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Should we use the FES-cycling exercise in clinical practice? Physiological and clinical effects systematic review with meta-analysis

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Abstract

Objective: To examine the evidence regarding FES-cycling's physiological and clinical effects. **Data Sources:** The study was conducted in accordance with PRISMA. PubMed, EMBASE, Cochrane Review, CINAHL, Scopus, Sport Discus, and Web of Science databases were used. **Study Selection:** Randomized controlled trials involving FES-cycling were included. Studies that didn't involve FES-cycling in the intervention group or without the control group were excluded. Two reviewers screened titles and abstracts and then conducted a blinded full-text evaluation. A third reviewer resolved discrepancies. **Data Extraction:** Meta-analysis was performed using inverse variance for continuous data with effect measured by mean difference and random effects analysis model. A 95%

confidence interval was adopted. The significance level was set at $p<.05$, and trends were declared at $p=.05$ to $\leq .10$. The I^2 method was used for heterogeneity analysis. The minimal clinically important difference was calculated. Methodological quality was assessed by the risk-of-bias tool for randomized trials. The GRADE method was used for the quality of the evidence analysis. **Results:** A total of 52 studies were included. Metabolic, cardiocirculatory, ventilatory, and peripheral muscle oxygen extraction variables presented statistical ($p<.05$) and clinically important differences favoring FES-cycling, with moderate to high certainty of evidence. It also presented statistical ($p<.05$) and clinically important improvement in cardiorespiratory fitness, leg and total body lean mass, power, physical fitness in intensive care (moderate to high certainty of evidence), and torque (low certainty of evidence). It presented a trend ($p=.05$ to $\leq .10$) of improvement in muscle volume, spasticity, and mobility (low to moderate certainty of evidence). It showed no difference ($p>.10$) in six-minute walking distance, muscle cross-sectional area, bone density, and length of ICU stay (low to moderate certainty of evidence). **Conclusions:** FES-cycling exercise is a more intense stimulus modality than other comparative therapeutic modalities and presented clinically important improvement in several clinical outcomes.

Keywords: FES-cycling, electrical stimulation, exercise, physiology, clinical, functional capacity, muscle.

Introduction

Reduced physical capacity is an independent factor for morbidity and all-cause mortality[1], with physical exercise being an important treatment component. Highly impaired patients may experience difficulties adhering to conventional physical exercise therapies. Restorative and substitutive technologies can play an important role in these cases, highlighting the benefits of physical exercise even in complex physical limitations.

Functional Electrical Stimulation cycling (FES–cycling) was developed initially in the 1980s[2] and evolved over the last 40 years. The basis of this technology is the association of an electrical stimulator with a cycle ergometer, a dedicated computer then provides the synchronism of both devices. From an operational point of view, the electrical stimulation device and the cycle ergometer can be adjusted in several modalities in clinical practice according to therapeutic goals and clinical situations. Stationary cycle ergometers allow a motor-powered fixed pedal cadence or a motor-fixed power resistance with a free pedal cadence. Non-stationary cycle ergometers allow free pedal cadence with power resistance due to gear combination and field circuit characteristics. Many commercial devices utilize a pulsed, rectangular, biphasic waveform with a constrained total electrical charge. However, contemporary devices can deliver pulse widths up to 1000 microseconds, intensities reaching 250 milliamperes, and frequencies as high as 250 hertz[3].

Initially used for spinal cord injury treatment, its applicability has greatly expanded for the most diverse pathological models (stroke[4], COVID-19[5], and critical illness[6], for example) and therapeutic objectives. Physiologically, FES-cycling enhances metabolic, ventilatory, and cardiovascular demands[7]. Several physiological effects have been reported for acute use of this technology, including changes in the oxygen consumption[8], peripheral muscle oxygen extraction[9], stroke volume[10], and minute ventilation[11]. Clinically, FES-cycling may provide enough physical stress to enable multi-systemic adaptations. Many clinical effects were described for short and long-term use of this therapeutic tool, encompassing adaptations on cardiorespiratory fitness[12], lean body mass[13], muscle performance[14], and functional capacity[15].

Although a growing body of literature supports this technology, robust evidence-based best practices for its clinical application by healthcare professionals remain insufficiently established. Consequently, the objective of this review is to critically assess the evidence pertaining to the physiological and clinical impacts of FES-cycling.

Methods

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Statement (PRISMA)[16] and Methodological Expectations of Cochrane Intervention Reviews

(MECIR)[17]. The study was registered in PROSPERO, the International Prospective Register of Systematic Reviews, under CRD42023425647 number.

Eligibility criteria

Studies that described FES-cycling effects were considered eligible. We included randomized control trial (RCT) studies involving FES-cycling use in healthy volunteers, spinal cord injuries, cerebral palsy, neuromuscular diseases, stroke, critical illness, COVID-19, cardiovascular diseases, or lung diseases, regardless of age and sex. To be included, studies could not have a control group that had undergone FES-cycling. The control group must have received electrical stimulation alone, cycling alone, or any complementary therapy other than FES-cycling (same received by the intervention group). It were excluded studies with therapies not involving FES-cycling in the intervention group. Studies without a control group were excluded also.

Information sources

The search was conducted on the following databases: PubMed, EMBASE, Cochrane Review, CINAHL, Scopus, Sport Discus, and Web of Science. We didn’t restrict our search by using a filter for RCTs and sought to identify all types of trials. Data were extracted from inception of the databases until 03 November 2022.

Search strategy

The main keywords with combinations of used terms were FES-cycling, functional electrical stimulation cycling, electrical stimulation, oxygen consumption, stroke volume, pulmonary ventilation, spinal cord injury, neuromuscular diseases, lung diseases, cardiovascular diseases, critical illness, functional capacity, cardiorespiratory fitness, and mobility limitation. Detailed keywords with combinations of used terms are presented in supplemental appendix 1. Due to the large number of studies/outcomes, the review was devided into physiological and clinical effects.

Selection process

The search results were imported into COVIDENCE platform. After removing duplicate files, data were analyzed in two parts. Initially, two reviewers (MF and TGF) independently screened the titles and abstracts in phase one, resolving discrepancies with the help of a third reviewer (GC). After the final selection of eligible papers, phase two began with the same two reviewers conducting a blinded full-text evaluation of the research, accounting for the third reviewer's participation. A list of all potentially relevant studies that were read in full-text form but excluded from the review is provided in supplemental appendix 2.

Data collection process

Following the PRISMA checklist recommendation[16], the characteristics of each primary study were extracted using a pre-pilot data extraction in the COVIDENCE platform were utilized to extract details regarding the methods, participants, interventions, comparators, outcomes, and research design. Outcomes data were also extracted in duplicate for effect measure calculation.

Data items

The physiological outcomes evaluated were a) Metabolic: oxygen consumption (VO_2), carbonic gas production (VCO_2), energy expenditure, and lactate; b) Cardiocirculatory: heart rate, stroke volume, oxygen pulse, and cardiac output; c) Peripheral muscle oxygen extraction: arterial—mixed venous oxygen content difference and deoxyhemoglobin; and d) Ventilatory: minute ventilation. All instruments used to measure the variables are in supplemental appendix 3.

Clinical outcomes evaluated were a) Functional capacity, including cardiorespiratory fitness, six-minute walking distance, and sedentary time/walking or running time; b) Body composition: utilizing muscle cross-sectional area, muscle volume, leg and total body lean mass, fiber type composition, and bone density; c) Spasticity: via pendulum test relaxation time, Ashworth scale and Hoffman reflex; d) Mobility: via gait speed, motricity index, upright motor control test, gross motor function measure 88, time for independent ambulation and time for marching in place; e) Muscle performance: torque and power and f) Critical illness: physical fitness in intensive care test, patients discharged from hospital to home, ICU length of stay and delirium incidence. All instruments used to measure the variables are in supplemental appendix 3.

The meta-analysis procedure was considered when at least three studies presented similar outcomes, and the calculation was performed utilizing the RevMan web. The statistical method used was inverse variance for continuous data with effect measured by mean difference and random effects analysis model. The confidence interval adopted was 95%. The significance level was set at $p<.05$, and trends were declared at $p=.05$ to $\leq .10$. Minimal clinically important difference (MCID) was calculated by the distribution-based method[18]. It was used 0.4 x baseline standard deviation values of the FES-cycling group variables. Between-study variability was examined for heterogeneity, using the I^2 statistic for quantifying inconsistency. The heterogeneity thresholds were set at I^2=25% (low), I^2=50% (moderate), and I^2=75% (high)[19]. Sub-group analyses were performed in peripheral muscle oxygen extraction (because the data for this variable were collected with two different measurement instruments) and cardiorespiratory fitness (because there was a huge difference in training protocol duration) variables. If articles with a discrepant risk of bias are presented for any outcome, a subgroup analysis based on this criterion was be performed.

For isolated studies (single or 2 studies with similar outcomes), analysis was also used on the RevMan Cochrane platform. The statistical method used was inverse variance for continuous data with effect measured by mean difference and Random effects analysis model or Mantel-Haenszel for dichotomous data with effect measured by odds ratio and Radom effects analysis model. The confidence interval adopted was 95%. The significance level was set at $p<.05$, and trends were declared at $p=.05$ to $\leq .10$.

Study risk of bias assessment

The risk-of-bias tool for randomized trials (RoB2) was used to assess the methodological quality of the included articles. Two reviewers used the Rob2 independently. It assessed the risk of bias according to the following domains: randomization process, deviations from intended intervention, missing outcome data, measurement of the outcome, and selection of the reported result.

GRADE

The Grading of Recommendations Assessment, Developing, and Evaluation (GRADE) method was used to assess the quality of the evidence.

Synthesis methods

The following information was provided: author and year, design, sample size, exercise type, duration, volume of training, and outcome measures. A meta-analysis was performed if three or more studies provided similar outcomes.

Results

Characteristics of the studies

Screening results are detailed in Figure 1. Only 1 study was manually included (published after 03 November 2022). 52 studies were included for review: 19 FES-cycling physiological effects studies[7-11, 20-33], and 33 FES-cycling clinical effects studies[4-6, 12-15, 34-59].

Table 1 presents the characteristics of the 19 physiological studies. There were 198 healthy or neurological participants, with critical illness or COPD as the primary disease. The mean age was 42 ± 13 years old. In declared FES parameter sets, there was a mean 330 ± 47µs pulse width, 20 to 145mA range intensity, and a mean 41 ± 17Hz frequency.

Table 2 presents the characteristics of the 33 clinical studies. There were 1010 participants with neurological, critical illness, or COVID-19 as a primary disease. The mean age was 41 ± 19 years old. In declared FES parameter sets, there was a mean 344 ± 88µs pulse width, 0 to 300mA range intensity, and mean

38 ± 18Hz frequency. There was a mean 9-week intervention period, ranging from 3 to 7 times per week intervention protocol.

Methodological quality

Figure 2 shows the risk of bias in physiological studies. 42% of the studies presented an overall low risk of bias, 58% presented some concerns about the risk, and none presented a high risk of bias. Figure 3 shows the risk of bias in clinical studies. 18% of the studies presented an overall low risk of bias, 67% presented some concerns about the risk of bias, and 15% presented a high risk of bias.

Physiological effects

Metabolic

Oxygen consumption

Figure 4 shows a mean 0.21L/min improvement in VO_2 favors FES-cycling (95% CI=0.14 to 0.28, p<0.00001), considering an MCID of 0.04L/min (Table 3), with high heterogeneity (I^2=91%, p<0.00001) and high certainty of evidence (Table 4).

Carbonic gas production

Figure 4 shows a mean 0.23L/min improvement in VCO_2 favors FES-cycling (95% CI=0.08 to 0.38, p=0.002), considering an MCID of 0.06L/min (Table 3), with high heterogeneity (i^2=84%, p<0.00001) and high certainty of evidence (Table 4).

Energy expenditure

Only two studies analyzed the effects of FES-cycling on energy expenditure. Frazão et al[a]. showed a mean 103W improvement in energy expenditure favors FES-cycling (95% CI=74.19 to 131.81, p<0.00001). Frazão et al[b]. showed a mean 69W improvement in energy expenditure favors to FES-cycling (95% CI=37.83 to 100.17, p<0.0001).

Lactate

Figure 4 shows a mean 2.35mmol/L improvement in lactate favors to FES-cycling (95% CI=0.53 to 4.16, p<0.00001), considering an MCID of 0.28mmol/L (Table 3), with high heterogeneity (i^2=91%, p<0.00001) and high certainty of evidence (Table 4).

Cardiocirculatory

Heart rate

Figure 5 shows a mean 9.94 beats/min improvement in heart rate favors FES-cycling (95% CI=2.26 to 17.25, p=0.008), considering an MCID of 4.20 beats/min (Table 3), with high heterogeneity (i^2=88%, p<0.00001) and moderate certainty of evidence (Table 4).

Stroke volume

Figure 5 shows a mean 13.88mL improvement in stroke volume favors FES-cycling (95% CI=4.52 to 23.24, p=0.004), considering an MCID of 2.80mL (Table 3), with high heterogeneity (i^2=84%, p=0.0003) and high certainty of evidence (Table 4).

Oxygen pulse

Figure 5 shows a mean 3.02mL/beat improvement in oxygen pulse favors FES-cycling (95% CI=2.06 to 3.97, p<0.00001), considering an MCID of 0.70mL/beat (Table 3), with no heterogeneity (i^2=4%, p=0.35) and high certainty of evidence (Table 4).

Cardiac output

Figure 5 shows a mean 1.46L/min improvement in cardiac output favors to FES-cycling (95% CI=0.63 to 2.28, p=0.0005), considering an MCID of 0.40L/min (Table 3), with high heterogeneity (i^2=95%, p<0.00001) and high certainty of evidence (Table 4).

Peripheral muscle oxygen extraction

Figure 6 shows the subgroup analysis. The arterial-mixed venous content difference showed a mean 24.29% improvement in peripheral muscle oxygen extraction favors to FES-cycling (95% CI=5.41 to 43.17, p=0.01), considering an MCID of 8.76% (Table 3), with high heterogeneity (i^2=94%, p<0.00001). Near-infrared spectroscopy-deoxyhemoglobin showed no difference between groups (a non-significant mean of 3.85% favors FES-cycling; 95% CI=-22.74 to 30.44, p=0.78), with high heterogeneity (i^2=98%, p<0.00001). Overall measurement analysis showed a trend mean 15.25% improvement in peripheral muscle oxygen extraction favors to FES-cycling (95% CI=-0.56 to 31.05, p=0.06), considering an MCID of 8.76% (Table 3), with high heterogeneity (i^2=97%, p<0.00001) and moderate certainty of evidence (Table 4).

Ventilatory

Figure 7 shows a mean 6.71L/min improvement in minute ventilation favors to FES-cycling (95% CI= 1.95 to 11.47, p=0.006), considering an MCID of 0.86L/min (Table 3), with high heterogeneity (i^2=98%, p<0.00001) and high certainty of evidence (Table 4).

Clinical effects

Functional capacity

Cardiorespiratory fitness

Figure 8 shows the subgroup analysis. Interventions with more than 8 weeks showed a mean 132.89mL/min oxygen consumption improvement in cardiorespiratory fitness favors FES-cycling (95% CI=5.35 to 260.43, p=0.04), considering an MCID of 0.80mL/min (Table 5), with no heterogeneity (i^2=0%, p=0.98). Interventions up to 8 weeks showed no difference between groups (a non-significant mean 9.40mL/min oxygen consumption favors FES-cycling; 95% CI=-130.48 to 149.28, p=0.90), with no heterogeneity (i^2=0%, p=0.89). Overall time interventions showed no difference between groups (a non-significant mean 76.83mL/min oxygen consumption in cardiorespiratory fitness favors FES-cycling; 95% CI=-17.41 to 171.08, p=0.11), with no heterogeneity (i^2=0%, p=0.91) and high certainty of evidence (Table 6).

Six-minute walking distance

Figure 8 shows no difference between groups (a non-significant mean 5.47m improvement in six-minute walking distance favors the control; 95% CI=-89.31 to 78.37, p=0.90), considering a MCID of 44m (Table 5), with no heterogeneity (i^2=0%, p=0.99) and moderate certainty of evidence (Table 6).

Sedentary / walking or running daytime

Only one study analyzed the effects of FES-cycling on sedentary / walking or running during the daytime. A 200.9 min/day reduction in sedentary time favors FES-cycling (95% CI=-236.45 to -138.35, p<0.00001). There was a 22.20 min/day improvement in walking or running time favoring FES-cycling (95% CI=18.83 to 29.75, p<0.00001).

Body composition

Muscle cross-sectional area

Figure 9 shows no difference between groups (a non-significant mean 30.40% improvement in muscle cross-sectional area favors FES-cycling; 95% CI=-4.31 to 65.12, p=0.11), with high heterogeneity (i^2=92%, p<0.00001) and a low certainty of evidence (Table 6).

Muscle volume

Figure 9 shows a trend mean 70.82cm^3 improvement in muscle volume favors to FES-cycling (95% CI= -2.36 to 144.01, p=0.06) considering an MCID of 66cm^3 (Table 5), with high heterogeneity (i^2=99%, p<0.00001) and low certainty of evidence (Table 6).

Leg and total body lean mass

Figure 9 shows a significant mean 2.93Kg improvement in leg lean mass favors to FES-cycling (95% CI=0.71 to 5.15, p=0.010) considering an MCID of 0.88Kg (Table 5), with high heterogeneity (i^2=76%, p=0.0006). Total body lean mass presented a mean of 5.04Kg favors FES-cycling (95% CI=0.82 to 9.27, p=0.02) considering an MCID of 2.52Kg (Table 5), with moderate heterogeneity (i^2=70%, p=0.04) (figure 9) and moderate certainty of evidence (Table 6).

Fiber type composition

Only one study analyzed FES-cycling effects on fiber type composition. There was no difference between groups. A non-significant mean of 4.90% type I fiber improvement favors FES-cycling (95% CI=-25.64 to 35.44, p=0.75). A non-significant mean of 3.10% type IIa fiber improvement favors FES-cycling (95% CI=-23.04 to 29.24, p=0.82). A non-significant mean of 2.50% type IIx fiber improvement favors FES-cycling (95% CI=-11.63 to 16.63, p=0.73).

Bone density

Figure 9 shows no difference between groups (a non-significant mean 0.04g/cm^2 improvement in bone density favors FES-cycling; 95% CI=-0.02 to 0.10, p=0.18) and considering an MCID of 0.01g/cm^2 (Table 5), with no heterogeneity (i^2=0%, p=0.95) and moderate certainty of evidence (Table 6).

Spasticity

Pendulum test – relaxation index

Figure 10 shows a trend mean 0.09 score improvement in the pendulum test relaxation index favoring FES-cycling (95% CI=-0.00 to 0.17, p=0.06) considering an MCID of 0.07 score (Table 5), with no heterogeneity (i^2=3%, p=0.39) and moderate certainty of evidence (Table 6).

Ashworth Scale

Figure 10 shows a significant mean 0.33 score reduction in the Ashworth scale favors FES-cycling (95% CI=-0.60 to -0.05, p=0.02), with no heterogeneity (i^2=3%, p=0.39) considering an MCID of 0.40 score (Table 5) and low certainty of evidence (Table 6).

Hoffman reflex (H/M ratio)

Figure 10 shows a trend mean 0.10 score reduction in Hoffman reflex favors FES-cycling (95% CI=-0.21 to 0.02, p=0.09) considering an MCID of 0.09 score (Table 5), with no heterogeneity (i^2=0%, p=0.60) and moderate certainty of evidence (Table 6).

Mobility

Gait speed

Only one study analyzed FES-cycling effects on gait speed. There was no difference between groups (a non-significant mean of 0.10m/s improvement favors FES-cycling; 95% CI=-0.29 to 0.49, p=0.62).

Motricity index

Figure 11 shows no difference in the mean 0.19 score of the motricity index (95% CI=-2.07 to 2.45, p=0.06), considering an MCID of 4.60 scores (Table 5). There is no heterogeneity (i^2=0%, p=0.87) and moderate certainty of evidence (Table 6).

Upright motor control

Only two studies analyzed FES-cycling effects on upright motor control tests. Amborisini et al. showed a trend mean of 1.70 score improvement favors FES-cycling (95% CI=-0.34 to 3.70, p=0.10), while Ferrante et al. showed no difference between groups a non-significant mean of 0.40 score improvement favors to FES-cycling; 95% CI=-0.67 to 1.74, p=0.46).

Gross Motor Function Measure 88

Figure 11 shows no difference between groups (a non-significant mean 3.99 score improvement in gross motor function measure 88 favors FES-cycling; 95% CI=-17.01 to 25.00, p=0.71), considering an MCID of 11.50 score (Table 5), with no heterogeneity (i^2=0%, p=0.94) and moderate certainty of evidence (Table 6).

Time for independent ambulation

Only one study analyzed the effects of FES-cycling on time for independent ambulation. There was no difference between groups (a non-significant mean 12.00 days reduction favors FES-cycling; 95% CI=-32.30 to 8.30, p=0.25).

Time for marching in place

Only one study analyzed FES-cycling effects on time for marching in place. There was no difference between groups (a non-significant mean 3.72 days reduction favors to FES-cycling; 95% CI=-13.41 to 5.97, p=0.45).

Muscle performance

Torque

Figure 12 shows a significant mean 20.31N improvement in torque favors to FES-cycling (95% CI=0.99 to 39.63, p=0.04), considering an MCID of 11N (Table 5), with high heterogeneity (i^2=84%, p=0.0006) and low certainty of evidence (Table 6).

Power

Figure 12 shows a significant mean 7.81W improvement in power favors to FES-cycling (95% CI=5.86 to 9.75, p<0.00001) considering an MCID of 3.8W (Table 5), with no heterogeneity (i^2=0%, p=0.83) and high certainty of evidence (Table 6).

Critical illness

Physical Fitness in Intensive Care Test (PFIT)

Figure 13 shows a significant mean 1.21 score improvement in physical fitness in intensive care test favors to FES-cycling (95% CI=0.04 to 2.38, p=0.04), considering an MCID of 1.12 score (Table 5), with low heterogeneity (i^2=49%, p=0.14) and high certainty of evidence (Table 6).

Patients discharged from hospital to home

Only two studies analyzed FES-cycling effects on the percentage of patients discharged from the hospital to home. Berney et al. showed a trend mean 11% improvement favors to FES-cycling, with an odds ratio = 1.59 (95% CI=0.90 to 2.81, p=0.10). Parry et al. showed a significant mean 42% improvement favoring FES-cycling, with an odds ratio = 8.14 (95% CI=4.09 to 16.23, p<0.000001).

ICU length of stay

Figure 13 shows no difference between groups (a non-significant mean 0.54 days reduction in ICU length of stay favors to FES-cycling; 95% CI=-2.42 to 1.34, p=0.57), considering an MCID of 1.84 days (Table 5), with low heterogeneity (i^2=40%, p=0.19) and moderate certainty of evidence (Table 6).

Delirium incidence

Only two studies analyzed FES-cycling effects on the percentage of delirium incidence. Berney et al. showed no difference between groups (a non-significant mean 4% reduction favors to FES-cycling, with an odds ratio = 0.85; 95% CI=0.48 to 1.49, p=0.57). Parry et al. showed a significant mean 62% reduction favors to FES-cycling, with an odds ratio = 0.05 (95% CI=0.02 to 0.10, p < 0.000001).

Discussion

Physiological effects

Higher VO_2 differences were especially greater when FES-cycling was compared to passive cycling[7, 8, 28, 29]. However, it was also higher when compared to isolated electrical stimulation (without cycling)[7] or associated with arm crank exercise[9, 10, 23, 31]. VO_2 normally increases close to linearly as power output increases[60]. Two isolated analyses showed that muscle contraction can be viewed as converting chemical energy into mechanical work. FES-cycling promotes a higher level of energy expenditure due to muscle contraction substantially increasing[7].

VCO_2 and lactate were significantly higher during FES-cycling in almost all studies reviewed. The two greatest VCO_2 differences were when FES-cycling was compared to passive cycling[7] and associated with arm crank exercise[31]. It suggests greater metabolic stress, exercise intensity, and glycolytic fiber recruitment. At this exercise intensity, CO_2 comes from two distinct sources: it is produced from aerobic metabolism and also from the buffering of lactic acid[61]. The three studies with the highest levels of blood lactate[11, 23, 32] in the FES-cycling group had the highest FES intensity. The amount of motor unit recruitment is related to the electrical intensity[62]. As lactate accumulation also comes from lactic acid buffering, it suggests a large amount of glycolytic fiber recruitment.

The highest heart rate difference achieved was when FES-cycling was compared to passive cycling[29]. However, the highest stroke volume and oxygen pulse differences were when associated with the arm crank exercise[9, 31]. Greater muscle activity promotes greater blood demand and pumping (blood return), which is drained from the periphery to the heart, improving stroke volume. Three studies showed greater cardiac output when comparing FES-cycling to the passive cycling[7, 28, 29]; two showed greater cardiac output when associated with the arm crank exercise[9, 10], and one when compared to isolated electrical stimulation (without cycling)[(7)]. The highest cardiac output difference was when compared to passive cycling. Heart rate adjustments seem more relevant to cardiac output than stroke volume.

Peripheral muscle oxygen extraction results depended on the data extraction/analysis modality. Arterial-mixed venous oxygen content difference analysis showed a clinically important difference that favors FES-cycling. Near-infrared spectroscopy (NIRS) analysis did not capture any superiority of FES-cycling. There was a clinically important significant difference trend in favor of FES-cycling. Delving deeper into deoxyhemoglobin analysis, one study[30], strongly moves the diamond away from significance. On the other hand, the other three other studies[26] pull the diamond to the significance. Interestingly, both are from the same research group. The earlier study analyzed active FES-cycling against active cycling plus FES placebo. The late ones compared passive FES-cycling to passive leg mobilization, passive cycling, and isolated electrical stimulation (without cycling). The later study showed a higher deoxyhemoglobin[28] compared passive FES-cycling to passive cycling. Voluntary muscle contraction plays a role in this case. During muscle contraction, arterioles have a greater vasodilatation, irrigating the active muscles with increased muscular blood perfusion[63].

Clinical effects

FES-cycling exercise improves cardiorespiratory fitness but is closely related to the duration of the exercise program. FES-cycling exercise needs more than 8 weeks to enhance oxygen consumption capacity. Intervention periods of up to 8 weeks are insufficient to promote cardiorespiratory fitness adaptations. The relation between cardiorespiratory fitness improvement and exercise program duration is well established. Nonoyama et al.[64] previously reported a VO_2 improvement throughout rehabilitation programs in individuals with respiratory, cardiac, or no comorbidities. Ward et al.[65] showed the importance of total training volume supported by greater improvements in VO_2 peak with programs > 12 weeks compared with those 6 to 12 weeks in duration and a positive trend between the total number of training sessions and change in VO_2 peak.

Reduction in sedentary time and improvement in active time was reported in a short therm exercise (4 weeks) single study with COVID-19 patients immediately after ICU hospitalization. Short-therm FES-cycling increases physical activity levels independently of gains in cardiorespiratory fitness. Even though gains in cardiorespiratory fitness are more important for reducing the risk of chronic heart and cardiovascular diseases, increasing physical activity levels promotes a protective effect already[66].

The six-minute walking distance is a worldwide functional capacity marker used in several pathological conditions. This review measured it in Myotonic Dystrophy Type I, Stroke, and Cerebral Palsy. FES-cycling had no superior effect in all these situations compared to control therapy. Curiously, all reviewed studies reported a short-term exercise program duration (ranging from 15 days to 6 weeks). As a longer exercise training duration is necessary for cardiorespiratory fitness improvement, it may also be necessary for six-minute walking distance improvement.

Lean mass was greatly improved with the FES-cycling exercise. All reviewed studies reported high FES intensity levels (up to 140 mA). Beyond leg lean mass, total body mass also improved, suggesting that a systemic growth effect may have been achieved. High-intensity current stimulation induces up-regulation of IGF-1 and modulation of MuRF-1 (a muscle-specific atrophy-related gene). It also induces up-regulation of relevant markers of differentiating satellite cells and extracellular matrix remodeling, reducing fibrosis[67]. Besides improvement in lean mass, FES-cycling provided only a trend of improvement in muscle volume and no improvement in muscle cross-sectional area. A single study showed no effects of FES-cycling on fiber type composition. Despite muscle mass changes, FES-cycling didn't bring any additional benefits to bone density.

FES-cycling showed spasticity reduction in Ashworth Scale analysis and a trend to decrease in Pendulum Test and Hoffman Reflex analysis. Most studies evaluated an acute effect of FES-cycling using a low electrical stimulation frequency (20Hz), with only 1 to 3 sessions of therapy. Two plausible reasons for spasticity reduction may be the repetitive and reciprocal stretching exercise during cycling and the effects of electrical stimulation on muscle tone. The elastic and parallel elastic components influence the resistance produced when muscles are stretched. These 2 components of the muscle might be changed after being stretched[59]. Additionally, whole-leg blood flow is lower in individuals with greater spasticity[68]. Previous studies demonstrated that electrical stimulation improves muscle blood flow[69, 70], which can reduce muscle tone.

Regarding mobility improvement, FES-cycling showed a favorable trend (without a clinically important difference) in the Motricity Index and no difference in Gross Motor Function Measure 88. Isolated analysis showed no differences (or slight trend) in gait speed, upright motor control, time for a march in place, and time to independent ambulation.

Strength and power are key elements to the capacity of the muscle to do work (muscle performance). To improve this capacity, these two aspects should be regarded. Torque (strength) and power were deeply improved with FES-cycling. For this improvement to be reached, many studies [37, 39, 46, 47] used high FES intensity levels (up to 140, up to 150, or up to 300 mA). Higher intensities induce higher motor unit recruitment, higher intramuscular tissue pressure, and, consequently, ischemia[71]. The adaptation mechanisms for the repeated muscle tension generation may be involved in muscle performance improvement. Good muscle performance improves functional capacity[72] and reduces the risk of cardiovascular disease[73] and mortality[74]. Additionally, the increases in torque and power strongly impact the motor recovery[14].

FES-cycling improved physical function in critically ill patients. There is a relationship between effectiveness and FES parameter adjustments. Higher FES parameters induced higher improvement. Parry et al.[6] reported a 2.4 gain in physical function score using a 300-400 μs pulse width and a maximum of 140 mA of pulse. Meanwhile, Berney et al.[15] achieved only a 1.3 gain using 250 μs (average-sized legs) or 300 μs (legs with edema) pulse width with a pulse amplitude varying from 20–30 mA. Waldauf et al.[58] reached a -0.2 PFIT score with a 250 μs pulse width and a pulse amplitude varying from 0–60 mA. Critically ill patients commonly present neuromuscular electrophysiological disorders[75].

Figueiredo et al.[76] showed that critically ill patients have a high stimulation cost (i.e., the total electrical charge delivery rate per watt of output power).

FES-cycling didn't affect the ICU length of stay besides better physical function. However, patients can be discharged from the hospital for better physical function and sent home without requiring ambulatory rehabilitation. The study with better physical function outcomes also presented a higher odds ratio of discharge from the hospital to the home[6]. The same study also reduced the incidence of delirium.

The use of FES cycling in Clinical Practice

There is a moderate to high level of evidence that FES-cycling induces higher physiological effects with a clinically important difference. FES-cycling exercise seems more intense and may provide enough physical stress for multi-systemic adaptation. There is a moderate to high level of evidence that FES-cycling improves cardiorespiratory fitness, leg and total body lean mass, power, and physical fitness in the intensive care unit, with a clinically important difference. However, some precautions must be taken. Long-term duration programs (more than 8 weeks) are needed for cardiorespiratory fitness improvement. Lean body mass and muscle performance improvement demand high-intensity electrical stimulation. High pulse width and intensity electrical stimulation are necessary in critically ill patients.

Strengths and Limitations

This is the first systematic review focused on using FES-cycling for clinical practice. We carefully reviewed several physiological and clinical outcomes to provide the best evidence available, helping healthcare professionals understand the use of this technology in direct patient care. Precisely, the reader will have the opportunity to know in which clinical and physiological outcomes the intervention surpasses the minimal clinically important difference and the certainty of evidence for each outcome.

The major limitation of this review was that it was not possible to perform meta-analysis on some clinically very important variables, such as time for independent ambulation, because the number of studies for some specific outcomes was limited.

Conclusions

FES-cycling exercise provides an intense stimulus modality. In general, metabolic, cardiocirculatory, ventilatory, and peripheral muscle oxygen extraction variables presented clinically important differences favoring FES-cycling (moderate to high certainty of evidence). It also presented clinically important improvement in cardiorespiratory fitness, leg and total body lean mass, power, physical fitness in intensive care (moderate to high certainty of evidence), and torque (low certainty of evidence). It presented a trend of improved muscle volume, spasticity, and mobility (low to moderate certainty of evidence). It showed no difference in six-minute walking distance, muscle cross-sectional area, bone density, and length of ICU stay (low to moderate certainty of evidence). On the evidence provided by this review, FES-cycling will provide positive changes in several clinical outcomes for patients.

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Figures legends

Figure 1 – Studies screening flow.

Figure 2 - Risk of bias in physiological studies**.**

Figure 3 - Risk of bias in clinical studies.

Figure 4 – Metabolic effects.

Figure 5 - Cardiocirculatory effects.

Figure 6 - Peripheral muscle oxygen extraction effects.

Figure 7 – Ventilatory effects.

Figure 8 - Functional capacity effects.

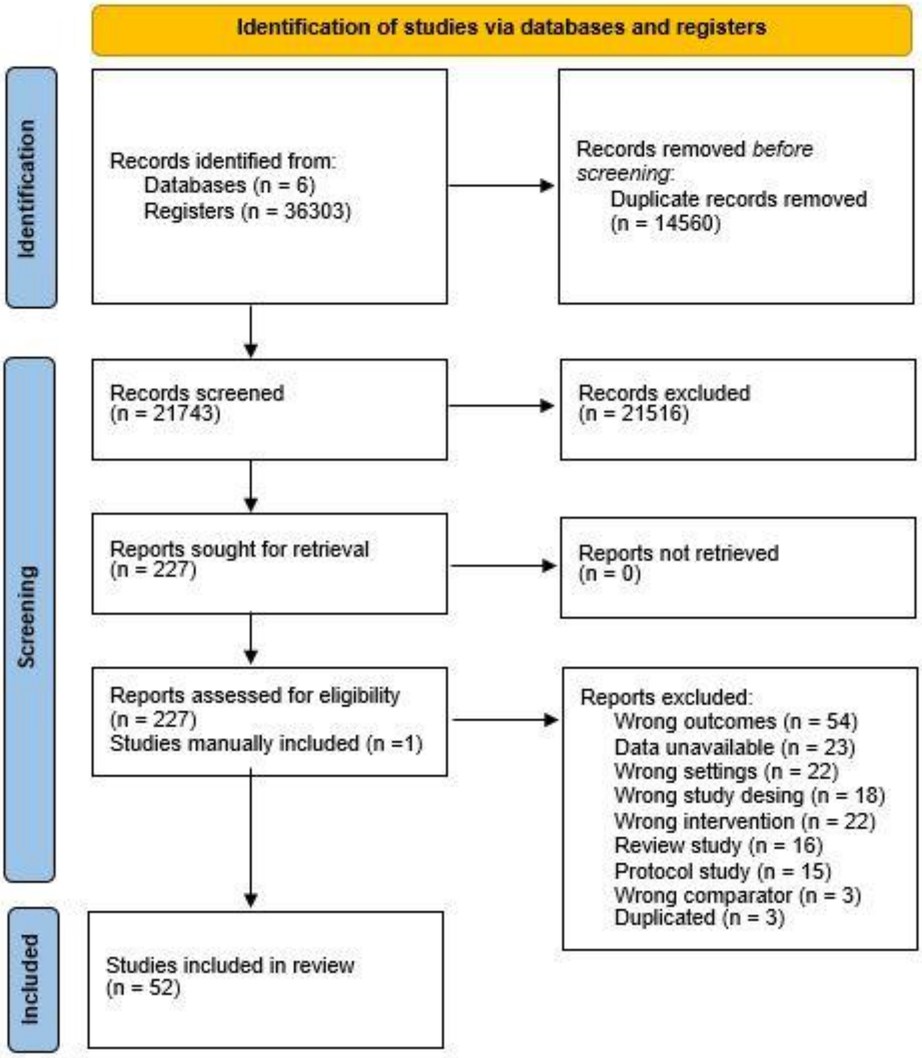
Figure 9 - Body composition effects.

Figure 10 – Spasticity effects.

Figure 11 – Mobility effects.

Figure 12 - Muscle performance effects.

Figure 13 - Critical illness effects.



Identification of studies via databases and registers
Identification
Records identified from:
Databases (n = 6)
Registers (n = 36303)
Records removed before screening:
Duplicate records removed
(n = 14560)
Screening
Records screened
(n = 21743)
Records excluded
(n = 21516)
Reports sought for retrieval
(n = 227)
Reports not retrieved
(n = 0)
Reports assessed for eligibility
(n = 227)
Studies manually included (n =1)
Reports excluded:
Wrong outcomes (n = 54)
Data unavailable (n = 23)
Wrong settings (n = 22)
Wrong study desing (n = 18)
Wrong intervention (n = 22)
Review study (n = 16)
Protocol study (n = 15)
Wrong comparator (n = 3)
Duplicated (n = 3)
Included
Studies included in review
(n = 52)

Unique ID	Study ID	Experimental	Comparator	Outcome	Weight	D1	D2	D3	D4	D5	Overall
1	Edwards 2018	Active FES-cycling	Passive cycling	VO2 and Heart Rate	1	+	+	+	+	+	+
2	Fornusek 2014	Passive FES-cycling	FES alone	VO2 and Heart Rate	1	!	+	+	+	+	!
3	Frazão 2022	Passive FES-cycling	Passive cycling or FES alone	VO2, VCO2, Cardiac Output, Oxygen pulse, Ca-vO2 and VE	1	+	+	+	+	+	+
4	Gojda 2019	Passive FES-cycling	Active cycling	Lactate	1	+	+	+	+	+	+
5	Kjaer 1994	Passive FES-cycling	Active cycling	VO2, Lactate, Cardiac Output, Heart Rate and VE	1	!	+	+	+	+	!
6	Hamzaid 2018	Passive FES-cycling	Arm cycling	Heart Rate	1	!	+	+	+	+	!
7	Hasnan 2013	Passive FES-cycling + arm cycling	Arm cycling	VO2, Lactate and Ca-vO2	1	!	+	+	+	+	!
8	Hasnan 2018	Passive FES-cycling + arm cycling	Arm cycling	Deoxyhemoglobin	1	!	+	+	+	+	!
9	Hooker 1992	Passive FES-cycling + arm cycling	Arm cycling	VO2, Cardiac Output, Stroke volume, Heart Rate, Ca-vO2 and VE	1	!	+	+	+	+	!
10	Medrinal 2015	Active FES-cycling	Active cycling	VO2, VCO2 and VE	1	!	+	+	+	+	!
11	Medrinal 2018	Passive FES-cycling	Passive leg mobilization or passive cycling or FES alone	Cardiac Output, Heart Rate and Deoxyhemoglobin	1	+	+	+	+	+	+
12	Medrinal 2018.2	Active FES-cycling	Placebo Active FES- cycling	VO2, VCO2, Lactate, Heart Rate and VE	1	+	+	+	+	+	+
13	Muraki 2007	Passive FES-cycling	Passive cycling	VO2, Cardiac Output, Stroke volume, Heart Rate, Deoxyhemoglobin and VE	1	!	+	+	+	+	!
14	Nash 1995	Passive FES-cycling	Passive cycling	VO2, Cardiac Output, Stroke volume, Heart Rate and Ca-VO2	1	+	+	+	+	+	+
15	Prieur 2019	Active FES-cycling	Placebo Active FES- cycling	Deoxyhemoglobin	1	+	+	+	+	+	+
16	Raymond 1999	Passive FES-cycling + arm cycling	Arm cycling	VO2, Cardiac Output, Stroke volume, Heart Rate, Ca-VO2 and VE	1	!	+	+	+	+	!
17	Raymond 1997	Passive FES-cycling + arm cycling	Arm cycling	VO2, VCO2, Heart Rate, Oxygen pulse and VE	1	!	+	+	+	+	!
18	Paulson 2014	Passive FES-cycling + arm cycling	Arm cycling	VO2, Lactate and Heart Rate	1	!	+	+	+	+	!
19	Máté 2024	Active FES-cycling	Active cycling	VO2	1	!	+	+	+	+	+

+ Low risk
! Some concerns
− High risk

D1 - Randomisation process
D2 - Deviations from the intended interventions
D3 - Missing outcome data
D4 - Measurement of the outcome
D5 - Selection of the reported result

Unique ID	Study ID	Experimental	Comparator	Outcome	Weight	D1	D2	D3	D4	D5	Overall
1	Ambrosini 2012	Passive FES-cycling	Placebo FES-cycling	Torque	1	+	+	+	+	+	+
2	Ambrosini 2011	Active FES-cycling	Placebo FES-cycling	Torque and motricity index	1	+	!	+	+	+	!
3	Armstrong 2020	Active FES-cycling + Usual care	Usual care	Power AND GMFM88	1	+	+	+	+	+	+
4	Bakkum 2015	Passive FES-cycling + Arm cycling	Arm cycling	Cardiorespiratory Fitness -VO2 and power	1	+	!	+	+	+	!
5	Baldi 1998	Passive FES-cycling	no FES training or FES alone	Leg Lean mass and total body Lean mass	1	!	!	+	+	+	!
6	Bauer 2014	Active FES-cycling	Active cycling	Motricity index	1	!	+	+	+	+	!
7	Berney 2021	FES-cycling + Usual care	Usual care	PFIT, Muscle CSA and ICU LOS	1	+	+	+	+	+	+
8	Bloomfield 1996	Passive FES-cycling	no FES-cycling training	Bone density	1	–	!	+	+	+	–
9	Brurok 2011	Passive FES-cycling + Arm cycling	no FES-cycling training	Cardiorespiratory Fitness - VO2 and power	1	–	!	+	!	+	–
10	Cudia 2016	FES-cycling	resistance + aerobic training	6MWT	1	–	–	+	!	+	–
11	deSousa 2016	FES-cycling	Usual care	Torque	1	+	+	+	+	+	+
12	Demchak 2005	Passive FES-cycling	no FES-cycling training	Muscle CSA	1	!	!	+	+	+	!
13	Dolbow 2020	Passive FES-cycling + nutrition	nutrition	Leg Lean mass and Total body Lean mass	1	+	!	+	+	+	–
14	Ferrante 2008	Passive FES-cycling + standard rehabilitation	Standard Rehabilitation	Motricity index, UMCT, Toquer and Power	1	+	!	+	+	+	!
15	Galea 2017	Passive FES-cycling	Passive cycling	Muscle CSA and Leg Lean mass	1	+	+	+	+	+	+
16	Janssen 2008	Active FES-cycling	Active placebo FES-cycling	Cardiorespiratory Fitness - VO2, 6MWT, Motricity index, Torque and Power	1	!	!	+	+	+	!
17	Johnston 2009	Passive FES-cycling	Passive cycling or FES alone	Cardiorespiratory Fitness - VO2	1	+	!	+	+	+	!
18	Johnston 2011	Passive FES-cycling	Passive cycling or FES alone	Muscle volume and Torque	1	+	!	+	+	+	!
19	Johnston 2011	Passive FES-cycling	Passive cycling or FES alone	Muscle volume	1	!	!	+	+	+	!
20	Johnston 2011	Passive FES-cycling	Passive cycling or FES alone	Torque	1	+	!	+	–	+	–
21	Krause 2008	Passive FES-cycling	Passive cycling	Pendulum test and Ashworth Scale	1	+	!	+	+	+	!
22	Lai 2010	Passive FES-cycling	No FES-cycling training	Bone density	1	!	!	+	+	+	!
23	Lauer 2011	Passive FES-cycling	Passive cycling or FES alone	Bone density	1	+	!	+	+	+	!
24	Lo 2012	Active FES-cycling	Active cycling	Pendulum Test and Hoffmann's reflex	1	+	!	+	+	+	!
25	Lo 2009	Active FES-cycling	Active cycling or arm exercise	Pendulum Test, Ashworth Scale and Hoffmann's reflex	1	!	!	+	+	+	!
26	Özen 2021	Passive FES-cycling	Placebo passive FES-cycling or usual care	6MWT, Ashworth Scale and GMFM88	1	+	!	+	+	+	!
27	Panisset 2022	Passive FES-cycling	Passive cycling	Muscle volume	1	+	!	+	+	+	!
28	Parry 2014	Passive FES-cycling + usual care	Usual care	PFIT and ICU LOS	1	!	!	+	+	+	!
29	Ralston 2013	Passive FES-cycling + usual care	Usual care	Ashworth Scale	1	+	+	+	+	+	+
30	Sadowsky 2013	Passive FES-cycling	no FES-cycling training	Muscle volume	1	!	!	+	+	+	!
31	Sansare 2021	Active FES-cycling	Active cycling or no intervention	Cardiorespiratory Fitness - VO2	1	+	!	+	+	+	!
32	Waldauf 2021	Passive FES-cycling + usual care	Usual care	PFIT, Muscle CSA and ICU LOS	1	+	+	+	+	+	+
33	Yeh 2010	Active FES-cycling	Active cycling	Pendulum Test and Ashworth Scale	1	+	!	+	+	+	!

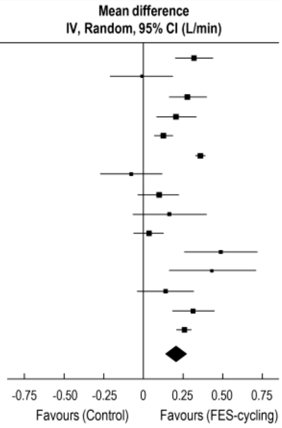
+ Low risk
! Some concerns
– High risk

D1 - Randomisation process
D2 - Deviations from the intended interventions
D3 - Missing outcome data
D4 - Measurement of the outcome
D5 - Selection of the reported result

Oxygen consumption

Study or Subgroup	FES-cycling Mean (L/min)	FES-cycling SD (L/min)	FES-cycling Total	Control Mean (L/min)	Control SD (L/min)	Control Total	Weight	Mean difference IV, Random, 95% CI (L/min)
Edwards 2018	0.38	0.13	6	0.06	0.06	5	7.3%	0.32 [0.20, 0.44]
Fornusek 2014	0.45	0.19	8	0.46	0.20	8	5.5%	-0.01 [-0.20, 0.18]
Frazão 2022[a]	0.26	0.15	10	-0.02	0.11	10	7.3%	0.28 [0.16, 0.40]
Frazão 2022b	0.26	0.15	10	0.05	0.12	10	7.2%	0.21 [0.09, 0.33]
Hasnan 2013	0.59	0.06	9	0.46	0.06	9	8.5%	0.13 [0.07, 0.19]
Hooker 1992	0.79	0.02	8	0.43	0.02	8	8.9%	0.36 [0.34, 0.38]
Kjaer 1994	0.72	0.20	8	0.79	0.19	8	5.5%	-0.07 [-0.26, 0.12]
Máté 2024	0.50	0.13	10	0.39	0.16	10	7.0%	0.10 [-0.03, 0.23]
Medrinal 2015	0.94	0.22	6	0.77	0.18	6	4.7%	0.17 [-0.06, 0.40]
Medrinal 2018.2	0.39	0.15	23	0.36	0.17	23	7.8%	0.04 [-0.05, 0.13]
Muraki 2007	0.53	0.16	4	0.04	0.16	4	4.8%	0.49 [0.27, 0.71]
Nash 1995	0.43	0.32	6	-0.01	0.11	6	3.9%	0.44 [0.17, 0.71]
Paulson 2014	1.00	0.15	5	0.86	0.14	5	5.7%	0.14 [-0.04, 0.32]
Raymond 1997	1.33	0.12	7	1.01	0.12	7	7.0%	0.32 [0.19, 0.45]
Raymond 1999	0.96	0.05	10	0.70	0.04	10	8.8%	0.26 [0.22, 0.30]
Total (95% CI)			**130**			**129**	**100.0%**	**0.21 [0.14, 0.28]**

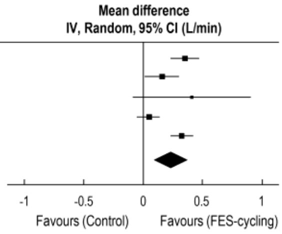
Heterogeneity: Tau² = 0.01; Chi² = 150.61, df = 614 (P < 0.00001); I² = 91%
Test for overall effect: Z = 5.75 (P < 0.00001)
Test for subgroup differences: Not applicable



Carbonic gas production

Study or Subgroup	FES-cycling Mean (L/min)	FES-cycling SD (L/min)	FES-cycling Total	Control Mean (L/min)	Control SD (L/min)	Control Total	Weight	Mean difference IV, Random, 95% CI (L/min)
Frazão 2022a	0.31	0.16	10	-0.04	0.10	10	23.1%	0.35 [0.23, 0.47]
Frazão 2022b	0.31	0.16	10	0.15	0.17	10	21.5%	0.16 [0.02, 0.30]
Medrinal 2015	0.99	0.38	3	0.59	0.31	6	6.6%	0.41 [-0.09, 0.91]
Medrinal 2018.2	0.58	0.16	23	0.54	0.16	23	24.5%	0.04 [-0.05, 0.13]
Raymond 1997	1.56	0.08	7	1.24	0.10	7	24.3%	0.32 [0.23, 0.41]
Total (95% CI)			**53**			**56**	**100.0%**	**0.23 [0.08, 0.38]**

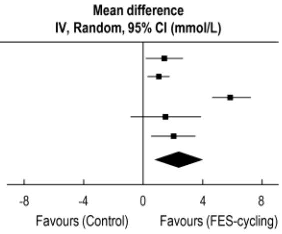
Heterogeneity: Tau² = 0.02; Chi² = 24.57, df = 4 (P < 0.0001); I² = 84%
Test for overall effect: Z = 3.07 (P = 0.002)
Test for subgroup differences: Not applicable



Lactate

Study or Subgroup	FES-cycling Mean (mmol/L)	FES-cycling SD (mmol/L)	FES-cycling Total	Control Mean (mmol/L)	Control SD (mmol/L)	Control Total	Weight	Mean difference IV, Random, 95% CI (mmol/L)
Godja 2019	0.7	1.06	14	-0.7	2.18	14	20.6%	1.40 [0.13, 2.67]
Hasnan 2013	3.9	0.85	9	2.9	0.54	9	22.2%	1.00 [0.34, 1.66]
Kjaer 1994	7.2	1.70	8	1.4	0.81	8	20.5%	5.80 [4.50, 7.10]
Medrinal 2018.2	2.1	4.63	23	0.6	3.17	23	16.8%	1.48 [-0.81, 3.77]
Paulson 2014	3.9	1.56	5	1.9	0.65	5	19.9%	2.00 [0.52, 3.48]
Total (95% CI)			**59**			**59**	**100.0%**	**2.35 [0.53, 4.16]**

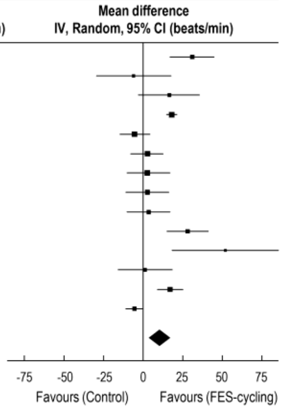
Heterogeneity: Tau² = 3.76; Chi² = 42.23, df = 4 (P < 0.00001); I² = 91%
Test for overall effect: Z = 2.53 (P = 0.01)
Test for subgroup differences: Not applicable



Heart rate

Study or Subgroup	FES-cycling Mean (beats/min)	FES-cycling SD (beat/min)	FES-cycling Total	Control Mean (beats/min)	Control SD (beat/min)	Control Total	Weight	Mean difference IV, Random, 95% CI (beats/min)
Edwards 2018	33.6	15.62	6	2.0	7.21	5	7.1%	31.60 [17.59, 45.61]
Formusek 2014	37.0	23.26	8	43.0	25.08	8	4.8%	-6.00 [-29.70, 17.70]
Hamzaid 2018	25.8	17.86	5	9.0	10.16	4	5.9%	16.80 [-1.77, 35.37]
Hooker 1992	51.0	2.24	8	33.0	2.83	8	9.5%	18.00 [15.50, 20.50]
Kjaer 1994	66.8	6.96	8	71.9	11.41	8	8.3%	-5.16 [-14.12, 4.10]
Medrinal 2018.2	10.1	17.30	23	7.5	16.88	23	8.2%	2.60 [-7.28, 12.48]
Medrinal 2018a	3.0	21.28	19	0	20.53	19	7.3%	3.00 [-10.30, 16.30]
Medrinal 2018b	3.0	21.28	19	0	22.01	19	7.2%	3.00 [-10.77, 16.77]
Medrinal 2018c	3.0	21.28	19	-1.0	22.31	19	7.1%	4.00 [-9.86, 17.86]
Muraki 2007	23.0	12.08	4	-5.0	5.10	4	7.4%	28.00 [15.15, 40.85]
Nash 1995	40.0	31.40	6	-12.2	28.90	6	3.1%	52.20 [18.05, 86.35]
Paulson 2014	105.0	11.00	5	104.0	16.00	5	6.3%	1.00 [-16.02, 18.02]
Raymond 1997	69.0	7.81	7	52.0	7.07	7	8.7%	17.00 [9.20, 24.80]
Raymond 1999	44.0	5.39	10	49.0	6.71	10	9.1%	-5.00 [-10.33, 0.33]
Total (95% CI)			**147**			**145**	**100.0%**	**9.94 [2.62, 17.25]**

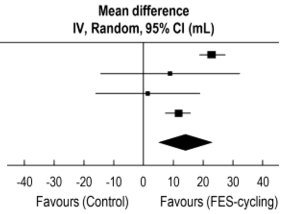
Heterogeneity: Tau² = 145.06; Chi² = 106.45, df = 13 (P < 0.00001); I² = 88%
Test for overall effect: Z = 2.66 (P = 0.008)
Test for subgroup differences: Not applicable



Stroke volume

Study or Subgroup	FES-cycling Mean (mL)	FES-cycling SD (mL)	FES-cycling Total	Control Mean (mL)	Control SD (mL)	Control Total	Weight	Mean difference IV, Random, 95% CI (mL)
Hooker 1992	17.0	3.61	8	-6.0	4.24	8	36.4%	23.00 [19.14, 26.86]
Murki 2007	14.0	11.40	4	5.0	21.02	4	11.3%	9.00 [-14.43, 32.43]
Nash 1995	3.0	20.51	6	1.5	8.07	6	16.3%	1.50 [-16.14, 19.14]
Raymond 1999	29.5	4.83	10	17.7	4.74	10	36.0%	11.80 [7.61, 15.99]
Total (95% CI)			**28**			**28**	**100.0%**	**13.88 [4.52, 23.24]**

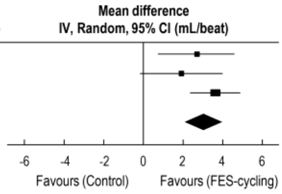
Heterogeneity: Tau² = 58.73; Chi² = 18.55, df = 13 (P = 0.0003); I² = 84%
Test for overall effect: Z = 2.91 (P = 0.004)
Test for subgroup differences: Not applicable



Oxygen pulse

Study or Subgroup	FES-cycling Mean (mL/beat)	FES-cycling SD (mL/beat)	FES-cycling Total	Control Mean (mL/beat)	Control SD (mL/beat)	Control Total	Weight	Mean difference IV, Random, 95% CI (mL/beat)
Frazão 2022a	2.2	2.58	10	-0.5	1.66	10	24.6%	2.70 [0.80, 4.60]
Frazão 2022b	2.2	2.58	10	0.3	2.05	10	21.4%	1.90 [-0.14, 3.94]
Raymond 1997	12.2	1.20	7	8.6	1.20	7	54.0%	3.60 [2.34, 4.86]
Total (95% CI)			**27**			**27**	**100.0%**	**3.02 [2.06, 3.97]**

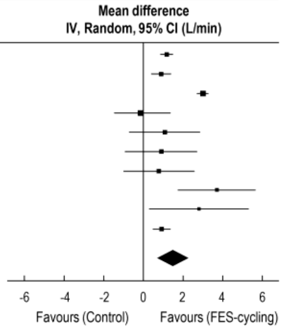
Heterogeneity: Tau² = 0.03; Chi² = 2.08, df = 2 (P = 0.35); I² = 4%
Test for overall effect: Z = 6.17 (P < 0.00001)
Test for subgroup differences: Not applicable



Cardiac output

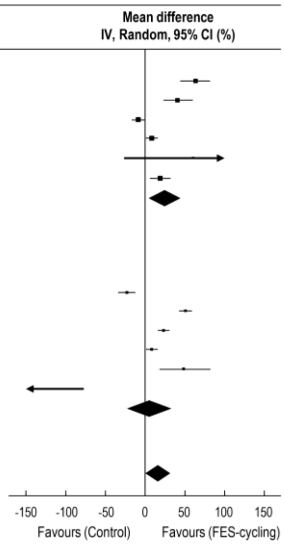
Study or Subgroup	FES-cycling Mean (L/min)	FES-cycling SD (L/min)	FES-cycling Total	Control Mean (L/min)	Control SD (L/min)	Control Total	Weight	Mean difference IV, Random, 95% CI (L/min)
Frazão 2022a	1.1	0.28	10	-0.1	0.28	10	13.1%	1.20 [0.95, 1.45]
Frazão 2022b	1.1	0.28	10	0.2	0.63	10	12.8%	0.90 [0.47, 1.33]
Hooker 1992	5.5	0.22	8	2.5	0.22	8	13.2%	3.00 [2.78, 3.22]
Kjaer 1994	9.9	1.47	8	9.9	1.34	8	9.7%	-0.08 [-1.46, 1.30]
Medrinal 2018a	1.0	2.86	19	-0.1	2.64	19	8.3%	1.10 [-0.65, 2.85]
Medrinal 2018b	1.0	2.86	19	0.1	2.79	19	8.2%	0.90 [-0.90, 2.70]
Medrinal 2018c	1.0	2.86	19	0.2	2.79	19	8.2%	0.80 [-1.00, 2.60]
Muraki 2007	3.5	1.30	4	-0.2	1.49	4	7.7%	3.70 [1.76, 5.64]
Nash 1995	2.5	2.58	6	-0.3	1.72	6	6.0%	2.80 [0.32, 5.28]
Raymond 1999	6.5	0.54	10	5.6	0.47	10	12.8%	0.90 [0.46, 1.34]
Total (95% CI)			**113**			**113**	**100.0%**	**1.46 [0.63, 2.28]**

Heterogeneity: Tau² = 1.33; Chi² = 186.98, df = 9 (P < 0.00001); I² = 95%
Test for overall effect: Z = 3.47 (P = 0.0005)
Test for subgroup differences: Not applicable



Peripheral muscle oxygen extraction

Study or Subgroup	FES-cycling Mean (%)	FES-cycling SD (%)	FES-cycling Total	Control Mean (%)	Control SD (%)	Control Total	Weight	Mean difference IV, Random, 95% CI (%)
Arterial-mixed venus oxygen content difference								
Frazão 2022a	56.9	22.4	10	-5.9	18.6	10	8.8%	62.80 [44.75, 80.85]
Frazão 2022b	56.9	22.4	10	15.7	14.9	10	8.9%	41.20 [24.53, 57.87]
Hasnan 2013	12.8	5.8	9	21.6	5.7	9	9.8%	-8.80 [-14.11, -3.49]
Hooker 1992	83.6	5.9	8	75.4	5.9	8	9.8%	8.20 [2.42, 13.98]
Nash 1995	55.8	93.3	6	-4.1	51.0	6	2.6%	59.90 [-25.18, 144.98]
Raymond 1999	128.3	14.6	10	109.8	13.8	10	9.3%	18.50 [6.05, 30.95]
Subtotal (95% CI)			**53**			**53**	**49.1%**	**24.29 [5.41, 43.17]**
Heterogeneity: Tau² = 442.50; Chi² = 90.72, df = 5 (P < 0.00001); I² = 94%								
Test for overall effect: Z = 2.52 (P = 0.01)								
Near infrared spectroscopy - Deoxyhemoglobin								
Hasnan 2018	-22.15	9.7	8	-0.06	0.03	8	9.7%	-22.09 [-28.81, -15.37]
Medrinal 2018a	24.00	9.0	19	-27.11	11.44	19	9.7%	51.11 [44.56, 57.66]
Medrinal 2018b	24.00	9.0	19	1.39	10.70	19	9.7%	22.61 [16.32, 28.90]
Medrinal 2018c	24.00	9.0	19	15.87	11.07	19	9.7%	8.13 [1.71, 14.55]
Muraki 2007	28.75	32.7	4	-21.50	4.46	4	7.0%	50.28 [17.91, 82.59]
Prieur 2019	84.00	29.0	8	212.00	65.00	8	5.0%	-128.00 [-177.32, -78.68]
Subtotal (95% CI)			**77**			**77**	**50.9%**	**3.85 [-22.74, 30.44]**
Heterogeneity: Tau² = 984.13; Chi² = 280.77, df = 5 (P < 0.00001); I² = 98%								
Test for overall effect: Z = 0.28 (P = 0.78)								
Total (95% CI)			**130**			**130**	**100.0%**	**15.25 [-0.56, 31.05]**
Heterogeneity: Tau² = 657.59; Chi² = 388.52, df = 11 (P < 0.00001); I² = 97%								
Test for overall effect: Z = 1.89 (P = 0.06)								
Test for subgroup differences: Chi² = 1.51, df = 1 (P = 0.22); I² = 33.7%								

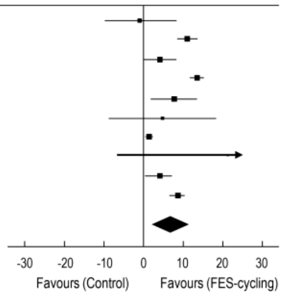


Ventilatory

Study or Subgroup	FES-cycling Mean (L/min)	FES-cycling SD (L/min)	FES-cycling Total	Control Mean (L/min)	Control SD (L/min)	Control Total	Weight	Mean difference IV, Random, 95% CI (L/min)
Fornusek 2014	22.3	8.90	8	23.1	9.08	8	8.7%	-0.80 [-9.61, 8.01]
Frazão 2022a	11.0	3.16	10	0.0	2.24	10	12.1%	11.00 [8.60, 13.40]
Frazão 2022b	11.0	3.16	10	7.0	6.08	10	11.3%	4.00 [-0.25, 8.25]
Hooker 1992	29.7	0.82	8	15.9	0.73	8	12.4%	13.80 [13.04, 14.56]
Kjaer 1994	23.8	6.82	8	16.1	5.23	8	10.4%	7.67 [1.71, 13.63]
Medrinal 2015	18.8	11.55	6	13.9	12.06	6	6.3%	4.85 [-8.51, 18.21]
Medrinal 2018.2	25.0	1.50	23	23.6	1.50	23	12.4%	1.40 [0.53, 2.27]
Muraki 2007	23.7	14.63	1	2.1	1.97	4	2.2%	21.60 [-7.14, 50.34]
Raymond 1997	39.8	2.31	7	35.9	3.96	7	11.7%	3.90 [0.50, 7.30]
Raymond 1999	27.8	2.28	10	19.2	1.24	10	12.3%	8.60 [6.99, 10.21]
Total (95% CI)			**91**			**94**	**100.0%**	**6.71 [1.95, 11.47]**

Heterogeneity: Tau² = 47.27; Chi² = 464.70, df = 9 (P < 0.00001); I² = 98%
Test for overall effect: Z = 2.76 (P = 0.006)
Test for subgroup differences: Not applicable

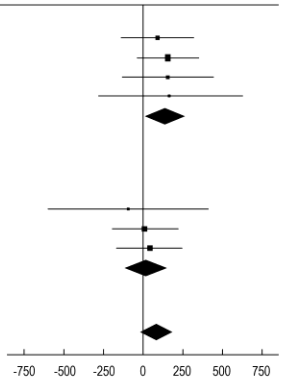
Mean difference IV, Random, 95% CI (L/min)



Cardiorespiratory fitness

Study or Subgroup	FES-cycling Mean (mL/min)	FES-cycling SD (mL/min)	FES-cycling Total	Control Mean (mL/min)	Control SD (mL/min)	Control Total	Weight	Mean difference IV, Random, 95% CI (mL/min)
More than 8 weeks								
Bakkum 2015	140	290.0	10	50	240.8	10	16.3%	90.00 [-143.63, 323,63]
Brurok 2011	160	178.0	6	10	162.8	6	23.8%	150.00 [-43.01, 343.01]
Johnston 2009a	100	344.0	8	-50	248.4	8	10.3%	150.00 [-144.03, 444.03]
Johnston 2009b	100	344.0	8	-60	566.0	8	4.2%	160.00 [-298.97, 618.97]
Subtotal (95% CI)			**32**			**32**	**54.6%**	**132.89 [5.35, 260.43]**
Heterogeneity: Tau² = 0.00; Chi² = 0.19, df = 3 (P = 0.98); I² = 0%								
Test for overall effect: Z = 2.04 (P = 0.04)								
Up to 8 weeks								
Janssen 2008	100	424.0	6	200	424.2	5	3.5%	-100.00 [-603.34, 403.34]
Sansare 2021a	23	228.0	14	21	291.5	11	20.2%	2.00 [-207.61, 211.61]
Sansare 2021b	23	228.0	14	-11	276.6	11	21.7%	34.00 [-168.44, 236.44]
Subtotal (95% CI)			**34**			**27**	**45.4%**	**9.40 [-130.48, 149.28]**
Heterogeneity: Tau² = 0.00; Chi² = 0.24, df = 2 (P = 0.89); I² = 0%								
Test for overall effect: Z = 0.13 (P = 0.090)								
Total (95% CI)			**66**			**59**	**100.0%**	**76.83 [-17.41, 171.08]**
Heterogeneity: Tau² = 0.00; Chi² = 2.06, df = 6 (P = 0.91); I² = 0%								
Test for overall effect: Z = 1.60 (P = 0.11)								
Test for subgroup differences: Chi² = 1.63, df = 1 (P = 0.20); I² = 38.8%								

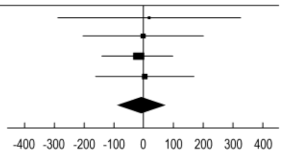
Mean difference IV, Random, 95% CI (mL/min)



Six-minute walking distance

Study or Subgroup	FES-cycling Mean (meters)	FES-cycling SD (meters)	FES-cycling Total	Control Mean (meters)	Control SD (meters)	Control Total	Weight	Mean difference IV, Random, 95% CI (meters)
Cudia 2016	58.0	181.2	4	40.0	250.0	4	7.7%	18.00 [-284.58, 320.58]
Janssen 2008	25.0	199.6	6	25.0	149.6	6	17.6%	0.00 [-199.59, 199.59]
Özen 2021a	30.9	137.0	9	48.6	122.9	9	48.6%	-17.67 [-137.91, 102.57]
Özen 2021b	30.9	137.0	9	24.2	185.9	7	26.1%	6.67 [-157.57, 170.91]
Total (95% CI)			**28**			**26**	**100.0%**	**-5.46 [-89.31, 78.37]**
Heterogeneity: Tau² = 0.00; Chi² = 0.09, df = 3 (P = 0.99); I² = 0%								
Test for overall effect: Z = 0.13 (P = 0.90)								
Test for subgroup differences: Not applicable								

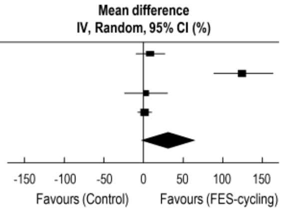
Mean difference IV, Random, 95% CI (meters)



Muscle cross-sectional area

Study or Subgroup	FES-cycling Mean (%)	FES-cycling SD (%)	FES-cycling Total	Control Mean (%)	Control SD (%)	Control Total	Weight	Mean difference IV, Random, 95% CI (%)
Berney 2021	-6.8	63.8	80	-15.5	49.1	82	26.5%	8.70 [-8.86, 26.26]
Demchack 2005	63.4	29.2	5	-61.7	31.3	5	21.3%	125.10 [87.58, 162.62]
Galea 2017	-10.1	38.0	10	-13.6	23.4	11	24.2%	3.50 [-23.81, 30.81]
Waldauf 2021	-11.0	20.8	57	-13.0	22.0	54	28.0%	2.00 [-5.97, 9.97]
Total (95% CI)			**152**			**152**	**100.0%**	**30.40 [-4.31, 65.12]**

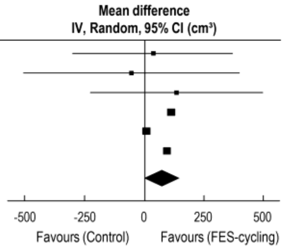
Heterogeneity: Tau² = 1104.07; Chi² = 39.66, df = 3 (P < 0.00001); I² = 92%
Test for overall effect: Z = 1.72 (P = 0.09)
Test for subgroup differences: Not applicable



Muscle volume

Study or Subgroup	FES-cycling Mean (cm³)	FES-cycling SD (cm³)	FES-cycling Total	Control Mean (cm³)	Control SD (cm³)	Control Total	Weight	Mean difference IV, Random, 95% CI (cm³)
Johnston 2011a	55.0	447	8	20.0	186	8	4.1%	35.00 [-300.50, 370.50]
Johnston 2011b	55.0	447	8	110.0	469	8	2.4%	-55.00 [-503.96, 393.96]
Panisset 2022	-45.1	501	10	-172.4	268	9	3.7%	127.30 [-229.18, 483.78]
Sadowsky 2013a	368.0	15	25	253.0	15	20	29.9%	115.00 [106.18, 123.82]
Sadowsky 2013b	81.0	5	25	71.0	5	20	30.0%	10.00 [7.06, 12.94]
Sadowsky 2013c	297.0	20	25	201.0	20	20	29.8%	96.00]84.24, 107.76[
Total (95% CI)			**101**			**85**	**100.0%**	**70.82 [-2.36, 144.01]**

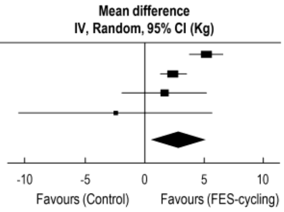
Heterogeneity: Tau² = 4641.09; Chi² = 640.35, df = 5 (P < 0.00001); I² = 99%
Test for overall effect: Z = 1.90 (P = 0.06)
Test for subgroup differences: Not applicable



Leg lean mass

Study or Subgroup	FES-cycling Mean (Kg)	FES-cycling SD (Kg)	FES-cycling Total	Control Mean (Kg)	Control SD (Kg)	Control Total	Weight	Mean difference IV, Random, 95% CI (Kg)
Baldi 1998a	1.55	0.95	9	-3.59	1.86	9	35.8%	5.14 [3.78, 6.50]
Baldi 1998b	1.55	0.95	9	-0.83	1.22	8	37.9%	2.38 [1.33, 3.43]
Dolbow 2020	0.60	1.98	5	-1.10	3.59	5	19.8%	1.70 [-1.89, 5.29]
Galea 2017	-0.50	8.90	10	1.90	9.96	11	6.4%	-2.40 [-10.47, 5.67]
Total (95% CI)			**33**			**33**	**100.0%**	**2.93 [0.71, 5.15]**

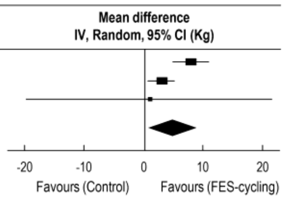
Heterogeneity: Tau² = 3.09; Chi² = 12.61, df = 3 (P = 0.006); I² = 76%
Test for overall effect: Z = 2.59 (P = 0.010)
Test for subgroup differences: Not applicable



Total body lean mass

Study or Subgroup	FES-cycling Mean (Kg)	FES-cycling SD (Kg)	FES-cycling Total	Control Mean (Kg)	Control SD (Kg)	Control Total	Weight	Mean difference IV, Random, 95% CI (Kg)
Baldi 1998a	2.9	1.7	9	-4.83	4.2	9	45.5%	7.73 [4.77, 10.69]
Baldi 1998b	2.9	1.7	9	-0.05	2.7	8	50.7%	2.95 [0.77, 5.13]
Dolbow 2020	0.5	21.4	5	-0.40	9.9	5	3.9%	0.90 [-19.77, 21.57]
Total (95% CI)			**23**			**22**	**100.0%**	**5.04 [0.82, 9.27]**

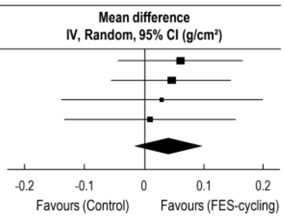
Heterogeneity: Tau² = 7.94; Chi² = 6.63, df = 2 (P = 0.04); I² = 70%
Test for overall effect: Z = 2.34 (P = 0.02)
Test for subgroup differences: Not applicable



Bone density

Study or Subgroup	FES-cycling Mean (g/cm²)	FES-cycling SD (g/cm²)	FES-cycling Total	Control Mean (g/cm²)	Control SD (g/cm²)	Control Total	Weight	Mean difference IV, Random, 95% CI (g/cm²)
Bloomfield 1996	0.048	0.131	7	-0.012	0.060	8	32.7%	0.06 [-0.05, 0.17]
Lai 2010	-0.022	0.090	12	-0.067	0.151	12	36.9%	0.05 [-0.05, 0.14]
Lauer 2011a	0.015	0.206	10	-0.014	0.169	9	12.8%	0.03 [-0.14, 0.20]
Lauer 2011b	0.015	0.206	10	0.006	0.102	9	17.6%	0.01 [-0.14, 0.15]
Total (95% CI)			**39**			**38**	**100.0%**	**0.04 [-0.02, 0.10]**

Heterogeneity: Tau² = 0.00; Chi² = 0.34, df = 3 (P = 0.95); I² = 0%
Test for overall effect: Z = 1.35 (P = 0.18)
Test for subgroup differences: Not applicable

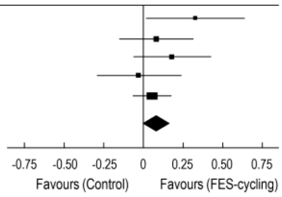


Pendulum test – relaxation index

Study or Subgroup	FES-cycling Mean (score)	FES-cycling SD (score)	FES-cycling Total	Control Mean (score)	Control SD (score)	Control Total	Weight	Mean difference IV, Random, 95% CI (score)
Krause 2008	0.39	0.14	5	0.06	0.32	5	8.1%	0.33 [0.02, 0.64]
Lo 2009a	0.19	0.33	17	0.11	0.33	17	15.2%	0.08 [-0.14, 0.30]
Lo 2009b	0.19	0.33	17	0.01	0.38	17	13.2%	0.18 [-0.06, 0.42]
Lo 2012	0.06	0.22	10	0.09	0.37	10	10.6%	-0.03 [-0.30, 0.24]
Yeh 2010	0.10	0.16	16	0.05	0.17	16	52.8%	0.05 [-0.06, 0.16]
Total (95% CI)			**65**			**65**	**100.0%**	**0.09 [0.00, 0.17]**

Heterogeneity: Tau² = 0.00; Chi² = 4.14, df = 4 (P = 0.39); I² = 3%
Test for overall effect: Z = 1.91 (P = 0.06)
Test for subgroup differences: Not applicable

Mean difference IV, Random, 95% CI (score)

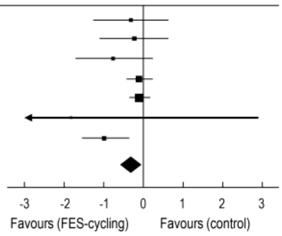


Ashworth Scale

Study or Subgroup	FES-cycling Mean (score)	FES-cycling SD (score)	FES-cycling Total	Control Mean (score)	Control SD (score)	Control Total	Weight	Mean difference IV, Random, 95% CI (score)
Krause 2008	-1.25	0.58	5	-0.92	0.85	5	7.8%	-0.33 [-1.23, 0.57]
Lo 2009a	-0.59	1.11	10	-0.35	1.14	17	8.2%	-0.24 [-1.12, 0.64]
Lo 2009b	-0.59	1.11	10	0.18	1.35	17	7.3%	-0.77 [-1.71, 0.17]
Özen 2021a	-0.62	0.22	9	-0.50	0.43	9	28.3%	-0.12 [-0.44, 0.20]
Özen 2021b	-0.61	0.22	10	-0.50	0.27	7	33.3%	-0.11 [-0.35, 0.13]
Ralston 2013	-2.80	5.14	14	-1.00	7.32	14	0.3%	-1.80 [-6.49, 2.89]
Yeh 2010	-1.00	0.56	16	0.00	1.06	16	14.9%	-1.00 [-1.59, -0.41]
Total (95% CI)			**74**			**85**	**100.0%**	**-0.33 [-0.60, -0.05]**

Heterogeneity: Tau² = 0.05; Chi² = 9.75, df = 6 (P = 0.14); I² = 38%
Test for overall effect: Z = 2.31 (P = 0.02)
Test for subgroup differences: Not applicable

Mean difference IV, Random, 95% CI (score)

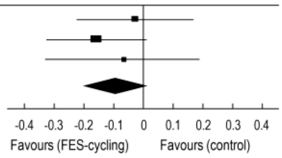


Hoffman reflex (H/M ratio)

Study or Subgroup	FES-cycling Mean (score)	FES-cycling SD (score)	FES-cycling Total	Control Mean (score)	Control SD (score)	Control Total	Weight	Mean difference IV, Random, 95% CI (score)
Lo 2009a	-0.13	0.30	17	-0.10	0.28	17	34.5%	-0.03 [-0.23, 0.17]
Lo 2009b	-0.13	0.30	17	0.03	0.19	17	46.1%	-0.16 [-0.33, 0.01]
Lo 2012	-0.21	0.20	10	-0.14	0.37	10	19.3%	-0.07 [-0.33, 0.019]
Total (95% CI)			**44**			**44**	**100.0%**	**-0.10 [-0.21, 0.02]**

Heterogeneity: Tau² = 0.00; Chi² = 1.03, df = 2 (P = 0.60); I² = 0%
Test for overall effect: Z = 1.67 (P = 0.09)
Test for subgroup differences: Not applicable

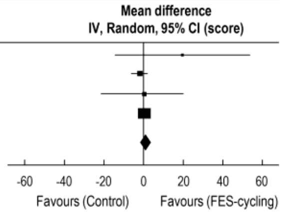
Mean difference IV, Random, 95% CI (score)



Motricity index

Study or Subgroup	FES-cycling Mean (score)	FES-cycling SD (score)	FES-cycling Total	Control Mean (score)	Control SD (score)	Control Total	Weight	Mean difference IV, Random, 95% CI (score)
Ambrosini 2011	30.0	41.6	12	10.0	46.1	13	0.4%	20.00 [-14.38, 54.38]
Bauer 2014	11.0	6.6	19	12.0	6.4	19	29.9%	-1.00 [-5.13, 3.13]
Ferrante 2008	26.0	17.7	10	26.5	28.7	10	1.2%	-0.50 [-21.40, 20.40]
Janssen 2008	0.9	2.9	6	0.3	1.8	6	68.5%	0.60 [-2.13, 3.33]
Total (95% CI)			**47**			**48**	**100.0%**	**0.19 [-2,07, 2.45]**

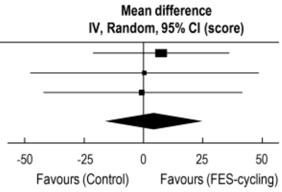
Heterogeneity: Tau² = 0.00; Chi² = 1.68, df = 3 (P = 0.64); I² = 0%
Test for overall effect: Z = 0.17 (P = 0.87)
Test for subgroup differences: Not applicable



Gross Motor Function Measure 88

Study or Subgroup	FES-cycling Mean (score)	FES-cycling SD (score)	FES-cycling Total	Control Mean (score)	Control SD (score)	Control Total	Weight	Mean difference IV, Random, 95% CI (score)
Armstrong 2020	9.8	33.3	11	2.5	32.8	10	55.1%	7.30 [-20.99, 35.59]
Özen 2021a	4.3	46.3	9	3.6	57.3	9	19.0%	0.75 [-47.39, 48.89]
Özen 2021b	4.3	46.3	9	5.0	38.0	7	25.8%	-0.67 [-42.00, 40.66]
Total (95% CI)			**29**			**26**	**100.0%**	**3.99 [-17.01, 25.00]**

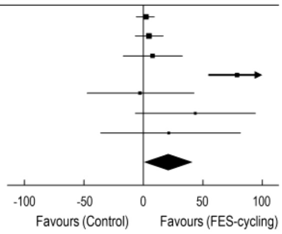
Heterogeneity: Tau² = 0,00; Chi² = 0.12, df = 2 (P = 0.94); I² = 0%
Test for overall effect: Z = 0.37 (P = 0.71)
Test for subgroup differences: Not applicable



Torque

	FES-cycling			Control				Mean difference	Mean difference
Study or Subgroup	Mean (Newtons)	SD (Newtons)	Total	Mean (Newtons)	SD (Newtons)	Total	Weight	IV, Random, 95% CI (Newtons)	IV, Random, 95% CI (Newtons)
Ambrosini 2011	-0.5	8.25	12	-1.7	7.87	13	21.4%	1.20 [-5.13, 7.53]	
Ambrosini 2012	6.8	16.75	13	2.1	12.09	13	20.4%	4.71 [-6.52, 15.94]	
deSousa 2016	14.7	39.77	20	6.9	41.36	20	16.0%	7.80 [-17.35, 32.95]	
Ferrante 2008	84.3	40.22	10	5.2	2.47	10	16.1%	79.12 [54.14, 104.10]	
Janssem 2008	9.7	44.40	4	12.7	18.20	15	10.1%	-3.00 [-47.48, 41.48]	
Johnston 2011a	55.8	58.07	9	11.7	52.78	9	8.6%	44.10 [-7.17, 95.37]	
Johnston 2011b	55.8	58.07	9	33.3	68.03	9	7.3%	22.50 [-35.94, 80.94]	
Total (95% CI)			**77**			**89**	**100.0%**	**20.31 [0.99, 39.63]**	

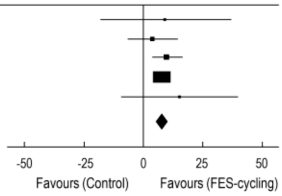
Heterogeneity: Tau² = 442.73; Chi² = 37.79, df = 6 (P < 0.00001); I² = 84%
Test for overall effect: Z = 2.06 (P = 0.04)
Test for subgroup differences: Not applicable



Power

	FES-cycling			Control				Mean difference	Mean difference
Study or Subgroup	Mean (Watts)	SD (Watts)	Total	Mean (Watts)	SD (Watts)	Total	Weight	IV, Random, 95% CI (Watts)	IV, Random, 95% CI (Watts)
Armstrong 2020	14.6	27.8	11	5.3	30.8	8	0.5%	9.30 [-17.65, 36.25]	
Bakkun 2015	5.9	12.8	10	1.8	10.8	10	3.5%	4.10 [-6.24, 14.44]	
Brurok 2011	10.0	5.8	6	0.0	4.2	6	11.4%	10.00 [4.23, 15.77]	
Ferrante 2008	4.4	3.3	10	-3.2	1.0	10	84.0%	7.60 [5.48, 9.72]	
Janssen 2008	15.3	23.9	6	0.0	19.2	6	0.6%	15.30 [-9.24, 39.84]	
Total (95% CI)			**43**			**40**	**100.0%**	**7.81 [5.86, 9.75]**	

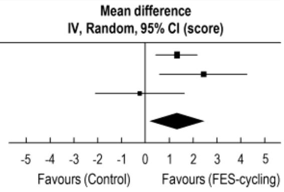
Heterogeneity: Tau² = 0.00; Chi² = 1.46, df = 4 (P = 0.83); I² = 0%
Test for overall effect: Z = 7.87 (P < 0.00001)
Test for subgroup differences: Not applicable



Physical Fitness in Intensive Care Test (PFIT)

Study or Subgroup	FES-cycling Mean (score)	FES-cycling SD (score)	FES-cycling Total	Control Mean (score)	Control SD (score)	Control Total	Weight	Mean difference IV, Random, 95% CI (score)
Berney 2021	6.4	2.4	80	5.1	3.0	82	49.6%	1.30 [0.46, 2.14]
Parry 2014	5.3	1.9	8	2.9	1.8	8	25.6%	2.40 [0.59, 4.21]
Waldauf 2021	9.4	4.2	37	9.6	4.2	42	24.8%	-0.20 [-2.06, 1.66]
Total (95% CI)			**125**			**132**	**100.0%**	**1.21 [0.04, 2.38]**

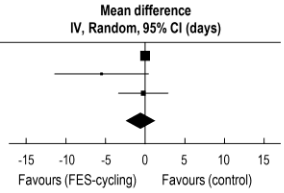
Heterogeneity: Tau² = 0.53; Chi² = 3.90, df = 2 (P = 0.14); I² = 49%
Test for overall effect: Z = 2.03 (P = 0.04)
Test for subgroup differences: Not applicable



ICU length of stay

Study or Subgroup	FES-cycling Mean (days)	FES-cycling SD (days)	FES-cycling Total	Control Mean (days)	Control SD (days)	Control Total	Weight	Mean difference IV, Random, 95% CI (days)
Berney 2021	6.0	1.8	80	6.0	1.8	82	66.4%	0.00 [-0.55, 0.55]
Parry 2014	9.0	3.4	8	14.5	7.8	8	8.9%	-5.50 [-11.40, 0.40]
Waldauf 2021	13.7	8.5	75	13.9	10.5	75	24.7%	-0.20 [-3.26, 2.86]
Total (95% CI)			**163**			**165**	**100.0%**	**-0.54 [-2.42, 1.34]**

Heterogeneity: Tau² = 1.31; Chi² = 3.32, df = 2 (P = 0.19); I² = 40%
Test for overall effect: Z = 0.56 (P = 0.57)
Test for subgroup differences: Not applicable



Study ID	Title	Population	Sample size	Mean age (SD)	Intervention	Control	Pulse width	Intensity	Frequency	Outcome variables
Edwards 2018	Cardiorespiratory demand of acute voluntary cycling with functional electrical stimulation in individuals with multiple sclerosis with severe mobility impairment.	Multiple sclerosis	11	58 (6)	Active FES-cycling	Passive cycling	250	NA	50	VO2, Heart Rate
Fornusek 2014	Cardiorespiratory responses during functional electrical stimulation cycling and electrical stimulation isometric exercise	Spinal cord injury	8	48 (14)	Passive FES-cycling	FES alone	300	40 to 140	35	VO2, Heart Rate
Frazão 2022	Metabolic, ventilatory and cardiovascular responses to FES-cycling: A comparison to NMES and passive cycling	Healthy	10	40 (15)	Passive FES-cycling	Passive cycling or FES alone	400	20 to 35	100	VO2, VCO2, Energy expenditure, Cardiac Output, Oxygen pulse, Ca-vO2, VE

Gojda 2019	Lactate production without hypoxia in skeletal muscle during electrical cycling: Crossover study of femoral venous-arterial differences in healthy volunteers	Healthy	14	31 (8)	Passive FES-cycling	Active cycling	NA	25 to 67	NA	Lactate
Kjaer 1994	Cardiovascular and ventilatory responses to electrically induced cycling with complete epidural anaesthesia in humans	Healthy	8	27 (2)	Passive FES-cycling	Active cycling	350	up to 130	30	VO2, Lactate, Cardiac Output, Heart Rate, VE
Hamzaid 2018	Heart rate and blood pressure following functional electrical stimulation evoked activity amongst inpatients with spinal cord injury	Spinal cord injury	9	42 (8)	Passive FES-cycling	Arm cycling	NA	NA	NA	Heart Rate

Hasnan 2013	Exercise responses during functional electrical stimulation cycling in individuals with spinal cord injury	Spinal cord injury	9	41 (1)	Passive FES-cycling + arm cycling	Arm cycling	300	up to 140	35	VO2, Lactate, Ca-vO2
Hasnan 2018	Muscle oxygenation during hybrid arm and functional electrical stimulation-evoked leg cycling after spinal cord injury	Spinal cord injury	8	42 (1)	Passive FES-cycling + arm cycling	Arm cycling	300	up to 140	35	Deoxyhemoglobin
Hooker 1992	Metabolic and hemodynamic responses to concurrent voluntary arm crank and electrical stimulation leg cycle exercise in quadriplegics	Spinal cord injury	8	33 (1)	Passive FES-cycling + arm cycling	Arm cycling	375	up to 130	35	VO2, Cardiac Output, Stroke volume, Heart Rate, Ca-vO2, VE
Medrinal 2015	Metabolic effects of electrotherapy combined with bedside cycle-	Healthy	6	23 (2)	Active FES-cycling	Active cycling	300	44 to 61	50	VO2, VCO2, VE

	ergometry: Preliminary study									
Medrinal 2018	Comparison of exercise intensity during four early rehabilitation techniques in sedated and ventilated patients in ICU: a randomized cross-over trial.	Critically ill	19	65 (10)	Passive FES-cycling	Passive leg mobilization or passive cycling or FES alone	300	NA	35	Cardiac Output, Heart Rate, Deoxyhemoglobin
Medrinal 2018.2	Functional Electrical Stimulation—A New Therapeutic Approach to Enhance Exercise Intensity in Chronic Obstructive Pulmonary Disease Patients: A Randomized, Controlled Crossover Trial.	COPD	23	63 (11)	Active FES-cycling	Placebo Active FES-cycling	300	38 ± 9	35	VO2, VCO2, Lactate, Heart Rate, VE
Muraki 2007	Muscle oxygenation during prolonged electrical	Spinal cord injury	4	35 (11)	Passive FES-cycling	Passive cycling	400	up to 140	30	VO2, Cardiac Output, Stroke volume,

	stimulation-evoked cycling in paraplegics									Heart Rate, Deoxyhemoglobin, VE
Nash 1995	Effects of electrically stimulated exercise and passive motion on echocardiographically-derived wall motion and cardiodynamic function in tetraplegic persons	Spinal cord injury	6	26 (3)	Passive FES-cycling	Passive cycling	375	up to 130	40	VO2, Cardiac Output, Stroke volume, Heart Rate, Ca-vO2
Prieur 2019	Functional Electrical Stimulation Changes Muscle Oxygenation in Patients with Chronic Obstructive Pulmonary Disease During Moderate-Intensity Exercise: A Secondary Analysis	COPD	23	63 (11)	Active FES-cycling	Placebo Active FES-cycling	300	38 ± 9	35	Deoxyhemoglobin

Raymond 1999	Cardiorespiratory responses to arm cranking and electrical stimulation leg cycling in people with paraplegia	Spinal cord injury	10	36 (2)	Passive FES-cycling + arm cycling	Arm cycling	375	up to 132	35	VO2, Cardiac Output, Stroke volume, Heart Rate, Ca-vO2, VE
Raymond 1997	Oxygen uptake and heart rate responses during arm vs combined arm/electrically stimulated leg exercise in people with paraplegia.	Spinal cord injury	7	32 (3)	Passive FES-cycling + arm cycling	Arm cycling	NA	NA	NA	VO2, VCO2, Heart Rate, Oxygen pulse, VE
Paulson 2014	Inflammation-mediating cytokine response to acute hand-cycling exercise with/without functional electrical stimulation-evoked lower-limb cycling.	Spinal cord injury	5	44 (15)	Passive FES-cycling + arm cycling	Arm cycling	NA	up to 145	35	VO2, Lactate, Heart Rate
Máté 2024	Functional electrical stimulation combined with	Multiple sclerosis	10	52 (10)	Active FES-cycling	Active cycling	300	NA	35	VO2

	voluntary cycling increases the VO2 response in people with severe multiple sclerosis: A pilot study									

FES: functional electrical stimulation, NA: non-available. VO2: oxygen consumption, VCO2: carbonic gas production, Ca-vO2: arterial-mixed venous oxygen content difference, VE: minute ventilation.

Study ID	Title	Population	Sample size	Mean age (SD)	Intervention	Control	Pulse width	Intensity	Frequency	Intervention time	Protocol	Outcome variables
Ambrosini 2012	Cycling induced by electrical stimulation improves muscle activation and symmetry during pedaling in hemiparetic patients	Stroke / traumatic brain injury	30	59 (10)	Passive FES-cycling	Placebo FES-cycling	300	20 to 60	20	4 weeks	5 times/week	Torque
Ambrosini 2011	Cycling Induced by Electrical Stimulation Improves Motor Recovery in Post acute Hemiparetic Patients: A Randomized Controlled Trial	Stroke / traumatic brain injury	30	59 (10)	Active FES-cycling	Placebo FES-cycling	300	20 to 60	20	4 weeks	5 times/week	Gait speed, Motricity index, Upright motor control test, Torque

Armstrong 2020	Functional electrical stimulation cycling, goal-directed training, and adapted cycling for children with cerebral palsy: a randomized controlled trial	Cerebral palsy	21	9 (3)	Active FES-cycling + Usual care	Usual care	90 to 250	10 to 50	40 to 50	8 weeks	3 times/week	Gross Motor Function Measure 88
Bakkum 2015	Effects of hybrid cycling versus handcycling on wheelchair-specific fitness and physical activity in people with long-term spinal cord injury: a 16-week randomized controlled trial	Spinal Cord Injury	20	48 (10)	Passive FES-cycling + Arm cycling	Arm cycling	NA	0 to 150	NA	16 weeks	2 times/week	Cardiorespiratory Fitness - VO2, Power

Baldi 1998	Muscle atrophy is prevented in patients with acute spinal cord injury using functional electrical stimulation	Spinal Cord Injury	26	28 (6)	Passive FES-cycling	no FES training or FES alone	375	0 to 140	60	6 months	3 times/week	Leg Lean mass, Total body Lean mass
Bauer 2014	Functional electrical stimulation-assisted active cycling--therapeutic effects in patients with hemiparesis from 7 days to 6 months after stroke:a randomized controlled pilot study	Stroke	40	59 (14)	Active FES-cycling	Active cycling	300 to 450	NA	20 to 60	4 weeks	3 times/week	Motricity index
Berney 2021	Functional electrical stimulation in-bed cycle ergometry in mechanically	Critically ill	162	61 (51-69)	FES-cycling + Usual care	Usual care	250 to 300	20 to 30	50	During ICU stay	5 times/week	Physical Function in Intensive Care Test (PFIT), Muscle CSA,

	ventilated patients: a multicentre randomized controlled trial											ICU length of stay, Patients Discharged to home, Delirium incidence
Bloomfield 1996	Bone mass and endocrine adaptations to training in spinal cord injured individuals	Spinal Cord Injury	17	28 (2)	Passive FES-cycling	no FES-cycling training	350	up to 130	50	9 months	NA	Bone density
Brurok 2011	Effect of Aerobic High-Intensity Hybrid Training on Stroke Volume and Peak Oxygen Consumption in Men with Spinal Cord Injury.	Spinal Cord Injury	6	40 (11)	Passive FES-cycling + Arm cycling	no FES-cycling training	NA	up to 140	NA	8 weeks preceeded by 7 weeks of regular daily activity	3 times/week	Cardiorespiratory Fitness - VO2, Power

Cudia 2016	Effects of Functional Electrical Stimulation Lower Extremity Training in Myotonic Dystrophy Type I: A Pilot Controlled Study	Myotonic Dystrophy Type I	8	53 (14)	FES-cycling	resistance + aerobic training	200	50 to 80	30	15 days	5 times/week	6MWT
deSousa 2016	Functional electrical stimulation cycling does not improve mobility in people with acquired brain injury and its effects on Torque are unclear: a randomized trial	Acquired brain injury	40	62 (15)	FES-cycling	Usual care	450	NA	50	4 weeks	5 times/week	Torque
Demchak 2005	Effects of functional electric stimulation cycle	Spinal Cord Injury	10	22 (5)	Passive FES-cycling	no FES-cycling training	NA	up to 140	NA	13 weeks	3 times/week	Muscle CSA, Fiber type composition

	ergometry training on lower limb musculature in acute SCI individuals											
Dolbow 2020	Electrically induced cycling and nutritional counseling for counteracting obesity after spinal cord injury: A pilot study	Spinal Cord Injury	10	34 (5)	Passive FES-cycling + nutrition	nutrition	350	up to 140	40	8 weeks	3 times/week	Leg Fat mass, Total body Fat, Leg Lean mass, Total body Lean mass
Eser 2003	Effect of electrical stimulation-induced cycling on bone mineral density in spinal cord-injured patients	Spinal Cord Injury	38	33 (11)	Passive FES-cycling + passive standing	passive standing	300 to 400	up to 140	30 to 60	6 months	3 times/week	Bone Density
Ferrante 2008	Cycling induced by functional electrical stimulation improves the	Stroke	20	51 (12)	Passive FES-cycling + standard rehabilitation	Standard Rehabilitation	NA	NA	NA	4 weeks	7 times/week	Motricity index, Upright motor control test, Torque, Power

	muscular Torque and the motor control of individuals with post-acute stroke											
Galea 2017	A Randomized Controlled Trial Investigating the Efficacy and Safety of Functional Electrical Stimulation–Assisted Cycling and Passive Cycling Initiated Early After Traumatic Spinal Cord Injury	Spinal Cord Injury	24	39 (15)	Passive FES-cycling	Passive cycling	300 to 500	up to 140	35	12 weeks	4 times/week	Muscle CSA, Leg Fat mass, Total body Fat, Leg Lean mass
Janssen 2008	Effects of electric stimulation-assisted cycling training in people with	Stroke	12	54 (11)	Active FES-cycling	Active placebo FES-cycling	NA	110 to 300	35	6 weeks	2 times/week	Cardiorespiratory Fitness - VO2, 6MWT, Motricity index,

	chronic stroke											Torque, Power
Johnston 2009	A randomized controlled trial on the effects of cycling with and without electrical stimulation on cardiorespiratory and vascular health in children with spinal cord injury	Spinal Cord Injury	30	10 (3)	Passive FES-cycling	Passive cycling or FES alone	150 to 300	up to 140	33	6 months	3 times/week	Cardiorespiratory Fitness - VO2
Johnston 2011	Muscle Changes Following Cycling and/or Electrical Stimulation in Pediatric Spinal Cord Injury	Spinal Cord Injury	30	11 (3)	Passive FES-cycling	Passive cycling or FES alone	150 to 300	up to 140	33	6 months	3 times/week	Muscle volume, Torque
Krause 2008	Changes in spastic muscle tone	Spinal Cord Injury	5	47 (12)	Passive FES-cycling	Passive cycling	500	up to 99	20	1 session		Pendulum Test -

	increase in patients with spinal cord injury using functional electrical stimulation and passive leg movements											relaxation index, Pendulum Test - peak velocity, Ashworth Scale
Lai 2010	Effects of functional electrical stimulation cycling exercise on bone mineral density loss in the early stages of spinal cord injury	Spinal Cord Injury	24	29 (5)	Passive FES-cycling	no FES-cycling training	300	NA	20	3 months	3 times/week	Bone density
Lauer 2011	Effects of cycling and/or electrical stimulation on bone mineral density in children with spinal cord injury	Spinal Cord Injury	30	11 (3)	Passive FES-cycling	Passive cycling or FES alone	150 to 300	up to 140	33	6 months	3 times/week	Bone density

Lo 2012	Cycling exercise with functional electrical stimulation improves postural control in stroke patients	Stroke	20	48 (3)	Active FES-cycling	Active cycling	NA	NA	NA	1 session		Pendulum Test - relaxation index, Hoffmann's reflex
Lo 2009	Effects of a functional electrical stimulation-assisted leg-cycling wheelchair on reducing spasticity of patients after stroke	Stroke	17	56 (7)	Active FES-cycling	Active cycling or arm exercise	300	40-64	20	3 sessions		Pendulum Test - relaxation index, Ashworth Scale, Hoffmann's reflex
Mateo 2021	Functional electrical stimulation-cycling favors erectus position restoration and walking in patients with critical COVID-19.	COVID-19	14	63 (9)	Active FES-cycling	Active cycling	NA	32 to 52	NA	4 weeks	3 times/week	Sedentary day time, Walking/running day time

	A proof-of-concept controlled study											
Özen 2021	Effectiveness of Functional Electrical Stimulation - Cycling Treatment in Children with Cerebral Palsy	Cerebral Palsy	25	6 (2)	Passive FES-cycling	Placebo passive FES-cycling or usual care	250-300	up to 100	30 to 45	4 weeks	5 times/week	6MWT, Ashworth Scale, Gross Motor Function Measure 88
Panisset 2022	Factors influencing thigh muscle volume change with cycling exercises in acute spinal cord injury - a secondary analysis of a randomized controlled trial	Spinal Cord Injury	24	40 (17)	Passive FES-cycling	Passive cycling	300 to 500	up to 140	35	12 weeks	4 times/week	Muscle volume
Parry 2014	Functional electrical stimulation with cycling in the	Critically ill	16	62 (18)	Passive FES-cycling + usual care	Usual care	300 to 400	up to 140	30 to 50	During ICU stay	5 times/week	Physical Function in Intensive Care Test (PFIT),

	critically ill: A pilot case-matched control study												Time for independent ambulation, Time to marching in place, ICU length of stay, patients discharged to home, delirium incidence
Ralston 2013	Functional electrical stimulation cycling has no clear effect on urine output, lower limb swelling, and spasticity in people with spinal cord injury: a randomized cross-over trial	Spinal Cord Injury	14	25 (25 to 32)	Passive FES-cycling + usual care	Usual care	350	up to 140	33	2 weeks	NA		Ashworth Scale
Sadowsky 2013	Lower extremity functional electrical	Spinal Cord Injury	45	35 (12)	Passive FES-cycling	no FES-cycling training	500	up to 140	100	3 months	NA		Muscle volume

	stimulation cycling promotes physical and functional recovery in chronic spinal cord injury.											
Sansare 2021	Aerobic Responses to FES-Assisted and Volitional Cycling in Children with Cerebral Palsy	Cerebral Palsy	36	14 (2)	Active FES-cycling	Active cycling or no intervention	NA	40	50	8 weeks	NA	Cardiorespiratory Fitness - VO2
Waldauf 2021	Functional electrical stimulation-assisted cycle ergometry-based progressive mobility programme for mechanically ventilated patients: randomized	Critically ill	150	60 (15)	Passive FES-cycling + usual care	Usual care	250	0-60	40	During ICU stay		Physical Function in Intensive Care Test (PFIT), Muscle CSA, ICU length of stay

	controlled trial with 6 months follow-up											
Yeh 2010	Effect of a Bout of Leg Cycling With Electrical Stimulation on Reduction of Hypertonia in Patients With Stroke	Stroke	16	55 (8)	Active FES-cycling	Active cycling	300	up to 100	20	1 session		Pendulum Test - relaxation index, Ashworth Scale

FES: functional electrical stimulation, NA: non-available, CSA: cross-sectional area, ICU: intensive care unit, 6MWT: six-minute walking test.

Table 3: Minimal clinically important difference (MCID) for FES-cycling compared to control – Physiological effects.

Variable	Minimal clinically important difference
Metabolic	
Oxygen consumption (L/min)	0.04
Carbonic gas (L/min)	0.06
Lactate (mmol/L	0.28
Cardiocirculatory	
Heart rate (beats/min)	4.20
Stroke volume (mL)	2.80
Oxygen pulse (mL/beat)	0.70
Cardiac output (L/min)	0.40
Muscle oxygen extraction	
Peripheral muscle oxygen extraction (%)	8.76
Ventilatory	
VE (L/min)	0.86

Table 4: GRADE analysis for FES-cycling physiological effects compared to control.

Certainty assessment							№ of patients		Effect	Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	FES-cycling	Control	Absolute (95% CI)	
Oxygen consumption										
15	randomised trials	not serious	not serious	not serious	not serious	none	130	129	MD 0.21 L/min higher (0.14 higher to 0.28 higher)	⊕⊕⊕⊕ High
Carbonic gas production										
5	randomised trials	not serious	not serious	not serious	not serious	none	53	56	MD 0.23 L/min higher (0.08 higher to 0.38 higher)	⊕⊕⊕⊕ High
Lactate										
5	randomised trials	not serious	not serious	not serious	not serious	none	59	59	MD 2.35 mmol/L higher (0.53 higher to 4.16 higher)	⊕⊕⊕⊕ High
Heart Rate										
14	randomised trials	not serious	serious[a]	not serious	not serious	none	147	145	MD 9.94 beats/min higher (2.62 higher to 17.25 higher)	⊕⊕⊕◯ Moderate
Stroke										
4	randomised trials	not serious	not serious	not serious	not serious	none	28	28	MD 13.88 mL higher (4.52 higher to 23.24 higher)	⊕⊕⊕⊕ High
Oxygen pulse										
3	randomised trials	not serious	not serious	not serious	not serious	none	27	27	MD 3.02 mL/beat higher (2.06 higher to 3.97 higher)	⊕⊕⊕⊕ High

Certainty assessment							№ of patients		Effect	Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	FES-cycling	Control	Absolute (95% CI)	
Cardiac output										
10	randomised trials	not serious	not serious	not serious	not serious	none	113	113	MD 1.46 L/min higher (0.63 higher to 2.28 higher)	⨁⨁⨁⨁ High
Peripheral muscle oxygen extraction										
12	randomised trials	not serious	serious[a]	not serious	not serious	none	130	130	MD 15.25 % higher (0.56 lower to 31.05 higher)	⨁⨁⨁◯ Moderate
Minute ventilation										
10	randomised trials	not serious	not serious	not serious	not serious	none	91	94	MD 6.71 L/min higher (1.95 higher to 11.47 higher)	⨁⨁⨁⨁ High

CI: confidence interval; MD: mean difference.

Explanations: a. Eyeball test and I square showing a substantial heterogeneity;

Table 5: Minimal clinically important (MCID) difference for FES-cycling compared to control – Clinical effects.

Variable	Minimal clinically important difference
Functional capacity	
Cardiorespiratory fitness (mL/min)	80
Six-minute walking distance (meters)	44
Body composition	
Muscle cross-sectional area (%)	11.20
Muscle volume (cm^3)	66
Leg lean mass (kg)	0.88
Total body lean mass (kg)	2.52
Bone density (g/cm^2)	0.01
Spasticity	
Pendulum test (score)	0.07
Ashworth scale *(score)*	0.40
Hoffmann reflex *(score)*	0.09
Mobility	
Motricity index(score)	4.60
Gross Motor Function Measure 88 (score)	11.50
Muscle performance	
Torque (Newtons)	11
Power (Watts)	3.80
Critical illness	
Physical Fitness in Intensive Care Test (score)	1.12
Intensive care unit length of stay (days)	1.84

Table 6: GRADE analysis for FES-cycling clinical effects compared to control.

Certainty assessment							№ of patients		Effect	Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	FES-cycling	Control	Absolute (95% CI)	
Cardiorespiratory fitness										
7	randomised trials	serious[a]	not serious	not serious	not serious	strong association	66	59	MD 76.83 mL/min higher (17.41 lower to 171.08 higher)	⊕⊕⊕⊕ High
Six-minute walking distance										
4	randomised trials	serious[a]	not serious	not serious	not serious	none	28	26	MD 5.47 meters lower (89.31 lower to 78.37 higher)	⊕⊕⊕◯ Moderate
Muscle cross sectional area										
4	randomised trials	not serious	very serious[b]	not serious	not serious	none	152	152	MD 30.4 % higher (4.31 lower to 65.12 higher)	⊕⊕◯◯ Low
Muscle volume										
6	randomised trials	serious[a]	serious[b]	not serious	not serious	none	101	85	MD 70.82 cm^3 higher (2.36 lower to 144.01 higher)	⊕⊕◯◯ Low
Leg lean mass										
4	randomised trials	serious[c]	not serious	not serious	not serious	none	33	33	MD 2.93 Kg higher (0.71 higher to 5.15 higher)	⊕⊕⊕◯ Moderate
Total body lean mass										
3	randomised trials	serious[a]	not serious	not serious	not serious	none	23	22	MD 5.04 Kg higher (0.82 higher to 9.27 higher)	⊕⊕⊕◯ Moderate

Certainty assessment							№ of patients		Effect	Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	FES-cycling	Control	Absolute (95% CI)	
Bonde density										
4	randomised trials	serious[a]	not serious	not serious	not serious	none	39	38	MD 0.04 g/cm² higher (0.02 lower to 0.1 higher)	⊕⊕⊕◯ Moderate
Pendulum test – relaxation index										
5	randomised trials	serious[a]	not serious	not serious	not serious	none	65	65	MD 0.09 higher (0 to 0.17 higher)	⊕⊕⊕◯ Moderate
Ashworth Scale										
7	randomised trials	serious[a]	not serious	not serious	serious[d]	none	74	85	MD 0.33 lower (0.6 lower to 0.05 lower)	⊕⊕◯◯ Low
Hoffman reflex										
3	randomised trials	serious[a]	not serious	not serious	not serious	none	44	44	MD 0.1 lower (0.21 lower to 0.02 higher)	⊕⊕⊕◯ Moderate
Motricity index										
4	randomised trials	serious[a]	not serious	not serious	not serious	none	47	48	MD 0.19 higher (2.07 lower to 2.45 higher)	⊕⊕⊕◯ Moderate
Gross Motor Function Measure 88										
3	randomised trials	serious[a]	not serious	not serious	not serious	none	29	26	MD 3.99 higher (17.01 lower to 25 higher)	⊕⊕⊕◯ Moderate
Torque										

Certainty assessment							№ of patients		Effect	Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	FES-cycling	Control	Absolute (95% CI)	
7	randomised trials	serious[a]	serious[b]	not serious	not serious	none	77	89	MD 20.31 Newtons higher (0.99 higher to 39.63 higher)	⊕⊕◯◯ Low
Power										
5	randomised trials	serious[a]	not serious	not serious	not serious	strong association	43	40	MD 7.81 Watts higher (5.86 higher to 9.75 higher)	⊕⊕⊕⊕ High
Physical Fitness in Intensive Care Test										
3	randomised trials	not serious	not serious	not serious	not serious	none	125	132	MD 1.21 higher (0.04 higher to 2.38 higher)	⊕⊕⊕⊕ High
Intensive care unit length of stay										
3	randomised trials	not serious	serious[e]	not serious	not serious	none	163	165	MD 0.54 days lower (2.42 lower to 1.34 higher)	⊕⊕⊕◯ Moderate

CI: confidence interval; MD: mean difference.

Explanations: a. ROB2 pointed that more than 50% of the studies are some concerns; b. Eyeball test an I square showing a considerable heterogeneity; c. ROB2 pointed that 50% of the studies are some concerns, 25% are high risk and 25% are low risk; d. Below minimal clinically important difference; e. Eye ball test showing heterogeneity.