REFLECTION, EVIDENCE AND PROFESSIONAL SKILLS – LEVEL 6

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What is the efficacy of Transcutaneous electrical nerve stimulation (TENS) in patients with osteoarthritis of the knee?

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ABBREVIATIONS

AL TENS	Acupuncture-like TENS
CCT	Controlled Clinical Trial
CINAHL	Cumulative index in nursing and allied health (database)
CMPT	Cutaneous Mechanical Pain Threshold
HF-TENS	High Frequency TENS
IFC	Interferential current
KIN	Kinesiotherapy
KOA	Knee osteoarthritis
LF-TENS	Low Frequency TENS
MEDLINE	Medical literature analysis and retrieval system online (database)
NICE	National institute for health and care excellence
NHP	Nottingham Health Profile
NMES	Neuromuscular electrical stimulation
NIN	Non invasive interactive neurostimulation
OA	Osteoarthritis
PENS	Percutaneous electrical nerve stimulation
PES	Pulsed electrical stimulation
PGA	Patient Global Assessment
PPT	Pressure Pain Threshold
RCT	Randomise control trial
ROM	Range of motion
SF36	Health Status Survey
SWD	Shortwave diathermy
tDCS	Transcranial direct current stimulation
TENS	Transcutaneous Electrical Nerve Stimulation
TKA	Total knee arthroplasty
VAS	Visual analogue scale
WOMAC	Western Ontario and McMaster Universities Arthritis Index
US	Ultrasound
6-MWT	6-Minute Walk Test in meters

ABSTRACT

Background: Osteoarthritis (OA) is a disease that affects synovial joints causing degeneration and destruction of hyaline cartilage. To date, no curative treatment for OA exists. The primary goals for OA therapy are to relieve pain and maintain or improve functional status. Transcutaneous electrical nerve stimulation (TENS) is a non-invasive modality that is commonly used to control both acute and chronic pain arising from several conditions.

Aims: To assess the effectiveness of TENS in the treatment of knee OA. The primary outcomes of interest were effect on pain relief and functional status. The secondary objective was to determine the most effective mode of TENS application for pain control.

Methods: CINAHL, MEDLINE and SPORTDiscus were searched from 1st of December up until 1st February 2017 using a strategy to describe TENS and knee OA pain. Inclusion criteria were primary research papers, participants with knee OA, intervention to include TENS, and pain and function as primary outcome measures. Eligible papers were critically appraised using CASP checklists, given a quality grading and summarised in tables. The papers' results and common themes were identified and discussed.

Results: Six RCTs papers were included in the review with methodological quality ratings ranging from fair to excellent. Five studies compares the effect of TENS against sham and one with before/after design.

Discussion: Even though there was variety in the methodological quality of the studies there was sufficiently common evidence across all of the papers to confirm that TENS resulted in reduction of pain and improved function and quality of life in patients presenting with knee OA. Nevertheless, its effect was overall similar to sham intervention. However, the studies commonly had too small a sample for their results to be generalised and there was a lack of evidence regarding the long-term effects.

Conclusions: Although active TENS is shown not to be as effective as sham TENS treatment, this review provides evidence for the use of TENS in management of knee OA due to the reduction of its symptoms in comparison to baseline. There was no significant difference in effectiveness of different type of TENS against each other. The current systematic review is inconclusive, hampered by the inclusion of only small trials. More well designed studies with a standardized protocol and adequate numbers of participants are needed to conclude the effectiveness of TENS in the treatment of OA of the knee.

Key Words: Knee Osteoarthritis, Transcutaneous Electrical Nerve Stimulation, Knee OA management.

INTRODUCTION

Osteoarthritis (OA) is an age-related chronic arthropathy characterised by disruption and potential loss of joint cartilage along with other joint changes, including bone hypertrophy (osteophyte formation). Symptoms include gradually developing pain aggravated or triggered by activity, stiffness lasting less then 30 minutes on awakening and after inactivity, and occasional joint swelling. OA mainly affects the elderly population. The prevalence of OA in populations older than 60 years of age is more than 50% (Solomon, 1997). Obesity is another common risk factor. This, along with the aging population, is contributing to the increasing number of people with osteoarthritis. The usual complaints in people with knee OA are pain exacerbated by movement or weight bearing, stiffness, swelling and deformity and restricted walking distance. Osteoarthritis is occurring more frequently in women than in men (Hope et al, 1998). Knee OA is expected to be the fourth highest cause of disability in women and is responsible for the deterioration of quality of life and functional capacity (Tok et al, 2009).

The total cost of osteoarthritis to the UK economy is estimated at 1% of annual gross national product. In 2010, 36 million working days were lost because of OA, costing the economy nearly £3.2 billion in lost production. Just over half of all

people consulting about osteoarthritis have knee osteoarthritis. The financial burden in secondary care due to joint replacement is large and increasing. In 2010 there were 116,000 hip and knee joint replacements in the UK, at a cost of £890 million pounds (Arthritis Research UK, 2013)

According to Arthritis Research UK (2013) “4.71 million people in the UK have sought treatment for osteoarthritis of the knee and 4.11 million people in England have knee OA. Although little research has been carried out in the area, conservative (non-joint replacement) management of osteoarthritis may not be satisfactory, with up to 80% of people reporting constant pain and a third of these reporting their pain as unbearable”. There is a pressing need to improve osteoarthritis management and provide standards describing high quality and cost-effective care across the care pathway (NICE, 2015).

There is no cure for osteoarthritis (NHS Choices, 2016). No therapies exist currently that can reverse this process. Non-operative treatment of knee OA has changed very slightly over the past 40 years. Nonsteroidal anti-inflammatory drugs (NSAIDs) and analgesics relieve pain and help knee OA patients function better, but many patients fail or do not tolerate these medications.

The objectives of the management of knee osteoarthritis are to relieve pain and to maintain or improve its function. The treatment options include non-pharmacological intervention, drug therapy, and surgery (File, 1997). Different modalities of manual therapy have been shown to help improve clinical symptoms and function of knee OA, with fewer adverse effects than medical treatment. Transcutaneous electrical nerve stimulation (TENS) is among these non-invasive therapies. The NICE clinical guideline for the treatment OA states: “Healthcare professionals should consider the use of Transcutaneous Electrical Nerve Stimulation (TENS) as an adjunct to core treatments for pain relief” (National Institute for Health and Clinical Excellence (NICE) centre for clinical practice, 2014)

TENS is the application of any electrical current through the skin with the aim of pain modulation and is a frequently used modality in knee osteoarthritis (Osiri et al, 2002). It is based on the 'Gate-Control Theory' of pain perception as

described by Melzack and Wall (Melzack & Wall, 1965). Gate control theory asserts that activation of nerves which do not transmit pain signals, called non-nociceptive fibers, can interfere with signals from pain fibers, thereby inhibiting pain. The theory suggests that the stimulation of large diameter, (A-beta) primary sensory afferent cutaneous fibers, activates inhibitory interneurons in the spinal cord dorsal horn and, thereby, may attenuate the transmission of nociceptive signals from the small diameter A-delta and C fibers. In Transcutaneous Electrical Nerve Stimulation (TENS), non-nociceptive fibers are selectively stimulated with electrodes in order to produce this effect and thereby lessen the pain (Kandel, Schwartz & Jessell, 2000). Other suggested mechanisms include a stimulation of β endorphin production. Several studies have shown that TENS may stimulate endogenous opiates secretion (Andersson et al., 1976) (Grimmer, 1992) (Mayer & Prince, 1989). Meanwhile, in animal studies, Lippiello et al. (1990) measured the physical characteristics of natural electrical fields generated by articular cartilage and designed a device to deliver this pulsed electrical signal to knee cartilage from surface electrodes applied over the knee. In a rabbit model of OA, this device altered repair of injured cartilage to regenerate hyaline cartilage instead of typical scar tissue and fibrocartilage. This positive effect needs to be studied in humans with acute cartilage injury.

Knee OA causes severe disability in millions of people. Those with moderate or severe disease who fail analgesics and/or NSAIDs have limited therapeutic options. Some choose total knee arthroplasty (TKA) or other types of surgery, but many are unwilling or are too young, too old, or too enfeebled by co-morbid disease to consider surgery. TENS offers a safe, non-invasive option for such patients, and may reduce the need for TKA as well.

The most commonly used TENS types described in Table 1.

Table 1. TENS commonly used in clinical practice.

TENS type	Parameters	Affect	Note
TENS HF (high frequencies)	40 to 150 Hz, 50 to 100 µsec pulse width, moderate intensity	To stimulate sensory nerve fibers.	The most common Conventional transcutaneous electrical nerve stimulation
TENS LF(low frequencies)	1 to 4 Hz, 100 to 400 µsec pulse width, high intensity	To stimulate both motor and sensory fibers. The stimulation may be painful, and the intensity of the current will depend on the patient's individual pain tolerance	Also known as Acupuncture-like TENS (AL TENS)
TENS Burst (Burst frequency)	1 to 4Hz with high internal frequency, 100 to 250 µsec pulse width, high intensity	to stimulate motor and sensory fibers. It uses short bursts of high frequency current which are repetitively applied at low intensity and a burst frequency of around 5 Hz,	Burst TENS was developed to minimise patients' discomfort, as experienced with AL TENS
Hyperstimulation TENS	100 Hz and 150 to 250 µsec pulse width. Intensity vary	To stimulate not only motor and sensory, but also nociceptor fibers.	Intensity adjusted to the level of the maximal, tolerated by the patient
PES - Pulsed electrostimulation	100 Hz and a pulse width of 640 to 1800 µsec. Intensity vary	To stimulate both motor and sensory fibers. Portable device, allowing application times of several hours rather than 15 to 60 minutes, as is the case for convenient TENS.	Device, typically using knee garments with flexible, embedded electrodes and a small battery-operated generator. (Appendix G, image 1)
IFC - interferential current stimulation	one current 4000 Hz the other from 4000 to 4100 Hz. Result is 80 and 230 Hz in area of intercrossing	To stimulate both motor and sensory fibers .The high frequency of the carrier currents in inferential current stimulation leads to a considerably lower impedance of skin and subcutaneous tissue as compared with conventional TENS and minimises patients' discomfort.	Stationary device typically consists two sets of electrodes with four electrical poles;

NIN – noninvasive Interactive Neurostimulation	Frequencies and intensities are varying, depends on skin resistant	To stimulate motor, sensory, and nociceptor fibers. Device adjusts the impulses it sends in response, thereby providing the optimal stimulus throughout the treatment session.	Device identifies key low impedance points related to the condition and requiring treatment. This diagnostic feedback regarding skin impedance informs the therapist which areas to treat and when treatment of a location is complete.

Despite the use of TENS for pain relief by some health professionals, there is an uncertainty about the efficacy of this method to manage symptoms of the knee osteoarthritis. A recent systematic review showed that TENS was not effective for the knee osteoarthritis pain (Rutjes et al, 2009). This is in direct contrast to an earlier systematic review conducted by Osiri et al. (2000) that concluded that TENS was effective for the knee OA pain and a meta-analysis that demonstrated a significant reduction in the knee OA pain with TENS (Bjordal et al, 2007). Several limitations in the included trials may explain the lack of TENS effect; these include small sample size, poor methodological quality, and inadequate randomization and blinding.

According to Fawkes et al. (2010), 3.4% of patients present to osteopathic clinic with knee pain. Osteopaths could benefit from being aware of the alternative methods of pain management in patients with knee OA. Reduced pain level may allow patients to utilise the affected joint and maintain an active lifestyle. This improvement in ability to perform physical effort is very important because physical exercise is also considered a valuable tool to reduce the risk of cardiovascular and endocrine diseases and to improve bone and muscle conditioning. These medical conditions may affect patients with OA due to the high level of inactivity and body disuse found in these patients. National Academy of Osteopathy (Toronto) recommends osteopaths to implement TENS to their practice (Hosseni, 2011).

The primary aim of this literature review is to evaluate the effectiveness of TENS in the management of osteoarthritis of the knee by assessing its effect on pain, joint function and quality of life in patients. The secondary objective was to determine the most effective mode of TENS application for symptoms control.

METHODS

Criteria for considering studies for this review

Types of studies: Randomized controlled trials (RCTs) and Controlled clinical trials (CCTs) that were eligible according to an a priori protocol.

Types of interventions: All types of TENS were included in this review (Table 1). Trials that compared TENS intervention with standard treatment and/or placebo were included.

Types of outcome measures: Pain, Stiffness, Physical function and Quality of life.

Study selection process

An electronic search was conducted between December 2016– February 2017. Published clinical trials of TENS for knee OA were identified through a search of the three databases MEDLINE, CINAHL and SPORTDiscus. Only primary research papers (RCTs and CCTs) were included in the review (Table 3) using search terms listed in tables 2a, 2b and 2c and using TENS and knee OA as main concepts. The example of MEDLINE Boolean search history can be found in Appendix A. After database searches were completed, duplicates were removed and titles were screened for inclusion/exclusion titles criteria (table 3a) and abstracts using inclusion/exclusion criteria for abstracts (Table 3b). Then remaining full text articles were retrieved from Staffordshire University's online journal library and finally assessed using inclusion/exclusion full text criteria (Table 3c) to determine the eligibility for inclusion into review. The study identification process is summarised in Figure 1 (page 12). Six papers fulfilled the inclusion and exclusion criteria and were finally identified eligible for review (Vance et al (2012), Fary et al (2011), Atamaz et al (2012), Mascarin et al (2012), Selfe, Bourguignon & Taylor (2008) and Garland et al. (2007)).The abstracts of selected papers can be found in Appendix F.

Table 2a MEDLINE Boolean Search

MEDLINE Concept 1 and Concept 2. 147 papers identified

	AND	
OR	Concept 1. TENS	Concept 2. Knee OA
	Transcutaneous electrical nerve stimulation (7808)	Osteoarthritis knee pain (9209)
	MH “TENS” MeSH (9811)	Knee osteoarthritis (26455)
	Pulsed electrical stimulation (1067)	Osteoarthritis knee (26642)
	MH “PES” (3218)	
	Neurostimulation (1732)	
	Electrotherapy (73799)	
	“TENS” Keyword (17710)	
	“PES” Keyword (7520)	
	MH = MeSH search for MEDLINE	

Table 2b CINAHL Boolean Search

CINAHL Concept 1 and Concept 2. 218 papers identified

	AND	
OR	Concept 1. TENS	Concept 2. Knee OA
	Transcutaneous electrical nerve stimulation (8019)	Osteoarthritis knee pain (12854)
	MH “TENS” (9989)	Knee osteoarthritis (28704)
	Pulsed electrical stimulation (1166)	Osteoarthritis knee (29006)
	MH “PES” (3675)	
	Neurostimulation (1836)	
	Electrotherapy (78790)	
	“TENS” Keyword (217122)	
	“PES” Keyword (8036)	
	MH = MeSH search for CINAHL	

Table 2c SPORTDiscus Boolean Search

SPORTSDiscus concept 1 and concept 2. 12 papers identified

	AND	
OR	Concept 1. TENS	Concept 2. Knee OA
	Transcutaneous electrical nerve stimulation (2022)	Osteoarthritis knee pain (3891)
	TENS (1477)	Knee osteoarthritis (7917)
	Pulsed electrical stimulation (243)	Osteoarthritis knee (9102)
	PES (1756)	
	Neurostimulation (619)	
	Electrotherapy (12034)	

Table 3 – Inclusion / Exclusion criteria for studies

	CRITERIA	**JUSTIFICATION**
INCLUSION	Randomised Controlled Trials (RCT)	Golden standard of research. Near the top of the hierarchy of evidence pyramid. Well designed RCT's likely to provide reliable result.
	Controlled Clinical Trials (CCT)	These studies compare intervention group. Feature high on evidence pyramid, but not as reliable as RCTs
	RCT which include pain and function as outcome measures	To reflect the aim of this literature review
	Studies to include Knee OA as primary cause of pain	Reflect the aim of the review. There are large number of researches on knee pain not caused by Knee OA.
	TENS as primary intervention	Reflect the aim of this review.
	Studies that included Pulsed Electro Stimulation (PES) as primary intervention	Pulsed Electro Stimulation (PES) is on of the type of TENS. Reflect the aim of this review.
	TENS administered as a solo intervention	Reflect the aim of this review. (except to standard form of treatments such as paracetamol, exercise and education)
EXCLUSION	Not primary research	Articles, protocols, editorials, case reports or guideline are not reliable source of data and could be subjective and caring low evidence value.
	Other Systematic Review	Although Systematic Review are top in hierarchy of evidence value, this literature review is limited to reviewing primary researches. The last review on similar subject was published on the base of RCTs conducted before 2007. With modern devices and altered protocols the outcomes could be different.

	Studies included other form of electrotherapy such as electroacupuncture or other forms of PENs, MES or tDCS used in combination with TENS	Not reflect the aim of the review
	RCT using TENS as adjunctive to other form of non-standard treatments such as laser or magnetic therapy	Not reflect the aim of the review
	RCTS older than 10 years	Up to date researches. There are modifications in equipment. There is similar review on RCTs dated before 2007.
	Not written in English or Russian	Inability to understand. There are potentially valuable researches written in Turkish.
	Studies that include TENS treatment to knee pain due to trauma or postoperative pain	There are numerous conditions causing knee pain. Not reflecting the aim of the review
	TENS is used in conjunction with Opioid treatment.	The aim of the review is to assess the effectiveness of TENS as solo treatment, though NSAIDs are acceptable as the standard treatment to knee OA.

Table 3a - Inclusion and exclusion criteria for title.

	CRITERIA	**JUSTIFICATION/** /No of papers rejected
INCLUSION	Electrotherapy as intervention	TENS is form of electrotherapy
	Neurostimulation as intervention	TENS is neurostimulation
	Pulsed electro stimulation as intervention	One of the type of TENS
	TENS or PES as abbreviation	reflect the aim of the review
	Knee osteoarthritis as source of pain	reflect the aim of the review
	Symptoms of knee OA as object of study	Pain is one of the symptom of Knee OA
	Management of knee OA	Implicate the pain management and function improvement
EXCLUSION	OA of different joints (elbow, wrist)	Not reflect the aim of the review (89)
	Knee pain due to trauma or postoperative pain, pregnancy or in conjunction with opioid treatment.	Not reflect the aim of the review (27)
	Review, protocols, editorials or guidelines.	Low in earache of research than RCT (39)
	Not included TENS as intervention	Not reflect the aim of the review (19)
	Animal studies	It is unclear whether animal studies will have similar effect in people
	Transcranial direct current stimulation (tDCS) as intervention	Not relevant to the topic(4)
	PENS or other form of Electroacupuncture as intervention	Not reflecting the aim of review (6)

	TENS as adjunctive to other non-standard treatment (such as laser or other form of electrotherapy)	Not reflecting the aim of review

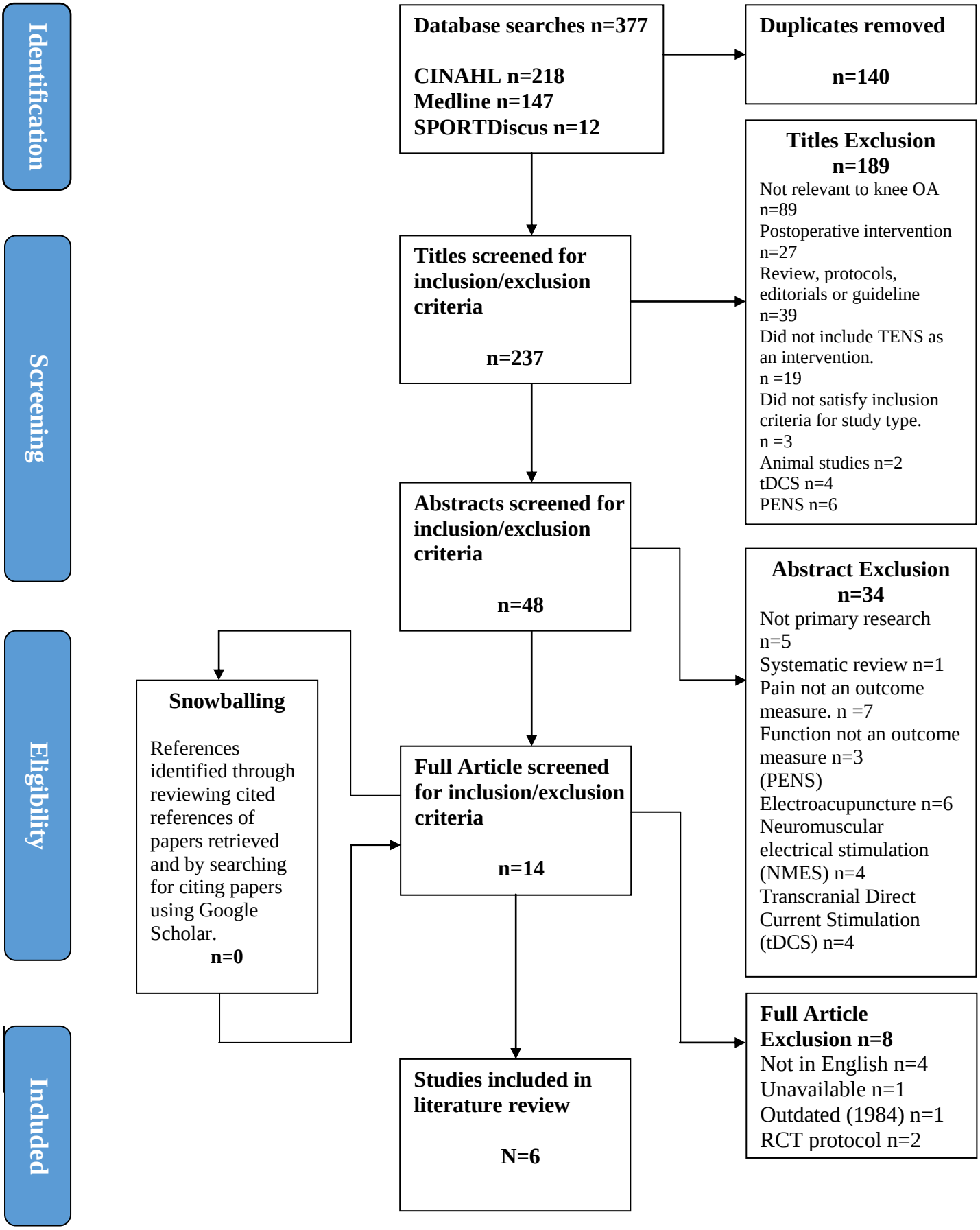
Table 3b - Inclusion and exclusion criteria for abstract.

	CRITERIA	JUSTIFICATION/ /No of papers rejected
INCLUSION	RCT	Golden standard of research
	RCTS with Control group or sham treatment.	Increase the reliability of RCT and clarity of the review
	RCT with before and after study design	Still has good reliability. Demonstrate the effectiveness of intervention.
	Pain, Function and Quality of life as outcome measures	This outcome mesures are included in NICE guidline for clinical studies. (NICE, 2010)
EXCLUSION	Not primary research	Articles, protocols, editorials or guideline are not reliable source of data and could be subjective.(5)
	Other systematic Review	The last review on similar subject was published on the base of RCTs conducted before 2007. With modern devices and altered protocols the outcomes could be different.(1)
	Pain and Function are not an outcome measure	They are primary outcome measures in assessment of management. Not reflecting the aim of the review (6)
	RCT using TENS as adjunctive to other form of treatments.	Not reflecting the aim of the review (2)
	Studies included other form of electrotherapy such as Electroacupuncture or other forms of PENs, ultrasound or NMES	Not reflecting the aim of the review (10)
	TENS not non-adjunctive treatment (except to standard form of treatments such as NSAIDs, exercise and education)	TENS is used in combination with other treatments such as Laser or Opioids . Not reflecting the aim of the review (2)

Table 3c - Inclusion and exclusion criteria for full text.

	CRITERIA	JUSTIFICATION/ /No of papers rejected
INCLUSION	Availability of published full text	Full text is not available (withdrawn) (1)
	Written in English or Russian	Ability to understand the language. There are potentially valuable researches written in Turkish and Chinese (4)
EXCLUSION	The equipment or protocol is no longer in use	Up to date researches. There are modifications in equipment. There is similar review on RCTs dated before 2007.(1)
	RCT protocol	Not primary research (1)

Fig 1: Flow diagram for Inclusion – Exclusion process



Critical Appraisal Methodology

All six papers were read and critically appraised using checklist from the Critical Appraisal Skills Programme (CASP). An example of CASP checklist can be found in Appendix B. Once checklists were completed, the Quality Rating was assessed using guidance by Greenhalgh (2007), the example can be found in Appendix C. Finally the Quality Grading Grid (Thompson, 2015) was used to determine the quality rating for each paper. The Quality Grading Grid can be found in Appendix D.

RESULTS

The aim of this literature review is to evaluate the effectiveness of TENS on pain, function and quality of life in people with knee OA. Papers represent in total 483 participants with 203 controls, while study duration ranging from single intervention to six months long trials. A variety of devices are used in the studies to deliver TENS treatments such as convenient TENS (Atamaz et al (2012), Mascarin et al (2012) and Vance et al (2012)) and its divergences: PES (Fary et al (2011), Garland et al. (2007)) and NIN (Selfe, Bourguignon & Taylor (2008)). Five studies included sham TENS control, while one study compared the effect of intervention using “before and after” study design. Three papers compare TENS variants against each other and/or with other physical therapies (KIN and US). The papers ranged from Excellent to Good in Quality rating. None of the selected papers have being included in previously conducted systematic reviews.

Table 4: Research Paper Reviewed

No		Study Type
1	ATAMAZ, F. C. et al. (2012) Comparison of the efficacy of Transcutaneous electrical nerve stimulation, Interferential currents, and Shortwave diathermy in knee osteoarthritis: A double-blind, Randomized, controlled, Multicenter study. *Archives of Physical Medicine and Rehabilitation*. 93 (5). pp. 748–756.	Randomised Control Study
2	FARY, R. E. et al. (2011) The effectiveness of pulsed electrical stimulation in the management of osteoarthritis of the knee: Results of a double-blind, randomized, placebo-controlled, repeated-measures trial. *Arthritis & Rheumatism*. 63 (5). pp. 1333–1342.	Randomised Control Study
3	GARLAND, D. et al. (2007) A 3-month, randomized, double-blind, placebo-controlled study to evaluate the safety and efficacy of a highly optimized, capacitively coupled, pulsed electrical stimulator in patients with osteoarthritis of the knee. *Osteoarthritis and Cartilage*. 15 (6). pp. 630–637.	Randomised Control Study
4	MASCARIN, N. et al. (2012) Effects of kinesiotherapy, ultrasound and electrotherapy in management of bilateral knee osteoarthritis: Prospective clinical trial. *BMC Musculoskeletal Disorders*. 13 (1). p. 182.	Prospective Clinical Trial
5	SELFE, T. K., BOURGUIGNON, C. & TAYLOR, A. G. (2008) Effects of Non-invasive interactive Neurostimulation on symptoms of osteoarthritis of the knee: A Randomized, sham-controlled study. *The Journal of Alternative and Complementary Medicine*. 14 (9). pp. 1075–1081.	Randomised Control Study
6	VANCE, C. G. T. et al. (2012) Effects of Transcutaneous electrical nerve stimulation on pain, pain sensitivity, and function in people with knee osteoarthritis: A Randomized controlled trial. *Physical Therapy*. 92 (7). pp. 898–910.	Randomised Control Study

Production of Summary Tables and Identification of Themes

All six papers are summarised individually (Tables 7,8,9,10,11,12) and the final quality rating result is presented in Table 5, and detailed within the individual summary table. One papers was “Excellent” in quality and five were “Good”, however there was the variation in study design, number of participants, gender ratio and trials duration.

Table 5: Summary of Paper Quality Rating

Paper number	1	2	3	4	5	6
Author / year	Atamaz et al (2012)	Fary et al (2011)	Garland et al. (2007)	Mascarin et al (2012)	Selfe, Bourguignon & Taylor (2008)	Vance et al (2012)
No. of participants	203	70	58	40	37	75
No. of controls	104	36	19		19	25
Controlled Study	V	V	V		V	V
Before / After cohort				V		
Participants Blinded	V	V	V		V	V
Examiners Blinded	V	V	V			V
Control/Sham	V	V	V		V	V
Peer reviewed	V	V	V	V	NS	V
Paper quality rating	Good	Excellent	Good	Good	Good	Good

NS = Not specified
V = Tick

Themes

Four themes were identified: 1. Effect of TENS on pain, 2. Effect of TENS on function, 3. Effect TENS on quality of life and 4.Comparison of different type of TENS against each other and to other physical therapies.

Table 6.. Themes identified

Themes / No.	Pain	Function	Life quality	Comparison
1. Atamaz et al (2012)	v	v	v	v
2. Fary et al (2011)	v	v	v	
3. Garland et al. (2007)	v	v	v	
4. Mascarin et al (2012)	v	v		v
5. Selfe, Bourguignon & Taylor (2008)	v	v	v	
6. Vance et al (2012)	v	v		v

V = Tick

Table 7. Summary table for "Comparison of the efficacy of Transcutaneous electrical nerve stimulation, Interferential currents, and Shortwave diathermy in knee osteoarthritis: A double-blind, Randomized, controlled, Multicenter study". ATAMAZ et al, 2012. (Serial Number 1)

Aim	Participants and Recruitment process	Outcome Measures	Method Intervention Device	Result Analysis	Conclusion	Limitations And Quality Rating
To compare the effectiveness of transcutaneous electrical nerve stimulation (TENS), interferential currents (IFCs), and shortwave diathermy (SWD) against each other and sham intervention with exercise training and education	N=203 Age 50-80 Female n=167 Male n=36 6 treatment groups: TENS n=37 Sham TENS n=37 IFCs n=31 Sham IFCs n=35 SWD n=31 Sham SWD n=32 Recruited at 3 centers	Pain 1. VAS pain (100mm) 2.Paracetamol intake (in grams) Function 1. WOMAC stiffness and function 2. ROM 3. Time to walk a distance of 15m Life quality 1. NHP (Nottingham Health Profile) Comparison 1. Pain 1.1 VAS 1.2 Paracetamol 2. Function 3. Life quality	A double-blind, randomized, controlled trial. Duration of treatment is 20min All interventions were applied 5 times a week for 3 weeks Assessments made at baseline and at months 1, 3 and 6. Each treatment group was compared with its sham group by using paired t test. Device: TENS (Bio-stim SD-980,Endomed CV-405 and Sonopuls 492b)	Pain 1. VAS-improved in all active groups ($p<0.05$), compare to baseline (no differences b/n groups) 2. All active group used a lower amount of paracetamol at 6 months ($p<0.05$) in comparison with sham groups. Function 1. WOMAC (stiffness and function) – improved in all groups ($p<0.05$), compare to baseline (no differences b/n groups)) 2. ROM – no effect 3. 15m timed walk – improved in all groups ($p<0.05$), compare to sham groups Life quality 1. NHP - – improved in all groups ($p<0.05$), without significant difference between groups. Comparison 1. Pain 1.1 VAS- no difference 1.2 IFC was more efficient in paracetamol intake then TENS and SWD ($p=0.03$). 2. Function - no difference b/n devices 3.Life quality - no difference b/n devices	Although all groups showed significant improvements, we can suggest that the use of physical therapy agents in knee OA provided additional benefits in improving pain because paracetamol intake was significantly higher in the patients who were treated with 3 sham interventions in addition to exercise and education.	No info how patients were recruited ("..at our centres..") No details about sham TENS devices (only mention "TENS sham stimulation") Intervention was in combination with exercise, its unclear if the result would be the same when TENS applied alone Quality Rating: Good

SWD Shortwave diathermy a form of electromagnetic therapy produces an oscillating electromagnetic field, which results in movement of ions, distortion of molecules, and creation of eddy currents; subsequently, heat is produced in the deep tissue.

Table 8. Summary table for "The effectiveness of pulsed electrical stimulation in the management of osteoarthritis of the knee: Results of a double-blind, randomized, placebo-controlled, repeated-measures trial." FARY et al, 2011. (Serial Number 2).

Aim	Participants and Recruitment process	Outcome Measures	Method Intervention Device	Result Analysis	Conclusion	Limitations And Quality Rating
To determine the effectiveness of subsensory, pulsed electrical stimulation (PES) in the symptomatic management of osteoarthritis (OA) of the knee.	N=70 mean age 70 53% men 2 Groups: Active PES n=34 Placebo PES n=36 Recruitment: Through media and telephone	Pain 1. VAS 100mm 2. WOMAC (pain) Function 1.WOMAC (function) 2.WOMAC (stiffness) Quality of Life 1. SF-36 2. PGA (Patient Global Assessment on 100-mm VAS)	Randomized, double-blind, placebo-controlled, repeated-measures trial. Participants were wearing the device for 7 hours a day Measurement were taking at baseline and then at 4, 16 and 26 weeks Devise is commercially available TENS (Metron Digi-10s) was modified by a biomedical engineer to deliver PES current	Pain 1. VAS-Significant improvement in both groups, but no difference between groups. 2. WOMAC-no effect Function 1&2. WOMAC Improvement in both groups, on both scores, but no difference between groups Quality of Life SF-36 and PGA: Improvement in both groups on both scores, but no difference between groups. Note: 56% of the PES-treated group achieved a clinically relevant 20-mm improvement in VAS pain score at 26 weeks compared with 44% of controls (p=0.04) Analysis: linear mixed model (appropriate)	Subjects with mild-to-moderate symptoms and moderate-to-severe radio-graphic OA of the knee, 26 weeks of PES was no more effective than placebo. (Both had good results)	Placebo device turned off after 3min (still intervention) Sample size could be bigger. Males >than females may not represent OA population. Unusually high, compare with other studies placebo effect well explained in discussion Quality Rating: Excellent with minor flaws

SF-36 Short-Form Health Survey (Quality of life health survey)
PES Pulsed Electrical Stimulation

Table 9. Summary table for "A 3-month, randomized, double-blind, placebo-controlled study to evaluate the safety and efficacy of a highly optimized, capacitively coupled, pulsed electrical stimulator in patients with osteoarthritis of the knee." GARLAND et al, 2007. (Serial Number 3)

Aim	Participants and Recruitment process	Outcome Measures	Method Intervention Device	Result Analysis	Conclusion	Limitations And Quality Rating
To investigate the efficacy and safety of a capacitively coupled pulsed electrical stimulation (PES) device in treating knee osteoarthritis (OA).	N=58 Age 64-70 Male 20 Female 38 Groups: Active n=39 Control n=19 Patients from two orthopedic surgery and one rheumatology practices	Pain 1. VAS (100mm) 2. WOMAC (pain) Function 1. WOMAC function 2. WOMAC stiffness Life Quality 1. PGA (Patient Global Asessment)	Controlled randomized, double-blind trial. Treatment duration 6 – 14 hours a day (using portable devise at home) Measurement at the baseline and at the end of 12-th weeks Commercially available TENS Model BIO-1000™ (BioniCare Medical Technologies, Inc.,)	Pain 1. VAS – improve in active for 31.2% (p=0.038) compare to control 2. WOMAC (pain)- no effect (p=0.110) Function 1. WOMAC (function) – improvement in active for 29.46% (p=0.013) 2. WOMAC (stiffness) – improvement in active for 25.06% (p=0.03) Life Quality 1. PGA – improvement in active for 50.56% (p=0.031) compare to control Analysis: Student's t test was used to compare percent changes in outcome measures between the baseline and final visits. Distribution of Kellgren–Lawrence scores between groups was compared	A highly optimized, capacitively coupled, pulsed electrical stimulus device significantly improved symptoms and function in knee OA without causing any serious side effects.	Sample size could be bigger Only 2 measurement were taken No limitation outlined in the text Quality Rating: Good

PES Pulsed Electrical Stimulation

Table 10. Summary table for "Effects of kinesiotherapy, ultrasound and electrotherapy in management of bilateral knee osteoarthritis: Prospective clinical trial." MASCARIN et al, 2012. (Serial Number 4)

Aim	Participants and Recruitment process	Outcome Measures	Method Intervention Device	Result Analysis	Conclusion	Limitations And Quality Rating
The purpose was to investigate the effects of kinesiotherapy (KIN) and electrotherapy on functional exercise capacity, ROM, severity of knee pain perceived health and physical function	N=40 Age 48-77 Only female with bilateral knee OA Groups: TENS n=12 KIN n=16 US n=10 Recruited from Rheumatology Clinic	Pain 1. VAS 100 mm Function 1. WOMAC (function) 2. ROM 3. 6-MWT Comparison 1. Pain (VAS) 2. Function 2.1 WOMAC 2.2 ROM 2.3 6-MWT	Before and after Clinical trial Treatment duration 20min Twice per week for 12 weeks Measurements were performed before and after the intervention Device: conventional TENS (Neurodyn II, Ibramed, Brazil)	Pain 1. VAS- improvement in all groups, compare to baseline ($p<0.05$) Function 1. WOMAC - improvement in all groups, compare to baseline ($p<0.05$) 2. ROM – increase in TENS and KIN ($p<0.05$) no effect in US group 3. 6-MWT – increased in all groups ($p<0.05$) compare to baseline Comparison 1. Pain (VAS) – no difference between active groups 2. Function 2.1 WOMAC – TENS and KIN done better then US ($p<0.05$) 2.2 ROM increased extension in KIN and TENS ($p<0.05$), but not in US group 2.3 6-MWT- KIN and US done better then TENS Analysis: Kolmogorov-Smirnov tests. Two-way repeated-measure analyses of variance (ANOVA) were used to assess group (KIN *vs.* TENS *vs.* US) and time (before vs. after) differences in the variables measured.	All treatments were effective for reducing pain and improving the WOMAC index. KIN and US groups had significantly higher 6-MWT distances compared with their respective pre-intervention values.	Female only does not represent OA population but good for comparative study, making sample more homogeneous. No control, but this is comparative studies. Only on pre- and post-test No follow up Sample size could be bigger Quality Rating: Good

US Ultrasound
6-MWT Six-minute walk test in meters

Table 11. Summary table for “Effects of Noninvasive interactive Neurostimulation on symptoms of osteoarthritis of the knee: A Randomized, sham-controlled study. “ SELFE et al, 2008. (Serial Number 5)

Aim	Participants and Recruitment process	Outcome Measures	Method Intervention Device	Result Analysis	Conclusion	Limitations And Quality Rating
To explore the effects of noninvasive interactive neurostimulation (NIN) on pain and other symptoms in adults with osteoarthritis of the knee.	N=37 Age 50-91 Female n=25(68%) Male n=12 (32%) Groups: Active n=18 Sham n=19 Recruitment: media in public places. Incl. criteria- older then 50 years	Pain 1. NRS 11 points (once a week) 2. WOMAC (pain) Function 1. WOMAC (function and stiffness) Quality of Life 1. SF-36 2. PGA (Patient global assessment)	Randomized, sham-controlled trial. 20-30min long treatment in clinic X3/52 weeks 1-3 X2/52 weeks 4-6 X1/52 weeks7-8 Measurement taking at baseline and weeks 4, 8, and 12. The hand-held, 9V battery-powered NIN device (InterX5000, Neuro Resource Group, Plano, TX)	Pain 1. NRS- Pain improved compare to baseline (p=0.002) in both groups, but no differences between groups (p>0.05). Note: clinically important reduction in pain was maintained at week 12 by the active NIN but not the sham group. 2. WOMAC-pain improved (p=0.001) in both groups, but no differences between groups p>0.05 Function 1. WOMAC function and stiffness both improved (p=0.001)) in both groups, but no differences between groups p>0.05 Quality of Life 1. SF-36- improved (p=0.017) in both groups, but no differences between groups (p>0.05) 2. PGA – improved (p=0.053) in both groups, but no differences between groups (p>0.05) Analysis: Separate repeated measures analysis of variance (ANOVA) model	Clinically important reductions in knee pain were maintained at week 12 in the active, but not the sham, NIN group. Active NIN group improvement on the patient global assessment from baseline to week 8 compared to the sham NIN group. Overall NIN therapy was not shown to be statistically superior to sham therapy in reducing knee pain	Older then 50 years Examiners were not blinded Sample size could be bigger Placebo effect could be high due to clinic specific environment. Quality Rating: Good

NRS Eleven-point numeric rating scale with the anchors 0 “no pain” and 10 “worst pain possible
WOMAC Western Ontario and McMaster Universities Osteoarthritis Index
SF-36 Short-Form Health Survey

Table 12. Summary table for "Effects of Transcutaneous electrical nerve stimulation on pain, pain sensitivity, and function in people with knee osteoarthritis: A Randomized controlled trial." VANCE et al, 2012. (Serial Number 6).

Aim	Participants and Recruitment process	Outcome Measures	Method Intervention Device	Result Analysis	Conclusion	Limitations and Quality Rating
1. To determine the efficacy of LF-TENS and HF-TENS for knee OA pain 2. To determine which outcome measures (pain at rest, movement-evoked pain, pain sensitivity and function) are most likely to be affected by LF-TENS and HF-TENS in people with pain.	N=75 (29 men 46 women) 31-94 years of age High TENS n=25 Low TENS n=25 Placebo TENS n=25 Recruitment: Tertiary care centre	Pain 1. VAS (100mm) 3. PPT 2. CMPT 4. HPT 5. HTS Function 1.TUG (for function) Comparison 1. Pain 2. Function 3. Life Quality	Randomised Control Trial. Treatment duration is 20min. All Measurements were taking before and after single treatment (in clinic) Device is commercially available TENS unit (Rehabilicare Maxima, DJO Inc.)	Pain 1.VAS- decreased in all groups (p=0.001, p=0.01,p=0.001) 3. PPT-pain decreased in both HF and LF group, but not in placebo group (p=0.002, p=0.0001, p=0.26) 2. CMPT- no effect (p>0.05) 4. HPT-no effect (p>0.05) 5. HTS-no effect (p>0.05) Function 1.TUG- decreased in all groups (p=0.001, p=0.03, p=0.001) Comparison 1. Pain- no difference 2. Function- no difference 3. Life Quality- no difference between HF and LF TENS	Both HF-TENS and LF-TENS increased PPT in people with knee OA; placebo TENS had no significant effect on PPT. Pain at rest and during the TUG was significantly reduced by HF-TENS, LF-TENS, and placebo TENS Cutaneous pain measures (CMPT, HPT, HTS.)were unaffected by TENS. Subjective pain ratings at rest and during movement were similarly reduced by active TENS and placebo TENS, suggesting a strong placebo component of the effect of TENS.	This study tested only a single TENS treatment. Short term effect only with No follow up. Sample size could be bigger Used placebo (sham) TENS produces current. All subjects were recruited at the same centre. More female than male ratio (good-represent OA population) A linear mixed-model analysis for repeated measures was used. (appropriate) Quality Rating: Good

LF-TENS Low Frequency TENS
HF-TENS High Frequency TENS
CMPT Cutaneous Mechanical Pain Threshold
PPT Pressure Pain Threshold
HPT Heat Pain Threshold
HTS Heat Temporal Stimulation
TUG "Timed Up and Go" Test (The TUG is a standardized test in which people arise from a chair with no arm rest, ambulate approximately 3 m (9.8 ft) as quickly as possible, turn, ambulate back, turn, and return to sitting in the chair.[34] Participants were timed in a standardized fashion from the moment the upper back left the chair until return to the full sitting position with the back in contact with the chair.)

DISCUSSION

Theme 1: TENS effect on pain

The latest previously conducted systematic Cochrane review “Transcutaneous electrostimulation for osteoarthritis of the knee” (Rutjes et al. (2009)) studied the effect of TENS against sham or non-specific intervention on pain in individuals with knee OA. This systematic review found little evidence of a significant effect for electrostimulation compared to sham or no intervention on pain in knee OA. The authors attributed these results to the poor quality of the trials and the high degree of heterogeneity across the studies. Rutjes et al (2009) completed their data search and the study selection process on 05.08.2008. All six papers included to this latest research were conducted or published since this date; hence they have not been included in Rutjes et al. (2009) systematic Cochrane review (Figure 1 on page 12).

The predominantly used tool across all six selected trials for pain assessment was VAS, while Vance et al. (2012) utilised the other highly technological means such as PPT, CMPT, HPT and HTS (Table13).

Table 13. Outcome measures used in studies for effect TENS on pain.

Outcome measure	Paper No.	Description and Comment
VAS (100mm)	1,2,3, 4,6	The pain VAS is a continuous scale comprised of a horizontal (HVAS) or vertical (VVAS) line 10 centimeters (100 mm) in length, anchored by 2 verbal descriptors, one for each symptom (“no pain” and “worst imaginable pain”) The participants are asked to use the scale to indicate their current level of pain. Higher values suggest more intense pain. The values (in centimeters or millimeters) are recorded for the statistical analysis.
Pain Numerical Scale (NRS)	5	NRS is segmented numeric version of VAS in horizontal line where responded selects a whole number (0-10) that best reflects the intensity of their pain. (Physio-pedia, 2016)

Pressure Pain Threshold (PPT)	6	Pressure Pain Threshold (PPT) is defined as the minimal amount of pressure that produces pain. A simple handheld pressure algometer (PA) with a spring is commonly used . (Kinser & Sand, 2009)
Cutaneous mechanical pain threshold (CMPT)	6	Cutaneous mechanical pain threshold (CMPT). The CMPT is assessed with a set of 20 von Frey filaments (North Coast Medical, Gilroy, California) applied to the test sites in ascending order (0.008–300 g). The tip of the filament is applied perpendicular to the site and pressed until bending occurred.
Heat Pain Threshold (HPT)	6	Heat Pain Threshold (HPT) is typically assessed by use of a TSA II NeuroSensory Analyzer (Medoc Ltd, Ramat Yishai, Israel) with a 5-cm^2 probe. The probe is placed at the middle of the 3 marks at each site. The temperature to be initially set at 37°C and increased 1°C/s to a maximum of 52°C. Participants indicated when they first felt pain (1/10) by pushing a button that terminated the stimulus.
Heat Temporal Summation (HTS)	6	Heat Temporal Summation (HTS) is measured with a TSA II NeuroSensory Analyzer. A tonic heat stimulus of 45.5°C is applied for 20 seconds. After the first 5 seconds of the heat stimulus application, participant rates pain every 5 seconds for 15 seconds. A difference between the pain rating (first rating) at 5 seconds and the pain rating at 15 seconds is used for analysis. Thermal measures have good test-retest reliability (ICC=.77) in people with knee OA
WOMAC (pain)	2,5	Specific questions about perceived pain in WOMAC questioner. (Appendix E)
Paracetamol intake in grams	1	Participant's reported reduction in Paracetamol intake is interpreted as pain relieving effect of intervention

The results of all selected papers demonstrate that active TENS was found to be no more effective then placebo for pain reduction in four (Atamaz et al (2012), Fary et al (2011), Selfe, Bourguignon & Taylor (2008) and Vance et al (2012); studies number: 1,2,5 & 6) studies out of five, which used sham/placebo TENS, whereas only one study (Garland et al. (2007)) reported significantly improvement against sham/control (Table 14). All six papers concluded that TENS associated with pain reduction compared to

baseline (but no more then in sham/control group), possibly suggesting big placebo effect of TENS. This is regardless of the device used and duration of experiment.

Table 14. Summary of Studies measuring effect of TENS on pain, including the numbers of participants in selected outcomed cathegories.

Pain Reduction	Active Ttt more effective then Sham	Active Ttt no more effective then Sham	Pain Improvement over baseline	Before and After study design
Paper No	3	1,2,5,6	1,2,3,4,5,6	4
Total active TENS participants (n=)	39	201	n/a	12
Total sham TENS Participants (n=)	19	184	n/a	n/a
Total study TENS Participants (n=)	58	385	455	12

Ttt = Treatment

Garland et al. (2007) (paper number 3) reported more pain reduction in active versa sham group. The device (portable PES) was similar in all parameters to equipment used by Fary et al. (2011) in his research. Both studies used VAS as outcome measure for pain and have similar study design (both double-blinded randomized and placebo control). They have adequately similar number of participants in active groups: 34 in Fary et al. (2011) and 39 in Garland et al. (2007). However Fary et al. (2011) reported contradictable similar pain reduction in both active and sham TENS groups.

The difference between studies was in the duration of the experiment: 26 weeks in Fary et al. (2011) and 12 weeks in Garland et al. (2007). The other variations were number of participants in sham TENS group (36 participants in Fary et al. (2011) versa 19 in Garland et al. (2007)) and the total number of participants (70 in study by Fary et al. (2011) against 58 by Garland et al. (2007)). In addition, the measurements were taken in study by Fary et al. (2011) on weeks 4, 16 and 26, in contrast to Garland et al. (2007)

where it was only at baseline and at the end of week 12. Therefore in direct comparison of those two RCTs, Fary et al. (2011) would score better in Quality Rating due to higher number of participants, total amount of measurements and longer study duration. This reflects in quality rating: Excellent for Fary et al. (2011) and Good for Garland et al. (2007)(Table 5, page14).

Fary et al, (2011) explains: “It may be that PES is more effective in some subgroups of people with OA. It is well recognized that OA is a heterogeneous disease and that causes of pain and pain mechanisms in OA are multifactorial. TENS may be a more appropriate treatment modality in those patients in whom local pain mediators, which rely on membrane ion channels that may be affected by externally applied electrical stimulation, are the main cause of pain. In contrast, those in whom biomechanical changes or psychosocial factors are the main contributors to pain production may be less responsive”.

In four trials some minor advantage of active TENS over sham TENS groups were reported. Vance et al. (2012) revealed increased PPT at affected knee, Fary et al. (2011) described VAS pain reduction at week 26, Selfe, Bourguignon & Taylor (2008) mentioned elevated pain toleration on week 12 and Atamaz et al. (2012) stated the paracetamol reduced intake in active group (Table 15).

Table 15. TENS effect on pain. Summary result across papers

Paper	TENS Active (n=)	TENS Sham (n=)	Duration weeks	Result on pain	Note	Device
Vance et al (2012)	50	25	Single Ttt	Similar reduction pain by active TENS and placebo TENS	Increased PPT at knee	TENS
Fary et al (2011)	34	36	26	Similar reduction pain by active TENS and placebo TENS	VAS pain reduction at 26 weeks	PES
Selfe, Bourguignon & Taylor (2008)	18	19	12	Similar reduction pain by active TENS and placebo TENS	Reduction in pain on week 12	NIN

Atamaz et al (2012)	99	104	26	Similar reduction pain by active TENS and placebo TENS	Paracetamol intake lower in active TENS	TENS IFC
Mascarin et al (2012)	12	N/A	12	Pain reduction, compare to baseline		TENS
Garland et al. (2007)	39	19	12	Reduction on pain in active TENS over placebo TENS		PES
Total	252	203				

Ttt - Treatment

(n=) - Number of Participants

The possible explanation of significant resemblance in pain reduction ability of both active and placebo treatments is that the sham device used for control still generates the electrical current though they are not exactly a placebo as they might have a therapeutic value. In study by Vance et al. (2012) sham TENS device produced 10% lower intensity for 15 sec then active equipment. In this experiment, 57% of participants correctly identified sham treatment ($p>0.05$). Fary et al. (2011) study's active device used for 3 min served as control (53% correct identification ($p=0.9$)). Garland et al. (2007) applied less time (about 5 min) treatment duration of active device to simulate placebo intervention (no data on correct sham identification). Selfe, Bourguignon & Taylor (2008) also employed less time usage of active equipment to produce sham intervention with 54% correct identification. Atamaz et al. (2012) utilised the same usage time, but reduced intensity (no data on correct sham identification). The percentage of patient's recognition of sham treatment is significant among studies.

Therefore, such sham devices with probably some therapeutic effect might contribute to high placebo group result. This was argued by Fary et al. (2011) stating "the possibility should be considered that the 3 minutes of placebo treatment could be therapeutic. However, since the placebo device used by Zizic et al (1995) and Garland et al (2007) also delivered 3 minutes of treatment and did not show a therapeutic effect, this is unlikely to be the case".

Due to the difficulty producing sham treatment without possible therapeutic effect, more extensive study is needed based on waiting list or before/after design. In summary, all

selected studies showed improvement over the baseline regardless of devices and protocol used. It may be concluded that the use of TENS could be beneficial for reduction pain in knee OA. However, the studies had too small a sample for their results to be generalised and there was a lack of evidence regarding the long-term effects.

Theme 2: TENS effect on function

Table 16. Outcome measures used in studies for effect TENS on function

Outcome measure	Paper number	Description and Comment
WOMAC (function and stiffness) Western Ontario and McMaster Universities Arthritis Index	1,2,3,4,5	A disease-specific index of disability, the WOMAC Osteoarthritis Index, was used as a subjective measure of perceived health and physical function. The WOMAC Osteoarthritis Index is a three-part questionnaire that can be completed by the subject in approximately 10 minutes, consists of 24 questions and probes clinically important symptoms in the areas of pain (5 questions), stiffness (2 questions), and physical function (17 questions) for patients with OA of the hip and/or knee. Patients make their responses on a five-point scale (0 = none, 1 = mild, 2 = moderate, 3 = severe, 4 = extreme). The higher the score achieved, the lower the level of perceived health and physical function. The WOMAC is a reliable, valid, responsive instrument that has been recommended by the Outcome Measures in Rheumatology Trials (OMERACT) guidelines as an outcome measure for clinical trials of OA of the hip or knee. (Appendix E)
ROM (Range of Motion)	1,4	Knee flexion and extension ROM in degrees are to be measured bilaterally in a supine position. To this end, the lateral femoral condyle is used as a landmark for the measurement of knee flexion and extension. The central pivot of a goniometer is placed over the midpoint of the lateral joint margin, with the stationary arm of the goniometer aligned with the great trochanter. The moving arm of the goniometer is then aligned with the lateral malleolus with the neutral position taken as zero. For the knee flexion measurement, initially the hip is at zero degrees of extension, abduction, and adduction, but as the patients maximally flexes the knee, the hip also flexes. Thus, the examiner supportes the lower limb and stabilizes the femur to prevent rotation, abduction, and adduction of the hip. For the knee extension, the measurement to be made with the lower limb extended. The previous precautions to prevent compensations (i.e., adduction, abduction, and rotation) needed to be taken. (Physio-pedia, 2016)

TUG (Timed Up and Go test)	6	The TUG is a standardized test in which people arise from a chair with no arm rest, ambulate approximately 3 m (9.8 ft) as quickly as possible, turn, ambulate back, turn, and return to sitting in the chair. Participants are timed in a standardized fashion from the moment the upper back left the chair until return to the full sitting position with the back in contact with the chair. The TUG has good reliability in elderly populations and has good construct validity and significant correlations with gait speed , the Berg Balance Scale, and step length (Hughes, Osman & Woods, 1998) (Steffen & Mollinger, 2002)
6-MWT (The six-minute walking test)	4	The 6-MWT to be performed to evaluate functional exercise capacity in a 100 m-long indoor hallway free of obstacles. The length of the corridor is marked every 1 m. The participants are instructed to walk at a self-selected regular pace to cover as much distance as they could during the allotted time. If necessary, slowing down and stopping to rest is allowed. The distance covered (in meters) is used for the statistical analysis. The test-retest reliability of the 6-MWT has been ascertained in patients with knee OA (Kennedy et al, 2005)
Time to walk distance of 15m	1	Time to walk distance of 15m is measured with stopwatch

Five out of six studies used WOMAC to assess the function. In addition to WOMAC Atamaz et al. (2012) used ROM and timed 15m walk, Mascarin et al. (2012) - ROM and 6min timed walk, Vance et al. (2012) used TUG test to assess the function (Table 17)

Table 17. Summative result of the effect TENS on function

Paper	No. ptns	Test					Result	Device	Duration weeks	Note
		TUG	ROM	WOMAC	6-MWT	15m Timed				
Vance et al (2012)	75	v					Similar improvement of function by active TENS and placebo TENS	TENS	Single Ttt	
Fary et al (2011)	70			v			Similar improvement of function by active TENS and placebo TENS	PES	26	
Selfe, Bourguignon & Taylor (2008)	37			v			Similar improvement of function by active TENS and placebo TENS	NIN	12	
Atamaz et al (2012)	203		v	v		v	Improvement of function by active TENS over placebo TENS on WOMAC and 15mTW, but not ROM	TENS IFC SWD	26	TENS had no effect on ROM
Mascarin et al (2012)	40		v	v	v		Improvement of function by TENS, compared to baseline	TENS KIN US	12	KIN and US higher 6-MWT
Garland et al. (2007)	58			v			Improvement of function in active TENS over placebo TENS	PES	12	

All six studies report improved function compared to baseline in all used tests regardless of device and treatment duration. One study by Garland et al. (2007) reports significant improvement in active group but not in sham group in term of function. However, similar in most parameters Fary et al. (2011) study reports improvement in both active and sham with no significant difference between groups. However, it is possible to hypothesise, that active TENS is more effective then sham as a short term (up to 12 weeks) solution. This finding correlates with Fary et al. (2011) where active PES demonstrates greater improvement than control from baseline on week 16, compared to week 4 and week 26, but no *p* calculation provided in his study for this particular measurement. However, the quality rating of Fary et al. (2011) is higher then Garland et al. (2007). This could lead to the conclusion, that data provided is not sufficient enough to confirm or disregard the statement that active PES devices are

more effective then sham in the short term (12 weeks) with regard to improvement of function.

Overall active TENS is no more effective than sham TENS on function, probably due to difficulty in providing sham device with no possible therapeutic effect (this was discussed in previous section). However all studies demonstrate self-reported function improvement over baseline, which may lead to conclusion, that use of TENS could be beneficial for reduction pain in knee OA. However, the studies had too small population for their results to be generalised and there was a lack of evidence regarding the long-term effects.

Theme 3: TENS Effect on Life Quality

Table 18. Summary of Outcome measures used in studies for effect TENS on quality of life

Outcome measure	Paper number	Description and Comment
Health Status Survey (SF36)	2,5	Health Status Survey (SF36) is a generic health survey compares the relative burden of disease and differentiates the health benefits produced by a wide range of treatments. 8 scale profiles about functional health and well-being psychometrically based with physical and mental health summaries. It takes 5-10 min to complete. Contains 36 questions in 8 health domains in either Physical health or Mental health. Available at: http://seepdf.net/doc/pdf/download/orthodoc__aaos__org--DrAlShaikh--SF36.pdf
Patient Global Assessment (PGA)	2,5,3	Patient Global Assessment is measured using an 11-point numeric rating scale (0 being “as well as possible” and 10 being “as bad as possible”) for this instruction: “Considering all the ways your knee arthritis affects you, circle the number that best describes how well you have been doing over the last month.” This is a recommended way to assess this outcome. (Gentelle-Bonnassies et al, 2000)

Nottingham Health Profile (NHP)	1	Nottingham Health Profile (NHP) is a general patient reported outcome measure which seeks to measure subjective health status. It is a questionnaire designed to measure a patient's view of their own health status, in a number of areas. It can be completed in 5 minutes. The NHP consists of two parts. The first part focuses on health and comprises 38 items which deal with pain, energy, sleep, mobility, emotional reaction and social isolation. The 2-nd part focuses on life areas affected and consists of 7 items which deal with problems regarding occupation, housework, social life, family life, sexual function, hobbies and holidays. All questions have only yes/no answer options and each section score is weighted. The higher the score, the greater the number and severity of problems. The highest score in any section is 100 Available at: http://reseauconceptuel.umontreal.ca/rid%3D1J1WXGYDK-CPP19Z-1ZQY/

Four studies assessed the effect of TENS on quality of life (2,3,4 & 6) using predominantly PGA and SF-36, one study by Atamaz et al. (2012) used NHP. All four studies report improvement in Life Quality compared to baseline, regardless of treatment duration Three studies (1,2 & 3) used TENS and PES devices while using outcome measures SF-36, PGA and NHP. The improvement in perceived life quality was similar between active and sham treatment groups ($p<0.05$) in three out of four papers. However Selfe, Bourguignon & Taylor (2008) using NIN report similar finding in regard to improvement while using SF-36, but different outcome in PGA. Personal Global Assessment test result in active TENS group was reported higher than in sham group. The summary of findings can be found in Table 19.

Table 19. Summative result of effect of TENS on assessments of quality of life

Paper	No. Ptns.	Test			Result	Device	Duration weeks	Note
		NHP	PGA	SF-36				
Fary et al (2011)	70		v	v	Similar improvement of life quality by active TENS and placebo TENS	PES	26	

Selfe, Bourguignon & Taylor (2008)	37		v	v	Similar improvement of life quality by active TENS and placebo TENS on SF-36	NIN	12	Improvement of life quality by active TENS not sham TENS on PGA from baseline to 8-th weeks
Atamaz et al (2012)	203	v			Similar improvement of life quality by active TENS and placebo TENS	TENS IFC SWD	26	
Garland et al. (2007)	58		v		Similar improvement of life quality by active TENS and placebo TENS	PES	12	

Three studies conducted by Fary et al. (2011), Garland et al. (2007) and Selfe, Bourguignon & Taylor (2008) used PGA as the outcome measure of their research. Fary et al. (2011) and Garland et al. (2007) found similar improvements of life quality by active TENS and placebo TENS, while Selfe, Bourguignon & Taylor (2008) reported better improvement of life quality by active TENS not sham TENS on PGA from the baseline to the end of 8-th week. In regards to the weight of evidence, studies conducted by Fary et al. (2011) and Garland et al. (2007) scored hire than Selfe, Bourguignon & Taylor (2008). Fary et al. (2011) and Garland et al. (2007) studies (in summary) consisted 128 participants, while Selfe, Bourguignon & Taylor (2008) had 37 participants. In addition, Fary et al. (2011) study was significantly longer (26 weeks) than Selfe, Bourguignon & Taylor (2008) (12 weeks). However, Fary et al. (2011) and Garland et al. (2007) used PES device to produce TENS, while Selfe, Bourguignon & Taylor (2008) utilised NIN in his research.

Therefore, there is a possibility that NIN device scores better in life quality improvement in short term (8 weeks). Although, taking into account Selfe, Bourguignon & Taylor (2008) small study population (37 participants) and employment of SF-36 which found no difference between active and sham groups, the statement about superiority on NIN over other types of TENS might not be founded.

In summary, life quality improvement induced by active TENS was found to be no better than sham TENS devices. However, all four papers demonstrated self-reported contribution to patient's life quality compared to baseline. Therefore the use of TENS might be beneficial therapy in management of knee OA in regard to improvement of Quality of Life. However, the studies population is inadequate for their results to be generalised and there was inconclusive evidence regarding the long-term effects.

Theme 4: Comparison of different types of TENS against each other and evaluation of efficacy of TENS compared to other physical interventions.

The final theme of this review is to investigate how different TENS devices might influence the effect of electrotherapy on pain, function and life quality. This section might also demonstrate the efficacy of TENS as electrotherapy in comparison to other form of physical therapies. There are three studies that compare different types of TENS between each other and with other forms of interventions. The summary of the results can be found in Table 20.

Table 20. Comparison of TENS to other form of physical therapy. Summary result across papers.

Paper	No. ptns (n=)	Type	No. ptns (n=)	Pain	Function	Life Quality	Notes/ Result
Vance et al (2012),	75	LF-TENS	25	No difference between groups	No difference between groups	N/A	No difference b/n LF and HF
		HF-TENS	25				
Atamaz et al (2012)	203	TENS	74	No difference between TENS and SWD on VAS, but IFC scores better in paracetamol intake reduction	No difference between groups	No difference between groups	IFCs group used a lower amount of paracetamol at 6 months (P<.05) in comparison with the IFCs sham group.
		IFC	66				
		SWD	63				
Mascarin et al (2012)	40	TENS	12	No difference between groups	Before/After design TENS KIN and US are the similar on ROM, WOMAC but KIN and US scores better on 6-MWT	N/A	KIN and US groups had significantly longer 6-MWT distances compared with baseline
		KIN	16				
		US	10				

No. ptns (n=) - Number of patients

According to studies Vance et al. (2012) and Atamaz et al. (2012) no significant difference was found regarding types of TENS used. They both displayed similar effect on symptoms of OA. The study of Atamaz et al. (2012) indicated that IFC group scored better then TENS and SWD in reduction of paracetamol intake; however the scores on VAS were similar between groups. The author interpreted the result as possible advanced analgesic ability of IFC compared to TENS and SWD. However, the other studies conducted by Johnson & Tabasam (2003) and Johnson & Tabasam (1999) had found that analgesic effect of IFC is no more superior to TENS.

The study of Mascarin et al. (2012) compares TENS with other forms of physical therapy such as US and KIN. They established no diversity in pain reduction efficacy, between interventions. However there was indication that their ability to improve function differ. The Function was assessed by using ROM, WOMAC and 6-MWT tools. The result was similar between groups when assessed by ROM and WOMAC tests. Nonetheless 6-MWT revealed that KIN and US groups demonstrated better result compared to TENS group. The test-retest reliability of the 6-MWT has been ascertained in patients with knee OA (Kennedy et al, 2005). However it has being noted that 6MWT test evaluates the global and integrated responses of all the systems involved during exercise, including the pulmonary, cardiovascular and muscular systems.

Previously conducted study (Enright & Sherrill, 1998) established a reference equation that incorporates subject characteristics such as age, body mass and height. These subject characteristics were shown to be associated with the distance walked during the 6-MWT. When applying this reference equation to the current data, the results revealed that the KIN, US and TENS groups walked 74%, 79% and 85%, respectively, of the predicted values found by the Enright & Sherrill (1998) equation in the pre-evaluation. Mascarin et al. (2012) suggested: “These modest values demonstrate the low functional exercise capacity, and consequently low health status, of the patients evaluated in the present study. The difference in this study is that our sample is homogeneous because we recruited only women with bilateral knee OA.” This is valuable note due to its relevancy to most motion tests.

In summary neither type of TENS demonstrated significant advantage in contrast one over the other. The comparison TENS to KIN or US reveals no considerable differentiation in efficacy of the therapies to affect pain, function or life quality.

LIMITATION

This review is based on six papers from three searched databases. There is the possibility of different outcome if more databases were searched with more papers reviewed. The current systematic review is inconclusive, hampered by the inclusion of only small trials. The other limiting factor is relative heterogeneity of the studies and its population. Greater specification in term of devices and population would add value and reliability to the review.

CONCLUSION

All reviewed studies demonstrated high placebo group result. This might be for the reason that sham TENS devices produce electrostimulation. This research revealed difficulty in providing conclusive control due to technical complexity in the creation of a sham TENS device with no possible therapeutic effect.

Although active TENS is shown not to be as effective as sham TENS treatment, this review provides evidence for the use of TENS in management of knee OA due to the reduction of its symptoms in comparison to baseline. There was no significant difference in effectiveness of different type of TENS against each other. The current systematic review is inconclusive, hampered by the inclusion of only small trials. More well designed studies with a standardized protocol and adequate numbers of participants are needed to conclude the effectiveness of TENS in the treatment of OA of the knee.

BIBLIOGRAPHY

ATAMAZ, F. C. et al. (2012) Comparison of the efficacy of Transcutaneous electrical nerve stimulation, Interferential currents, and Shortwave diathermy in knee osteoarthritis: A double-blind, Randomized, controlled, Multicenter study. *Archives of Physical Medicine and Rehabilitation*. 93 (5). pp. 748–756.

FARY, R. E. et al. (2011) The effectiveness of pulsed electrical stimulation in the management of osteoarthritis of the knee: Results of a double-blind, randomized, placebo-controlled, repeated-measures trial. *Arthritis & Rheumatism*. 63 (5). pp. 1333–1342.

GARLAND, D. et al. (2007) A 3-month, randomized, double-blind, placebo-controlled study to evaluate the safety and efficacy of a highly optimized, capacitively coupled, pulsed electrical stimulator in patients with osteoarthritis of the knee. *Osteoarthritis and Cartilage*. 15 (6). pp. 630–637.

MASCARIN, N. et al. (2012) Effects of kinesiotherapy, ultrasound and electrotherapy in management of bilateral knee osteoarthritis: Prospective clinical trial. *BMC Musculoskeletal Disorders*. 13 (1). p. 182.

SELFE, T. K., BOURGUIGNON, C. & TAYLOR, A. G. (2008) Effects of Noninvasive interactive Neurostimulation on symptoms of osteoarthritis of the knee: A Randomized, sham-controlled pilot study. *The Journal of Alternative and Complementary Medicine*. 14 (9). pp. 1075–1081.

VANCE, C. G. T. et al. (2012) Effects of Transcutaneous electrical nerve stimulation on pain, pain sensitivity, and function in people with knee osteoarthritis: A Randomized controlled trial. *Physical Therapy*. 92 (7). pp. 898–910.

References:

ANDERSSON, S. A. et al. (1976) Evaluation of the pain Suppressive effect of different frequencies of peripheral electrical stimulation in chronic pain conditions. *Acta Orthopaedica Scandinavica.* 47 (2). pp. 149–157.

ARTHRITIS RESEARCH UK (2013). Osteoarthritis in General Practice. [Online]. Available from: https://www.arthritisresearchuk.org/~/media/Files/.../Arthritis%20key%20facts.ashx [Accessed 01 Feb 2017]

BJORDAL, J. M. et al. (2007) Short-term efficacy of physical interventions in osteoarthritic knee pain. A systematic review and meta-analysis of randomised placebo-controlled trials. *BMC Musculoskeletal Disorders*. 8 (1). p. 51. [Online] Available from: http://bmcmusculoskeletdisord.biomedcentral.com/articles/10.1186/1471-2474-8-51 [Accessed: 01.Feb2017]

CRITICAL APPRAISALS SKILLS PROGRAMME. 'CASP Randomised Control Trial Checklist'. www.casp-uk.net. Accessed 1 Feb 2017.

CRITICAL APPRAISALS SKILLS PROGRAMME. 'CASP Case Control Checklist'. www.caspuk.net. Accessed 1 Feb 2017.

CRITICAL APPRAISALS SKILLS PROGRAMME. 'CASP Qualitative Checklist'. www.casp-uk.net. Accessed 1 Feb 2017.

ENRIGHT, P. L. & SHERRILL, D. L. (1998) Reference equations for the Six-Minute walk in healthy adults. *American Journal of Respiratory and Critical Care Medicine*. 158 (5). pp. 1384–1387.

CHOICES, N. (2016) Osteoarthritis. [Online] Available from: http://www.nhs.uk/Conditions/Osteoarthritis/Pages/treatment.aspx. [Accessed: 2 Feb 2017].

FAWKES, C., LEACH, J., MATHIAS, S., MOORE, A. (2010). 'Standardised data collection within osteopathic practice in the UK: development and first use of a tool to profile osteopathic care in 2009'. NCOR. University of Brighton, England. [Online]. Available from: http://www.ncor.org.uk/wp-content/uploads/2013/05/standardised_data_collection_finalreport_24062010.pdf [Accessed: 09 Jan 2017]

FILE, R.S. (1997) Osteoarthritis: A. Epidemiology, pathology, and pathogenesis. In: KLIPPER, J. editor(s). *Primer on the rheumatic diseases. 11th Edition*. Atlanta: Arthritis Foundation, pp. 216-8.

GARLAND, D. et al. (2007) A 3-month, randomized, double-blind, placebo-controlled study to evaluate the safety and efficacy of a highly optimized, capacitively coupled, pulsed electrical stimulator in patients with osteoarthritis of the knee. *Osteoarthritis and Cartilage*. 15 (6). pp. 630–637.

GENTELLE-BONNASSIES, S. et al. (2000) Comparison of the responsiveness of symptomatic outcome measures in knee osteoarthritis. *Arthritis & Rheumatism*. 13 (5). pp. 280–285.[Online]. Available from: http://onlinelibrary.wiley.com/resolve/openurl?genre=article&sid=nlm:pubmed&issn=0893-7524&date=2000&volume=13&issue=5&spage=280 [Accessed: 09 Jan 2017]

GREENHALGH, T. (2007). 'How to Read a Paper: the basics of evidence based medicine'. BMJ Book, Blackwell Publishing, London, England.

GRIMMER, K. (1992) A controlled double blind study comparing the effects of strong burst mode TENS and high rate TENS on painful osteoarthritic knees. *Australian Journal of Physiotherapy*. 38 (1). pp. 49–56.

HOPE, R.A., LONGMORE, J.M., MCMANUS, S.K. & WOOD-ALLUM, C.A. (1998). 'Oxford Handbook of Clinical Medicine'. Forth edition. Oxford University Press, Oxford, UK.

HOSSENI, S.A.G. (2011). How manual osteopaths can benefit by adding physiotherapy modalities to their services [Online]. *National Academy Of Osteopathy*
Available from:
http://www.nationalacademyofosteopathy.com/documents/research_papers/how_osteopathy_can_benefit_by_adding_physiotherapy_modalities_to_their_services.pdf

HUGHES, C., OSMAN, C., WOODS, A.K. (1998). Relationship among performance on stair ambulation, Functional Reach, and Timed Up and Go tests in older adults. *Issues on Ageing*. 21. pp. 18–22

JOHNSON, M. I. & TABASAM, G. (2003). An investigation into analgesic effects of interferential currents and transcutaneous electrical nerve stimulation on experimentally induced ischemic pain in otherwise pain-free volunteers. *Physical Therapies Journal* (83) pp. 208-23.

JOHNSON, M. I. & TABASAM, G. (1999) A double blind placebo controlled investigation into the analgesic effects of inferential currents (IFC) and transcutaneous electrical nerve stimulation (TENS) on cold-induced pain in healthy subjects. *Physiotherapy Theory and Practice*. 15 (4). pp. 217–233.

KANDEL, E.R., SCHWARTZ, J.H. & JESSELL, T.M. (2000). *Principles of Neural Science (4th edition.).* New York: McGraw-Hill. pp. 482–486.

KENNEDY, D. M. et al. (2005). Assessing stability and change of four performance measures: a longitudinal study evaluating outcome following total hip and knee arthroplasty*. BMC Musculoskeletal Disorders.* 6 (1). p. 3.

LIPPIELLO, L., CHAKKALAKAL, D. & CONNOLLY, J. F. (1990) Pulsing direct current-induced repair of articular cartilage in rabbit osteochondral defects*. Journal of Orthopaedic Research*. 8 (2). pp. 266–275.

MAYER, D.J. & PRINCE, D.D. (1989). The neurobiology of pain. In: Snyder-Mackper L, Robinson A editor(s). *Clinical Electrophysiology, Electrotherapy and Electrophysiologic Testing. 1st Edition*. Baltimore, MD: Williams & WIlkins, pp. 141-201.

MELZACK, R. & WALL, P. D. (1965) Pain mechanisms: A new theory. *Science.* 150 (3699). pp. 971–978.

NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE centre for clinical practice [Online]. Available from: https://www.nice.org.uk/guidance/cg177/documents/osteoarthritis-update-final-scope2. [Accessed: 1 Feb 2017].

NEURO RESOURCE GROUP. Advanced InterX Technology: A Breakthrough in Neuro Stimulation. [Online]. Available from: www.nrg-unlimited.com/interx_technology_overview.php. [Accessed: 27 Dec 2016]

NHS CHOICES (2016) Osteoarthritis [online] Available from: htIn-text citations: (NHS Choices,2016) http://www.nhs.uk/Conditions/Osteoarthritis/Pages/treatment.aspx. [Accessed: 11 January 2017].

NICE (2014) Osteoarthritis: Care and management [online] Available from: https://www.nice.org.uk/guidance/cg177/chapter/1-Recommendations#diagnosis-2. [Accessed: 2 February 2017].

OSIRI, M., WELCH, V., BROSSEAU, L. et al (2000). Transcutaneous electrical nerve stimulation for knee osteoarthritis. *Cochrane Database Systematic Review*.(4):CD002823 [Online]. Available from: http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD002823/full [Accessed 23 Jan 2017]

RUTJES, A.W., NUSCH, E., STERCHI, R., et al. (2009). Transcutaneous electrostimulation for osteoarthritis of the knee. *Cochrane Database Systematic Review* (4):CD002823 [Online]. Available from: http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD002823.pub2/full

[Accessed: 30 Jan 2017]

SHULTZ, S. P., DRIBAN, J. B. & SWANIK, C. B. (2007). The evaluation of Electrodermal properties in the identification of Myofascial trigger points*. Archives of Physical Medicine and Rehabilitation.* 88 (6). pp. 780–784.

SLUKA, K. A. & WALSH, D. (2003) Transcutaneous electrical nerve stimulation: Basic science mechanisms and clinical effectiveness. *The Journal of Pain.* 4 (3). pp. 109–121.

SOLOMON, L.(1997) Clinical features of osteoarthritis. In: Kelly WN, Harris ED Jr, Ruddy S, Sledge CB editor(s).*Textbook of Rheumatology. 5th Edition*. Vol. 2, Philadelphia: WB Saunders, pp. 1383-93.

STEFFEN, T. M. & MOLLINGER, L. A. (2005) Age- and gender-related test performance in community-dwelling adults. *Journal of Neurologic Physical Therapy*. 29 (4). pp. 181–188. [Online]
Available: https://www.ncbi.nlm.nih.gov/pubmed/11856064 [Accessed 15 Jan 2017]

THOMPSON, J. (2015). 'Critical Assessment Guidelines 2014-2015'. The College of Osteopaths. Middlesex. UK

TOK, F., AYDEMIR, K., PEKER, F., SAFAZ, I., TASKAYNATAN, M.A. & OZGUL, A. (2009) The effects of electrical stimulation combined with continuous passive motion versus isometric exercise on symptoms, functional capacity, quality of life and balance in knee osteoarthritis: Randomized clinical trial. *Rheumatology International.* 31 (2). pp. 177–181.

WHITE, P. F., LI, S. & CHIU, J. W. (2001) Electroanalgesia: Its role in acute and chronic pain management. *Anesthesia and Analgesia*. pp. 505–513.

ZIZIC, T.M., HOFFMAN, K.C., HOLT, P.A., HUNGERFORD, D.S., O'DELL, J.R., JACOBS, M.A., et al. (1995) The treatment of osteoarthritis of the knee with pulsed electrical stimulation. *Journal of Rheumatolojy* (22) pp. 1757–61.

APPENDIX A Search History example

Search history table for MEDLINE

#	Query	Limiters/Expanders	Last Run Via	Result
S12	S10 AND S11	Search mode Boolean/Phrase	Interface- EBSCOhost Research Databases Search Screen- Advanced Search Database- MEDLINE with Full Text	147
S11	S7 OR S8 OR S9	Search mode Boolean/Phrase	Interface- EBSCOhost Research Databases Search Screen- Advanced Search Database- MEDLINE with Full Text	26703
S10	S1 OR S2 OR S3 OR S4 OR S5 OR S6	Search mode Boolean/Phrase	Interface- EBSCOhost Research Databases Search Screen- Advanced Search Database- MEDLINE with Full Text	18083
S9	Osteoarthritis knee pain	Search mode Boolean/Phrase	Interface- EBSCOhost Research Databases Search Screen- Advanced Search Database- MEDLINE with Full Text	9209
S8	Osteoarthritis knee	Search mode Boolean/Phrase	Interface- EBSCOhost Research Databases Search Screen- Advanced Search Database- MEDLINE with Full Text	26642
S7	Knee osteoarthritis	Search mode Boolean/Phrase	Interface- EBSCOhost Research Databases Search Screen- Advanced Search Database- MEDLINE with Full Text	26455
S6	Transcutaneous electrical nerve stimulation	Search mode Boolean/Phrase	Interface- EBSCOhost Research Databases Search Screen- Advanced Search Database- MEDLINE with Full Text	7808
S5	MH “TENS”	Search mode Boolean/Phrase	Interface- EBSCOhost Research Databases Search Screen- Advanced Search Database- MEDLINE with Full Text	9811
S4	Pulsed electrical stimulation	Search mode Boolean/Phrase	Interface- EBSCOhost Research Databases Search Screen- Advanced Search Database- MEDLINE with Full Text	1067
S3	MH ”PES”	Search mode Boolean/Phrase	Interface- EBSCOhost Research Databases Search Screen- Advanced Search Database- MEDLINE with Full Text	3218
S2	Neurostimulation	Search mode Boolean/Phrase	Interface- EBSCOhost Research Databases Search Screen- Advanced Search Database- MEDLINE with Full Text	1732
S1	Electrotherapy	Search mode Boolean/Phrase	Interface- EBSCOhost Research Databases Search Screen- Advanced Search Database- MEDLINE with Full Text	73799
“TENS” Keyword (17710)				
“PES” Keyword (7520)				
MH = MeSH search for MEDLINE				

APPENDIX B FACTORS EFFECTING VALIDITY AND RELIABILITY

Aspect of Methodology	Explanation of effect on validity/reliability
Clearly focussed question (CFQ)	A CFQ improves validity by allowing the reader to determine how accurately the study has measured what was intended. A CFQ enables a trial to be accurately repeated by clearly defining what is to be measured thus improving reliability.
Clearly described methods (CDM)	CDM are required in order to produce the results needed to answer the paper's question, which adds to the paper's validity. CDM allow the study's methods to be repeated more accurately, improving reliability.
Random sampling from defined population (RS)	RS improves validity by ensuring a study measures what was intended against a representative population. RS reduces the risk of systematic bias, which would otherwise adversely affect a study's reliability.
Random allocation of participants to test groups (RA)	RA ensures test groups are comparable and that differences in the results are due to the intervention and not pre-existing differences in the population, this improves both validity and reliability. RA improves reliability by ensuring that the mix of participants to treatment and control are similar and can be repeated.
Use of controls	The use of controls can improve reliability and validity by ensuring that when results are considered, differences identified can be confirmed as due to the intervention as well as natural progression allowing relevant comparisons to be made.
Use of placebos	Placebo controls ensure that when results are compared, any differences are due to the intervention rather than psychological effects of treatment, which can improve both validity and reliability of a study.
Blinding	Blinding stops expectations from affecting results and ensures a trial can be more accurately repeated by avoiding the introduction of additional, unwanted variables such as psychological influences.
Use of validated outcome measures	Validated outcome measures can improve reliability and validity of a paper by ensuring that measurements of what was intended can be relied on for accuracy.

(Greenhalgh, 2007)

APPENDIX C CRITICAL APPRAISAL SKILLS PROGRAMME EXAMPLE

CHECKLIST FOR A TRIAL
Three broad issues need to be considered when appraising the report of a randomised controlled trial:
□Are the results of the trial valid? (Section A)
□What are the results? (Section B)
□Will the results help locally? (Section C)

The 11 questions on the following pages are designed to help you think about these issues
systematically.
The first two questions are screening questions and can be answered quickly. If the answer to both is
yes, it is worth proceeding with the remaining questions.
There is some degree of overlap between the questions, you are asked to record a yes, no or can't
tell to most of the questions. A number of prompts are given after each question. These are designed
to remind you why the question is important. Record your reasons for your answers in the spaces
provided.

(A) Are the results of the trial valid?

Screening Questions:

1. Did the trial address a clearly focused issue?
□Yes
□Can't tell □No
Consider: An issue can be 'focused' in terms of
□The population studied
□The intervention given
□The comparator given
□The outcomes considered

2. Was the assignment of patients to treatments randomised?
□Yes
□Can't tell □No
Consider:
□How was this carried out, some methods may produce broken allocation concealment
□Was the allocation concealed from researchers?
Is it Worth Continuing?
Detailed Questions

3. Were patients, health workers and study personnel blinded?

□Yes
□Can't tell □No
Consider:
□Health workers could be; clinicians, nurses etc
□Study personnel – especially outcome assessors

4. Were the groups similar at the start of the trial?
□Yes
□Can't tell □No
Consider:
□Other factors that might affect the outcome such as age, sex, social class, these may be called baseline characteristics.

5. Aside from the experimental intervention, were the groups treated equally?
□Yes
□Can't tell □No

6. Were all of the patients who entered the trial properly accounted for at its conclusion?
□Yes
□Can't tell □No
(B) What are the results?

7. How large was the treatment effect?
Consider:
□What outcomes were measured?
□Is the primary outcome clearly specified?
□What results were found for each outcome?
□Is there evidence of selective reporting of outcomes?

8. How precise was the estimate of the treatment effect?
Consider:
□What are the confidence limits?
□Were they statistically significant?
(C) Will the results help locally?

9. Can the results be applied in your context (or to the local population?)
□Yes
□Can't tell □No
Consider:
□Do you have reason to believe that your population of interest is different to that in the trial?
□If so, in what way?

10. Were all clinically important outcomes considered?
□Yes
□Can't tell □No
11. Are the benefits worth the harms and costs?
□Yes
□Can't tell □No
Consider:
□Even if this is not addressed by the trial, what do you think?

APPENDIX D Quality Grading Grid

Quality Grades	Descriptor
Excellent	Well-designed and executed study, with care taken to avoid bias. Very few weaknesses
Good	Reasonable study design with minor flaws or omissions. Strengths outweigh weaknesses.
Fair	Study has flaws and limitations design, conclusions to be viewed with caution. Strengths and weaknesses equally balanced.
Poor	Significant problems with the study and/or major omissions. Weaknesses outweigh strengths.
Unusable	Study suffers from so many serious flaws that it is not usable as evidence. Very few strengths

(Thompson, 2015)

APPENDIX E

The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC)

Name:_____ Date:_____

Instructions: Please rate the activities in each category according to the following scale of difficulty: 0 = None, 1 = Slight, 2 = Moderate, 3 = Very, 4 = Extremely

Circle **one number** for each activity_____

Pain	1. Walking.	0 1 2 3 4
	2. Stair Climbing	0 1 2 3 4
	3. Nocturnal	0 1 2 3 4
	4. Rest	0 1 2 3 4
_____	5. Weight bearing	0 1 2 3 4
Stiffness	1. Morning stiffness	0 1 2 3 4
_____	_ 2. Stiffness occurring later in the day	0 1 2 3 4
Physical Function	1. Descending stairs	0 1 2 3 4
	2. Ascending stairs	0 1 2 3 4
	3. Rising from sitting	0 1 2 3 4
	4. Standing	0 1 2 3 4
	5. Bending to floor	0 1 2 3 4
	6. Walking on flat surface	0 1 2 3 4
	7. Getting in / out of car	0 1 2 3 4
	8. Going shopping	0 1 2 3 4
	9. Putting on socks	0 1 2 3 4
	10. Lying in bed	0 1 2 3 4
	11. Taking off socks	0 1 2 3 4
	12. Rising from bed	0 1 2 3 4
	13. Getting in/out of bath	0 1 2 3 4
	14. Sitting	0 1 2 3 4
	15. Getting on/off toilet	0 1 2 3 4
	16. Heavy domestic duties	0 1 2 3 4
	17. Light domestic duties	0 1 2 3 4

Total Score: _____ / 96 = _____%

Comments / Interpretation (to be completed by therapist only):

APPENDIX F

Selected papers abstracts

Abstract 1 *Effects of transcutaneous electrical nerve stimulation on pain, pain sensitivity, and function in people with knee osteoarthritis: a randomized controlled trial.*

BACKGROUND: Transcutaneous electrical nerve stimulation (TENS) is commonly used for the management of pain; however, its effects on several pain and function measures are unclear.

OBJECTIVE: The purpose of this study was to determine the effects of high-frequency TENS (HF-TENS) and low-frequency TENS (LF-TENS) on several outcome measures (pain at rest, movement-evoked pain, and pain sensitivity) in people with knee osteoarthritis.

DESIGN: The study was a double-blind, randomized clinical trial.

SETTING: The setting was a tertiary care centre.

PARTICIPANTS: Seventy-five participants with knee osteoarthritis (29 men and 46 women; 31-94 years of age) were assessed.

INTERVENTION: Participants were randomly assigned to receive HF-TENS (100 Hz) (n=25), LF-TENS (4 Hz) (n=25), or placebo TENS (n=25) (pulse duration=100 microseconds; intensity=10% below motor threshold).

MEASUREMENTS: The following measures were assessed before and after a single TENS treatment: cutaneous mechanical pain threshold, pressure pain threshold (PPT), heat pain threshold, heat temporal summation, Timed "Up & Go" Test (TUG), and pain intensity at rest and during the TUG. A linear mixed-model analysis of variance was used to compare differences before and after TENS and among groups (HF-TENS, LF-TENS, and placebo TENS).

RESULTS: Compared with placebo TENS, HF-TENS and LF-TENS increased PPT at the knee; HF-TENS also increased PPT over the tibialis anterior muscle. There was no effect on the cutaneous mechanical pain threshold, heat pain threshold, or heat temporal summation. Pain at rest and during the TUG was significantly reduced by HF-TENS, LF-TENS, and placebo TENS.

LIMITATIONS: This study tested only a single TENS treatment.

CONCLUSIONS: Both HF-TENS and LF-TENS increased PPT in people with knee osteoarthritis; placebo TENS had no significant effect on PPT. Cutaneous pain measures were unaffected by TENS. Subjective pain ratings at rest and during movement were similarly reduced by active TENS and placebo TENS, suggesting a strong placebo component of the effect of TENS.

Abstract 2 *Effects of kinesiotherapy, ultrasound and electrotherapy in management of bilateral knee osteoarthritis: prospective clinical trial.*

BACKGROUND: Although recent advances in knee osteoarthritis (OA) treatment and evaluation were achieved, to the best of our knowledge, few studies have evaluated the longitudinal effect of therapeutic modalities on the functional exercise capacity of patients with knee OA. The purpose was to investigate the effects of kinesiotherapy and electrotherapy on functional exercise capacity, evaluated using the six-minute walk test (6-MWT) in patients with bilateral knee OA. Secondary measurements included range of OBJECTIVE: To determine the effectiveness of subsensory, pulsed electrical stimulation (PES) in the symptomatic management of osteoarthritis (OA) of the knee.

METHODS: This was a double-blind, randomized, placebo-controlled, repeated-measures trial in 70 participants with clinical and radiographically diagnosed OA of the knee who were randomized to either PES or placebo. The primary outcome was change in pain score over 26 weeks measured on a 100-mm visual analogue scale (VAS). Other measures included pain on the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), function on the WOMAC, patient's global assessment of disease activity (on a 100-mm VAS), joint stiffness on the WOMAC, quality of life on the

Medical Outcomes Study Short-Form 36 (SF-36) health survey, physical activity (using the Human Activity Profile and an accelerometer), and global perceived effect (on an 11-point scale).

RESULTS: Thirty-four participants were randomized to PES and 36 to placebo. Intent-to-treat analysis showed a statistically significant improvement in VAS pain score over 26 weeks in both groups, but no difference between groups (mean change difference 0.9 mm [95% confidence interval -11.7, 13.4]). Similarly, there were no differences between groups for changes in WOMAC pain, function, and stiffness scores (-5.6 [95% confidence interval -14.9, 3.6], -1.9 [95% confidence interval -9.7, 5.9], and 3.7 [95% confidence interval -6.0, 13.5], respectively), SF-36 physical and mental component summary scores (1.7 [95% confidence interval -1.5, 4.8] and 1.2 [95% confidence interval -2.9, 5.4], respectively), patient's global assessment of disease activity (-2.8 [95 motion (ROM), severity of knee pain (VAS), and a measure of perceived health and physical function, evaluated using the Western Ontario and McMaster Universities (WOMAC) Osteoarthritis Index.

METHODS: A total of 40 women with bilateral knee OA were assigned to three groups: kinesiotherapy (KIN, n = 16), transcutaneous electrical nerve stimulation (TENS, n = 12), or ultrasound (US, n = 10). The groups underwent 12 weeks of intervention twice per week. The participants were subjected to the 6-MWT, ROM, VAS and WOMAC index. These tests were performed before and after the intervention. The study was focused on outpatients and was carried out at Universidade Estadual de Campinas, Brazil.

RESULTS: At follow-up, the KIN and US groups had significantly higher 6-MWT distances (19.8 ± 21.7 and 14.1 ± 22.5%, respectively) compared with their respective pre-intervention values. All treatments were effective for reducing pain and improving the WOMAC index.

CONCLUSIONS: We demonstrated that the 6-MWT is a tool that can be used to evaluate improvements in the functional exercise capacity of patients submitted to a clinical intervention.

Abstract 3 *The effectiveness of pulsed electrical stimulation in the management of osteoarthritis of the knee: results of a double-blind, randomized, placebo-controlled, repeated-measures trial.*

% confidence interval -13.9, 8.4]), or activity measures. Fifty-six percent of the PES-treated group achieved a clinically relevant 20-mm improvement in VAS pain score at 26 weeks compared with 44% of controls (12% [95% confidence interval -11%, 33%]).

CONCLUSION: In this sample of subjects with mild-to-moderate symptoms and moderate-to-severe radiographic OA of the knee, 26 weeks of PES was no more effective than placebo.

Abstract 4 *A 3-month, randomized, double-blind, placebo-controlled study to evaluate the safety and efficacy of a highly optimized, capacitively coupled, pulsed electrical stimulator in patients with osteoarthritis of the knee.*

OBJECTIVE: To investigate the efficacy and safety of a capacitively coupled, pulsed electrical stimulation device in treating knee osteoarthritis (OA).

DESIGN: Fifty-eight outpatients with moderate to severe OA of the knee entered a 3-month, double-blind, placebo-controlled trial, using either an active or placebo device at home for 6 to 14 h/day. Outcome measures included a patient global evaluation, a patient report of knee pain severity, and the Western Ontario and McMaster Universities (WOMAC) questionnaire.

RESULTS: Active treatment provided superior outcomes between baseline and 3-month follow-up measurements: 50.6% greater improvement than placebo in patient global (P=0.03), 31.2% in patient pain (P=0.04), 25.1% in WOMAC stiffness (P=0.03), 29.5% in WOMAC function (P=0.01), 19.9% in WOMAC pain (P=0.11), and 27% in total WOMAC (P=0.01). The percent of patients who improved by more than 50% was 38.5 active vs 5.3 placebo in patient global (P=0.01), 43.6 vs 15.8 in patient pain (P=0.04), 38.5 vs 10.5 in WOMAC pain (P=0.03), 28.2 vs 5.3 in WOMAC stiffness (P=0.08), 23.1 vs 5.3 in WOMAC function (P=0.14), and 23.1 vs 5.3 in total WOMAC (P=0.14). Twenty-

one percent of placebo and 18% of actively treated patients developed a transient rash at the electrode sites. No other adverse device effects were reported.

CONCLUSION: A highly optimized, capacitively coupled, pulsed electrical stimulus device significantly improved symptoms and function in knee OA without causing any serious side effects.

Abstract 5 *Effects of noninvasive interactive neurostimulation on symptoms of osteoarthritis of the knee: a randomized, sham-controlled study.*

OBJECTIVE: To explore the effects of noninvasive interactive neurostimulation used as an adjunct to usual care, on pain and other symptoms in adults with osteoarthritis of the knee.

DESIGN: Randomized, sham-controlled trial.

SETTING: A university in the southern United States.

SUBJECTS: Thirty-seven (37) adults with knee osteoarthritis (based on American College of Rheumatology diagnostic criteria).

INTERVENTIONS: Seventeen (17) noninvasive interactive neurostimulation (active or sham) sessions over 8 weeks with a week 12 follow-up.

OUTCOME MEASURES: Eleven-point numeric rating scale for weekly pain; Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), patient global assessment, and Short-Form Health Survey (SF-36) completed at baseline and weeks 4, 8, and 12.

RESULTS: For the main outcome, pain, the differences between the groups over time did not reach statistical significance (all $p > 0.05$). However, a clinically important reduction in pain (defined as a 2-point or 30% reduction on an 11-point numeric rating scale) was maintained at week 12 by the active noninvasive interactive neurostimulation

group (2.17 points, 34.55% reduction) but not the sham group (1.63, 26.04% reduction). Pain improved over time in participants regardless of group membership (numeric rating scale average pain, $p = 0.002$; numeric rating scale worst pain, $p < 0.001$; and WOMAC pain, $p < 0.001$), as did WOMAC function, WOMAC stiffness, and WOMAC total score (all $p < 0.001$). Repeated measures ANOVA revealed a statistically significant difference between the groups over time for the SF-36 Vitality scale, $F (3, 105) = 3.54$, $p = 0.017$. In addition, the active device group improved on the patient global assessment from baseline to week 8 compared to the sham device group, $F (1, 35) = 4.025$, $p = 0.053$.

CONCLUSIONS: In this pilot study, clinically important reductions in knee pain were maintained at week 12 in the active, but not the sham, non-invasive interactive neurostimulation group. Further study of this non-invasive therapy is warranted.

Abstract 6 Comparison *of the efficacy of transcutaneous electrical nerve stimulation, interferential currents, and shortwave diathermy in knee osteoarthritis: a double-blind, randomized, controlled, multicenter study.*

OBJECTIVE: To compare the effectiveness of transcutaneous electrical nerve stimulation (TENS), interferential currents (IFCs), and shortwave diathermy (SWD) against each other and sham intervention with exercise training and education as a multimodal package.

DESIGN: A double-blind, randomized, controlled, multicenter trial.

SETTING: Departments of physical medicine and rehabilitation in 4 centers.
PARTICIPANTS: Patients (N=203) with knee osteoarthritis (OA).

INTERVENTIONS: The patients were randomized by the principal center into the following 6 treatment groups: TENS sham, TENS, IFCs sham, IFCs, SWD sham, and SWD. All interventions were applied 5 times a week for 3 weeks. In addition, exercises and an education program were given. The exercises were carried out as part of a home-based training program after 3 weeks' supervised group exercise.

MAIN OUTCOME MEASURES: Primary outcome was a visual analogue scale (0-100mm) to assess knee pain. Other outcome measures were time to walk a distance of 15m, range of motion, Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), Nottingham Health Profile, and paracetamol intake (in grams).

RESULTS: We found a significant decrease in all assessment parameters (P<.05), without a significant difference among the groups except WOMAC stiffness score and range of motion. However, the intake of paracetamol was significantly lower in each treatment group when compared with the sham groups at 3 months (P<.05). Also, the patients in the IFCs group used a lower amount of paracetamol at 6 months (P<.05) in comparison with the IFCs sham group.

CONCLUSIONS: Although all groups showed significant improvements, we can suggest that the use of physical therapy agents in knee OA provided additional benefits in improving pain because paracetamol intake was significantly higher in the patients who were treated with 3 sham interventions in addition to exercise and education.