Author Year; Country Score Research Design Total Sample Size	Methods	Outcome
FES-Cycling		
Lai et al. 2010 Taiwan Prospective controlled Study Level 2 N = 24	**Population:** 24 participants; 12 treatment (10 men, 2 women; age: 28.9 ± 5.3 years; TPI: 35.3 ± 6.1 days; C5 – T7) and 12 control (10 men, 2 women; age: 28.2 ± 5.7 years; TPI: 34.9 ± 8.0 days; C5 – T7). **Treatment**: FES-cycling 3x/week for first 3 months, suspended for next 3 months. Cycling time gradually increased up to 30 min. **Outcome Measures:** Right femoral neck BMD and distal femur BMD between femoral condyles 2cm above knee joint space (DXA). Measurements at baseline, after 3-month intervention, and 3 months post-intervention	1. Baseline: no significant differences in BMD between groups at femoral neck and distal femur 2. End of 3 months program BMD at femoral neck and distal femur significantly lower in both groups, but ↓ in distal femur BMD absolute values significantly lower in FES group than control (0.02 g/cm^2 (SD 0.01) vs. 0.07 g/cm^2 (SD 0.01), $p<0.01$) 3. From the end of cycling to 3 months after discontinuation, both groups decreased at the femoral neck and distal femur site, with no group differences.
Eser et al. 2003 Switzerland Prospective controlled trial	**Population:** 38 participants (34 men, 4 women); age: 32.9 years; complete traumatic injuries between C5-T12, (19 participants, 19 controls). **Treatment**: FES-cycling. Progressive training sessions until able to cycle for 30 minutes, then 3x/week for 6 months from this	1. Both groups had 0-10% decrease in tibial cortical BMD at 3-10 months. There was no difference between groups for BMD after the intervention.

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Level 2 N=38	baseline. On the remaining 2 days of the week, there was passive standing. Control group performed 30 min of passive standing 5 days/week. **Outcome measures:** cortical BMD of right tibia diaphysis (50% site, and 5cm proximal and distal to the 50% site) computed tomography (CT)	
NMES		
Arija-Blázquez et. al 2014 Spain RCT Level 1 PEDro = 8 N=8	**Population:** 8 men with acute motor complete traumatic SCI were allocated to Treatment group (n=5; AIS A; T4 – T 12; age: 42 years; TPI: 5.5 weeks) or Control group (n=3; age: 36years; TPI: 5.8 weeks). **Treatment:** 14 weeks of NMES training (47 minutes/day, 5 days/week). One session consisted of 80 muscle contractions during 47 minutes divided into 10 contraction sets with a 60-second rest between sets. Every 2 sets, knee angle was changed throughout 10°, 35°, 60°, and 85° (0° full extension). NMES (T-ONE MEDIPRO, Electromedical Mediterranea, S.L., Spain): electrodes were located over the rectus femoris, vastus	1. No difference in mean group change in BMD (g/cm^2) and T-score between pre vs pre and pre vs post-NMES treatment between two groups. In fact, both groups showed a trend (i.e. not significant) for BMD decline in all areas (e.g. Treatment group: leg=-2.92%; trochanteric=-9.94%; Control group: leg=-3.34%; trochanteric=-8.12%), except lumbar (+3.47%). 2. Although serum OC increased >50% (pre: 10.64±5.5 ng/ml) and CTX and serum cortisol decreased by >26 (pre: 1.26±0.6 ng/ml) and >20%

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	medialis and vastus lateralis. Stimulation pattern: 200 μs pulse duration, at 30 Hz and with a maximum current of 140 mA. Amplitude was adjusted in the Treatment group to elicit similar isometric torque during the 14 weeks. **Outcome Measure:** Bone mineral density (BMD; DXA): legs from whole-body scan, lumbar spine, total hip, femoral neck, trochanteric and intertrochanteric areas. Bone biomarkers: Serum cortisol (ARCHITECT c4000 (Abbott Laboratories S.A, Madrid, Spain), Serum OC (Diasource kit (DIAsource ImmunoAssays S.A., Barcelona, Spain) and Serum CTX (E 170 module for MODULAR ANALYTICS - Roche Diagnostics, S.L., Madrid, Spain).	(pre: 13.5 ±3.6 ug/dl), respectively, these differences were not statistically significant.
	Effect Sizes: Forest plot of standardized mean differences (SMD ± 95%CI) as calculated from pre- and post-intervention data	

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	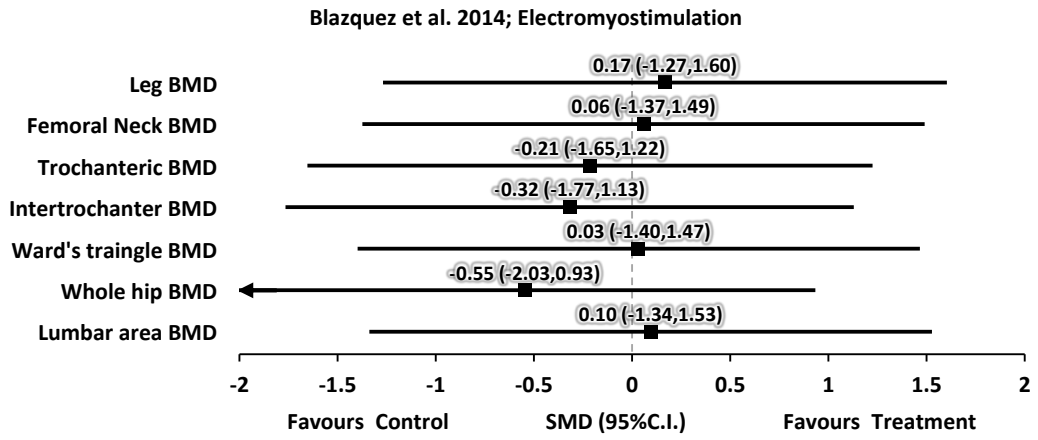	
Groah et al. 2010 USA PEDro =6 RCT Level 1 N=26	**Population**: 26 participants (22 men, 4 women) with traumatic SCI; age: ≥18 years; AIS A or B at time of entry, TPI: 39.5 days; above T12. **Treatment**: Randomized to usual inpatient SCI program [n=10; 26.2 years (range 19-71), 15 men and 1 woman] or intervention group [(n=16; 31.1 years (range 18-44), 7 men and 3 women]. Usual care and additional 1-hour NMES to quadriceps bilaterally (using Complex Motion Stimulator) for 1 hour (or until fatigue) 5 days/week for 6 weeks. **Outcome Measures**: Measurements at baseline, post-intervention, 3 months post-intervention. 1) BMD at lumbar spine and bilateral femoral neck, distal femur, proximal tibia (DXA). 2)	1. No group differences in BMD decline or biomarkers over time. However, the NMES group experienced 50% less distal femur BMD loss (not significant).

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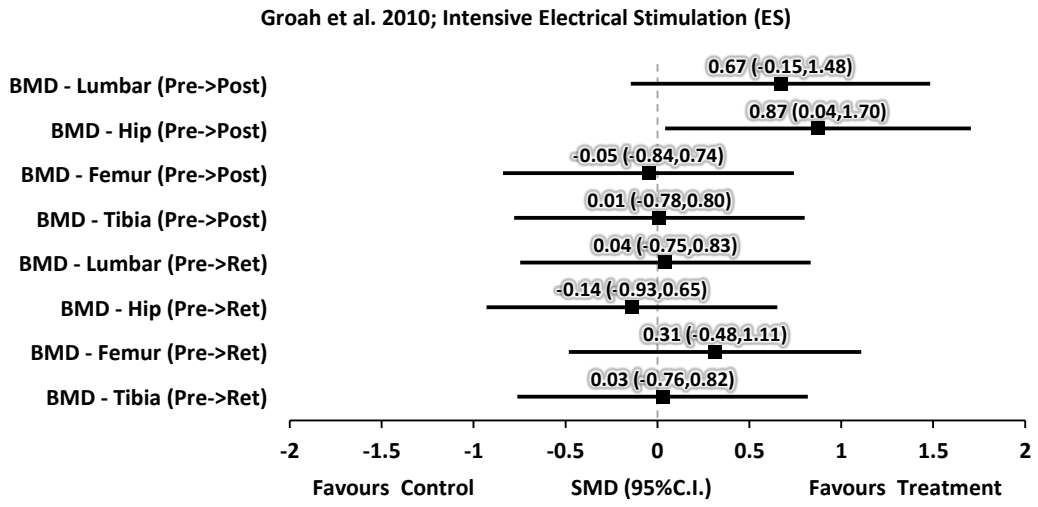
	Serum OC 3) Urinary NTX and 24-hour urine calcium	
	Effect Sizes: Forest plot of standardized mean differences (SMD ± 95%CI) as calculated from pre- to post-intervention data and pre-intervention to retention/follow-up data 	
Arija-Blázquez et al. 2013 Spain	**Population:** 10 participants with recent traumatic thoracic SCI (10 men, AIS A); age: 39.4 ± 12.3 years; TPI: 8 weeks; BMI: 25.1 ± 3.6 kg/m^2. 10 age-matched non-disabled participants for comparison; age: 36.7 ± 8.9 years, BMI: 23.3 ± 3.3 kg/m^2. **Treatment:** Immediately after basal blood samples were drawn, NMES was conducted (1 set of currents was applied bilaterally at each knee angle; total of 80 contractions; total	1. No significant differences between right and left leg BMD. 2. Basal levels of testosterone were not significantly different in SCI and non-disabled groups. There was a significant decrease in testosterone 15 min post-NMES (SCI = -11.9%, non-disabled=-6.8%). In the SCI group, testosterone remained lowered 30 min

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Prospective Controlled Trial Level 2 N=20 (10 SCI)	NMES time was 47 min per participant). **Outcome Measures:** BMD lower limb, total hip, femoral neck, intertrochanteric region (DXA), muscle cross-sectional area (MRI), testosterone, cortisol, and Type I collagen CTX (blood samples)	post-NMES (-7.4%). No differences in mean testosterone concentrations were observed between SCI and non-disabled groups at any time point. 3. Mean cortisol levels were not significantly different in SCI and non-disabled groups at any time point. In the SCI group, 30 min post-NMES mean cortisol levels dropped significantly (-18.5%). 4. Mean OC levels were not significantly different between SCI and non-disabled groups at any time point. 5. At all time points, CTX levels were significantly higher in the SCI group than non-disabled group. In the SCI group, CTX levels significantly declined post-NMES at 0 min (-27.0%), 15 min (-23.4%), 30 min (-27.1%), and 24h post-NMES (-10.2%). In the non-disabled group, CTX levels declined at 15 min (-13.7%) and 30 min (-15.6%) post-NMES.

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Dudley-Javoroski & Shields 2008a USA Case-control Level 3 N=19 (12 SCI)	**Population:** 12 men with motor complete SCI; age: 21–72 years; TPI: 0.3–22 years; C5–T11; AIS A–B; 9 matched SCI subjects as controls. 7 matched non-SCI controls. **Treatment:** Unilateral soleus NMES 5x/week 15 Hz every 2 s for 120 contractions (8000 contractions/month). **Outcome measures:** pQCT (trabecular vBMD of distal tibia 4% site) of one leg versus the other leg annually for up to 6 years.	1. A sustained between-limb difference in posterior distal tibia trabecular vBMD of 76.1 mg/cm3 (p = 0.04).
Dudley-Javoroski & Shields 2008b USA Case Report Level 5 N=1	**Population:** 1 man; T4 AIS A traumatic paraplegia; age: 21 years; TPI: 7 weeks. **Treatment:** Four bouts of 125 soleus contractions over 30 minutes 5 times per week in one leg; actual 8,000 contractions per month **Outcome** measures: trabecular vBMD of distal tibia 4% site (pQCT) of one leg versus the other leg after 1 year, 3 years	1. After 1 year, no difference in trabecular architecture; 4.5% difference in trabecular vBMD After 3 years, 15%/year vBMD decline in of untrained tibia and 7.6%/year vBMD decline in trained limb. Lower decline attributed to posterior portion which lost 2.59%/year.
Clark et al. 2007 Australia Prospective Controlled trial Level 2	**Population:** 33 participants; 15 tetraplegia and 18 paraplegia; AIS A-D. **Treatment**: NMES, 5 months Low-intensity stimulation to leg muscles, 15 min, 2x/day 5 days/week, 5 months (n=23; age	1. NMES was safe and well-tolerated, but there was only a minimal difference between groups for total body BMD only at 3 months post-injury (p<.01). Other DXA measures (hip

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N=33	28.6 ± 8.6 years; C4–T10, 13 tetraplegic; ; n=21 traumatic; n=2 nontraumatic); or control group (no treatment) (n=10; age: 31.0 ± 10.7 years; C5–T12, 4 tetraplegic; n=9 traumatic; n=1 nontraumatic). **Outcome measures:** total body, lumbar spine and hip BMD (DXA) at 3 weeks, 3- and 6-months post-injury.	and spine BMD) did not differ between groups at any time point.
Shields et al. 2007 USA Pre-Post Level 4 N=4	**Population:** 4 men with SCI; age: 52.3 ± 11.2 years; T1-7; AIS A; TPI: 8.9 ± 4.1 years. **Treatment:** Trained 1 leg using an isometric plantarflexion NMES protocol (the untrained limb serving as within-subject control) for 30min/day, 5 days/week, for 6 to 11 months. Mean estimated compressive loads delivered to the tibia were ~110% body weight. **Outcome Measures:** BMD of the proximal tibia by DXA at baseline and post-intervention.	1. Unchanged BMD of proximal tibia before and after training for trained and untrained limb ($p>0.05$). Trained limb of 2 subjects had ~0.02g/cm^2 gain in BMD but not statistically significant. 2. Untrained proximal tibia BMD did not differ from trained limb proximal tibia BMD either before or after training.
Shields et al. 2006a USA Prospective Controlled trial Level 2 N=6	**Population:** 6 participants with complete injuries from C5-T10; age: 27.6 years (range: 21-43); TPI: 2.1 months; 70% training compliance. Within-participant design. **Treatment**: NMES at 1.5 times bodyweight for 3 years. Treatment leg only received a home program	1. There was a greater decline in tibia BMD of the untrained limb compared with the trained limb (10% vs. 25%) ($p<0.05$)

Author Year; Country Score Research Design Total Sample Size	Methods	Outcome
	of NMES to stimulate leg plantar flexors with a 35-min protocol (4 bouts with 5-min rest between bouts) for 5x/week **Outcome measures:** BMD of the spine, hips and knee regions (proximal tibial analysis protocol) by DXA at baseline and 1,2 and 3 years.	
Shields et al. 2006b USA Prospective Controlled trial Level 2 N= 7	**Population:** 7 men with complete injuries from C5-T10; age: 29.1 years (range: 21-43); TPI: < 4.5 months. Within-participant design. **Treatment**: NMES at 1.5 times body weight; 2-3 years. Treatment leg only received a home program of NMES to stimulate leg plantar flexors with a 35-min protocol (4 bouts/day with 5-min rest between bouts) for 5x/week). **Outcome measures:** cortical BMD of the tibia bilaterally at the 4%, 38%, and 66% sites (pQCT).	1. No significant differences in cortical BMD of the tibia at the 38% and the 66% sites 2. Higher distal tibia trabecular BMD at 4% site in trained compared with untrained limb.
Standing/Walking		
Ben et al. 2005 Australia PEDro=9 Within-participant RCT	**Population:** 20 participants (16 men and 4 women); TPI: 4 ± 2 months; age: 34 ± 15; 8 paraplegia, 12 tetraplegia. Within-participant design. **Treatment:** Tilt-table standing, 12 weeks	1. No difference in proximal femur BMD between the treatment and the control leg.

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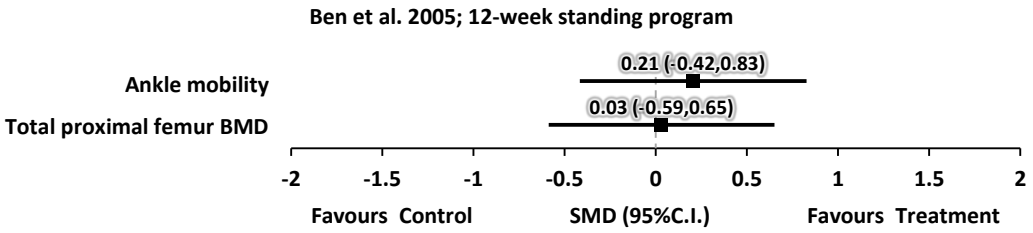
Level 2 N=20	Treatment leg only received weight-bearing on a tilt-table for 30 min, 3x/week. Wedge applied to treatment leg to provide adequate dorsiflexion and weight-bearing to the ankle. Control leg was not loaded in standing. **Outcome measures:** BMD of proximal femur (DXA).	
	Effect Sizes: Forest plot of standardized mean differences (SMD ± 95%CI) as calculated from pre- and post-intervention data  **Both heels of each subject randomized to different groups (control or intervention) such that each sucject acts as his/her own control**	
de Bruin et al. 1999 Switzerland PEDro=6 RCT Level 1 N=19	**Population:** 19 men; ages 19-59; traumatic injuries between C4-T12; AIS: A-D. **Treatment:** Standing/Walking. Group 1 had 0-5 hour per week loading exercises with a standing frame. Group 2 had 5+hour of standing exercises per week (standing). Group 3 had 5+hours of standing and treadmill (walking). Interventions lasted 25 weeks **Outcome measures:** trabecular BMD, cortical BMD moment of	1. Marked decrease in trabecular BMD. (site not specified) at the left tibia for the immobilized group but minimal decrease in trabecular BMD in Group 2 and 3

Author Year; Country Score Research Design Total Sample Size	Methods	Outcome
	inertia of the left tibia proximal to the ankle joint line and in the diaphysis (pQCT).	
Dudley-Javoroski & Shields 2013 USA Longitudinal Level 2 N=12	**Population:** 12 participants (9 men, 3 women; age: 22-48 years) non-disabled controls and 12 (11 men, 1 woman; age: 16-44 years old; 11 AIS A, 1 AIS B; 10 out of 12 subjects had TPI <1-year at first scan) participants with SCI. **Treatment:** Individuals with SCI experienced active-resisted stance with FES of the quadriceps (n=7) or passive stance (n=5) for up to 3 years. **Outcome Measures:** trabecular BMD of the distal femur 12% femur length measured distal to proximal (pQCT)	1. Over 1.5 years, the slope of distal femur trabecular MD decline over time was slower at all quadrants for the active-resisted stance limbs. 2. At >2 years of training, trabecular BMD was significantly higher for the active-resisted stance group than for the passive stance group. 3. Trabecular BMD was preferentially spared in the posterior quadrants of the femur with active-resisted stance.
Treadmill Training		
Giangregorio et al. 2005 Canada Pre-post Level 4 N=5	**Population:** 5 participants (2 men, 3 women); age: 19-40 years, traumatic injuries between C3-C8; AIS: B and C; no controls; TPI: 114.2 days. **Treatment:** Body-weight supported treadmill training. Initial session started at 5mins and was increased gradually to 10-15 mins in all but 1 participant during 48 sessions of 2x/week-training over 6-8 months.	1. Lumbar spine BMD changes ranged from 0.2 to -7.4%. 2. Decrease in BMD for all participants at almost all lower limb sites after training, ranging from -1.2 to -26.7% (DXA). 3. No consistent changes in bone geometry at distal femur and proximal tibia (pQCT).

Author Year; Country Score Research Design Total Sample Size	Methods	Outcome
	Outcome measures: BMD lumbar spine, hip, distal femur and proximal tibia by DXA and mid femur 60% site and proximal tibia 66% site CT; bone turnover markers (osteocalcin, DPD).	4. Did not alter the expected pattern of change in biochemical bone markers over time.
Ultrasound		
Warden et al. 2001 Australia PEDro=11 RCT Level 1 N=15	**Population:** 15 men; age: 29 years (range: 17-40); traumatic injuries between C5-T10; AIS: A-B; TPI: 110.3 days; within-group design. **Treatment:** Pulsed therapeutic ultrasound. Applied to both calcanei for each participant for 20 min/day, 5x/week over a consecutive 6-week period. Right and left calcaneus within each participant was randomized. **Outcome measures:** BMD of the calcaneus by DXA and quantitative ultrasound of the calcaneus (QUS).	1. For the specified dose of pulsed ultrasound, no significant effects were on BMD measured via DXA or QUS for any parameter ($p>0.05$).
	Effect Sizes: Forest plot of standardized mean differences (SMD ± 95%CI) as calculated from pre- and post-intervention data	

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	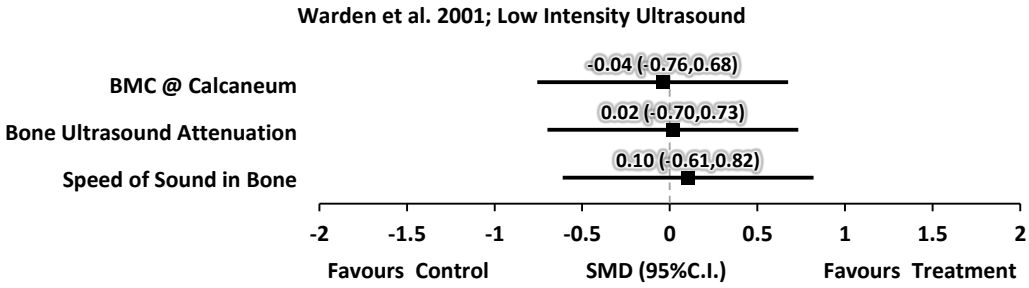 **Both heels of each subject randomized to different groups (control or intervention) such that each sucject acts as his/her own control**	
Physical Activity		
[Astorino et al. 2013] USA Pre-post Level 4 N=13	**Population:** 13 participants with SCI (11 men, 2 women); 2 chronic, 11 acute SCI; age: 29.4 ± 7.8 years; TPI: 1.9 ± 2.7 years. **Treatment:** 2-3h/day of activity-based therapy targeting regions below the level of injury a minimum of 2 days/week for 6 months. Activity-based therapy consisted of the following modalities: active assisted exercise, upper/lower body and core resistance training, load-bearing, cycle ergometry, gait training and vibration. **Outcome measures:** BMD of the whole body, lumbar spine, right and left total hip, femoral neck and intertrochanteric region distal femur, proximal tibia (DXA) at baseline, 3 and 6 months. Serum P1NP; serum CTX;	1. Total-body BMD significantly declined (2.5%) from 0 to 6 months, accompanied by reductions in total hip BMD, right and left femoral neck BMD, and right and left trochanter BMD. 2. The two participants with chronic SCI showed increased total body (1.0 and 1.8%), total femur (0.5 and 1.3%) and trochanter BMD (2.6 and 6.8%) in response to training. 3. Activity-based therapy had no effect on P1NP and serum CTX.

* All data expressed as mean±SD, unless expressed otherwise.