (± SD) time since injury 88 (± 63.2) months. Treatment: Participants received 12 one- hour training sessions for 3 weeks. Patients walked on floor and wore a harness connected to a mobile	1. 2.	The only treatment-related AEs were skin redness (n=5) and ischial skin abrasion (n=1) with a complete resolution. Postural parameters: All patients succeeded in standing up, sitting down and standing up for two min at the 6th and 12th session. At the 6th session, all the patients passed the U- turn test with some assistance,

	suspension system (without weight bearing) to prevent from falling, while using the Atalante exoskeleton. Outcome Measures: The ability to walk 10 m, without human or material assistance; 10MWT; the ability to sit down without human assistance, then maintain a balanced position for at least 5 s; the ability to stand still without support for 2 min; the ability to keep balance in exercise positions, with intrinsic perturbations such as arm and upper body movements; the ability to turn 180° in less than 3min (U-turn); and the ergonomics of Atalante exoskeleton were assessed at the 6 th and at the 12 th session.	whereas during the 12th session two patients performed the U- turn without any help.
Kim et al. (2021); Korea Pre-post Level 4 N=10	Population: 10 non-ambulatory patients with SCI with sufficient postural stability to sit independently, ability to transfer from wheelchair to bed independently, and sufficient bilateral upper extremity strength to manage crutches, among others; 7 males and 3 females; mean age 48.1 years; AIS A (n=7), AIS B (n=1), and AIS C (n=2); level of injury C6 (n=1), T1 (n=1), T4 (n=1), T8 (n =1), T10 (n=4), T11 (n=1), and L1 (n=1); and mean time since injury 5.7 years. Treatment: The program was performed 3 times per week, over 10 weeks. Each training session consisted of standing up from sitting on a chair, walking across a flat floor, and sitting down on a chair with the exoskeleton H-MEX for 60 min. Outcome Measures: 6MWT, TUG test, and Korean version of the FES-I (KFES-I)	 There were no severe AEs, but there were three minor events (two skin abrasions and one near fall). Statistically significant improvement between the pre- training and post-training assessments were reported for the TUG test (x2 = 11.400, P = 0.03). The mean score in the KFES-I questionnaire was reduced post-training (36.00 ± 9.09) compared to pre-training (37.80 ± 8.40), but this result was not statistically significant (p=0.475).
	were assessed at pre-training and post- training. *6MWT and TUG test were also assessed at mid-training (15 sessions).	
Hong et al. (2020); USA Pre-post Level 4 N=50	Population: 50 participants with chronic (> 6 months) SCI who were non- ambulatory; 38 males and 12 females; mean (± SD) age 38.7 (± 14.2) years; AIS A/B (n=31) and AIS C/D (19); and mean (± SD) time since injury 4.69 (± 5.18) years.	1. There were four "possibly study- related" severe AEs and there were 49 total study-related AEs which included 39 skin abrasions/bruising, eight musculoskeletal/edema, and two falls. All study-related skin

	 Treatment: Eligible participants were randomized within site to one of two groups for 12 weeks (3 months): Group 1 received EAW first for 12 weeks then crossover to usual activity for a second 12 weeks. Group 2 received usual activity first for 12 weeks then crossover to EAW for 12 weeks of training. Participants were divided by four neurological deficit sub-groups: motor complete tetraplegia (<i>n</i>=4); motor incomplete paraplegia (<i>n</i>=27); and motor incomplete paraplegia (<i>n</i>=9). The EAW arm consisted of EAW training, three sessions per week (4–6 h/week) for 36 sessions. Two powered exoskeleton devices were used depending individual characteristics of each participant, namely the ReWalk[™] and the Ekso[™]. Most participants with injury level of T3 or lower used the ReWalk (<i>n</i>=28) and participants with injury level higher than T3 used the Ekso (<i>n</i>=22). The usual activity arm consisted of the identification of usual activities for each participant and encouragement to continue with these activities throughout the 12-week usual activity arm. Outcome Measures: 10MWT, 6MWT and TUG were performed at 12, 24, and 36 sessions. 	2.	abrasions and musculoskeletal AEs were resolved, and participants continued in study. There were two falls during EAW, but no injuries occurred. Participants who used the ReWalk had significantly better performance during the IOMWT, 6MWT and TUG than participants using the Ekso at session 36 (p<0.0001, p<0.0001, p=0.0011, respectively). There were significant improvements in the performance of the IOMWT, 6MWT, and TUG from session 12 to session 36 (p<0.0001); but there were no significant differences between sub- groups in terms of improvements from 12 to 36 sessions on the IOMWT, 6MWT, and TUG (p>0.07).
<u>Tefertiller et al.</u> (2017); USA Pre-post Level 4 N=32	Population: 32 non-ambulatory participants with SCI; 27 males and 5 females; mean age 37 years; injury level T4-L2; and AIS A (n=21), AIS B (n=5), and AIS C (n=6). Time since injury not stated. Treatment: The participants completed 24 training sessions at a frequency of 3 times per week for 8 weeks. Throughout the trial, participants were asked to perform various gait-related tasks while wearing the Indego exoskeleton.	1. a	A combined total of 66 AEs were reported: a. Eleven of these AEs were directly device related and were reported on six participants. The majority (9/11) of the device-related AEs were skin redness, small abrasions, mild joint edema, or mild bruising on the lower legs and hips that were

	Outcome Measures: 10MWT (indoor and outdoor assessments); 6MWT; TUG; and 600-meter walk test were assessed. The 10MWT, 6MWT and TUG were completed midway (session 11, 12, or 13) and during the final walking sessions (session 24 or 25) utilizing the device and an appropriate assistive device. The 600- meter walk test was completed once during the trial on indoor surfaces between the midway and final assessments.	 resolved with improved padding and pressure relief. b. Sixty-four of 66 AEs were minor and were not device-related. c. Two events were categorized as moderate (right greater trochanteric blister due to pressure and friction while walking in the device, and ankle sprain while walking in the device, and the device), without interruption in training for either participant. 2. TUG improved from a midpoint average of 102.1 s (± 28.3) to a final of 83.6 s (± 19.8).
Baunsgaard et al. (2018a; 2018b); Denmark, Germany, the Netherlands, Norway, Spain, Sweden and Switzerland. Pre-post Level 4 N=52	Population: 52 participants with SCI; 36 males and 16 females; mean age 47.0 years; injury level C5–L2; AIS A-B-C (n=33) and AIS D (n=19); and time since injury were subgrouped (recently injured [TSI ≤ 1 year], n=25; chronically injured [TSI > 1 year], n=27). Treatment: The training protocol consisted of gait training three times per week for eight weeks, as an "add on" to existing training. Two exoskeletons were used, the Ekso (n=8) and the Ekso GT (n=44). Outcome Measures: Total up time (time standing plus time walking), walk time (time in walk motion) and number of steps, recorded by the device during the training session, alongside the walk- mode and the assistive device used. LEMS and SCIM-III mobility subscore were assessed at baseline, at end of the training period (TS24) and at a follow-up session. Participants who had or acquired gait function during the training period performed 10MWT, TUG, BBS, and WISCI II at baseline, midway (TS12), at end (TS24) and at follow-up.	 All training characteristics (up time, walk time, and steps) increased significantly from TS1 to TS24 (p<0.001), including all sub-groups: recently and chronically injured, paraplegia and tetraplegia, and incomplete and complete injury (p<0.001). The recently injured participants significantly improved 10MWT, TUG, BBS, LEMS and mobility subscore of SCIM-III but not WISCI II from baseline to TS24. The chronically injured participants did not significantly improve 10MWT, WISCI II, mobility subscore of SCIM-III or LEMS from baseline to TS24; but they showed a significant improvement in TUG and BBS. These changes were retained at follow-up in both groups.
<u>Benson et al.</u> <u>(2016)</u> ;	Population: 10 participants with traumatic SCI; 10 males; age ranged from 23 to 43 years; injury level: C8 to L1; AIS A	 Out of 60 candidates, ten (17%) were enrolled and five (8%) completed the training

UK Pre-post Level 4	(n=7) and AIS C (n=3); and time since injury ranged from 15 months to 21 years. Treatment: Participants performed 20		program. Primary reasons for not enrolling were ineligibility (<i>n</i> =24, 40%) and limited interest
N=10	exoskeleton (ReWalk [™]) training sessions over a 10-week training period. Each training session lasted a total of two hours, which included one hour of exoskeleton training and time required for device set up and data collection. Training sessions took place twice weekly. A prespecified training program consisting of progressive training modules was developed. Each training session was tailored to suit the individual's progress and needs. Outcome Measures: TUG Test were	2.	to engage in a 10- week training program (<i>n</i> =16, 27%). Five out of ten enrolled participants experienced grade I/II skin aberrations. For TUG with exoskeleton, all 5 participants shown improvements; additionally, only three participants could perform the TUG test without exoskeleton and two of these showed improvements.
	measured before, during and after the study, with and (where possible) without use of the exoskeleton.		
	Population: 7 participants with SCI and financial coverage for the inpatient exoskeleton-training; mean (SD) age: 48.3 (10.2) years; 2 females and 5 males; AIS: AIS A (n=6) and AIS C (n=1), level of injury: T5-L1, and mean (SD) time since injury: 11.4 (10.1) years.	1.	All participants who commenced the device- training completed the course of training and achieved basic competences to use the system, that is, the ability to stand up, sit down, keep balance while
<u>Platz et al. (2016);</u> Germany	Treatment: Participants performed a training with an exoskeleton (ReWalk) for 4-5 weeks during inpatient stay. Each session lasted 60 minutes and was performed from Monday through Friday. Further therapeutic exercises were individually indicated.		standing, and walk indoors, at least with a close contact guard.
Pre-post Level 4 N=7	The skills to be learned during the exoskeleton training included (1) sit-to- stand, (2) stand-to-sit, (3) 2-arm standing balance, (4) 1-arm standing balance, (5) walking straight ahead, (6) walking in a curve, when stable indoor overground walking capability was gained, (7) stair climbing (individual cases), and (8) outdoor walking.		
	Outcome Measures: Device-training milestone achievements (the number of device-training sessions until the following milestone were achieved was documented: (a) Sit-to-stand, (b) Stand- to-sit, (c) Standing balance for 1 minute with both crutches, (d) Walk 10 meters		

	straight, (e) Walk 10 meters straight and in curve, (f) Ascend, turn around, and descend a flight of 12 stairs, and (g) Walk 500 meters (outdoors).	
Sale et al. (2018); Italy Pre-post Level 4 N=8	Population: 8 participants with chronic SCI; ability to tolerate upright standing for a minimum of 30 min; joint range of motion within normal functional limits for ambulation; sufficient upper body strength to balance themselves using the walker while wearing the exoskeleton; 6 males, 2 females; mean age: 43.2 years; injury level: TI-L2; and AIS A (n=3), AIS B (n=4), and AIS C (n=1). Treatment: Participants underwent a rehabilitation mobility training consisting of a treatment cycle of 20 sessions of robotic training (45 min for 5- 4 times per week, for 4-5 weeks) using the Ekso [™] system device (exoskeleton), according to individually tailored exercise scheduling. Outcome Measures: TUG test was	After the training, all participants showed significant (p=0.008) improvements for TUG (T0: 86.83 ± 28.64 s; TI: 58.06 ± 12.7 s).
	assessed while wearing the exoskeleton at baseline (inclusion) (T0) and after 20 sessions of adaptive training (T1).	
Sale et al. (2016); Italy Pre-post Level 4 N=3	Population: 3 participants with chronic SCI; ability to tolerate upright standing for a minimum of 30 min; joint range of motion within normal functional limits for ambulation; sufficient upper body strength to balance themselves using the walker while wearing the exoskeleton; 2 males, 1 female; mean age: 36 years; injury level: T6 (n=1), T10 (n=1), and L1 (n=1); and AIS A (n=2) and AIS C (n=1). Treatment: Participants underwent a rehabilitation mobility training consisting of a treatment cycle of 20 sessions of robotic training (50 min for 3/4 times per week) using the Ekso™ system device (exoskeleton), according to individually tailored exercise scheduling.	The results of TUG test showed a non-significant (p>0.05) decrement of -44 % in time (TO 89 ± 24,25 and TI 56,53 ± 9,036).
	Outcome Measures: TUG test was assessed at baseline and after 20 training sessions.	

<u>Kolakowsky-</u> <u>Hayner et al.</u> <u>(2013):</u>	Population: 10 participants with complete SCI (AIS A); mean age: 29.8 years; 5 males, 2 females; level of injury: T4-T11; and mean time since injury: 311.3 days.	1.	Loss of balance and falls were infrequent.
USA Pre-post Level 4	Treatment: Participants performed six weekly sessions with graduated time (from 20 to 60 minutes) and less assistance in the Ekso exoskeleton.		
N=10	Outcome Measures: Losses of balance and number of falls during the sessions were assessed.		

There is understandable excitement around the proliferation of exoskeleton technologies for regaining the ability to stand and ambulate (Fritz et al. 2019). Despite the promising results and enthusiasm regarding robotic exoskeletons' potential, there are still several limitations to their use as a rehabilitation therapy tool and as a personal mobility device, such as device safety, setup requirements, slow speeds for community ambulation, level and completeness of injury, body composition and weight, range of motion required for use, and high cost (<u>Heinemann et al. 2020</u>; Gorgey 2018). Interestingly, van Dijsseldonk et al. (2021) studied the validity of some parameters as predictors of performances related to the use of the ReWalk device, in people with chronic SCI. Factors such as an active lifestyle, young age at the time of the injury, low lesion level and low body mass index were found to be factors significantly correlated to the achievement of required motor tasks during training (i.e., maintenance of upright position and walking) (van Dijsseldonk et al. 2021). As previously shown in BWSTT intervention, the time since injury seems to be a predictor of the recovery of ambulation in exoskeleton-assisted training. One pre-post study assessed a gait training protocol using the exoskeleton Ekso in 52 participants with SCI who were subgrouped according to the time since injury (Baunsgaard et al. 2018a; Baunsgaard et al. 2018b). It was shown that after 8 weeks of training, the recently injured participants (n=25) significantly improved 10MWT, LEMS, TUG and BBS from baseline; while the chronically injured (n=27) showed a significant improvement only in TUG and BBS scores; with these changes being retained at four weeks of follow-up (Baunsgaard et al. 2018a; Baunsgaard et al. 2018b). However, according to the meta-regression analysis of Zhang et al. (2022), for comparing baseline demographic and clinical characteristics, it was shown that age, time after injury, and the AIS score had no impact on the outcomes of patients undergoing wearable EAW and Lokomat training.

Recent systematic reviews have been conducted to assess the safety, feasibility, and effects on gait and/or standing balance performance (and other health outcomes) of the use of different overground powered lower limb exoskeletons in patients with SCI (<u>Duddy et al. 2021; Federici et al. 2015; Lajeunesse et al. 2015; Louie et al. 2015; Rodriguez-Tapia et al. 2022; Shackleton et al. 2019; Tamburella et al. 2022; Zhang et al. 2022</u>). In a systematic review, Rodriguez-Tapia et al. (2022) found, from 570 participants with SCI who had been included, a total of 174 AEs, with

a significantly higher occurrence in a population with paraplegia (n=157, 90%) compared to the population with tetraplegia (n=17, 10%). The systematic review of Tamburella et al. (2022) also showed that from the 41 studies included, 13 reported different AEs during training with exoskeletons. It was noted that the most frequent AEs were skin lesions, while the less frequent ones were the presence of extreme fatigue, falls, bone fractures or muscle strains (Tamburella et al. 2022). However, these and other results from Table 13, show that gait training using wearable powered exoskeletons may be a safe intervention after paraplegia (Miller et al. 2016) and tetraplegia (Rodriguez-Tapia et al. 2022).

Regarding standing balance outcomes, the systematic review and meta-analysis of Shackleton et al. (2019) included seven studies which studied over-ground robotic locomotor training and showed for TUG, a positive pooled effect of 0.74 (95% CI 0.36, 1.11) with no heterogeneity ($I^2 = 0\%$, p=0.0001). To date, the only network meta-analysis of RCTs and non-RCTs to assess the clinical effects (i.e. 10MWT, WISCI II, and TUG) of two different types of RAGT (Lokomat and wearable EAW) in patients with SCI was conducted by Zhang et al. (2022). It was shown that TUG scores were significantly improved from baseline by using wearable EAW [1.19 (95% CI=0.74, 1.64); I^2 =44%]. However, these (and other) benefits need to be confirmed through RCTs with larger sample sizes and higher quality because the small number of studies with a control group did not allow to establish if the benefits deriving from the use of exoskeletons are greater or lesser than conventional physical therapy (Duddy et al. 2021; Shackleton et al. 2019; Tamburella et al. 2022).

Regarding training dosage, Shackleton et al. (2019) showed that the most common intervention length was eight weeks and typically, training was conducted three times per week for 60 min per session; but there is still some degree of variability in training dosage according to other systematic reviews (Fang et al. 2020; Rodriguez-Tapia et al. 2022; Shackleton et al. 2019; Tamburella et al. 2022).

In line with previous systematic reviews published until the date assessing gait interventions with the use of exoskeletons (Rodriguez-Tapia et al. 2022; Tamburella et al. 2022; Shackleton et al. 2019), the two most studied exoskeletons models in people with SCI for standing balance outcome measures and falls assessed in this section are the Ekso® (Baunsgaard et al. 2018a; Baunsgaard et al. 2018b; Chang et al. 2018; Edwards et al. 2022; Hong et al. 2020; Sale et al. 2018; Sale et al. 2016; Kolakowsky-Hayner et al. 2013) and the ReWalk (Benson et al. 2016; Hong et al. 2020; Platz et al. 2016). Despite the promising results overall described, only a few high-quality studies have been conducted, comparing locomotor training interventions using exoskeletons with other locomotor interventions.

One high-quality study compared the use of a wearable exoskeleton with a traditional orthosis (Rodríguez-Fernández et al. 2022). The cross-over RCT of Rodríguez-Fernández et al. (2022) included 10 patients with chronic motor-complete and thoracic SCI who performed two overground training programs (with sit-to-stand and stand-to-sit transitions, and standing and walking exercises using one of the two devices [KAFO vs. ABLE exoskeleton]) of 10 sessions of 90 min duration. At the end of the study, it was shown that walking with the robotic device improved gait kinematics and spatiotemporal parameters compared to walking with knee ankle

foot orthoses (KAFOs) (<u>Rodríguez-Fernández et al. 2022</u>). However, the performance during the clinical evaluations (6MWT, 10MWT, and TUG) and the energy consumption were similar (p > 0.05) (<u>Rodríguez-Fernández et al. 2022</u>). These results are of interest, as traditional orthoses represent a more accessible option than exoskeletons in people with SCI. Future studies comparing training interventions using these devices would be necessary to elucidate whether both devices provide similar improvements in standing balance outcomes or, on the contrary, one of them provides larger improvements in this function.

The RCT of Edwards et al. (2022) included 25 participants with chronic motor incomplete SCI who were randomly assigned to one of three interventions (i.e., Ekso robotic standing/up and walking and, if possible, overground training without BWS; BWSTT, and again, if possible, overground training without BWS; and continuing with daily activities as normal). After 12 weeks of training, gait speed (10MWT), walking endurance (6MWT), and standing balance (TUG test) improved in each of the three groups, with the highest improvements shown in the Ekso group, but without reaching statistical significance (Edwards et al. 2022). The authors stated that with a larger sample size, the promising results of the intervention with the Ekso exoskeleton might have appeared (Edwards et al. 2022).

The prospective controlled trial of Tamburella et al. (2020b) aimed to provide more data after promising results in gait speed, walking endurance and standing balance in four participants with incomplete motor SCI shown in the pre-post study of Tamburella et al. (2020a). Tamburella et al. (2020b) assessed the effects on gait and balance of a training program based on standing balance and gait training using the Achilles ankle exoskeleton (or not) for 10 sessions in eight patients with incomplete motor SCI. At the end of the training, there were significant improvements in spatio-temporal parameters (gait speed, gait cycle time, and step length) only for the experimental group; similar but not significant improvements in standing balance and manual muscle testing were shown in both groups (Tamburella et al. 2020b). These two studies are the only ones included in the present systematic review which assessed the effects of an ankle exoskeleton (developed to assist plantar/dorsiflexion during walking) for standing balance and walking performance; being of particular interest because the rest of the exoskeletons traditionally provide assistance reaching the lumbar/pelvis/hip joints. More research on interventions for improving standing balance, focusing on the ankle joint and muscle groups, could be important to carry out. For example, it has been shown that ankle muscle activity cocontractions may be a compensatory strategy for individuals with incomplete SCI to accommodate for decreased motor function, but co-contractions may result in increased ankle mechanical joint stiffness and consequently postural sway (Fok et al. 2021); or that individuals with incomplete SCI show larger postural sway compared with participants without SCI during quiet standing, primarily due to larger ankle joint acceleration (Lee et al. 2021).

Conclusions

There is level 1 evidence (from 1 RCT: <u>Rodríguez-Fernández et al. 2022</u>) that an overground training program with the ABLE exoskeleton provides a better improvement in gait kinematics and spatiotemporal parameters, but similar improvement in performance (6MWT, 10MWT, and TUG) compared to a training program with KAFOs in patients with chronic motor-complete and thoracic SCI.

There is level 2 evidence (from 1 RCT: <u>Edwards et al. 2022</u>) that walking training with an Ekso exoskeleton provides similar benefits in gait speed (10MWT) and endurance (6MWT), and standing balance (TUG test) than a BWSTT in patients with chronic motor incomplete SCI.

There is level 2 evidence (from 1 RCT: <u>Chang et al. 2018</u>) that three weeks of conventional physical therapy designed to facilitate gait improvement, but not exoskeleton-assisted gait training, provides significant improvements in standing balance (TUG) in people with incomplete and chronic SCI.

There is level 2 evidence (from 1 prospective controlled trial: <u>Tamburella et al. 2020b</u>) that the use of an NeuroMuscular Controller-controlled Achilles exoskeleton during 10 sessions of gait and balance training provides more improvements in walking distance (6MWT), but does not provide better improvement in lower limb strength (LEMS) nor standing balance (BBS), than the same training program performed without the use of the ankle exoskeleton, in patients with chronic and motor incomplete SCI.

There is level 4 evidence (from several pre-post studies) that wearable exoskeletons can enable safe walking and improvements in walking function and standing balance (TUG, BBS, among other outcome measures) in patients with SCI and different levels of injury (mostly paraplegia), AIS level, or time since injury (mostly chronic).

Key Points

Even though wearable exoskeleton-assisted gait training has been studied primarily to improve gait performance, it can enable safe walking and provide improvements in standing balance in patients with SCI and different levels of injury, AIS level, or time since injury.

There is little consensus regarding training regimens and exoskeleton models used, and we found a high number of studies with adverse events.

There is insufficient evidence regarding whether wearable exoskeleton-assisted training provides better walking function, balance performance, or energy expenditure outcomes, compared with other approaches (such as RAGT with Lokomat or KAFOs) or in the community setting in patients with SCI.

Some aspects of Powered Exoskeleton use in rehabilitation need to be improved, as they may be cumbersome to use, have a high cost, and are not generally available for home use.

4.5 Neuromodulation for Standing Balance

Neuroplasticity refers to the capacity of the nervous system to modify its structural and functional organization, adjusting itself to a changing environment (<u>De Ridder et al. 2016</u>). Neuromodulation is linked to neuroplasticity and can be defined as the induction of neuroplastic changes via local application of electrical, magnetic, acoustic, optic, tactile, or pharmacological

stimuli (De Ridder et al. 2016). The International Neuromodulation Society defines neuromodulation as "a technology that acts directly upon nerves. It is the alteration—or modulation—of nerve activity by delivering electrical or pharmaceutical agents directly to a target area" (<u>https://www.neuromodulation.com/about-neuromodulation</u>). More specifically, the SCIRE YouTube channel (<u>https://www.youtube.com/watch?v=ks-RkYNjPZQ</u>) refers to neuromodulation as the modification of nerve function through a number of ways, including chemically (intrathecal baclofen), via electrical stimuli (FES and epidural stimulation), and magnetic fields (transcranial magnetic stimulation). Neuromodulation can be applied to three main areas of the body: the brain, the spinal cord and the peripheral nerves, through invasive and/or non-invasive approaches.

Researchers, clinicians, and people with SCI are excited about the promising therapeutic potential in neuromodulation for movement, sensation, bowel, bladder, and sexual function. In recent years, the combination of rehabilitative training with neuromodulation of the brain or the spinal cord has been investigated as a means to enhance the excitability of motor circuits and to increase training efficacy, promoting motor recovery (Hofer & Schwab 2019). Over the last few years, the translation of stimulation-enhanced activity-based rehabilitation from the pre-clinical to a clinical setting has been carried out successfully, yielding substantial improvements in motor functionality (Hofer & Schwab 2019).

4.5.1 Functional Electrical Stimulation (FES) for Standing Balance

The idea of compensating for paralyzed function using electrical stimulation was introduced as early as the 1960s (Liberson et al. 1961). FES of the common peroneal nerve was found to be effective in assisting foot clearance during the swing phase (Liberson et al. 1961). There has also been a report of attempts to stimulate the ankle plantarflexor muscles to assist push-off at the end of stance and enhance the initiation of the swing phase in participants with incomplete SCI (Bajd et al. 1999). Approaches that focus on swing phase activity are more suitable for less severely disabled persons who have adequate balance to support their stance leg during gait. There are also more complex systems that involve several channels of stimulation that support proper extension as well as foot clearance during swing (e.g., Sigmedics 2000). These are more suitable for patients who require assistance in standing as well as gait, such as those with neurologically complete SCI. FES systems such as the Parastep or ALT-2 provide stimulation of thigh extensor muscles (quadriceps, gluteal muscles) to support extension and standing, as well as stimulation of the common peroneal nerve to assist with swing phase movements. FES may also be combined with bracing to counter trunk and hip instability (Solomonow et al. 1997). FES to assist with foot clearance during swing (drop-foot) has been studied more extensively in the stroke population (Bosch et al. 2014) and may provide some evidence for people with incomplete SCI who present with hemiparesis similar to stroke.

One of the limitations of surface FES is possible skin irritation, discomfort under the electrodes, or difficulties with proper positioning of the electrodes. With improvements in electronic technology, FES systems have become smaller and more practical for everyday use. In addition, some patients have opted for implanted FES systems that may be inserted without surgery. These systems offer a more precise delivery of stimulation, enabling greater muscle selectivity and the ability to access deeper muscles, such as the hip flexors (Kobetic et al. 1997).

Percutaneous electrodes, which are inserted through the skin with a hypodermic needle, offer one possibility to circumvent complications with surface electrodes (Kobetic et al. 1997; <u>Marsolais & Kobetic 1986</u>). However, there may be complications due to infection or irritation at the site of insertion, and electrode movement or breakage (Agarwal et al. 2003). More recently, there was a case study reporting the positive effects with a BION microstimulator in a participant with incomplete tetraplegia with drop-foot (Weber et al. 2004). Thus, preliminary reports of the use of such innovative FES technology are promising, but further study is warranted to determine the long-term efficacy of such implanted systems.

Author Year Country Research Design Score Total Sample Size	Methods	Outcome
Galea et al. (2018); Australia RCT PEDro=7 Level 1 N=116	 Population: 116 participants who had sustained a SCI above the level TI2; 98 males and 18 females; mean age 41.45 years; level of injury C2-C8 (n=62), TI-T6 (n=31), and T7-TI2 (n=23); AIS A (n=57), AIS B (n=17), AIS C (n=12), and AIS D (n=30); and mean time since injury 4.7 years. Treatment: The intervention consisted of 36 sessions over 12 weeks. Participants were randomly assigned to: Full-body exercise program (n=60: Participants in received a triad of interventions comprising locomotor training (BWSTT for 30 min), FES-assisted cycling (for 10-60 min), and trunk and upper and lower extremity exercise. Upper body exercise program (n=56): Participants received a circuit-based exercise program for the upper body, incorporating resistance and aerobic training. Outcome Measures: SCIM, Spinal Cord Injury–Falls Concern Scale (SCI-FCS), 6MWT, and 10MWT were assessed at baseline, 12 weeks, and 24 weeks after randomization. 	 There were no statistically significant between-group differences for 6MWT, 10MWT, SCIM, and SCI-FCS after 12 weeks of training or at 6 months follow-up. AEs: 31 serious AEs (16 full- body exercise, 15 upper body exercise) and 719 minor AEs (404 full-body exercise, 309 upper body exercise) were recorded over the 6-month trial period. One serious AE in full- body exercise (bilateral medial femoral condyle and tibial plateau subchondral insufficiency fractures) was considered to be related to the intervention. Another serious AE in full- body exercise (severe worsening back pain) was considered probably related to the intervention. In upper body exercise, 1 serious AE (feeling off balance, pain and loss of strength in upper limbs)

		was considered possibly related to the intervention.
Kapadia et al. (2014); Canada RCT PEDro=5 Level 2 N=27	6MWT (Pre->Post) -0.27 10MWT (Pre->Post) -0.27 TUG (Pre->Post) -0.27 FIM Locomotor (Pre->Post) -0.29 10MWT (Pre->Ret) -0.29 10MWT (Pre->Ret) -0.29 TUG (Pre->Ret) -0.29 FIM Locomotor (Pre->Ret) -0.2 SCIM Mobility (Pre->Ret) -2 -2 -1.5 -1	 SCIM mobility sub-score significantly improved over time for the intervention group (p<.01) but not for the control group (baseline/12 months: 17.27/21.33 vs. 19.09/17.36, respectively). On all other outcome measures the intervention and control groups had similar improvements. Walking speed, endurance, and balance during ambulation all improved upon completion of therapy and the majority of participants retained these gains at long- term follow-ups. an differences (SMD ± 95%C.I.) as the and pre-intervention to Electrical Stimulation (1.19,0.80) (1.19,0.80) (1.19,0.64) 0.05 (1.06,0.96) 0.07 (0.84,0.69) 0.03 (0.98,1.05) (0.78 (0.03,1.59)
<u>Kuhn et al. (2014);</u> Germany Cohort Study Level 2	Population : 30 participants; average age 44 ± 15.5y; motor complete and incomplete spinal cord injuries in the cervical, lumbar, and thoracic regions; AIS A=10, B=3, C=15, D=2; 0-122 months post injury.	 For the 5 patients with partial walking ability at the start of the study, the time for TUG was reduced from 11.7±21.9 to 10.1±18.1 s (p=0.5).

N=30	Treatment : During the 4-week study period, all patients received eight 20min FES interventions at the beginning and end of each week. At every intervention, circumferential measurement and spasticity testing before and after FES cycling (pretest/post-test) were performed. Ultrasound, walking tests, and manual muscle testing were only performed at the beginning of week 1 (TI) and at the end of week 4. Outcome Measures: Circumferential measurement, muscular ultrasound measurement, spasticity measured by Modified Ashworth Score, Walking (6MWT, TUG).		
Houston et al. (2020; 2021) Canada Pre-post Level 4 N=5	 Population: 5 participants with chronic incomplete SCI; 1 male and 4 females; age range 55-68 years; level of injury CI (n=1), C3 (n=1), C5 (n=1), T6 (n=1) and TIO (n=1); AIS C (n=3) and AIS D (n=2); and mean time since injury 46.8 months. Treatment: Participants completed three 1h training sessions per week for 4 weeks consisting of FES applied bilaterally to the ankle plantarflexors and dorsiflexors while they performed visual VFBT exercises. A closed-loop FES system was used in which the CoP was continually monitored and the level of electrical current administered was automatically adjusted. Outcome Measures: Outcome measures were collected before beginning the intervention, after completion of training, and 4 and 8 weeks after the intervention: Clinical assessment: BBS, Mini-BESTest and ABC scale. Biomechanical assessment: Static balance test (in standing) (measuring postural sway through calculation of CoP velocity and the root-mean-square of the CoP displacement in both anterior-posterior and medio-lateral directions) and dynamic balance test (in standing) (evaluating the LOS). 	1. 2. 3.	Improvements were seen for four of the five participants on at least one of the clinical scales following completion of the training intervention. All participants showed greater maximal CoP excursion area during the LOS test after the training intervention, whereas only one participant demonstrated a reduction in postural sway. Regarding the semi- structured interviews, risk of falling was perceived as slightly reduced or unchanged, but participants felt that their balance confidence had increased. No training-related AEs were reported.

Semi-structured interviews were conducted after completion of the balance training intervention and 8-weeks post- training to understand participants' experiences.	
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To date, there are few studies assessing different training protocols which include some type of FES intervention for balance outcomes in people with chronic SCI (<u>Galea et al. 2018</u>; Houston et al. <u>2020</u>, <u>2021</u>; <u>Kapadia et al. 2014</u>; <u>Kuhn et al. 2014</u>).

In an RCT, Galea et al. (2018) assessed 116 patients with chronic SCI who were randomly assigned to receive a multimodal exercise training program (comprising BWSTT, FES cycling and trunk and upper and lower limb exercises) or an upper body exercise program for 12 weeks. The findings of the study do not support the hypothesis that an intensive full-body exercise program might lead to neurological recovery, walking improvement, or falls concern-balance in participants with chronic SCI (Galea et al. 2018). The authors stated that the heterogeneity of their sample, which included participants with a range of injury levels and severity (AIS A and B, n=74; AIS C and D, n=42), may have contributed to these results (Galea et al. 2018). Kapadia et al. (2014) found in participants with chronic and incomplete SCI that FES-assisted BWSTT (intervention group) and an aerobic and resistance training program (control group) significantly improved standing balance (TUG) function after 16 weeks of training. However, these improvements were not statistically different between groups (Kapadia et al. 2014).

Other lower-quality studies were carried out for FES-cycling interventions, such as the cohort study of Kuhn et al. (2014), which assessed 30 participants with complete and incomplete SCI during their rehabilitation in a special acute care unit (median time since injury: 2 months). After 4 weeks of 20-min FES-cycling program for 2 days per week, only the five participants with partial walking ability at the start of the study showed a non-significant improvement in TUG (p=0.5) (Kuhn et al. 2014).

The two pre-posts of Houston et al. (2020) and Houston et al. (2021) included three patients with tetraplegia and two with paraplegia who received three 1h training sessions per week for four weeks, consisting of FES applied bilaterally to the ankle plantarflexors and dorsiflexors while they performed visual feedback balance training (VFBT) exercises. After the intervention, improvements were seen in four of five participants on at least one balance scale (BBS and/or Mini-BESTest), with less impact on balance confidence (ABC scale) (Houston et al. 2020). Additionally, some of the biomechanical parameters (area of maximal CoP excursion) increased for all participants, while there was little effect on quiet stance assessments (Houston et al. 2020). In semi-structured interviews assessed at the end of the intervention, participants perceived that the risk of falling was slightly reduced or unchanged, but they felt that their balance confidence had increased (Houston et al. 2021). The authors highlighted the fact that FES+VFBT was able to elicit improvements in balance ability despite a small training dosage, so this intervention could be a promising intervention for standing balance rehabilitation among

people with incomplete SCI, which has to be confirmed in larger and higher-quality studies (<u>Houston et al. 2020</u>).

Conclusions

There is level 1 evidence (from 1 RCT: <u>Galea et al. 2018</u>) that a multimodal exercise training program (comprising BWSTT, FES cycling, and trunk and upper and lower limb exercises) does not provide better balance (Spinal Cord Injury – Falls Concern Scale [SCI-FCS]DCS), neurological or walking improvements than an upper body exercise program in patients with chronic SCI.

There is level 2 evidence (from 1 RCT: <u>Kapadia et al. 2014</u>) that a program consisting of FESassisted BWSTT compared with another of aerobic and resistance training, for 16 weeks, provides significant, but similar improvements, in standing balance (TUG) function in participants with chronic and incomplete SCI.

There is level 2 evidence (from 1 cohort study: <u>Khun et al. 2014</u>) that two days per week of 20minute FES-cycling for four weeks in a special acute care unit does not provide significant improvement in standing balance (TUG) in participants with partial walking ability due to acute SCI.

Key Points

Some RCTs involving BWSTT coupled with FES or FES-cycling have shown improvements in standing balance outcomes or functional independence, and some have not.

Specific balance interventions with larger sample sizes, coupled with FES could be carried out to determine if this addition could be an effective complement.

4.5.2 Transcranial Direct Current Stimulation (tDCS) for Standing Balance

Transcranial direct current stimulation (tDCS) is increasingly used in rehabilitation research as a neuromodulation approach to influence the excitability of cortical and cerebellar networks (<u>Evans et al. 2022</u>). The aim is often to "prime" neural circuits to increase corticospinal activation and to augment the effects of motor skill training (<u>Evans et al. 2022</u>). The majority of the studies published on the combination of tDCS and motor rehabilitation is related to upper limb, and studies examining the effects of tDCS on lower limb motor learning in persons with motor-incomplete SCI are still limited (<u>Kumru et al. 2016</u>).

Table 15. Transcranial Direct Current Stimulation	(tDCS) for Standing Balance
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Author Year Country Methods Research Design	Outcome
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Score Total Sample Size				
Overground Training in Combination With tDCS				
Klamruen et al. (2024); Thailand RCT PEDro=8 Level 1 N=34	 Population: 34 participants with SCI and the ability to walk at least 15 m independently (with or without a walking device): Anodal Group (n=17): Mean (SD) age: 41.88 (13.50) years; 13M, 4F; etiology: Traumatic (n=13) and non-traumatic (n=4); AIS: AIS C (n=7) and AIS D (n=10); level of injury: Tetraplegia (n=8) and paraplegia (n=9); and median (IQR Q1-Q3) time since injury: 17.0 (8.0-22.50) months. Sham Group (n=17): Mean (SD) age: 48.41 (13.36) years; 12M, 5F; Etiology: Traumatic (n=2) and non-traumatic (n=5); AIS: AIS C (n=5) and AIS D (n=12); Level of injury: Tetraplegia (n=9) and paraplegia (n=8); and Median (IQR Q1-Q3) time since injury: 12.0 (12.0-16.0) months. Treatment: Participants were randomly assigned into one of the following two groups: Anodal Group (n=17): Anodal transcranial direct current stimulation (tDCS)vDCS was administered over the vertex (lower-limb motor area) at an intensity of 2 mA for 20 min while sitting. Sham Group (n=17): Participants received the delivered current only for the first 30 seconds before it was automatically terminated, and the electrodes remained on the participant's head for 20 minutes. After tDCS, all participants underwent overground gait training at a moderate intensity (RPE level of 5). The total gait training time was 40 minutes. The intervention program was administered for 5 consecutive days. 	1.	No serious AEs of tDCS were observed. The anodal group reported itching (42% of participants) and tingling (44% of participants) sensations only during the stimulation period. The sham group reported itching sensations a moment after starting stimulation, which disappeared after a few (1- 2) minutes of stimulation. For TUG, changes over time in the anodal (p<.001) and sham (p=.007) groups were shown. No between-group differences were found for all time points.	

	to the fifth lumbar spinous process with a belt for assessing cadence, stride length, and stride duration; TUG test, FTSST; and WHOQOL-BREF were assessed at pre- intervention (PRE), immediately post the 5 sessions on the same day (POST), at 1- month follow-up (1M), and at 2-month follow-up (2M).	
Evans et al. (2022); USA RCT PEDro=10 Level 1 N=26	 Population: 25 participants with chronic motor-incomplete SCI; 18 males and 7 females; mean age 48.6 years; level of injury C4 (n=9), C5 (n=7), C6 (n=2), C7 (n=4), T6 (n=1), and T8 (n=2); AIS C (n=2) and AIS D (n=23); and mean time since injury 85.85 months. Treatment: Participants were randomly allocated to one of two groups: MST+tDCS group (n=14). MST+tDCS group (n=11). Interventions were carried out during 3 consecutive days and consisted of: Motor Skill Training (MST): Each of the six motor task activities was performed in consecutive order and repeated four times as a circuit. Participants were asked to complete as many repetitions as possible in 60 s with the intent to maintain a moderate exercise intensity (40–60% heart rate reserve). The MST activities were intended to challenge upright standing balance and promote rapid volitional activation and deactivation of lower extremity muscles. tDCS was delivered via two electrodes for 20 min, which was delivered concurrently with MST. Outcome Measures: Overground walking speed (10MWT); spatiotemporal gait characteristics (cadence and stride length), peak trailing limb angle and intralimb coordination (this kinematic data was obtained during each 10MWT using a 3D inertial measurement unit motion capture system); and balance function (assessed using the BBS and the FES-I). Outcomes were assessed at baseline on Day-1 and 24-h post-intervention on Day-5. To examine 	 AEs included cases of mild- to-moderate headache following tDCS and delayed onset muscle soreness following MST. Analyses revealed a significant effect of the MST circuit, with improvements in walking speed, cadence, bilateral stride length, stronger limb trailing limb angle, weaker limb intralimb coordination, BBS, and FES-I observed in both groups. No differences in outcomes were observed between groups.

	within-day (online) and between-day (offline) effects of intervention on outcome measures associated with walking, a subset of selected outcomes was assessed pre- (D2pre, D3pre, D4pre) and post- intervention (D2post, D3post, D4post) on each intervention day. BWSTT in Combination with tDC	S	
Simis et al. (2021); Brazil RCT PEDro=9 Level 1 N=43	 Population: 43 participants with incomplete SCI; 33 males and 10 females; median (IQR) age 38 (28-45) years; injury level paraplegic (n=28) and tetraplegic (n=15); AIS C (n=20) and AIS D (n=23); and median (IQR) time since injury 16 (6.5-23.5) months. Treatment: Participants were randomly allocated to receive 30 sessions of active (n=21) or sham (n=22) tDCS immediately before RAGT with Lokomat. All participants received 20-min tDCS sessions; 30-min sessions of Lokomat training; and their normal rehabilitation program. During RAGT sessions, the participant body weight, guidance force and training speed were progressively incremented depending on each participant. tDCS was performed using a monophasic current device with the anode placed over the primary motor cortex region and the cathode placed over the supraorbital region, contralateral to the anode. Outcome Measures: WISCI II; BBS; 10MWT; 6MWT; TUG test; and Lower Extremity Isokinetic Dynamometry were assessed before the beginning of the intervention (baseline), after 15 sessions (intermediate), after 30 sessions (post-treatment) and three months after treatment (follow-up). 	1.	All the participants tolerated tDCS sessions, without unexpected AEs. One participant did not tolerate Lokomat training due to pain related to the straps of the BWS mechanism and was excluded from the study. Regardless of intervention group, statistical improvement existed between baseline and the other periods as measured by BBS, TUG, 10MWT, and 6MWT. Regarding the improvement in the BBS, 10MWT, 6MWT and TUG, there was no statistical difference between groups for the tested periods.
Raithatha et al. (2016); USA RCT PEDro=9 Level 1 N=15	Population: 15 participants with traumatic SCI; 10 males and 5 females; mean (range) age 47.5 ($24 - 67$) years; level of injury C4 (n=1), C5 (n=1), C5-C6 (n=1), C6 (n=5), C8 (n=1), T2 (n=1), T6 (n=2), T12 (n=1), and L1 (n=2); AIS B (n=1), AIS C (n=11) and AIS D (n=3); and mean (range) time since injury 7.9 (1 – 39) years.	1. 2.	There were no AEs during the intervention period. Within-group changes from baseline to post- intervention indicated overall improvement on all outcome measures for both groups. Statistically

	1	
 Treatment: All participants attended to 36 sessions (3/week for 12 weeks) of tDCS immediately before locomotor training with a robot-assisted gait orthosis (LT-RGO). They were randomly allocated into 2 groups: Active anodal tDCS paired with LT-RGO (active group, n=9). Sham tDCS paired with LT-RGO (control group, n=6). <i>tDCS</i>: Each participant in the active tDCS group received 20 min of tDCS. <i>LT-RGO</i>: The Lokomat was used with a novel approach to LT-RGO (with progressively decreased treadmill speed and guidance force in order to minimize momentum and thereby avoid eliciting passive movement). 	3.	significant improvement was evident on SCIM-III and TUG in the sham tDCS group. Between-groups comparison of changes from baseline to post- intervention revealed that the sham tDCS group improved significantly more than the active tDCS group on TUG.
Outcome Measures: Muscle strength (assessed by manual muscle testing) of hips (flexion, extension, abduction, adduction, internal and external rotation), knees (flexion, extension), ankles (dorsiflexion, plantarflexion), great toes (flexion, extension), and toes (flexion, extension); 10MWT; 6MWT; TUG; BBS, and SCIM-III were assessed at baseline, post- intervention, and 1-month follow-up timepoints.		

One high-quality study assessed the effects of the combination of tDCS and motor skill training in patients with chronic motor-incomplete SCI (Evans et al. 2022). Patients received the intervention during three consecutive days and were randomly allocated to one of two groups: 20 min of tDCS delivered concurrently with motor skill training (patients had to perform a circuit of 6 motor task activities of standing balance exercises for 60 s, repeated 4 times) or a sham application of tDCS in combination with the same training intervention (Evans et al. 2022). It was shown that the locomotor-related motor skill training, with and without tDCS, provided significant increases in overground walking speed (10MWT), walking distance (2MWT), cadence, bilateral stride length, and balance function (BBS and FES-I), but the addition of tDCS was not associated with greater improvements compared with the sham application (Evans et al. 2022). Another RCT assessed participants with incomplete chronic SCI who were assigned to receive anodal tDCS over the vertex while sitting or to a sham tDCS application (Klamruen et al. 2024). After the tDCS application, all participants underwent overground gait training at a moderate intensity (Klamruen et al. 2024). After 5 days of consecutive sessions, both groups showed similar significant improvements in standing balance (TUG); however, higher

improvements were observed in the experimental group for walking speed (10MWT) (<u>Klamruen</u> et al. 2024).

Two high-quality studies assessed the effects of the combination of tDCS and BWSTT in patients with chronic and motor-incomplete SCI (Simis et al. 2021; Raithatha et al. 2016). In the RCT of Simis et al. (2021), patients with chronic SCI received 20 min of active or sham tDCS immediately before BWSTT with Lokomat for 30 min. After 30 sessions, there was a statistically significant difference in the percentage of participants that improved in WISCI II (33% in the sham group vs. 70% in the active group) and in the follow-up; however, other outcome measures related to walking (10MWT and 6MWT) or balance (BBS and TUG) improved significantly in both groups, but without statistical differences between groups (Simis et al. 2021). Lastly, the study of Raithatha et al. (2016) was the very first to evaluate the effects of combining tDCS with locomotor training to facilitate gait recovery for people with incomplete and chronic SCI. Patients were randomly allocated into two groups: 20 min of tDCS immediately before locomotor training with Lokomat (Raithatha et al. 2016). Balance, as measured by BBS, improved in both groups nearly equally (and TUG improved only in the sham group), suggesting that while LT-RGO can improve balance, tDCS may not enhance this improvement (Raithatha et al. 2016).

It should be noted that tDCS seems to be a feasible and safe intervention. Studies by Raithatha et al. (2016) and Simis et al. (2021) stated that all patients tolerated the intervention with no complications. Evans et al. (2022) and Klamruen et al. (2024) found that four participants in the active tDCS group (n=14) had mild-to-moderate poststimulation headache related to the tDCS intervention (but it was not stated if the AE occurred in the active or the sham group), and 42-44% of participants in the experimental group reported itching and tingling sensations, respectively.

Conclusions

There is level 1 evidence (from 1 RCT: <u>Evans et al. 2022</u>) that a brief intensive motor skill training involving a circuit of ballistic, cyclic locomotor-related skill activities improved overground walking speed (10MWT), walking distance (2MWT), cadence, bilateral stride length, and balance function (BBS and FES-I); however, concurrent application of tDCS did not further enhance the effects of motor skill training in patients with motor-incomplete SCI.

There is level 1 evidence (from 1 RCT: <u>Klamruen et al. 2024</u>) that anodal or sham tDCS in a sitting position prior to overground gait training at moderate intensity for five days provide similar improvements in standing balance (TUG), but higher improvements in 10MWT for the anodal tDCS in patients with incomplete and chronic SCI.

There is level 1 evidence (from 2 RCTs: <u>Simis et al. 2021</u>; <u>Raithatha et al. 2016</u>) that the application of tDCS immediately before BWSTT with Lokomat improved significantly more the walking ability (WISCI II) and lower extremity motor function (manual muscle testing), and similarly the walking speed (10MWT), walking distance (6MWT) and balance (BBS and TUG), compared to the same intervention but with sham stimulation in patients with motor-incomplete and chronic SCI.

Key Points

Concurrent application of tDCS did not further enhance the effects on walking, balance and strength outcomes of motor skill training, overground walking training, or BWSTT in patients with motor-incomplete SCI.

4.5.3 Repetitive Transcranial Magnetic Stimulation (rTMS) and Other Approaches for Standing Balance

Repetitive transcranial magnetic stimulation (rTMS) has been widely explored as a tool for treating a variety of disorders, including depression (Martin et al. 2003; Couturier et al. 2005), pain (Lima & Fregni 2008), or motor disorders following Parkinson's disease (Elahi et al. 2009) and stroke (Corti et al. 2011). Experimental studies in humans have shown that low-frequency rTMS (<1 Hz) can reduce the excitability of the motor cortex whereas high-frequency rTMS (>1 Hz) causes an increase in motor cortical excitability (Kobayashi & Pascual-Leone 2003). Given the ability for rTMS to modulate cortical excitability, there has been much interest in exploring its potential to facilitate supraspinal connectivity or restore the balance of interhemispheric inhibition (in stroke) as a means to promote motor recovery and function. The recovery of functional ambulation following motor-incomplete SCI has been shown to be associated with enhanced excitability of motor cortical areas (Winchester et al. 2005) and corticospinal connectivity to the lower limb (Thomas & Gorassini 2005).

Recently, other related neuromodulation approaches have been developed, such as the non-invasive brain stimulation (rTMS and simultaneous transvertebral direct current stimulation [tvDCS]) (<u>Naro et al. 2022</u>).

Author Year Country Research Design Score Total Sample Size	Methods	Outcome
Krogh et al. (2021); Denmark RCT <u>PEDro=7</u> Level 1 N=20	Population: 20 participants with motor-incomplete SCI and capable of participating in lower limb resistance training; 15 males and 4 females; mean age 54.45 years; injury level C2 (n=2), C4 (n=4), C5 (n=4), C8 (n=1), T3 (n=1), T9 (n=1), T10 (n=1), T11 (n=1), T12 (n=1), L1 (n=1), and L2 (n=2); AIS A (n=1), AIS C (n=5), and AIS D (n=13); and mean time since injury 89.3 days.	 A seizure during stimulation (n=1 in REAL group) and mild and transitory headaches following their first treatment session (n=2 in SHAM group) were reported as AEs. Apart from

Table 16. Repetitive Transcranial Magnetic Stimulation (rTMS) and Other Approaches for Standing Balance

	 Treatment: All participants received lower limb resistance training (twice weekly) and lower limb physical therapy (thrice weekly) for 4 weeks; and were randomly assigned to receive active stimulation (REAL group) (n=11) or sham stimulation (SHAM group) (n=9) rTMS with a double-cone coil over bilateral leg motor cortex, daily (Monday- Friday) immediately before training sessions. Lower limb resistance sessions lasted 60 min and strength exercises, for each major functioning muscle group, were performed (3 x 10 at moderate to vigorous [50–80% one repetition maximum] loading intensity). Lower limb physical training included stair climbing, balance and mobility exercises, OL, BWSTT, FES, and stretching/mobilization. Participants were engaged in additional clinical activities as part of their usual care, such as hydrotherapy, occupational therapy, activities of daily living training, and upper extremity resistance training classes. Outcome Measures: Maximal voluntary contraction, LEMS, and gait function* (10MWT, 6MWT, and TUG) were assessed the day before the first rTMS session and the day after the last session; except for LEMS assessment, which was performed at admission and within 1 week of discharge. *Gait function was assessed in a sub-group of ambulators (REAL group, n=8; SHAM group, n=8). 	2.	that, only harmless side effects such as drowsiness, twitching facial muscles, and tingling/poking sensations in the scalp were occasionally reported. Both groups improved in the 6MWT and TUG at POST with no clear main effects (treatment: p<0.76, treatment x time: p<0.90, time: p<0.76).
Benito et al. (2012); Spain RCT PEDro=6 Level 1 N=17	 Population: 17 participants - 13 males and 4 females; incomplete SCI; all AIS D; level of injury: C4 – T12; age range= 18 – 60y; mean time since injury: 6.9 months Treatment: Patients were randomized to active rTMS or sham stimulation. Three patients from the initial group of 10 randomized to sham stimulation entered the active rTMS group after a 3-week washout period. Therefore, a total of 10 patients completed each study condition. Both groups were homogeneous for age, gender, time since injury, etiology, and ASIA scale. Active rTMS consisted of 15 days of daily sessions of 20 trains of 40 pulses at 20 Hz and an intensity of 90% of resting motor threshold. rTMS was applied with a double cone coil to the leg motor area. Outcome Measures: LEMS, Modified Ashworth Scale, WISCI II, 10MWT, Step length and cadence (assessed during 10MWT), TUG. 	1.	There was a significant improvement in LEMS in the active group but not in the sham group. Both the active and sham groups showed significant improvements in TUG scores.

	Population:	1.	Thorowore policida
	 15 participants with incomplete and thoracic SCI (> 6 months since injury) and with 	2. T t k v c g 3. T s s c c r r 4. T r L s	There were no side effects during or after the training. The 6MWT and TUG test improved in both groups, but without significant differences between groups. There was no significant effect of patients' stratification depending on ASIA on clinical outcome measure changes (all p>0.1). The significant predictors of recovery were the LEMS, age, and time since injury (all p<0.0001).
	spasticity; 6 males and 9 females; mean (± SD) age 38 (± 9); level of injury T3 (n=3), T4 (n=1), T5 (n=3), T6 (n=1), T7 (n=1), T8 (n=2), and T9 (n=4); AIS C (n=6) and AIS D (n=9); and mean (± SD) time since injury 10 (± 4) months.		
	 25 matched-SCI persons with spasticity; 11 males and 14 females; mean (± SD) age 44 (± 14); level of injury T3 (n=4), T4 (n=2), T5 (n=3), T6 (n=6), T7 (n=2), T8 (n=4), T9 (n=2), T10 (n=2); AIS C (n=12) and AIS D (n=13); and mean (± SD) time since injury 12 (± 3) months. 		
	Treatment: Participants were divided into:		
<u>Naro et al. (2022);</u> Italy	 Robot-assisted rehabilitation (RAR) + non- invasive brain stimulation (NIBS) group (n=15) (RAR + NIBS). 		
Case control Level 3	 RAR – NIBS group (n=25): Matched-SCI persons who previously underwent the same amount or RAR without NIBS. 		
N=40	Patients were provided with a daily (six sessions weekly) NIBS session followed by a RAR session, for eight consecutive weeks.		
	 NIBS consisted of a rTMS carried out simultaneously with a transvertebral direct current stimulation (tvDCS). 		
	 Patients performed a 40-min session per day of RAR with LokomatPro. The amount of BWS was initially set at 70% of the patient's weight, then progressively decreased, and the gait speed was individually adjusted. 		
	Patients underwent conventional physical therapy twice a day and five-times a week using the Bobath principles, occupational therapy, and FES.		
	Outcome Measures: 6MWT, 10MWT, TUG, WISCI II, FIM-L, and LEMS were assessed at baseline (TO), after (T1), and three months after (T2) the training.		

Few studies have investigated the effects of rTMS on gait, balance, and strength outcomes in patients with acute or subacute SCI (<u>Benito et al. 2012</u>; <u>Krogh et al. 2021</u>; <u>Naro et al. 2022</u>). Krogh et al. (<u>2021</u>) compared 22 min of active or sham application of rTMS immediately before training sessions, which consisted of lower limb resistance training (twice a week) and lower limb physical therapy (thrice a week) in 20 participants with motor-incomplete and acute SCI. After 4

weeks of training, LEMS improved significantly more in the active group; meanwhile, both groups improved in the TUG test, 6MWT and 10MWT (<u>Krogh et al. 2021</u>). Benito et al. (2012) showed that after 15 consecutive rTMS sessions applied before overground gait training in patients with subacute and motor incomplete SCI there were significant improvements in LEMS and 10MWT in the rTMS group, though both groups showed similar improvements in standing balance (TUG).

It should be noted that rTMS seems to be safe; however, there were some side effects during the trials. Krogh et al. (2021) reported that one patient in the real stimulation group dropped out due to a seizure during stimulation and two participants in the sham stimulation group reporting mild and transitory headaches following their first treatment session. Benito et al. (2012) stated that all participants tolerated the intervention, with the participants in real rTMS reported only mild undesired effects (slightly uncomfortable twitching of facial muscles during real rTMS [n=6]).

The case control of Naro et al. (2022) was the first study assessing both rTMS and tvDCS (namely non-invasive brain stimulation [NIBS]) with robot-aided rehabilitation. Forty participants with incomplete thoracic SCI were retrospectively divided based on whether they received a daily NIBS intervention before BWSTT or only BWSTT (Naro et al. 2022). After 8 weeks of training and at 3 months follow-up assessment, both groups improved in gait-related (10MWT, 6MWT, WISCI II and FIM-L), strength-related (LEMS), balance-related (TUG), and spasticity-related (Modified Ashworth Score) outcomes; but walking speed, FIM-L, strength and walking ability were found to have more significant increases following robot-assisted rehabilitation + NIBS compared to robot-assisted rehabilitation alone (Naro et al. 2022). However, this combined approach and its promising data need to be confirmed with more extensive RCTs incorporating objective clinical and neurophysiological measures of corticospinal and spinal excitability.

Conclusions

There is level 1 evidence (from 1 RCT: <u>Krogh et al. 2021</u>) that the application of rTMS immediately before lower limb training sessions provides significant improvements in LEMS, but similar improvements in walking-related outcomes (TUG test, 6MWT and 10MWT) compared with the same intervention but with a sham rTMS application in participants with motor-incomplete and acute SCI.

There is level 1 evidence (from 1 RCT: <u>Benito et al. 2012</u>) that rTMS before overground locomotor training provides significant improvements in lower limb strength (LEMS) and walking speed (10MWT); however, may not afford further benefits in dynamic balance (TUG) over overground locomotor training alone (with sham stimulation) in patients with motorincomplete and subacute SCI.

There is level 3 evidence (from 1 case control study: <u>Naro et al. 2022</u>) that the addition of rTMS plus tvDCS to BWSTT with Lokomat provides significantly more improvements in walking speed (10MWT), FIM-L, strength (LEMS) and walking ability (WISCI II) in comparison with BWSTT alone, but not in walking endurance (6MWT) and balance (TUG) in patients with incomplete and subacute SCI with spasticity.

rTMS and NIBS combined with locomotor or exercise training do not seem to provide more benefits in standing balance and walking function than exercise alone in patients with SCI; however, they may provide positive effects on lower limb strength.

4.6 Emerging Experimental Approaches

Greater understanding of the mechanisms underlying locomotor pattern generation, neuroplasticity, and motor recovery naturally leads to the development of new experimental approaches for improving locomotor function and balance following SCI. The usage of technology in rehabilitation and in medicine is increasing generally. In this section, we highlight some innovative emerging experimental approaches that have been studied in people with SCI.

4.6.1 Whole-Body Vibration (WBV)

Whole-body vibration (WBV) can be defined as standing or training on a vibrating platform, which transmits sinusoidal oscillations to the whole body via feet (<u>Cardinale & Bosco 2003</u>).

Alashram et al. (2019) conducted a systematic review to examine the effects of WBV training on motor impairments among patients with neurological disorders. The authors assessed 20 studies and concluded that there was weak evidence for a positive effect of short-term WBV training on spasticity of lower limbs, balance, and postural control, as well as any long-term benefits in mobility in patients with neurological disorders (Alashram et al. 2019). In addition, optimal WBV training parameters to treat patients with neurological disorders remain unclear (Alashram et al. 2019). It should be noted that the RCT of Bosveld and Field-Fote (2015) was the only study with participants with SCI included in this systematic review.

Author Year Country Research Design Score Total Sample Size	Methods	Outcome
In et al. (2018);	Population: 28 participants with cervical	 Both groups showed
Republic of Korea	(level C6 or C7) SCI; 19 males and 9 females;	significant improvements in
RCT	mean age 48 years; AIS D; and mean time	balance and walking ability. There were significant
<u>PEDro=7</u>	since injury 14 months.	differences between the
Level 1	Treatment: All patients were randomly	WBV and control groups for
N=28	assigned to two groups:	the changes in postural

Table 17. Whole-Body Vibration (WVB)

 WBV group (n=14): Participants received 16 min of WBV training, twice a day, 5 days a week for 8 weeks. The frequency was set at 30 Hz, and a vertical displacement was 2–4 mm. Patients were required to stand on the platform and were instructed to hold a semi-squatting position. WBV training consisted of four sets of 45 s of stimulation, and a minute break between each session. 	sway length (p=0.045 with eyes open and p=0.014 with eyes closed), TUG (p=0.016), and 10MWT (p=0.005); which were bigger in the experimental group than in the control group.
 Control group (n=14): Participants received the same WBV procedure but without vibration (placebo). 	
Both groups were treated with a conventional physical therapy protocol consisting of range of motion and mat exercises, and gait training for 30 min per day.	
Outcome Measures: Postural imbalance (analyzed based on PS length using a force plate device) and walking ability (by TUG and 10MWT) were assessed at baseline and at post training.	

One good quality RCT found that a WBV 8-week training program had a significant effect on walking speed (10MWT) and standing balance (TUG test and postural sway length) in patients with cervical and chronic SCI (<u>In et al. 2018</u>). It should be noted, however, that the control group participants also made significant improvements with range of motion training, mat exercises, and walking practice over the same period, though their gains were not as great as the WBV group.

Of note, in a meta-analysis of patients with stroke, Zeng et al. (2024) found that WBV demonstrated significant reductions in spasticity (SMD=-0.33, 95% CI =-0.61 to -0.06, p=0.02), improvements in motor function (SMD=0.39, 95% CI = 0.16 to 0.61, p<0.01), and enhancements in balance function (SMD=0.28, 95% CI = 0.09 to 0.47, p<0.01) but not in gait. In their subgroup analyses, Zeng et al. (2024) determined that WBV protocols differed; variable frequency vibration and side-alternating vibration reduced spasticity and improved motor and balance functions, while fixed frequency vibration and vertical vibration did not.

Conclusions

There is level 1 evidence (from 1 RCT: <u>In et al. 2018</u>) that a period of a minimum of four weeks of WBV training could have beneficial effects on walking speed and on standing balance in patients with chronic and motor-incomplete SCI.

There is some evidence that WBV could improve walking speed and standing balance in people with chronic and incomplete SCI.

4.6.2 Acute Intermittent Hypoxia (AIH) to Augment Standing Balance

Acute intermittent hypoxia (AIH) refers to brief (acute), repetitive (intermittent) episodes of breathing oxygen-deprived air (hypoxia) alternating with breathing ambient room air (<u>Tan et al.</u> 2020). AIH is a novel, noninvasive means to induce spinal plasticity, strengthening spared pathways to motoneurons after incomplete SCI (<u>Hayes et al. 2014</u>). Previously, studies have shown AIH triggers rapid mechanisms of neuroplasticity and improves respiratory and non-respiratory motor function in rats with cervical SCI; recent studies have provided foundational support that AIH also induces improvements in breathing capacity, lower limb, and upper limb function in people with SCI (<u>Tan et al. 2020</u>).

Author Year Country Research Design Score Total Sample Size	Methods	Outcome
Navarrete-Opazo et al. (2017a); Chile RCT PEDro=4 Level 2 N=35	 Population: 35 participants with chronic and incomplete SCI; 31 males and 4 females; mean (± SD) age 41 (± 17) years; injury level C4 (n=1), C5 (n=3), C6 (n=6), C7 (n=2), T1 (n=1), T3 (n=2), T4 (n=1), T6 (n=3), T9 (n=3), T10 (n=1), T12 (n=4), L1 (n=3), L3 (n=3), L4 (n=1); AIS C (n=13) and AIS D (n=22); and mean (± SD) time since injury 53 (± 40) months. Treatment: Participants were randomly allocated into two groups: Experimental group (n=18): The intermittent hypoxia (IH) protocol consisted of 90sec of 9% O₂ interspersed with 90 sec of 21% O₂, 15 times a day, for 5 consecutive days, followed by IH three times per week for 3 additional weeks. Control group (n=17): The placebo protocol consisted of 	 The interventions were well tolerated by all participants with no side effects being reported. Within-group and between- group comparisons showed that exposure to IH elicits a greater decrease in TUG time in IH group at all assessment points, but without significant differences (p>0.05).

Table 18. Acute Intermittent Hypoxia (AIH)

	continuous normoxia (Nx) (21% O ₂) for 45 min for 5 consecutive days followed by three times per week for 3 weeks. Following the IH/Nx protocol, all participants performed BWSTT for 45 min (for 5 consecutive days the first week and 3 times per week for 3 additional weeks). Outcome Measures: 10MWT, 6MWT,	
	and TUG were assessed at baseline, day 5, weekly from weeks 2–4, and at a 2- week follow-up.	
Navarrete-Opazo et al. (2017b); Chile RCT PEDro=4 Level 2 N=35	 Population: 35 participants with chronic and incomplete SCI; 31 males and 4 females; mean (± SD) age 41 (± 17) years; injury level C4 (n=1), C5 (n=3), C6 (n=6), C7 (n=2), T1 (n=1), T3 (n=2), T4 (n=1), T6 (n=3), T9 (n=3), T10 (n=1), T12 (n=4), L1 (n=3), L3 (n=3), L4 (n=1); AIS C (n=13) and AIS D (n=22); and mean (± SD) time since injury 52 (± 40) months. Treatment: Intervention protocol was described above in (Navarrete-Opazo et al. 2017a). Outcome Measures: Standing and dynamic balance was tested by the APDM Mobility Lab at baseline and at post-intervention: Instrumented sway (standing balance): Participants were instructed to maintain an upright standing position with arms crossed on the chest and heel-to-heel distance fixed at 10cm for 30 s. The instrumented sway measures included in this study were (1) normalized jerk: smoothness of sway from the time derivative of the lumbar's acceleration (normalized to the range of the sway trajectory's excursion and duration), and (2) root-mean-square of sway (m x s²) of the sway trajectory. Instrumented TUG test (dynamic balance): (1) duration of a 180° turn (s), (2) number of 	 The interventions were well tolerated with no side effects being reported. Standing balance: There were no significant within-group MDs in jerkiness and absolute values of root-mean-square of sway in either group. There were also no significant differences between groups. Dynamic balance: Within-group comparisons showed that participants receiving IH plus BWSTT significantly reduced their median turning duration and turn-to-sit duration compared with baseline, whereas no significant change was observed in participants receiving Nx plus BWSTT. Between-group median comparison showed that the IH plus BWSTT group had a significantly faster turning duration and turn-to-sit duration than the Nx plus BWSTT group. Within-group comparisons showed that participants receiving IH plus BWSTT significantly faster turning duration and turn-to-sit duration than the Nx plus BWSTT group. Within-group comparisons showed that participants receiving IH plus BWSTT significantly reduced their median number of steps compared with baseline, whereas no significant change was observed in participants

steps in a turn, and (3) turn-to- sit duration (s) were assessed.	receiving Nx plus BWSTT. Between-group median comparison showed there was a mild, although statistically significant, greater median number of steps in the IH plus BWSTT group compared with the Nx plus BWSTT group.
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Two RCTs testing the effects of AIH on standing balance have been conducted in people with chronic incomplete SCI (albeit using the same participants and protocol in both studies; <u>Navarrete-Opazo et al. 2017a</u>; <u>Navarrete-Opazo et al. 2017b</u>). Navarrete-Opazo et al. (2017a) found that daily AIH, along with BWSTT, elicited a greater walking speed and endurance, but not up-and-go time, compared with the sham intervention plus BWSTT. Navarrete-Opazo et al. (2017b) found that daily intermittent hypoxia (IH), along with BWSTT, elicited a faster turning duration, cadence during a 180 turn, and turn-to-sit duration, but not changes in standing balance measures (normalized jerk and root-mean-square instrumented sway parameters), compared with the sham protocol plus BWSTT.

Other studies have shown that a single AIH treatment enhances motor behaviors important for functional walking (Tan et al. 2020) and lower limb strength (Trumbower et al. 2012; Tan et al. 2020; Lynch et al. 2017; Sandhu et al. 2019). Despite the potential for AIH as a treatment for SCI, further research is necessary to understand the treatment's enduring effects in a large cohort of people with SCI (Tan et al. 2020). Several studies involving animal models and non-SCI humans show IH protocols that involve less than 9% oxygen concentration and episodes that exceed 48/day result in serious pathologies across multiple physiological systems simultaneously (Tan et al. 2020). Thus, moving toward clinical translation will require careful consideration of AIH devices and delivery methods that prevent administration of more severe protocols (Tan et al. 2020).

Conclusions

There is level 2 evidence (from 2 RCTs: <u>Navarrete-Opazo et al. 2017a</u>; <u>Navarrete-Opazo et al.</u> <u>2017b</u>) that an IH protocol followed by BWSTT produces a greater walking speed and endurance, and a faster turning duration, but not up and go time, or changes in standing balance measures compared with a sham intervention followed by BWSTT; in patients with incomplete and chronic SCI.

Limited evidence shows that AIH has the potential to improve walking capacity (walking speed and walking endurance), but not standing balance, in people with incomplete and chronic SCI.

Further research is necessary to understand the treatment's safety limitations as well as enduring effects in larger and better controlled studies in people with SCI.

4.6.3 Eccentric Resistance Exercise Using the Eccentron

The Eccentron (BTETech, Hanover, MD, USA; see figure 3 is a motor driven eccentric stepper; and could be an ideal modality for those with incomplete SCI (<u>Stone et al. 2019</u>). Originally designed to train older adults, athletes, or those who have had cardiopulmonary complications, the Eccentron delivers a controlled and measurable negative muscular overload (<u>Stone et al. 2019</u>). Training on the Eccentron allows a person with incomplete SCI to bilaterally work the limbs and visually track the accuracy of force production during repetitions (<u>Stone et al. 2019</u>). The Eccentron may assist in concurrently improving lower extremity muscle strength and reciprocal limb activation, both of which may improve ambulatory function (<u>Stone et al. 2019</u>).



Figure 3. The Eccentron. From <u>www.btetechnologies.com</u>

Author Year Country Research Design	Methods	Outcome
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Table 19. Eccentric Resistance Exercise Using the Eccentron

Score Total Sample Size			
Stone et al. (2019); USA Pre-post Level 4 N=11	 Population: 11 participants; 7 males and 4 females; mean (± SD) age 39.0 (± 15.9) years; AIS B (n=4), AIS C (n=4), and AIS D (n=3); level of injury cervical (n=6), thoracic (n=4) and lumbar (n=1); and mean (± SD) time since injury 9.5 (± 4.7) years. Treatment: Participants trained twice a week for 12 weeks on an eccentrically biased recumbent stepper (Eccentron), which targets the gluteal, hamstring, and quadriceps muscles. Participants started training at 50% one-repetition maximum (intensity was individually adjusted) for 2 to 3 sets of 8 repetitions at 12 rpm. Outcome Measures: SCIM, TUG, 10MWT, and WISCI II during 10MWT were assessed at baseline, after 6 weeks, and after 12 weeks. Daily step physical activity on four consecutive days was also assessed. 	1. 2. 3.	There were no AEs or elevated pain associated with the eccentric resistance training. There was a significant (p=0.034) eccentric resistance training effect on TUG performance from pre-test (158.36 \pm 165.84 s) to post-test (56.31 \pm 42.42 s). Participants did not improve total SCIM scores from pre- test to post-test (F (1.22, 12.20) = 0.87, MSE = 33.14, p=.20), nor on mobility subscale of SCIM (F (1.66, 16.56) = 2.75, P=0.10).

Stone et al. (2019) assessed 11 participants with chronic SCI who performed an eccentric resistance training program for 12 weeks. For the training program, an eccentrically biased recumbent stepper (i.e., Eccentron, which targets the gluteal, hamstring, and quadriceps muscles) was used for training twice a week, with an intensity of 50% one-repetition maximum and a dosage of 2-3 sets of 8 repetitions at 12 rpm (Stone et al. 2019; Stone et al. 2018). Participants significantly improved their walking speed (10MWT), walking ability (WISCI II) and standing balance (TUG test) from baseline to 6 weeks to 12 weeks post-training (Stone et al. 2019). It should be noted that the improvement in 10MWT performance across the intervention was positively correlated with the change identified in daily step physical activity (Stone et al. 2019). Lower limb eccentric and isometric strength also improved; however, daily step physical activity remained unchanged (Stone et al. 2018).

Conclusions

There is level 4 evidence (from 1 pre-post study: <u>Stone et al. 2019</u>) that an eccentric resistance training program for the lower limbs, using the Eccentron device, performed twice a week for 12 weeks with an intensity of 50% one-repetition maximum improves standing balance, walking speed, walking ability, and isometric and eccentric strength, but not daily step physical activity on participants with chronic SCI.

An eccentric resistance training program for the lower limbs, using the Eccentron device, provides improvements in walking function, lower limb strength in participants with chronic SCI, but further high-quality studies need to be performed to confirm these promising effects.

4.6.4 Underwater Treadmill Training (UTT)

Underwater treadmill training (UTT) is largely unexamined as a means of improving walking performance and balance in people with SCI (<u>Morgan & Stevens 2024</u>). Primarily used in animal rehabilitation and sports medicine facilities, this water-based therapy to improve mobility and physical function in persons with neurological disease is new and innovative (<u>Morgan & Stevens 2024</u>). The use of a treadmill submerged in a self-contained, water-filled tank allows for the precise control of water depth, walking speed, and water temperature, a trio of variables that can markedly influence training responses (<u>Stevens et al. 2015</u>).

Author Year Country Research Design Score Total Sample Size	Methods		Outcome
	Population : 7 males and 5 females; average age 47.7y; >1y post injury; AIS C and D.	1.	Participants improved in leg strength (57%), balance (39%), preferred walking speed (34%),
<u>Stevens et al.</u> (2015); USA Pre-post Level 4 N=11	Treatment : Participants completed 8 weeks (3 × /week) of UTT. Each training session consisted of three walks performed at a personalized speed, with adequate rest between walks. BWS remained constant for each participant and ranged from 29 to 47% of land body weight. Increases in walking speed and duration were staggered and imposed in a gradual and systematic fashion.		rapid walking speed (34%), rapid walking speed (61%), 6MWT (82%), and daily step activity (121%) following UTT.
	Outcome Measures: Lower-extremity strength, balance (BBS), preferred and rapid walking speeds, 6MWT, and daily step activity.		
<u>Marinho-Buzelli</u> <u>et al. (2019);</u>	Methods: To assess the influence of the aquatic environment on quasi-static	1.	Larger medians of CoP in water than on land for all participants.

Table 20. Underwater Treadmill Training (UTT)

Canada Case series Level 4	posture by measuring CoP sway and trunk acceleration parameters after incomplete SCI in water and on land.	2.	Participants with low dynamic gait used power wheelchair mobility.
N=6	Population: 6 participants with incomplete SCI (4 cervical/2 thoracic injuries, AIS D) were enrolled. Mean age = 56.8 years. 2F;4M.	3.	Perception of balance improved over time for participant 2.
	Treatment: Participants stood on a waterproof force plate for one minute per trial on land and in water; participants completed testing with their eyes open or closed in random order over 10 trials.		
	Outcome Measures: Baseline balance was assessed by the BBS and Mini- BESTest, CoP sway and trunk acceleration,		

Treadmill training performed in a water environment has been shown to serve as an effective alternative or support to land-based physical activity and walking programs in adults who experience balance problems and lower-limb muscle weakness (Stevens et al. 2015); however, there is limited research on this intervention for persons with SCI. Stevens et al. (2015) found significant gains (p<0.05) of moderate to large magnitude in leg strength (57%), balance (39%), preferred and rapid walking speed (34% and 61%, respectively), 6-min walk distance (82%), and daily step activity (121%). In a small case series study, the majority of individuals reported that water felt like a safer environment in which to stand (although most participants perceived that they swayed more in water, in contrast to on land) (Marinho-Buzelli et al. 2019).

Although more research is needed, mainly because the sample size and quality of studies were low; the use of smaller, portable underwater treadmills may also extend the accessibility of UTT beyond the research environment and into public fitness settings to enhance ambulatory status and physical function in people with SCI and other severe neuromuscular disorders (Morgan & Stevens 2024).

Conclusions

There is level 4 evidence (from 1 pre-post study: <u>Stevens et al. 2015</u>) that eight weeks of UTT provides significant gains of moderate to large magnitude in leg strength, balance, preferred and rapid walking speed, 6MWT, and daily step activity in participants with incomplete and chronic SCI.

UTT could be an interesting and helpful alternative approach to dry land BWSTT for improving walking performance, standing balance, and lower limb strength in people with SCI; however, further high-quality studies need to be performed to confirm these promising effects.

4.6.5 Robot-Aided Ankle Rehabilitation

Ankle rehabilitation plays an important role as it aims at stemming drop foot consequences in weakened lower limb muscles, which affects static and dynamic balance and gait performance negatively and favors the recovery of stepping ability (<u>Calabró et al. 2021</u>). Improving ankle functionality requires targeting the ranges of motions (i.e., plantar/dorsiflexion, inversion/eversion, and abduction/adduction) and the ankle plantar and dorsiflexion muscle strength, and perceptual abilities and proprioceptive capacity of the ankle (<u>Calabró et al. 2021</u>). Therefore, it is possible to minimize the risk of falls and enhance walking speed and efficiency; thus, the adoption of an intensive and task-oriented motor practice is essential (<u>Calabró et al. 2021</u>).

Nevertheless, little evidence is available concerning the efficacy and neurophysiological underpinning of robot-aided ankle rehabilitation in persons with SCI compared to conventional physiotherapy (<u>Calabró et al. 2021</u>). Thus, a pilot study was conducted to assess the neurophysiological underpinnings and the efficacy in improving gait performance and balance of robot-aided ankle rehabilitation using the ankle rehabilitation platform-robot Hunova® (Movendo Technology, Genoa, Italy) (<u>Calabró et al. 2021</u>).

Author Year Country Research Design Score Total Sample Size	Methods	Outcome
<u>Calabró et al.</u> <u>(2021);</u> Italy Case control (pre-	 Experimental group (n=10): Participants with SCI and at least a palpable or visible contraction of 	 None of the participants reported any side effects during the rehabilitative sessions.
post for the experimental group and retrospective for the control [matched group])		 2. There were more significant improvements in experimental group than control group for: a. 10MWT: Experimental group from 0.43 ± 0.11 to

r		
Level 3 N=20	(n=1); AIS C (n=5) and AIS D (n=5); and mean (± SD) time since injury 8 (± 4) months.	0.51 ± 0.09 m/s, p=0.006; control group from 0.4 ± 0.13 to 0.45 ± 0.12, p=0.01;
	 Control group (n=10): Participants who previously underwent conventional ankle rehabilitation were retrospectively matched: 5 males and 5 females; mean (± SD) age 39 (± 7) years; level of injury C5 (n=1), C6 (n=2), T1 (n=1), T2 (n=2), T5 (n=2), T6 (n=1), and T9 (n=1); AIS C (n=4) and AIS D (n=6); and mean (± 	group-comparison p=0.006. b. 6MWT: Experimental group from 231 ± 13 to 274 ± 15 m, p<0.001; control group from 236 ± 13 to 262 ± 15 m, p=0.003; group- comparison p=0.01. c. TUG: Experimental group
	 SD) time since injury 9 (± 3) months. Treatment: All persons underwent an intensive treatment (6 days weekly) consisting of FES of lower limb muscles (a daily 30-min session), conventional physiotherapy (two 1-h sessions daily), and occupational therapy (a 1-h session, three times weekly) for 4 weeks. Additionally: The experimental group received robot-aided ankle rehabilitation using Hunova device for a one-hour 	 from 70 ± 18 to 45 ± 15 s, p=0.002; control group from 68 ± 21 to 48 ± 18 s, p=0.01; group-comparison p=0.001. d. SCIM: Experimental group from 53 ± 7 to 38 ± 11, p<0.001; control group from 53 ± 5 to 45 ± 8, p<0.001; group- comparison p<0.001.
	 daily session. The control group underwent an equal amount of conventional ankle rehabilitation. Outcome Measures: SCIM-III; 10MWT; 6MWT; and TUG were assessed at baseline (PRE) and after the trial completion (POST). 	3. Patients belonging to the experimental group showed better stability in static and dynamic balance instrumental testing (Hunova) than the control group concerning both center of pressure root mean square and velocity.

There was one case-control study that evaluated the effects of robot-aided ankle rehabilitation vs. conventional ankle rehabilitation in persons with incomplete SCI using corticomuscular coherence data (Calabró et al. 2021). After 4 weeks of training, there were more significant improvements in the experimental group than in the control group for walking speed (10MWT), walking distance (6MWT), TUG, static and dynamic balance outcomes (confirmed by instrumental assessment: center-of-pressure values), independence in daily living activities (SCIM-III), and muscle activation of dorsal and plantar flexors. These changes were paralleled by widespread modifications in functional synchronization between the sensorimotor cortex and lower limb distal muscles (assessed by the corticomuscular coherence) (Calabró et al. 2021). The potential application of a platform-based robot-aided ankle rehabilitation as a clinical rehab tool for people with incomplete SCI has been suggested, although more studies with larger sample sizes and including a follow-up assessment will be necessary for the implementation of this intervention in clinical practice.

Conclusions

There is level 3 evidence (from 1 case control study: <u>Calabró et al. 2021</u>) that the addition of a robot-aided ankle rehabilitation (in comparison with conventional ankle rehabilitation) to an intensive program consisting of FES of lower limb muscles, conventional physiotherapy and occupational therapy sessions provides more significant improvements on gait performance (10MWT and 6MWT), TUG and other static and dynamic balance outcomes (i.e., center-of-pressure values and corticomuscular coherence) in patients with acute SCI.

Key Points

The addition of a robot-aided ankle rehabilitation to an intensive therapy program seems to improve walking, and static and dynamic balance in patients with acute SCI. However, further high-quality studies need to be performed to confirm these promising effects.

4.6.6 Robotic Upright Stand Trainer (RobUST)

A novel cable-driven robotic upright stand trainer (RobUST) has been designed and validated in adults without SCI to provide trunk perturbations and standing balance assistance-as-needed through trunk and pelvic force fields (<u>Khan et al. 2019c</u>; Luna et al. 2020). RobUST has also been shown to be a potential training device for upright postural control in one individual with SCI, resulting in complete functional independence and the ability to stand and ambulate independently (<u>Santamaria et al. 2021</u>). There have been recent studies providing some evidence for the use of this device in participants with SCI.

Author Year Country Research Design Score Total Sample Size	Methods		Outcome
<u>Bowersock et al.</u> <u>(2023);</u> USA Post-test N=4	Population: N=4 (3 motor complete and 1 incomplete). Mean age: 37.5 years; 3M, 1F; Level of injury: C4 (n=2), T1 (n=1), T2 (n=1). AIS A (n=2), AIS B (n=1), AIS C (n=1).	1.	 Stable standing with force field-free hands was observed in two participant and did not require RobUST FF activation meanwhile the other two needed assistance with trunk control.
	Treatment: RobUST device with aluminum frame with 12 mounted motors and cables that provide controlling forces for		
	participants. Outcome Measures: Motor force, kinematic data, force plates data, ground reaction	2.	Stable standing with RobUST FF and free hands resulted in 8.5% larger weight bearing (d=1.19),

Table 22. Robotic Upright Stand Trainer (RobUST)

	forces, trunk displacement, and EMG of trunk and lower limb muscles		larger trunk mean velocity (d=0.96), and larger activation of representative trunk muscles.
Bowersock et al. (2024); USA Post-test N=5	 Population: N=5, all motor complete. Mean age: 35 years 4M, 1F Level of injury: C4 (n=3), C7 (n=1), T2 (n=1) AIS: AIS A (n=2), AIS B (n=3) Treatment: total of 16 hands-on and 16 free-hand perturbations were attempted. RobUST trunk motors exerted a low-level constant force (30 N) that provided appropriate cable tension to remove any slack in the cables before perturbations without hindering or promoting trunk movement. Perturbations were characterized by a trapezoidal force with 0.15 sec rise time, 0.8 sec constant time, and 0.15 sec fall time. Perturbation magnitude was selected during an acclimation session and was relative to the participant's body weight. Perturbation magnitudes equal to 10, 15, and 20% BW. Outcome Measure: Successful perturbation control, motor force, trunk kinematic data, force plate data, and EMG. 	1.	Lower limb postural responses were generally more frequent, larger in magnitude, and appropriately modulated during the free-hands condition. This was associated with trunk displacement and lower limb loading modulation that were larger in the free- hands condition.
Rejc et al. (2024a); USA Pre-post Level 4 N=6	Population: Six individuals with chronic SCI who were already implanted with a spinal cord epidural stimulation (scES) unit for the recovery of motor function. Mean age: 34.7 years 5M, 1F Level of injury: C3 (n=1), C4 (n=3), C7 (n=1), and T2 (n=1) AIS: AIS A (n=3) and AIS B (n=3) * Prior to enrollment in this study, these individuals had already undergone an average of 112 – 92 overground stand training sessions with Stand-scES using assistive devices (i.e., a standing apparatus or walker) as part of other interventional studies, and had demonstrated the ability to stand with bilateral independent knees extension. Treatment: A novel RobUST with scES, performed with free hands, to restore upright postural control was implemented on average 80±10 training sessions (1 h/day; 5 days/week). Robotic upright postural	1.	Robotic postural training re- enabled and/or largely improved the participants' ability to control steady standing, self-initiated trunk movements and upper limb reaching movements while standing with free hands, receiving only external assistance for pelvic control. These improvements were associated with neuromuscular activation pattern adaptations above and below the lesion. Note: a second <u>Rejc (2024b</u>) study also tested the RobUST and sitting outcomes with the same protocol; neither statistically significant differences nor

training was always performed with Stand- scES in the RobUST frame.	large effect sizes were found.
* The RobUST is a motorized cable-driven device that can provide assistance as needed and deliver controlled perturbation forces at the trunk and pelvis.	
Outcomes Measures: Steady upright postural control and proactive upright postural control (in which self-initiated trunk movements and upper limb reaching movements were attempted while standing) were collected immediately prior to the beginning of robotic postural training (Pre), after 45 – 7 (Mid), and after 80 – 10 robotic postural training sessions.	

Two studies by Bowersock et al. (2023, 2024) provided the foundation for the pre-post study of Rejc et al. (2024a), which included six individuals with chronic SCl who had been implanted with a spinal cord epidural stimulation (scES) unit for the recovery of motor function. The RobUST, a motorized cable-driven device that can provide assistance as needed and deliver controlled perturbation forces at the trunk and pelvis, was used for upright postural training (Rejc et al. 2024a). After an average of 80 sessions, robotic postural training re-enabled and/or largely improved the participants' ability to control steady standing, self-initiated trunk movements and upper limb reaching movements while standing with free hands, receiving only external assistance for pelvic control (Rejc et al. 2024a); but not in sitting balance outcomes (Rejc et al. 2024b). These improvements were associated with neuromuscular activation pattern adaptations above and below the lesion, suggesting that the human spinal cord below the level of injury can generate meaningful postural responses when its excitability is modulated by scES, and can learn to improve these responses (Rejc et al. 2024a). However, longitudinal studies involving more participants and populations with different injury severity are needed to test this hypothesis (Rejc et al. 2024a).

Conclusions

There is level 4 evidence (from 2 pre-post studies: <u>Rejc et al. 2024a</u>; <u>Rejc et al. 2024b</u>) that 80 sessions (1 h/day; 5 days/week) of robotic postural stand training with the RobUST device (a motorized cable driven device that can provide assistance as needed and deliver controlled perturbation forces at the trunk and pelvis), which included periods of standing with steady trunk control, self-initiated trunk and arm movements, and trunk perturbations; re-enables and/or largely improves the participants' ability to control steady standing, self-initiated trunk movements and upper limb reaching movements while standing with free hands, but does not improve sitting balance performance in people with chronic and motor complete tetraplegia who are already implanted with a scES unit for the recovery of motor function.

One small study shows promising effects in the restoration and/or improvement of the ability to control steady standing, self-initiated trunk movements and upper limb reaching movements while standing with free hands (receiving only assistance for pelvic control) after robotic (RobUST) postural stand training in people with chronic and motor complete tetraplegia who were already implanted with a scES; however, further studies with larger sample sizes need to be conducted to assess the safety and confirm these promising effects.

4.6.7 Brain-Spine Interface (BSI)

Although the majority of SCIs do not directly damage the neurons located in the lumbosacral spinal cord, which receive executive commands from the brain in order to walk, the disruption of descending pathways interrupts the brain-derived commands that are necessary for these neurons to produce walking (<u>Arber & Costa 2018</u>; <u>Courtine & Sofroniew 2019</u>). The consequence is permanent paralysis (<u>Lorach et al. 2023</u>).

A spinal cord stimulation system can restore standing and basic walking in people with paralysis due to a SCI (Lorach et al. 2023). However, this recovery requires wearable motion sensors to detect motor intentions from residual movements or compensatory strategies to initiate the preprogrammed stimulation sequences (Rowald et al. 2022). Consequently, the control of walking was not perceived as completely natural; moreover, the participants showed limited ability to adapt leg movements to changing terrain and volitional demands (Rowald et al. 2022).

Recently, Lorach et al. (2023) suggested that a digital bridge between the brain and spinal cord would enable volitional control over the timing and amplitude of muscle activity, restoring more natural and adaptive control of standing and walking in people with paralysis due to SCI.

Author Year Country Research Design Score Total Sample Size	Methods	Outcome
<u>Lorach et al.</u> (2023); Switzerland Case Report Level 5 N=1	Population: One male with incomplete and chronic SCI and able to step with the help of a front-wheel walker; 38 years old of age; injury level C5/C6; and time since injury 10 years. Treatment: The communication between the brain and the region of the spinal cord	1. The BSI was calibrated within a few min with high reliability. This reliability has remained stable over one year, including during independent use at home.

Table 23. Brain-Spine Interface (BSI)

The case report of Lorach et al. (2023) was carried out as part of the ongoing clinical feasibility study STIMO-BSI ('Brain-controlled Spinal Cord Stimulation in Patients with Spinal Cord Injury'), which investigates the safety and preliminary efficacy of brain-controlled spinal cord stimulation after SCI (clinicaltrials.gov, NCT04632290). Before enrolment in the STIMO-BSI study, the participant was implanted with a spinal cord stimulation system, and completed a five-month intensive neurorehabilitation program, followed by a two-year period of independent use at home (Lorach et al. 2023). The results showed that the reliability of the brain–spine interface (BSI) remained stable over one year (including during independent use at home), that the BSI enabled natural control over the movements of the legs of the participant to stand, walk, climb stairs, and traverse complex terrains. Objective improvements were observed in standing balance (BBS and TUG), walking ability (WISCI II), and walking distance (6MWT), and the participant regained the ability to walk with crutches overground even when the BSI was switched off (Lorach et al. 2023). Although these promising results need to be replicated in larger studies,

and broader implementation of such a device will require time and resources, the authors suggest that "the concept of a digital bridge between the brain and spinal cord augurs a new era in the treatment of motor deficits due to neurological disorders" (Lorach et al. 2023).

Conclusions

There is level 5 evidence (from 1 case report study: <u>Lorach et al. 2023</u>) that a brain-spine interface device enables natural control over the movements of the legs to stand, walk, climb stairs and even traverse complex terrains.

Key Points

One case study shows promising effects of natural walking pattern restoration after the implantation of a brain-spine interface in one patient with chronic and incomplete tetraplegia; however, further studies with larger sample sizes need to be conducted to assess the safety and confirm these promising effects.

4.7 Standing Balance Summary

Numerous studies have investigated the effects of different interventions on standing balance function in people with SCI. Although further studies are needed focusing on the standing balance function in people with SCI, taking all the results from this review together and from a clinical perspective:

- The inclusion of VR and/or other biofeedback approaches (e.g., EMG biofeedback or visuotemporal cues) to exercise programs could help in providing significant effects in standing balance in people with SCI, especially in those with chronic injuries.
- Different exercise interventions, especially conventional intensive balance training, taskspecific training (consisting of stepping practice), and walking training programs on a walking track with different surfaces, among others, provide the most positive effects on standing balance or balance confidence for people with SCI, specifically those with motor incomplete and chronic injuries.
- On the other hand, different body-weight supported training interventions (e.g., BWSTT or wearable exoskeleton-assisted training) do not provide higher effects on standing balance function when compared with other approaches (e.g., body-weight supported training interventions, overground walking training interventions, use of KAFOs, or usual care) in people with acute and chronic SCI, and complete/incomplete injuries.
- The application of FES to cycling or BWSTT interventions does not provide larger effects in standing balance in comparison with the same interventions without adding the electrical stimulation in participants with chronic SCI. Similarly, the combination of different neuromodulation approaches, such as tDCS or rTMS, to, mainly, gait training interventions does not provide higher improvements than the same interventions with

sham stimulation in participants with chronic and incomplete SCI, and with acute and incomplete SCI, respectively.

• Promising effects have been shown for standing balance from different novel approaches (such as WBV training, eccentric resistance training program using the Eccentron, UTT, the addition of a robot-aided ankle rehabilitation to an intensive rehabilitation program, robotic postural stand training with the RobUST device, and a brain-spine interface device). However, more research is needed to assess the safety and effectiveness of these interventions in different subpopulations of people with SCI. In addition, these approaches may not yet be available to therapists.

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Abbreviations

2MWT	2-minute walk test
6MWT	6-minute walk test
10MWT	10 meter walk test
AE	adverse event
ABC scale	activities-specific balance confidence scale
ABLE	Activity-based Balance Level
ABT	activity-based therapy
AIH	acute intermittent hypoxia
AIS	ASIA Impairment Scale
ASIA	American Spinal Injury Association
Balance CAT	Balance Computerized Adaptive Test
BBS	Berg Balance Scale
BSI	brain-spine interface
BWS	body-weight support
BWSTT	body-weight supported treadmill training
BWSLT	body-weight supported locomotor training
CB&M	Community Balance and Mobility Scale
CI	confidence interval
CoP	center of pressure
СРТ	conventional physical therapy
DGI	Dynamic Gait Index
EAW	exoskeleton-assisted walking
EMG	electromyography
EMG-ES	electromyography triggered electrical stimulation
FAC	Functional Ambulation Category
FES	functional electrical stimulation
FES-I	Falls Efficacy Scale - International

FIM	Functional Independence Measure
FIST	function in sitting test
FRT	functional reach test
FTSTS	Five Times Sit to Stand Test
iSCI	incomplete spinal cord injury
ISNCSCI	ASIA International Standards for Neurological Classification of Spinal Cord Injury
HR	heart rate
IH	intermittent hypoxia
KAFOs	knee ankle foot orthoses
LEMS	lower extremity motor score
LOS	limit of stability
MCID	minimal clinically important difference
MD	mean difference
MDC	minimal detectable change
mFRT	modified functional reach test
Mini-BESTest	Mini-Balance Evaluation Systems Test
MST	Motor Skill Training
MVC	maximum voluntary contraction
NIBS	non-invasive brain stimulation
Nx	normoxia
PEDro	Physiotherapy Evidence Database
RAGT	robotic-assisted gait training
RAR	robot-assisted rehabilitation
RCT	randomized controlled trial
RoBUST	robotic upright stand trainer
RPE	rate of perceived exertion
rTMS	repetitive transcranial magnetic stimulation
scES	spinal cord epidural stimulation

Sitting and Standing Balance Following Spinal Cord Injury

SCI	spinal cord injury
SCI-FAP	Spinal Cord Injury – Functional Ambulation Profile
SCI-FCS	Spinal Cord Injury – Falls Concern Scale
SCIM	Spinal Cord Independence Measure
SMD	standardized mean difference
tDCS	transcranial direct current stimulation
TUG (test)	Timed Up and Go Test
TSCS	transcutaneous electrical spinal cord stimulation
TSR	task-specific rehabilitation
tvDCS	transvertebral direct current stimulation
UTT	underwater treadmill training
VFBT	visual feedback balance training
VR	virtual reality
WISCI	walking index for spinal cord injury
WPHF-FES	wide pulse/high frequency FES
WVB	whole-body vibration