Research Request – Efficacy of Rehabilitation Training Machines

Brief

Efficacy of Rehabilitation Training Machines (Motomed/Active passive trainer/FES Cycling):

- Evidence of use in populations such as SCI, MS, stroke, Parkinson's disease and cerebral palsy
- Evidence of benefits including health outcomes and carryover into functional benefits
- Dosages trialled and recommended
- Any comparisons made to standard treatment regimes

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Summary

<u>MOTOmed and/or Active Passive Trainer</u>

-Quality of research is generally of medium-high quality across stroke, SCI, Parkinson's disease and cerebral palsy. Although, many studies conclude that further research is needed which included larger controlled samples and utilise consistent outcomes measures and interventions.

-Results vary between conditions as different outcome measures are used, however, there is evidence to suggest that these rehabilitation trainers can increase cardiovascular, musculoskeletal and neurological outcomes.

- Long term health and functional related outcomes were rarely reported. The longest intervention duration reported was 12 weeks

- Dosages vary significantly. On average, studies investigated interventions which lasted 20-30 minutes, 2-3 times a week

-Refer to individual disorders for separate research on MOTOmed and/or Active Passive Trainers

-Very few studies investigated the devices in a home setting

<u>FES cycling</u>

-Quality of research into FES cycling for multiple sclerosis and cerebral palsy was low to very low. There is a paucity of evidence looking at FES cycling for those with Parkinson's disease with only a single subject design study discovered. Stork and spinal cord injury had greater – quality research evidence ranging from medium to high.

-Research from all diseases showed mixed results across cardiorespiratory and functional performance, as well as musculoskeletal and psychological outcomes. For example, some studies found reduced spasticity in those with SCI and others did not. See individual diseases for exact findings.

-Differences in the duration and effort of intervention, as well as outcome measures used led to significant heterogeneity and inability to directly compare results within and between diseases

- Significant variation in dosages ranging from 10-90 minutes, 2-7 times per week over 2 to 24 weeks.

- Long term health and functional related outcomes were rarely reported. The longest intervention duration reported was 24 weeks.

-Very few studies investigated the devices in a home setting

Where possible, conventional exercise training programs are also provided if a systematic review existed on the topic. This allows for some comparison to regular physical therapy interventions that are currently delivered to these cohorts of patients.

1. Efficacy of Rehabilitation Training Machines

1.1 Multiple Sclerosis

1.1.1 MOTOmed and/or Active Passive Trainer

A single randomised controlled trial (RCT) [1] has investigated the effectiveness of a neuro-physiotherapy programme based on feedback cycling for improving gait in patients with multiple sclerosis (MS) using a **MOTOmed device**.

This study included 61 patients with mild to moderate MS. Half performed one 30 minute session per week for three months using the MOTOmed Viva2 Movement Trainer in addition to a personalised exercise program to be completed at home. The control group only received the personalised at home exercise program.

No significant differences in walking speed or cadence (steps per minute) between groups. Intervention group showed statistically significant improvements in Functional Ambulatory Performance (FAP) across all time intervals. Stride length significantly improved in the intervention group across all time intervals and between baseline and final measurement in the control group.

Quality = Medium

- Results suggest that visual biofeedback cycling training may be a viable. However, larger studies are required with different treatment intervals to determine efficacy

An RCT by Barclay et al. (2019) [2] evaluated the feasibility of a progressive, four week lower limb cycling programme using **active passive trainers (APT's)** on spasticity, cardiovascular fitness, function and quality of life in people with moderate to severe MS.

- Intervention group
  - 30 min of APT cycling (2 min passive warm up, 26 min active cycling and 2 min passive cool down)
  - 20 sessions (5 days per week for four weeks in addition to usual care)
- Control group
  -Individualised therapy programme, delivered Monday to Friday
- Performed in a clinical setting

Results

- Average power output, distance cycled and speed improved in the intervention group but this did not translate to statistical changes in the outcome measures.
- Improvements were shown across both groups for physical health and mental health. Effect Size = 0.93 intervention and 0.46 control
- Cardiovascular health = Medium effect size in intervention (0.36) compared to control group (0.07)

Quality = Medium

- Small sample size and intervention group also underwent usual care so difficult to separate effect of the intervention.

1.1.2 FES cycling

Two systematic reviews [3, 4] examining the outcomes of people with MS with mobility impairment following Functional Electrical Stimulation (FES) cycling have been conducted.

Both reviews found that intervention duration ranged from 10-60 minutes, 2-3 times per week over 2 to 24 weeks. The majority were performed in clinical settings (89%). Stimulation parameters for most trials involved a pulse width of 200–300 µ sec at a frequency of 20–50 Hz and a cycling cadence of 10–50 rpm. All stimulated the quadriceps, hamstrings, and gluteal muscle groups, with the exception of one trial.

- **Cardiorespiratory performance** (VO2 max, peak aerobic capacity, peak work rate, power generation) = No improvement
- **Functional performance** (2-min walk test, 25-foot walk test, 10m walk test or 12 item MS walking scale) **=** No significant improvement
- **Musculoskeletal outcomes =** No improvement in lower body strength (knee and hip parameters) or long term improvements in spasticity
  - Significant reduction in spasticity directly post FES
- **Psychological outcomes =** No improvement in Quality of Life (QOL) or mental health scores
  - High levels of participant satisfaction
- **Adverse events =** 10 adverse events reported across studies including skin irritation, increased spasticity, bowel dysfunction and fatigue

Quality – Low

These reviews included studies of low quality (pre-post studies with no control group, retrospective and case studies) and a single RCT which didn't perform blinding or achieve a sufficient sample size which introduces bias and limits generalisability. This precludes any definitive conclusions regarding the efficacy of FES cycling for MS.

1.1.3 Conventional Exercise Training Programs

Two systematic reviews examining the benefits of 'exercise training' in patients with MS have been conducted.

1) Latimer-Cheung et al. (2013) [5] investigated patients with mild-moderate MS and performed a meta-analysis and combined the below interventions;

-Ergometer
-Technogym equipment
-Resistance training with simultaneous electrostimulation
-Static bike
-Plyometric exercises
-Walking
-Balancing
-Stretching
-Swimming

-Treadmill
-Calisthenics
-Yoga
-Therabands

Results

-Consistent and strong evidence that aerobic and resistance exercise performed 2 times per week at a moderate intensity increases physical capacity and muscular strength, respectively.
- Evidence supporting the benefits of exercise on mobility and fatigue is promising, there is insufficient evidence to definitively establish the prescriptive amounts, intensities, or types of exercise to improve these outcomes.
-Not enough good-quality evidence to date supporting the benefits of exercise for improving Health related QOL outcomes.
-No evidence that FES cycling is effective for increasing strength.

Quality – High

Inclusion of high quality RCTs (29/54). Consistent finding and ability to perform a meta-analysis shows homogeneity in outcome measures

2) Edwards et al. (2017) [6] investigated studies which included participants with severe MS (severe mobility issues). The number of studies were limited compared to those which investigate mild-moderate MS.

Results

Mixed results across all outcomes for all treatment types

- **Conventional exercise training:** no statistically significant improvements in any of the outcomes
- **Conventional resistance exercise training**
  -Significant improvements in muscular strength, muscle endurance, balance, fatigue symptoms, and QOL when combined with neuromuscular electrical stimulation
- **Bodyweight support treadmill training**
  -Mixed results (some positive others no change) across outcomes on level of disability, knee extensor strength, walking, endurance, walking speed, gait kinematics, balance and agility, fatigue, QOL
- **Total body recumbent stepper training (one study)**
  -No change in disability or physical function reported. Fatigue significantly reduced after the intervention.

Quality – Medium

Significant heterogeneity led to **inability to perform meta-analysis.** Further research is necessary to determine the most efficacious and effective exercise approaches for individuals with MS with severe mobility disability due to the limited amount of quality evidence

Table 1					
Author (year) and country	**Study aim**	**Method/participants characteristics**	**Treatment/Intervention/ Setting**	**Outcome/summary**	**Quality of evidence** **Low/Medium/ High**
Multiple Sclerosis					
Hochspung et al. (2017) [1]	To analyse the effectiveness of a neuro-physiotherapy programme based on feedback cycling for improving gait in patients with MS.	**RCT (double-blind)** 61 patients with mild to moderate MS Inclusion criteria: (*1*) referral by neurologist (*2*) diagnosis of definite MS according to the McDonald criteria at least 2 years previously; (*3*) EDSS score between 2 and 6 (*4*) age between 20 and 70 years; (*5*) clinical stability during the 3 months previous to recruitment; (*6*) no cognitive impairment according to the	-During the study period, none of the participants received other types of physiotherapy. **Intervention group** - stationary bicycle with a coordination feedback programme to work on lower limb strength asymmetry using 75% of the maximum resistance - one 30-minute session per week for 3 months using the MOTOmed Viva2 Movement Trainer - personalised exercise programme to be completed at home **Control group** - personalised exercise programme to be completed at home	No significant differences in walking speed or cadence were observed between stages in any of the groups **Functional Ambulatory Performance (FAP)** - intervention group showed statistically significant changes between stages 0 and 1 ($P < .014$) and between stages 0 and 2 ($P < .002$) - no such differences were observed in the control group **Stride length** - significant differences in stride length between stages 0 and 2 ($P < .001$) and between stages 1 and 2 ($P < .002$) - controls only displayed significant differences in stride length between stages 0 and 2 ($P < .004$)	**Medium** -Lack of follow-up and the small size prevent generalisation of results. -Significant improvements only in FAP and stride length -12 sessions not enough for long term results -Results show that visual biofeedback cycling training may be a viable, effective treatment in patients with MS but larger studies are required.

		Mini-Mental State Examination			
Barclay et al. (2019) [2]	To evaluate the feasibility of a progressive, four week lower limb cycling programme using **active passive trainers (APT's)** on spasticity, cardiovascular fitness, function and quality of life in people with moderate to severe MS.	**Randomised Trial** not powered to show statistically significant changes Inclusion: (a) Confirmed diagnosis of MS, (b) aged over 18, (c) expanded Disability Status Scale (EDSS) of between 6.0 and 8.5. Exclusion: (a) Significant cognitive impairment, (b) co-morbidities which would preclude them taking part in exercise, (c) visual Impairment, (d) unable to be seated appropriately in a wheelchair for 30 min.	**Clinic setting** **APT group (intervention)**: - 30 min of APT cycling (2 min passive warm up, 26 min active cycling and 2 min passive cool down) -20 sessions (Five days per week for four weeks in addition to usual care) **Usual care:** Individualised therapy programme, delivered Monday to Friday, and could include PT, OT, SLT and Psychology.	15 intervention and 9 control -Improvements were noted in the majority of outcome measures, although no statistically significant group differences were found. -The average power output, distance cycled and speed improved in the intervention group but this did not translate to statistical changes in the outcome measures. -lack of objective change in spasticity -Improved walking speed in 7/16 participants in the intervention group compared to 2 in the control Improvements were shown across both physical health (PH) and mental health (MH). ES = 0.93 intervention and 0.46 control Medium effect in intervention (0.36) for cardiovascular health and negligible (0.07) for control	**Medium** -Small sample -Very few clinical or significant effects -Intervention group also underwent usual care so difficult to separate effects of the intervention from the intensive therapy
Scally et al. (2020) [3]	To systematically examine the outcomes of people with MS with mobility impairment	**Systematic Review** (1) human participants with definite diagnosis of MS	Intervention duration ranged between 2 and 24 weeks 8 studies in clinic setting 1 in home	**Cardiorespiratory performance** **Functional performance** -No significant changes in 2-min walk test, 25-foot walk test, 10m walk test or 12 item MS walking scale	**Low** Low quality (study design and sample sizes) of the literature base precludes any

	following **FES cycling** intervention.	(2) aged 18 years and over (3) average EDSS 6.0 or above, or an equivalent mobility impairment (4) evaluate FES cycling as an intervention study 5 pre-post studies with no control group, 2 randomised controlled trials (RCTs), 1 retrospective study and 1 case study.	Average 2-3 sessions per week Min 10-60 minutes per session	**Musculoskeletal outcomes** -No improvement in lower body strength (knee and hip parameters) - Significant reduction in spasticity directly post FES - No long term improvements in spasticity **Psychological outcomes** -No improvement in QOL or mental health scores **Adverse events** 10 adverse events reported across studies including skin irritation, increased spasticity, bowel dysfunction and fatigue	definitive conclusions regarding the efficacy of FES cycle training in improving cardiovascular health in MS and higher EDSS scores. RCT's did not blind participants or providers and not sufficient power to detect a difference. FES cycle training appears to be well tolerated in MS with mobility impairment, with no serious adverse events.
Pilutti et al. (2019) [4]	Summary of the current evidence for FES cycling as an exercise training modality in persons with MS	**Systematic Review** Acute and chronic FES cycling as an exercise modality in persons with MS 8 included studies, only 1 RCT Samples were small (n = 1–14) participants had	Intervention -Durations ranged between 2 and 24 weeks -Sessions delivered 2–3×/ week for between 10 and 60 min/session. -Stimulation parameters for most trials involved a pulse width of 200–300 μ sec at a frequency of 20–50 Hz and a cycling cadence of 10–50 rpm. -All stimulated the quadriceps, hamstrings, and	**Safety and tolerability** -Preliminary evidence supports the safety and tolerability of FES cycling exercise Acute effects -Studies support the potential for modification of muscle spasticity, cycling kinematics, and cardiorespiratory metabolism with single sessions of FES cycling - Acute benefits may, with chronic exposure to FES cycling, result in long-term adaptations Chronic effects - potential for strength adaptations with	**Low** limited but promising evidence for the application of FES cycling exercise among persons with MS who have moderate-to-severe disability. High-quality RCTs of FES cycling exercise are now needed to establish the safety and efficacy of this promising modality

		Moderate-to-severe disability (EDSS range reported = 4.0–7.5).	gluteal muscle groups, with the exception of one trial	FES cycling likely depends on the specific muscle groups that are peripherally Stimulated - changes in body composition in response to FES cycling exercise in persons with MS are unclear - no effect of FES cycling delivered between 2 and 24 weeks on spasticity -No improvements in QOL -High levels of participant satisfaction	for people living with MS
Latimer-Cheung et al. (2013) [5]	To conduct a systematic review of evidence surrounding the effects of **exercise training** on physical fitness, mobility, fatigue, and Health related quality of life in adults with multiple sclerosis (MS).	**Systematic Review** Both randomised and non-randomised studies included (29 high level RCT) Diagnosis of MS (mild-moderate) Focus on: fitness, mobility, fatigue or health related quality of life benefits	Clinic and Home -Ergometer -Technogym equipment -Resistance training with simultaneous electrostimulation -Static bike -Plyometric exercises -Walking -Balancing -Stretching -Swimming -Treadmill -Calisthenics -Yoga -Therabands	54 included studies There was consistent and strong evidence that aerobic and resistance exercise performed 2 times per week at a moderate intensity increases physical capacity and muscular strength, respectively. While the evidence supporting the benefits of exercise on mobility and fatigue is promising, there is insufficient evidence to definitively establish the prescriptive amounts, intensities, or types of exercise to improve these outcomes. There is not enough good-quality evidence to date supporting the benefits of exercise for improving HRQOL outcomes. **There is no evidence that electrical stimulation-assisted cycling is effective for increasing strength.**	**High** -More than half of included studies were RCTs of moderate-high quality
Edwards et al. (2017) [6]	Provide a summary of the potential benefits of **exercise training** in persons with MS with severe	**Systematic Review** randomized and nonrandomized controlled trials, and	conventional exercise training (aerobic and resistance exercise) (n= 5)	Further research is necessary to determine the most efficacious and effective exercise approaches for individuals with MS with severe mobility disability due to the limited amount of quality evidence.	**Medium** -Small samples

	mobility disability, and a future research agenda for developing effective strategies for managing disability through exercise training.	pre-post intervention designs Diagnosis of MS (severe mobility issues)	body-weight support treadmill training (BWSTT) (n= 7) total-body recumbent stepper training (TBRST) (n = 1) Functional clectrical stimulation assisted cycling (n = 5)	**Conventional exercise training** - no statistically significant improvements in any of the outcomes **Conventional resistance exercise training** -Significant improvements in muscular strength, muscle endurance, balance, fatigue symptoms, and QOL when combined with neuromuscular electrical stimulation -Low level evidence **Bodyweight support treadmill training** -Mixed results (some positive others no change) across outcomes on level of disability, knee extensor strength, walking, endurance, walking speed, gait kinematics, balance and agility, fatigue, QOL **Total body recumbent stepper training (one study)** -No change in disability or physical function reported. -Symptoms of fatigue were significantly reduced after the intervention **Electrical stimulation assisted cycling** <u>(functional electrical stimulation (FES) and neuromuscular electrical stimulation (NMES) cycling)</u> - Two studies reported significant improvements in physical fitness assessed as thigh circumference and muscle oxygen consumption (mVO2) -No significant improvements in physical function	-Mixed results across all outcomes for all treatment types -Significant heterogeneity led to inability to perform meta-analysis

				-Mixed evidence for the effects of ESAC on spasticity, walking speed, and other participatory outcomes	

1.2 Spinal Cord Injury

1.2.1 MOTOmed and/or Active Passive Trainer

Phadke et al. (2019) [7] performed a systematic review to assess the effectiveness of **passive leg** cycling interventions on cardiovascular, neuromuscular, and musculoskeletal outcomes post spinal cord injury (SCI).

Devices utilised in included studies: Ergo-Dom, FNS leg cycle, ERGYS 1 leg cycle, Sevo-dynamically controlled recumbent ergometer and MOTOmed cycle.

Intervention duration
Single intervention:
5 to 100 minutes per session

Multiple sessions - frequency of the exercise sessions ranged from one to three times per day, 20 to 90 minutes per session, 2 to 6 days per week, and 6 to 12 weeks total duration

Results

-Two included RCTs reported significant benefits of multiple sessions of passive cycling on **cardiovascular** (improved leg blood flow velocity), **musculoskeletal** (improved joint range of motion and markers of muscle hypertrophy), and **neurological** outcomes (improved spasticity and reflex excitability)
-No clear picture emerged with single session studies, with about half the studies showing a statistically significant improvement in acute responses in **cardiovascular** (blood flow velocity) and **neurological** outcomes (short interval intra-cortical inhibition and spasticity), while the rest reported no change.

Quality – Medium

Only 11 included studies of which only 2 were RCT. More evidence is required to understand the best parameters for single and multiple sessions of passive cycling.

1.2.2 FES cycling

Multiple literature and systematic reviews have been conducted relating to FES cycling as a treatment for patients with spinal cord injury (SCI) [8-11]. Two were of higher quality and will be summarised here [8, 9]. The remaining two were low quality narrative/literature reviews [10, 11] and can be found in Table 2.

1) Alashram et al. (2020) [8] investigated the effects of the FES-cycling on the lower extremities spasticity in patients with SCI and found:
- Significant reduction in Modified Ashworth Scale (assess muscle tone and level of spasticity) and Numerical-Rating-Scale spasticity scores (reduce spasticity) after FES-cycling post-treatment, and at three and six months follow ups ($P < 0.05$).
- Intervention details were not reported in some of the selected studies so unable to identify the treatment effect size and the effective treatment protocol

Quality – Medium

Several low quality studies included due to the paucity of evidence. Small sample sizes and heterogeneity of studies meant a meta-analysis was not conducted.

2) Thomaz et al. (2019) [9] evaluated the effect of electrical stimulation (ES) on skeletal muscle volume and spasticity in individuals with SCI, however, only results for FES cycling were retrieved.
   - Intervention: 30-45 minutes, 3-4x per week
   - Overall effect on muscle volume was statistically significant in patients with acute SCI (mean difference: 0.86; 95% CI: 0.04 to 1.69; $p < 0.04$).
   - Non-significant (mean difference: 0.55; 95% CI: −0.31 to 1.41; $p = 0.21$) effect for spasticity of the lower limb.

Quality – High
High quality RCTs

1.2.3 Conventional Exercise Training Programs

Hicks et al. (2011) [12] conducted a systematic review of evidence surrounding the effects of exercise on physical fitness in people with SCI. Broad range of study types included covering resistance training, arm ergometry, wheelchair exercise and FES, step training and strength training.

<u>Intervention:</u> All studies performed the desired intervention 2-5x a week, over a range of 5-12 weeks (one study performed over 26 weeks)

<u>Results</u>

Overall, Exercise is effective in increasing physical capacity and muscular strength among people with chronic SCI. There is no evidence to suggest that exercise is harmful to this population.

See Table 2 for outcomes on Power Output, Aerobic capacity, Muscle strength, Body weight, Muscle mass Wheelchair propulsion and skills, Walking and Standing across intervention types

Quality – Medium

Inclusion of very low quality (level 5) studies may impact results. Although results were relatively consistent across studies.

Table 2					
Author (year) and country	**Study aim**	**Method/ participants characteristics**	**Treatment/ Intervention/ Setting**	**Outcome/summary**	**Quality of evidence** **Low/Medium /High**
Spinal Cord Injury					
Phadke et al. (2019). [7]	To assess the effectiveness of passive leg cycling interventions on cardiovascular, neuromuscular, and musculoskeletal outcomes post SCI, and to describe intensity, duration, and type of passive leg cycling post SCI	**Systematic Review** Inclusion: passive leg cycling prospectively in adult participants (age ≥18 years) with SCI 11 included studies (2 RCT, 1 cross-over trial, 8 pre-post)	**Cycling training parameters** Single intervention: 5 to 100 minutes per session Multiple sessions - frequency of the exercise sessions ranged from one to three times per day, 20 to 90 minutes per session, 2 to 6 days per week, and 6 to 12 weeks total duration. **Devices used** Ergo-Dom, FNS leg cycle, ERGYS 1 leg cycle, Sevo-dynamically controlled recumbent ergometer,	**Outcome measures used to assess the effects of cycling** -Two RCTs reported significant benefits of multiple sessions of passive cycling on **cardiovascular** (improved leg blood flow velocity), **musculoskeletal** (improved joint range of motion and markers of muscle hypertrophy), and **neurological** outcomes (improved spasticity and reflex excitability) -No clear picture emerged with single session studies, with about half the studies showing a statistically significant improvement in acute responses in **cardiovascular** (blood flow velocity) and **neurological** outcomes (short interval intra-cortical inhibition and spasticity), while the rest reported no change. -The studies reviewed here showed a diversity of cycling protocols and outcomes across multiple body systems.	**Medium** Evidence from this systematic review indicates that multiple sessions of passive leg cycling showed some form of beneficial changes across cardiovascular, musculoskeletal, and neurological systems -More evidence is required to understand the best parameters for single and multiple sessions of passive cycling.

			Motomed cycle **Comparisons** No intervention, FES cycling, resting, Active + FES cycling,		
Alashram et al. (2020) [9]	to investigate the effects of the FES-cycling on the lower extremities spasticity in patients with SCI.	**Systematic Review** - individuals with SCI -examined lower extremities spasticity. 2 randomised cross-over trials 6 pilot studies 2 cohort studies 161 total participants	See note on intervention details in outcome/summary section	-The selected studies demonstrated a significant reduction in the Modified Ashworth Scale (assess muscle tone and level of spasticity) and Numerical-Rating-Scale spasticity scores (reduce spasticity) after FES-cycling post-treatment, and at three and six months follow ups (P < 0.05). -Comparison study found significant reduction in the spasticity in the experimental FES-cycling group (P = 0.02) than in the standard care control group. -One reported AE relating to an increase in spasticity and a bowel accident -Intervention details were not reported in some of the selected studies such as: frequency of treatment, treatment time period, session duration, number of electrodes, pulse type, type of FES-cycling system, pulse width, frequency, and RPM. So unable to identify the treatment effect size and the effective treatment protocol.	**Medium** -2 high quality studies but remaining were low-quality and included due to the paucity of studies published about this issue. -Small samples - Heterogeneity of studies meant a meta-analysis was not conducted.
Thomaz et al. (2019) [9]	Evaluate the effect of electrical stimulation (ES) on skeletal muscle volume and spasticity in individuals with	**Systematic Review and Meta-Analysis** Only RCT included Patients with SCI	Treatment (relating to FES cycling studies) 30 minutes 3x per week 30-45 minutes 4x per week	ES is effective at promoting a discrete, but significant increase in skeletal muscle volume in patients with SCI with a subsequent reduction in atrophy and an effect on muscle volume that is similar in patients with complete and incomplete injuries. -ES on muscle volume of the lower limbs, the overall effect was statistically significant in patients with acute SCI (mean difference: 0.86; 95% CI: 0.04 to 1.69; p < 0.04).	**High** studies included in this meta-analysis were homogeneous and evaluated a respectable number of participants

	spinal cord injury	Intervention = ES Comparison = other intervention or no intervention 7 included studies		-ES for spasticity of the lower limb, the overall effect was non-significant (mean difference: 0.55; 95% CI: −0.31 to 1.41; p = 0.21).	
Deley et al. (2015) [10]	To discuss some evidence-based physiological and methodological considerations for optimal use of FES for training in paraplegia. Particular attention is given to the comparison of the different FES methods	**Narrative Review** Poor search strategy (only PubMed and Google Scholar) Study types included are not reported All in clinical setting	Unclear duration, dosage etc	FES allows the participation of greater muscle mass through hybrid exercises (FES–cycling associated with arms ergometer or FES–rowing). These different forms of exercise are associated with major benefits to all systems of the body—muscular, cardiovascular and pulmonary—and induce important training adaptations when used regularly. FES appears to be a beneficial and safe method for training in paraplegic individuals FES rowing appears to provide the greatest outcomes	**Low** -Lack of methodological explanation of studies included -Narrative review and no quantitative analysis -Poor outcome reporting or intervention
Mayson et al. (2014) [11]	To review the evidence on FES cycling intervention in youth with SCI	**Literature Review** <21 years with SCI 6 included studies	Interventions included FES cycling, Passive leg cycling and ES only 5 studies performed 1 hour sessions 3x/ week for 6 months	FES cycling is safe for youth with SCI Based on RCT: FES cycling can positively influence VO2, as well as quadriceps muscle strength and Volume. However, ES alone may be more beneficial in reducing cholesterol levels and increasing thigh muscle volume	**Low** Due to the limited number of intervention publications, five of which involved the

		-4 RCT (one study spread across 4 publications) -1 case series -1 prospective case series Total 40 participants	1 study 30 minutes sessions 3x/ week for 9 months FES cycling parameters -Applied to: quadriceps, hamstrings, gluteal muscles -Frequency: 33 Hz -Pulse duration: 150, 200, 250 or 300 µs -Amplitude: <140 mA -Resistance adjusted by 0.14 nm to maintain 50 rpm		same small sample, it is impossible to recommend optimal parameters for use of FES cycling in children and adolescents with SCI.
Hicks et al. (2011) [12]	To conduct a systematic review of evidence surrounding the effects of exercise on physical fitness in people with spinal cord injury (SCI).	**Systematic Review** Physical activity or exercise training intervention in persons diagnosed with an SCI (paraplegia or tetraplegia).	Include at least one of the fitness measures below: -strength, oxygen uptake/consumption, power output, peak work capacity, body composition, exercise performance or functional performance.	**Power Output** <u>Combined resistance and arm ergometry exercise:</u> -Level 1 and 4 studies have shown the combination of resistance and aerobic training to improve power output of the upper limbs. -**B**enefits when performed 2-3x per week over 12 weeks <u>Wheelchair exercise:</u> This single level 4 study showed non-significant improvements in upper limb power output. **Aerobic capacity** <u>Arm ergometry exercise:</u>	**Medium** Exercise is effective in increasing physical capacity and muscular strength among people with chronic SCI. There is no evidence to

		Case studies, experimental and quasi experimental designs were included.	69 included studies on chronic SCI	-All level 4 studies, arm ergometry has been shown to be very effective in improving aerobic capacity. -3x per week showed benefits after 5 weeks <u>Wheelchair ergometry exercise:</u> -Level 4 and 5 studies. Most show improvements in aerobic capacity following 3x per week training for as little as 4 weeks. <u>Combined resistance and arm ergometry exercise:</u> -Level 4 trials produced conflicting results; two studies (one level 4 study, and the RCT) showed significant improvement in aerobic capacity following training 3x per week for 7 and 12 weeks, while the other (level 4 study) showed no improvement following 3x per week training for 6 weeks. <u>Resistance training exercise:</u> -Although resistance training is not traditionally used to improve aerobic capacity, a single level 4 study yielded significant improvements in aerobic capacity. Further, the magnitude of improvement was comparable to that seen in most other exercise studies. <u>Functional electrical stimulation:</u> - In these level 4 and 5 studies, FES exercise has shown to be very effective in improving aerobic capacity in as little as 4–6 weeks. -Exercise schedule 2-3x per week is sufficient for improvement. **Muscle strength** <u>Combined resistance and arm ergometry exercise:</u> - Level 4, pre–post training studies consistently show that participation in any form of exercise training that ‘overloads’ the muscle will result in increases in muscle strength. -Training frequencies of 3x per week, the level 1 RCT demonstrated significant improvements in muscle strength with a frequency of 2x per week. -Training intensities ranged between 50–80% 1RM.	suggest that exercise is harmful to this population.

				<u>Functional electrical stimulation:</u> -Level 4, pre–post training studies utilizing FES show that muscle strength can significantly increase in the paralyzed muscles -3x per week over 8 weeks of training -There is level 1 evidence that FES-assisted arm ergometry training is more effective in improving triceps strength than arm ergometry alone. **Body weight** Resistance and aerobic exercise: All of these level 4 studies reported non-significant increases or decreases in body weight and utilized a training frequency of 3_ per week with an intensity ranging from 40 to 80% max. HR. <u>Functional electrical stimulation</u> -Level 4 studies reported non-significant increases or decreases in body weight. -Frequency of training was 3-5x per week. **Muscle mass** <u>Resistance exercise</u> -One level 4 study of vibration exercise reported significant increases in fat free mass with training -5x per week for 12 weeks -No other significant changes in lean tissue mass were reported. <u>Functional electrical stimulation:</u> A level 2 study reported significant increases in quadriceps cross-sectional area with a treadmill training frequency of 2x per week for 26 weeks. **Wheelchair propulsion and skills** <u>Resistance and aerobic exercise:</u>	

				-Significant improvements in maximum power output during wheelchair propulsion were reported -Most studies trained 3x per week, at moderate–heavy intensities. **Walking** Step training: -Findings were mixed. Most found significant improvements in overground walking following body weight supported treadmill training (BWSTT) both with and without FES. -Changes in treadmill training parameters emerged in most, but not all studies, depending on the parameters measured. -Training ranged from 2 -5x per week; intensity varied considerably and was often individually determined. Strength training -Improvements in overground walking (significance not reported) were noted after 12 weeks of training, 2–3x per week at 70–85% of 1RM. **Standing** Step training: This level 5 study showed progressive BWSTT, 3x per week, led to improvements in the ability to stand with a walker.	

1.3 Stroke

1.3.1 MOTOmed and/or Active Passive Trainer

1) A systematic review investigating the effectiveness of the MOTOmed trainer was performed by Shen et al. (2018) [13]. All included studies were RCTs and a total of 1099 participants were recruited.

Intervention duration

- 20 minutes in 11 studies
- 30 minutes in 6 studies
- 40 minutes in 1
- Unclear in 1 study
- Average 1-2 times per day and 5-7 days per week
- Over 4 to 12 weeks

All studies compared conventional rehabilitation to MotoMed + conventional rehabilitation.

Results

- MOTOmed movement therapy effectively improves mobility and activities of daily living in stroke patients with hemiplegia.
- Fugl-Meyer Assessment (assess motor functioning, balance, sensation and joint functioning) $Z = 7.33$, $P < 0.0001$
-Modified Ashworth Scale (muscle tone) $Z = 9.19$, $P < 0.00001$
-Berg Balance Scale $Z = 8.39$, $P < 0.00001$
- Functional Ambulation Category $Z = 9.61$, $P < 0.00001$
-10m walk test $Z = 4.49$, $P < 0.00001$
-Barthel Index (activities of daily living) $Z = 15.6$, $P < 0.00001$

Quality – High
Consistent findings across all included RCTs

2) A narrative literature review of the efficacy and safety of passive exercise interventions was conducted by Brenner (2018) [14]. **C**ontinuous Passive Motion (CPM) and Motorized-cycle ergometers were reviewed.

Results
CPM exercise
-Can significantly reduce physiological symptoms such as oedema, muscle stiffness and/or spasticity.
-Shoulder joint stability can be increased following 4 weeks of training, 5 × /week/ 25 min per session (plus warm-up and cool-down)

Motorised-cycle ergometers
-Duration of training programs ranged from 3 to 5 weeks

-Improvements in motor control, trunk stability and cognition were reported following this type of passive exercise training
-Regular passive arm exercise led to an increase in the range of motion in the affected arm
- No standard protocols or best practice guidelines exist for either modality in stroke

Quality – Low

Small number of included studies of moderate-low quality. More information is required on the type of device, the frequency and duration of each exercise session as well as the intensity and how long the therapy should be continued (i.e., length of treatment).

1.3.2 FES cycling

1) A high quality systematic review by Shariat et al. (2019) [15] has investigated the effectiveness of different protocols of cycling with/without FES on functional mobility after stroke.

Intervention: Cycling with/without FES to the lower limbs
- Frequency: 1 to 7 sessions per week
- Session length: 10 to 90 minutes
- Duration of interventions: 3 to 16 weeks (for cycling alone 3–72 weeks and for cycling with FES about 4 weeks)
- Total dose of the stimulation: between 4 and 16 hours.

Comparison: cycling alone, cycling with FES, control, placebo, or other interventions
Outcomes: Balance, walking speed, mobility
Study design: All included studies were RCTs

Results

- Walking speed: Effect size (ES) 0.30 (95% CI, 0.05 – 0.55) P <0.02
- Walking ability: ES 0.41 (95% CI, 0.11 – 0.71) P <0.007
- Cycling vs control on balance: ES 0.32; 95% CI, 0.06 – 0.57, P <0.01
- Cycling with FES vs control on balance: ES 1.48; 95% CI, 0.99 –1.97, *P* < 0.00001

Quality – High

-Cycling with FES has a significant and positive effect on balance compared to cycling without FES
-Additional studies are needed comparing FES cycling directly with other modalities of exercise such as balance training, strength training, power training or combinations to determine its relative efficacy
-No outcomes for functional mobility such as falls and fall-related injuries

2) An additional RCT comparing a standard rehabilitation program to MOTOmed cycle + FES and found that the intervention and control group both improved on all outcome measures, however, the intervention group had significantly less shoulder pain. Full summary of the study by Karaahmet et al. (2018) [16] can be found in Table 3.

Table 3					
Author (year) and country	**Study aim**	**Method/participants characteristics**	**Treatment/Intervention/Setting**	**Outcome/summary**	**Quality of evidence** **Low/Medium/High**
Stroke					
Shen et al. (2018) [13]	To estimate the effectiveness of MOTOmed® movement therapy in increasing mobility and activities of daily living in stroke patients with hemiplegia.	**Systematic Review** Only RCTs included (all performed in China) 19 Trials including 1099 patients Stroke with hemiplegia **Age range 46.5-83.4**	Duration of MotoMed therapy: - 20 minutes in 11 studies - 30 minutes in 6 studies - 40 minutes in 1 - Unclear in 1 study - 1-2 times per day and 5-7 days per week - Lasting 4 to 12 weeks All studies compared conventional rehabilitation to MotoMed + conventional rehabilitation	The main finding of this systematic review and meta-analysis is that MOTOmed movement therapy effectively improves mobility and activities of daily living in stroke patients with hemiplegia. Significant effects in favour of Motomed for: - Fugl-Meyer Assessment (assess motor functioning, balance, sensation and joint functioning) $Z = 7.33$, $P < 0.0001$ -Modified Ashworth Scale (muscle tone) $Z = 9.19$, $P < 0.00001$ -Berg Balance Scale $Z = 8.39$, $P < 0.00001$ - Functional Ambulation Category $Z = 9.61$, $P < 0.00001$ -10m walk test $Z = 4.49$, $P < 0.00001$ -Barthel Index (activities of daily living) $Z = 15.6$, $P < 0.00001$	**High** Inclusion of only RCTs. Consistent findings across all
Brenner (2018) [14]	To investigate the efficacy and safety of passive exercise interventions for	**Literature Review** 1. Continuous Passive Motion (CPM)	See results/outcomes	**CPM exercise** -Can significantly reduce physiological symptoms such as oedema, muscle stiffness and/or spasticity.	**Low** Non-systematic search strategy.

	patients with hemiplegia with a focus on those interventions that could be used in the home setting	2. Motorized-cycle ergometers		-Shoulder joint stability can be increased following 4 weeks of training, 5 × /week/ 25 min per session (plus warm-up and cool-down) Motorised-cycle ergometers -Two studies investigated passive leg-cycle and one on arm ergometer exercise on functional measures -Duration of training programs ranged from 3 to 5 weeks -Improvements in motor control, trunk stability and cognition were reported following this type of passive exercise training -Regular passive arm exercise led to an increase in the range of motion in the affected arm --No adverse effects were reported in the literature, can perform at home - No standard protocols or best practice guidelines exist for either modality in stroke	Small number of included studies of moderate-low quality More information is required on the type of device, the frequency and duration of each exercise session as well as the intensity and how long the therapy should be continued (i.e., length of treatment).
Shariat et al. (2019) [15]	To quantify the effectiveness of different protocols of cycling with/without functional electrical stimulation on functional mobility after stroke.	**Systematic Review** 1. Participants: Human subjects post-stroke (Adults ≥18 within 5 years after stroke). 2. Intervention: Cycling with/without functional electrical stimulation (FES) to the lower limbs 3. Comparison: cycling alone, cycling with FES,	Frequency: 1 to 7 sessions per week Session length: 10 to 90 minutes Duration of interventions: 3 to 16 weeks (for cycling alone 3–72 weeks and for cycling with FES about 4 weeks)	Walking speed: ES 0.30 (95% CI, 0.05 – 0.55) P <0.02 Walking ability: ES 0.41 (95% CI, 0.11 – 0.71) P <0.007 Cycling vs control on balance: ES 0.32; 95% CI, 0.06 – 0.57, P <0.01 Cycling with FES vs control on balance: ES 1.48; 95% CI, 0.99 –1.97, *P* < 0.00001	**High** -Literature suggests that more studies are needed comparing FES cycling directly with other modalities of exercise such as balance training, strength training,

		control, placebo, or other interventions 4. Outcomes: Balance, walking speed, mobility 5. Study design: **Randomized clinical trial** **14 trials including 680 participants who completed final follow up** **Mean age 42.5 to 85 years**	Total dose of the stimulation between 4 and 16 hours. -Electrical stimulation varied across studies as the frequency ranged from 20 to 60 Hz and pulse width from 300 to 450 ms. **control intervention** - 10 studies used sham stimulation - 4 studies participants received no stimulation	Long term effects and the most effective protocols are unclear due to study heterogeneity	power training or combinations, to determine its relative efficacy -Cycling is superior to control for improving walking speed, walking ability, and balance. -Cycling with FES has a significant and positive effect on balance compared to cycling without FES. -Although more research is needed, patients post stroke with lower limb disability could use cycling with FES as part of their rehabilitation program. -No outcomes for functional mobility such as falls and fall-related injuries
Karaahmet et al. (2018) [16]	To determine the effects of FES-cycling on shoulder pain and	**RCT**	-Both groups were trained with a standard rehabilitation program	The only significant finding was that severity of shoulder pain decreased in the FES-cycling group compared to the control	**Medium**

	subluxation, and secondarily to evaluate the improvement of upper extremity motor function in patients with acute–subacute stroke	-Age between 18 and 80 years, -First stroke Exclusion: sensory aphasia, recurrent stroke or bilateral hemiplegia, vasomotor instability, lower motor neuron disorder, limitation/ instability/dislocation of the shoulder joints, severe spasticity, and uncontrolled epilepsy 21 participants (12 intervention, 9 control)	(range of motion, stretching and strengthening exercises) program -5x a week lasting 30 min each -20 sessions Intervention group - Motomed cycle-ergometer used - Surface electrodes applied to anterior and the posterior deltoid, biceps, and triceps muscles - Pulse width of 300 µs and a stimulation frequency of 20 Hz - 5-min warm-up of passive cycling, a 15-min training of FES-cycling, and a 5-min cool-down of passive cycling	All other measures improved significantly between baseline and post-test for both intervention and control groups	Insufficient sample size to observe the effects of FES training

1.4 Parkinson's disease

1.4.1 MOTOmed and/or Active Passive Trainer

A literature review summarising the state of the evidence of **forced exercise's** impact on individuals with Parkinson's disease (PD) has been conducted by Miner et al (2020) [17]. Included studies utilised MOTOmed, Theracycle or a Tandem Bike.

Intervention
- On average, the intervention was delivered;
  - 3 times per week
  - 5-10 minute warm up at an average pedalling rate of 40-50 rpm
  - 30-40 minute forced exercise session (average 80-90 rpm)
  - 5-10 minute cool down
  - Over 8-12 weeks

Results
Acute effects
- Forced exercise has the potential to cause similar therapeutic effects as antiparkinsonian medication to improve motor symptoms of PD.
- Last for up to 48hr

Effects on motor function
-Best when used to treat rigidity, bradykinesia, and tremor

Physical fitness
-Muscular strength improved by>30% in the upper and lower body (only one study)

Mobility performance
-difficult to draw conclusions on the effects of forced exercise on mobility performance in individuals with PD as most of the results were confounded by a ceiling effect in the outcome measures selected

Incorporating forced exercise as an adjunctive treatment could provide significant added benefit to task specific training, or gait and balance training for individuals with PD.

Clinical recommendations summary comparing Tandem cycling to MotoMed (or equivalent) can be found in Figure 1.

Quality – Moderate
- Various methodological flaws which limit the generalizability
-longer term follow-up studies with larger sample sizes are needed to inform the ability of forced exercise to alter the trajectory of PD

1.4.2 FES cycling

There is a paucity of research in this area. Findings from a single subject design study [18] can be found in Table 4. No conclusions can be drawn from the findings provided.

Table 4					
Author (year) and country	**Study aim**	**Method/participants characteristics**	**Treatment/Intervention /Setting**	**Outcome/summary**	**Quality of evidence** **Low/Medium/High**
Parkinson's Disease					
Miner at al.(2020) [17]	to summarize the state of the evidence of **forced exercise's** impact on individuals with PD and to determine the utility of this intervention in the clinical decision making for this patient population.	**Review** Unclear what the search methodology was for this review. No methods section Single subject, RCT, quasi-experimental MOTOmed Theracycle Tandem Bike	Treatment frequency - 3 times per week - 5-10 minute warm up at an average pedalling rate of 40-50 rpm - 30-40 minute forced exercise session (average 80-90 rpm) - 5-10 minute cool down -Duration 8-12 weeks	Clinical recommendations summary comparing Tandem cycling to MotoMed (or equivalent) can be found in Figure 1 below) Incorporating forced exercise as an adjunctive treatment could provide significant added benefit to task specific training, or gait and balance training for individuals with PD. **Acute effects** -Forced exercise has the potential to cause similar therapeutic effects as antiparkinsonian medication to improve motor symptoms of PD. -Last for up to 48hr **Effects on motor function** -highlights the importance of individuals being actively engaged in the exercise intervention -Best when used to treat rigidity, bradykinesia, and tremor **Physical fitness** -Muscular strength improved by>30% in the upper and lower body (only one study)	**Low** -Small numbers of patients - Include studies had various methodological flaws which limit the generalizability -longer term follow-up studies with larger sample sizes are needed to inform the ability of forced exercise to alter the trajectory of disease progression related to motor function

				Mobility performance -difficult to draw conclusions on the effects of forced exercise on mobility performance in individuals with PD as most of the results were confounded by a ceiling effect in the outcome measures selected	
Bellman et al. (2016) [18]	provides the results of an experiment conducted with one subject with PD to establish feasibility of FES-assisted cycling in this population	**Case study** Four able-bodied male subjects 25–27 years old were recruited from the University of Florida, and one male subject with PD, 60 years old, with a modified Hoehn and Yahr disability score of 2.5	Device -stationary, recumbent exercise cycle (AudioRider R400, NordicTrack) Stimulation -Frequency was fixed at 60 Hz Gluteal, quadriceps femoris, and hamstrings muscle groups stimulated	Results suggest that FES-assisted cycling using the developed switched controller may improve the ability of people with PD to track a desired cadence	**Very Low** Only one participant with PD. Only outcome measure is cadence Significant additional testing beyond the scope of this paper is needed to determine clinical efficacy.

Clinical recommendations and summary.

	Tandem cycling	MOTOmed or comparable model
Warm-up (minutes)	5 (40–50 RPM)	5 (40–50 RPM)
Forced Exercise Session (minutes)	30–40 (80–90 RPM or 30% above voluntary rate; 60–80% target HR)	30–40 (80–90 RPM or 30% above voluntary rate; 60–80% target HR)
Cool-down (minutes)	5–10 (40–50 RPM)	5–10 (40–50 RPM)
Frequency (x per week)	3–5 (at least 3)	3–5 (at least 3)
Duration (of entire treatment)	12 weeks; Re-Evaluate Every 6 Months	12 weeks; Re-Evaluate Every 6 Months
Pros	Temporal variability of pedal cadence of tandem cycling may provide more afferent drive to improve motor output. Trainer on tandem bicycle can give patient encouragement, social, emotional support which may improve effort, compliance, adherence to exercise program No significant differences in improvements between tandem forced cycling and motorized forced cycling	Ease of access to the bike; patient can sit in a chair in front of the bicycle and there is no need to mount and dismount. Increased Safety No trainer necessary Could potentially be performed in the home setting No significant differences in improvements between tandem forced cycling and motorized forced cycling
Cons	Safety- Patients with impaired balance may find it difficult to mount and dismount bicycle Trainer must be available to ride the bike and change gears Investment in bike and bike stand are expensive, but less so than MOTOmed	Expensive Lack of partner involvement via a trainer may cause decreased patient motivation/effort, compliance, adherence to exercise program

1.5 Cerebral Palsy

1.5.1 MOTOmed and/or Active Passive Trainer

A single high quality, well powered RCT has been conducted by Damiano et al. (2017) [19]. The aim was to quantify and compare the effectiveness of a motor-assisted cycle (MOTOmed) and a novel alternative (elliptical), in cerebral palsy (CP) to improve inter-limb reciprocal coordination.

Intervention
Devices were randomised to participants and delivered to their homes
-Instructed to exercise above 40 rpm for 20 minutes, 5 days a week for 12 weeks.

Results
-Device cadence at self-selected and fast speeds for all participants improved markedly and significantly as a result of training
-No significant changes were seen in gait speed for time or group, nor did parent-reported functional mobility
-Knee extensor strength increased in both

Quality – Medium
Single study but excellent sample size with positive findings. Training dose provided likely insufficient for maximum results.

1.5.2 FES cycling

Several case studies and pilot work has been conducted on the feasibility and benefits of FES cycling in CP [20-22].

Intervention

- Duration: most commonly used 30 minutes at a time for 3 times a week
- FES applied to the bilateral quadriceps and/or hamstrings
- One delivered intervention in the participants home [22]

Results

- Positive results for Modified Ashworth scale (MAS), cadence, power output, and heart rates, quadriceps and hamstring strength, Timed “Up & Go” .
- Participants were able to tolerate the application of FES and complete testing

Quality – Low to Very Low

No control groups. Very small sample (total of 5 participants).

1.5.3 Conventional Exercise Training Programs

The impact of resistance training on the motor functions of children with CP has been investigated in a systematic review and meta-analysis by Collado-Garrido et al (2019) [23].

Outcome measures

- Gross Motor Function Measure
- Lateral Step Up
- Time Up and Go
- Mobility Questionnaire

Results

- Large effect of 0.75 (95% CI 0.41-1.08) for duration ≤6 weeks compared to 7-12 weeks
- Large effect of 1.08 (95% CI = 0.52 to 1.64) when duration was less than 30 minutes compared to 30-60 minutes and 60-90 minutes
- Large effect for fewer than three days a week. 1.59 (95% CI = 0.67 to 2.50), compared to studies with sessions applied three days a week
- Larger effect when using the "functional exercises" protocol. 1.25 (95% CI = 0.46 to 2.04)

Quality – High

Majority RCT of high quality. Statistically significant positive effect on motor function in favour of the use of resistance therapy in weakened musculature in children with CP

Table 5					
Author (year) and country	**Study aim**	**Method/ participants characteristics**	**Treatment/ Intervention/ Setting**	**Outcome/summary**	**Quality of evidence** **Low/Medium /High**
Cerebral Palsy					
Damiano et al. (2017) [19]	To quantify and compare effectiveness of a motor-assisted cycle and a novel alternative, an elliptical, in CP to improve inter-limb reciprocal coordination through intensive speed-focused leg training.	**RCT** 27 children with bilateral spastic CP, and a mean age of 10.3 years Reached power MOTOMed Elliptical	assigned device was delivered to their home, and they were instructed to exercise above 40 rpm for 20 minutes, 5 days a week for 12 weeks. Each participant was tested 3 times at 3-month intervals,	Device cadence at self-selected and fast speeds for all participants, improved markedly and significantly as a result of training No significant changes were seen in gait speed for time or group, nor did parent-reported functional mobility Knee extensor strength increased in both	**Medium** Single study Positive across both groups Training dose is insufficient
Peng et al. (2010) [20]	Review FES cycling system; the therapeutic benefits of FESCE in subjects with SCI; clinical efficacy of FES in subjects with stroke; a pilot study of FESCE in subjects with cerebral palsy Will only review CP case	**Case study** 3 children with quadriplegic CP (mean age 3 years)	-FES sequentially applied to the bilateral quadriceps and hamstrings to achieve a rhythmic pedaling motion. -30 minutes, 3x per week -Exercise protocol based on the muscle status of their lower limbs	-Preliminary results showed all measured MAS scores decreased after FES cycling	**Very low** The results implied that FES cycling might acutely alleviate spastic conditions of children with CP.

			-Gradual increase in load -Modified Ashworth scale (MAS), leg drop pendulum test, and myotonometric measurements were conducted pre and post-test		
Harrington et al. (2012) [21]	to adapt methods and assess the feasibility of applying FES cycling technology in adolescents with CP, determine methods of performing cycling tests in adolescents with CP, and evaluate the immediate effects of FES assistance on cycling performance.	**Pilot study** four participants (2 male) with spastic CP between the ages of 12–14 years (mean 13 ± 1.2 years) tricycle-based system (a sport tricycle (KMXKarts; United Kingdom) mounted on a cycle trainer	-Bilateral quadriceps muscles were stimulated during the limb extension phase of the cycling -2–4 sessions with at least 24 hours of rest between cycling sessions and with all testing occurring within a two-week period for each participant -Target for the constant load test was set at 80% of the peak power output	-All participants were able to tolerate the application of FES and complete testing -FES-assisted cycling resulted in increased cadence, power output, and heart rates and decreased variability in cycling performance compared with volitional cycling without FES assistance.	**Low**

Johnston et al. (2011) [22]	describes the effects of cycling with FES (FES cycling) in an adult with CP.	**Mixed methods case report** 49-year-old man with spastic diplegic CP	-Cycled with FES at home for 30 minutes, 3 times per week, for 12 weeks Volitional efforts were augmented by FES of the bilateral quadriceps, gastrocnemius, and gluteal muscles. Tested 4 weeks after withdrawal	-Quadriceps muscle strength improved by 22.2% -Hamstring muscle strength improved by 18.5%, -Timed "Up & Go" Test time decreased from 11.9 to 9.0 seconds -Patient reported increased performance and satisfaction for self-identified goals and his score on the Medical Outcomes Study 36-Item Health Survey questionnaire increased from 62.1 to 77.6. -Reported increased back pain	**Very low** **Single case study** Patient made gains in body structure and function, activity, and participation
Collado-Garrido et al. (2019) [23] Related to resistance training but not specific to Motomed, APT, FES cycling etc.	To analyse, through a meta-analysis of published primary studies, the impact of resistance therapy on the parameters of the motor function in children with CP	**Systematic Review and Meta-Analysis** Controlled (randomized or quasi-randomized) and non-controlled clinical trials Intervention based on resistance therapy School-aged CP patients (≤18 years)	"progressive strength training" functional training static bicycle outcome measure -Gross Motor Function Measure - Lateral Step Up -Time Up and Go -Mobility Questionnaire	Intervention duration -Large effect of 0.75 (95% CI 0.41-1.08) for duration ≤6 weeks compared to 7-12 weeks -Large effect of 1.08 (95% CI = 0.52 to 1.64) when duration was less than 30 minutes compared to 30-60 minutes and 60-90 minutes -Large effect for fewer than three days a week. 1.59 (95% CI = 0.67 to 2.50), compared to studies with sessions applied three days a week -larger effect when using the "functional exercises" protocol with an SMD of 1.25 (95% CI = 0.46 to 2.04)	**High** statistically significant positive effect on motor function in favour of the use of resistance therapy in weakened musculature in children with CP

		12 RCT and 3 non-randomised clinical trials electrostimulation as resistance therapy			

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