Evidence Based Review

The effectiveness of ERGYS - A Functional Electrical Stimulation Device used to improve the health and well-being of persons with spinal cord injuries.

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Date report completed	3rd of June

Please note:

This evidence based review summarises information on the effectiveness of Functional Electrical Stimulation and cycle ergometry in rehabilitation for spinal cord injured patients. It is not intended to replace clinical judgement or to be used as a clinical protocol. A reasonable attempt has been made to find and review papers relevant to the focus of this report. It does not claim to be exhaustive. This document has been prepared by staff of the ACC Evidence Based Healthcare Advisory Group. The content does not necessarily represent the official view of ACC or represent ACC policy. This report is based upon information retrieved up to the end of May 2005.

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1. Executive Summary

Background

An evidence based review of the effectiveness of ERGYS, a Functional Electrical Stimulation (FES) device used to restore muscle function and capacity for spinal cord injury patients was investigated. Currently ACC does not fund FES-cycle ergometer equipment for tetraplegics or paraplegics and a request for evidence which supports the appropriateness of ACC funding for these claimants was requested by a branch manager. The Evidence Based Healthcare Advisory Group has therefore reviewed the effectiveness of ERGYS as a rehabilitation intervention.

Objectives

To investigate the amount and range of information available which examines the effectiveness of ERGYS, a functional electrical stimulation device cycle ergometer, and if possible, determine guidelines as to whether ACC should fund this device for spinal cord injured patients.

Search strategy

Relevant databases and websites including Medline, Cinahl, and AMED were searched in February 2005 and in May 2005.

Selection criteria

Meta-analyses, systematic reviews and primary quantitative and qualitative studies of the effectiveness of FES-cycle ergometry in rehabilitation were included in the review if: (i) published in English; and (ii) published during or after 1996. References suggested by the requestor were also taken into consideration that dated back to 1996.

Data Collection and Analysis

Included studies were appraised and graded for methodological quality according to an evidence grading system developed by the Scottish Intercollegiate Guidelines Network.

Main results

A total of 29 papers met the selection criteria and were included in the review. All studies included adults only with either tetraplegia or paraplegia with varying post injury times. All outcomes were physiological rather than functional. The quality of the studies were moderate with only four papers graded with a 1- rating indicating that there is some evidence of effectiveness of FES-cycle ergometry. Three papers were controlled trials and hence were graded a level 2. The majority of other studies were case series or pre post tests where intervention measures were observed before and after intervention.

Reviewer's conclusions

Overall, there is moderate evidence for FES cycle ergometry. It appears beneficial for Spinal Cord Injured (SCI) users in terms of cardiovascular and muscle outcomes (morphology and function) given there is consistent use for a 3 month period or greater. There is insufficient evidence to suggest that FES-cycle ergometry reduces bone demineralisation.

It is recommended that ACC purchase on a case-by-case basis, where a clear exercise regime is stipulated over a 3 month or greater period and that the individual meets all of the criteria required for the safe use of such a piece of equipment. The other consideration is to fund FES cycle ergometers for communal use in spinal injury units such as Burwood Spinal Unit in Christchurch or Otara Spinal Unit in Auckland.

2. Background

Spinal Cord Injury (SCI) involves primarily damage to the neural components within the spinal canal and occasionally the injury may involve the nerve roots. SCI severely affects multiple organ systems and induce reduced or absent motor function. In addition the SCI individual may have alteration of bladder and bowel function, disturbed sexual activity and altered function of the sympathetic nervous system. Paraplegia involves the loss of leg function, whereas tetraplegia involves functional loss of the arms, trunk and legs. Persons with an "incomplete injury" have some spared sensory or motor function below the level of injury, that is, the spinal cord was not totally damaged or disrupted. In comparison "complete injury" refers to no motor or sensory function is preserved below the level of injury. The lifespan of the SCI patient has increased dramatically; however, it is still lower than the average life expectancy of the able bodied individual (Wilder *et al*, 2002)[37]

In recent years there has been a growing awareness of the need for physical exercise in SCI patients. One of the leading causes of death in the SCI population is cardiovascular disease which is associated with exercise inactivity. There is strong confirmation that functional electrical stimulation (FES) can significantly improve cardiovascular function in individuals with SCI (Wilder *et al*, 2002). [37]

FES is stimulation of the neuromuscular system by small electrical currents in functional or therapeutic applications. The FES cycle ergometer is one of the newer technologies on the market, and is used to enhance the health of patients suffering from SCI. The main goal of the FES cycle ergometer is to aid in the treatment of the cardiopulmonary and circulatory systems, muscles and bones which are severely affected due to injury by SCI.

2.1 Functional Electrical Stimulation

Functional Electrical Stimulation (FES) is a process where a computer generates low level electrical pulses that are carried through surface electrodes that are strategically placed over the motor nerves of the muscles. The electrical pulses stimulate the contraction of the targeted muscles. The computer controls all the stimulation parameters, including magnitude, frequency and sequence in order to produce a fluid pedalling motion (Wilder *et al*, 2002). [37]

2.2 Effects on the Cardiopulmonary and Circulatory Systems

SCI individuals have poor cardiopulmonary fitness as a result of their difficulty in exercising, loss of muscle mass and sympathetic autonomic impairment. Sympathetic autonomic impairment involves the separation of the peripheral sympathetic nervous system from control by the Central Nervous System (CNS) resulting in loss of control of sympathetic effector organs, including the myocardium and the smooth muscle of arteries and veins. This eventually limits exercise capacity and tolerance.

Tetraplegics and other SCI patients exhibit varying degrees of cardiac atrophy which involves the loss of Left Ventricular Mass. The atrophy is attributed to reduced venous return to the heart which in turn decreases cardiac wall stress and myocardial work resulting in changes to the structure and function of the heart. It has been shown that tetraplegics have a 26% smaller LV mass and that they also show reduced resting cardiac output, stroke volume, and mean arterial pressure in the sitting position.

It has been shown that exercise improves the cardiac and circulatory system of healthy, nondisabled persons[36,38]. Improvements in circulation lead to an enlargement of the LV Mass in persons with normal heart function. If exercise training is lessened or stopped, LV Mass will be reduced accordingly.

2.3 Effect on Muscle Morphology and Function

SCI patients lose the ability to use muscles below the level of the spinal cord lesion. This eventually leads to atrophy of the paralysed muscle fibres as well as a change in muscle fibre composition. Muscle deconditioning is a rapid process with most if it occurring within the first 6 months post injury.

Morphologic studies on muscles have shown that after SCI muscle fibres change from type I (slow, aerobic) to type II (fast, anaerobic) ((Wilder *et al*, 2002). [37]. There is also a reduction in mitochondria concentration, oxidative enzyme level and number of capillaries. This in turn results in a change in the contractile properties of muscles. Speed of contraction and relaxation increases and low level prolonged contractions can no longer be generated.

2.4 Effect on Bone mineral density

SCI patients suffer from a reduction in bone mass in the lower extremities due to a lack of exercise. Increased calcium excretion is associated with bone mass reduction and has been reported in the first 6 months of injury. (Mohr *et al*, 1997)[24] Bone mineral density in the tibia has been shown to diminish in the first two years post injury (Mohr *et al* 1997)[24]. Despite continued lack of physical stress, loss of bone mass does not continue indefinitely but stops at 6 -12 months after the SCI. Loss of bone mass can make a SCI individual more prone to low impact fractures.

2.5 FES Cycle Ergometers

Therapeutic Alliances (Fairborn, Ohio) and Electrologic of America (Beavercreek, Ohio) are the leading providers of FES cycle ergometers. Therapeutic Technologies became Therapeutic Alliances in 1993 and they introduced the REGYS™ Clinical Rehabilitation System in 1984. This was the first FES leg cycle ergometer used for clinical use. In 1985, the ERGYS®1 was designed for home and clinical use ((Wilder *et al*, 2002). [37]

REGYS and ERGYS 1 specifications include rectangular, monophasic waveforms with 0-130 mA constant current and sequential 30Hz frequency. The ERGYS 1 has a more user friendly adjustable seat, which allows for easier transfer of tetraplegics.

ERGYS 2 was released by Therapeutic Alliances in 1996. This contained more sophisticated computer programming and electronics along with other benefits such as stimulation technology which can be used by patients with partial and full sensation.

Electronic of America produced the StimMaster™ in 1995 and later in 2001 the StimMaster Orion was introduced. The newer model is medically optimized for 3 X 30 minute sessions per week. (Wilder *et al*, 2002). [37]

The cost must be factored into prescribing FES cycle exercise at home. Currently the ERGYs 2 is worth $15,665.00 (USD), ($22,050.80 NZD). All papers suggest that use must be consistent and a plan for ongoing regular exercise is required for maintenance of therapeutic effects. (www.musclepower.com/patientpricing.htm).

2.6 Current Practice In New Zealand

The ERGYS device or any other similar cycling device used in conjunction with FES is currently not used in New Zealand (Personal communication Dr. Sean Xiong- Burwood Spinal Unit, Christchurch) but is used in some centres in Australia. Functional electrical stimulation is routinely used as a training system or a beginning stage to move on to other forms of muscle strengthening. Functional Electrical Stimulation has proven to work well in many situations (Personal communication, Jason Nicolls, physiotherapist-Burwood Spinal Unit).

It is suggested that the main use of this ERGYS device in New Zealand would be to improve cardiovascular function and this would be incorporated into an already existing rehabilitation training schedule. It would not be used to replace existing rehabilitation regimes. It would depend on the individual and the nature of the injury as to whether the ERGYS would be suitable and effective as a rehabilitation tool.

3. Objectives

- To determine the effectiveness of ERGYS 1 and 2 and REGYS, functional electrical stimulation cycling devices used for the improved health of SCI individuals.

- To determine if ACC should fund ERGYS 2 for SCI patients.

4. Review Methodology

4.1 Criteria for selecting participants for this review:

Studies published in English from 1999 to May 2005, which investigated the effectiveness of functional electrical stimulation and cycle ergometry were selected for review. Papers selected by the reviewer were also critiqued which dated back to 1989.

4.1.1 Types of studies

Randomised controlled trials, case control studies and case series published since 1996.

4.1.2 Types of participants

Adults (aged 18 years and over) who were tetraplegic or paraplegic, with incomplete or complete injuries.

4.1.3 Types of interventions

FES and cycle ergometry and or cycle ergometry

4.1.4 Types of outcome measures

There were numerous outcome measures, mainly physiological, including cardiac output and stroke volume, immunoreactivity, blood circulation, glucose uptake rates, electromyogram recordings, increase in thigh girth, cardiorespiratory capacity, oxygen uptake rates, and an increase in exercise training time.

4.2 Search Strategy

A comprehensive literature search of major relevant bibliographic databases was undertaken.

A search strategy was devised and undertaken initially in February 2005 utilising the following medical databases:

Ovid MEDLINE 1999 to 11-02-2005
Ovid MEDLINE daily update 11-02-2005
ACP Journal Club
CCTR
CDSR
DARE
AMED 1999 till 24-02-2005
Cinahle 1999 till 24-02-2005
Medline In-Process & Other non indexed citation 24-02-2005
The exact search strategy is outlined in Appendix 1.

Key words and terms used were:

“ERGYS”, “REGYS”, “FUNCTIONAL ELECTRICAL STIMULATION”, “FES”, Quadriplegia”, “SCI”, “spinal cord injury”.

A comprehensive search to update the literature search results using Ovid databases and to search the web was done again from the 16th-18th of May, 2005. The search strategy was run again using the same Ovid databases {see Appendix 1}.Results were limited to “human” and had to be written in the English language. A filter was applied to limit the search to the period from 1999- May 2005.

A further search was undertaken using Scopus [www.scopus.com] which is a new navigation tool and an abstract and indexing database.

Scopus was searched using the Literature Search Strategies: “ERGYS”OR “REGYS”. The second strategy was using the following key terms: “Cycling” AND “Functional Electrical Stimulation”. A filter was applied to limit the search to the period from 1999- May 2005.

Hand searching of reference lists of articles already obtained was also undertaken, including the reference lists of the excluded articles.

A search for current guidelines on the following websites was also undertaken:

The Oxford Pain site: www.jr2.ox.ac.uk/bandolier/
Centre for Reviews and Dissemination www.york.ac.uk/inst/crd/welcome.htm
The National Institute for Clinical Excellence www.nice.org.uk
National Guideline Clearing House www.guideline.gov/resources/discussion_list.aspx
New Zealand Guidelines Group www.nzgg.org.nz
New Zealand Health Technology Assessment Clearing House http://nzhta.chmeds.ac.nz/
eGuidelines www.eguidelines.co.uk/
Scottish Intercollegiate Guidelines Network http://www.sign.ac.uk/
Trip+ http://www.tripdatabase.com/

4.3 Review methodology

The initial search resulted in 187 references being found. After screening these articles, 29 were obtained for review and appraised by the principal investigator using the Scottish Intercollegiate Guidelines Network (SIGN)[2] grading system (see Appendix 4) to determine the levels of evidence.

The type of study and study quality were determined by reviewing the methodology of each study. The following aspects of each study were analysed: condition for which ERGYs was being investigated, inclusion and exclusion criteria for participants, sample size, blinding, randomisation, outcome measurements, was the exercise continued after the trial and potential bias in the study. Evidence tables were created which summarised this information as well as the outcomes and level of evidence (see Appendix 2).

5. RESULTS

5.1 Description of studies

Twenty nine studies were included in this review, of which, 22, were cases series. The case series included all study subjects and described in detail the nature of each participant with explicit inclusion and exclusion criteria specified. In accordance with level 3 studies, the methodology was thorough and the techniques used were well described. Due to the nature of this type of injury, case series, may have been the most appropriate study technique in contrast to the Randomised Controlled Trial, whereby it would be harder to use controls. This could be due to the lack of active participants or people who would fit the inclusion criteria.

Four papers included in the study were allocated level 1- ratings. Each of these studies contained control groups who were not exposed to the cycling intervention. These papers tended to be more recent (from 96-2005). Other reasons for grading these papers as level 1 papers is that they eliminated bias by comparing two otherwise identical groups and that they enabled one single variable (FES-cycle ergometry) in a precisely defined patient group to be examined.

One study (by Sipski *et al*, 1989)[33] was allocated a level 3, due to the fact it reported a questionnaire. The questionnaire was included because the outcomes after cycle ergometry were relevant to this review. Although it was not quantitative in nature, the qualitative outcomes such as patient confidence and how patients perceived themselves after FES-cycling were of value to this evidence based review because it showed the effectiveness of something that was otherwise hard to measure.

Seven reviews were found that were narrative and hence were not assessed using the SIGN system but were cited throughout the report. [12,13,29,30,37,38.] The reviews did not clearly make a statement of materials and methods and therefore the methodology was not reproducible. This inferred that the methods may have been bias in identifying and rejecting studies and that the conclusions may not have been reliable or accurate. One of the reviews by Wilder *et al*: (2002)[37] was cited in this report due to the fact that there was some good background information regarding functional electrical stimulation and cycle ergometry.

Overall the sample sizes were relatively small. The number of participants from the Level 1 studies ranged from 10 to 26 and from 10 to 44 from the level 2 studies. There was wider variation with the level 3 studies from case reports of one person to 52 subjects. The average number of subjects was 12 for the level 3 papers.

Studies looked at the ERGYS and the REGYS cycle ergometer. The same company produces both machines. Typically, studies looked at the outcomes associated with regular cycling on various parameters such as cardiac, immunology, muscle size increase, or blood circulation flow. All outcomes were physiological in nature, apart from one study that was qualitative and focused on how SCI patients perceived their own self-image after using ERGYS.

5.2 Effect on Circulation

Many investigators have reported various characteristics of diminished lower extremity blood flow and general circulatory dysfunction in survivors of chronic spinal cord injury (SCI)[9,17,27,29.] Spinal Cord Injuries which alter the activity levels of the heart, transform the structure of the heart and alter its pumping efficiency.

One good quality level one study by Nash *et al*; 1996 [26] focused on whether lower extremity blood flow and hyperaemic responses to vascular occlusion differed among electrically stimulated exercise trained and sedentary tetraplegic persons and subjects without tetraplegia as a control group. This study was well designed with good quality controls. One group of ten tetraplegic men who had previously been exposed to electrically stimulated cycling exercise for 0.4-7 years were compared to 10 tetraplegic men who were sedentary and 10 nondisabled controls. Interestingly, many studies have a higher number of male subjects compared to female subjects. The main outcome measurements included heart rate, peak systolic velocity (PSV) cross sectional area of the femoral artery (CSA) flow velocity integral and computed CFA inflow volume (IV). It was observed that following occlusion, PSV, CSA and IV averaged 16.5%, 33.4% and 65.1% greater for trained tetraplegic persons, compared to tetraplegic patients ($p<0.05$) suggesting that tetraplegic persons conditioned by electrically stimulated cycling have greater lower extremity blood flow and hyperaemic responses to occlusion than do sedentary tetraplegics. The authors found their findings consistent with other studies that demonstrated that people without disability showed greater resting arterial inflow to an exercise trained rather than an untrained limb. Exercise training enlarges the cross sectional area of conductance arteries supplying trained muscles and exercise training enhanced the hyperemic response of limbs to occlusive challenge.

The difference in blood flow and hyperemic response between exercise trained and sedentary tetraplegic subjects may represent adaption favouring altered arterial compliance, skeletal muscle neovascularisation, or endothelial cell regulation of blood flow, as all have been reported to accompany exercise training in persons without disability.

Twelve papers were found which focused on circulation and cardiac response of tetraplegics before and after exercise training. All papers report a positive finding, albeit, they are level 3 papers. Table 1 describes the key findings of each study.

5.3 Effect on bone mineralization

Unlike the numerous scientific evidence for muscle enhancement after FES-cycling, there is less evidence (four studies) and somewhat mixed results for reversing bone atrophy. It is known that bone atrophy in spinal cord injured people is caused by immobilization and is initiated shortly after injury. Bone density can nearly be reduced by a factor of 10 resulting in a high incident of bone fractures among SCI people.

Eser *et al*; 2003[7] examined the effects of 19 patients who were subjected to 30 min FES cycling 3 x per week during a mean period of time of 6 months. The researchers wished to know if Bone Mineralization Density (BMD) of the tibia was affected by FES-cycling in recently injured (mean 4-5 weeks) SCI people. The control group and the intervention group showed a mean reduction in tibial cortical BMD of 0.7% (±0.8) and 0.3% (±0.6) respectively and the difference did not reach statistical significance. In fact the researchers report a decrease in BMD being correlated to a high initial BMD or the patients who were older lost more bone. The author's report that in neither group was bone loss associated with duration of immobilization or lesion level.

Similarly, BeDell (1996)[3] found that FES lower leg cycling did not significantly increase bone density in the hip parameters of chronic SCI patients but a positive trend was observed in the lumbar spine. The authors felt that further research was warranted during the first few months post SCI when BMD occurs rapidly.

In comparison, Mohr *et al* (1997)[24] found an increase in bone density at the proximal tibia of 10% during the first year of FES-cycling training, however, FES cycle exercise did not enhance BMD in the femoral neck or lumbar spine. A further study by Bloomfield *et al* (1996)[2] found an increase of 18% in the distal fermur in a subgroup of FES cyclists that achieved a power output of at least 18W, but no increase in the subgroup with lower power output. Both of these studies included severe SCI patients who were greater than 2 years post injury. Also, both of these studies showed that exercise needed to be carried out for long periods of time such as three sessions per week for 12 months versus one session per week for 6 months to maintain an increase in BMD.

5.4 Effect on Muscle Morphology and Function

There have been numerous scientific articles that indicate that muscle bulk, strength and endurance can markedly increase with different forms of FES training such as weight lifting, ergometry, or ambulation. In this study, twelve papers including three level one studies, describe the positive effects of FES cycling on muscle strength. All papers described a significant effect on either, reduction of muscle atrophy, an increase in muscle cross section area, accelerated collagen turnover, increased muscle mass, increase in thigh girth, increased glucose uptake and an increase in muscle fibre.

Skold et al[34] (2002) showed that patients who were subjected to FES cycling 3 X per week for 6 months exhibited increased muscle volume by an average of 1300cm^3 otherwise no changes in body composition were seen. Likewise, Baldi *et al*(1998)[1] showed that FES cycling ergometry was effective at preventing muscle atrophy in acute SCI after three months of training compared to unloaded isometric FES contractions. After 6 months training, hypertrophy was observed of the leg and buttocks muscles after 6 months of training. Screamin et al (1999)[31] also showed that muscle cross sectional area significantly increased as did the muscle to adipose tissue ratio of the lower extremities during a regular regime of 2.3 FES-induced lower extremity cycling sessions weekly. It was also observed that the distribution of changes was related to the proximity of muscles of the stimulating electrodes.

Kjaer *et al* (2001)[19] showed that patients who cycled at 30min per day (cycling) at comparable O_2 uptake rates had higher muscle glycogen breakdown, leg glucose uptake, carbohydrate oxidation and lactate release ($p < 0.05$) than those who did not perform electrically induced cycling.

Nash *et al*. (1996)[26] compared lower extremity blood flow and responses to occlusion ischemia in FES cycle-trained and sedentary tetraplegics. The results showed that tetraplegics who engaged in FES cycle training demonstrated enhanced resting lower extremity blood flow compared to their sedentary counterparts. FES cycle ergometry also enhanced capillary density and the cross sectional area around the stimulated muscle in tetraplegics. The findings from this report also showed that FES-trained tetraplegics exhibited greater hyperemic responses to occlusion than their sedentary counterparts.

FES cycle ergometry may also affect the muscles directly as seen in a clinical study by Mohr *et al* 1997[23] The study involved a 1 year long FES cycle training programme and they noted a 12% increase in muscle mass and a shift in muscle fibre type towards a more fatigue resistant "myosin heavy chain isoform IIA." Hooker *et al* (1995)[17] also showed a preferential selection for the Type II motor units by FES cycle ergometry. By increasing muscle mass, this leads to a significant increase in oxidative capacity, which was determined by the level of citrate synthase activity in muscle tissue.

Thus, FES cycle training increases both leg and muscle buttocks strength and endurance which are seen as two important components of overall physical fitness (Wilder et al, 2002). [37]

Ragnarsson *et al* 1991[30] reported that four weeks of electrically stimulated quadriceps training on 19 subjects all demonstrated increased strength and endurance. For example: the number of knee extensions increased as did the resistance against which these were completed.

Gerritis *et al* (2000)[12] reported that FES leg cycle ergometry training changed the physiological properties of the quadriceps muscle in people with SCI. The authors report that even after a small amount of training the stimulated muscles become more resistant to fatigue. The authors also reported that their study period was relatively short compared to many of the other studies, 30min sessions three times per week for six weeks. Other studies, who reported significant adaptations in structural, molecular and physiological properties of muscles, used considerable longer or more intensive training programs. Anderson and Mohr[23] used 6-12 month training program, others applied daily electrical stimulation for 1 hour per day during 13 weeks or 8h per day for 6-24 weeks. From these findings it is speculated that longer or more intensive training periods are required to induce muscular adaptations which would led to a detectable slowing of contractile speed characteristics in paralysed muscle of people with SCI.

5.5 Contraindications

Before beginning any exercise programme it is recommended that any SCI individual wishing to use FES-cycle ergometry should consult a physician. Use of the FES cycle is not recommended for individuals with the following conditions: implanted pacing devices, high or abnormal heart rate, high blood pressure, heart disease, possible blood clots, types of tumour, pregnancy, unhealed wounds, infection in the area of treatment, denervated muscle, severe osteoporosis, limited range of motion in joints where treatment is to occur, abnormal bone formation in treatment areas, severe muscle spasticity, autonomic dysreflexia, history of joint disarticulation of treatment limb, and high fever (Wilder *et al*, 2002).[37.]

5.6 Safety and Adverse effects

Few adverse effects were reported in the 29 studies included in this review. Fatigue was the most commonly reported safety issue. In these instances, cycling was slowed or stopped to allow the subject to recover. The "ERGYS 2" and "StimMaster Orion" models both have "closed-loop" control systems which have the ability to detect fatigue, when the pedalling rate drops below 35rpm. When fatigue is detected the ergometer goes into "cool-down mode" which is approximately 2 minutes of low level stimulus cycling. The safety precaution works to prevent blood pooling in legs by keeping the patient pedalling (Wilder *et al*; 2002)[37] FES-cycling therefore appears to be a reasonably safe intervention when practiced appropriately by properly trained therapists.

6. Discussion

6.1 Methodology Quality

The majority of evidence to date regarding functional electrical stimulation and cycle ergometers are mainly case series, or pre-post trials whereby SCI patients are subjected to cycling and certain parameters are measured before and after the test. Only four trials were found that were given a level 1 rating compared to 3 Level 2 papers and 21 level 3 papers. All papers indicated a positive response after using cycle ergometry in combination with functional electrical stimulation, however, some papers failed to mention follow-up, that is, after the trial were the outcomes maintained. 10 number of papers suggested that cycling needed to be maintained 3 x per week to remain effective and the majority of studies were over a long time frame in order to achieve desired results. The shortest time frame for a trial was 3 months with 6 months or greater having more desired results.

In all papers there were more male subjects than female subjects. Also, statistically, sample sizes were low ranging from 1 -52. Few of the level 1 papers described how randomisation was carried out, and most studies did not describe any follow-up. There was a significant lack of able bodied volunteers who would have acted as good controls.

Three papers described controlled trials that were not randomised. [2,8,21]. That is, the controls were specifically selected to match the experimental subjects in every way but were not subjected to the intervention. In the study by Kjaer *et al*, (2001)[21] six healthy body controls were used as the control group. Eser *et al*, (2003)[8] thought it was ethically correct to let the patients decide whether they should be in the control or intervention group.

There are limits to the cardiovascular benefits of FES ergometry, especially in those with lesions above T5. In these patients, there is a loss of supraspinal sympathetic control, which in turn limits the body's ability to increase heart rate, stroke volume and cardiac output (Ragnarsson *et al* 1991)[31] There is also inconclusive evidence as to whether FES cycling can retard or reverse the osteoporosis and bone deminiseralisation seen in patients with SCI. There is also inconclusive evidence regarding whether FES cycling can improve carbohydrate metabolism and insulin sensitivity in the same way that happens with able bodied persons.

6.2 Limitations of this review

This report excluded studies which were published in languages other than English. The authors acknowledge that this may exclude some valuable information relating to the effectiveness of FES – cycle ergometry. The omission of these studies was unavoidable, as the resources to translate the journal articles into English were not available to the authors of this report.

This report also excluded conference proceedings and studies which have only been published in abstract form. Sufficient information may not be available from study abstracts to extract adequate methodological detail to be able to evaluate the level of evidence. Furthermore, all study findings may not be reported in the study abstract.

The authors acknowledge that publication bias may exist, in that studies may not have been published which found a neutral outcome or an outcome that did not serve the purpose of the funding body.

Furthermore, other studies may have been conducted that found a contradictory result which have not yet been published.

7. Conclusions

On the basis of the studies reviewed, FES cycle ergometry appears beneficial for SCI users in terms of cardiovascular and muscle outcomes, given there is consistent use for a three month period or greater. There is insufficient evidence to suggest that FES-cycle ergometry reduces bone demineralisation.

7.1 Implications for Practice

Overall the quality of research available was moderate, however, the evidence from RCT's, controlled trials, and case series indicate that FES-cycle ergometry maybe effective in improving cardiopulmonary and circulatory function as well as lower extremity muscle atrophy. There is insufficient evidence to suggest that bone mass reduction is halted or stopped as a result of FES-cycling.

The majority of evidence indicates that exercise must be carried out frequently to be effective (at least 3 X 30 minute sessions per week) for at least three months or greater to obtain a desired result. FES cycle ergometry appeared to be a reasonably safe intervention ensuring all criteria and contraindications were observed.

7.2 Implications for Research

Research is needed into the effectiveness of cycle ergometry on preventing bone mineralization. At this stage it is unknown whether frequent cycling has a positive effect or not.

The bulk of evidence came from level 3 case series. To improve the quality of studies presented, researchers may want to consider incorporating control subjects and randomly assigning subjects to intervention or control groups.

There is a lack of papers that focus on functional outcomes after exercise training for SCI patients. That is, how do the physiological outcomes mentioned in this report improve the day to day life of a SCI patient? More research is required in this area.

7.3 Implications for Purchasing

Overall, there is moderate evidence for FES cycle ergometry. It appears beneficial for Spinal Cord Injured (SCI) users in terms of cardiovascular and muscle outcomes, given there is consistent use for a 3 month period or greater. There is insufficient evidence to suggest that FES-cycle ergometry reduces bone demineralisation.

It is recommended that ACC purchase on a case-by-case basis, where a clear exercise regime is stipulated over a 3 month or greater period and that the individual meets all of the criteria required for the safe use of such a piece of equipment. The other consideration is to fund FES cycle ergometers for communal use in spinal injury units such as Burwood Spinal Unit in Christchurch or Otara Spinal Unit in Auckland.

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9. Conflicts of Interest

None declared.

10. References

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APPENDIX 1- SEARCH STRATEGY

Research Literature Search Strategy for Medline

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Database: Ovid MEDLINE(R), Ovid MEDLINE(R) In-Process, Other Non-Indexed
Citations, Ovid MEDLINE(R) Daily Update
Search Strategy:


1      ERGYS.mp. [mp=ti, ot, ab, nm, hw]
2      REGYS.mp. [mp=ti, ot, ab, nm, hw]
3      1 or 2
4      (FUNCTIONAL adj ELECTRICAL adj STIMULATION).mp. [mp=ti, ot, ab,
5      FES.mp. [mp=ti, ot, ab, nm, hw]
6      4 or 5
7      (FUNCTIONAL adj ELECTRICAL adj STIMULATION).ti.
8      FES.ti.
9      7 or 8
10      Quadriplegia.mp. [mp=ti, ot, ab, nm, hw]
11      SCI.mp. [mp=ti, ot, ab, nm, hw]
12      (spinal adj cord adj injury).mp. [mp=ti, ot, ab, nm, hw]
13      10 or 11 or 12
14      3 or 6 or 9
15      13 and 14
16      limit 15 to english
17      limit 16 to yr=1999-2005
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APPENDIX 2 – CHARACTERISTICS OF INCLUDED STUDIES-Evidence Based Tables.

Study **Level 1 Studies**	Methods and Settings	Participants	Intervention	Outcomes and Results	Comments and Level of Evidence/Additional comments.
Skold et al, 2002.[34] Funding from The Swedish Medical Research Council, Norrbacka Eugenia foundation, the Karolinska Institute Committee for the caring sciences, The Swedish foundation for healthcare sciences and Allergy Research.	Randomly Selected Controlled Trial. Set in Stockholm, Sweden.	15 Spinal cord Injured (SCI) patients. Mean Age: 33years. Mean Time since injury : 9 years. Training period = 6 months. Male and Female numbers not specified.	Intervention group 8/15 Functional Electrical Stimulation (FES) cycling 3 X per week for 6 months. Control Group 7/15 – No FES cycling. Tested: Simultaneous Modified Ashworth Scale and electromyography (EMG) measurements, resistive torque (Kin-Com) and EMG measurements and self ratings with Visual Analogue Scale.	Muscle volume increased by an average of 1300cm^3 ($p<0.05$). Otherwise no changes in body composition were seen. No change in control group. Significant correlation found between individual EMG recordings and movement provoked modified Ashworth Scale ratings in 26% of the test situations. The objective and subjective evaluation of movement provoked passive and active resistance remained unchanged.	**1-**

Kjaer et al, 2001[19] Funding from the Danish Medical Research Council, Danish National Research Foundation, Danish sports Research Council.	Randomly controlled Trial. Copenhagen, Denmark.	10 SCI patients. 6 healthy volunteers served as controls.	Intervention Both groups exercised at 30min per day (cycling) at comparable O_2 uptake rates. Free Fatty Acid (FFA) turnover rate was monitored As well as • Fernoval arteriovenous differences • Blood flow • Muscle biopsies • Indirect Calorimetry • Leg Substrate balances.	Muscle glycogen breakdown, leg glucose uptake, Carbohydrate oxidation and Lactate release were higher ($p< 0.05$) in SCI than in controls during exercise. Insulin decrease only in Controls. FFA mobilization, delivery and fractional uptake are lower and muscle glycogen breakdown and glucose uptake are higher in SCI patients during electrically induced leg exercise compared with healthy subjects performing voluntary exercise.	**1-**
Baldi et al, 1998[1] Funding not stated	Randomly?controlled Trial Set in Ohio, USA.	26 subjects. 14-15 weeks post traumatic SCI were assigned to either • Control • FES-IC (isometric	3-6 month period Control group received no training. FES-CE-ERGYS 30 min 3X per week.	FES-cycle ergometry but not FES-isometric cycling training prevents muscle atrophy in acute SCI after 3	**1- RCT.**

		contractions) • Or FES-CE. (cycle ergometry)	FES-IC –subject to a biphasic waveform for 1 hour 5X per week.	months of training and causes significant hypertrophy after 6 months.	
Nash, et al,. 1996.[26] No funding specified.	Blinded cross-sectional comparison, control group. RCT	10 tetraplegics sedentary, male, 10 tetraplegic persons previously habituated to electrically stimulated cycling exercise for 0.4-7 years and 10 non-disabled controls.	Subjects underwent quantitative Doppler ultrasound examination of the common femoral artery (CFA). End diastolic arterial images and arterial flow velocity profiles obtained at rest and following five minutes of suprasystolic thigh occlusion were computer digitised for analysis of heart rate (HR), CFA Peak systolic velocity (PSV), CFA, cross sectional area (CSA) and Flow velocity intergral (FVI) and computed CFA inflow volume.	Tetra persons conditioned by electrically stimulated cycling have greater lower extremity blood flow and hyperaemic responses to occlusion than do their sedentary counterparts. Following occlusion, PSV, CSA, and IV averaged 16.5% 33.4% and 65.1% greater for trained tetraplegic persons, respectively, than sedentary tetraplegic subjects (p values< 0.05).	1- ERGYS- REGYS

Study **Level 2 Studies**	Methods and Settings	Participants	Intervention	Outcomes and Results	Comments and Level of Evidence/Additional comments.
Eser, et al 2003.[7] Funding support provided by the Swiss Paraplegic Foundation. University of Alberta, Edmonton, Alberta, Canada.	Controlled Trial, but not randomised.	Forty four recently injured para and tetraplegic rehab patients were recruited for the study. Post mean injury time is 4.5 weeks. Patients choose to enter intervention or control groups. Inclusion criteria included traumatic motor complete spinal cord lesions between C5 and T12. Exclusion criteria were fractures of the lower extremities at or after the time fo the SCI, thrombosis, contractures and ossifications reducing full range of motion of the hip or knee joint and diseases known to affect bone metabolism.	30 min. functional electrical stimulation cycling three times a week for the duration of primary rehabilitation (6 months). CT scans were taken of the right tibia at the beginning and the end of the intervention.	Both groups showed a reduction in tibial cortical BMD of 0-10% of initial values within 3-10 months. Mean decrease in BMD was 0.3% (± 0.6) per month in the intervention group and 0.7% (± 0.8) in the control group. Concluded that FES cycling applied shortly after SCI did not significantly attenuate bone loss.	**Stim master** **2.**
Kjaer *et al* 2001[20]	Controlled Trial	10 spinal cord injured subjects (6 tetraplegics	Performed FES cycling 29± 2 min. to	Levels of Calcitonin gene related peptide	2. REGYS1

Research was funded by the Danish Medical Research Council. National Research Foundation, The Novo Foundation, Danish Sports Research Council, Danish Medical Association Research Foundaiton.		(5 males/1 female) 20-32 yrs in age, 165-174cm and 60-78kg). Six healthy able bodied controlled subjects. All were neurologically stable with clinically complete motor lesion in the lower extremities.	fatigue. Workload low during the first 15 mins but increased too high during the last 15 mins. Does not mention how long the study went for.	(CGRP) increased during exercise (from 33.2±3.8 to 46.9± 3.6 pmol 1^{-1} to 46.9 ± 3.6 pmol-1 P<0.05). Heart rate increased more in paraplegic subjects (67± 7 to 132 ± 15bpm) compared with controls and tetraplegics (P<0.05).	
Bloomfield *et al;* 1996[2] Research was supported by the Spinal Cord Research Foundation of The Paralyzed Veterans of America.	Controlled Trial Control subjects were selected to closely match the test subjects.	Nine healthy individuals, 21-39 years of age. Mean age is 28.2 yrs. 5 male subjects and 4 female subjects. Average year since injury 6 years. Exclusion criteria included: independent factors affecting bone metabolism, including recent bone fracture, prolonged use of medications such as cortisone, prednisone, Pagets disease, malnutrition, alcoholism, history of hyper or	REGYS1 Clinical Rehab system was used first, 3 sessions per week consisting of up to 45 leg extensions. FES cycle ergometry utilising the ERGYS Home Rehabilitation System was then used- 30 min continuous cycling starting at 0 W, then 6 W for the next session. Total of 80 sessions Densitometry and collections of blood and urine were collected at 3 month	In a subset of subjects training at > 18 W for at least 3 months, BMD increased by 18% at the distal fermur. By 6 months of training a 78% increase in serum ostocalcin was observed, indicating an increase in bone turnover. Changes in BMD were not significant for the group as a whole at the femoral neck, distal fermur and proximal tibia.	2 REGYS1 ERGYS1

		hypothyroidism. Control subjects were independently recruited from the community. They met all exclusion and eligibility criteria and were virtually identical in weight, but had slightly greater % body fat, were approx 5cm shorter, and approx 6 yrs older as a group.	intervals.		

Study **Level 3 Studies**	Methods and Settings	Participants	Intervention	Outcomes and Results	Comments and Level of Evidence/Additional comments.
Eser et al. 2003[6] Funding not stated	Case series Switzerland	19 recently injured motor and sensory complete para and tetraplegics with lesions above T12	FES cycle training at 30, 50 and 60 Hz. Power output was measured continually.	The mean PO of the 30min, the PO of the last minute of each session and the minimum PO were significantly greater at 60and 50 HZ, respectively compared to 30Hz. The PO of the last minute of each session was higher at higher frequencies, indicating muscle fatigue could be detected in 30min FES cycling of any of the tested frequencies. Recommend using 50HZ for 30 min power cycling.	**3.** **This paper focused on the amount of Hz required for maximum Power output.**
BeDell et al: 1996[3] Funding not stated.	Case series, No control, Los Angeles, USA.	12 healthy SCI patients, all males. Aged between 23-46 years in age.	Patients participated in a three phase training programme. Phase 1: Quadricep	Functional Electrical stimulation-induced lower extremity cycling (FESILEC)	**3.** **No controls.** **Pre post test.** **Machine used:**

		2-19 years post injury. Ashworth spasticity 2-4.	muscle training Phase 2: pedal progession. FES was applied to the quadriceps, gluteals and hamstrings to achieve a rhythmical pedalling motion on the REGYS1 ergometer. Phase 3a: 24 X 30 min continuous sessions, performed three times per week of FES induced lower extremity cycling. 3b. Extra 24 X 30 min sessions with the addition of simultaneous arm ergometry.	did not significantly increase bone density in the hip parameters of chronic SCI patients- a positive trend was observed in the lumbar spine (P=0.056). Further research with acute intervention such as FESILEC during the first few months post SCI is warranted to further evaluate a treatment regime to prevent or reduce neurogenic osteopenia.	**REGYS1.**
Hooker et al; 1992[15]	Case series Los Angeles USA	10 people with quadriplegia and 8 people with paraplegia. 1 female, 17 male volunteers. Mean age was 30.6 ±0.45 yrs, mean weight was 76.1 ±0.76 and the mean time since injury was 6.1± 0.25 years,	ERGYS 1 ergometer 10' to 30' per day, 2-3 days per week for 12 to 16 weeks. A total of 36 sessions.	23% higher Oxygen uptake compared to controls. Pulmonary ventilation increased by 27%, Heartrate increased by 11%, Total peripheral resistance - 14% during FES. No significant differences were	3. ERGYS 1 Ergometer.

				noted for the peak level of any monitored variable.	
Pollack et al, 1989[28]	Case series New York, USA	11 SCI patients Seven cervical and four thoracic cord injured subjects ranging in age from 18-54 years. Post injury time: 6 months to 132 months. Weight ranged from 54.4-83.9 kg.	REGYS1 system Initial phase is weight lifting Initial phase of ergometer pedalling Final phase 36 sessions of continous ergometer pedalling against variable resistanc.e	FES exercise can increase the aerobic capacity of persons with SCI. Peak oxygen consumption and total stress time increased markedly. From 211± 13 mlo2/min to 252 ± 19 ml02/min after phase II.	3. Regys1 system.
Scremin et al: 1999[31] Funding not specified	Case series. Los Angeles USA	Thirteen men with neurologically complete motor sensory SCI. Time since injury ranged from 2 to 19 years. Age ranged from24 to 46 yrs of age. Body mass ranged from 61.1 kg to 106.3 kg.	All 13 men underwent a 3-phase FES induced, ergometry exercise program. Phase 1: Strengthening of quadriceps. Cycling progression. Phase 3: FES induced lower extremity cycling sessions weekly. Move from one phase to the next when certain criteria were met for the current phase. Measures included a	Muscle cross sectional area and the muscle to adipose tissue ratio of the lower extremities increased during a regular regimen of 2.3 FES-induced lower extremity cycling sessions weekly. The distribution of changes was related to the proximity of muscles to the stimulating electrodes.	3. REGYS ergometer was used.

			muscle cross sectional area and a proportion of muscle and adipose tissue.		
Mohr et al,. 1997[25] Funding by the Danish National Research Council, the Danish Medical Research council, Danish Heart Foundation.	Case series. Copenhagen Denmark.	10 SCI individuals 35.3 yrs ± 2.3 yrs and 12.5 ± 2.7 years post injury.	12 months of FES upright cycling for 30 min. per day, 3 days per week, followed by 6 months with only one weekly training session. Bone mineral Density (BMD) before training at 12 months and after 18 months was measured.	After 12 months BMD increased by 10%. After 18 months with reduced training the BMD in the proximal tibia had increased 10% from 0.49± 0.04 to 0.54 ± 0.04 g/cm^2 ($P<0.05$). It is concluded that in SCI the loss of bone mass in the proximal tibia can be partially reversed by regular long term FES cycle exercise. However, one exercise session per week is insufficient to maintain this increase.	3. Case series. No controls. BMD was measured in the lumbar spine, the femoral neck and the proximal tibia.
Koskinen *et al*:2000[22] Danish National Research Foundation, Danish Medical Research Council, the Finnish Ministry of	Case Study Copenhagen, Denmark.	8 men, 2 women,. With spinal cord Injury. Age 35 (27-45) Mean weight 78kg±3.8 (SE)	18 month programme of FES cycling, for 30 min 3 X per week for 1 year followed by one time per week for 6 months.	Accelerated type IV collagen turnover in skeletal muscle of SCI individuals especially after FES as part of adaptive	3. REGYS1 cycle ergometer.

Education, Finnish graduate school in Musculoskeletal problems.		Average of 12.5 years since injury.		process of the muscle.	
Mohr et al,. 1997.[23] Funding Nat Society of Polio and Accident victims, The Danish medical research council, the Danish National Research Foundation,. The Hamilton Foundation. Danish Hospital foundation for Medical Research, the Danish Heart foundation, the Foundation of J and O Madsen, the Danish Medical Association Research Foundation and Team Denmark.	Case series Copenhagen, Denmark	10 individuals. 6 with tetraplegia, 4 with paraplegia Aged 27-45 Time since injury 3-23 years.	Exercise trained for 1 year using an electrically induced computerised feedback controlled cycle ergometer, 3 X per week, 30 min on each occasion.	After 1 year, all individuals could perform 30 mins of continuous training and work output from 4± 1 to 17± 2 KJ per training bout. (p<0.05). Max oxygen uptake increased from 1.20± 0.08 litres per minute after training for 1 year measured after a few weeks habituation to the exercise to 1.43± 0.09 litres per minute after training for 1 year (P,0.05).Muscle mass increased by 12% (mean, P<0.05). Muscle Fibre type shifted towards more Type II fatigue resistant type. The authors	3 REGYS1 exercise ergometer.

				concluded that inactivity-associated changes in exercise performance capacity and skeletal muscle occurring in SCI individuals is reversible, even up to over 20 years after the injury. It follows that electrically induced exercise training of the paralysed limbs is an effective rehabilitation tool.	
Seymour *et al*,. 1989[32]	One case report.	21 yr old man with a T6 paraplegia. (2.5 yrs post injury due to a motor vehicle accident).	ERGYS 2 x per week (15 mins) for 18 months.	Increase in thigh girth Reverse of normal atrophy associated with spinal cord inury. No changes in blood pressure. Endurance increased from 6-7 min cycling to 25 min continuous cycling.	3. ERGYS 1 cycle ergometer
Chilibeck et al; 1999[4] Study carried out in	Case series	5 SCI patients, 4 men plus one women,. Ages ranged from 31-50 yrs.	Subjects trained using a computer controlled FES leg cycle ergometer, for a	Glut 1 levels increased by 52% and Glut 4 levels increased by 72%	3 Pre post test. ERGYS II cycle ergometer used.

the University of Alberta, Canada. No funding stated.		Exclusion criteria : Pacemakers, uncontrolled arrhythmia, angina, congestive heart failure, current deep vein thrombosis, pulmonary emboli, severe autonomic dysreflexia response to electrical stimulation, less than 90º flexion range of motion of the hips and knees, flaccid paralysis, nonresponsive to FES, severe lower-extremity spasticity, and those who were currently participating in regular exercise.	cumulated duration of 30 mins of cycling 3 days per week. Biopsy samples were obtained pre and post training analysis of Glut 1 and Glut 4 content on paralysed skeletal muscle before versus after FES leg-cycle ergo meter training.	with training. FES endurance training is effective to increase glucose transporter protein levels in paralysed skeletal muscle of individuals with SCI. The authors concluded that 8 weeks of FES exercise cycle training of paralysed muscle would be a sufficient stimulus for an increase in glucose transporters.	
Figoni, et, al,. 1990.[8] Funding from the Rehabilitation Research and Development Service of the US Department of Veterans Affairs.	Case series. Pre post test. Set in Ohio, USA.	30 SCI subjects, 17 quadriplegics, 13 paraplegics, 4 females, 26 males. Time since injury 5.5 yrs ± 3.9 (Paraplegics) and 6.0 ± 4.7 yrs (Quadriplegics).	FNS leg cycle ergometer, Discontinous graded FNS exercise test from rest to fatigue on an ERGYS 1 ergometer.	Cardiac output increased by (69%)and stroke volume increased (45%), Oxygen uptake increased by 255% Total peripheral vascular resistance decreased by 43%.	3. ERGYS 1 cycle ergometer.

				The authors conclude that Active FNS leg cycle ergometry elicts significant increases in aerobic metabolism, pulmonary ventilation, and cardiac volume loading above resting and passive exercise in SCI subjects.	
Mohr, et al, 2001.[24] Funding Nat Society of Polio and Accident victims, The Danish medical research council, the Danish National Research Foundation,. The Hamilton Foundation. Danish Hospital foundation for Medical Research, the Danish Heart foundation, the Foundation of J and O Madsen, the Danish Medical Association Research Foundation	Case series, Pre-post analysis. Set in: Copenhagen, Denmark.	Ten subjects with SCI, 35± 2 yrs, 73 ± 5 kg, level of lesion C6-Th4, Time since injury: 12± 2.5 yrs, performed one year of FES cycling,	One year of FES cycling, 30 mins, three times per week. 6 months after this, The training was reduced to 30 min, once per week. Glucose uptake rates were measured.	Glucose uptake rates increased after intensive training from 4.9 ± 0.5 $mg.min^{-1}.kg^{-1}$ to $6.2 \pm 0.6 mg.min^{-1}.kg-^{1.}$ ($p<0.008$)(step 1) and from $9.0 \pm 0.8 mg.min^{-1}.kg^{-1}$ to 10.6 ± 0.8 $mg.min.kg^{-1}$ ($p=0.103$)(step 2). It was observed with a reduction in training- glucose rates were reduced.	3.

and Team Denmark.					
Klokker et al: 1998[21] Danish Armed Forces, Health Services, The Danish Heart Foundation, The National Society of Polio and Accident Victims, and The Danish National Research foundation.	Case series, Set in Copenhagen, Denmark.	5 Paraplegics, and 6 quasdriplegics, (2 females and 9 males, aged 34 yrs, (range 25-47 yrs) weight, 74.8 kg (52.5-93.7kg) and height 1.8m.	30 min. electrically induced cycling exercise per day.	Natural killer cells concentration increased in the paraplegic group, but resumed to normal after 2 hours. The concentration of plasma growth hormones and catchaeloamines increased during exerscie. Epinephedrin was more pronounced in paraplegic than quadriplegic.	3. REGYS1 system was used.
Donaldson et al, 2000.[5] Funding not stated.	Single subject case report. Set in Salisbury, UK.	Subject was age 52, Male and 10 years post injury.	Near isometric or cycling exercise was performed at home for an avg of 21 minutes per day for 16 months.	The stimulated muscles increased in size, right quadriceps 28%, left quadriceps 14%, right calf 4%, left calf, 14%. The subject was able to cycle for 12km on the level. A substantial increase	3. . Exercise carried out on a recumbent tricycle.

				in measured voluntary strength of the knee extensors and subject reported improved leg function.	
Sipski et al; 1989[33] Funding not stated	Case series with qualitative outcomes-questionnaire.	52 patients were treated from June 1985 to November 1987 in the electrical stimulation ergometry program. 90% responded to questionnaire, 72% were quadriplegic, 28% were paraplegic. 37 males, 10 females. Ages ranged from 16-65 years, with a mean of 40.5 years. Post injury 6 months to 22 years.	Electrical Stimulation ergometry training Questionaire positive or negative (improved or worsened), on endurance, self image, apasticity, appearance, breathing, skin integrity, sleeping patterns, lower extremity dependent edema, bladder and bowel function, dysesthetic pain and sweating. Patients were divided into quadriplegic and paraplegic groups.	62% paraplegics improved endurance, 65% quadriplegics improved endurance. 62% paraplegics and 56% quadriplegics reported improved self image. 54% of paraplegics and 77% of quadriplegics perceived their appearance was better. 39% paraplegics and 24% of quadriplegics noted decreased lower extremity edema with training.	3 ERGYS I and REGYSI Cycle ergometry. 22 patients were discharged from the training due to a variety of reasons such as nausea, medical instability, dysreflexia, increased spactisicity, personal, insurance and college.
Twist, et al, 1992[36] Funding not specified.	Pre-post test, No controls. Case series	Nine patients, 6 male, 3 females, ranging in age from 22 to 50 years. Four patients were paraplegic, 5 were quadriplegic.	Phase I (0-19 weeks) Leg training, REGYS1, 30-40min sessions. Phase II: (19-30wk) Lower extremity	Regular exercise with computerised FES caused significantly ($p<0.05$) sustained increases in BEP-ir	3

		Post injury time: 1.2 to 33.5 years (mean+9.71 yr).	Bicycle Ergometry REGYSI chair. Phase III: three consecutive sessions 15-20 minutes. Measures included: Plasma levels of Beta endorphinlike immoreactivity (BEP-ir), cortisol levels and depression parameters.	in all patients and improved the regulation of cortisol. The greater the exercise training the greater increases in BEP-ir levels were seen. Depression scores also improved which the authors suggested a correlation between subjective mood and BEP-ir levels.	
Nash, et al; 1991[27] Research was funded by The Miami Project to Cure Paralysis and the Lucerne Rehabilitation Spinal Centre.	Case series.	Eight SCI volunteers from two SCI centres served as study subjects. All were quadriplegic males, between the ages of 22 and 39 years of age. Post injury 3-11 years duration. Inclusion criteria: Neurologically stable, No volitional bowel or bladder function Good health.	One month of electrically stimulated quadriceps strengthening followed by 6 months of FES cycle training.	6.5% increase in left ventricular internal dimension at end diastole ($p< 0.02$). with increases in interventricular septal and posterior wall thicknesses at end diastole of 17.8 ($p<0.002$) and 20.3% ($p<0.01$) respectively. Left ventricular mass increased by 35% following exercise training ($p=0.002$). Data indicates that	3

				myocardial atrophy is reversed in tetraplegics following electrically stimulated exercise training, and that changes in cardiac architecture are likely to be the result of pressure and volume challenge to the heart imposed by exercise.	
Hooker, et al, 1995[17] Funding not specified.	Case series.	Eight males with SCI, Mean age is 36. Mean post injury time is 9.8 yrs. None of the subjects had been involved in any regular endurance exercise or NMES leg cycle ergometry prior to the training programme.	NMES leg cycle ergometers 3 X per week for 12 weeks.	Significant increase in exercise, tolerance, and cardiorespiratory capacity in persons with SCI. A significant ($p<0.05$) increase was observed for peak VO_2 (+10%, 1.29±0.30 to 1.42 ± 0.39 $1.min^{-1}$). No other statistically significant differences were noted for any other peak variable.	3. REGYS1/NMES cycle ergmometer.

Hooker et al; 1990[16] Funding from the Rehabilitation Research and Development of Science of the US Dept of Veterans Affairs.	Case series. Pre post test.	7 persons with quadriplegia and 7 persons with paraplegia volunteered for the study. Each group included six men and one woman and groups were matched for age, weight and post injury. Quad group: Mean age : 26.7 yrs, Post injury: 6.7 yrs Paraplegic group: Mean age: 29 and post injury time 5.4.	30 mins. of continuous FNS leg cycling during which open circuit spirometry, impedance cardiography, auscultation and fingertip capillary blood sampling were used to assess metabolic and hemodynamic responses. No mention of length of time for this study.	30 mins of FES leg cycle exercise in a controlled environment does not result in an inappropriate physiologic responses in SCI individuals.	ERGYS 1 leg cycle ergometer. 3.
Gerritis et al 2001[11] No funding stated	Before after trial	Nine men with spinal cord lesions. Average age ranged from 26 to 61. duration of injury ranged from 1yr to 27 yrs. Exclusion criteria: Cardiac arrhythmia, high blood pressure, a pacemaker, pressure ulcers, metal implants in the area of stimulation, severely reduced mobility in hip or knee joints, absence of spinal	Six weeks of cycling using a functional electrically stimulated leg cycle ergometer.	Increase in diameter (p,0.05) peak systolic inflow volumes (PSIVs) mean inflow volumes and reduced velocity index (p<.01) where values in the common carotid remained unchanged. Concluded that six weeks of FES_LCE	3 Case series, before after trial. ERGYS 2.

		reflexes, and previous bone fractures.		training increased the cross sectional area of large conduit arteries and improved blood flow to the paralysed legs of individuals with SCI.	
Chilibeck et al 1999.[4] Research funded by the Glenrose Rehabilitation Hospital Research Fund. University of Alberta, Edmonton, Alberta, Canada.	Pre post test analysis	Six individuals with motor complete SCI (age 31-50 yrs, 3-25 yrs post injury). .	Trained using FES leg cycle ergometry for 30 min. 3 days per week for 8 weeks Biopsies of the muscle were obtained pre and post training and analysed for fibre composition, fibre size and capillarization	Average fibre area increased by 23% (p,0.05) with training. As a result of these proportional increases, capillarization expressed relative to fibre area was unchanged with training. Concluded that FES leg cycle ergometer training results in proportional increases in fibre area and capillary number in individuals with SCI	3.

Gerritis, H.L.*et al*: 2000.[10] No research funding stated.	Longitudinal training study, pre post design.	Muscles were studied in seven people with motor complete SCI. Seven male subjects, age range 28-61, post injury time ranged from 1 yr to 27 yrs.	30min per week for 6 weeks. Contractile Speed and fatigue characteristics of electrically stimulated isometric contractions were compared before and after 6 weeks of FES LCE.	Fatigue resistance improved, following FES-LCE training. Maximal rate of force was unaffected. The speed of relaxation increased and a change in force-frequency relationship.	3 ERGYS2.

APPENDIX 3 – CHARACTERISTICS OF EXCLUDED STUDIES

1. Akers JM, Smith BT, Betz RR, Mulcahey MJ. Implantable functional electrical stimulation (FES) technology in growing animals... The Howard H. Steel Conference on Pediatric Spinal Cord Injury, Rancho Mirage, California, December 3-5, 1999. *Topics in Spinal Cord Injury Rehabilitation* 2000;6Suppl::251. Excluded: Animals
2. Bajd T, Kralj A, Stefancic M, Lavrac N. Use of functional electrical stimulation in the lower extremities of incomplete spinal cord injured patients. *Artificial Organs.* 1999;23(5):403-9.
3. Bajd T, Munih M, Kralj A. Problems associated with FES-standing in paraplegia. *Technology & Health Care.* 1999;7(4):301-8. Excluded:Standing
4. Beadling L. Evolution of neural prostheses increases promise for spinal cord injury patients: functional electrical stimulation technology has restored hand flexion and grasp in nearly 200 patients with cervical spine cord injuries. *Orthopedics Today.* 2001;21(1):32-3. Excluded: grasping only.
5. Betz RR, Johnston TE, Smith BT, Mulcahey MJ, McCarthy JJ. Three-year follow-up of an implanted functional electrical stimulation system for upright mobility in a child with a thoracic level spinal cord injury. *Journal of Spinal Cord Medicine.* 2002;25(4):345-50. Excluded children
6. Betz RR, Mulcahey MJ. Restoration of function in children with spinal cord injuries and cerebral palsy: progress, current state, and future vision of functional electrical stimulation research at the Shriners Hospitals for Children... The Howard H. Steel Conference on Pediatric Spinal Cord Injury, Rancho Mirage, California, December 3-5, 1999. *Topics in Spinal Cord Injury Rehabilitation* 2000;6Suppl::110-24.Excluded children
7. Betz RR, Mulcahey MJ, Smith BT, Triolo RJ, McCarthy JJ. Implications of hip subluxation for FES-assisted mobility in patients with spinal cord injury. *Orthopedics.* 2001;24(2):181-4. Excluded:non-cycling
8. Bhambhani Y, Tuchak C, Burnham R, Jeon J, Maikala R. Quadriceps muscle deoxygenation during functional electrical stimulation in adults with spinal cord injury. *Spinal Cord.* 2000;38(10):630-8.Excluded non-cycling.
9. Bobet J. Can muscle models improve FES-assisted walking after spinal cord injury?. [Review] [67 refs]. *Journal of Electromyography & Kinesiology.* 1998;8(2):125-32. Excluded: more on modelling
10. Bonaroti D, Akers J, Smith BT, Mulcahey MJ, Betz RR. A comparison of FES with KAFO for providing ambulation and upright mobility in a child with a complete thoracic spinal cord injury. *Journal of Spinal Cord Medicine.* 1999;22(3):159-66.Excluded: children
11. Bonaroti D, Akers JM, Smith BT, Mulcahey MJ, Betz RR. Comparison of functional electrical stimulation to long leg braces for upright mobility for children with complete thoracic level spinal injuries. *Archives of Physical Medicine & Rehabilitation.* 1999;80(9):1047-53. Excluded children
12. Brissot R, Gallien P, Le Bot MP, Beaubras A, Laisne D, Beillot J, et al. Clinical experience with functional electrical stimulation-assisted gait with Parastep in spinal cord-injured patients. *Spine.* 2000;25(4):501-8. Excluded: non-cycling
13. Davis SE, Mulcahey MJ, Smith BT, Betz RR. Outcome of functional electrical stimulation in the rehabilitation of a child with C-5 tetraplegia. *Journal of Spinal Cord Medicine.* 1999;22(2):107-13. Excluded: Children
14. Degnan GG, Wind TC, Jones EV, Edlich RF. Functional electrical stimulation in tetraplegic patients to restore hand function. [Review] [43 refs]. *Journal of Long-Term Effects of Medical Implants.* 2002;12(3):175-88. Excluded: Hand function
15. Ferrarin M, Palazzo F, Riener R, Quintern J. Model-based control of FES-induced single joint movements. *IEEE Transactions on Neural Systems & Rehabilitation Engineering.* 2001;9(3):245-57. Excluded: Model theory

16. Franco JC, Perell KL, Gregor RJ, Scremin AM. Knee kinetics during functional electrical stimulation induced cycling in subjects with spinal cord injury: a preliminary study. *Journal of Rehabilitation Research & Development*. 1999;36(3):207-16. Excluded: knee kinetics
17. Frazier CR. The development of a nursedirectedcomputerized functional electrical stimulation program... reprinted from SCI Nursing 16:2. *SCI Nursing*. 2003;20(3):164-70. Excluded: programme theory
18. Gider F, Bajd T. Influence of functional electrical stimulation on gait efficiency in a subject with incomplete spinal cord injury: a case study. *Fizyoterapi Rehabilitasyon* 2002;13(1):31-6. Excluded Gait
19. Giuffrida JP, Crago PE. Reciprocal EMG control of elbow extension by FES. *IEEE Transactions on Neural Systems & Rehabilitation Engineering*. 2001;9(4):338-45. Excluded: elbow extension
20. Greenwald D, Keith MW, Aguiar J, Singh S. Current surgical therapy for quadriplegia: functional electrical stimulation. [Review] [22 refs]. *Plastic & Reconstructive Surgery*. 2002;109(4):1378-85. Excluded: Surgery therapy
21. Gschwind CR. Functional electrical stimulation: a new horizon for quadriplegic patients.[comment]. *Australian & New Zealand Journal of Surgery*. 2000;70(8):549-50. Excluded: non -cycling
22. Hartkopp A, Murphy RJ, Mohr T, Kjaer M, Biering-Sorensen F. Bone fracture during electrical stimulation of the quadriceps in a spinal cord injured subject. *Archives of Physical Medicine & Rehabilitation*. 1998;79(9):1133-6. Excluded: non-cycling.
23. Hesse S, Werner C, Bardeleben A. Electromechanical gait training with functional electrical stimulation: case studies in spinal cord injury. *Spinal Cord*. 2004;42(6):346-52. Excluded: Gait
24. Ichie M, Handa Y. [Restoration of motor function by functional electrical stimulation]. [Review] [28 refs] [Japanese]. *No Shinkei Geka - Neurological Surgery*. 2001;29(1):11-20. Excluded: Non-cycling
25. Jezernik S, Wassink RG, Keller T. Sliding mode closed-loop control of FES: controlling the shank movement. *IEEE Transactions on Biomedical Engineering*. 2004;51(2):263-72. Excluded: more on shank movement.
26. Johnston TE, Betz RR, Smith BT, Mulcahey MJ. Implanted functional electrical stimulation: an alternative for upright mobility in pediatric spinal cord injury... Platform & poster presentations for CSM 2000... Combined Sections Meeting. *Neurology Report*. 2001;25(4):127. Excluded: Poster presentation
27. Johnston TE, Betz RR, Smith BT, Mulcahey MJ. Implanted functional electrical stimulation: an alternative for standing and walking in pediatric spinal cord injury. *Spinal Cord*. 2003;41(3):144-52. Excluded: children
28. Johnston TE, Finson RL, Smith BT, Bonaroti DM, Betz RR, Mulcahey MJ. Functional electrical stimulation for augmented walking in adolescents with incomplete spinal cord injury. *Journal of Spinal Cord Medicine*. 2003;26(4):390-400. Excluded: walking
29. Kameyama J, Handa Y, Hoshimiya N, Sakurai M. Restoration of shoulder movement in quadriplegic and hemiplegic patients by functional electrical stimulation using percutaneous multiple electrodes. *Tohoku Journal of Experimental Medicine*. 1999;187(4):329-37. Excluded: non-cycling
30. Kern H, Boncompagni S, Rossini K, Mayr W, Fano G, Zanin ME, et al. Long-term denervation in humans causes degeneration of both contractile and excitation-contraction coupling apparatus, which is reversible by functional electrical stimulation (FES): a role for myofiber regeneration? *Journal of Neuropathology & Experimental Neurology*. 2004;63(9):919-31.Excluded:Non-cycling

31. Kern H, Hofer C, Strohhofer M, Mayr W, Richter W, Stohr H. Standing up with denervated muscles in humans using functional electrical stimulation. *Artificial Organs.* 1999;23(5):447-52. Excluded:standing
32. Kjaer M, Mohr T, Biering-Sorensen F, Bangsbo J. Muscle enzyme adaptation to training and tapering-off in spinal-cord-injured humans. *European Journal of Applied Physiology.* 2001;84(5):482-6. Excluded: non-cycling
33. Krause P, Straube A. Repetitive magnetic and functional electrical stimulation reduce spastic tone increase in patients with spinal cord injury. *Supplements to Clinical Neurophysiology* 2003;56:220-5. Excluded: non-cycling
34. Kuzelicki J, Kamnik R, Bajd T, Obreza P, Benko H. Paraplegics standing up using multichannel FES and arm support. *Journal of Medical Engineering & Technology.* 2002;26(3):106-10 .Excluded:Arm support
35. Mangold S, Keller T, Curt A, Dietz V. Transcutaneous functional electrical stimulation for grasping in subjects with cervical spinal cord injury. *Spinal Cord.* 2005;43(1):1-13. Excluded: grasping
36. Maxwell DJ, Granat MH, Baardman G, Hermens HJ. Demand for and use of functional electrical stimulation systems and conventional orthoses in the spinal lesioned community of the UK. *Artificial Organs.* 1999;23(5):410-2. Excluded: non-cycling
37. Memberg WD, Crago PE, Keith MW. Restoration of elbow extension via functional electrical stimulation in individuals with tetraplegia. *Journal of Rehabilitation Research & Development.* 2003;40(6):477-86. Excluded: elbow extension
38. Middleton JW, Keast JR. Artificial autonomic reflexes: using functional electrical stimulation to mimic bladder reflexes after injury or disease. [Review] [140 refs]. *Autonomic Neuroscience-Basic & Clinical.* 2004;113(1-2):3-15. Excluded: bladder reflex.
39. Mirbagheri MM, Ladouceur M, Barbeau H, Kearney RE. The effects of long-term FES-assisted walking on intrinsic and reflex dynamic stiffness in spastic spinal-cord-injured subjects. *IEEE Transactions on Neural Systems & Rehabilitation Engineering.* 2002;10(4):280-9. Excluded: walking.
40. Okuma I, Hayashi J, Kaito T, Funahashi M, Kuno S, Kato Y, et al. Functional electrical stimulation (FES) for spinal cord injury. *Acta Neurochirurgica - Supplement* 2003;87:53-5. Exlcluded: Not available in English
41. Pfurtscheller G, Muller GR, Pfurtscheller J, Gerner HJ, Rupp R. 'Thought'--control of functional electrical stimulation to restore hand grasp in a patient with tetraplegia. *Neuroscience Letters.* 2003;351(1):33-6. Excluded: hand function
42. Popovic D, Stein RB, Oguztoreli N, Lebiedowska M, Jonic S. Optimal control of walking with functional electrical stimulation: a computer simulation study. *IEEE Transactions on Rehabilitation Engineering.* 1999;7(1):69-79. Excluded walking not cycling.
43. Saccavini M, Bizzarrini E, Galassi F, Dolfo E, Zampa A, Cappellazzo A, et al. Normal myoelectric signal and its use in functional electrical stimulation in spinal cord injury patients. *Europa Medicophysica* 2001;37(1):11-3. Excluded: Not English
44. Sampson EE, Burnham RS, Andrews BJ. Functional electrical stimulation effect on orthostatic hypotension after spinal cord injury. *Archives of Physical Medicine & Rehabilitation.* 2000;81(2):139-43. Excluded: effect on hypotension.
45. Shimada Y, Chida S, Matsunaga T, Misawa A, Ito H, Sakuraba T, et al. Grasping power by means of functional electrical stimulation in a case of C6 complete tetraplegia. *Tohoku Journal of Experimental Medicine.* 2003;201(2):91-6. Excluded: not available in Japanese.
46. Sinkjaer T, Haugland M, Inmann A, Hansen M, Nielsen KD. Biopotentials as command and feedback signals in functional electrical stimulation systems. [Review] [93 refs]. *Medical Engineering & Physics.* 2003;25(1):29-40.
47. Excluded: non cycling

48. Stanic U, Kandare F, Jaeger R, Sorli J. Functional electrical stimulation of abdominal muscles to augment tidal volume in spinal cord injury. *IEEE Transactions on Rehabilitation Engineering.* 2000;8(1):30-4. Excluded: abdominal muscles
49. Steers WD, Wind TC, Jones EV, Edlich RF. Functional electrical stimulation of bladder and bowel in spinal cord injury. [Review] [20 refs]. *Journal of Long-Term Effects of Medical Implants.* 2002;12(3):189-99 Excluded: bladder and bowel function.
50. Stieglitz T. Neural prostheses and functional electrical stimulation. *Biomedizinische Technik.* 2004;49(4):70-1.Excluded: not available in English
51. Thorsen R, Spadone R, Ferrarin M. A pilot study of myoelectrically controlled FES of upper extremity. *IEEE Transactions on Neural Systems & Rehabilitation Engineering.* 2001;9(2):161-8. Excluded: upper extremity only.
52. Tinsley SL, Eldridge E, Carver K, Vazquez M. The cardiovascular effects of ambulation with the advanced reciprocating gait orthosis (ARGO) vs ARGO coupled with functional electrical stimulation (FES) in a patient with thoracic level spinal cord injury (SCI)... Platform & poster presentations for CSM 2003. *Neurology Report.* 2002;26(4):212. Excluded: poster presentation.
53. Tong KY, Granat MH. Reliability of neural-network functional electrical stimulation gait-control system. *Medical & Biological Engineering & Computing.* 1999;37(5):633-8. Excluded: Gait control
54. van der Salm A, Nene AV, Maxwell DJ, Veltink PH, Hermens HJ, MJ IJ. Gait impairments in a group of patients with incomplete spinal cord injury and their relevance regarding therapeutic approaches using functional electrical stimulation. *Artificial Organs.* 2005;29(1):8-14. Excluded: Gait improvements, non-cycling.
55. Winslow J, Jacobs PL, Tepavac D. Fatigue compensation during FES using surface EMG. *Journal of Electromyography & Kinesiology.* 2003;13(6):555-68. Excluded: non-cycling.

APPENDIX 4 – Scottish Intercollegiate Guidelines Network (SIGN) revised grading system*

Levels of evidence

1++	High quality meta analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias
1+	Well conducted meta analyses, systematic reviews of RCTs, or RCTs with a low risk of bias
1 -	Meta analyses, systematic reviews of RCTs, or RCTs with a high risk of bias
2++	High quality systematic reviews of case-control or cohort studies High quality case-control or cohort studies with a very low risk of confounding, bias, or chance and a high probability that the relationship is causal
2+	Well conducted case control or cohort studies with a low risk of confounding, bias, or chance and a moderate probability that the relationship is causal
2 -	Case control or cohort studies with a high risk of confounding, bias, or chance and a significant risk that the relationship is not causal
3	Non-analytic studies, e.g. case reports, case series
4	Expert opinion

2003 * From http://www.sign.ac.uk/guidelines/fulltext/50/section6.html. In this review, controlled studies without randomisation have been given a “2” grading.

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