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# Neuromuscular electrical stimulation in the treatment of knee osteoarthritis: a systematic review and meta-analysis

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**OM Giggins, BM Fullen and GF Coughlan**

## Abstract

**Objective:** To assess the effectiveness of surface neuromuscular electrical stimulation in the treatment of knee osteoarthritis.

**Design:** Systematic review and meta-analysis of randomized controlled and controlled clinical trials

**Methods:** Studies were identified from databases (MEDLINE, EMBASE, CINAHL, Sports Discus, PEDro and the Cochrane Library) searched to January 2011 using a battery of keywords. Two reviewers selected studies meeting inclusion criteria. The methodological quality of the included studies was assessed using the Thomas Test and the strength of the evidence was then graded using the Agency for Health Care Policy and Research guidelines. Data were pooled and meta-analyses were performed.

**Results:** Nine randomized controlled trials and one controlled clinical trial, studying a total of 409 participants ( $n=395$  for randomized controlled trials, and  $n=14$  for controlled trial) with a diagnosis of osteoarthritis were included. Inconsistent evidence (level D) was found that neuromuscular electrical stimulation has a significant impact on measures of pain, function and quadriceps femoris muscle strength in knee osteoarthritis.

**Conclusion:** The role of neuromuscular electrical stimulation in the treatment of knee osteoarthritis is ambiguous. Therefore, future work is needed in this field to clearly establish the role of neuromuscular electrical stimulation in this population.

## Keywords

Electrical stimulation, knee osteoarthritis, rehabilitation interventions

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## Introduction

Osteoarthritis is the most common form of arthritis predominantly affecting the large weight-bearing joints of the body such as the knee. Symptoms associated with knee osteoarthritis include joint instability, pain on weight-bearing and/or at rest, reduced

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range of motion and disuse atrophy and weakness of the quadriceps femoris muscle. Functional disability arises from pain and loss of quadriceps femoris strength, both of which reduce quality of life and increase the risk of further morbidity and mortality.<sup>1</sup> Exercise therapy aims to decrease pain and increase quadriceps femoris strength, therefore improving functional capacity for those with knee osteoarthritis. The American College of Rheumatology has approved regular exercise as a therapeutic approach<sup>2</sup> with both aerobic and strengthening exercises shown to improve pain and physical function in patients with knee osteoarthritis.<sup>3</sup>

Neuromuscular electrical stimulation consists of electrically stimulating muscle and/or nerves to induce a muscle contraction. It increases the load on the muscle using an electrically induced contraction and can therefore be used to improve muscle strength.<sup>4</sup> Evidence suggests that neuromuscular electrical stimulation can increase strength of the quadriceps femoris muscle and decreases pain in knee osteoarthritis,<sup>5,6</sup> however this has not been thoroughly investigated. A previous systematic review published in 2000 identified strong evidence for the beneficial application of neuromuscular electrical stimulation in knee osteoarthritis, however the authors highlighted limitations which included the limited number of included studies, their small sample sizes and flawed allocation procedures.<sup>7</sup> In addition, patients post total knee arthroplasty were included as was the use of transcutaneous electrical nerve stimulation for pain relief.

Because of the expansion of research in the area of neuromuscular electrical stimulation in the past decade, an update on the current evidence is required. Hence this study was undertaken to systematically review the literature to determine the efficacy of surface neuromuscular electrical stimulation as a method of improving quadriceps femoris muscle strength, pain and function in patients with knee osteoarthritis.

## Methodology

The review comprised three phases. In phase 1 an extensive literature search of the following databases

was conducted up to January 2011: MEDLINE, EMBASE, CINAHL, Sports Discus, PEDro and the Cochrane Library. The search terms relating to osteoarthritis and neuromuscular electrical stimulation used in the MEDLINE search were modified for the other databases (Appendix 1). Citation lists from all included studies were also searched.

Inclusion criteria included randomized controlled trials and controlled clinical trials, published in English, or translated into English between 1986 and 2011, and conducted on human adults with a diagnosis of unilateral or bilateral knee joint osteoarthritis. Studies that used neuromuscular electrical stimulation in combination with any other therapeutic intervention or exercise programme, as well as those comparing neuromuscular electrical stimulation to exercise interventions/non-exercise interventions or combinations of exercise with different conservative treatments were included. Exclusion criteria included participants who had undergone total knee replacement or uni-compartmental replacement or had any history of inflammatory disease such as rheumatoid arthritis. Studies that investigated the use of transcutaneous electrical nerve stimulation or pulsed electromagnetic stimulation were also excluded, along with studies that used implantable electrodes.

In phase 2, two reviewers (OMG and GFC) assessed studies generated from the search strategy for inclusion using the title and/or the abstract if there was ambiguity in the study title. Full copies of potentially relevant studies were then obtained for detailed examination. The two reviewers then reviewed the full text of the potential studies to determine their suitability. Where disagreement existed between the reviewers on the inclusion of a study, a third independent reviewer (BMF) was assigned to review the manuscript. A detailed proforma was developed to capture and categorize the results of the included studies into three main themes: the effects of neuromuscular electrical stimulation on pain, on function and on quadriceps femoris muscle strength.

In phase 3, the quality of the studies was assessed using the Thomas Test<sup>9</sup> which has been identified in the literature<sup>8</sup> as the most appropriate tool for quality assessment for studies involving both randomized and non-randomized controlled trials. Two reviewers (OMG and GFC) independently graded

the quality of the included studies according to the following components: selection bias, study design, confounders, blinding, data collection methods, withdrawals and drop-outs. These component ratings then gave a global rating of strong, moderate or weak. The strength of the evidence was then graded according to the grading system used in the Agency for Health Care Policy and Research (AHCPR) guidelines.<sup>8</sup> Minor amendments were made to the grading system<sup>9</sup> to include level B category for trials of moderate quality. Where appropriate, study results were pooled and meta-analyses were undertaken. Considering the clinical heterogeneity of the included studies the meta-analyses were limited to studies where outcome measures included the Western Ontario and McMaster Osteoarthritis Index (WOMAC) pain and function scores, and walking tests. The analysis was undertaken using Review Manager Software package RevMan 5 (version 5.0.25, updated 2010 Cochrane Collaboration). For the continuous data where different scales were employed by different studies for the assessment of the same outcome (e.g. walking test) the standardized mean difference (SMD) with 95% confidence intervals (CI) were calculated using a random effect model. Where the same scale was employed (e.g. for pain and function (WOMAC)), the mean differences with 95% CI were used. Authors were contacted in cases of incomplete data.

## Results

Nine randomized controlled trials and one controlled clinical trial were included in the review. Figure 1 summarizes the results of all database searches. There was full agreement between the reviewers on the inclusion of all of the studies. A summary of the study characteristics is shown in Table 1.

### *Participants studied*

In total, 409 patients (female  $n = 312$ , male  $n = 83$ , not reported  $n = 14$ ) with knee osteoarthritis were included in the ten studies ( $n = 395$  for randomized controlled trials and  $n = 14$  for controlled clinical trials), where patient numbers in each intervention

study ranged from 7 to 57. All participants had either radiographic evidence (>grade 1 on the Kellgren and Lawrence Scale) of knee osteoarthritis, or where radiographic evidence was not reported, clinical evidence of knee osteoarthritis.<sup>10,11</sup> Participants were recruited from a range of clinical settings: an osteoarthritis database, an outpatient department in the study centre, from a total knee arthroplasty waiting list or by self-selection (advertisements). Four studies did not detail the method of participant recruitment.<sup>1,6,12,13</sup> All but one study<sup>10</sup> identified the proportion of male and female participants, with a greater proportion of females participating in every study. The participants' age ranged from 52 to 71 years. Mean body mass index ranged from 29.3–32.9 kg/m<sup>2</sup>. Three studies did not detail the body mass index of the participants studied.<sup>1,10,11</sup>

### *Treatment approaches*

The neuromuscular electrical stimulation treatment protocols employed in each study are summarised in Table 1. All but one study reported the parameters used.<sup>14</sup> The neuromuscular electrical stimulation pulse frequency used ranged from 25 to 50 Hz, with 50 Hz the most common frequency employed.<sup>1,5,12,15–17</sup> Choice of machine, treatment times and electrode placement varied between the studies.

### *Outcome measures*

Both self-report and objective outcome measures were included (Table 1). Self-report measures included disease-specific questionnaires (WOMAC and Lequense Index) and measures of pain (visual analogue scale, WOMAC pain subscale, McGill pain questionnaire, the pain subscale of the Arthritis Impact Measurement Scale 2, the Pain Rating Index Total, pain diary and the Present Pain Intensity scale). Quality of life measures (Short Form Health Survey 36, the Nottingham Health Profile) and a self reported measure of function (the Functional Performance Inventory) were also included.

Objective outcome measures included strength measurements (one-repetition maximum (1RM)

Table 1. Study characteristics

Author	Study design	Participants	Outcome measures	Intervention	Outcome	Conclusion
Burchi <sup>15</sup>	RCT	N = 109, K-L scale grade > 1 OA. Group 1: IF plus NMES (n = 54, 36 female, 18 male, age: 62.6 ± 10.5, BMI: 29.3 ± 5.4) Group 2: TENS (n = 55, 43 female, 12 male, age: 60.8 ± 11.4, BMI: 31.7 ± 5.8)	(i) WOMAC: pain, stiffness and function subscales (ii) Pain VAS (iii) Quality of life VAS	For both groups 35 min therapy was applied daily for 8 weeks. Group 1: 15 min of IF followed by 20 min of NMES. IF 5000 Hz and premodulated beat frequency sweeping between 1 and 150 Hz. NMES parameters: biphasic square wave, frequency 50 Hz, duty cycle 200 ms every 1500 ms, pulse width 3.39–102.2 µs, intensity 60 mA Group 2: 35 min of TENS, biphasic square wave with a 0.2 Hz frequency, amplitude of 60 mA, pulse width adjusted to give peak output of 73 nC	(i) Significantly greater reductions in WOMAC pain (P=0.002), stiffness (P=0.004) and function (P=0.003) subscales in IF + NMES group (ii) IF + NMES group had a greater, but non-significant decrease in overall pain (P=0.29) (iii) The mean change from baseline to follow-up in the quality of life VAS ratings were similar between the two groups (P=0.99)	An NMES combined with IF intervention demonstrated significantly greater improvements in self-reported measures of pain, stiffness and function following an 8 week intervention compared to a TENS intervention
Durmuş <sup>12</sup>	RCT	N = 50, female, K-L scale grade 1, 2, 3 OA Group 1: NMES (n = 25, age: 54.76 ± 20, BMI: 32.69 ± 0.70) Group 2: BF assisted isometric exercise (n = 25, age: 54.68 ± 1.77, BMI: 32.77 ± 0.89)	(i) Pain: VAS in activity, at night and at rest (ii) WOMAC pain score (iii) WOMAC function, 50-m timed walk, timed stairs climb (iv) Strength: IRM and IORM	For both groups 20 min therapy was applied 5 days/week for 4 weeks Group 1: Asymmetric biphasic wave, frequency 50 Hz, pulse width 200 µs, duty cycle 10 s on–10 s off, intensity 70–120 mA Group 2: Isometric contractions held for 10 s, 50 s relaxation. Patient asked to increase the visual and auditory signals that she perceived at every contraction	(i) Both groups showed significant improvements in VAS and WOMAC pain, physical function and stiffness scores, 50 m walking time and 10 step stair climb, IRM and IORM No SD between the groups in any measure after therapy (P>0.05)	A 4 week NMES intervention is as effective as an exercise intervention in improving pain, function and strength in knee osteoarthritis
Gaines <sup>6</sup>	RCT	N = 38, K-L scale grade 1–4 OA. Group 1: NMES plus education (n = 20, 17 female, 3 male, age: 70.75, BMI: 31.52 ± 5.43) Group 2: education only (n = 18, 13 female, 5 male, age: 70.94, BMI: 31.55 ± 7.25)	(i) NMES pain diary (ii) Pain using PPI Scale, PRIT and McGill Pain Questionnaire (iii) AIMS2	12 week intervention Group 1: Biphasic rectangular wave, frequency 50 Hz, pulse width not reported, ramp up 3 s 10 s on–50 s off, intensity for first 4 weeks at 10–20% MVC, weeks 5–8 20–30% MVC, weeks 9–12 30–40% MVC. 15 min duration. Electrodes (4 in × 5 in) positioned over the vastus medialis oblique and proximal vastus lateralis Group 2: Arthritis self-help course, 12 h community-based education	(i) Significant decrease in knee pain after an NMES session (P<0.001) (ii) No SD between groups in pain on the PPI and the PRIT following the intervention (iii) Non-significant 7% increase in pain for the NMES group and a significant 66% increase in pain for the education-only group on the AIMS2	NMES results in an immediate decrease in knee pain 15 min after treatment However, no long-term improvement in knee pain was observed in either group after a 12 week intervention period

Author	Study design	Participants	Outcome measures	Intervention	Outcome	Conclusion
Gibson <sup>10</sup>	CCT	14 participants, two groups: Group 1: NMES ( $n=7$ , age: 67) Group 2: control ( $n=7$ , age: 75)	QF MVC, force, relaxation rate and fatiguability Markers of muscle protein synthesis QF histology	Group 1: Stimulation on the side of knee OA. Square wave, frequency 30 Hz, pulse width $300 \pm 45 \mu\text{s}$ , duty cycle 2 s on–9 s off. Electrodes ( $9 \text{ cm} \times 5 \text{ cm}$ ) placed over proximal and distal QF. side. Muscle protein synthesis 1 h stimulation per day for 28 days Group 2: No treatment	NMES group: No SD in muscle protein concentration or fibre diameter between stimulated (osteoarthritic) and non-stimulated (healthy) concentration, however there was no evidence of increased QF MVC following the intervention Control group: Higher rate of protein synthesis on the side of knee OA	A 4 week NMES intervention results in an increase in quadriceps protein concentration, however there was no evidence of increased QF MVC following the intervention
Kocaman <sup>14</sup>	RCT	$N=38$ K-L scale grade $>1$ OA, NMES group: ( $n=19$ , 15 female, 4 male, age: $61.6 \pm 10.1$ , BMI: $29.4 \pm 3.9$ ) Exercise group: ( $n=19$ , 14 female, 5 male, age: $60.4 \pm 7.6$ , BMI: $31.2 \pm 6.1$ )	(i) Pain: VAS (ii) Knee range of motion (iii) Thigh and knee circumference (iv) Timed stairs climb (v) CSA of RF (vi) Lequesne and WOMAC	NMES: 23 min 5 times/week for 4 weeks. Stimulation parameters not reported Exercise: Maximal quadriceps contractions: 3 sets of 10 repetitions. 5 times/week for 4 weeks	Significant improvements in pain, thigh circumference, activity time, CSA of RF and Lequesne and WOMAC indices in both groups ( $P<0.05$ ) No SD between the groups Significant improvement in active knee range of motion in both groups, the improvement in the exercise group was more prominent ( $P<0.05$ )	A 4 week NMES intervention is as effective as a 4 week exercise intervention in improving knee osteoarthritis symptoms and improving quality of life, however the exercise intervention results in significantly greater improvements in active knee range of motion than the NMES intervention

(Continued)

Table 1. (Continued)

Author	Study design	Participants	Outcome measures	Intervention	Outcome	Conclusion
Oldham <sup>11</sup>	RCT	N = 30 participants (n = 17 female, n = 13 male) allocated to one of 4 groups	(i) QF torque, QF CSA (ii) Function: timed walk and timed sit-to-stand (iii) Quality of life: Nottingham Health Profile	(i) Uniform frequency stimulation: 8.4Hz (ii) Patterned neuromuscular stimulation (PNMS): Stimulation replicating the discharge of a fatigued QF MU (iii) Random pattern: stimulation pattern generated by randomly shuffling the interspike intervals in the fatigued QF MU discharge train (iv) or sham treatment. Stimulation protocol: Biphasic asymmetrical wave, pulse width 300 $\mu$ s, duty cycle 30s on-15s off. Stimulation of QF for 3h per day/6 weeks	No SD between all 4 groups in MVIT and endurance, Group (i) showed significant improvements in MVIT over group (ii) ( $P=0.05$ ) and (iv) ( $P=0.002$ ) Significant improvements ( $P<0.05$ ) in endurance at 3 weeks in group (ii) and (iv) No SD between the groups in function and quality of life	No stimulation pattern emerged as being significantly better than the other in improving strength, function or quality of life
Palmieri-Smith <sup>17</sup>	RCT	N = 30. Female. K-L scale grade > 2 OA. Intervention group (n = 16, age: 58 $\pm$ 2.7, BMI: 32.7 $\pm$ 4.1). Control group (n = 14, age: 56.8 $\pm$ 2.9, BMI: 32.1 $\pm$ 5.1)	(i) QF strength and activation. (ii) WOMAC pain, function and stiffness (iii) 40-foot walk test	Intervention: NMES 3/week for 4 weeks. Waveform not reported, frequency 50Hz, pulse width not reported, duty cycle ramp up 2s, 10s on-50s off, intensity adjusted to at least 35% of MVC. 10 QF contractions Control group: no treatment; standard of care	(i) No SD in QF strength or activation for intervention group versus the control group (ii) No SD between groups in terms of WOMAC scores (iii) No SD between groups for 40-foot walk	A 4 week NMES intervention did not induce significant gains in QF muscle strength or activation as compared to a standard care control group. No significant improvements were observed either in the measures of pain, stiffness or function

Author	Study design	Participants	Outcome measures	Intervention	Outcome	Conclusion
Rosemffet <sup>13</sup>	RCT	N = 26 participants (n = 20 female, n = 6 male), K-L scale grade > 2 OA, allocated to one of 3 groups. Group A (n = 8, BMI: 32.86) Group B (n = 10, BMI: 29.31) Group C (n = 8, BMI: 31.13)	(i) Pain: VAS (ii) WOMAC (iii) QF torque (iv) 6-metre walk test (m)	8 week intervention Group A: NMES, 3 times/week for 30 min monophasic wave, 0.2 mls amplitude, frequency 25 Hz, pulse width not reported, duty cycle 5 s on–5 s off, voltage 60–80V (n = 8) Group B: exercise programme, 1 h 15 min twice a week (n = 10) Group C: Combined NMES and exercise (n = 8)	(i) VAS pain improved significantly in all 3 groups (P < 0.05) (ii) WOMAC indices improved significantly in all 3 groups (P < 0.05) (iii) QF torque improved significantly in groups B and C (P < 0.05) (iv) Walk test improved significantly in group B only (P < 0.05)	A combined NMES and exercise intervention is more effective than either treatment modality alone in increasing QF muscle strength in knee OA. Significant improvements in pain levels were observed following all 3 interventions. Significant improvements in walking function were only observed following the exercise-only intervention.
Talbot <sup>5</sup>	RCT	N = 34 K-L scale grade > 1 OA Group 1: NMES+ education (n = 18, female n = 15, male n = 3, age: 70.3 ± 5.6, BMI: 29.5 ± 4.1) Group 2: Education only (n = 16, female n = 12, male n = 4, age: 70.8 ± 4.9, BMI: 31.6 ± 5.9)	(i) AIMS2 and Functional Performance Inventory (ii) Maximal Isometric QF force (iii) Physical activity monitoring: accelerometer (iv) Timed 100-foot walk, stair climb, chair rise (s) (v) McGill pain Questionnaire	12 week intervention Group 1: symmetrical biphasic rectangular wave, frequency 50 Hz, pulse width 300 μs, duty cycle 3 s ramp-up 1.5 ramp-down 10 s on–10 s off, intensity adjusted to 10–40% of MVC. 2 (4 × 5 in) electrodes stimulated the QF muscle. 15 min 3/week for 12 weeks Group 2: Participants attended arthritis self-help course	Significant increase in QF strength in NMES group (P < 0.05) SD in chair rise time and timed walk in NMES group (P < 0.05) No SD in the severity of pain reported following intervention in both groups	A 12 week NMES intervention appears to increase QF strength and improve function in adults with knee OA. However no SD was observed in measures of pain between the control and NMES group following the intervention period

(Continued)

Table 1. (Continued)

Author	Study design	Participants	Outcome measures	Intervention	Outcome	Conclusion
Tok <sup>1</sup>	RCT	N=40 K-L scale grade 2 or 3 OA Group 1 (n=20, female n=16, male n=4, age range: 42–80) Group 2 (n=20, female n=14, male n=6, age range: 59–72)	(i) VAS (ii) WOMAC (iii) SF-36 (iv) Knee and thigh circumference (v) Isokinetic dynamometry (vi) Balance	Group 1: Infrared, IF current, US and combined continuous passive movement and NMES; asymmetrical biphasic wave, frequency 50 Hz, pulse width 200 ms, duty cycle 10 s on–10 s off, intensity 70–120 mA. Stimulation for 20 min via 4 surface electrodes to QF and HS muscles Group 2: Infrared, IF current, US and isometric exercise Treatment for 5 days/week for 3 weeks	Group 1: SD in VAS, WOMAC, flexor work and dynamic balance (P<0.05). SD also in static balance (P=0.009) and flexor peak torque (P=0.001) Group 2: SD in VAS, WOMAC, dimensions of SF-36 (P<0.05), dynamic and static balance scores (P<0.001) NO SD between groups following a 3 week intervention	It was demonstrated that NMES and conventional exercise combined with other therapeutic interventions are equally effective in improving measures of pain, function and strength following a 3 week intervention

RCT, Randomized controlled trial; CCT, controlled clinical trial; OA, osteoarthritis; NMES, neuromuscular electrical stimulation; TENS, transcutaneous electrical nerve stimulation; IF, interferential; US, ultrasound; QF, quadriceps femoris; RF, rectus femoris; MU, motor unit; HS, hamstring; WOMAC, Western Ontario MacMaster Osteoarthritis Index; VAS, visual analogue scale; IRM, one-repetition maximum; 10RM, ten-repetition maximum; PPI, Present Pain Intensity; PRIT, Pain Rating Index Total; AIMS2, Arthritis Impact Measurement Scale 2; MVC, maximum voluntary contraction; CSA, cross-sectional area; SF-36, Short Form 36 Health Survey; NR, not reported in text; MYC, maximum voluntary contraction; MVT, maximal voluntary isometric torque; CSA, cross-sectional area; SD, significant difference; BMI, body mass index; K-L scale, Kellgren and Lawrence scale.

and ten-repetition maximum (10RM), maximum voluntary contraction and force of the quadriceps femoris) and functional assessments/physical activity measurements (timed walk, timed stair climb, timed sit-to-stand, balance, accelerometry). Other objective measurements included knee range of motion, knee and thigh circumference, quadriceps femoris cross-sectional area and protein synthesis and histological markers.

### Study quality

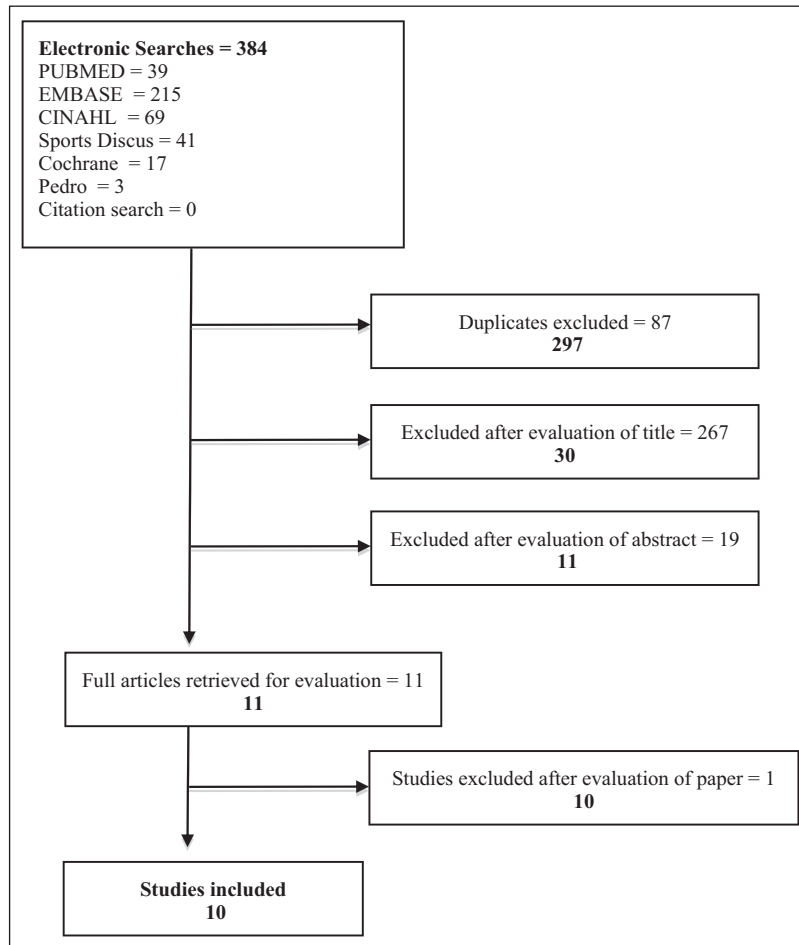
The Thomas Test rated the quality of two studies as strong,<sup>5,15</sup> four studies as moderate<sup>1,11–13</sup> and four studies as weak.<sup>6,10,14,17</sup> The component ratings and global ratings are summarized in Table 2.

### Impact of neuromuscular electrical stimulation on pain

Eight studies investigated the impact of neuromuscular electrical stimulation on pain.<sup>1,5,6,12–15,17</sup> A range of self-report outcome measures were used: visual analogue scale,<sup>1,12–15</sup> WOMAC pain subscale,<sup>1,12–15,17</sup> the Pain Rating Index Total,<sup>6</sup> a pain diary,<sup>6</sup> the pain subscale of the Arthritis Impact Measurement Scale 2,<sup>6</sup> the Present Pain Intensity scale<sup>6</sup> and the McGill Pain Questionnaire.<sup>5,6</sup>

Inconsistent evidence (level D) from eight papers found that neuromuscular electrical stimulation alone, or in combination with other therapeutic interventions, had a significant impact on self-reported pain in osteoarthritis.

Four studies of moderate or strong methodological quality,<sup>1,12,13,15</sup> reported that neuromuscular electrical stimulation alone or combined with other therapeutic interventions, such as infrared, interferential ultrasound and continuous passive movement,<sup>1</sup> interferential therapy<sup>15</sup> and exercise,<sup>13</sup> can significantly improve pain in knee osteoarthritis. One study of weak methodological quality reported that neuromuscular electrical stimulation alone was as effective as conventional exercise in improving knee pain in osteoarthritis.<sup>14</sup> However, three studies (one strong and two weak methodological quality studies) reported no significant difference in the



**Figure 1.** Search results.

severity of pain following a neuromuscular electrical stimulation intervention.<sup>5,16,17</sup>

### *Impact of neuromuscular electrical stimulation on function*

Eight studies investigated the impact of neuromuscular electrical stimulation on patient function.<sup>1,5,11–15,17</sup> A range of self-report and objective outcome measures were used: WOMAC function subscale,<sup>1,12–15,17</sup> timed walk,<sup>5,12,13,17</sup> timed stairs climb,<sup>5,11,12,14</sup> timed sit-to-stand,<sup>5,11</sup> balance measure<sup>1</sup> and the Functional Performance Inventory.<sup>5</sup>

Inconsistent evidence (level D) was found in the eight papers that neuromuscular electrical stimulation significantly improved patient function.

Four investigations demonstrated that neuromuscular electrical stimulation alone, or when combined with other therapeutic interventions (infrared, interferential therapy, ultrasound and continuous passive movement<sup>1</sup>) or exercise<sup>13</sup> is as effective as conventional exercise in improving measures of function in knee osteoarthritis.<sup>1,12–14</sup> Similarly, two investigations found that neuromuscular electrical stimulation is capable of significantly improving levels of function greater than a control

**Table 2.** Thomas Test component ratings

Author	Selection bias	Study design	Confounders	Blinding	Data collection methods	Withdrawals/ drop-outs	Global rating
Burch <sup>15</sup>	Strong	Strong	Strong	Strong	Strong	Strong	Strong
Durmuş <sup>12</sup>	Moderate	Strong	Strong	Weak	Strong	Strong	Moderate
Gaines <sup>6</sup>	Strong	Strong	Weak	Weak	Strong	Moderate	Weak
Gibson <sup>10</sup>	Moderate	Strong	Weak	Moderate	Strong	Weak	Weak
Kocaman <sup>14</sup>	Moderate	Strong	Strong	Weak	Strong	Weak	Weak
Oldham <sup>11</sup>	Moderate	Strong	Weak	Moderate	Strong	Strong	Moderate
Palmieri-Smith <sup>17</sup>	Weak	Strong	Strong	Weak	Strong	Strong	Weak
Rosemffet <sup>13</sup>	Moderate	Strong	Strong	Moderate	Strong	Moderate	Moderate
Talbot <sup>5</sup>	Moderate	Strong	Strong	Moderate	Strong	Strong	Strong
Tok <sup>1</sup>	Strong	Strong	Strong	Strong	Weak	Strong	Moderate

intervention.<sup>5,15</sup> However, two studies reported no significant difference between intervention and control group; in a timed walk and timed sit-to-stand following interventions with different stimulation patterns,<sup>11</sup> or in terms of self-reported function following a four-week neuromuscular electrical stimulation intervention.<sup>17</sup>

### *Impact of neuromuscular electrical stimulation on strength*

Eight studies investigated the impact of neuromuscular electrical stimulation on quadriceps femoris muscle strength.<sup>1,5,10–14,17</sup> Objective measures of strength included one and ten repetition maximum,<sup>12</sup> manual muscle testing<sup>14</sup> and quadriceps femoris torque measurements.<sup>1,5,10,11,13,17</sup> There is inconsistent evidence (level D) from the eight papers that neuromuscular electrical stimulation alone, or in combination with other therapeutic interventions, had a significant positive impact on measures of quadriceps femoris muscle strength in knee osteoarthritis.

Significant improvements in quadriceps femoris strength measures were noted following a neuromuscular electrical stimulation intervention in three studies.<sup>5,12,14</sup> One paper<sup>1</sup> reported that combined continuous passive movement and neuromuscular electrical nerve stimulation is

effective in increasing strength in this population. However, three studies demonstrated no significant improvements in strength following a neuromuscular electrical stimulation intervention.<sup>10,13,17</sup> It has been suggested that there may be a significant placebo effect associated with neuromuscular electrical stimulation, as strength gains were observed in this study following sham stimulation.<sup>11</sup>

### *Meta-analyses results*

Pooled data from six studies examining pain and function outcome measures were included in the meta-analyses.<sup>1,5,12,13,15,17</sup> One study was excluded as original data could not be obtained from the authors.<sup>14</sup> A meta-analysis was undertaken to determine the impact of neuromuscular electrical stimulation on the WOMAC function scores. From a total of 233 patients, the point estimate for differences between the experimental and control groups at follow-up was  $-5.31$  ( $-10.32$  to  $-0.40$ ) in favour of the experimental group (Table 3).

A pooled analysis was also undertaken for the WOMAC pain scores. From a total of 225 patients, the point estimate for differences between the experimental and control groups at follow-up was  $-1.32$  ( $-2.40$  to  $-0.23$ ) in favour of the experimental group (Table 4).

**Table 3.** Meta-analysis of neuromuscular electrical stimulation and WOMAC function scores

Study or Subgroup	Experimental		Control		Total	Weight	Mean Difference	
	Mean	SD	Mean	SD			IV, Random, 95% CI	IV, Random, 95% CI
Burch (15)	19.94	5.8	26.96	6.3	53	38.1%	-7.02	[-9.34, -4.70]
Durmus (12)	8.72	1.68	10.4	1.39	25	41.1%	-1.68	[-2.53, -0.83]
Palmieri-Smith (17)	22.85	9.04	35.5	17.66	18	17.2%	-12.65	[-21.72, -3.58]
Tok (1)	105.47	43.15	98.91	37.04	20	3.6%	6.56	[-18.36, 31.48]
<b>Total (95% CI)</b>		<b>117</b>			<b>116</b>	<b>100.0%</b>	<b>-5.31</b>	<b>[-10.22, -0.40]</b>

Heterogeneity:  $\text{Tau}^2 = 15.07$ ;  $\text{Chi}^2 = 23.42$ ,  $\text{df} = 3$  ( $P < 0.0001$ );  $I^2 = 87\%$   
 Test for overall effect:  $Z = 2.12$  ( $P = 0.03$ )

**Table 4.** Meta-analysis of neuromuscular electrical stimulation and Western Ontario McMaster (WOMAC) osteoarthritis index pain scores

Study or Subgroup	Experimental		Control		Total	Weight	Mean Difference	
	Mean	SD	Mean	SD			IV, Random, 95% CI	IV, Random, 95% CI
Burch (15)	5.62	0.99	7.4	0.47	53	43.7%	-1.78	[-2.08, -1.48]
Durmus (12)	2.44	0.51	3.04	0.48	25	44.0%	-0.60	[-0.87, -0.33]
Palmieri-Smith (17)	7.23	3.03	10.3	4.83	14	10.5%	-3.07	[-6.00, -0.14]
Tok (1)	30.36	13.03	27.61	12.51	20	1.8%	2.75	[-5.17, 10.67]
<b>Total (95% CI)</b>		<b>113</b>			<b>112</b>	<b>100.0%</b>	<b>-1.32</b>	<b>[-2.40, -0.23]</b>

Heterogeneity:  $\text{Tau}^2 = 0.68$ ;  $\text{Chi}^2 = 35.24$ ,  $\text{df} = 3$  ( $P < 0.00001$ );  $I^2 = 91\%$   
 Test for overall effect:  $Z = 2.38$  ( $P = 0.02$ )

**Table 5.** Meta-analysis of neuromuscular electrical stimulation and walking tests

Study or Subgroup	Experimental		Control		Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI
	Mean	SD	Mean	SD			
Durmus (12)	49.92	2.69	48.1	1.1	29.2%	0.87 [0.29, 1.45]	
Palmieri-Smith (17)	1.4	0.13	1.44	0.2	25.0%	-0.23 [-0.95, 0.49]	
Roseff (13)	484	25	458	85.3	18.3%	0.39 [-0.60, 1.38]	
Talbot (5)4.78	29.6	4.78	30.23	4.83	27.5%	-0.13 [-0.77, 0.51]	
<b>Total (95% CI)</b>		<b>69</b>		<b>65</b>	<b>100.0%</b>	<b>0.23 [-0.33, 0.80]</b>	

Heterogeneity: $\tau^2 = 0.20$ ; $\text{Chi}^2 = 7.54$ , $\text{df} = 3$ ( $P = 0.06$ ); $I^2 = 60\%$
Test for overall effect: $Z = 0.81$ ( $P = 0.42$ )

A meta-analysis was also undertaken to determine the impact of neuromuscular electrical stimulation on a walking test. From a total of 134 patients, the point estimate for differences between the experimental and control groups at follow-up was 0.23 (-0.33 to 0.80), indicating no significant difference between the experimental and control groups (Table 5).

### Discussion

Ten studies investigating the impact of neuromuscular stimulation in the treatment of knee osteoarthritis fulfilled the inclusion criteria for the review. The quality of the studies was strong ( $n = 2$ ), moderate ( $n = 4$ ) or weak ( $n = 4$ ). Overall there is inconsistent evidence (level D) that neuromuscular electrical stimulation significantly reduced pain and increased strength and function in patients with knee osteoarthritis. However, the results of the pooled analyses from six studies found that neuromuscular electrical stimulation improved levels of self-reported pain and function, but not objective measures of function in this population. Nonetheless, these results should be interpreted with caution due to the heterogeneity of studies and the low number of studies included as demonstrated by the  $I^2$  statistic.

The results of the present review should be considered with respect for the following limitations. Both randomized controlled trials and a controlled clinical trial were included in this review. While there is less agreement on critical appraisal tools for the evaluation of non-randomized studies, a valid and reliable tool previously used in systematic reviews (Thomas Test) rated the quality of the studies. In addition only studies published in English or translated into English were included, meaning that some studies may have been overlooked. The limited number of studies included in the meta-analyses due to study heterogeneity may also limit findings.

The development of treatment protocols for the management of symptoms (pain, reduced strength and function) in patients with knee osteoarthritis is important. It is estimated that 10% of people older than 55 years have symptoms of osteoarthritis, a quarter of whom are severely disabled.<sup>18</sup> As a

disease, osteoarthritis is now also being identified in adults at younger ages,<sup>19</sup> thus if effective interventions are not developed, joint replacement surgery will be needed at earlier ages to maintain mobility and quality of life.

In the elderly population with knee osteoarthritis reduced quadriceps strength and increased postural sway have been reported, both of which may be related to falls.<sup>20,21</sup> Falls in the older population has been recognized as a significant health issue in today's society.<sup>22</sup> It is estimated that one in every three people over the age of 65 and one in two people over the age of 80 years fall every year<sup>23</sup> with fall-related injuries the leading cause of injury and disability among adults greater than 65 years.<sup>24</sup> Given the expected rise in the age of the population in Europe,<sup>25</sup> developing protocols to maximize strength and proprioception in the lower extremity is important.

A previous systematic review has provided strong evidence demonstrating that conventional exercise has significant benefits in terms of knee pain and physical function in knee osteoarthritis.<sup>26</sup> Neuromuscular electrical stimulation has been suggested as a method for increasing strength of the quadriceps femoris and decreasing pain in knee osteoarthritis, but findings to date have been inconclusive. The findings of the current review concur with the findings reported by Monaghan et al.<sup>4</sup> who found that there was inconclusive evidence regarding the effectiveness of surface neuromuscular electrical stimulation as a means of improving quadriceps femoris strength in knee osteoarthritis patients both before and after total knee replacement. This review was very small with only two studies included, both with a high risk of methodological bias. Hulme et al.<sup>27</sup> also reported inconclusive findings in their review regarding the effects of pulsed electromagnetic stimulation in the treatment of osteoarthritis. Conversely, Marks and colleagues<sup>7</sup> suggested that there was strong evidence to support the application of neuromuscular electrical stimulation to strengthen the quadriceps femoris muscle; however, confidence in these conclusions is weakened by the limitations presented earlier.

The challenge of developing protocols for this patient cohort is that in the published literature

there is no consistency in the neuromuscular electrical stimulation parameters used. In the current review six studies employed neuromuscular electrical stimulation at a frequency of 50 Hz<sup>1,5,6,12,15,17</sup> to produce smooth tetanic muscle contractions,<sup>10,28</sup> a condition which is favourable for strengthening the quadriceps femoris muscle.<sup>29</sup> However, a range of other frequencies were also included (25 Hz,<sup>13</sup> 30 Hz<sup>10</sup> and pulse patterns at a frequency of 8.4 Hz<sup>11</sup>). In addition, parameters of pulse width versus duration and intensity showed great variability between studies: one paper<sup>5</sup> applied stimulation at an intensity which produced quadricep femoris contractions at 10–40% of maximum voluntary contraction, while a second<sup>17</sup> reported using stimulation intensities which produced at least 35% of maximum voluntary contraction. Further research is necessary to clearly establish the optimal neuromuscular electrical stimulation parameters for use in this population. In addition, standardizing interventions is warranted in the development of protocols for use in the clinical setting to maximize the impact of this intervention. In the current review the lack of consistency between studies makes this difficult: six studies<sup>10–14,17</sup> investigated the application of neuromuscular electrical stimulation alone, while a further four studies combined neuromuscular electrical stimulation with other therapeutic interventions.<sup>1,5,6,15</sup>

The conflicting data from the studies identified in the current review does not allow any definitive conclusion to be made with regard to the use of neuromuscular electrical stimulation to reduce pain and to increase quadriceps femoris strength and function in knee osteoarthritis. Nevertheless, the existing evidence is promising, with a greater number of moderate–strong quality randomized controlled trials suggesting the use of neuromuscular electrical stimulation in this population. In particular, neuromuscular electrical stimulation may prove to be a useful therapeutic alternative for individuals with knee osteoarthritis who are unable to carry out conventional exercise due to the presence of coexisting disease. Future studies in this field should be conducted to establish protocols using neuromuscular electrical stimulation to increase patient function, reduce pain and maximize quality of life.

### Clinical messages

- There is inconsistent evidence regarding the impact of neuromuscular electrical stimulation on measures of pain, function and quadriceps femoris muscle strength in knee osteoarthritis.
- Future work is needed in this field to clearly establish the role of neuromuscular electrical stimulation in knee osteoarthritis and to determine the optimal neuromuscular electrical stimulation protocol to use in this population.

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## Appendix I – Online database search strategy for MEDLINE Database

'Electric Stimulation' [MeSH] OR  
 'Neuromuscular Electrical Stimulation' OR  
 'Functional Electrical Stimulation' OR  
 'Electrical Stimulation Therapy' OR  
 'Electric Stimulation Therapy' OR  
 'NMES' OR  
 'FES' OR  
 'EMS'  
 AND  
 'Osteoarthritis' [MeSH] OR  
 'Arthritis' OR  
 'Knee Osteoarthritis'  
 Limits: Humans, English, Randomised controlled trials,  
 Clinical trial