Washington State Health Care Authority

HEALTH TECHNOLOGY ASSESSMENT

UPDATED

HTA FINAL REPORT
ELECTRICAL NERVE STIMULATION FOR THE TREATMENT OF PAIN

UPDATED

DATE: FRIDAY, NOVEMBER 13, 2009

Health Technology Assessment Program
676 Woodland Square Loop SE
P.O. Box 42712
Olympia, WA 98504-2712
http://www.hta.hca.wa.gov

ELECTRICAL NERVE STIMULATION FOR THE TREATMENT OF PAIN

Provided by:

Spectrum Research, Inc.

Prepared by:

Jocelyn M. Weiss, PhD, MPH
Andrea C. Skelly, PhD, MPH
Nora Henrikson, PhD, MPH
Lisa Kercher, PhD, MPH
Joseph R. Dettori, PhD, MPH

With assistance from:
Erika D. Ecker, BS

This technology assessment report is based on research conducted by a contracted technology assessment center, with updates as contracted by the Washington State Health Care Authority. This report is an independent assessment of the technology question(s) described based on accepted methodological principles. The findings and conclusions contained herein are those of the investigators and authors who are responsible for the content. These findings and conclusions may not necessarily represent the views of the HCA/Agency and thus, no statement in this report shall be construed as an official position or policy of the HCA/Agency.

The information in this assessment is intended to assist health care decision makers, clinicians, patients and policy makers in making sound evidence-based decisions that may improve the quality and cost-effectiveness of health care services. Information in this report is not a substitute for sound clinical judgment. Those making decisions regarding the provision of health care services should consider this report in a manner similar to any other medical reference, integrating the information with all other pertinent information to make decisions within the context of individual patient circumstances and resource availability.

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INTRODUCTION

According to the Centers for Disease Control and Prevention (CDC), pain is one of the most common causes of disability in the United States. The CDC's National Center for Health Statistics reported in 2006 that one in four U.S. adults report a day-long bout of pain in the past month, and one in 10 say the pain lasted at least a year[1]. Low back pain, headache, and joint pain, aching or stiffness are among the most common complaints. Data from the 1999–2002 National Health and Nutrition Examination Survey (NHANES) revealed back pain to be the most commonly reported of all types, with more than 25% of adults reporting low back pain in the prior 3 months, with pain most commonly reported among adults 45 years of age and over. Annually, an estimated 46 million (21.6%) U.S. adults (about 1 in 5) report doctor-diagnosed arthritis[2]. In 2003, the total cost of arthritis was $128 billion, including $81 billion in direct costs (medical) and $47 billion in indirect costs (lost earnings)[3].

There are many treatments, increasing in number, that are available to manage acute and chronic pain. Treatments include physical therapies, medications, neural blockade, neuroaugmentation, biofeedback-relaxation technique and psychotherapy, as well as complementary and alternative practices, such as acupuncture, herbal medications, and massage. Many of these treatments, however, are prescribed despite clear evidence of their efficacy or effectiveness.

Schatman et al.[4] have outlined six criteria to consider when evaluating the effectiveness of a particular treatment: 1) knowledge of the mechanisms involved as the source or the cause of pain; 2) individual variations in patients treated; 3) the criteria used to determine success; 4) the methods used for assessing these criteria; 5) the design of the studies that attempt to establish effectiveness; and 6) the data analytic methods selected to evaluate the outcomes. This technology assessment aims to address the latter two criteria and evaluate the efficacy, effectiveness, safety and cost-effectiveness of transcutaneous electrical nerve stimulation (TENS) for the treatment of pain.

To that end, the following key questions developed by the Washington State Health Technology Assessment Program will be addressed:

In patients being treated for acute and chronic pain:

1. What is the evidence of efficacy and effectiveness of TENS for the treatment of acute and chronic pain?

2. What is the evidence about the safety profile for TENS?

3. What is the evidence of cost implications and cost effectiveness of TENS?

METHODS FOR EVALUATING COMPARATIVE EFFECTIVENESS

Spectrum Research, Inc.'s (SRI) method for technology assessment involves formal, structured systematic search of the peer-reviewed literature across a number of databases in addition to searches of pertinent databases related to clinical guidelines and previously performed assessments. Included systematic reviews, meta-analyses and individual studies are critically appraised using appropriate checklists and/or SRI's Level of Evidence (LoE) system which evaluates the methodological quality based on study design as well as factor which may bias studies. An overall Strength of Evidence (SoE) takes into account the LoE, along with the quantity of studies and consistency of the findings. The SoE can be interpreted to mean how confident one should be that these estimates will remain stable as further research becomes available. Included economic studies were also formally appraised based on criteria for quality of economic studies and pertinent epidemiological precepts.

Previously published Cochrane Reviews comparing transcutaneous electrical nerve stimulation (TENS) to placebo, control, or other treatments provided the basis for this Health Technology Assessment (HTA), as these are considered to provide the highest quality of evidence. Results and conclusions from these reports are summarized. Individual studies and meta-analyses reviewed in these reports were not re-evaluated. Comparative studies that were published in peer-reviewed journals after the most recent Cochrane updates were also reviewed for inclusion, again with a focus on the highest level of available evidence. The criteria for inclusion and exclusion used in the Cochrane Reviews were applied to any new comparative studies.

Throughout the process, SRI sought clinical review to assure that the clinical components are accurately represented. In addition, peer-review by clinical experts, health services researchers and those with expertise in economic and outcomes evaluation provided an assessment of the systematic review methodology, analyses and report conclusions at the time of the publication of the public draft.

SUMMARY AND IMPLICATIONS

Summary with respect to efficacy and effectiveness of transcutaneous electrical nerve stimulation (TENS) in the treatment of acute and chronic pain

- Findings regarding efficacy described in this technology assessment report are primarily taken from previously published Cochrane Reviews of randomized studies (LoE I/II) and from randomized trials (LoE II/III) published since the most recent updates of the reviews.
    - The overall strength of evidence (SoE) ranged from moderate to very low, depending on the degree of literature support for the different conditions and outcomes examined.
    - Evidence for a benefit of effect in the treatment osteoarthritis of the knee was moderate; TENS was found to be superior to placebo (sham), with the differences both statistically significant and clinically important.
    - Although the primary evidence in this assessment comes from Cochrane Reviews, meta-analysis for most of the studies was not appropriate given the heterogeneity in study populations, intervention characteristics, and outcome measures.

Acute Pain [5]

- A total of 12 studies covering the following conditions were included in one Cochrane Review of acute pain: pain associated with medical procedures (e.g. sigmoidoscopy), hemophiliac pain, acute trauma (e.g. sprains or fractures), postpartum uterine contraction, acute oro-facial pain, post thoracotomy, and rib fractures.

- The overall SoE across studies of acute pain is *low* given the number of LoE I/II studies. Although 12 studies were included in this review, data could only be extracted from 6 of them.
- Acute pain relief (measured using a numerical rating scale or a visual analogue scale) was not significantly different between TENS and sham or control group for the treatment of procedural and post-treatment pain. Significantly greater pain relief was reported for patients treated with TENS that those treated with sham after two days of treatment, however, this finding was based on a single study of 50 patients.
- In comparisons between types of TENS, pain relief was significantly greater for patients treated with high amplitude (intensity) TENS than those treated with low amplitude TENS. Patients treated with conventional (high frequency) TENS and acupuncture-like TENS (ALTENS; low frequency) did not differ in acute pain relief post-treatment. These findings, however, are based on two individual studies of 60 and 20 patients, respectively.
- Sample sizes for most of the studies were small and significant clinical and methodological heterogeneity precluded pooling of data.
- Due to insufficient extractable data in the studies included in this review, the authors of this review concluded that definitive conclusions about the effectiveness of TENS as an isolated treatment for acute pain in adults cannot be made.

Labor Pain [6]

- One Cochrane review comprised of 19 studies compared conventional TENS and ALTENS, pharmacological treatment and epidural and one more recently published RCT were identified.
- Overall, results are mixed with regard to the effectiveness of TENS for the relief of labor pain. It appears to depend on the type of TENS and how it is applied.
- The overall SoE across TENS is *moderate* with regard to pain relief.
- For treatment of labor pain, TENS tended to reduce pain to a greater degree than sham treatment (2 studies), but this finding failed to reach statistical significance. TENS applied to acupuncture points led to statistically significant differences in the number of women reporting severe pain during labor based on 2 studies.
- Women treated with TENS were significantly more satisfied with their pain relief (5 studies) and would be more likely to use TENS again in a future labor than women treated with sham (4 studies) and the SoE for these outcomes is *high*.
- When compared to pharmacologic relief, TENS applied to the back was not significantly different with respect to patient satisfaction with pain relief (pain scores were not reported) in 3 studies.
- TENS combined with epidural did not lead to significantly different pain or delivery outcomes from epidural alone, except when TENS was applied to the cranium (for which there was a longer duration of pain relief from first injection).
- The authors of this review concluded that there is only limited evidence that TENS reduces pain in labor and it does not seem to have any impact (either positive or negative) on other outcomes for mothers or babies.
- A recent RCT comparing TENS to traditional treatment (controls) did not find statistically significant differences between the two groups with respect to pain scores at any point during labor or covering the entire delivery or number of women needing epidural analgesia; these findings do not change the overall conclusions.

Dysmenorrhea [7]

- A Cochrane review of 7 studies, some of which had small sample sizes, comparing low and high frequency TENS was identified.
- Overall, when all types of TENS were considered together for relief of dysmenorrhea, results were mixed, leading to an overall SoE that is *low*. Small sample sizes and wide confidence intervals for some studies bring the stability of estimates into question.
- For treatment of dysmenorrhea pain, high frequency TENS (HFTENS) led to greater reductions in pain than placebo, however, the estimate was not precise.
- There was not a statistically significant difference in overall pain experience (categorical measure) when low frequency TENS (LFTENS) was compared to placebo. Although HFTENS led to a significantly greater number of women with positive overall pain experiences than LFTENS, there was no difference in pain relief on the VAS.
- When LFTENS was compared to placebo TENS and placebo pill, three studies reported no significant differences between the groups in number of women with an overall positive pain experience, another small study measuring VAS pain relief also did not observe a significant difference between LFTENS and placebo TENS. Two additional studies reported statistically significant greater pain relief for LFTENS, but did not provide descriptive data.
- Women treated with LFTENS reported significantly less analgesic usage than placebo in a study of 24 women.
- When compared to pharmacologic treatments, ibuprofen was shown to be significantly better at reducing pain, but did not influence consumption of additional analgesics; no significant differences in pain scores were reported when TENS was compared to naproxen.
- The authors of this review concluded that high frequency TENS was effective for the treatment of dysmenorrhea by a number of small trials, but evidence was insufficient to determine the effectiveness of low frequency TENS.
- A recent small study did not find any differences between TENS and interferential current therapies, however, each led to reductions in menstrual pain, referred lower limb pain, and low back pain. Without sham or no treatment control comparisons, these differences should be interpreted with caution.

Chronic Pain [8]

- A Cochrane review of TENS use for chronic pain (> 3 months) that included 25 studies (1281 participants) included those with rheumatoid arthritis, osteoarthritis, pancreatitis, myofascial pain, diabetic neuropathy, and low back pain. .
- Numerical data were not summarized in this review and authors provided information on the numbers of studies which overall showed a positive effect of TENS on pain relief.
- The overall SoE for chronic pain is *moderate* based on the number and quality of studies, but numerical data were not presented and a description of consistency across studies was not explicit.
- For treatment of chronic pain, patients treated with TENS were more likely to report overall positive effects of treatment when compared to sham within the first week of treatment, but this advantage decreased over time (follow-up for most studies did not exceed four weeks); when analyses were restricted to HFTENS and sham, the results were similar.
- While almost all of the studies reported on the immediate effects and those effects within the first four weeks, only three studies described long-term efficacy of relief.
- Clinical importance of effect of TENS on pain relief cannot be commented on.

- The authors of this review concluded that the published literature lacks the methodological rigor or robust reporting needed to make confident assessments of the role of TENS in chronic pain management. Large multi-center RCTs of TENS in chronic pain are still needed.

Chronic Low Back Pain [9]

- A Cochrane Review of TENS use in chronic low back pain (LBP) included only four studies representing 585 persons. Two additional small RCTs were identified. Sample sizes in most studies were small.
- For the relief of chronic LBP, the overall SoE for the effectiveness of any type of TENS is *low*, based on a total of 6 RCTs (LoE I/II) with small sample sizes.
- Only one small study reported statistically significant pain relief with TENS use.
- Therefore, of 6 RCTs (LoE I/II) evaluating the efficacy of TENS for LBP, only one study showed statistically significant pain relief compared to placebo TENS.
- The authors of this review concluded that evidence from the small number of placebo-controlled trials does not support the use of TENS in the routine management of chronic LBP.

Osteoarthritis of the Knee [10]

- A Cochrane Review of seven studies (N = 254) and two recently published RCTs were identified.
- The overall SoE for relief of knee pain across types of TENS (compared with placebo) in patients with osteoarthritis is *moderate* based on the small sample sizes of included studies and mixed results when newer trials were considered.
- Overall, TENS appears to be associated with a significant improvement in pain compared with placebo. In meta-analyses of five studies, patients treated with TENS were almost 4 times as likely as those in the placebo group to report improvement immediately after treatment (Peto OR 3.91, 95% CI 2.13, 7.17).
- With respect to other more functional outcomes, patients who received TENS or acupuncture-like TENS (ALTENS) showed greater improvement in knee stiffness (MD -5.97, 95% CI -9.89, -2.06) compared to placebo in a meta-analysis of two studies (n=90).
- The authors of this review concluded that TENS and ALTENS are effective in pain control over placebo. Heterogeneity of the included studies was observed, which might be due to the different study designs and outcomes used. 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.
- In one recent RCT, there were no statistically significant differences in pain relief reported by patients in the TENS and hyaluronic acid treatment groups, after 6 months of follow-up (50.2% and 56.7%, respectively; $p>0,05$). Although knee stiffness showed greater improvement for the patients in the TENS group at one-month follow-up ($p<0.05$), this difference was no longer statistically different by the 6-month follow-up.
- In another new study, three-week treatment with PNT, VAS pain relief was significantly better for the PNT group than the placebo group immediately post-treatment ($p<0.04$), however, this difference did not remain statistically significant at later follow-up times. Median pain intensity difference (PID) across all time periods indicated that pain relief was significantly greater in the PNT group than the placebo group (14.5 mm vs. 6.5 mm, $p<0.01$).

- Using the criterion of 0.80 to indicate a large effect, differences in pain relief when comparing TENS/ALTENS to placebo and high rate TENS to placebo could be considered clinically important (SMDs -0.79 and -1.12, respectively).

Rheumatoid arthritis in the hand [11]

- A Cochrane Review of three small studies was identified. The studies were too heterogeneous with respect to TENS treatment (type, treatment schedule) to allow for meta-analysis.
- The overall SoE for pain relief is *very low* since studies of similar comparisons were few and were likely to be underpowered.
- Results from small three studies comparing TENS with placebo were mixed: One study showed a statistically significant improvement in pain while the other two did not.
- One comparison of C-TENS with ALTENS, reported no statistically significant difference between the two types of TENS in patient-reported improvement.
- The authors of the review concluded that given there conflicting effects of TENS on pain outcomes in patients with RA, more well designed studies with a standardized protocol and adequate number of subjects are needed to fully conclude the effect of C-TENS and AL-TENS in the treatment of RA of the hand.

Neck disorders [12]

- A Cochrane Review included 5 studies looked at TENS and 1 looked at IFC therapy (referred to as diadynamic current) compared with use of a cervical collar; two of these studies included TENS as part of a multimodal treatment (in combination with other therapies), so it was not possible to delineate the individual effects of TENS.
- The overall SoE is for use of either TENS for IFC was *low* for neck pain relief.
- Only one study of 38 patients that compared a single 20-minute treatment with TENS to placebo reported greater reduction in pain intensity for the TENS group.
- No statistically significant differences in pain relief were observed when TENS was used in combination with collar and compared to manual therapy + collar or collar alone.
- There was no significant difference in pain intensity after 5 days when diadynamic (interferential) current therapy was compared to placebo in a study of 40 patients.
- The authors of the review concluded that definitive statements on electrotherapy for mechanical neck disorders could not be made. The current evidence on electrical nerve stimulation is either lacking, limited, or conflicting. Future trials should have larger patient samples and include more precise standardization and description of all treatment characteristics.

Post-stroke shoulder pain [13]

- A Cochrane Review included 4 of studies comparing TENS, functional electrical stimulation (FES) and high frequency TENS (HFTENS) with placebo or control. Only two of these studies assessed pain relief.
- Results from this small number of studies are mixed; patients treated with electrical stimulation had lower pain scores than control but those treated with TENS did not.
- Neither FES nor TENS had significantly different new reports of shoulder pain when compared to control.
- The overall SoE for pain relief is *very low* since studies of similar comparisons were few and were likely to be underpowered. There is evidence from 2 studies that FES and TENS may improve passive humeral later rotation.

- Overall, TENS applied to the shoulder after stroke had no significant effect on subjective reports of pain, based on 4 studies.
- The authors of the review concluded that the evidence from RCTs does not confirm or refute that electrical stimulation around the shoulder after stroke influences reports of pain, but there do appear to be benefits for passive humeral lateral rotation. A possible mechanism is through the reduction of glenohumeral subluxation. Further studies are required.

Cancer pain [14]

- A Cochrane Review included only two small studies of TENS effect on cancer pain.
- The overall SoE for cancer pain relief is *very low* given the paucity of studies.
- No statistically significant differences in pain relief between TENS and control groups in either study.
- The authors of this review concluded that the results were inconclusive due to a lack of suitable RCTs, and that large multi-centre RCTs are required to assess the value of TENS in the management of cancer-related pain in adults.

Summary with respect to the safety of transcutaneous electrical nerve stimulation

- TENS is generally regarded as a safe, non-invasive therapy.
- Other than minor skin irritation (burning, tingling or discomfort) at the electrode site, no major adverse events have been associated with its use; for many of the RCTs included in this report, there were no side effects reported.
- TENS is contraindicated for patients with pacemakers, as it could inhibit or interfere with their operation.
- It is also recommended that electrodes not be placed close to the carotid sinus, over the eyes, open wounds, irritated skin or internally.

Summary with respect to economic studies

- None of the previously reported HTAs contained formal economic analyses specific to TENS. No full economic analyses were found in the published peer-reviewed literature.
- There is insufficient evidence from one costing study on chronic pain to evaluate the economic value of TENS. No studies pertaining to acute pain were found.
- Data from one costing study on chronic pain suggests that the number of persons using pain medications and muscle relaxants after six months of TENS use decreased significantly as did the number of visits for physical or occupational therapy. Simulated cost savings estimates for medications over 12 months ranged from $240-$560 (in 1994) US Dollars per patient and $1052 assuming 12 PT/OT visits in 6 months.
- Paths of clinical care are not delineated in the literature and the costs and consequences of TENS use would most likely vary by pain condition and clinical pathway.

Table 1. Overall Strength of Evidence (SoE) Criteria

SoE	Description	Further Research Impact	Domain Criterion Met		
			Quality	Quantity	Consistency
1	High	Very unlikely to change confidence in effect estimate	+	+	+
2	Moderate	Likely to have an important impact on confidence in estimate and *may* change the estimate	+	-	+
			+	+	-
3	Low	Very likely to have an important impact on confidence in estimate and *likely* to change the estimate	+	-	-
			-	+	+
4	Very Low	Any effect estimate is uncertain	-	+	-
			-	-	+
			-	-	-

Table 2. Summary of Evidence for each Key Question 1

Key Question 1: Evidence regarding efficacy and effectiveness of TENS for acute pain		
Outcome	**Efficacy**	**Results**
Pain relief	**LOW**	• Previously published HTAs generally report that, on the whole, there is insufficient consistent evidence to make a decision about the efficacy or effectiveness of TENS; TENS may be useful in certain situations (e.g. reducing analgesic need during labor). • TENS is generally not recommended for acute or subacute pain by guidelines found in the Clinical Guidelines Clearinghouse. The Ottawa Panel only found a small clinical benefit for low frequency TENS applied to the hand and wrist. *Acute Pain* • When looking at acute pain as a whole, the only significant results indicating a benefit of TENS were seen after two days of treatment in a study of 50 patients and when high frequency TENS was compared to a no treatment control in a study of 20 patients. • Due to insufficient extractable data in the studies included in this review, the authors of this review concluded that definitive conclusions about the effectiveness of TENS as an isolated treatment for acute pain in adults cannot be made. *Labor pain* • Pain relief during labor was not significantly different for women treated with TENS applied to their back, but there was a significant difference in the number of women reporting severe labor pain when TENS was applied to acupuncture points in 2 studies. • In a study of cranial TENS, duration of pain relief when TENS was given along with epidural was significantly longer than when epidural was given alone. • The authors of this review concluded that there is only limited evidence that TENS reduces pain in labor and it does not seem to have any impact (either positive or negative) on other outcomes for mothers or babies. • Recent evidence from a large study of 293 women did not observe any significant differences between TENS and placebo treatment. *Primary Dysmenorrhea* • More women reported high frequency TENS (HFTENS) to improve overall pain relief than placebo when measured categorically (2 studies) or using a VAS (1 study), but not those receiving low frequency TENS (LFTENS) (4 studies). • In studies of LFTENS, 3 studies that evaluated number of women with a positive overall pain experience and 1 study that measured pain relief on a VAS reported no significant differences with placebo. Two studies that did not provide descriptive data, however, reported LFTENS to be more effective than placebo in relieving pain. • When compared to medical treatment, TENS was less effective at reducing pain than ibuprofen (1 study). • A significantly greater number of women treated with high frequency TENS reported a

		positive overall experience with pain relief than those treated with low frequency TENS in a study of 42 women, but there was no difference in this same study when pain relief was measured by VAS. • There were a limited number of high quality studies and significant heterogeneity across studies with respect to TENS delivery. TENS treatments varied in frequency, amplitude, electrode placement, duration of each session, total duration of treatment. Most of the Cochrane Reviews could not combine data for meta-analysis. • The authors of this review concluded that high frequency TENS was effective for the treatment of dysmenorrhea by a number of small trials, but evidence was insufficient to determine the effectiveness of low frequency TENS. • A recent RCT compared TENS to interferential current therapy and found both to be effective at reducing pain; this study did not include a placebo or no treatment control group.
Patient satisfaction	**MODERATE**	*Labor pain* • Use of TENS for control of pain during labor was preferred by more women than was placebo, whether applied to the back or acupuncture points (5 studies); in one study, women receiving TENS at acupuncture points were more likely to use TENS in a future labor.
Analgesic consumption	**LOW**	*Primary dysmenorrhea* • In two studies, there was not a significant difference between high frequency TENS and placebo in the number of women who requested additional analgesics or the number of tablets taken (n=64 and 24, respectively), • In another study of 24 women, the number of tablets of additional analgesic used was significantly less for the low frequency TENS group than the placebo TENS group.
Functional outcomes	**VERY LOW**	• Not reported

Key Question 1: Evidence regarding efficacy and effectiveness of TENS for chronic pain		
Outcome	**Efficacy**	**Results**
Pain relief	**MODERATE**	• Previously published HTAs generally report that, on the whole, there is insufficient consistent evidence to make a decision about the efficacy or effectiveness of TENS; TENS may be useful in certain situations (e.g. reducing analgesic need during labor). • The Clinical Guidelines Clearinghouse contains very little info on TENS for use specific chronic pain conditions. The only recommendations made for the use of TENS are with back pain and osteoarthritis of the knee, but still the evidence is described as being limited. TENS is not recommended for treatment of headache. *Chronic Pain* • Patients treated with TENS were more likely to report overall positive effects of treatment when compared to sham within the first week of treatment, but this advantage decreased over time (follow-up for most studies did not exceed four weeks). • Only three studies described long-term efficacy of relief. • When TENS was used in multiple dose treatments, only 3 of 7 were considered to be in favor of the active TENS. • For active controlled studies (HFTENS vs. LFTENS), 5 of 7 studies found no difference in analgesic efficacy between HFTENS and LFTENS at any time point. • Clinical importance of effect of TENS on pain relief cannot be commented on. • The authors of this review concluded that the published literature lacks the methodological rigor or robust reporting needed to make confident assessments of the role of TENS in chronic pain management. *Osteoarthritis of the knee* • Statistically significant improvements in pain with TENS treatment, measured as reductions in VAS pain intensity, were observed in 6 studies (n=254) that compared TENS and ALTENS to placebo TENS. • Patients treated with TENS were four times as likely than those in the placebo group to report improvement immediately after treatment (5 studies, n=214) and during follow-up (2 studies, n=62). • In a study of 40 patients, comparing ALTENS to placebo, there was not a statistically significant difference in pain relief between groups. • In subgroup analyses, pain improvement was statistically significant in high quality studies, studies of repeated TENS applications, and studies with treatment durations of at least 4 weeks. • A recent RCT comparing TENS to hyaluronic acid injection in 52 patients observed reductions in pain after 3 weeks of treatment, but did not find any significant difference between the two groups. • The only study to evaluate percutaneous neuromodulation therapy (PNT) in 63 patients reported greater pain immediately post-treatment when compared to placebo but this did not remain significant at later follow-up times. • The authors of this review concluded that TENS and ALTENS are effective in pain control over placebo. Heterogeneity of the included studies was observed, which might be due to the different study designs and outcomes used. 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. • Using the criterion of 0.80 to indicate a large effect, differences in pain relief when comparing TENS/ALTENS to placebo and high rate TENS vs. placebo could be considered clinically important (SMDs -0.79 and -1.12, respectively).
	LOW	*Chronic Low Back Pain (LBP)* • No statistically significant differences in pain intensity or pain relief were observed for conventional TENS when compared to ALTENS 4 weeks after treatment (1 study) or placebo 2 weeks after treatment (1 study).

- One study of 27 patients reported reduced pain and activity pain scores for patients treated with TENS and reduced pain for ALTENS when compared to placebo.
- A recent RCT of 23 female patients with chronic LBP found no statistically significant differences between low frequency TENS and placebo up to 8 weeks post-treatment.
- The authors of this review concluded that evidence from the small number of placebo-controlled trials does not support the use of TENS in the routine management of chronic LBP.

Rheumatoid Arthritis in the Hand

- After 3 weeks of treatment in a study of 32 patients, those patients receiving ALTENS treatment reported significantly lower pain intensity and grip pain scores than placebo, however, the latter was not statistically significant.
- In a study of 22 patients treated with conventional TENS, there were no statistically significant differences in resting pain score, improvement in VAS score or number of tender joints compared to ALTENS after a single treatment of 20 minutes.
- Although there was a statistically significant difference in reduction of joint tenderness scores, the scores did not meet the reviewer's criterion of 15% relative improvement for clinical benefit.
- Five-minute daily treatments over a period of 15 days with conventional TENS did not result in statistically significant differences in the number of patients reporting improvement.
- The authors of the review concluded that given there conflicting effects of TENS on pain outcomes in patients with RA, more well designed studies with a standardized protocol and adequate number of subjects are needed to fully conclude the effect of C-TENS and AL-TENS in the treatment of RA of the hand.

Neck Disorders

- A single 20-minute treatment with TENS showed significantly reduced pain intensity and trigger point tenderness compared to placebo in a study of 38 patients.
- No statistically significant differences in pain relief were reported in a study of 20 patients comparing TENS + collar, manual therapy + collar, and collar alone.
- There was no statistically significant difference in pain intensity after 5 days when diadynamic (interferential) therapy was compared to placebo in a study of 40 patients.
- The authors of the review concluded that definitive statements on electrotherapy for mechanical neck disorders could not be made. The current evidence on electrical nerve stimulation is either lacking, limited, or conflicting. Future trials should have larger patient samples and include more precise standardization and description of all treatment characteristics.
- The authors of the review concluded that the evidence from RCTs does not confirm or refute that electrical stimulation around the shoulder after stroke influences reports of pain, but there do appear to be benefits for passive humeral lateral rotation. A possible mechanism is through the reductionof glenohumeral subluxation. Further studies are required.

Post-Stroke Shoulder Pain

- There were no statistically significant differences in VAS pain intensity or new reports of shoulder pain between TENS and control
- Electrical stimulation led to significantly greater pain improvement than control, but there were no differences in new reports of shoulder pain.

Cancer Pain

- No significant differences were reported between TENS and transcutaneous spinal electroanalgesia or between ALTENS and placebo.
- The authors of this review concluded that the results were inconclusive due to a lack of suitable RCTs, and that large multi-centre RCTs are required to assess the value of TENS in the management of cancer-related pain in adults.

Patient satisfaction	**LOW**	*Osteoarthritis of the knee* • Patients treated with PNT were more likely than those treated with placebo to report positive outcomes with respect to overall satisfaction with treatment after 48 hours and one week of follow-up. *Rheumatoid Arthritis in the Hand* • A clinically important benefit (21% risk difference) on patient assessment of change in disease was reported for conventional TENS over ALTENS. • There was no statistically significant differences in patient-rated improvement after 5 days when diadynamic (interferential) therapy was compared to placebo in a study of 40 patients *Cancer Pain* • TENS was only found to be advantageous over transcutaneous spinal electroanalgesia on one dimension of a patient satisfaction questionnaire.
Analgesic consumption	**LOW**	*Osteoarthritis of the knee* • Patients treated with PNT (one study, n=63) were more likely than those treated with placebo to report reductions in medication after one week of follow-up.
Functional outcomes	**VERY LOW**	*Chronic Low Back Pain (LBP)* • No statistically significant differences were reported for conventional TENS on the Oswestry Disability Index and Low Back Pain Outcome Scale in a study of 27 patients, but significant benefit was seen on 4 out of 8 sections of the SF-36; significant benefit was seen for 2 out of 8 sections on the SF-36 for ALTENS. *Osteoarthritis of the Knee* • When compared to placebo, patients treated with ALTENS were shown to have greater improvement in knee stiffness, quadriceps muscle strength, and knee flexion in one study of 50 patients. *Rheumatoid Arthritis in the Hand* • There were no statistically significant differences between TENS and placebo in power score or work score at the end of 3 weeks treatment in a study of 32 patients. *Post-Stroke Shoulder Pain* • Patients treated with high intensity TENS or functional electrical stimulation showed greater improvement in passive lateral humeral rotation when compared to control.

Table 3. Summary of Evidence for each Key Question 2

Key Question 2: Evidence regarding safety in patients with acute pain		
Adverse events	**LOW**	** SoE moderate given that most studies report either minimal or no adverse effects. • Previous HTAs have either not reported on safety or report that no serious adverse events have been reported with TENS use. *Acute Pain* • Adverse effects not reported in 4/12 included studies. • Five studies reported a range of side effects, however, only shoulder pain occurred more often in TENS patients than control group; nausea, bradycardia, dizziness were more common in control group. *Labor Pain* • No adverse effects were reported in the included studies. *Dysmenorrhea* • In a study of 64 women, minor adverse events were more common in the high frequency TENS group (4/32) than the placebo group. • Adverse events reported included: muscle vibrations, tightness, headaches after use, and slight redness or burning of the skin. • When compared to ibuprofen in a study of 24 women, significantly more women (10/12) treated with TENS experienced minor adverse effects (described as 'pain from treatment). • The women who reported pain from TENS in one study stated that they were prepared to accept the short-term pain from the treatment in return for relief of dysmenorrhea.
Key Question 2: Evidence regarding safety in patients with chronic pain		
Adverse Events	**LOW**	** SoE 2 given that most studies report either minimal or no adverse effects. • Previous HTAs have either not reported on safety or report that no serious adverse events have been reported with TENS use. *Chronic Pain* • Only one of the 25 included studies detailed methods to detect adverse effects; this study found no difference in side effects between the groups. • Other studies indicated skin rash, irritation or burning at electrode site; most only reported adverse effects for a small number of patients and others did not specify how many patients experienced adverse effects. • Three studies made a clear statement that no participants experienced side effects. *Chronic LBP* • Typically minor skin irritations observed equally in the treatment and placebo groups. One participant developed a severe rash four days after the start of treatment. *Osteoarthritis of the Knee* • None reported. *Rheumatoid Arthritis in the Hand* • Review authors state that adverse effects were not reported in the included studies. *Neck Disorders* • Review authors state that adverse effects were not reported in the included studies.

		Post-stroke Shoulder Pain • Review authors state that no adverse effects were noted. *Cancer Pain* • Review authors state that adverse effects were monitored and 'minimal' in 1 of the 2 included studies.

Table 4. Summary of Evidence for each Key Question 3

Key Question 4: Evidence regarding cost-effectiveness for treatment of acute pain		
	NO EVIDENCE	• No economic studies on use of TENS for acute pain were identified
Key Question 4: Evidence regarding cost-effectiveness for treatment of chronic pain		
Cost savings	**VERY LOW**	• No full economic analyses were identified in the peer reviewed literature and none were done as part of previous HTAs • The number of persons using pain medications and muscle relaxants after six months of TENS use decreased significantly as did the number of visits for physical or occupational therapy. • Simulated cost savings estimates for medications over 12 months ranged from $240-$560 (in 1994) US Dollars per patient and $1052 assuming 12 PT/OT visits in 6 months.

APPRAISAL

TENS FOR THE TREATMENT OF ACUTE AND CHRONIC PAIN

FINAL SCOPE

RATIONALE FOR THE APPRAISAL

TENS is a commonly prescribed treatment for both acute and chronic pain. Estimates of use are limited, but there were 275,000 reported TENS prescriptions in 1991[15]. Proponents estimate that 50% to 80% of chronic pain patients and 6% to 44% of acute pain patients benefit from TENS therapy.[16] The bulk of the evidence from which these estimates are drawn, however, arises from studies of questionable methodological quality.

TENS has been widely adopted for the relief of pain, even though studies have been of questionable quality and some reviews have concluded that clear benefit has not been established for relief of pain from various etiologies. TENS may be used in a wide range of clinical settings and by a number of different provider types. Patients may use TENS units for a number of months at home following initial use. Even with what seem to be relatively inexpensive technologies, if they are widely used without evidence of benefit, questions regarding cost-effectiveness arise. There are a number of unanswered questions regarding the use of TENS for pain relief. Some of these include:

- Are there specific conditions for which TENS is effective?
- What specific guidelines are there for the use of TENS for the relief of acute and chronic pain? What are the optimal conditions and duration for its use?
- Does TENS decrease the need for other, less effective and/or perhaps more costly or less safe treatment options?
-

The public health burden and overall cost of treating chronic pain in particular is high. To make best use of available resources, it is logical to undertake critical evaluation of TENS and better understand how and when it may be most effective to assist in pain management.

OBJECTIVES

The primary aim of this assessment is to systematically review, critically appraise and summarize research evidence describing efficacy and safety of TENS as a treatment for acute and chronic pain. Available information on the economic impact of this will also be summarized and critically appraised.

KEY QUESTIONS

When used as a treatment for acute and chronic pain:

1. What is the evidence of efficacy and effectiveness of TENS for the treatment of acute and chronic pain when compared to placebo, control, or other established pharmacologic and non-pharmacologic treatments?

2. What is the evidence regarding the safety of TENS?

3. Is there evidence of differential efficacy or safety issues with the use of TENS? What is the evidence of cost implications and cost effectiveness of TENS?

OUTCOMES

The main focus of this report is on pain relief associated with TENS treatment in patients with acute or chronic pain. Therefore, the difference between pre- and post-treatment pain intensity, measured with a visual analog scale (VAS) or other validated measure, is the primary outcome to be described. Secondary outcomes such as patient satisfaction, analgesic consumption, and functional status are summarized as well.

1. BACKGROUND

1.1 THE CONDITIONS: ACUTE AND CHRONIC PAIN

Pain is described by the International Association of the Study of Pain (IASP) as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage" [17]. In other words, pain is the symptom felt when inflammation or other changes to the nervous system dues to illness or injury are transmitted to the brain, producing a physical sensation [1]. Typically, the inflammation subsides or the wound heals, the pain lessens, and eventually goes away. In some cases, however, pain can persist for longer than expected.

Acuity and chronicity of pain are based on how long pain is expected to persist, and whether it lasts longer than expected. Types of acute pain, for example, include pre- and post-operative pain, post-traumatic acute pain, tinnitus, dental procedures and labor pain. Conditions that can lead to chronic pain are arthritis, low back pain, and other musculoskeletal problems.

Chronic pain can result when acute pain is not adequately evaluated and/or treated. Therefore, in a small but significant number of acute pain patients, the pain continues and even intensifies in nature. The physical sensation of pain is complicated by physical factors such as inactivity and psychological factors such as depression. Environmental factors such as compensation (i.e. insurance or worker's compensation benefits) may influence patient report of pain.

1.2 THE TECHNOLOGY AND ITS COMPARATORS

Transcutaneous Electrical Nerve Stimulation

Transcutaneous electrical nerve stimulation (TENS) is one of the most commonly used treatments for acute and chronic pain. The idea of electrical nerve stimulation as a form of pain control was revived in the 1960's after the publication of the gate-control hypothesis proposed by Melzack and Wall.[18] The gate control hypothesis is based on the idea that pain sensation represents a balance of factors acting upon spinal pain-transmission cells. Large-diameter, myelinated primary afferents were proposed to inhibit, and small-diameter (myelinated and unmyelinated) primary afferents to excite, the pain-transmission cells. They also posited that pain-transmission cells are under the control of descending influences from the brain. Therefore, input to the spinal cord from large-diameter myelinated axons inhibits (or 'closes the gate' on) putative pain-transmitting neurons.[19]

Large-diameter myelinated axons have lower electrical thresholds for externally applied currents than smaller-diameter axons and do not produce pain when activated. Herein lies the theory behind TENS - that selectively activating the large-diameter axons in a non-invasive way through externally applied currents on the skin can provide pain relief. In addition, TENS is purported to induce the release of

endogenous endorphins and enkephalins within the central nervous system, thereby suppressing the transmission and perception of noxious stimuli from the periphery.[20-22] Adaptations to the theory behind TENS propose that TENS-mediated hypoalgesia (a diminished sensation of pain resulting from a raised pain threshold) occurs as a result of direct peripheral effects as well.[23] Low-frequency TENS, for example, produces a local increase in cutaneous blood flow.[24]

Treatment with TENS involves the transmission of electrical energy from an external stimulator to the peripheral nervous system via cutaneously placed conductive gel pads. TENS units usually have a single channel (with two electrodes) or dual channels (with four electrodes). The manner in which this energy, or current, is delivered can vary in frequency, intensity, pulse width, electrode placement and duration. The pulse forms can be exclusively positive or negative (monophasic) or bipolar (biphasic), and the frequency can be controlled. Although definitions vary:

- High frequency (conventional) TENS generally ranges from 25-150 Hz (or pulses per second) in frequency and 1-2 mA in amplitude, or intensity. With conventional TENS, the patient feels a constant tingling/prickling sensation, or even numbness. High frequency TENS is usually applied for acute pain.

- Low frequency (acupuncture-like) TENS, on the other hand, ranges from 1-10 Hz in frequency and 15-20 mA in intensity. Here, the intensity is set close to the tolerance limit of the patient, leading to muscle contraction that is usually less comfortable for the patient. Low frequency TENS is usually applied for chronic pain.

Pulsed (burst) TENS is a third method in which the stimulus is low-intensity firing in high frequency bursts; the recurrent bursts discharge at 12 Hz, and the frequency of impulses within each burst is at 100 Hz. This latter method, however, has not been found to be advantageous and is used much less frequently than conventional and ALTENS.

As noted above, TENS treatment induces the release of endorphins and enkephalins. Other neurotransmitters, including acetylcholine, norepinephrine, and gamma-aminobutyric acid, mediate its effects as well. High and low frequency TENS are each thought to involve different mechanisms, with low frequency TENS involving μ-opioid and 5-HT_2 and 5-HT_3 receptors and high frequency TENS involving ∂-opioid receptors and reduction of aspartate and glutamate levels in the spinal cord.[25]

Pulse duration (width) is set anywhere from 10-1000 microseconds; width is generally shorter for conventional TENS (e.g. 40-75 μsec) than for acupuncture-like TENS (ALTENS) (e.g. 150-250 μsec). Placement of the electrodes is usually at the site of pain, but other locations (e.g. over cutaneous nerves, trigger points, acupuncture sites) are commonly used as well.

TENS is typically used for a single session or for multiple sessions over a short period of time for acute pain, while multiple treatment sessions over a longer period of time are generally recommended for chronic pain.

Indications for the use of TENS include neurogenic pain, musculoskeletal pain, and visceral pain. More specific recommendations for using TENS include:

- Counseling of the patient before the start of treatment.
- Using a trained nurse to communicate the technical instructions is highly desirable.

- Because the induction time for TENS to produce analgesia varies widely, the patient should be confident with the feeling of strong stimulation and view self-treatment without fear.
- The effect of TENS is cumulative, and the duration of an individual treatment session depends on the severity of the pain.

Percutaneous Neuromodulation Therapy

Percutaneous neuromodulation therapy (PNT) is the most recent adaptation of TENS. PNT is not the same as what is typically called percutaneous electrical nerve stimulation (PENS; described below). Treatment with PNT involves a premixed modulated envelope of two high-frequency electronic waveforms ("feed signals") into deep tissue via a larger feed electrode and a smaller pain site electrode called a percutaneous array. The percutaneous electrode array is comprised of 1014 microneedles, each of which is 0.73 mm in length and housed within a 2.5-inch diameter hydrogel-based electrode. The array is thought to allow for delivery of the stimulation into deep tissue by providing a direct conductive pathway for current through the outermost layers of skin.[26] The active electrode is placed over the pain site, while the feed electrode (conventional self-adhesive electrode) is placed opposite the site of pain. The Biowave deep tissue neuromodulation pain therapy device (Deepwave®; FDA-approved) is the only PNT device to be studied in a randomized controlled trial.

Comparators

In studies of TENS, many different treatments have been used as comparisons – placebo, control, and other pharmacologic and non-pharmacologic interventions:

- A **placebo (or sham)** is generally regarded as the best comparator Although it is not possible to produce the same sensations (i.e. tingling, muscle contraction) as with active TENS, use of an inactive TENS unit is likely the best way to ensure blinded assessment by the participants and investigators. Exclusion of patients with prior TENS experience (inclusion of only TENS-naïve patients) can further improve on use of a placebo unit; patients can be instructed that it is possible for them to not feel any sensation in response to treatment.

- A **control** group also does not receive active treatment, but rather than a sham device, these patients typically receive either usual care or no treatment at all.

- **TENS versus TENS** comparisons have also been performed to determine if particular treatment characteristics improve outcome. Comparisons of conventional (high frequency) and acupuncture-like (low frequency) TENS are common.

- Traditional **acupuncture** is a technique of relieving pain in which fine filiform needles are inserted into specific points on the body, located on meridians along which qi, or vital energy (according to traditional Chinese medicine), is believed to flow. The use of acupuncture requires skilled therapists and remains controversial among Western medically researchers and clinicians. A recent review, specifically looking at Cochrane reviews of acupuncture, reported that the evidence does not suggest this treatment is effective for a wide range of conditions.[27]

- **Electroacupuncture** is a form of acupuncture that involves the use of electrical stimulation delivered to traditional acupuncture points on the body, either through electrodes or needles.

- **Percutaneous electrical nerve stimulation (PENS)** is essentially electroacupuncture that involves the insertion of 32-gauge (ultra-fine) acupuncture needle probes into the soft tissues or muscles to electrically stimulate peripheral nerve fibers in the sclerotomal, myotomal, or dermatomal distribution corresponding to the patient's pain symptoms.

- **Pharmacologic treatments** used as comparators in include epidural, narcotic medications, hyaluronic acid injection and non-steroidal anti-inflammatory drugs (NSAIDs).

- **Non-pharmacologic treatments** including, but not limited to, physical therapy, neck collars, manipulation, bio-feedback and relaxation techniques have been used for TENS comparisons.

For this report, only the comparison of TENS to placebo, control, other forms of TENS, and established pharmacologic and non-pharmacologic treatments have been considered. Comparisons of TENS with acupuncture, PENS, deep brain stimulation, or spinal cord stimulation, have not been included as comparators.

Safety
TENS is generally considered to be a safe therapy. Other than minor skin irritation at the electrode site or discomfort with the stimulation, no major adverse events have been associated with its use. TENS is contraindicated for patients with pacemakers, as it could inhibit or interfere with their operation. It is also recommended that electrodes not be placed close to the carotid sinus, over the eyes, open wounds, irritated skin or internally. Although TENS is often used in an effort to reduce consumption of narcotics, caution is still recommended when using these devices on patients who are taking concomitant narcotic medications.

1.3 CLINICAL GUIDELINES

National Guideline Clearinghouse (NGC)
A search of the NGC returned 7 potential guidelines on the use of TENS for pain management. Of those, 6 specifically describe conditions for TENS use and provide specific recommendations. In general, very little information specific to the use of TENS with regard to chronic conditions like low back pain, rheumatoid arthritis, headache, and neuropathic pain were described. Two guidelines that described management of acute pain conditions, concluded that TENS therapy was generally not recommended. The following provides a summary of the guidelines that were most relevant.

University of Iowa Gerontological Nursing Interventions Research Center, Research Translation and Dissemination Core [28]
There is good evidence that transcutaneous electrical nerve stimulation (TENS) can be used as a non-pharmacological, physical method for the treatment of persistent pain in older adults. Although other therapies have been found to be useful, the evidence is still preliminary or inconclusive. Referral to trained specialists is recommended for all physical modalities of treatment. This guideline did not refer to other types of persistent pain or the use of percutaneous neuromodulation therapy (PNT).

- TENS reduced pain in knee osteoarthritis and in chronic back pain [29, 30]. *Evidence Grade = B*)

American College of Occupational and Environmental Medicine (ACOEM) [31] Occupational medicine practice guidelines: evaluation and management of common health problems and functional recovery in workers.

The only recommendation for use of TENS therapy by the ACOEM was TENS therapy for low back pain, however, the evidence was described as limited and it was only recommended for select appropriate patients. All other electrical nerve stimulation modalities were not recommended or described.

- TENS (single or dual channel) is recommended for select use in chronic low back pain or chronic radicular pain syndrome as an adjunct for more efficacious treatments (*Evidence Grade = C*)
- TENS is not recommended for acute or subacute LBP or acute radicular pain syndromes (*Evidence Grade = I, insufficient evidence*)

Ottawa Panel evidence-based clinical practice guidelines for electrotherapy and thermotherapy interventions in the management of rheumatoid arthritis in adults. [32]

The Ottawa Panel's evidence-based practice guidelines on electrotherapy for the management of rheumatoid arthritis are generally in accordance with other evidence-based practice guidelines, including those from the American College of Rheumatology, the American Pain Society, and the American Occupational Therapy Association. Overall, only low frequency TENS applied to the hand and wrist showed a small clinical benefit. The following is a summary of their findings.

- Low-frequency TENS applied to the hand and wrist versus no stimulation (*Evidence Grade = I* (RCT): *Grade A* for pain at 3 weeks (clinically important benefit), *grade C+* for 10 of 14 power at 3 weeks (clinical benefit), *grade C* for work at 3 weeks, no benefit).
- High-frequency TENS applied to the hand and wrist versus placebo, *Evidence Grade = I* (RCT): *Grade C* for pain and joint tenderness, same day, no benefit).
- High- versus low-frequency TENS applied to the hand and wrist, (*Evidence Grade = I* (RCT): *Grade C* for global patient (patient's assessment of overall disease activity or improvement) [32] at 2 weeks, clinical benefit).
  (*Evidence Grade = I, insufficient evidence*)

Institute for Clinical Systems Improvement (ICSI) [33]

In a guideline describing several treatments for headache, the ICSI found TENS units for migraine or muscle contraction headache have not been found to be more beneficial than placebo when evaluated in a controlled study.

National Headache Foundation [34] According to the National Headache Foundation, the use of TENS has been reserved primarily for the treatment of body or extremity pains because of fear of potential epileptogenic effects of electric current running through the head. With proper placement of electrodes and the use of low-intensity currents, it appears to be safe to apply this technique to the head. However, there is little objective evidence about the efficacy of TENS. Considering the inconvenience and the limited efficacy, this treatment was not recommended.

European Federation of Neurological Societies (EFNS) guidelines on neurostimulation therapy for neuropathic pain. [35]

The EFNS stated it was difficult to come to conclusive recommendations for the use of TENS. There were a limited number of patients with ascertained neuropathic pain, diseases, comparators, and the results varied considerably from study to study. Stimulation parameters also vary considerably between the studies, using different pulse waveforms and a wide range of frequencies, in addition to the number and duration of the sessions. They concluded standard high-frequency TENS might be better than placebo (*Evidence Grade = C*). The guideline developers did not draw any conclusion for PNT.

[Stroke Rehabilitation] Clinical practice guidelines for transcutaneous electrical nerve stimulation (TENS) [11]

This guideline does not address the use of TENS for pain relief specifically, but describes TENS for decrease in spasticity, and increase in functional status (motor function, gait speed, passive shoulder range of motion, and sensation).

American Pain Society

In a published guideline from the American Pain Society (APS), it was concluded that there was insufficient evidence to accurately judge the efficacy of TENS versus other interventions for chronic low back pain or for acute low back pain.[36] In a more recent guideline, TENS was not listed as an interventional therapy (as part of an interdisciplinary rehabilitation approach) for patients with low back pain.[37]

National Institute for Health and Clinical Excellence

No specific guidelines were found for TENS from the National Institute for Health and Clinical Excellence (NICE), which provides guidance on health technologies and clinical practice for the National Health Service in England and Wales.

1.4 PREVIOUS TECHNOLOGY ASSESSMENTS

Previous technology assessments concluded there is little evidence of the effectiveness of electrical nerve stimulation in treating both acute and chronic pain. All reviews noted more multi-center, randomized-controlled trials are necessary. The complete report from the most recent HTA is not available in English. The others reflect an older literature base including articles only until the year 2000. Table 5 summarizes the previous assessments.

Table 5. Overview of previous technology assessments of electrical nerve stimulation for pain management.

Assessment (year)	Literature search dates	Device evaluated	Evidence base available*†	Critical Appraisal‡	Comments	Primary Conclusions
Institute for Clinical Effectiveness and Health Policy (2007) *Transcutaneous electrical nerve stimulation (TENS-PENS) for back pain*	through 2006	N/A	• 4 HTAs • 7 SRs • 12 RCTs (% f/u NR); N = NR	yes	HTA in Spanish; only English summary available	**Efficacy:** It has not been categorically demonstrated that the effects of TENS/PENS exceed those of placebo. **Safety:** N/A **Economic:** N/A
The Canadian Coordinating Office for Health Technology Assessment (1995, updated 2006) *Transcutaneous electrical nerve stimulation (TENS) and pain management*	03/1985 to 03/1994	N/A	• 29 RCTs (% f/u NR); N = 1,345; compared TENS with sham treatment, placebo, or narcotic • 15 case series (% f/u NR); N = 2,058	yes	Both acute and chronic pain evaluated; studies found conflicting evidence	**Efficacy**: 13 of 29 RCTs found TENS was significantly more effective at reducing pain, increasing mobility, or decreasing the amount of analgesics required. The remaining 16 studies found no difference. Therefore, good evidence does not exist for the use of TENS for the management of pain.

						Safety: Not addressed. **Economic**: No cost-benefit analysis was available at the time of this report.
Hayes, Inc. (2000) *Transcutaneous electrical nerve stimulation for the treatment of pain.*	1966 to 07/2000	N/A	• 17 RCTs (%f/u NR); N = 1,583; compared TENS with sham treatment, control, or narcotic	not described	Only RCTs were evaluated	**Efficacy:** TENS may provide analgesia in certain situations for some patients; however, there is insufficient scientific evidence from well-designed randomized controlled trials to conclude that TENS is efficacious in pain management. **Safety**: No serious complications have been reported with TENS. **Economic**: Not addressed
Health Technology Assessment NHS R&D HTA Programme (1997) *Systematic review of outpatient services for chronic pain control: Transcutaneous electrical nerve stimulation (chapter 8)*	1966 to 01/1996	N/A	• 55 RCTs (%f/u NR); N = 786, only acute pain studies reported. • 8 reports (%f/u NR); N = 712, only labor pain reported.	yes	Evaluated acute, chronic, and labor pain.	**Efficacy:** TENS is of no value in acute pain. TENS is of possible value in labor pain because it may be used in place of other analgesic interventions. TENS may be beneficial in chronic pain but there is no useful evidence. **Safety**: No serious complications have been reported with TENS. **Economic**: Not addressed

NR: Not Reported
N/A: Not Available
*Percent follow-ups were not given for all RCTs or case series
†N reflects numbers before loss to follow-up
‡Critical appraisal refers to formal evaluation of individual study quality using criteria such as the Jadad or GRADE methods of scoring and the determination of overall strength of evidence.

1.5 MEDICARE AND REPRESENTATIVE PRIVATE INSURER COVERAGE POLICIES

Coverage policies are consistent for electrical nerve stimulation for the Centers for Medicare and Medicaid Services and selected bell-weather payers. The payers will provide coverage for TENS, as long as a disposable or durable medical device is used and certain patient conditions are met. With the exception of CMS and Aetna, payers consider the use of PNT investigational and will not cover this procedure. Table 6 provides an overview of policy decisions.

Medicare (National Coverage Determination)

Electrical nerve stimulation is an accepted modality for assessing a patient's suitability for ongoing treatment with a transcutaneous or an implanted nerve stimulator. Accordingly, program payment may be made for the following techniques when used to determine the potential therapeutic usefulness of an electrical nerve stimulator. The Centers for Medicare and Medicaid Services (CMS) will cover the use of TENS for the relief of acute post-operative pain. TENS may be covered whether used as an adjunct to the use of drugs, or as an alternative to drugs.

- TENS devices, whether durable or disposable, may be used in furnishing this service.
- In cases where TENS is used for longer than 30 days, TENS is then considered used for chronic pain, in which case the device may be covered as durable medical equipment.
- PNT is covered only when performed by a physician or incident to physician's service. If pain is effectively controlled by PNT, implantation of electrodes is warranted.

Aetna

Aetna considers TENS medically necessary durable medical equipment when used as an adjunct or as an alternative to the use of drugs either in the treatment of acute post-operative pain in the first 30 days after surgery, or for certain types of chronic pain not adequately responsive to other methods of treatment including, as appropriate, physical therapy and pharmacotherapy.

Aetna considers percutaneous neuromodulation medically necessary DME for up to a 30-day period for the treatment of members with chronic low back pain secondary to degenerative disc disease when PNT is used as part of a multi-modality rehabilitation program that includes exercise. PNT is considered investigational for the treatment of chronic neck pain and all other indications and is not covered.

Blue Cross/Blue Shield (Regence)

TENS may be considered medically necessary for the treatment of chronic intractable musculoskeletal pain or acute postoperative musculoskeletal pain. A TENS unit is considered not medically necessary for non-musculoskeletal pain including, but not limited to pain associated with headache and visceral or abdominal pain. PNT is considered investigational and is not covered.

Cigna

Cigna covers the use of TENS as medically necessary for either of the following:

- Chronic pain when there is a failure of at least a 30-day trial of conventional medical management including medications and physical therapy.
- As an adjunct to conventional post-operative pain management within 30-days of surgery.

Cigna does not cover the use of PNT devices, because it is considered experimental for the treatment of any condition.

Table 6. Overview of payer technology assessments and policies for electrical nerve stimulation**.**

Payer (year)	Lit search dates	Evidence base available*†	Policy	Rationale/comments
Centers for Medicare and Medicaid Services, #35-46 (2003)	N/A	Not described	(CMS) will cover the use of TENS for the relief of acute post-operative pain. TENS may be covered whether used as an adjunct to the use of	• No rationale for policy stated.

			drugs, or as an alternative to drugs. o TENS devices, whether durable or disposable, may be used in furnishing this service. o In cases where TENS is used for longer than 30 days, TENS is then considered used for chronic pain, in which case the device may be covered as durable medical equipment. o PNT only covered if performed by a physician.	
Aetna Clinical Policy Bulletin, #0011 (2009)	through 2009	• 1 HTA • 2 case series (% f/u NR, 1 month) N = 159 • Listed 41 other references for policy	o Considers TENS medically necessary durable medical equipment when used as an adjunct or as an alternative to the use of drugs either in the treatment of acute post-operative pain in the first 30 days after surgery, or for certain types of chronic pain not adequately responsive to other methods of treatment including, as appropriate, physical therapy and pharmacotherapy o PNT considered medically necessary DME for up to a 30-day period for the treatment of members with chronic low back pain secondary to degenerative disc disease when PNT is used as part of a multi-modality rehabilitation program that includes exercise. PNT is considered investigational for the treatment of chronic neck pain and all other indications and is not covered.	• No rationale for policy stated • CPT codes if selection criteria is met: 64550
BCBS Regence Medical Policy, #11, #44 (2009)	through 2008	• BCBS Medical Policy Reference Manual	TENS may be considered medically necessary for the treatment of chronic intractable musculoskeletal pain or acute postoperative musculoskeletal pain. A TENS unit is considered not medically necessary for non-musculoskeletal pain including, but not limited to pain associated with headache and visceral or abdominal pain. PNT is considered investigational and is not covered.	• No rationale for policy given • CPT codes if selection criteria is met: 64550
Cigna Medical Coverage Policy, #0160 (2008)	through 2008	• 1 HTA • 4 SRs	Cigna covers the use of TENS as medically necessary for either of the following: o Chronic pain when there is a failure of at least a 30-day	• The evidence in the peer-reviewed literature supports the use of TENS for the treatment of pain in the acute post-operative period (i.e.,

			trial of conventional medical management including medications and physical therapy. o As an adjunct to conventional post-operative pain management within 30-days of surgery. o PNT is considered investigational.	within 30 days of surgery) and the use of TENS as a secondary treatment for patients with chronic pain when conventional therapies (e.g., nonsteroidal anti-inflammatory drugs, physical therapy) have failed. TENS is also a well-established treatment modality for these indications • CPT codes if selection criteria are met: 64550

N/A: Not Available
*Medicare and BCBS do not report the current evidence available.
†N reflects numbers before loss to follow-up

1.6 WASHINGTON STATE UTILIZATION AND COST DATA

The following data were provided from the Washington State Health Care Authority and represent estimates for costs and utilization from the Uniform Medical Plan, Labor and Industry and Medicaid.

Devices* by Year

UMP, Medicaid & L&I

HCPCS CODES	2005	2006	2007	2008	Total
E0720 (TENS, 2 lead)	4	15	47	29	**95**
E0730 (TENS, 4 lead)	5,336	6,676	7,485	8,982	**28,479**
Total	**5,340**	**6,691**	**7,532**	**9,011**	**28,574**

*Includes multiple instances, such as rental units

Distinct Patient Counts by Year

UMP, Medicaid & L&I*

HCPCS CODES	2005	2006	2007	2008
E0720 (TENS, 2 lead)	3	7	26	18
E0730 (TENS, 4 lead)	1,792	2,163	2,661	2,998
Total	**1,795**	**2,170**	**2,687**	**3,016**

* 70% of L&I patients receive rental units

Device Payments by Year

UMP, Medicaid & L&I

	2005	2006	2007	2008	Total
Total	**$537,852**	**$655,163**	**$748,314**	**$907,229**	**$2,848,558**

Includes A4365, A4450, A4452, A4455, A4556, A4557, A4558, A4595, A4630, A5120, A5126, A6250, E0720, E0730, E0731, K0739

Per Patient Per Year Costs

UMP, Medicaid & L&I

	2005	2006	2007	2008
Total	**$300**	**$302**	**$278**	**$301**

Total amount divided by distinct patient count.

PT/HCPCS Codes

TENS

Code	Brief Description
HCPCS	
A4365	Adhesive Remover Wipes, any type, per 50
A4450	Tape, nonwaterproof, per 18 square inches
A4452	Tape, waterproof, per 18 square inches
A4455	Adhesive remover or solvent (for tape, cement or other adhesive),
A4556	Electrodes, (For example, apnea monitor), per pair
A4557	Lead wires, (For example, apnea monitor), per pair
A4558	Conductive paste or gel, for use with electrical device
A4595	ENS Supp 2 lead per month
A4630	Repl batt TENS own by pt
A5120	Skin barrier, wipes or swabs, each
A5126	Adhesive or non adhesive; disk or foam pad
A6250	Skin sealants, protectorants, moisturizers, ointments, any type, any size
E0720	TENS, 2 lead
E0730	TENS, 4 lead
E0731	Form-fitting conductive garment for delivery of TENS or NMES
K0739	Repair or nonroutine service for durable medical equipment other than oxygen requiring the skills of a technician, labor component, per 15 minutes.

PENS

BILLING/CODING INFORMATION:

There are no specific CPT codes for PENS or PNT. CPT codes for percutaneous implantation of neurostimulator electrodes (i.e., 64553, 64554, 64555, 64556, 64557, 64558, 64559, 64560, 64561, 64562, 64563, 64564, and 64565) are not appropriate since PENS and PNT use percutaneously inserted needles and wires rather than percutaneously implanted electrodes. The stimulation devices used in PENS and PNT are not implanted so CPT code 64590 is also not appropriate.

Policy Guidelines

The correct CPT code to use for PENS and PNT is the unlisted CPT code 64999. CPT codes for percutaneous implantation of neurostimulator electrodes (i.e., 64553–64565) are not appropriate since PENS and PNT use percutaneously inserted needles and wires rather than percutaneously implanted electrodes. The stimulation devices used in PENS and PNT are not implanted so CPT code 64590 is also not appropriate.

Note: CPT code 64999 (unlisted procedure, nervous system) is most likely not appropriate in the UMP data due to the majority being surgeries of various types.

2. THE EVIDENCE

2.1 SYSTEMATIC REVIEW

Objectives
The primary aim of this assessment was to systematically review, critically appraise and analyze research evidence comparing the efficacy, effectiveness, and safety of electrical nerve stimulation for

the treatment of pain. Available information on the economic impact of this will also be summarized and critically appraised.

2.2 METHODS

Inclusion/exclusion

- **Previously published formal systematic reviews or similar reports** that assessed TENS via critical review and summarization of randomized controlled trials formed the basis of this HTA, with the most recently performed reports considered to be the most up-to-date. Reports that were publicly available or available via Spectrum's contract with the State were used. The report focuses on the most complete and methodologically rigorous systematic reviews, namely Cochrane Reviews.
- **Randomized controlled trials (RCTs) published after the Cochrane Reviews** that assessed TENS via comparison with placebo, control, or other treatments were considered to present a higher level of evidence than non-randomized trials or cohort studies. Thus, RCTs provide the focus for new evidence since Cochrane review publication.
- The inclusion and exclusion criteria for individual **studies published after the currently available Cochrane Reviews** (most recent updates) correspond to those described for each individual review (Appendix C).

Table 7. Inclusion and exclusion criteria for this assessment

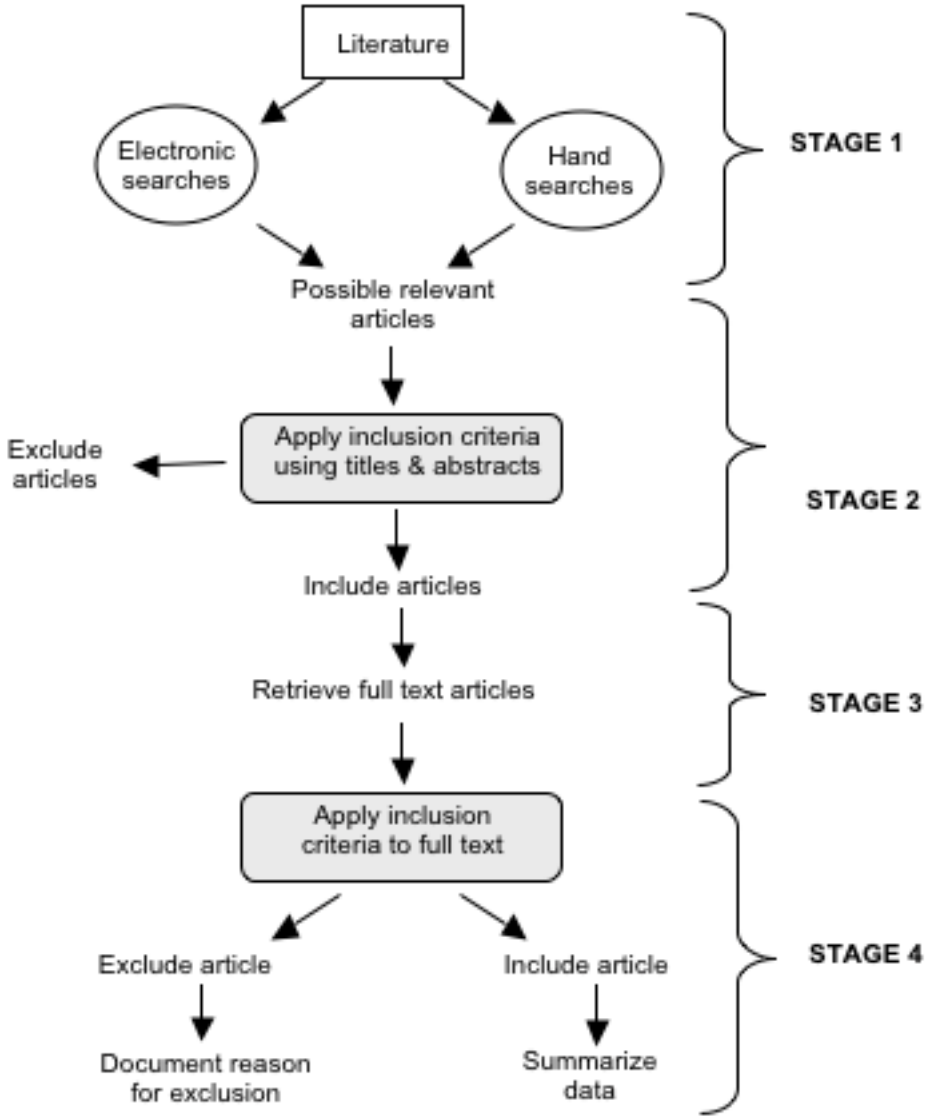
Study Component	Inclusion	Exclusion
Participants	• Patients with acute or chronic pain	· Pediatric populations
Intervention	• Transcutaneous electrical nerve stimulation (TENS) • Interferential current (IFC) therapy • Percutaneous neuromodulation therapy (PNT)	• Percutaneous electrical nerve stimulation (PENS) involving needles • Acupuncture/electroacupuncture • Spinal cord stimulation, deep brain stimulation.
Comparators	• Placebo (sham) TENS • Control (no treatment/routine care) • Pharmacologic interventions • Non-pharmacologic interventions • Other standard forms of ENS	• Invasive techniques (same as intervention exclusions)

Study Component	Inclusion	Exclusion
Outcomes	Studies reporting the following outcomes Primary clinical outcomes • pain intensity (pre- and post-treatment) measured with VAS or other validated pain scales • analgesic consumption Secondary outcomes (if reported) • functional outcomes • patient-reported outcomes: satisfaction with treatment, quality of life Safety • adverse events Economic • economic parameters	
Study Design	• Systematic reviews or meta-analyses of RCTs • Only comparative studies (e.g. randomized controlled trials (RCTs)) are considered for questions 1 and 2. • Formal, full economic studies will be sought for question 3	• For question 1 and 2, studies other than randomized controlled trials have been excluded • Case reports • Case series • Costing studies, partial economic analyses if full economic analyses are available
Publication	• Studies published in English in peer-reviewed journals or publicly available FDA reports • For Key Question 3- Full formal economic analyses (e.g. cost-utility studies) published in English in a peer-reviewed journal published after those represented in previous HTAs.	• Abstracts, editorials, letters • Duplicate publications of the same study which do not report on different outcomes • Single reports from multicenter trials • White papers • Meeting abstracts, presentations or proceedings • Narrative reviews • Articles identified as preliminary reports when results are published in later versions • Incomplete economic evaluations such as costing studies

Data sources and search strategy

The reports and clinical studies included in this report were identified using the algorithm shown in Figure 1 below. The search took place in four stages. The first stage of the study selection process consisted of a comprehensive literature search using electronic means and hand searching. We then screened all possible relevant articles using titles and abstracts in stage two; two individuals did this. Those articles that met a set of *a priori* retrieval criteria based on the criteria above were included. Any disagreement between screeners that were unresolved resulted in the article being included for the next stage. Stage three involved retrieval of the full text articles remaining. The final stage of the study selection algorithm consisted of the selection of those studies using a set of a priori inclusion criteria. Those articles selected form the evidence base for this report.

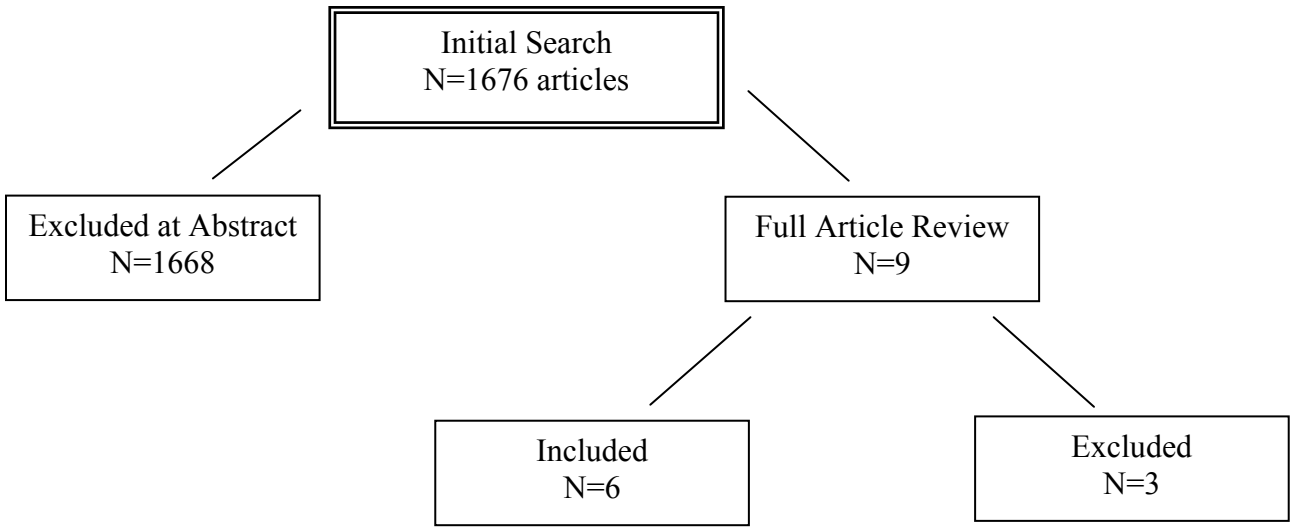
Figure 1. Algorithm for article selection.



For this HTA, the search for new comparative studies was limited to studies published since the most recent updates of each review (1998-2009). Only citations that met the inclusion criteria set *a priori* that had not already been included in a Cochrane review were retained. A list of included Cochrane reviews and studies is found in Appendices C and D.

The Cochrane Review Database was first searched to identify the Cochrane Reviews relevant to this assessment. Following identification of the included Cochrane Reviews, the search strategies from each of the 10 included reviews were re-run to identify RCTs that had been published after the most recent update of each review. Details of the search strategy can be found in Appendix A.

Figure 2. Search Results



Categorization of studies and outcomes
Information from randomized controlled trials presented in the Cochrane Reviews as well as data from studies published afterward were used to evaluate efficacy, effectiveness and safety. Formal economic analyses those that formally evaluate the incremental costs and benefits for outcomes related to treatment efficacy and could include cost-utility analyses, cost-effectiveness analyses and cost-benefit analyses. Studies that provide only costing information are not considered full economic analyses.

The primary intent of TENS in treating pain is relief of that pain and thus is the primary outcome reported in this assessment.

For purposes of this report, the following outcomes are discussed under efficacy and effectiveness for comparative studies of TENS:

- Primary outcomes: pain intensity (pre- and post-treatment)
- Secondary outcomes: patient-reported satisfaction, analgesic consumption, functional outcomes

Pain intensity and pain relief were primarily measured using a visual analogue scale (VAS) or similar tool. Some reports included patient-assessed pain or pain relief, which was typically presented categorically (e.g. rating pain based on categories of 'none' up to 'worst possible pain'). Patient satisfaction with pain relief was also a common outcome, with either yes/no responses or categories reflecting how satisfied patients were after treatment. Concomitant analgesic (pain medication) consumption was collected for some studies either as a yes/no response of whether additional analgesics were needed, as a number of patients requiring additional analgesics, or as the amount of additional analgesics consumed (e.g. number of pills).

With respect to safety, there are few risks reported with TENS treatment. Any reported adverse events (typically skin irritation or pain/tingling at the electrode site) are noted. Outcomes from formal economic analyses would ideally include various incremental cost-effectiveness ratios and related parameters, e.g. cost per quality of life year gained.

Data extraction

Reviewers extracted data from the included previously done Cochrane reviews and new studies for each common outcome of interest where feasible. General characteristics of the Cochrane reviews or randomized controlled trials (RCTs) were abstracted and general population and treatment-specific information were abstracted if provided. Interested readers should consult the original publications for detailed information.

For new clinical studies, the data extracted include: study population characteristics, study type, study interventions, study outcomes, follow-up time, complications, and adverse events.

Study quality assessment: Quality of Cochrane reviews and level of evidence evaluation
Details of assessment of study quality are found in Appendix B.

The method used by Spectrum Research, Inc. (SRI) for assessing the quality of evidence of individual studies as well as the overall quality of evidence incorporates aspects of the rating scheme developed by the Oxford Centre for Evidence-based Medicine[38] precepts outlined by the Grades of Recommendation Assessment, Development and Evaluation (GRADE) Working Group,[39] and recommendations made by the Agency for Healthcare Research and Quality (AHRQ).[40]

Table 8. Definition of the different levels of evidence for articles on therapy.

Level	Study type	Criteria
I	Good quality RCT	• Concealment • Blind or independent assessment for important outcomes • Co-interventions applied equally • F/U rate of 85% + • Adequate sample size • Intent-to-treat
II	Moderate or poor quality RCT	• Violation of one or more of the criteria for a good quality RCT
	Good quality cohort	• Blind or independent assessment in a prospective study, or use of reliable data* in a retrospective study • Co-interventions applied equally • F/U rate of 85% + • Adequate sample size • Controlling for possible confounding†
III	Moderate or poor quality cohort	• Violation of any of the criteria for good quality cohort
	Case-control	
IV	Case-series	

†Authors must provide a description of robust baseline characteristics, and control for those potential variables associated with outcome that are unequally distributed between treatment groups.

The methodological characteristics of previously published Cochrane reviews were assessed using a checklist that incorporates aspects of the AMSTAR checklist[41] and areas for critical appraisal outlined by "Users Guides" developed by the evidenced –based working groups at McMaster University[29] (See Appendix B).

Table 9. Assessment checklist for HTAs, systematic reviews and meta-analyses.

Methodological Principle*	
Purpose, aim, study question, and/or hypothesis stated	
Literature search described	
Unpublished sources sought	
Inclusion/exclusion criteria stated	
Characteristics of included studies provided	
Quality of included studies formally assessed and method described	
Overall quality of included studies (LoE) given primary purpose/aim	
Quantitative analysis	
• Studies appraised critically	
• Magnitude and direction of effect sizes evaluated	
• Consistency of effect sizes evaluated	
• Stability of effect sizes (e.g. confidence intervals) evaluated	
• Scientific quality of studies considered in conclusions	
• Methods to enhance objectivity incorporated	
Quantitative analysis	
• Heterogeneity evaluated	
• Heterogeneity explored, if present	
• Missing data handled appropriately	
• Effect sizes pooled appropriately	
• Sensitivity analysis conducted	
• Publication bias explored	
Potential conflict of interest stated	

It was beyond the scope of this report to evaluate individual studies described in previous HTAs or meta-analyses. Therefore, since Cochrane reviews use randomized trials as their basis, the overall quality of the included studies was considered to be LoE I or II.

There is no universally accepted, standardized approach to critical appraisal of economic evaluation studies. The criteria described in the Quality of Health Economic Studies (QHES) tool[42] provided a basis for the critical appraisal of included economic studies and was augmented with the application of epidemiologic appraisal precepts (see Appendix B). The QHES employs widely accepted criteria for appraisal, such as choice and quality of cost and outcomes measures, transparency of model and presentation, use of incremental analysis, uncertainty analysis, and discussion of limitations and funding source and was primarily used to facilitate description of primary strengths and limitations of the studies. A weighted global score can be obtained based on these measures with a possible range of scores from 0 (worst) to 100 (best), theoretically providing a common metric to compare study quality. This tool and the weighted score have not yet undergone extensive evaluation for broad use but provide a valuable starting point for critique.
Two individuals critically appraised each study independently using the QHES. Discrepancies were resolved by discussion to arrive at a final appraisal. In addition, elements of critical appraisal consistent with epidemiologic principles and evaluation of bias (e.g., selection bias) were applied.

Evaluation of the overall strength of evidence across studies for specific key questions, considers the quality and quantity of available studies as well as the consistency of study estimates.

DATA ANALYSIS

2.3 QUALITY OF LITERATURE AVAILABLE

The literature search for recent RCTs resulted in 9 potentially relevant citations for reports or studies using search strategies outlined in Appendix A. Most of the 1676 articles identified in the search strategy were excluded at the abstract level because they were irrelevant, had already been included or excluded from the Cochrane Reviews, or it was evident at the abstract-level that they did not meet inclusion criteria for the assessment.

A total of four HTAs or similar reports were found.[43-45] [46] They are summarized in section 1.4. The complete report for the most recent evaluation (2007) is not available in English. The other HTAs are older with literature up to the year 2000 represented. Thus, the Cochrane Reviews represent the most up to date evidence available and are therefore the basis of this report.

Eleven Cochrane reviews were found, however, one on chronic headache pain was excluded because TENS was given as part of a multimodal treatment (concurrently with other therapies, so it would not be possible to tease out the effect of TENS alone). Based on these reports for purposes of this assessment, conditions considered under acute pain included: labor pain; primary dysmenorrhea; and a general review of TENS for acute pain, which included procedural pain procedures (cervical laser treatment, office hysteroscopy, screening flexible sigmoidoscopy, flexible cystoscopy and venipuncture), hemophiliac pain, acute trauma (e.g. sprains or fractures), postpartum uterine contraction, acute oro-facial pain, post thoracotomy, rib fractures, and neuropathic pain. Conditions considered under chronic pain included: low back pain, osteoarthritis of the knee; rheumatoid arthritis in the hand; cancer pain; neck disorders; post-stroke shoulder pain; and a general review of TENS for chronic pain, which included rheumatoid arthritis, osteoarthritis, pancreatitis, myofascial pain, diabetic neuropathy, and LBP.

Randomized controlled trials that were published since the most recent Cochrane review updates, that met the inclusion criteria, examined TENS for the treatment of pain due to: labor, primary dysmenorrhea, chronic low back pain, and osteoarthritis of the knee. These studies included comparisons of TENS to control, placebo, interferential current (IFC), and hyaluronic acid injection and one study comparing percutaneous neuromodulation therapy (PNT) to placebo PNT.

Quality of studies retained: Cochrane reviews

All of the reports were based on data from RCTs. Summaries of the methodological quality of each Cochrane Review are provided below.

The most common limitation of the reviews was variability across trials in not only what outcomes the studies assessed, but also how they were assessed. For example, while some studies used a visual analogue scale to measure pain intensity, others used a numerical rating scale or frequency of analgesic use to qualify changes in pain status. Such differences, combined with clinical heterogeneity across studies precluded use of formal meta-analysis for some conditions. Some reviews provided descriptions of study findings but little or no numerical data.

Six out of 10 included reviews performed meta-analyses, and for most of these they could only do so for a portion of the outcomes due to the heterogeneity across studies with respect to treatment characteristics and outcomes reported.

Table 10. Study quality assessment: Cochrane reviews of acute pain, labor pain, primary dysmenorrhea.

	Walsh	Dowswell	Proctor
Methodological Principle*			
Purpose, aim, study question, and/or hypothesis stated	■	■	■
Literature search described	■	■	■
Unpublished sources sought	■		■
Inclusion/exclusion criteria stated	■	■	■
Characteristics of included studies provided	■	■	■
• Quality of included studies formally assessed and method described		■	■
• Overall quality of included studies (LoE) given primary purpose/aim	LoE I/II	LoE I/II	LoE I/II
Qualitative analysis			
• Studies appraised critically	■	■	■
• Magnitude and direction of effect sizes evaluated	■	■	■
• Consistency of effect sizes evaluated	■	■	■
• Stability of effect sizes (e.g. confidence intervals) evaluated	■	■	■
• Scientific quality of studies considered in conclusions	■	■	■
• Methods to enhance objectivity incorporated	■	■	■
Quantitative analysis			
• Heterogeneity evaluated *	NA	■	■
• Heterogeneity explored, if present	■	■	■
• Missing data handled appropriately			
• Effect sizes pooled appropriately	■	■	■
• Sensitivity analysis conducted	■		■
• Publication bias explored			
Potential conflict of interest stated			

** refers only to reviews that conducted meta-analyses of the data*

Table 11. Study quality assessment: Cochrane reviews of chronic pain, chronic LBP, osteoarthritis of the knee and rheumatoid arthritis in the hand.

	Nnoaham	Khadilkar	Brosseau	Osiri
Methodological Principle*				

Purpose, aim, study question, and/or hypothesis stated	■	■	■	■
Literature search described	■	■	■	■
Unpublished sources sought		■	■	■
Inclusion/exclusion criteria stated	■	■	■	■
Characteristics of included studies provided	■	■	■	■
Quality of included studies formally assessed and method described	■	■	■	■
Overall quality of included studies (LoE) given primary purpose/aim	LoE I/II	LoE I/II	LoE I/II	LoE I/II
Qualitative analysis				
• Studies appraised critically	■	■	■	■
• Magnitude and direction of effect sizes evaluated		■	■	■
• Consistency of effect sizes evaluated		■		■
• Stability of effect sizes (e.g. confidence intervals) evaluated		■		■
• Scientific quality of studies considered in conclusions	■	■	■	■
• Methods to enhance objectivity incorporated	■	■	■	■
Quantitative analysis				
• Heterogeneity evaluated *	NA	NA	NA	■
• Heterogeneity explored, if present				■
• Missing data handled appropriately				
• Effect sizes pooled appropriately				■
• Sensitivity analysis conducted				■
• Publication bias explored				
Potential conflict of interest stated				

** refers only to reviews that conducted meta-analyses of the data*

Table 12. Study quality assessment: Cochrane reviews of cancer pain, chronic headache, neck disorders, and post-stroke shoulder pain

	Robb	Kroeling	Price
Methodological Principle*			
Purpose, aim, study question, and/or hypothesis stated	■	■	■
Literature search described	■	■	■
Unpublished sources sought		■	■
Inclusion/exclusion criteria stated	■	■	■
Characteristics of included studies provided	■	■	■
Quality of included studies formally assessed and method described	■	■	■
Overall quality of included studies (LoE) given primary purpose/aim	LoE I/II	LoE I/II	LoE I/II
Qualtitative analysis			
• Studies appraised critically	■	■	■
• Magnitude and direction of effect sizes evaluated		■	■
• Consistency of effect sizes evaluated		■	■

	Robb	Kroeling	Price
Methodological Principle*			
• Stability of effect sizes (e.g. confidence intervals) evaluated		■	■
• Scientific quality of studies considered in conclusions	■	■	■
• Methods to enhance objectivity incorporated	■	■	■
Quantitative analysis			
• Heterogeneity evaluated *	NA	NA	■
• Heterogeneity explored, if present			■
• Missing data handled appropriately			
• Effect sizes pooled appropriately			■
• Sensitivity analysis conducted			■
• Publication bias explored			
Potential conflict of interest stated	■ *		

† Although not involved in the review of her own paper, one of the reviewers is lead author on one of the included studies.

QUALITY OF STUDIES RETAINED: NEW CLINICAL TRIALS

Randomized controlled trials published after the Cochrane reviews were all LoE II and III.

Table 13. Study quality assessment: New studies on acute pain (labor, primary dysmenorrhea).

Methodological Principle	Borup	Tugay
Study design		
Randomized controlled trial	■	■
Cohort Study		
Case-series		
Statement of concealed allocation*	■	
Intent-to-treat*	■	
Independent or blind assessment		
Co-interventions applied equally		■
Complete follow-up of ≥85%		■
Adequate sample size	■	■
Controlling for possible confounding	■	
Evidence Class	**II**	**II**

.

Table 14. Study quality assessment: New studies on chronic pain

Methodological Principle	Kofotofolis	Itoh	Paker	Kang
Study design				
Randomized controlled trial	■ *	■		■
Cohort Study			■ **	

Case-series				
Statement of concealed allocation			■	■
Intent-to-treat	■			
Independent or blind assessment			■	■
Co-interventions applied equally		■	■	■
Complete follow-up of ≥85%	■		■	■
Adequate sample size	■		■	■
Controlling for possible confounding	■	■		■
Evidence Class	**II**	**II**	**III**	**II**

* *Quasi-randomized; sequential allocation.*

*** Investigators used 'simple charts' to randomly assign patients to groups; no details provided.*

2.4 OUTCOME MEASURES

The reviews and studies included in this assessment used many different measures to assess outcomes after treatment. The 100-mm visual analogue scale and 10-point verbal scale were the most commonly used tools for assessing pain intensity and pain relief. Visual and verbal pain scales are used in studies of pain treatment as a tool for quantifying pain relief or improvement between pre- and post-treatment measurements; the changes in pain intensity are compared between treatment groups.

The *visual analogue scale (VAS)* comes in many variants, the most common of which are lines (often 100 millimeters in length) with the left and right ends labeled 'no relief of pain' and 'complete relief of pain', respectively. The ends can alternatively be labeled as 'no pain' and 'worst possible pain'. Patients are instructed to mark the line at the point that represents their pain. The scores are then determined by measuring the distance between 0 (no relief) and the patient's mark. The VAS is the preferred method for assessing pain intensity, as it is relatively easy to use and score, avoids imprecise descriptive terms and provides a wide range for patients to choose from when describing their pain.

Verbal numerical scales correlate well with 100mm VAS scores.[47] Verbal numerical scales usually range from 0 to 10. With respect to pain intensity, 0 corresponds to 'no pain' and 10 corresponds with 'maximum possible pain'. Alternatively, when measuring pain relief, 0 corresponds with 'no relief' and 10 with 'complete relief. A few of the studies included in this assessment used a numerical rating scale rather than the VAS.

Standardized mean difference

The values reported in the pain scales described above are used not only to quantify pain intensity and pain relief within patients, but also to compare outcomes between patients. One way to do this is by calculating the absolute benefit, or the improvement in the treatment group less the improvement in the control (comparison) group. The standardized mean difference, referred to as *d*[48] is useful for comparing treatment groups across studies as in meta-analyses. The standardized mean difference is calculated as the difference in means between treatment groups, divided by the pooled standard deviation of the measurements.[49] By this transformation, the outcome becomes dimensionless and the scales become uniform (e.g., for the same degree of pain, values measured on a 100-mm analog scale would be expected to be 20 times larger than values measured on a 5-point ranking scale) but the standard deviation would also be expected to be 20 times larger. The standardized mean difference is useful for comparing studies that measure the same outcomes, but use different methods to do it.

Similar to the standardized mean difference is the weighted mean difference, which is also used in meta-analyses to compare treatment groups across studies. The mean differences in outcome between the groups being studied are weighted to account for different sample sizes and differing precision between studies (large studies with greater precision are assigned higher weights). Unlike the standardized mean difference, the weighted mean difference is an absolute number that takes on the units of the original outcome measure.

The Cochrane reviews presented in this report most commonly report the standardized mean difference to compare treatment groups. Interpretation is not necessarily intuitive, but the standardized mean difference measures the size of the treatment effect in terms of the standard deviation. For example, an estimate of 0.5 indicates that the treatment changed the mean by half of a standard deviation; similarly, an estimate of 1.0 indicates that the size of the treatment effect is equal to one whole standard deviation.

Clinical importance
Statistical significance (in differences between treatment groups) is only one criterion used to judge whether an outcome is clinically important. Although outcomes might be statistically different between two treatment groups, however, this does not necessarily translate to clinically important differences in outcome.

Clinical importance is defined in the literature in many difference ways – it depends not only on the conditions and outcomes being assessed, but also the opinions of individual investigators or clinical panels. The American College of Rheumatology defines clinical improvement in rheumatoid arthritis as ≥20% improvement in tender or swollen joints in combination with ≥20% improvement in 3 of 5 other outcomes (patient pain, patient global assessment, physician global assessment, patient self-assessed disability, acute-phase reactant).[50] A 15% improvement is recommended by the Philadelphia Panel as a minimally important change for back pain.[11, 30, 51]. Other researchers use 50% relief as the outcome to derive relative efficacy of analgesics McQuay et al.[52], and still others recommend a cut-off of 30% relief because this is the level of relief below which it has been observed that patients need to remedicate.[53]

When interpreting standardized mean deviations in terms of clinical importance, there are some rules of thumb. The most widely used is that by Cohen[48], even though it was originally intended for the social sciences. In this interpretation, an SMD value of 0.2 represents a small effect, 0.5 a moderate effect, and 0.8 a large effect. It is important to note, however, that this interpretation reflects only the magnitude of the effect size. Interpretation of both the statistical significance and clinical importance should be taken in context, with consideration for patient and physician beliefs important outcomes.

Categorical scales involve the patient picking the most appropriate word to describe their pain. The number of words and exact wording used can differ across research groups. Many groups use four words (none, mild, moderate and severe) to describe pain intensity, while others use five categories (none, slight, moderate, good or lots, and complete) to describe pain relief. To score the results, numbers are assigned to each of the verbal categories (i.e. for pain relief, non = 0, mild = 1, moderate = 2, severe = 3; and for pain relief, none = 0, slight = 1, moderate = 2, good or lots = 3, complete = 4).[44] The data can now be combined across individuals to allow comparison between treatment groups (e.g. means and standard errors). Quantified categorical measurements correlate well with VAS measurements, however, the limited number of categories may not allow for an entirely accurate description of a patient's pain. In the studies presented here, success of treatment was sometimes based on more global questions asked of the patients such as "how satisfied are you with your pain relief" or "would you use this treatment again." Categorical outcomes were assessed in the reviews and studies included here in addition to, or in some cases in place of, the visual analogue scale or similar tool.

Outside of pain relief itself, another goal of electrical nerve stimulation is to reduce a patient's need for analgesic medications. Pain medications such as non-steroidal anti-inflammatory drugs and narcotics, both of which often have potential side effects associated with their use. To this end, analgesic consumption was a secondary outcome assessed in some of the studies that allowed for concomitant medication use.

Functional and quality of life outcomes were also compared between treatment groups. The functional outcomes were often specific to the condition being treated. For instance, passive humeral lateral rotation is a functional outcome that was used to measure shoulder restriction; trunk extension range of motion, dynamic endurance of trunk flexion and static endurance of trunk extension were used to measure functional outcomes in patients with chronic low back pain.

Validated questionnaires were also used by many studies to assess pain, function and quality of life; these include:

- *McGill Pain Questionnaire*: This questionnaire consists primarily of 3 major classes of word descriptors--sensory, affective and evaluative--that are used by patients to specify subjective pain experience. It also contains an intensity scale and other items to determine the properties of pain experience.

- *Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) Questionnaire*: This is a self-administered test that yields summary scores for pain, stiffness, and level of physical function limitation.

- *Roland-Morris Disability Questionnaire (R-MDQ)*: This questionnaire awards a point for questions answered affirmatively, with higher scores equating with greater disability.

- *Lequesne Index:* used to assess pain and limitation in function of the patient with knee OA (1-4, mild; 5-7, moderate; 8-10, severe; 11-13, very severe; >=14, extremely severe). Valid and reproducible test that is easy and quick to perform and useful for follow-up of patients with knee OA.

- The SF-36 is a health survey that consists of 8 subscales and a total of 36 questions; it is used to evaluate the physical and mental health of patients.

3. RESULTS

3.1 KEY QUESTION 1: What is the evidence of efficacy and effectiveness of TENS for the treatment of acute and chronic pain?

ACUTE PAIN

Acute Pain

A 2009 Cochrane Review by Walsh, et al.[5] looked at acute pain as whole. Conditions included in the review were: procedural pain procedures (cervical laser treatment, office hysteroscopy, screening flexible sigmoidoscopy, flexible cystoscopy and venipuncture), hemophiliac pain, acute trauma (e.g. sprains or fractures), postpartum uterine contraction, acute oro-facial pain, post thoracotomy, rib fractures, and neuropathic pain.

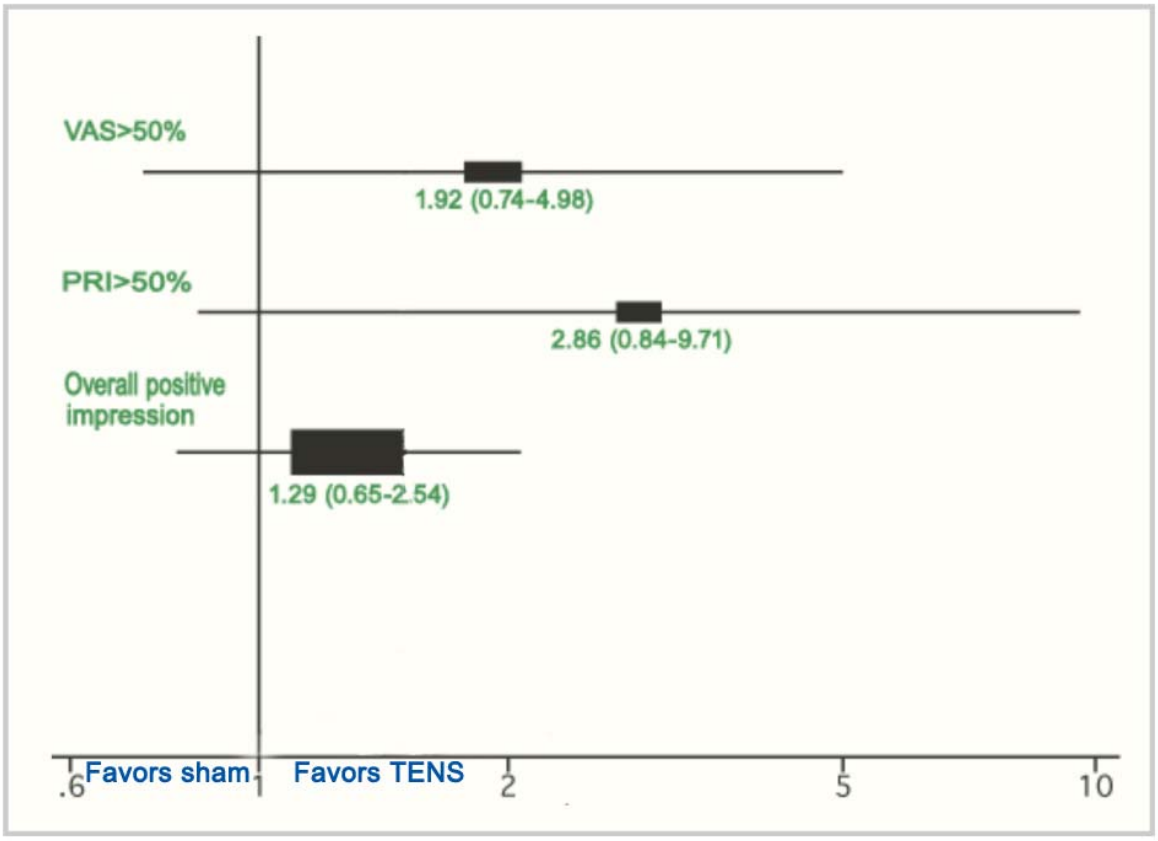
For six of the twelve studies included in this review, it was not possible to extract data. The authors cite that extraction was not possible due to the way data were presented (e.g. median and interquartile range), ambiguity of the data presented, and mixed age groups that included participants under the age of 16. The remaining six studies were too heterogeneous to allow for meta-analysis, so data were presented separately for each. Note that for continuous outcomes, weighted mean differences were used for outcomes given on the same scale and standardized mean differences when the outcomes were presented on difference scales. The reviewers, however, refer to both of these simply as mean differences

The authors of this Cochrane Review drew the following conclusions when all studies of TENS for treatment of acute pain were taken as a whole. Heterogeneity prevented meta-analysis, so each comparison reflects evidence from individual studies:

- *TENS versus sham TENS*
  - There was no significant difference in 50% improvement in visual analogue scale or pain rating index when measured post-treatment in two studies (62 and 36 patients, respectively).
  - Similarly, in a study of 30 patients, neither VAS pain intensity or overall patient impression (excellent/good rating) were significantly different post-treatment between TENS and sham patients.
  - Pain intensity measured using a numerical rating scale during a procedure did not significantly differ between groups in a study of 60 patients.
  - The only significant difference between TENS and sham TENS for the treatment of acute pain was seen after two days of treatment in a study of 50 patients.
- *High amplitude TENS versus low amplitude TENS*
  - Pain intensity during a procedure did not differ significantly between the two groups in a study of 60 patients.
- *High amplitude TENS versus no treatment control*
  - Patients treated with high amplitude TENS had significantly lower VAS pain scores and were less likely to report severe/worst possible discomfort post-treatment than patients treated with low amplitude TENS (1 study, n=20).
- *Conventional TENS versus AL-TENS*
  - There was no significant difference in 50% improvement in VAS when measured post-treatment.

There was no significant difference between treatment with TENS or placebo with respect to post-treatment pain relief defined as a >50% improvement in VAS (1 study, n=62) or pain rating index (PRI) (1 study, n=36). The review authors presumed assessment to be immediate, but it was not explicitly indicated in the studies. Reporting of an overall positive impression with TENS was also similar between TENS and placebo (1 study, n=30) [Figure 3]

Figure 3. Risk ratios for pain reduction of at least 50% and patient rating of excellent/good comparing TENS with sham TENS post-treatment based on three studies (one study per comparison).[2]

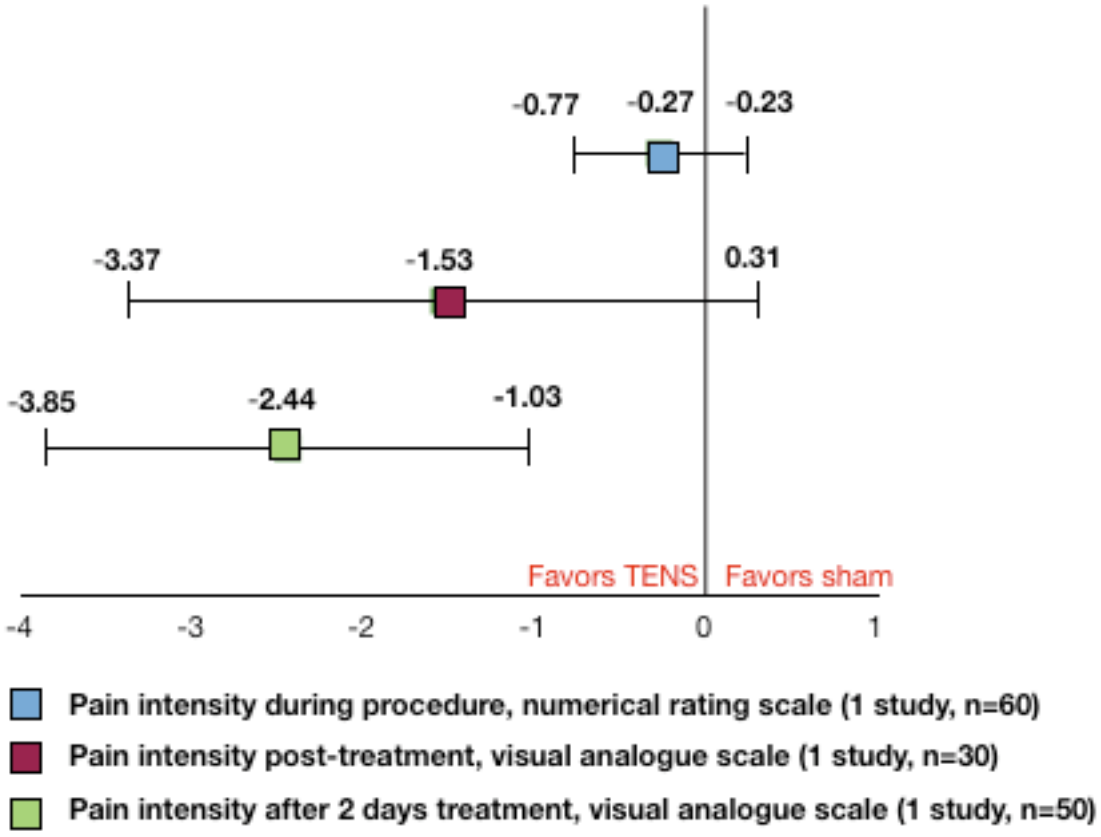


* Pain reduction of at least 50% as measured with VAS (1 study, n=62) or pain rating index (1 study, n=36). Overall positive impression with TENS was defined a rating of excellent/good on a 4-category scale (1 study, n=30).

** Each data point represents the risk ratio, or the likelihood of an outcome in the TENS group relative to the likelihood in the sham group. Any value above 1 for these comparisons favors treatment with TENS over treatment with sham. When the 95% confidence interval crosses 1.0 (indicating similar risk between the two groups), then any difference between the groups is not statistically significant.

There was no statistically significant difference in pain intensity either during a procedure or post-treatment (presumed to be immediate, but not explicitly indicated) measured using a numerical rating scale (NRS) and VAS, respectively. The mean difference in pain intensity between TENS and sham was -0.27 (95% CI -0.77, 0.23) during the procedure in one study with 60 patients and -1.53 (95% CI -3.37, 0.31) post-treatment in another study with 30 patients. The only statistically significant difference reported between TENS and sham procedure was at two days post-treatment (mean difference -2.44, 95% CI -3.85, -1.03) in a third study of 50 patients. When looking at mean differences, results are statistically significant when the confidence interval excludes zero [Figure 4].

Figure 4. Mean difference in pain intensity between TENS and placebo, measured during a procedure, immediately post-treatment, or after 2 days of treatment using a numerical rating scale (NRS) or visual analogue scale (VAS).[2].

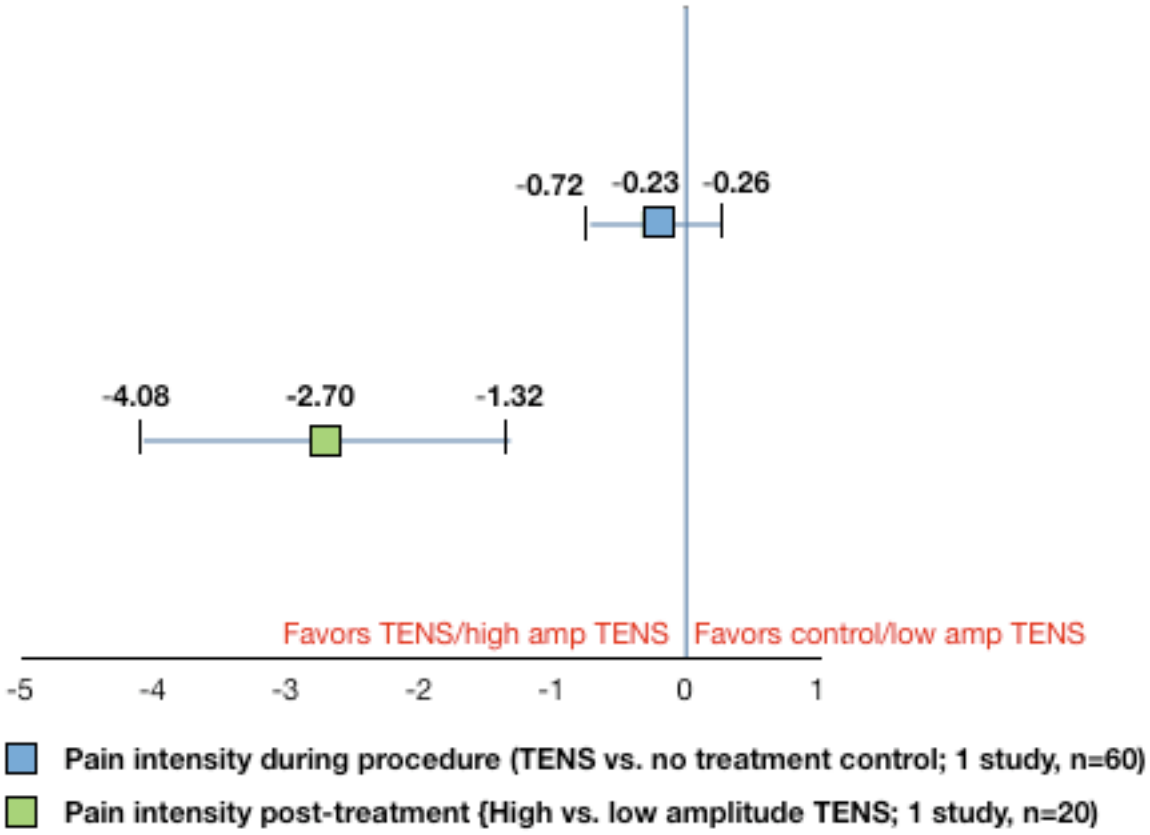


* Each data point represents the mean difference with 95% confidence interval for pain scores (at that particular time point) between TENS and sham groups. Any estimates to the left of 0 indicate lower pain scores with TENS treatment than with sham treatment. If the 95% confidence interval crosses 0 (mean difference = 0), then any difference between the groups is not statistically significant.

The same review of acute pain included three other studies comparing conventional TENS to other modalities. The figure below summarizes the mean difference in pain intensity at two different time points for two of these studies, only one of which reports a statistically significant result.

- In a study of TENS compared to a no treatment control, pain intensity during the procedure did not differ between the groups (mean difference: -0.23, 95% CI -0.72, 0.26).
- When high amplitude (intensity) TENS was compared to low amplitude TENS, high amplitude TENS showed significantly greater pain relief post-treatment (mean difference: -2.70, 95% CI -4.08, -1.32) [Figure 5].
- In the one comparison of conventional (high frequency) TENS to ALTENS (low frequency), there was no difference in VAS>50% pain relief post-treatments (RR 0.71, 95% CI 0.32, 1.54) [not shown].

Figure 5. Mean difference in pain intensity for comparisons of TENS vs. control and high vs. low amplitude TENS, measured either during a procedure or post-treatment using a numerical rating scale or visual analogue scale.[2]



* Each data point for the TENS vs. no treatment control comparison represents the mean difference and 95% confidence interval for pain scores during a procedure; for the high amplitude vs. low amplitude TENS comparison, each data point represents mean difference for pain relief. Any estimates to the left of 0 indicate lower pain scores for the TENS and high amplitude TENS groups than their comparators. If the 95% confidence interval crosses 0 (mean difference = 0), then any difference between the groups is not statistically significant.

Citing methodological issues of inadequate sequence generation, lack of blinding, and incomplete follow-up, the reviewers concluded that there is little evidence of a benefit with use of TENS for acute pain.

Labor Pain

In a separate Cochrane review,[6] a total of 19 studies comparing conventional TENS and acupuncture-like TENS (ALTENS) with placebo (sham TENS), control (no treatment; routine care), and pharmacologic treatment for the control of labor pain were included. Fifteen examined TENS applied to he back, two to acupuncture points and two to the cranium. Study sample sizes ranged from 20 to 300 women. Outcome definitions and measurements varied across studies. In addition to these studies a recent RCT of 607 women was identified; 314 of these women received acupuncture as an intervention, leaving 293 women who were eligible for inclusion in this assessment.

Based on their analysis, the authors of this Cochrane Review concluded the following:

- *TENS versus sham TENS or control*
  - There were no differences with respect to measures of pain relief or labor and delivery outcomes who had TENS treatment applied to their back. Women treated with TENS, however, were 54% more likely to use it again in a future labor than women treated with sham or control (4 studies, n=583).
- *TENS applied to acupressure points versus sham TENS*
  - Women treated with TENS applied to acupuncture points, on the other hand, were significantly less likely to report severe pain during labor (2 studies, n=190), were 5 times as likely to be satisfied with their pain relief (1 study, n=100), and 25% more likely to use TENS in a future labor (1 study, n=90).
- *TENS versus pharmacologic relief*
  - Pain scores were not reported, but there were no significant differences between the groups in patient satisfaction with pain relief.
  - The one reported advantage of TENS was a statistically significant decrease in duration of the second stage of labor.
- *TENS or cranial TENS plus epidural versus epidural alone*
  - There were no significant differences in pain or delivery outcomes when TENS was used in combination with epidural versus epidural alone.
  - In a study of cranial TENS plus epidural versus epidural alone, most pain and labor outcomes did not significantly differ between the groups; duration of pain relief from first injection, the one exception, was significantly longer for those women treated with cranial TENS.
- *Recent evidence from an RCT*
  - In a study of 144 women treated with TENS and 149 women treated with placebo, there were no statistically significant differences between the groups with respect to pain scores at any point during labor or covering the entire delivery or number of women needing epidural analgesia.

When TENS was applied to the back and compared to sham TENS or control (routine care) to control labor pain, there were no significant differences reported in pain score or reports of severe pain during labor, analgesic consumption, need for an epidural, or satisfaction with pain relief. When asked if they would use their assigned treatment in a future labor, however, more women in the TENS group said they would (RR 1.54, 95% CI 1.31, 1.80) [Table 15].

When applied to acupuncture points, TENS was shown to reduce severe pain during labor (RR 0.41, 95% CI 0.32-0.55) and lead to higher patient satisfaction (RR 4.81, 95% CI 1.81, 9.29) than sham or control. More women in the acu-point TENS group reported that they would use their assigned treatment in a future labor (RR 1.45, 95% CI 1.18, 1.79) [Table 15].

Table 15. TENS vs. sham TENS or control for labor pain: Pain- and satisfaction-related outcomes, with TENS applied either to the back or acupuncture points.[36]

	No. studies	N	RR (95% CI)	SMD (95% CI)	Favors TENS
Back					
Severe pain in labor *	2	147	0.77 (0.60, 1.00)		- [†]
Mean pain score in labor *	2	299		-0.16 (-0.39, 0.07)	-
Other analgesics needed *	5		0.88 (0.76, 1.01)		-
Analgesic consumption	2	358		-0.09 (-0.33, 0.14)	-
Epidural required	5	571	0.99 (0.59, 1.67)		-
Satisfied with pain relief *	5	452	1.25 (0.98, 1.60)		-
Would use TENS again	4	583	1.54 (1.31, 1.80)		+
Acu-points					
Severe pain in labor *	2	190	0.41 (0.32, 0.55)		+
Epidural required	1	100	0.40 (0.08, 1.97)		-
Satisfied with pain relief *	1	90	4.81 (1.81, 9.29)		+
Would use TENS in future	1	100	1.45 (1.18, 1.79)		+

* measured with different definitions and pain scales; + = favors TENS, - = favors placebo or control.

When looking at labor and delivery outcomes, there were no differences in need for caesarean section, assisted delivery, augmentation of labor, duration of the 1st or 2nd stage of labor, satisfaction with their labor/delivery, or fetal distress between TENS and sham or control. One exception was that women receiving TENS at acupuncture points were more likely to have an assisted delivery (RR 4.5, 95% CI 1.02, 19.79) based on a single study. The sample size and width of confidence interval, however, suggest that this may not be a stable effect estimate [Table 16].

Table 16. TENS vs. sham TENS: Labor and delivery outcomes, with TENS applied either to the back or acupuncture points.[36]

	No. studies	N	RR (95% CI)	SMD (95% CI)	Favors TENS
Back					
Caesarean section rate	8	868	1.35 (0.84, 2.17)		-
Assisted delivery	7	840	0.82 (0.56, 1.19)		-
Augmentation of labor	1	194	0.86 (0.59, 1.25)		-
Duration of 1st labor stage, min	3	318		14.10 (-36.73, 8.53)	-
Duration of 2nd labor stage, min	3	318		0.59 (-12.21, 12.39)	-
Satisfaction with labor/delivery	1	24		0.34 (-0.47, 1.15)	-
Fetal distress	1	200	0.33 (0.01, 8.09)		-
Acu-points					
Caesarean section rate	1	100	1.5 (0.26, 8.60)		-
Assisted delivery	1	100	4.5 (1.02, 19.79)		+
Augmentation of labor	1	100	0.93 (0.78, 1.11)		-
Duration of 1st labor stage, min	2	190		-55.77 (-170.30, 58.76)	-
Duration of 2nd labor stage, min	1	95		-3.0 (-14.87, 8.87)	-
Fetal distress	1	100	1.0 (0.06, 15.55)		-

* + = favors TENS, - = favors placebo or control.

In comparisons of TENS to pharmacologic relief (3 studies, n=325) pain scores were not reported, but there were no differences between the groups in patient satisfaction with pain relief. The one reported advantage of TENS was a decreased duration of the second stage of labor (SMD -2.20, 95% CI -3.64, -0.76) This result was presented in only one study and should be confirmed by additional studies [Table 17].

Table 17. TENS to the back vs. pharmacologic relief for treatment of labor pain.[36]

	No. studies	N	RR (95% CI)	SMD (95% CI)	Favors TENS
Satisfied with pain relief *	3	304	0.95 (0.80, 1.13)		-
Assisted delivery	1	200	0.20 (0.01, 4.11)		-
Duration of 1st labor stage, min	2	290		-92.54 (-272.43, 87.36)	-
Duration of 2nd labor stage, min	1	200		-2.20 (-3.64, -0.76)	+
Fetal distress	1	200	0.20 (0.01, 4.11)		-

* measured with different definitions and pain scales; + = favors TENS, - = favors placebo or control

.
When TENS was used in combination with epidural was compared to epidural alone, there were no differences in pain or delivery outcomes. In another study of cranial TENS plus epidural versus epidural alone, there was no significant difference for most comparisons. Duration of pain relief from first injection was, however, longer for those treated with cranial TENS (SMD, minutes: 22.00, 95% CI 9.09, 34.91).

Most of the studies included in this review were unclear about sequence generation and allocation concealment. In addition, several studies had unbalanced study groups (e.g. number of patients per group, characteristics such as parity). Lack of blinding, or lack of information on blinding, was prevalent. Although there is some evidence that women using TENS in labor are less likely to rate their pain as severe, the evidence is neither strong nor consistent.

Recent evidence

In a 2009 randomized trial by Borup et al.[54], patients treated with TENS or acupuncture for labor pain were compared to controls. The controls could choose between traditional analgesics of sterile water papules, nitrous oxide, warm tub bath, pethidine [British Pharmacopeia name for meperidine (Demerol)] or epidural analgesia. These traditional analgesics were also provided on request to the intervention groups if they requested supplemental analgesia. Participants recorded the degree of pain just before randomization, 1 hour after randomization, and subsequently every 2 hours until the baby was born; a final recording was made 2 hours after delivery assessing the woman's total pain experience. Two months after delivery, participants completed a questionnaire about their experience and satisfaction with delivery, pain relief, and possible side effects of the analgesics used. Birth experience assessed by 14 different questions adapted from a Canadian study.

Among 144 women treated with TENS and 149 women treated with placebo, there were no statistically significant differences between the groups with respect to pain scores at any point during labor or covering the entire delivery or number of women needing epidural analgesia. This study does not influence the interpretation of the evidence presented in the Cochrane Review.

Primary Dysmenorrhea

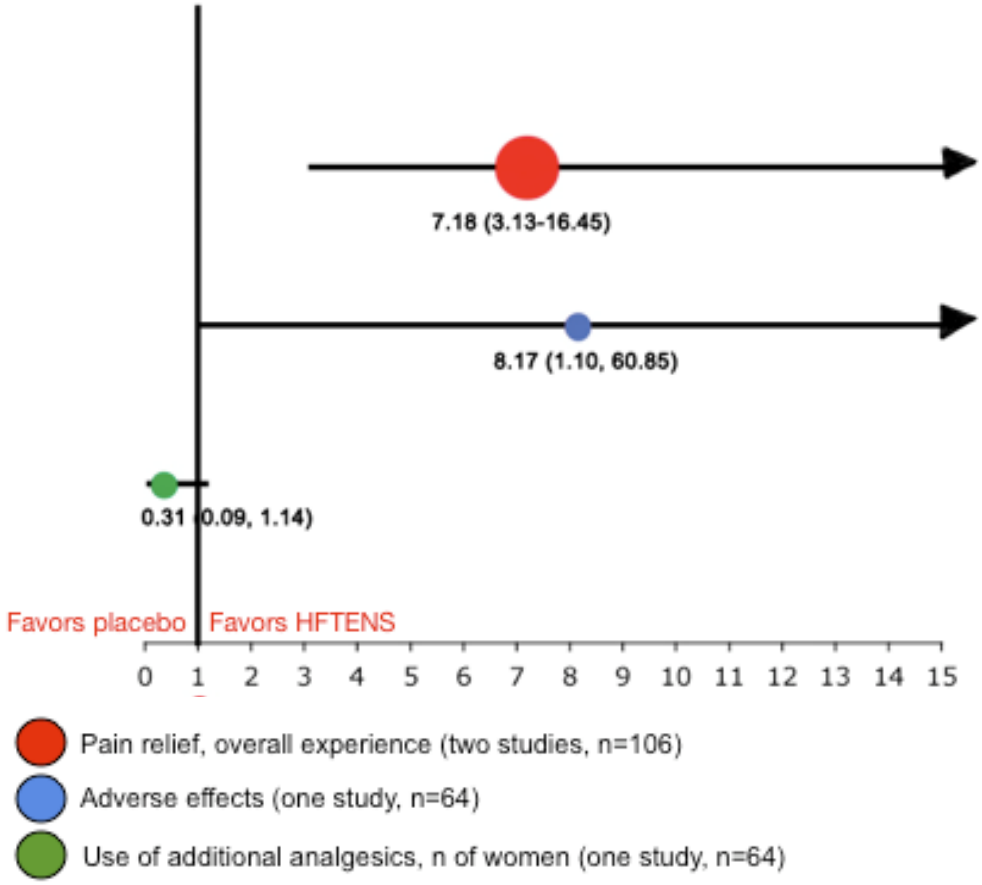
TENS and acupuncture were the topic of a Cochrane Review for treatment of pain associated with primary dysmenorrheal, or pain associated with menses.[7] Treatment with acupuncture is not in the scope of this assessment, so results will focus on the comparisons of high (conventional) and low frequency TENS (ALTENS) in the included 7 studies.

Based on their analysis, the authors of this Cochrane Review concluded the following:

- *HFTENS vs. placebo*
  - HFTENS was more significantly more effective at improving overall pain relief experience (measured categorically) compared to placebo (two studies, n=106).
  - HFTENS also led to significantly greater reductions in pain intensity in one study (n=18) compared to placebo when measured using a 100-point VAS.
  - There was not a significant difference in the number of women who requested analgesics between the groups (one study, n=64)
  - Minor adverse events were significantly more common in the HFTENS group (one study, no=64)
- *LFTENS vs. placebo TENS or placebo pill*
  - No statistically significant differences were seen in three studies reporting overall pain experience when compared to placebo TENS (two studies, n=50) or placebo pill (one study, n=21).
  - One study of 24 women reported less analgesic use in the LFTENS group.
- *LFTENS versus medical treatment*
  - Ibuprofen was significantly better at reducing pain in a study of 64 women.
  - In a study of 24 women there was no significant difference between TENS and naproxen with respect to pain relief, but TENS use led to significantly more adverse effects.
- *HFTENS versus LFTENS*
  - There was a statistically significant difference in pain relief, with women treated with HFTENS reporting greater pain relief than those treated with LFTENS in a study of 42 women.

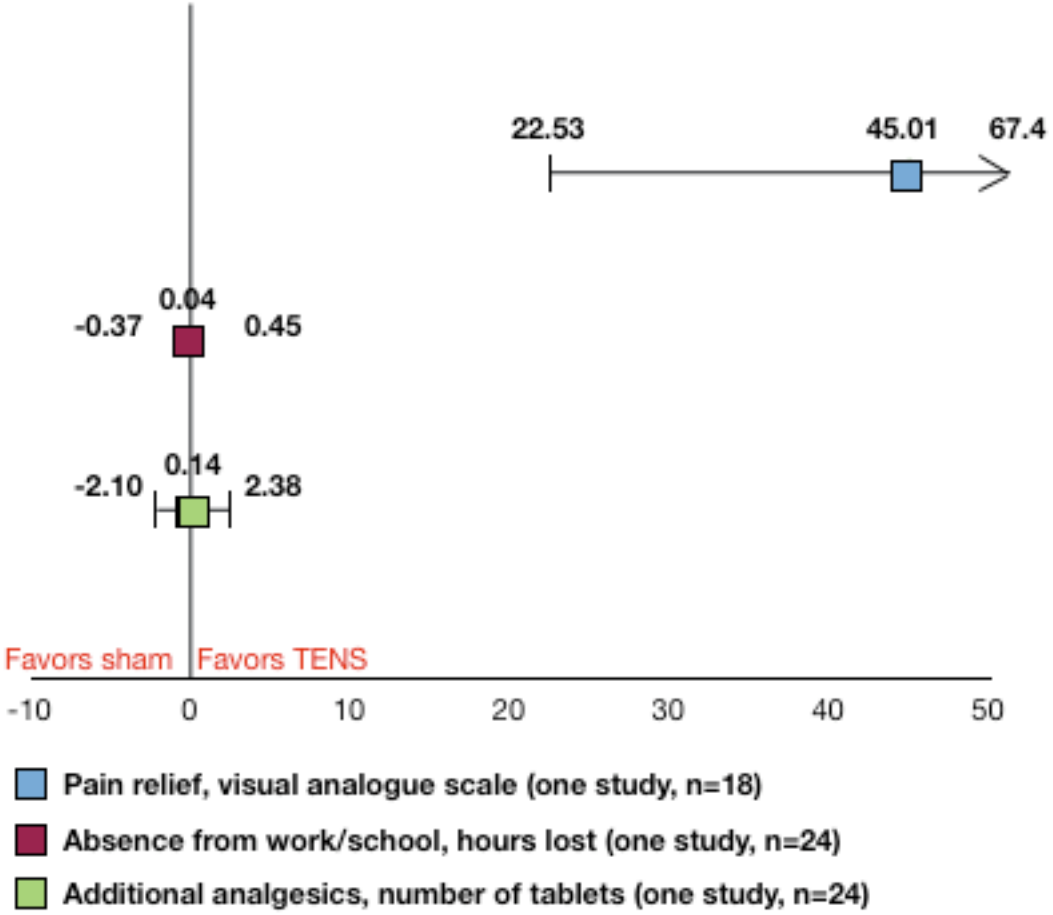
In comparisons of high frequency TENS (HFTENS) and placebo, HFTENS was shown to be more effective at improving overall pain relief experience compared to placebo in two studies (n= 106) using a categorical measure assessing whether they had a positive overall pain experience (combined Peto OR 7.18, 95% CI 3.13, 16.45) [Figure 6]. An 8-fold increased risk (Peto OR 8.17. 95% CI 1.10, 60.85) of adverse effects with HFTENS was reported in a study of 64 women; 4/32 women using HFTENS experienced muscle vibrations, tightness, headaches after use, and slight redness or burning of the skin. There were no reported adverse effects from placebo TENS. This same study reported that fewer patients treated with HFTENS tended to need additional analgesics than those treated with placebo (OR 0.31, 95% CI 0.09, 1.14), however, the difference was not statistically significant.

Figure 6. HFTENS vs. placebo for dysmenorrhea: Pain relief (overall experience), adverse effects, and additional analgesic requirement (no. of women) (Odds ratios, 95% CI).[6]



HFTENS also led to significantly greater reductions in pain intensity in one study (n=18) compared to placebo when measured using a 100-point VAS (weighted mean difference (WMD): 45.01, 95% CI 22.53, 67.47) [Figure 7]. Statistically significant differences between the treatment groups were not observed, however, in a study of 24 women for the number of additional analgesic tablets taken (WMD 0.14, 95% CI -2.10, 2.38) or number of hours lost from work or school (WMD 0.04, 95% CI -0.37, 0.45).

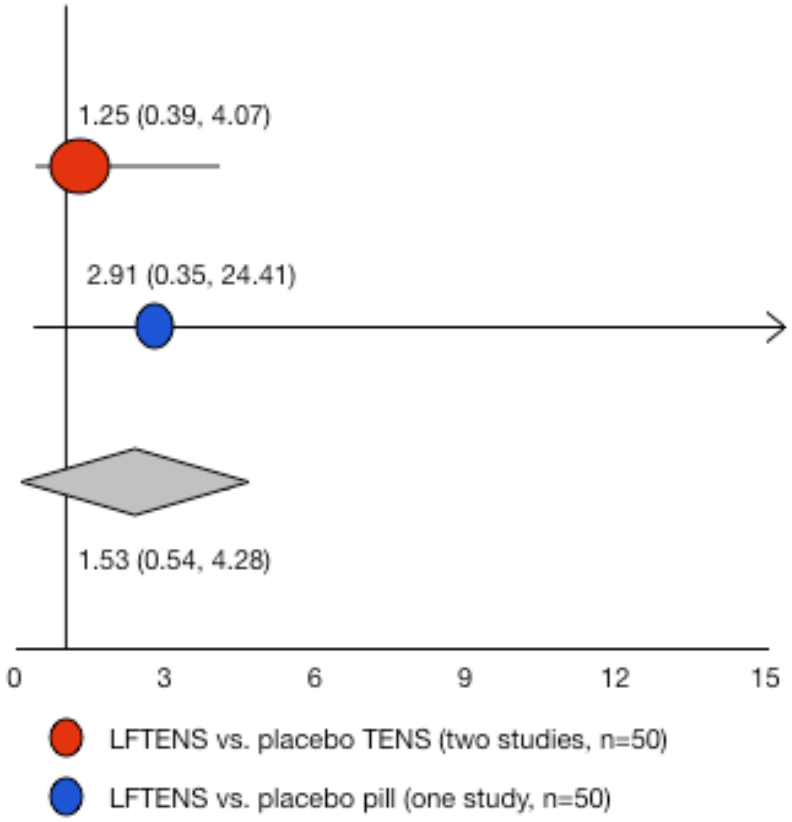
Figure 7. Weighted mean differences of pain relief (reduction in VAS score), analgesic requirement (no. of pills), and lost hours from work/school for HFTENS compared to placebo.[6]



* presented as weighted mean differences with 95% confidence intervals.

There were six studies comparing the use of low frequency TENS (LFTENS) with placebo TENS and two studies comparing LFTENS with a placebo pill, with three of these studies using a categorical measure of overall positive pain experience. No difference in overall pain experience was reported for LFTENS in two studies (n=50) compared to placebo TENS (Peto OR 1.25, 95% CI 0.39, 4.07) or placebo pill (Peto OR 2.91, 95% CI 0.35, 24.41) in another study (n=21); the combined OR across all three studies (n=71) was 1.53 (95% CI 0.54, 4.28) [Figure 8].

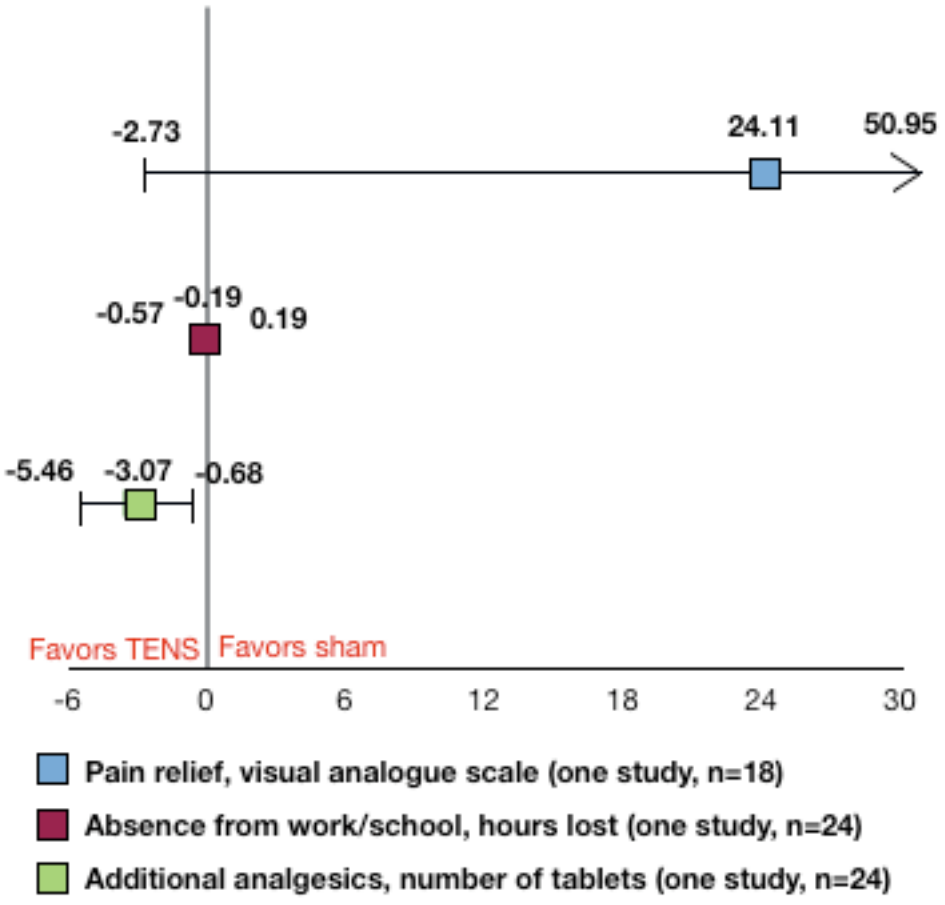
Figure 8. Positive overall experience with pain relief for LFTENS compared to placebo TENS and placebo pill for dysmenorrhea (Odds ratios, 95% CI).[6]



LFTENS did not lead to significantly greater reductions in pain intensity in another study (n=18) compared to placebo when measured using a 100-point VAS (WMD: 24.11, 95% CI -2.73, 50.95. One trial (n=24) reported the number of tablets of additional analgesic used, with the LFTENS group having used significantly less than the placebo TENS group (WMD -3.07, 95% CI -5.46, -0.68). This same trial reported no significant difference between the two groups for absence from work or school (WMD -0.19, 95% CI -0.57, 0.19) [Figure 9].

Two trials could not be included in the meta-analysis due to how the results were presented, but descriptive data were presented. One trial comparing LFTENS and placebo TENS reported a significant difference between the two groups in pain relief ($p<0.05$); the other trial showed that LFTENS is more effective at reducing pain than a placebo pill ($p<0.05$).

Figure 9. Weighted mean differences of pain relief (reduction in VAS score), analgesic requirement (no. of pills), and lost hours from work/school for LFTENS compared to placebo.[6]

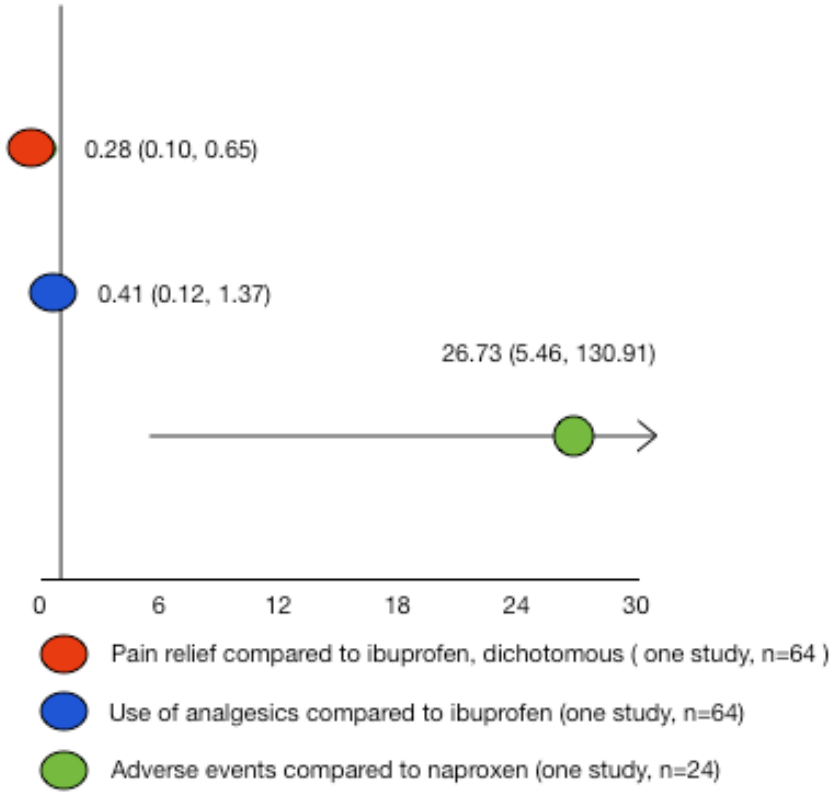


* presented as weighted mean differences with 95% confidence intervals.

There were two trials that compared a medical therapy with TENS; one trial compared ibuprofen (a nonsteroidal anti-inflammatory) with HFTENS. For the outcome of positive overall experience with pain relief, one study (n=64) showed that ibuprofen was significantly better at reducing pain (OR 0.28, 95% CI 0.10, 0.75) [Figure 10]. This trial also reported no significant difference between the two treatments for additional use of analgesics (OR 0.41, 95% CI 0.12, 1.37).

Another trial (n=24) compared high frequency/high intensity TENS with naproxen (a nonsteroidal anti-inflammatory drug). For the outcome of pain relief, reported only as descriptive data, there was no significant difference in the pain scores of each group. There was a significant difference between HFTENS and naproxen with respect to adverse effects, with women randomized to receive HFTENS significantly more likely to experience minor adverse effects (OR 26.73, 95% CI 5.46, 130.91). The extremely wide confidence interval, however, indicates that the estimate is not very precise [Figure 10]. Ten out of 12 women in the TENS group experienced pain from the treatment (pain or burning at the electrode site), while there were no adverse effects reported by those taking naproxen. The women who reported pain from TENS stated that they were prepared to accept the short-term pain from the treatment in return for relief of dysmenorrhea.

Figure 10. LFTENS vs. ibuprofen and naproxen: Pain relief, use of analgesics, and adverse events (Odds Ratio, 95% CI). [Proctor]



* For the first two comparisons of pain relief and use of analgesics, estimates to right of 1.0 favor TENS. For the third comparison of adverse events, estimates to the right of 1.0 favor medical treatment.

When HFTENS was compared to LFTENS in a study of 42 women, overall experience of pain relief was better for the HFTENS group (Peto OR 3.86, 95% CI 1.14, 13.04) but there was no difference in pain relief on a 100 point VAS. Use of additional analgesics and absence from work or school were similar between HFTENS and LFTENS groups (results not shown).

Overall, high frequency TENS was shown to be more effective for treating dysmenorrhea than placebo TENS. LFTENS was found to be no different in reducing pain than placebo TENS, although there is a trend towards efficacy. There were conflicting results regarding whether high frequency TENS is more effective than low frequency TENS. The small number of participants in the majority of included trials is reflected by the wide confidence intervals and lack of precision in many of the comparisons, meaning that clear recommendations for practice cannot be made.

Recent evidence

In a relatively small study of 32 women, Tugay et al.[55] compared TENS to interferential current therapy for the treatment of pain associated with primary dysmenorrhea. Patients in both treatment groups experienced statistically significant reductions in the intensity of menstrual pain, referring low back pain, and lower limb pain at each measurement (immediately post-treatment, 8 hours post-treatment and 24 hours post-treatment).

Although the intensity of referring low back pain in the first three measurement times was different between the TENS and interferential current groups ($P<0.05$), this difference is thought to be due to the baseline values of the groups. According to the differences from just after to 8 hours and from 8 to 24 hours after the applications, the relief of pain in each parameter was either maintained ($P > 0.05$) or improved ($P < 0.05$). The results of this study suggest that TENS and interferential current therapy are both effective in reducing menstrual pain, referred lower limb pain, and low back pain, which are the common symptoms of dysmenorrhea. The results, however, should be interpreted with caution since neither a placebo nor a control group were included and randomization did not result in an equal distribution of baseline pain intensities.

CHRONIC PAIN

Chronic Pain

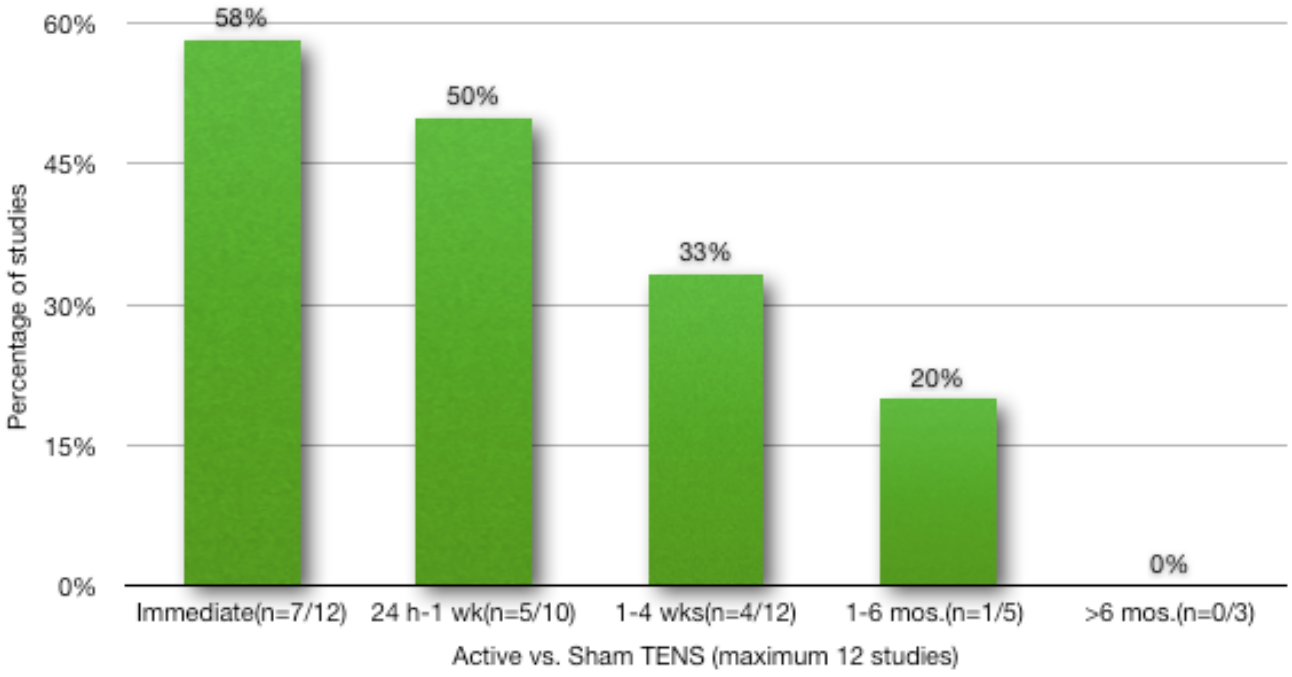
The review of TENS conducted by Nnoaham et al.[8] considered both HFTENS and LFTENS compared to placebo or no treatment control for the treatment of chronic pain across 25 studies (1281 participants). Conditions included were rheumatoid arthritis, osteoarthritis, pancreatitis, myofascial pain, diabetic neuropathy, and LBP. To be considered as chronic, pain had to be experienced by the patient for at least 3 months.

Based on their analysis, the authors of this Cochrane Review concluded the following:

- *TENS vs. placebo*
    - The greatest benefit of pain relief occurred within the first week of treatment and then gradually decreased over time.
    - Similar results were observed when they looked solely at HFTENS.

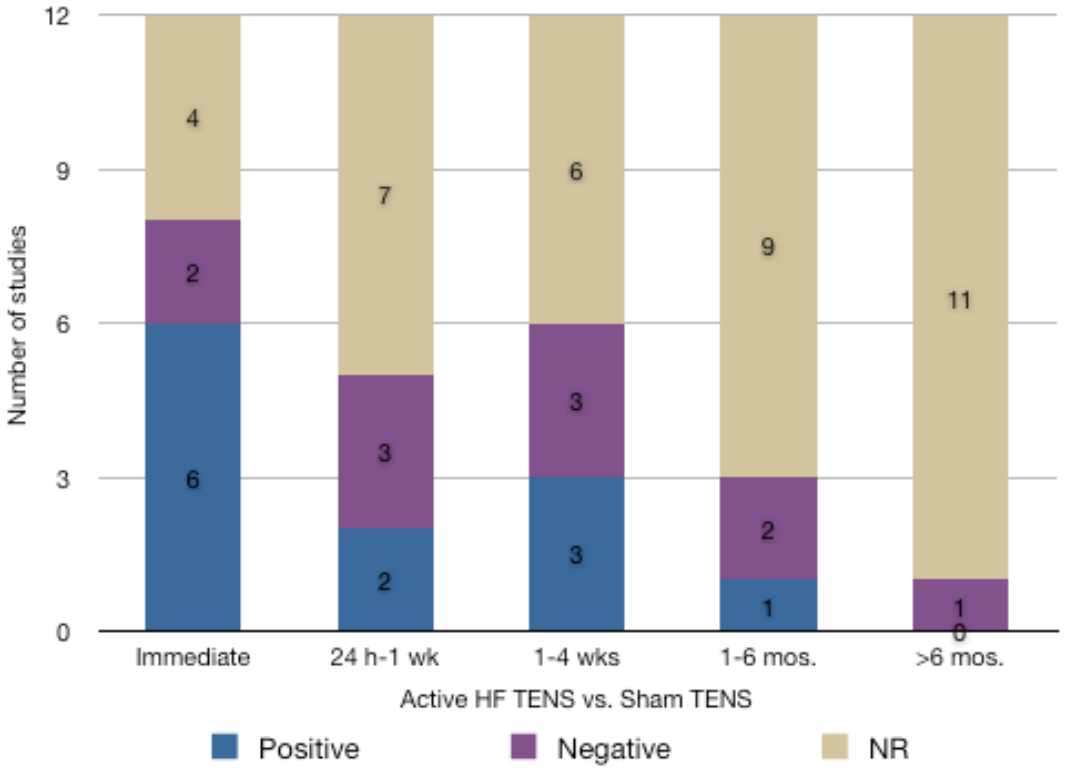
When TENS was compared to sham TENS, the greatest benefit of pain relief occurred within the first week of treatment and then gradually decreased over time. Most studies did not have follow-up continue longer than 4 weeks. The proportions of studies reporting overall positive effects of TENS immediately, 24 hours to 1 week, 1-4 weeks, 1-6 months and greater than 6 months post-treatment were 58%, 50%, 33%, 20% and 0%, respectively [Figure 11].

Figure 11. Proportion of studies of active TENS versus sham TENS for which an overall positive effect of TENS for relieving chronic pain (at different times post-treatment) was described.[7]



When high frequency TENS (HFTENS) was compared to sham TENS, similar results were shown. Immediately post-treatment, 24 hours to one week, 1-4 weeks, 1-6 months, and more than 6 months after treatment, the proportion of studies reporting positive outcomes for pain relief were 50%, 20%, 25%, 8% and 0%, respectively [Figure 12].

Figure 12. Evidence for analgesic efficacy after active HFTENS compared with sham TENS for the treatment of chronic pain over time.[7]



NR: not reported; data not available

When TENS was used in multiple dose treatments, only 3 of 7 were considered to be in favor of the active TENS. For active controlled studies (HFTENS vs. LFTENS), 5 of 7 studies found no difference in analgesic efficacy between HFTENS and LFTENS at any time point.

Eight of the 25 included studies in this review evaluated the effectiveness of single-dose stimulation with TENS. Although single dose studies are extremely useful and important in certain contexts (e.g. in acute postoperative pain), their relevance when evaluating the effectiveness of TENS in chronic pain is unclear.

While almost all of the studies reported on the immediate effects and those effects within the first four weeks, only three studies described long-term efficacy of relief. Again, it is unclear how appropriate relatively short follow-up is when evaluating efficacy of treatment in chronic (long-term) pain conditions. Methodological quality was rated as low by the reviewers for most of the included studies. Although some of the studies performed adequate randomization and accounted for loss to follow-up, the study methods were generally not well described and, for those that were, variation existed across studies with respect to methods, treatments, and outcome measurements.

Chronic Low Back Pain (LBP)

A Cochrane Review by Khadilkar et al.[9] considered comparisons of TENS and placebo (sham) for the treatment of chronic low back pain (LBP). Out of 47 studies identified, four (n=585) met the inclusion criteria.

Based on their analysis, the authors of this Cochrane Review concluded the following:

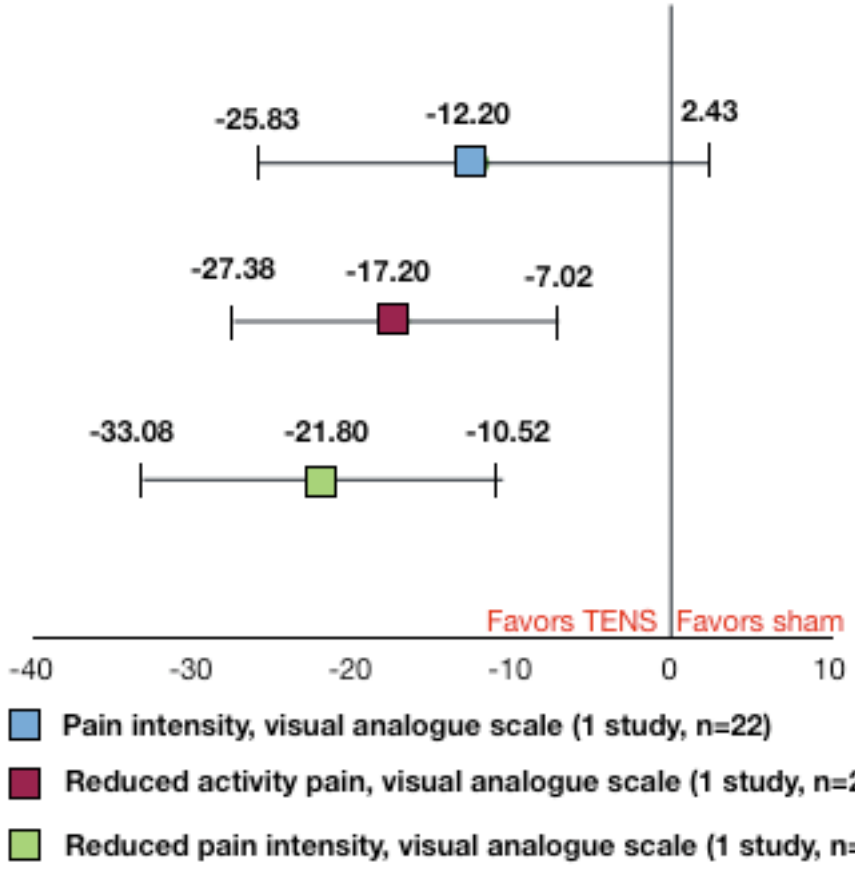
- *TENS +/- ALTENS vs. placebo*
  - After four weeks of treatment in a study of 125 patients with chronic LBP, there was no statistical difference in pain intensity or pain relief, whether measured categorically or using a VAS.
- *Conventional TENS vs. placebo*
  - After two weeks of treatment for chronic LBP, there was no statistical difference in pain intensity between conventional TENS and placebo when measured by VAS in a study of 22 patients.
  - In another study of 27 patients, statistically significant differences in pain relief, measured as reduced pain scores and reduced activity pain scores, was reported for conventional TENS after two weeks of treatment.
  - No statistically significant differences reported for Oswestry Disability Index and Low Back Pain Outcome Scale in this same study of 27 patients, but significant benefit on 4 out of 8 sections of the SF-36.
- *ALTENS vs. placebo*
  - In this same study of 27 patients, statistically significant differences in relief of activity pain were shown, with ALTENS treatment improving activity pain to a greater degree.
  - Significant benefit was seen on only 2 out of 8 sections of the SF-36.
- *Recent evidence from two RCTs*
  - In a recent study of 23 female patients with chronic LBP, no statistically significant differences were reported between low frequency TENS and placebo up to 8 weeks post-treatment.
  - Another poorly designed RCT of low back pain in 32 patients with chronic LBP did not report and significant differences in pain intensity or Roland Disability Questionnaire after 5 weeks of treatment.

In a study of conventional TENS and acupuncture-like TENS (ALTENS) in 125 patients with chronic low back pain, pain intensity and pain relief were not statistically different at the end of four weeks treatment between patients treated with conventional TENS +/- ALTENS and placebo (mean difference: -2.30, 95% CI -9.55, 4.95 and 5.20, 95% CI -6.55, 16.95) [Figure 13].

When categorical pain outcomes were used, pain improvement (1=pain entirely gone, 6=much worse) and frequency of pain (1=never, 5=all the time were similar between treatment and placebo groups (mean difference: 0.0, 95% CI -0.36, 0.36 and -0.10, 95% CI -0.50, 0.30). Generic health status (a modified version of the Sickness Impact Profile), self-rated activity level (1-3; 1=more active, 3=less active), flexion ROM (cm), Lasegue's SLR (degrees) and use of medical services did not differ between TENS and placebo groups.

Figure 13. Mean difference in pain relief and pain intensity measured by VAS and pain improvement and pain frequency measured categorically in comparisons of conventional TENS +/ ALTENS vs. placebo at the end of 4 weeks treatment in a study of 125 patients with chronic low back pain.

Figure 14. Mean differences in pain intensity and activity pain (measured by VAS) at the end of two weeks treatment in two studies of chronic low back pain.



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* From two studies: one study measured pain intensity using VAS (n=22) and the other measured both general and activity pain intensity using VAS (n=27)

In two studies that compared conventional TENS to placebo for the treatment of low back pain, one study (n=22) observed no difference in VAS pain score after two weeks of treatment (mean difference -12.20, 95% CI -25.83, 2.43), while the other study (n=27) reported reduced pain scores for the C-TENS group (mean difference -21.80, 95% CI -33.08, -10.52); this same study observed reduced activity pain in the C-TENS group after 2 weeks of treatment (mean difference -17.2, 95% CI -27.38, 7.02) [Figure 14].

When looking at more functional outcomes, the latter study[39] did not observe statistically significant differences between the C-TENS and placebo groups for the Oswestry Disability Index and Low Back Pain Outcome Scale. This same study, however, showed significant benefits for TENS on 4 of 8 subsections of the SF-36 (physical role limitations, emotional role limitations, general mental health, vitality) and for ALTENS on just 2 of 8 sections.

In analyses of ALTENS and pain intensity, significantly greater reductions in activity pain were seen for the ALTENS group when compared to placebo (mean difference -12.50, 95% CI -24.47, -0.53) (results not shown). With the exception of the isometric dead-lift test, which seemed to improve with ALTENS relative to placebo, there were no differences between treatment groups in other functional outcomes. Studies that separately compared C-TENS and ALTENS to placebo showed similar results.
There is not consistent evidence that TENS improves back-specific functional status to a clinically important degree whether conventional TENS or ALTENS. Although the reviewers rated the four included studies as high quality using Cochrane Back Review Group criteria (6-8 criteria out of 11 met), methodological issues that characterized the studies included unclear concealment of allocation number, blinding of care provider not clearly achieved (all four included studies), outcome assessor not reported to be blinded, low follow-ups of 70% and 74%, and intent-to-treat analyses not clearly performed. In addition, the findings are based on evidence from a few small studies.

Recent evidence
A 2008 study[56] of low frequency TENS (LFTENS) for the treatment of chronic LBP did not report any statistically significant differences in outcomes between TENS and placebo group after one month of treatment and two months of follow-up. The study population consisted of 23 female patients per arm in

a four-arm trial; since the Cochrane Review only included placebo TENS as a comparator, we did not include comparisons between the other two trial arms (LFTENS + rhythmic stabilization and rhythmic stabilization alone). Oswestry Index scores and back pain severity scores were similar between TENS and placebo patients, assessed pre-treatment, immediately after treatment, and 4 and 8 weeks post-treatment (all $p>0.05$). This small study does not change the interpretation of the evidence presented by the Cochrane Review with respect to treatment of chronic LBP.

A more recent 2009[57] study looked at TENS along with acupuncture for the treatment of chronic LBP. This was a small study that enrolled 32 patients, randomized to four treatment arms [TENS, TENS + acupuncture, acupuncture alone, and control (poultice)]. Statistically significant differences in pain intensity or Roland Disability Questionnaire score were not observed between the TENS and control groups after 5 weeks of treatment. Six participants dropped out of the study, however, leaving 26 participants. The methodological quality of this study was poor due to the low attrition rate, small sample size, lack of concealed allocation, and lack of blinding of either participants or those assessing outcome. This study adds little to evidence on use of TENS for the treatment of chronic LBP.

Osteoarthritis of the Knee

A Cochrane Review by Osiri et al.[10] considered comparisons of TENS and ALTENS with placebo (sham) for the treatment of osteoarthritis of the knee. Out of 210 studies identified, seven (n=294) met the inclusion criteria.

Based on their analysis, the authors of this Cochrane Review concluded the following:

- *TENS +/- ALTENS vs. placebo*
  - Statistically significant improvements in pain with TENS treatment, measured as reductions in VAS pain intensity, were observed in 6 studies (n=254) that compared TENS and ALTENS to placebo TENS.
- *Conventional TENS (C-TENS) vs. placebo*
  - Similar results were seen when analysis was restricted only to studies of TENS (5 studies, n=214).
  - Patients treated with TENS were four times as likely than those in the placebo group to report improvement immediately after treatment (5 studies, n=214) and during follow-up (2 studies, n=62). (Peto OR 3.91, 95% CI 2.13, 7.17). Similar results were reported by two of the studies that collected this information further along during follow-up
- *ALTENS vs. placebo*
  - In a study of 40 patients, there was not a statistically significant difference in pain relief between groups.

- *Subgroup analyses*
  - Pain improvement with TENS treatment was statistically significant in high quality studies, studies of repeated TENS applications, and studies with treatment durations of at least 4 weeks.
  - On the contrary, studies that were of low quality, applied TENS in a single treatment, or treated with TENS for less than 4 weeks, did not observe statistically significant differences in pain improvement.

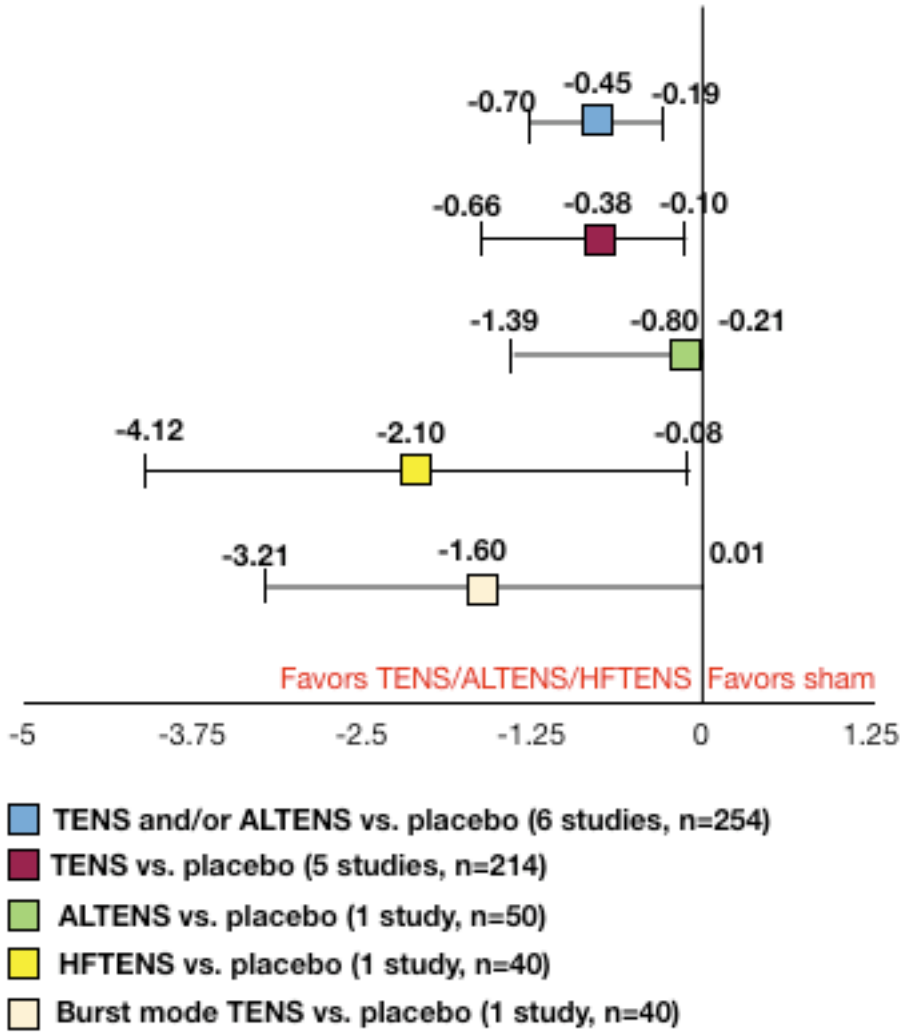
Recent evidence from two RCTs

- In one study[58] (n=52) comparing TENS to hyaluronic acid injection, patients in both groups experienced improvement after 3 weeks of treatment, but the difference in improvement was not statistically significant between the two groups.
- In the other study[26] (n=63), comparing percutaneous neuromodulation therapy (PNT) to placebo, there was a statistically significant difference in VAS pain relief immediately post-treatment that favored TENS, but this did not remain significant at later follow-up times.
- Patients treated with PNT were significantly more likely to report positive outcomes at 48-hour follow-up with respect to their pain control and overall satisfaction with treatment.
- At one-week follow-up, patients treated with PNT were more likely to report reductions in medication use and higher satisfaction levels.

When the combined efficacies of TENS and ALTENS compared to placebo were examined across 6 studies (n=254), significantly greater improvement in VAS pain relief was observed for the TENS/ALTENS groups (SMD -0.45 VAS, 95% CI: -0.70, -0.19)[Figure 15]. If only the studies of TENS application compared to placebo were analyzed (5 studies, n=214), pain relief measured on a VAS was still significantly better in the TENS group (SMD -0.38 VAS, 95% CI: -0.66 to -0.10). The result was similar when ALTENS was compared to placebo; the WMD of pain relief was -0.80 (95% CI: -1.39 to -0.21) in favor of ALTENS.

Reviewers did separate analysis of one study of two different kinds of TENS applications compared to placebo. After one application, pain relief with high frequency TENS (HFTENS) application was significantly better than placebo (WMD -2.10 cm, 95% CI: - 4.12, -0.08) while the difference in pain relief between strong burst mode TENS and placebo did not reach a significant level (WMD -1.60 cm, 95% CI: -3.21 to 0.01) [Figure 15].

Figure 15. Mean differences in VAS pain relief experienced between TENS/ALTENS, TENS alone, ALTENS alone, HFTENS, high burst TENS and placebo.[8]



* ALTENS = acupuncture-like TENS; HFTENS = high frequency TENS; presented as weighted mean differences and standardized mean differences with 95% confidence intervals.

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In meta-analyses of data from five studies (n=214) on categorical pain

improvement (number of patients with pain improvement), patients treated with TENS were almost 4 times as likely as those in the placebo group to report improvement immediately after treatment (Peto OR 3.91, 95% CI 2.13, 7.17) [Figure 16] Similar results were reported by two of the studies (n=62) that collected this information further along during follow-up (Peto OR 4.31, 95% CI 1.55, 12.01).

In subgroup analyses, pain improvement with TENS treatment was statistically significant in high quality studies, studies of repeated TENS applications, and studies with treatment durations of at least 4

weeks. On the contrary, studies that were of low quality, applied TENS in a single treatment, or treated with TENS for less than 4 weeks, did not observe statistically significant differences in pain improvement [Table 18].

Table 18. Compari

With respect to other more functional outcomes, patients who received TENS/ALTENS showed greater improvement in knee stiffness (mean difference -5.97, 95% CI -9.89, -2.06) compared to placebo in a meta-analysis of two studies (n=90). In comparisons with placebo, ALTENS was significantly favored with respect to 50-foot walking time, quadriceps muscle strength and knee flexion. When compared to each other, greater pain relief was reported for strong burst mode TENS and acupuncture-like TENS than for HFTENS.

Variations in the patient populations and study designs, along with potential biases, might have affected the study results. Although studies enrolled only patients with a definite diagnosis of OA, heterogeneity

in the disease (e.g. stage and severity of knee OA) and the people (e.g. lifestyle, co-morbid diseases and concomitant medication) might exist; detailed information on demographic data was incomplete. Appropriate randomization and treatment allocation, along with double blinding, would minimize baseline differences between treatment groups; these study design characteristics, however, were not reported in many of the studies. The evidence, however, suggests that TENS may be beneficial in the treatment of pain associated with osteoarthritis of the knee.

Recent evidence

There have been two recently conducted RCTs on use of TENS[58] and percutaneous neuromodulation therapy (PNT)[26] for treatment of pain associated with osteoarthritis of the knee.

In the study of 52 patients with osteoarthritis of the knee conducted by Paker et al.[58] three-week treatment with conventional TENS was compared to hyaluronic acid (Hylan) injection. Patients in both the TENS and Hylan treatment groups reported significant improvements in pain and functional outcomes (e.g. WOMAC stiffness score, Lequesne score, SF-36 score) between baseline and 6-month follow-up ($p<0.05$). There were no statistically significant differences in pain relief reported by patients in the TENS and Hylan treatment groups, however, after 6 months of follow-up (50.2% and 56.7%, respectively; $p>0,05$).). Although knee stiffness showed greater improvement for the patients in the TENS group at one-month follow-up ($p<0.05$), this difference was no longer statistically different by the 6-month follow-up.

It is important to note that although the participants were similar with respect to most baseline characteristics (height, weight, duration of disease, WOMAC pain score, WOMAC stiffness score, Lequesne score, and SF-36 score; all $p>0.05$), participants in the TENS group were significantly younger than those in the Hylan group (mean, 54.2 versus 64.0 years, respectively; $p<0.0001$), indicating that randomization was not entirely successful. The authors describe using 'simple charts' for randomization, without further details. The authors make no mention of adjusting for this age difference in the analyses. Of 60 enrolled patients, 52 (87%) completed the follow-up period through 6 months.

There are few studies, RCTs in particular, that have looked at percutaneous neuromodulation therapy (PNT). A 2007 study by Kang et al.[26] is the only one identified that fit inclusion criteria for this assessment. In this study of 63 patients, three-week treatment with PNT was compared to placebo for the relief of knee pain secondary to osteoarthritis. VAS pain relief was significantly better for the PNT group than the placebo group immediately post-treatment ($p<0.04$), however, this difference did not remain statistically significant at later follow-up times (differences at immediate, 6-, 24-, and 48-hour time points were 9.5 mm, 5.0 mm, 9.0 mm, and 7.0 mm, respectively). Median pain intensity difference (PID) across all time periods indicated that pain relief was significantly greater in the PNT group than the placebo group (14.5 mm vs. 6.5 mm, $p<0.01$). The TENS group was significantly more likely to report positive outcomes at the 48-hour follow-up with respect to their pain control (measured either categorically as 'none' to 'poor' or on a 0%-100% scale) and overall satisfaction with treatment. WOMAC scores showed significantly greater improvement in stiffness ($p=0.03$) but not pain or function ($p=0.15$ and 0.05, respectively). At one-week follow-up, patients treated with PNT were more likely to report reductions in medication use (54% vs. 0%) and satisfaction levels of 'good', 'very good', or 'excellent' (77% vs. 11%) than patients treated with placebo.
Of 70 enrolled patients, 63 (90%) completed the follow-up. The findings of this study suggest that PNT may be of use in the treatment of osteoarthritis of the knee. As this was the only identified RCT, however, more research is warranted.

Rheumatoid Arthritis in the Hand

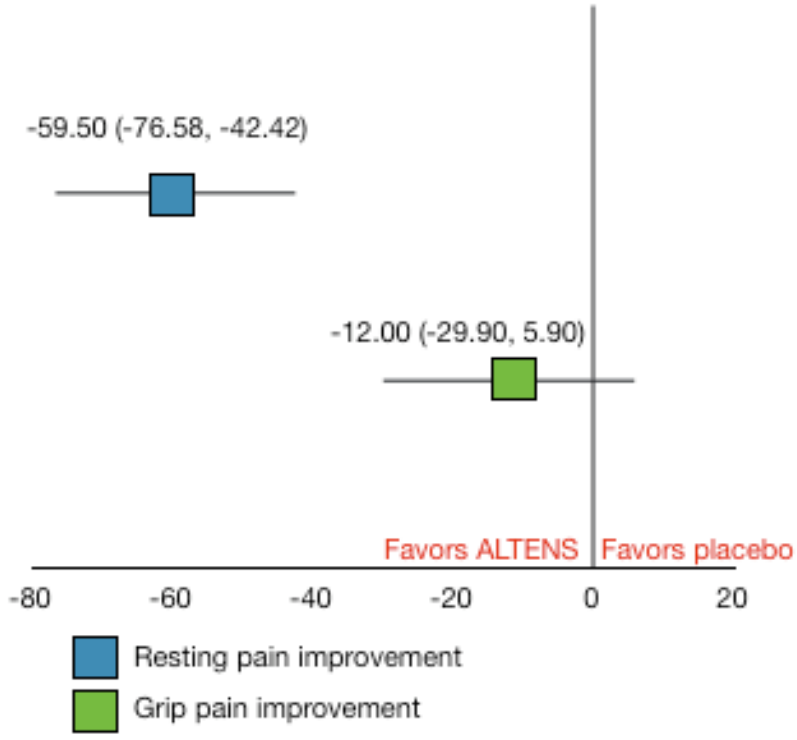
A Cochrane Review of rheumatoid arthritis in the hand [11] looked at conventional TENS and ALTENS compared to placebo. A total of three studies met their study inclusion. Due to heterogeneity of the data, meta-analyses were not performed and data was presented separately for each of the three included studies. For one comparison[59] the reviewers refer to TENS given at 70 Hz at ALTENS, however, this is a frequency typically used with conventional TENS therapy. We will refer to this treatment as ALTENS in the current assessment since that is how the results were presented. The authors of this review used a 15% minimum difference between groups as the criteria for clinical relevance.

Based on their analysis, the authors of this Cochrane Review concluded the following:

- *ALTENS versus placebo*
  - After 3 weeks of treatment in a study of 32 patients, those patients receiving ALTENS treatment reported significantly lower pain intensity and grip pain scores, however, the latter was not statistically significant.
- *Conventional TENS (C-TENS) versus ALTENS*
  - In a study of 22 patients, there were no statistically significant differences in resting pain score, improvement in VAS score or number of tender joints after a single treatment of 20 minutes.
  - Although there was a statistically significant difference in reduction of joint tenderness scores, the scores did not meet the reviewer's criterion of 15% relative improvement for clinical benefit.
  - Five-minute daily treatments over a period of 15 days with conventional TENS did not result in statistically significant differences in the number of patients reporting improvement.
  - A clinically important benefit (21% risk difference) on patient assessment of change in disease, however, was reported for conventional TENS over ALTENS.

When ALTENS was compared to placebo in a small study of 32 patients with rheumatoid arthritis, there was a significantly different, clinically relevant benefit of ALTENS treatment (3 weeks of treatment) on VAS intensity of pain while resting when compared to placebo (67% relative difference in change from baseline, absolute benefit of 45 points in a 100-mm scale) (WMD = -59.50, 95% CI -76.58, -42.42; p<0.00001) [Figure 17]. Grip pain scores measured by VAS were not significantly different between the ALTENS and placebo groups at the end of 3 weeks of treatment (WMD = -12.00, 95% CI -29.90, 5.90; p=0.19); these results also did not demonstrate any clinical benefit of treatment on grip pain.

Figure 17. Weighted mean difference in resting pain improvement and grip pain improvement comparing ALTENS to placebo after 3 weeks of treatment.



* weighted mean differences and 95% confidence intervals

Administration of 15 minutes of ALTENS once weekly, over 3 consecutive weeks, improved muscle power scores and work scores by a relative difference in the ALTENS group compared to placebo at 3 weeks. Although improvement in the muscle power score was deemed to be of clinically important benefit, the results were not statistically significant for either muscle power scores (WMD) = 0.71, 95% CI -0.33, 1.75; p=0.18) or work scores (WMD = 0.29 J, 95% CI: -0.39,0.97; p=0.4).

In another small study (n=22), no statistically significant differences were found between conventional TENS (C-TENS) and ALTENS (data not shown). In comparisons of C-TENS (one treatment of 20 minutes duration) to placebo, there was not a statistically significant difference in resting pain score (VAS) improvement (WMD = -0.20, 95% CI: -4.05,3.65; p=0.9) or gripping pain score (VAS) improvement (WMD = 0.70, 95% CI: -4.11,5.51; p=0.8).

There was also not a significant difference between C-TENS and placebo in the number of tender joints reported before and after treatment [WMD= 0.58 (number of tender joints over total joints assessed), 95% CI: 0.14, 2.48, p=0.50]. Although there was a statistically significant difference in reduction of joint tenderness scores (WMD = - 20.00 (22 point score), 95% CI: -33.79-6.21; p=0.004) for C-TENS treatment over placebo, the joint tenderness scores did not meet the reviewer's criterion of 15% relative improvement for clinical benefit.

In the third study (n=38) included in the Cochrane Review, C-TENS was compared to ALTENS, with daily 5-minute treatments given for 15 days. At the end of 15 days of treatment, there was not a statistically significant difference between the two types of TENS in number of participants improved, based on patient self-assessment of disease (OR 6.43, 95% CI: 0.67, 61.47; p=0.11) based on patient assessment of disease. There was evidence, however, of a clinically important benefit (21% risk difference; the number needed to treat was approximately 5) of C-TENS over AL-TENS on patient assessment of change in disease.

Only one of the three studies included in the Cochrane Review were rated of high methodological quality (4 out of 5 points); the other two studies scored a 1 and 3. The studies were too heterogeneous with respect to TENS treatment (type, treatment schedule) to allow for meta-analysis.

Neck Disorders

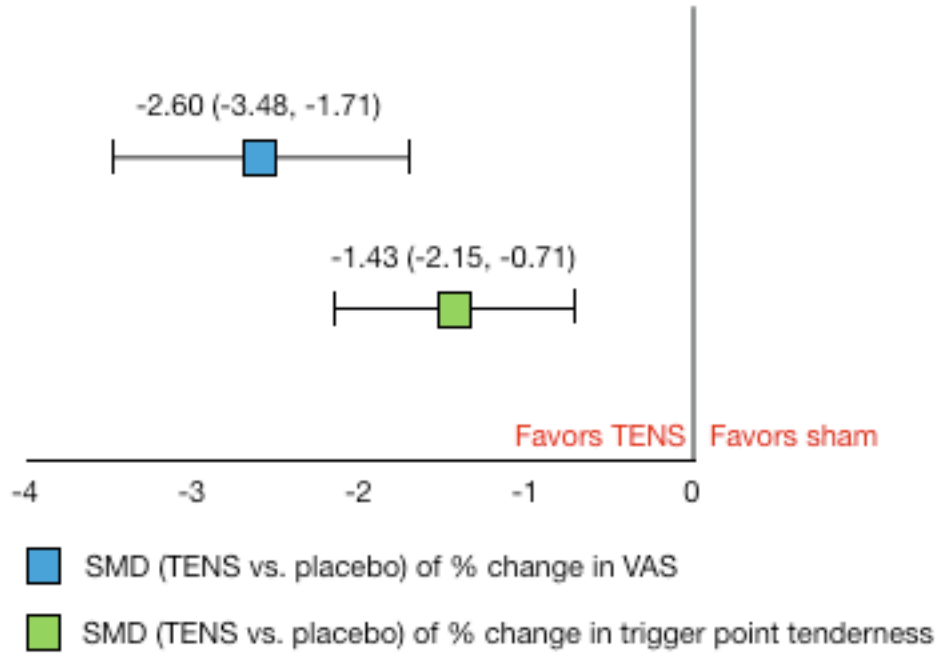
In the Cochrane Review of electrotherapy for neck disorders, Kroeling et al.[60] evaluated conventional TENS and interferential current (IFC) therapy for the treatment of pain caused by mechanical neck disorders, Although other forms of electrostimulation, (e.g. galvanic current, iontophoreses, electromagnetic fields, permanent magnets) were included in the review, they will not be evaluated because they were not within the scope of this assessment. We have placed this review under chronic pain, however, patients with acute pain were included as well. Of 11 total included studies, 5 studies looked at TENS and 1 looked interferential current therapy (referred to as diadynamic current).

Based on their analysis, the authors of this Cochrane Review concluded the following:

- *TENS versus placebo*
  - A single 20-minute treatment with TENS showed significantly reduced pain intensity and trigger point tenderness in a study of 38 patients.
- *TENS + collar, manual therapy + collar, collar alone*
  - No statistically significant differences in pain relief were reported in a study of 20 patients.
- *Diadynamic (interferential) current versus placebo*
  - There were no statistically significant difference in pain intensity or patient-rated improvement after 5 days treatment in a study of 40 patients.

When given as a single treatment (60 Hz, 20 minutes) in a study of 38 patients[44] TENS significantly reduced pain intensity (% change in VAS: SMD -2.60, 95% CI -3.48, -1.71) and trigger point tenderness (% change in pressure pain threshold: SMD -1.43, 95% CI -2.15, -0.71) in patients with trigger points (trapezius muscle) when compared to placebo [Figure 18].

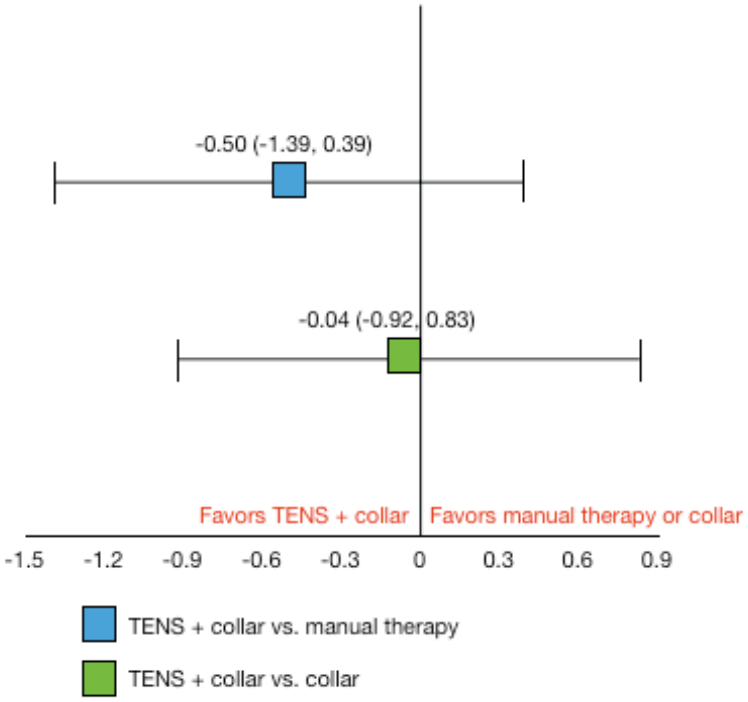
Figure 18. Single treatment TENS vs. placebo for neck pain: standardized mean difference of % change in pain intensity and % change in trigger point tenderness (1 study, n=38).



* presented as standardized mean differences and confidence intervals.

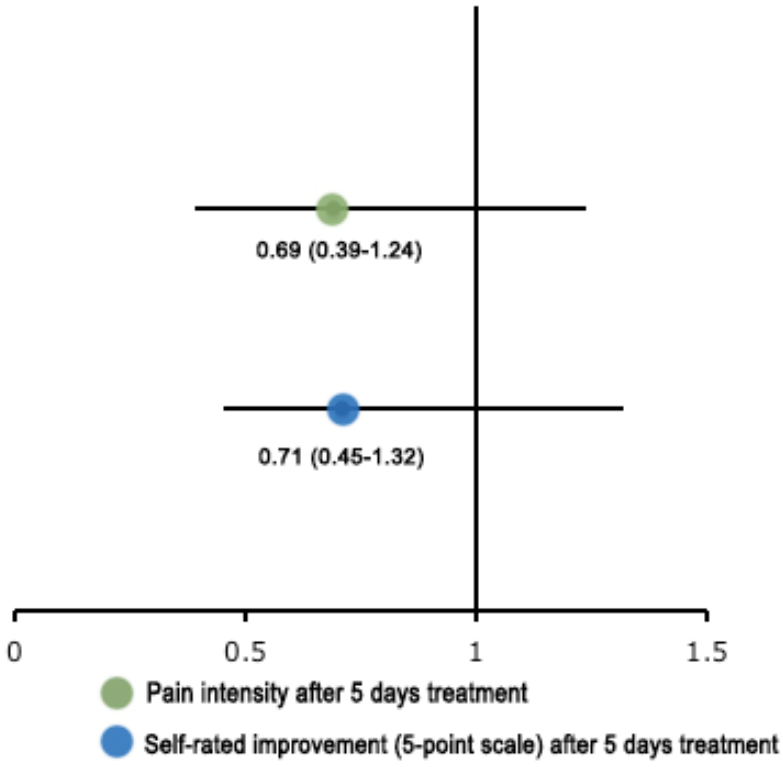
In another study of 20 patients[45], TENS plus collar (80 Hz, three 15-minute sessions) was compared to manual therapy plus collar or collar use alone in patients with mechanical neck disorder (MND). There was not a statistically significant difference in VAS pain relief (% change) between TENS plus collar and manual therapy plus collar (SMD -0.04, 95% CI -0.92, 0.83) or TENS plus collar and collar alone (SMD: -0.50, 95% CI -1.39, 0.39) [Figure 19]. The other three studies evaluating TENS are not assessed here; one investigated microamperage TENS (described as subliminal TENS) and the other two included TENS within multimodal care frameworks and it was not possible to delineate the effects of TENS alone.

Figure 19. Multiple treatment TENS vs. placebo for neck pain: standardized mean difference of % change in pain intensity (1 study, n=20) (standardized mean difference, 95% CI).



The one study of diadynamic (interferential) current therapy included in the review was performed on patients with MND with radicular symptoms and headache. The placebo group (instead of using a sham device) was treated with the current turned up until the patient felt a sensation in their neck, and then the device was turned off. In this study of 40 patients, there was not a statistically significant difference in pain intensity after 5 days treatment between the interferential current and placebo groups when measured using a VAS (RR 0.69, 95% CI 0.39, 1.24). Similarly, patient-rated improvement (the number of patients reported no pain/improved) on a 5-point categorical scale did not differ significantly between IFC and placebo (RR 0.71, 95% CI 0.45, 1.32) [Figure 20]. It is unclear from the review text how the relative risk for pain intensity was determined (i.e. whether it represented a comparison of post-treatment scores between groups or whether it represents comparison of changes in pain score from baseline).

Figure 20. Diadynamic (interferential) current therapy vs. placebo: Pain intensity and patient-rated improvement (number of patients reporting no pain/improved) after 5 days treatment (RR, 95% CI).[4]



The evidence for TENS and interferential current therapy in the treatment of patients with neck pain is limited. The methodological quality of the data is low due to the small number of trials, lack of power, and heterogeneity of methods (in study design and methods of TENS delivery). In addition, electrotherapy was often used in a multimodal setting (i.e. as part of a treatment regimen with other interventions). Details on treatment characteristics were poorly described or missing in many trials.

For the single dose study included here [61], the one trial to achieve statistical significance, the treatment session lasted 15 minutes to treat chronic trigger points. Many chronic pain experts believe that 30 to 40 minutes of stimulation twice a day for at least one month may be necessary to achieve significant pain

relief. [62] Pain reduction immediately post-treatment after a single session of TENS does not necessarily reflect the long-term palliative effects for a chronic condition.

Post-Stroke Shoulder Pain

The use of conventional TENS and ALTENS for the treatment of post-stroke shoulder pain was evaluated in the Cochrane Review by Price et al.[13] Time between stroke and study recruitment varied across the four included studies: <48 hours, average of 16.5 days, average of 12 weeks, and average of 8.7 months. The focus of each study varied in whether TENS was being used for treatment or prevention of shoulder pain: one study was clearly of TENS for treatment, one study did not record baseline pain, and two studies included mixed treatment and prevention populations, predominantly without pain at entry. The methods of TENS application also differed between the four included studies:

1) Two studies used stimulation intended to cause muscle contraction
    - One referred to as electrical stimulation (ES)
    - One referred to as functional electrical stimulation (FES)
2) One used a greater frequency set at the sensory threshold (low intensity TENS) and three times this amount (high intensity TENS); referred to as TENS and high intensity TENS.
4) One study applied stimulation with the intention of causing muscle contraction; referred to as TENS.

Treatment programs lasted anywhere from 4-12 weeks and duration of follow-up was anywhere from 8 weeks to 3 years after treatment.

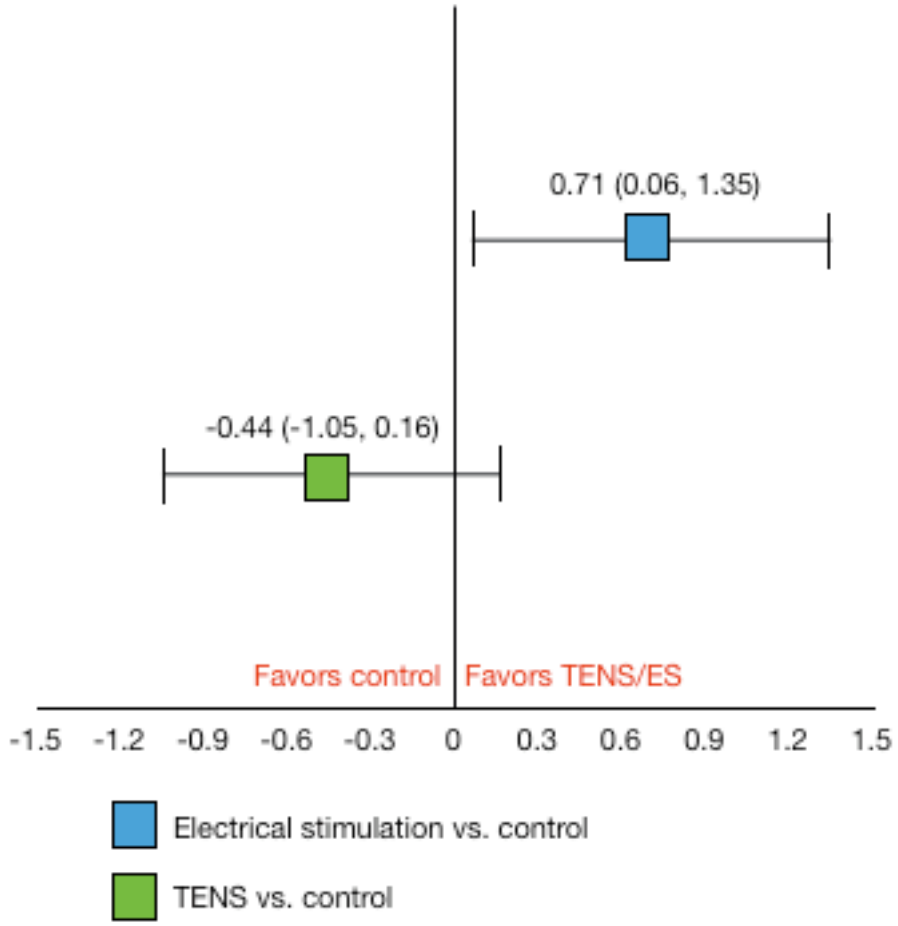
Based on their analysis, the authors of this Cochrane Review concluded the following:

- *TENS versus electrical stimulation and control*
    - There were no statistically significant differences in VAS pain improvement or new reports of shoulder pain between TENS and control groups.
    - There was a statistically significant difference in pain improvement observed for electrical stimulation when compared to control, but new reports of shoulder pain did not differ between the two groups.
    - Patients treated with high intensity TENS or functional electrical stimulation showed greater improvement in passive lateral humeral rotation when compared to control.

Reduction in pain intensity from baseline was explored in comparisons of electrical stimulation and TENS to control. Statistically significant differences in VAS pain intensity rating were observed for

electrical stimulation (SMD 0.71, 95% CI 0.06, 1.35) but not for TENS (SMD -0.44, 95% CI -1.05, 0.16) [Figure 21]. when compared to control. The review authors suggest that the reported improvement in pain intensity for electrical stimulation be viewed cautiously because higher baseline pain scores in the electrical stimulation group may have confounded the results. Although a combined estimate was calculated (SMD 0.10, 95% CI -0.34, 0.54) using a random effects model, heterogeneity between the studies was found to be significant (p=0.01) and therefore any combined estimate should be viewed cautiously.

Figure 21. Reduction in VAS pain intensity from baseline: electrical stimulation vs. control and TENS vs. control (standard mean difference, 95% CI).[5]

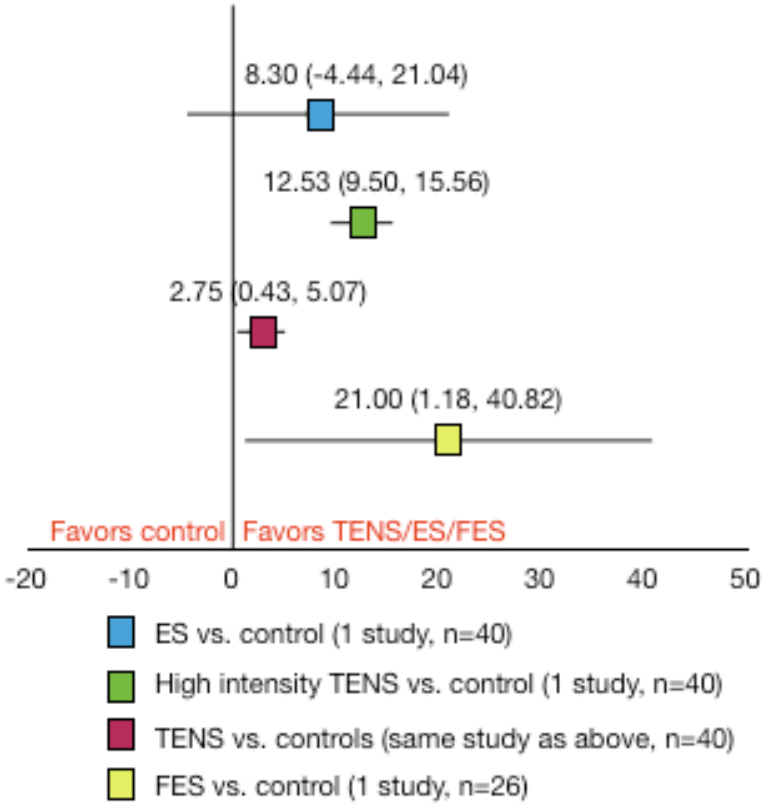


New reports of shoulder pain were a secondary outcome measure in two studies, one of which was not very precise. The combined estimate (Peto Odds Ratio) for new reports when comparing ENS and TENS to control was 0.64 (95% CI 0.19-2.14) [Figure 22].

Figure 22. New reports of

Improvement in passive lateral humeral rotation tended to be greater for all treatment groups, but only comparisons of high intensity TENS (mean difference 12.53, 95% CI 9.50, 15.56) and functional electrical stimulation (mean difference 21.00, 95% CI 1.18, 40.82) to control achieved statistical significance [Figure 22]. Heterogeneity was highly significant between studies for this outcome (p<00001) so again, the combined estimate (mean difference 6.53, 95% CI 4.71, 8.35) should be viewed cautiously.

Figure 22. Improvement in passive humeral lateral rotation (PHLR): TENS, electrical stimulation, and functional electrical stimulation compared to control (Mean difference, 95% CI; 3 studies).



Overall, TENS applied to the shoulder after stroke had no significant effect on subjective reports of pain, although there was a clear objective improvement in PHLR. This increase may be due to a reduction in glenohumeral subluxation, which was demonstrated by two studies. It is reasonable, given that there are non-mechanical causes for shoulder discomfort, that overall pain level does not significantly alter in the short term despite better congruity of the glenohumeral joint.

Cancer Pain

Of 37 identified studies, only two were included in the Cochrane Review.[63] In one study, TENS was only found to be advantageous over transcutaneous spinal electroanalgesia (TSE) on one dimension of a patient satisfaction questionnaire. No significant differences were reported in pain relief scores between TENS and sham TSE. In the other (small) study, no differences were observed between ALTENS and sham ALTENS. The two included studies were heterogenous with respect to study population, sample size, study design, methodological quality, mode of TENS, treatment duration, method of administration

and outcome measures used. The evidence from these studies provides insufficient evidence to judge whether TENS should be used to manage cancer-related and cancer treatment-related pain.

3.2 KEY QUESTION 2: What is the evidence about the safety profile for TENS?
Adverse effects associated with the use of TENS are generally mild, most often associated with irritation at the electrode site or discomfort with the sensation of TENS current.

Acute Pain

- Four of the included 12 studies did not report on adverse effects. Of the 8 studies that did report on adverse effects, three reported that there were none.
- 5 out of the 12 studies reported a range of adverse effects that were primarily related to sensations experienced at the electrode site or the muscle contractions associated with low frequency TENS (pain, burning, tingling at electrode site (n=60)

Labor Pain

- No adverse effects were reported.

Dysmenorrhea

Minor adverse effects were more common in patients treated with HFTENS in two studies.

- 4/32 participants receiving HFTENS reported adverse effects in one study, translating to an 8-fold increased risk compared to those receiving placebo. Adverse effects reported included: muscle vibrations, tightness, headaches after use, and slight redness or burning of the skin.
- A 26-fold increase in risk of adverse effects was observed when HFTENS was compared to ibuprofen in another study (described as 'pain from treatment'. The women who reported pain in this study stated that thy were prepared to accept the short-term pain from the treatment in return for relief from dysmenorrhea.
- For both of these studies, however, that there was a wide confidence interval around the estimates for adverse effects.

Chronic Pain

Adverse effects were not reported in 4 of the 12 included studies. In 3 of the remaining 8 studies, the authors reported that there were not adverse effects.

Five studies reported a range of adverse effects:

- In one study, most of the adverse effects were more common in the control groups(nausea bradycardia, dizziness). Shoulder pain, however, was more common in the TENS group (3% vs. 0%).
- Another study reported pain, burning, or tingling at the electrode site for 29/30 participants in the TENS group and 6/30 in the placebo TENS group.
- A third study reported that 2/48 active TENS participants could not tolerate TENS and 1/49 placebo TENS participants reported severe abdominal pain several hours after their procedure (flexible cystoscopy).
- In a study of high pulse amplitude TENS, 1/13 participants in the high amplitude group discontinued treatment due to discomfort during stimulation.
- In a study of low frequency TENS, most participants receiving low frequency TENS found the muscle twitches uncomfortable.

Chronic LBP

- Minor skin irritations were commonly observed equally in the treatment and placebo groups.
- One patient developed a severe rash four days after the start of treatment.

Osteoarthritis of the Knee

- No adverse effects reported (no clear statement that they were not observed in the included studies or the authors of the review did not include them).

Rheumatoid Arthritis in the Hand

- Review authors state that adverse effects were not reported in the included studies.

Neck Disorders

- Review authors state that adverse effects were not reported in the included studies.

Post-stroke Shoulder Pain

- Review authors state that no adverse effects were noted.

Cancer Pain

- Review authors state that adverse effects were monitored and 'minimal' in 1 of the 2 included studies.

3.3 KEY QUESTION 3: What is the evidence of cost implications and cost effectiveness of TENS?

Overall, there is very limited information on the cost-effectiveness of ENS. Two older previous HTAs, neither of which provides formal economic analyses [43, 44 64] and one older costing study in patients with chronic pain[48, 49] were found. No full economic evaluations were found. Overall, there is very low evidence regarding the cost-effectiveness of TENS.

Critical appraisal of the costing study based on the items of the Quality of Health Economic Studies (QHES) instrument and epidemiologic principles, indicates that there are insufficient data for full economic evaluation or extensive conclusions and that potential biases should be considered in the interpretation of these studies. Weighted QHES score was 44 [possible score 0 (worst) to 100 (best)] for this study by Chabal..

Economic analysis from other HTAs

None of the previous HTAs included economic analysis specific to ENS. Information on the cost effectiveness of ENS from two older HTAs (1995 and 1997) is limited. Both HTAs focus on economic considerations from systems outside of the United States, one on the Canadian system and one on the United Kingdom. A 2000 Hayes report[43] briefly cites the costing study mentioned above but provides no details.

The 1995 Canadian Coordinating Office for Health Technology Assessment (now CADTH) reported that no formal economic analyses for use of ENS for pain management were found in the published literature.[45] No formal cost-effectiveness evaluation was done as part of this HTA. Because ENS may be used in a wide array of settings by a number of different types of health care providers for varied conditions, the authors stated that was difficult to obtain a single system-wide estimate of cost for ENS

utilization. They provide only limited information on costs and do not perform a formal economic analysis.

Similarly, the 1997 HTA by McQuay [44] indicated that there was little information about the costs and benefits for chronic pain services, which includes use of TENS. The authors report that the lack of evidence on effectiveness of TENS for management of chronic pain at that time precluded evaluation of cost-effectiveness. In light of this, they focus on the cost-effectiveness of pain clinics. They conclude that use of pain clinics results in direct health services savings equal to twice their costs. Again, this approach does not elucidate the overall cost-effectiveness of TENS specifically.

Economic studies on TENS

Only one economic study specific to TENS use was found. This 1998 costing study by Chabal[65] is considered a partial economic analysis. It is well accepted that cost analyses are not considered full economic evaluations. Theoretically, a cost-minimization study (one that compares costs of the alternatives assuming equal effectiveness) might provide a complete economic evaluation, but because of uncertainty around costs and quality of life outcomes that likely differ between alternative interventions this is rarely possible.

Table 19. Costing study, Chabal 1998.[65]

	Design	Data sources and Population	Primary Strengths	Primary Limitations
Chabal (1998)	▪ Retrospective ▪ Cost simulation ▪ Perspective not stated ▪ Study funded by Empi ▪ Evaluation of service and medication use before and after	▪ N = 255 randomly selected from population of 2003 ▪ Chronic pain patients (39% had back pain as source) ▪ Costs of medication estimated from brand and generic price from random survey of pharmacies, and *Drug Topics Red Book* price (high and low estimates for each) ▪ Costs of PT/OT estimated from Washington State Department of Labor and Industries	▪ Random selection of patients but data are not from a randomized controlled trial ▪ Costs from several sources	▪ Cost of medication and PT/OT only ▪ Retrospective survey of TENS users may be subject to re and other biases ▪ No control group ▪ No probabilistic sensitivity analyses done

PT = physical therapy; OT = occupational therapy

In this study, the authors conducted telephone interviews with 376 chronic pain patients who had acquired a ENS device. They assessed several treatment outcomes: changes in medication use, number of pain medications, and use of physical and/or occupational therapy (PT/OT). Patients were asked to recall these outcomes retrospectively, both before ENS treatment and after six months of ENS use. These data provided the clinical values used for the cost simulation that they then conducted. The cost simulation estimated pain medication costs from a variety of sources, and estimates cost differences in ENS users at 6 months compared to before ENS initiation, both in aggregate and in per-patient forms. They provide six cost estimates for medications: Pharmacy *Red Book* high, *Red Book* low, and high and low values for brand and generic prices. Patients must have been using ENS for at least 6 months to be included in the interview study (n=376). Of those, only patients taking pain medications were included in the cost simulation (n=255).

The study population was drawn as a random sample from a larger population of 2003 "chronic pain patients," 39% of which had back pain as their primary complaint (other pain conditions were not described). Of the original 376, 74% reported using their ENS device for at least 6 months. Of these, 62.7% were female and 49.7% were worker's compensation patients.

Results

The interview results are reported elsewhere[66] and are briefly described in the Chabal[65] study. Briefly, the authors found that the number of pain-related medications (NSAIDs, opiates, steroids, sedatives/hypnotics, and muscle relaxants) were all reduced at 6 months after ENS use compared with use prior to ENS. Each drug class as well as overall number of pain medications were evaluated and the difference between pre- and post-ENS use reached statistical significance for each. Statistically significant reductions in PT/OT visits at the two time periods were also reported (Table 20).

Table 20: Effectiveness measures used for cost simulation: Chabal 1998

	Number using medications at ENS initiation	Number of medications after 6 months ENS use	P - value
NSAIDs	121	82	<0.003
Opiates	206	101	<0.001
Steroids	6	0	0.014
Sedatives/hypnotics	17	9	<0.05
Muscle relaxants	44	28	<0.01
PT/OT visits	327	108	<0.001

NSAID = non-steroidal anti-inflammatory drug; PT = physical therapy; OT = occupational therapy

Chabal reports that the simulated cost savings per patient (in 1994 USD) over 6 months when TENS was used ranged from $526 for 6 PT/OT visits to $1,052 for 12 visits. The simulated medication cost savings ranged from $120 to $480 over six months, and from $240 to $560 over 12 months (Table 21).

Table 21: Overall results for cost simulations from Chabal 1998

Simulation results (N = 255)	(1994 USD)
Medication cost savings over 6 months, per patient	120 - 480*
Medication cost savings over 12 months, per patient	240 - 560*
Cost savings assuming 6 PT/OT visits in 6 months, per patient	526
Cost savings assuming 12 PT/OT visits in 6 months, per patient	1052

* Describes lowest estimate (Red Book low) and highest estimate (brand high)

The patient population included 39% who had back pain as the primary complaint. It is not clear what other types of chronic pain are represented, and were not included in the model, so extrapolation of these findings to location-specific pain may not be appropriate.

The study's primary limitation is that it is not a full economic analysis and therefore no incremental estimate of cost-effectiveness based on a summary measure of benefit, either clinical (cost-effectiveness) or quality-adjusted survival (cost-utility) is available. In addition, the following should be considered in the interpretation of this study.

- Only costs related to use of medications and PT/OT visits were considered in the model. This implies a health services perspective; neither patient- nor society-relevant outcomes such as pain relief, adverse effects from therapy, productivity, functional status, health-related quality of life and costs besides medication or PT/OT (such as out-of-pocket costs for devices, subsequent diagnostic or interventional costs, lost productivity costs) are addressed in this study.
- No control group was included in the interview study or in the simulation.

- People who did not use the ENS device for a full six months or who were not taking pain-related medications were excluded from the cost simulation.
- No sensitivity analyses around model assumptions were done. The authors do provide a range of costs based on varied number of PT/OT visits, but information on factors which might drive the economic model are not explored.
- Patient data were gathered retrospectively via telephone interview. Although the authors indicate that the sampling allowed for at least six months ENS use, the precise timing of ENS use with respect to when the survey was conducted is not described. The potential for recall bias and the influence of a placebo effect should be considered in the interpretation. The effects of any pre-ENS treatment are also not known.

Full economic evaluation of TENS for pain in general may be challenging since it is applied in a variety of settings, by a range of providers for a broad range of pain indications. The authors do note limitations of their study that preclude a full economic evaluation, such as the lack of control group, recall bias, unmeasured extrinsic factors or trends affecting ENS use, and the inability with the data at hand to conduct a full economic evaluation. However, relevant information on the cost-effectiveness of TENS for treatment of pain in specific situations is theoretically possible. Future studies that make explicit the following would help to provide relevant information:

- Paths of care, including time horizons, need to be included. Modeling the path of care, including most relevant time horizon, for TENS use may depend on the pain condition and, in the absence of clear clinical practice guidelines for a given condition, presents a challenge. For example, in patients with intractable chronic low back pain, whether the costs and consequences of future surgery are considered will likely affect model results and generalizability.
- The perspective, including selection and measurement of costs and outcomes needs to be clearly defined. In general, a societal perspective that includes both indirect and direct costs, productivity, and patient-relevant outcomes such as pain relief is preferred and provides the highest quality economic evaluations. Given the subjective nature of pain, in this clinical area it is especially important to be explicit about the choice of perspective and outcome measures.[67] Other economic evaluations of pain control interventions have been specific about methodology and measurement.[68-70]

Conclusion: There is insufficient evidence to evaluate the economic value of TENS for pain management.

4. SUMMARY AND IMPLICATIONS

4.1 Summary with respect to efficacy and effectiveness of transcutaneous electrical nerve stimulation (TENS) in the treatment of acute and chronic pain

- Findings regarding efficacy described in this technology assessment report are primarily taken from previously published Cochrane Reviews of randomized studies (LoE I/II) and from randomized trials (LoE II/III) published since the most recent updates of the reviews.

    - The overall strength of evidence (SoE) ranged from moderate to very low, depending on the degree of literature support for the different conditions and outcomes examined.
    - Although the primary evidence in this assessment comes from Cochrane Reviews, meta-analyses for most of the studies was not appropriate given the heterogeneity in study populations, intervention characteristics, and outcome measures.
    - Evidence for a benefit of effect in the treatment osteoarthritis of the knee was moderate; TENS was found to be superior to placebo (sham), with the differences both statistically significant and clinically important.
    - Further research is warranted to evaluate the efficacy and effectiveness of TENS for the treatment of acute and chronic pain in populations that are more similar with respect to the conditions, treatment regimens, study designs, and outcomes assessed.

Acute Pain

- A total of 12 studies covering the following conditions were included in one Cochrane Review of acute pain: pain associated with medical procedures (e.g. sigmoidoscopy), hemophiliac pain, acute trauma (e.g. sprains or fractures), postpartum uterine contraction, acute oro-facial pain, post thoracotomy, rib fractures, and neuropathic pain.
- The overall SoE across studies of acute pain is low given the number of LoE I/II studies. Although 12 studies were included in this review, data could only be extracted from 6 of them.
- Acute pain relief (measured using a numerical rating scale or a visual analogue scale) was not significantly different between TENS and sham or control group for the treatment of procedural and post-treatment pain. Significantly greater pain relief was reported for patients treated with TENS that those treated with sham after two days of treatment, however, this finding was based on a single study of 50 patients.
- In comparisons between types of TENS, pain relief was significantly greater for patients treated with high amplitude (intensity) TENS than those treated with low amplitude TENS. Patients treated with conventional (high frequency) TENS and acupuncture-like TENS (ALTENS, low frequency) did not differ in acute pain relief post-treatment. These findings, however, are based on two individual studies of 60 and 20 patients, respectively.
- Sample sizes for most of the studies were small and significant clinical and methodological heterogeneity precluded pooling of data.
- Due to insufficient extractable data in the studies included in this review, the authors of this review concluded that definitive conclusions about the effectiveness of TENS as an isolated treatment for acute pain in adults cannot be made.

Labor Pain

- One Cochrane review comprised of 19 studies compared conventional TENS and ALTENS, pharmacological treatment and epidural and one more recently published RCT were identified.
- Overall, results are mixed with regard to the effectiveness of TENS for the relief of labor pain. It appears to depend on the type of TENS and how it is applied. The overall SoE across ENS is moderate with regard to pain relief.
- For treatment of labor pain, TENS tended to reduce pain to a greater degree than sham treatment (2 studies), but pooled estimates failed to reach statistical significance. TENS applied to acupuncture points led to statistically significant differences in the number of women reporting severe pain during labor based on 2 studies.
- Women treated with TENS were significantly more satisfied with their pain relief (5 studies) and would be more likely to use TENS again in a future labor than women treated with sham (4 studies) and the SoE for these outcomes is high.
- When compared to pharmacologic relief, TENS applied to the back was not significantly different with respect to patient satisfaction with pain relief (pain scores were not reported) in 3 studies.
- TENS combined with epidural did not lead to significantly different pain or delivery outcomes from epidural alone, except when TENS was applied to the cranium (for which there was a longer duration of pain relief from first injection).
- The authors of this review concluded that there is only limited evidence that TENS reduces pain in labor and it does not seem to have any impact (either positive or negative) on other outcomes for mothers or babies.
- A recent RCT comparing TENS to traditional treatment (controls) did not find statistically significant differences between the two groups with respect to pain scores at any point during labor or covering the entire delivery or number of women needing epidural analgesia.

Dysmenorrhea

- A Cochrane review of 7 studies, some of which had small sample sizes, comparing low and high frequency TENS was identified.
- Overall, when all types of ENS were considered together for relief of dysmenorrhea, results were mixed, leading to an overall SoE that is low. Small sample sizes and wide confidence intervals for some studies bring the stability of estimates into question.
- For treatment of dysmenorrhea pain, high frequency TENS (HFTENS) led to greater reductions in pain than placebo, however, the estimate was not precise.
- There was not a statistically significant difference in overall pain experience (categorical measure) when low frequency TENS (TENS) was compared to placebo. Although HFTENS led to a significantly greater number of women with positive overall pain experiences than LFTENS, there was no difference in pain relief on the VAS.
- When LFTENS was compared to placebo TENS and placebo pill, three studies reported no significant differences between the groups in number of women with an overall positive pain experience, another small study measuring VAS pain relief also did not observe a significant difference between LFTENS and placebo TENS. Two additional studies reported statistically significant greater pain relief for LFTENS, but did not provide descriptive data.
- Women treated with LFTENS reported significantly less analgesic usage than placebo in a study of 24 women.

- When compared to pharmacologic treatments, ibuprofen was shown to be significantly better at reducing pain, but did not influence consumption of additional analgesics; no significant differences in pain scores were reported when TENS was compared to naproxen.
- The authors of this review concluded that high frequency TENS was effective for the treatment of dysmenorrhea by a number of small trials, but evidence was insufficient to determine the effectiveness of low frequency TENS.
- A recent small study did not find any differences between TENS and interferential current therapies, however, each led to reductions in menstrual pain, referred lower limb pain, and low back pain. Without sham or no treatment control comparisons, these differences should be interpreted with caution.

Chronic Pain

- A Cochrane review of ENS use for chronic pain (> 3 months) that included 25 studies (1281 participants) included those with rheumatoid arthritis, osteoarthritis, pancreatitis, myofascial pain, diabetic neuropathy, and low back pain. .
- Numerical data were not summarized in this review and authors provided information on the numbers of studies which overall showed a positive effect of TENS on pain relief.
- The overall SoE for chronic pain is moderate based on the number and quality of studies, but numerical data were not presented and a description of consistency across studies was not explicit.
- For treatment of chronic pain, patients treated with TENS were more likely to report overall positive effects of treatment when compared to sham within the first week of treatment, but this advantage decreased over time (follow-up for most studies did not exceed four weeks); when analyses were restricted to HFTENS and sham, the results were similar.
- While almost all of the studies reported on the immediate effects and those effects within the first four weeks, only three studies described long-term efficacy of relief.
- Clinical importance of effect of TENS on pain relief cannot be commented on.
- The authors of this review concluded that the published literature lacks the methodological rigor or robust reporting needed to make confident assessments of the role of TENS in chronic pain management.

Chronic Low Back Pain

- A Cochrane Review of ENS use in chronic low back pain (LBP) included only four studies representing 585 persons. Two additional small RCTs were identified. Sample sizes in most studies were small.
- For the relief of chronic LBP, the overall SoE for the effectiveness of any type of ENS is low, based on a total of 6 RCTs (LoE I/II) with small sample sizes.
- Only one small study reported a statistically significant pain relief with ENS use.
- The authors of this review concluded that evidence from the small number of placebo-controlled trials does not support the use of TENS in the routine management of chronic LBP.
- The authors of this review concluded that evidence from the small number of placebo-controlled trials does not support the use of TENS in the routine management of chronic LBP.

Osteoarthritis of the Knee

- A Cochrane Review of seven studies (N = 254) and two recently published RCTs were identified.

- The overall SoE for relief of knee pain across types of ENS (compared with placebo) in patients with osteoarthritis is moderate based on the small sample sizes of included studies and mixed results when newer trials were considered.
- Overall, ENS appears to be associated with a significant improvement in pain compared with placebo. In meta-analyses of five studies, patients treated with TENS were almost 4 times as likely as those in the placebo group to report improvement immediately after treatment (Peto OR 3.91, 95% CI 2.13, 7.17).
- With respect to other more functional outcomes, patients who received TENS/ALTENS showed greater improvement in knee stiffness (MD -5.97, 95% CI -9.89, -2.06) compared to placebo in a meta-analysis of two studies (n=90).
- The authors of this review concluded that TENS and ALTENS are effective in pain control over placebo. Heterogeneity of the included studies was observed, which might be due to the different study designs and outcomes used. 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.
- In one recent RCT, there were no statistically significant differences in pain relief reported by patients in the TENS and hyaluronic acid treatment groups, after 6 months of follow-up (50.2% and 56.7%, respectively; $p>0,05$). Although knee stiffness showed greater improvement for the patients in the TENS group at one-month follow-up ($p<0.05$), this difference was no longer statistically different by the 6-month follow-up.
- In another new study, three-week treatment with PNT, VAS pain relief was significantly better for the PNT group than the placebo group immediately post-treatment ($p<0.04$), however, this difference did not remain statistically significant at later follow-up times. Median pain intensity difference (PID) across all time periods indicated that pain relief was significantly greater in the PNT group than the placebo group (14.5 mm vs. 6.5 mm, $p<0.01$).
- Using the criterion of 0.80 to indicate a large effect, differences in pain relief when comparing TENS/ALTENS to placebo and high rate TENS vs. placebo could be considered clinically important (SMDs -0.79 and -1.12, respectively).

Rheumatoid arthritis in the hand

- A Cochrane Review of three small studies was identified. The studies were too heterogeneous with respect to TENS treatment (type, treatment schedule) to allow for meta-analysis.
- The overall SoE for pain relief is very low since studies of similar comparisons were few and were likely to be underpowered.
- Results from small three studies comparing ENS with placebo were mixed: One study showed a statistically significant improvement in pain while the other two did not.
- One comparison of C-TENS with ALTENS, reported no statistically significant difference between the two types of TENS in patient-reported improvement.
- The authors of the review concluded that given there conflicting effects of TENS on pain outcomes in patients with RA, more well designed studies with a standardized protocol and adequate number of subjects are needed to fully conclude the effect of C-TENS and AL-TENS in the treatment of RA of the hand.

Neck disorders.

- A Cochrane Review included 5 studies looked at TENS and 1 looked at IFC therapy (referred to as diadynamic current) compared with use of a cervical collar; two of these studies included

TENS as part of a multimodal treatment (in combination with other therapies), so it was not possible to delineate the individual effects of TENS.

- The overall SoE is for use of either TENS for IFC was low for neck pain relief.
- Only one study of 38 patients that compared a single 20-minute treatment with TENS to placebo reported greater reduction in pain intensity for the TENS group.
- No statistically significant differences in pain relief were observed when TENS was used in combination with collar and compared to manual therapy + collar or collar alone.
- There was no significant difference in pain intensity after 5 days when diadynamic (interferential) current therapy was compared to placebo in a study of 40 patients.
- The authors of the review concluded that definitive statements on electrotherapy for mechanical neck disorders could not be made. The current evidence on ENS is either lacking, limited, or conflicting. Future trials should have larger patient samples and include more precise standardization and description of all treatment characteristics.

Post-stroke shoulder pain

- A Cochrane Review included 4 of studies comparing TENS, functional electrical stimulation (FES) and HFTENS with placebo or control. Only two of these studies assessed pain relief.
- Results from this small number of studies are mixed; patients treated with electrical stimulation had lower pain scores than control but those treated with TENS did not.
- Neither FES nor TENS had significantly different new reports of shoulder pain when compared to control.
- The overall SoE for pain relief is very low since studies of similar comparisons were few and were likely to be underpowered. There is evidence from 2 studies that FES and TENS may improve passive humeral later rotation.
- Overall, TENS applied to the shoulder after stroke had no significant effect on subjective reports of pain, based on 4 studies.
- The authors of the review concluded that the evidence from RCTs does not confirm or refute that electrical stimulation around the shoulder after stroke influences reports of pain, but there do appear to be benefits for passive humeral lateral rotation. A possible mechanism is through the reductionof glenohumeral subluxation. Further studies are required.

Cancer pain

- A Cochrane Review included only two small studies of TENS effect on cancer pain.
- The overall SoE for cancer pain relief is very low given the paucity of studies.
- No statistically significant differences in pain relief between TENS and control groups in either study.
- The authors of this review concluded that the results were inconclusive due to a lack of suitable RCTs, and that large multi-centre RCTs are required to assess the value of TENS in the management of cancer-related pain in adults.

4.2 Summary with respect to the safety of transcutaneous electrical nerve stimulation

- TENS is generally regarded as a safe, non-invasive therapy.
- Other than minor skin irritation (burning, tingling or discomfort) at the electrode site, no major adverse events have been associated with its use; for many of the RCTs included in this report, there were no side effects reported.

- TENS is contraindicated for patients with pacemakers, as it could inhibit or interfere with their operation.
- It is also recommended that electrodes not be placed close to the carotid sinus, over the eyes, open wounds, irritated skin or internally.
- Although TENS is often used in an effort to reduce consumption of narcotics, caution is still recommended when using these devices on patients who are taking concomitant narcotic medications.
- The limited availability of evidence on the safety of TENS, regardless of how safe it is believed to be, suggests that future studies should collect this information and report on the occurrence of adverse effects.

4.3 Summary with respect to economic studies

- None of the previously reported HTAs contained formal economic analyses specific to ENS. No full economic analyses were found in the published peer-reviewed literature.
- There is insufficient evidence from one costing study on chronic pain to evaluate the economic value of TENS. No studies pertaining to acute pain were found.
- Data from one costing study on chronic pain suggests that the number of persons using pain medications and muscle relaxants after six months of TENS use decreased significantly as did the number of visits for physical or occupational therapy. Simulated cost savings estimates for medications over 12 months ranged from $240-$560 (in 1994) US Dollars per patient and $1052 assuming 12 PT/OT visits in 6 months.
- Paths of clinical care are not delineated in the literature and the costs and consequences of TENS use would most likely vary by pain condition and clinical pathway.

Table 22. Overall Strength of Evidence (SoE) Criteria

SoE	Description	Further Research Impact	Domain Criterion Met		
			Quality	Quantity	Consistency
1	High	Very unlikely to change confidence in effect estimate	+	+	+
2	Moderate	Likely to have an important impact on confidence in estimate and *may* change the estimate	+	-	+
			+	+	-
3	Low	Very likely to have an important impact on confidence in estimate and *likely* to change the estimate	+	-	-
			-	+	+
4	Very Low	Any effect estimate is uncertain	-	+	-
			-	-	+
			-	-	-

Table 23. Summary of Evidence for each Key Question 1

Key Question 1: Evidence regarding efficacy and effectiveness of TENS for acute pain		
Outcome	**Efficacy**	**Results**

Pain relief	**LOW**	• Previously published HTAs generally report that, on the whole, there is insufficient consistent evidence to make a decision about the efficacy or effectiveness of TENS; TENS may be useful in certain situations (e.g. reducing analgesic need during labor). • TENS is generally not recommended for acute or subacute pain by guidelines found in the Clinical Guidelines Clearinghouse. The Ottawa Panel only found a small clinical benefit for low frequency TENS applied to the hand and wrist. *Acute Pain* • When looking at acute pain as a whole, the only significant results indicating a benefit of TENS were seen after two days of treatment in a study of 50 patients and when high frequency TENS was compared to a no treatment control in a study of 20 patients. • Due to insufficient extractable data in the studies included in this review, the authors of this review concluded that definitive conclusions about the effectiveness of TENS as an isolated treatment for acute pain in adults cannot be made. *Labor pain* • Pain relief during labor was not significantly different for women treated with TENS applied to their back, but there was a significant difference in the number of women reporting severe labor pain when TENS was applied to acupuncture points in 2 studies. • In a study of cranial TENS, duration of pain relief when TENS was given along with epidural was significantly longer than when epidural was given alone. • The authors of this review concluded that there is only limited evidence that TENS reduces pain in labor and it does not seem to have any impact (either positive or negative) on other outcomes for mothers or babies. • Recent evidence from a large study of 293 women did not observe any significant differences between TENS and placebo treatment. *Primary Dysmenorrhea* • More women reported high frequency TENS to improve overall pain relief than placebo when measured categorically (2 studies) or using a VAS (1 study), but not those receiving low frequency TENS (4 studies). • In studies of LFTENS, 3 studies that evaluated number of women with a positive overall pain experience and 1 study that measured pain relief on a VAS reported no significant differences with placebo. Two studies that did not provide descriptive data, however, reported LFTENS to be more effective than placebo in relieving pain. • When compared to medical treatment, TENS was less effective at reducing pain than ibuprofen (1 study). • A significantly greater number of women treated with high frequency TENS reported a positive overall experience with pain relief than those treated with low frequency TENS in a study of 42 women, but there was no difference in this same study when pain relief was measured by VAS. • There were a limited number of high quality studies and significant heterogeneity across studies with respect to TENS delivery. TENS treatments varied in frequency, amplitude, electrode placement, duration of each session, total duration of treatment. Most of the Cochrane Reviews could not combine data for meta-analysis. • The authors of this review concluded that high frequency TENS was effective for the treatment of dysmenorrhea by a number of small trials, but evidence was insufficient to determine the effectiveness of low frequency TENS. • A recent RCT found compared TENS to interferential current therapy and found both to be effective at reducing pain; this study did not include a placebo or no treatment control group.
Patient satisfaction	**MODERATE**	*Labor pain* • Use of TENS for control of pain during labor was preferred by more women than was placebo, whether applied to the back or acupuncture points (5 studies); in one study, women receiving TENS at acupuncture points were more likely to use TENS in a future labor.

Analgesic consumption	**LOW**	*Primary dysmenorrhea* • In two studies, there was not a significant difference between high frequency TENS and placebo in the number of women who requested additional analgesics or the number of tablets taken (n=64 and 24, respectively), • In another study of 24 women, the number of tablets of additional analgesic used was significantly less for the low frequency TENS group than the placebo TENS group.
Functional outcomes	**VERY LOW**	• Not reported

Key Question 1: Evidence regarding efficacy and effectiveness of TENS for chronic pain		
Outcome	**Efficacy**	**Results**
Pain relief	**MODERATE**	• Previously published HTAs generally report that, on the whole, there is insufficient consistent evidence to make a decision about the efficacy or effectiveness of TENS; TENS may be useful in certain situations (e.g. reducing analgesic need during labor). • The Clinical Guidelines Clearinghouse contains very little info on TENS for use specific chronic pain conditions. The only recommendations made for the use of ENS are with back pain and osteoarthritis of the knee, but still the evidence is described as being limited. TENS is not recommended for treatment of headache. *Chronic Pain* • Patients treated with TENS were more likely to report overall positive effects of treatment when compared to sham within the first week of treatment, but this advantage decreased over time (follow-up for most studies did not exceed four weeks) • Only three studies described long-term efficacy of relief. • When TENS was used in multiple dose treatments, only 3 of 7 were considered to be in favor of the active TENS. • For active controlled studies (HFTENS vs. LFTENS), 5 of 7 studies found no difference in analgesic efficacy between HFTENS and LFTENS at any time point. • Clinical importance of effect of TENS on pain relief cannot be commented on. • The authors of this review concluded that the published literature lacks the methodological rigor or robust reporting needed to make confident assessments of the role of TENS in chronic pain management. *Osteoarthritis of the knee* • Statistically significant improvements in pain with TENS treatment, measured as reductions in VAS pain intensity, were observed in 6 studies (n=254) that compared TENS and ALTENS to placebo TENS. • Patients treated with TENS were four times as likely than those in the placebo group to report improvement immediately after treatment (5 studies, n=214) and during follow-up (2 studies, n=62). • In a study of 40 patients, comparing ALTENS to placebo, there was not a statistically significant difference in pain relief between groups. • In subgroup analyses, pain improvement was statistically significant in high quality studies, studies of repeated TENS applications, and studies with treatment durations of at least 4 weeks. • A recent RCT comparing TENS to hyaluronic acid injection in 52 patients observed reductions in pain after 3 weeks of treatment, but did not find any significant difference between the two groups. • The only study to evaluate percutaneous neuromodulation therapy (PNT) in 63 patients reported greater pain immediately post-treatmetn when compared to placebo but this did not remain significant at later follow-up times. • The authors of this review concluded that TENS and ALTENS are effective in pain control over placebo. Heterogeneity of the included studies was observed, which might be due to the different study designs and outcomes used. 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. • Using the criterion of 0.80 to indicate a large effect, differences in pain relief when comparing TENS/ALTENS to placebo and high rate TENS vs. placebo could be considered clinically important (SMDs -0.79 and -1.12, respectively).
	LOW	*Chronic Low Back Pain (LBP)* • No statistically significant differences in pain intensity or pain relief were observed for conventional TENS when compared to ALTENS 4 weeks after treatment (1 study) or placebo 2 weeks after treatment (1 study).

- One study of 27 patients reported reduced pain and activity pain scores for patients treated with TENS and reduced pain for ALTENS when compared to placebo.
- A recent RCT of 23 female patients with chronic LBP found no statistically significant differences between low frequency TENS and placebo up to 8 weeks post-treatment.
- The authors of this review concluded that evidence from the small number of placebo-controlled trials does not support the use of TENS in the routine management of chronic LBP.

Rheumatoid Arthritis in the Hand

- After 3 weeks of treatment in a study of 32 patients, those patients receiving ALTENS treatment reported significantly lower pain intensity and grip pain scores than placebo, however, the latter was not statistically significant.
- In a study of 22 patients treated with conventional TENS, there were no statistically significant differences in resting pain score, improvement in VAS score or number of tender joints compared to ALTENS after a single treatment of 20 minutes.
- Although there was a statistically significant difference in reduction of joint tenderness scores, the scores did not meet the reviewer's criterion of 15% relative improvement for clinical benefit.
- Five-minute daily treatments over a period of 15 days with conventional TENS did not result in statistically significant differences in the number of patients reporting improvement.
- The authors of the review concluded that given there conflicting effects of TENS on pain outcomes in patients with RA, more well designed studies with a standardized protocol and adequate number of subjects are needed to fully conclude the effect of C-TENS and AL-TENS in the treatment of RA of the hand.

Neck Disorders

- A single 20-minute treatment with TENS showed significantly reduced pain intensity and trigger point tenderness compared to placebo in a study of 38 patients.
- No statistically significant differences in pain relief were reported in a study of 20 patients comparing TENS + collar, manual therapy + collar, and collar alone.
- There was no statistically significant difference in pain intensity after 5 days when diadynamic (interferential) therapy was compared to placebo in a study of 40 patients.
- The authors of the review concluded that definitive statements on electrotherapy for mechanical neck disorders could not be made. The current evidence on ENS is either lacking, limited, or conflicting. Future trials should have larger patient samples and include more precise standardization and description of all treatment characteristics.

Post-Stroke Shoulder Pain

- There were no statistically significant differences in VAS pain intensity or new reports of shoulder pain between TENS and control
- Electrical stimulation led to significantly greater pain improvement than control, but there were no differences in new reports of shoulder pain.
- The authors of the review concluded that the evidence from RCTs does not confirm or refute that electrical stimulation around the shoulder after stroke influences reports of pain, but there do appear to be benefits for passive humeral lateral rotation. A possible mechanism is through the reductionof glenohumeral subluxation. Further studies are required.

Cancer Pain

- No significant differences were reported between TENS and transcutaneous spinal electroanalgesia or between ALTENS and placebo.
- The authors of this review concluded that the results were inconclusive due to a lack of suitable RCTs, and that large multi-centre RCTs are required to assess the value of TENS in the management of cancer-related pain in adults.

Patient satisfaction	**LOW**	*Osteoarthritis of the knee* • Patients treated with PNT were more likely than those treated with placebo to report positive outcomes with respect to overall satisfaction with treatment after 48 hours and one week of follow-up. *Rheumatoid Arthritis in the Hand* • A clinically important benefit (21% risk difference) on patient assessment of change in disease was reported for conventional TENS over ALTENS. • There was no statistically significant differences in patient-rated improvement after 5 days when diadynamic (interferential) therapy was compared to placebo in a study of 40 patients *Cancer Pain* • TENS was only found to be advantageous over transcutaneous spinal electroanalgesia on one dimension of a patients satisfaction questionnaire.
Analgesic consumption	**LOW**	• *Osteoarthritis of the knee* • Patients treated with PNT (one study, n=63) were more likely than those treated with placebo to report reductions in medication after one week of follow-up.
Functional outcomes	**VERY LOW**	*Chronic Low Back Pain (LBP)* • No statistically significant differences were reported for conventional TENS on the Oswestry Disability Index and Low Back Pain Outcome Scale in a study of 27 patients, but significant benefit was seen on 4 out of 8 sections of the SF-36; significant benefit was seen for 2 out of 8 sections on the SF-36 for ALTENS. *Osteoarthritis of the Knee* • When compared to placebo, patients treated with ALTENS were shown to have greater improvement in knee stiffness, quadriceps muscle strength, and knee flexion in one study of 50 patients. *Rheumatoid Arthritis in the Hand* • There were no statistically significant differences between TENS and placebo in power score or work score at the end of 3 weeks treatment in a study of 32 patients. *Post-Stroke Shoulder Pain* • Patients treated with high intensity TENS or functional electrical stimulation showed greater improvement in passive lateral humeral rotation when compared to control.

Table 24. Summary of Evidence for each Key Question 2

Key Question 2: Evidence regarding safety in patients with acute pain		
Adverse events	**MODERATE**	** SoE 2 given that most studies report either minimal or no adverse effects • Previous HTAs have either not reported on safety or report that no serious adverse events have been reported with TENS use. *Acute Pain* • Adverse effects not reported in 4/12 included studies. • Five studies reported a range of side effects, however, only shoulder pain occurred more often in TENS patients than control group; nausea, bradycardia, dizziness were more common in control group. *Labor Pain* • No adverse effects were reported in the included studies. *Dysmenorrhea* • In a study of 64 women, minor adverse events were more common in the high frequency TENS group (4/32) than the placebo group. • Adverse events reported included: muscle vibrations, tightness, headaches after use, and slight redness or burning of the skin. • When compared to ibuprofen in a study of 24 women, significantly more women (10/12) treated with TENS experienced minor adverse effects (described as 'pain from treatment). • The women who reported pain from TENS in one study stated that they were prepared to accept the short-term pain from the treatment in return for relief of dysmenorrhea.
Key Question 2: Evidence regarding safety in patients with chronic pain		
Adverse Events	**MODERATE**	** SoE 2 given that most studies report either minimal or no adverse effects. • Previous HTAs have either not reported on safety or report that no serious adverse events have been reported with TENS use. *Chronic Pain* • Only one of the 25 included studies detailed methods to detect adverse effects; this study found no difference in side effects between the groups. • Other studies indicated skin rash, irritation or burning at electrode site; most only reported adverse effects for a small number of patients and others did not specify how many patients experienced adverse effects. • Three studies made a clear statement that no participants experienced side effects. *Chronic LBP* • Typically minor skin irritations observed equally in the treatment and placebo groups. One participant developed a severe rash four days after the start of treatment. *Osteoarthritis of the Knee* • None reported. *Rheumatoid Arthritis in the Hand* • Review authors state that adverse effects were not reported in the included studies. *Neck Disorders* • Review authors state that adverse effects were not reported in the included studies. *Post-stroke Shoulder Pain* • Review authors state that no adverse effects were noted.

		Cancer Pain • Review authors state that adverse effects were monitored and 'minimal' in 1 of the 2 included studies.

Table 25. Summary of Evidence for each Key Question 3

Key Question 4: Evidence regarding cost-effectiveness for treatment of acute pain		
	No evidence	• No economic studies on use of ENS for acute pain were identified
Key Question 4: Evidence regarding cost-effectiveness for treatment of chronic pain		
Cost savings	**VERY LOW**	• No full economic analyses were identified in the peer reviewed literature and none were done as part of previous HTAs • The number of persons using pain medications and muscle relaxants after six months of TENS use decreased significantly as did the number of visits for physical or occupational therapy. • Simulated cost savings estimates for medications over 12 months ranged from $240-$560 (in 1994) US Dollars per patient and $1052 assuming 12 PT/OT visits in 6 months.

BIBLIOGRAPHY

1. *Health, United States, 2006*: Centers for Disease Control, National Center for Health Statistics;2006.
2. Hootman J, Bolen J, Helmick C, Langmaid G. Prevalence of doctor-diagnosed arthritis and arthritis-attributable activity limitation - United States, 2003-2005. *MMWR.* 2006;55(40):1089-1092.
3. Arthritis: Meeting the Challenge. 2009; http://www.cdc.gov/nccdphp/publications/aag/arthritis.htm.
4. Schatman ME, Campbell A. *Chronic pain management : guidelines for multidisciplinary program development*. New York: Informa Healthcare; 2007.
5. Walsh DM, Howe TE, Johnson MI, Sluka KA. Transcutaneous electrical nerve stimulation for acute pain. *Cochrane Database Syst Rev.* 2009(2):CD006142.
6. Dowswell T, Bedwell C, Lavender T, Neilson JP. Transcutaneous electrical nerve stimulation (TENS) for pain relief in labour. *Cochrane Database Syst Rev.* 2009(2):CD007214.
7. Proctor ML, Smith CA, Farquhar CM, Stones RW. Transcutaneous electrical nerve stimulation and acupuncture for primary dysmenorrhoea. *Cochrane Database Syst Rev.* 2002(1):CD002123.
8. Nnoaham KE, Kumbang J. Transcutaneous electrical nerve stimulation (TENS) for chronic pain. *Cochrane Database Syst Rev.* 2008(3):CD003222.
9. Khadilkar A, Odebiyi DO, Brosseau L, Wells GA. Transcutaneous electrical nerve stimulation (TENS) versus placebo for chronic low-back pain. *Cochrane Database of Systematic Reviews.* 2008;(4)(CD003008).
10. Osiri M, Welch V, Brosseau L, et al. Transcutaneous electrical nerve stimulation for knee osteoarthritis. *Cochrane Database Syst Rev.* 2000(4):CD002823.
11. Brosseau L, Judd MG, Marchand S, et al. Transcutaneous electrical nerve stimulation (TENS) for the treatment of rheumatoid arthritis in the hand. *Cochrane Database Syst Rev.* 2003(3):CD004377.
12. Kroeling P, Gross AR, Goldsmith CH. A Cochrane review of electrotherapy for mechanical neck disorders. *Spine.* Nov 1 2005;30(21):E641-648.
13. Price CI, Pandyan AD. Electrical stimulation for preventing and treating post-stroke shoulder pain. *Cochrane Database Syst Rev.* 2000(4):CD001698.
14. Robb KA, Bennett MI, Johnson MI, Simpson KJ, Oxberry SG. Transcutaneous electric nerve stimulation (TENS) for cancer pain in adults. *Cochrane Database Syst Rev.* 2008(3):CD006276.
15. Braly D. *TENS market spurred by high end retail - transcutaneous electrical nerve stimulation devices*1993.
16. Lampl C, Kreczi T, Klingler D. Transcutaneous electrical nerve stimulation in the treatment of chronic pain: predictive factors and evaluation of the method. *Clin J Pain.* Jun 1998;14(2):134-142.
17. International Association for the Study of Pain (IASP) website. Available from:. http://www.iasp-pain.org/AM/Template.cfm?Section=Home&Template=/CM/HTMLDisplay.cfm&ContentID=3058#Pain.
18. Basbaum AI, Fields HL. Endogenous pain control mechanisms: review and hypothesis. *Ann Neurol.* Nov 1978;4(5):451-462.

19. Hillman P, Wall PD. Inhibitory and excitatory factors influencing the receptive fields of lamina 5 spinal cord cells. *Exp Brain Res.* 1969;9(4):284-306.

20. Facchinetti F, Sandrini G, Petraglia F, Alfonsi E, Nappi G, Genazzani AR. Concomitant increase in nociceptive flexion reflex threshold and plasma opioids following transcutaneous nerve stimulation. *Pain.* Jul 1984;19(3):295-303.

21. Gao M, He LF. [Increase of mu opioid receptor density in rat central nervous system following formalin nociception and its enhancement by electroacupuncture]. *Sheng Li Xue Bao.* Apr 1996;48(2):125-131.

22. Han JS, Chen XH, Sun SL, et al. Effect of low- and high-frequency TENS on Met-enkephalin-Arg-Phe and dynorphin A immunoreactivity in human lumbar CSF. *Pain.* Dec 1991;47(3):295-298.

23. Walsh DM, Lowe AS, McCormack K, Willer JC, Baxter GD, Allen JM. Transcutaneous electrical nerve stimulation: effect on peripheral nerve conduction, mechanical pain threshold, and tactile threshold in humans. *Arch Phys Med Rehabil.* Sep 1998;79(9):1051-1058.

24. Cramp AF, Gilsenan C, Lowe AS, Walsh DM. The effect of high- and low-frequency transcutaneous electrical nerve stimulation upon cutaneous blood flow and skin temperature in healthy subjects. *Clin Physiol.* Mar 2000;20(2):150-157.

25. Sluka K. TENS mechanism of action. In: Schmidt RF, Willis WD, eds. *Encyclopedia of pain (Muscle pain management)*. Berlin ; New York: Springer-Verlag; 2007:2406-2409.

26. Kang RW, Lewis PB, Kramer A, Hayden JK, Cole BJ. Prospective randomized single-blinded controlled clinical trial of percutaneous neuromodulation pain therapy device versus sham for the osteoarthritic knee: a pilot study. *Orthopedics.* Jun 2007;30(6):439-445.

27. Ernst E. Acupuncture: What Does the Most Reliable Evidence Tell Us? *Journal of Pain and Symptom Management.* April 2009;37(4):709-714.

28. McLennon S. *Persistent pain management.* Iowa City: AHRQ: National Guideline Clearinghouse; Aug 2005.

29. Grant DJ, Bishop-Miller J, Winchester DM, Anderson M, Faulkner S. A randomized comparative trial of acupuncture versus transcutaneous electrical nerve stimulation for chronic back pain in the elderly. *Pain.* Jul 1999;82(1):9-13.

30. Philadelphia Panel evidence-based clinical practice guidelines on selected rehabilitation interventions for knee pain. *Phys Ther.* Oct 2001;81(10):1675-1700.

31. Low back disorders. In: Hegmann KT, L.S. G, eds. *Occupational medicine practive guidelines: evaluation and management of common health problems and functional recovery in workers*. Elk Grove Village (IL) 2007.

32. Ottawa Panel evidence-based clinical practice guidelines for electrotherapy and thermotherapy interventions in the management of rheumatoid arthritis in adults. *Phys Ther.* 2004 Nov;84(11):1016-1043.

33. *Diagnosis and treatment of headache.* Bloomington, MN: Institute for Clinical Systems Improvement (ICSI);2007.

34. Mauskop A, Graff-Radford S. Special treatment situations: alternative headache treatments. *Standards of care for headache diagnosis and treatment*. Chicago (IL): National Headache Foundation; 2004:115-122.

35. Cruccu G, Aziz TZ, Garcia-Larrea L, et al. EFNS guidelines on neurostimulation therapy for neuropathic pain. *Eur J Neurol.* Sep 2007;14(9):952-970.

36. Chou R, Huffman LH. Nonpharmacologic therapies for acute and chronic low back pain: A review of the evidence for an American Pain Society/American College of Physicians clinical practice guideline. *Annals of Internal Medicine.* 02 2007;147(7):492-504.

37. Chou R, Loeser JD, Owens DK, et al. Interventional therapies, surgery, and interdisciplinary rehabilitation for low back pain: An evidence-based clinical practice guideline from the American pain society. *Spine.* 01 2009;34(10):1066-1077.

38. Phillips B, Ball C, Sackett D. Levels of evidence and grades of recommendation. Available at: http://www.cebm.net/levels_of_evidence.asp.

39. Atkins D, Best D, Briss PA, et al. Grading quality of evidence and strength of recommendations. *BMJ.* Jun 19 2004;328(7454):1490.

40. West S, King V, Carey TS, et al. Systems to rate the strength of scientific evidence. *Evid Rep Technol Assess (Summ).* Mar 2002(47):1-11.

41. Shea BJ, Bouter LM, Peterson J, et al. External validation of a measurement tool to assess systematic reviews (AMSTAR). *PLoS One.* 2007;2(12):e1350.

42. Ofman JJ, Sullivan SD, Neumann PJ, al. e. Examining the value and quality of health economic analyses: implications of utilizing the QHES. *J Manag Care Pharm.* Jan-Feb 2003(9):53-61.

43. Hayes I. *Transcutaneous electrical nerve stimulation for the treatment of pain.* Lansdale, PA August 2000.

44. McQuay HJ, Moore RA, Eccleston C, Morley S, Williams AC. Systematic review of outpatient services for chronic pain control. *Health Technology Assessment.* 1997;1(6).

45. *Transcutaneous electrical nerve stimulation (TENS) and pain management.* Ottowa, Ontario: Canadian Coordinating Office for Health Technology Assessment; April 1995.

46. Pichon RA, Augustovski F, Alcaraz A, et al. *Transcutaneous electrical nerve stimulation (TENS-PENS) for back pain.* Ciudad de Buenos Aires: Institute for Clinical Effectiveness and Health Policy (IECS);2007.

47. Murphy DE, McDonald A, Power C, Unwin A, MacSullivan R. Measurement of pain: a comparison of the visual analogue with a nonvisual analogue scale. *Clin J Pain.* 1988;3:197-199.

48. Cohen J, ed. *Statistical power analysis for the behavioral sciences, 2nd ed*. Hillside, NJ: Lawrence Erlbaur Associates; 1988.

49. Higgins J, Green S, Cochrane Collaboration. *Cochrane handbook for systematic reviews of interventions*. Chichester, West Sussex ; Hoboken NJ: John Wiley & Sons; 2008.

50. Felson DT, Anderson JJ, Boers M, et al. American College of Rheumatology. Preliminary definition of improvement in rheumatoid arthritis. *Arthritis Rheum.* Jun 1995;38(6):727-735.

51. Guyatt GH, Sackett DL, Sinclair JC, Hayward R, Cook DJ, Cook RJ. Users' guides to the medical literature. IX. A method for grading health care recommendations. Evidence-Based Medicine Working Group. *Jama.* Dec 13 1995;274(22):1800-1804.

52. McQuay HJ, Barden J, Moore RA. Clinically important changes-what's important and whose change is it anyway? *J Pain Symptom Manage.* May 2003;25(5):395-396.

53. Farrar JT, Berlin JA, Strom BL. Clinically important changes in acute pain outcome measures: a validation study. *J Pain Symptom Manage.* May 2003;25(5):406-411.

54. Borup L, Wurlitzer W, Hedegaard M, Kesmodel US, Hvidman L. Acupuncture as pain relief during delivery: a randomized controlled trial. *Birth.* Mar 2009;36(1):5--12.

55. Tugay N, Akbayrak T, Demirturk F, et al. Effectiveness of transcutaneous electrical nerve stimulation and interferential current in primary dysmenorrhea. *Pain Med.* May-Jun 2007;8(4):295-300.

56. Kofotolis ND, Vlachopoulos SP, Kellis E. Sequentially allocated clinical trial of rhythmic stabilization exercises and TENS in women with chronic low back pain. *Clinical Rehabilitation.* Feb 2008;22(2):99-111.

57. Itoh K, Itoh S, Katsumi Y, Kitakoji H. A pilot study on using acupuncture and transcutaneous electrical nerve stimulation to treat chronic non-specific low back pain. *Complement Ther Clin Pract.* Feb 2009;15(1):22-25.

58. Paker N, Tekdos D, Kesiktas N, Soy D. Comparison of the therapeutic efficacy of TENS versus intra-articular hyaluronic acid injection in patients with knee osteoarthritis: a prospective randomized study. *Adv Ther.* Mar-Apr 2006;23(2):342--353.

59. Abelson K, Langley GB, Sheppeard H, M. V, Wigley RD. Transcutaneous electrical nerve stimulation in rheumatoid arthritis. *New Zealand Medical Journal.* 1983;96(156-8).

60. Kroeling P, Gross A, Houghton PE. Electrotherapy for neck disorders. *Cochrane Database Syst Rev.* 2005(2):CD004251.

61. Hsueh TC, Cheng PT, Kuan TS, Hong CZ. The immediate effectiveness of electrical nerve stimulation and electrical muscle stimulation on myofascial trigger points. *Am J Phys Med Rehabil.* 1997;76(6):471-476.

62. Cheing GL, Tsui AY, Lo SK, Hui-Chan CW. Optimal stimulation duration of tens in the management of osteoarthritic knee pain. *J Rehabil Med.* Mar 2003;35(2):62-68.

63. Robb K, Oxberry SG, Bennett MI, Johnson MI, Simpson KH, Searle RD. A cochrane systematic review of transcutaneous electrical nerve stimulation for cancer pain. *J Pain Symptom Manage.* Apr 2009;37(4):746-753.

64. Reeve J, Menon D, Corabian P. Transcutaneous electrical nerve stimulation (TENS): a technology assessment. *Int J Technol Assess Health Care.* 1996;12(2):299-324.

65. Chabal C, Fishbain DA, Weaver M, Heine LW. Long-term transcutaneous electrical nerve stimulation (TENS) use: impact on medication utilization and physical therapy costs. *Clin J Pain.* Mar 1998;14(1):66-73.

66. Fishbain DA, Chabal C, Abbott A, Heine LW, Cutler R. Transcutaneous electrical nerve stimulation (TENS) treatment outcome in long-term users. *Clin J Pain.* Sep 1996;12(3):201-214.

67. Carey TS, Mielenz TJ. Measuring outcomes in back care. *Spine (Phila Pa 1976).* May 15 2007;32(11 Suppl):S9-14.

68. Calmels P, Queneau P, Hamonet C, et al. Effectiveness of a lumbar belt in subacute low back pain: an open, multicentric, and randomized clinical study. *Spine (Phila Pa 1976).* Feb 1 2009;34(3):215-220.

69. Freeman BJ, Steele NA, Sach TH, Hegarty J, Soegaard R. ISSLS prize winner: cost-effectiveness of two forms of circumferential lumbar fusion: a prospective randomized controlled trial. *Spine (Phila Pa 1976).* Dec 1 2007;32(25):2891-2897.

70. Hall AM, Maher CG, Latimer J, Ferreira ML, Lam P. A randomized controlled trial of tai chi for long-term low back pain (TAI CHI): study rationale, design, and methods. *BMC Musculoskelet Disord.* 2009;10:55.