Washington State Health Care Authority

Health Technology Assessment

HTA Final Appendices

Electrical Neural Stimulation for the Treatment of Pain

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Electrical Neural Stimulation for the Treatment of Pain

Provided by:

Spectrum Research, Inc.

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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APPENDIX A: SEARCH STRATEGIES

Once all relevant Cochrane Reviews were obtained from the Cochrane database, the search strategies were replicated to identify any studies published since the most recent update for that review.

OVID MEDLINE SEARCHES

Acute pain (Aug 2008 - Aug 2009)

1. exp Pain/
2. Pain Measurement/
3. Pain Threshold/
4. Pain Clinics/
5. Myofascial Pain Syndromes/
6. Hyperalgesia/
7. exp Headache Disorders/
8. (toothache$ or tooth-ache$ or ear-ache$ or earache$ or sciatic$ or neuralgi$ or migraine$ or headache$ or neuralgi$ or cephalalgi$ or metatarsalgia$ or bursitis or hyperalg$).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name]
9. pain$.ti.
10. pain$.ab.
11. exp Angina Pectoris/
12. angina.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name]
13. Metatarsalgia/
14. or/1-13
15. exp Transcutaneous Electric Nerve Stimulation/
16. “TENS”.ti.
17. “TENS”.ab.
18. “TNS”.ti.
19. “TNS”.ab.
20. “ENS”.ti.
21. “ENS”.ab.
22. (“transcutaneous electric$ nerve stimulation” or “transcutaneous nerve stimulation”).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name]
23. (“electric$ nerve stimulation” or “electrostimulation therap$” or “electro-stimulation therap$”).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name]
24. (“electric$ nerve therap$” or electroanalgesi$).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name]
25. transcutaneous electric$ stimulation.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name]
26. TES.ti,ab.
27. or/15-26
28. 14 and 27
29. RANDOMIZED CONTROLLED TRIAL.pt.
30. CONTROLLED CLINICAL TRIAL.pt.
31. RANDOMIZED CONTROLLED TRIALS.sh.
32. RANDOM ALLOCATION.sh.
33. DOUBLE BLIND METHOD.sh.
34. SINGLE BLIND METHOD.sh.
35. or/29-34

36. (ANIMALS not HUMAN).sh.
37. 35 not 36
38. CLINICAL TRIAL.pt.
39. exp CLINICAL TRIALS/
40. (clin$ adj25 trial$).ti,ab.
41. ((singl$ or doubl$ or trebl$ or tripl$) adj25 (blind$ or mask$)).ti,ab.
42. PLACEBOS.sh.
43. placebo$.ti,ab.
44. random$.ti,ab.
45. RESEARCH DESIGN.sh.
46. or/38-45
47. 46 not 36
48. 47 not 37
49. 37 or 48
50. 28 and 49
limits: abstract, humans, English

Primary Dysmenorrhea (Aug 2001 - Aug 2009)
1 exp Menstruation disorders/, exp Menstruation disorders/
2 Pelvic pain/
3 (pelvic adj5 pain).tw.
4 Dysmenorrhea/
5 dysmenorrh$.tw.
6 (painful adj5 menstrua$).tw.
7 (painful adj5 period$).tw.
8 menstrual disorder.tw.
9 or/1-8
10 Transcutaneous electric nerve stimulation/
11 transcutaneous electrical nerve stimulation.tw.
12 transcutaneous nerve stimulation.tw.
13 nerve stimulation.tw.
14 TENS.tw.
15 Acupuncture/
16 Acupuncture therapy/
17 acupuncture$.tw.
18 or/10-17
19 9 and 18
limits: abstract, humans, English

Chronic Pain (Apr 2008 - Aug 2009)
Search strategy not provided in review, therefore the following strategy was used.

1 “Clinical Trial” [publication type]
2 randomized [tiab]
3 placebo [tiab]
4 randomly [tiab]
5 trial [tiab]
6 groups [tiab]
7 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7
8 chronic [tiab]
9 pain [tiab]

10 #8 OR #9
11 Transcutaneous Electric Nerve Stimulation [mesh]
12 TENS [tiab]
13 TNS [tiab]
14 “transcutaneous electric$ nerve stimulation”
15 “transcutaneous nerve stimulation”
16 “electric$ nerve stimulation”
17 “electric$ neuromodulation”
18 “percutaneous neuromodulation”
19 #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18
20 #7 AND #10 AND #19
limits: abstract, humans, English

Chronic Low Back Pain (Jan 2007- Aug 2009)
1 exp “Clinical Trial [Publication Type]”/
2 randomized.ab,ti.
3 placebo.ab,ti.
4 dt.fs.
5 randomly.ab,ti.
6 trial.ab,ti.
7 groups.ab,ti.
8 or/1-7
9 Animals/
10 Humans/
11 9 not (9 and 10)
12 8 not 11
13 dorsalgia.ti,ab.
14 exp Back Pain/
15 backache.ti,ab.
16 (lumbar adj pain).ti,ab.
17 coccyx.ti,ab.
18 coccydynia.ti,ab.
19 sciatica.ti,ab.
20 sciatica/
21 spondylosis.ti,ab.
22 lumbago.ti,ab.
23 exp Low Back Pain/
24 low back pain.mp.
25 or/13-24
26 Transcutaneous Electric Nerve Stimulation/
27 TENS.mp.
28 ALTENS.mp.
29 transcutaneous nerve stimulation.mp.
30 TNS.mp.
31 transcutaneous electrical neurostimulation.mp.
32 TENMS.mp.
33 exp Electroacupuncture/
34 transdermal electrical stimulation.mp.
35 peripheral conditioning stimulation.mp.
36 percutaneous neural stimulation.mp.
37 microamperage electrical stimulation.mp.

38 cranial electrotherapy stimulation.mp.
39 transcutaneous cranial electrical stimulation.mp.
40 transabdominal neurostimulation.mp.
41 exp Electric Stimulation Therapy/
42 exp Electric Stimulation/
43 electroanalgesia.mp.
44 electrotherapy.mp.
45 or/26-44
46 12 and 25 and 45
limits: abstract, humans, English

Cancer Pain (April 2008 – Aug 2009)
1. TRANSCUTANEOUS ADJ ELECTRIC ADJ NERVE ADJ STIMULATION
2. TRANSCUTANEOUS-ELECTRIC-NERVE-STIMULATION.DE.
3. TNS
4. PERCUTANEOUS ADJ ELECTRIC ADJ NERVE ADJ STIMULATION
5. ELECTRIC ADJ STIMULATION ADJ THERAPY
6. ELECTRIC-STIMULATION-THERAPY.DE.
7. ELECTRIC ADJ STIMULATION
8. ELECTROSTIMULATION
9. ELECTROANALGESI$
10. ELECTROTHERA$
11. ELECTROMAGNETI$
12. INTERFERENTIAL
13. REBOX
14. CODETRON
15. LIKON
16. 1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13 OR 14 OR 15
17. CANCER$
18. NEOPLASMS#.W..DE.
19. TUMOUR$
20. TUMOR$
21. ONCOLO$
22. CARCINOMA$
23. MALIGNAN$
24. 17 OR 18 OR 19 OR 20 OR 21 OR 22 OR 23
25. PAIN$
26. PAIN#.W..DE.
27. PAIN ADJ MEASUREMENT
28. PAIN-MEASUREMENT.DE.
29. PAIN ADJ SCALE
30. 25 OR 26 OR 27 OR 28 OR 29
31. 16 AND 24 AND 30
limits: abstract, humans, English

Osteoarthritis of the Knee (Jan 1999 - Aug 2009)
1. pain.tw,hw.
2. activities of daily living/
3. (joint$ adj4 (mobility or flexibility)).tw.
4. (return$ adj3 (work or leisure)).tw.

5. (function$ adj2 (status or abilit$)).tw.
6. (stiffness or swelling or swollen or tender).tw.
7. (flexion or extension or abduction or adduction).tw.
8. range of motion, articular/
9. (range adj2 motion).tw.s
10. (strength or power).tw.
11. (grip$ or force or rotation).tw.
12. (dynamomet$ or goniomet$).tw.
13. absenteeism/ or absenteeism.tw.
14. (sick leave or sick day$ or absence).tw.
15. sick leave/
16. (disabilit$ or (work$ adj compensation)).tw.
17. cost$.tw.
18. exp economics/ or ec.fs.
19. or/1-18
20. exp electric stimulation therapy/
21. ((electric$ adj nerve) or therapy).tw.
22. ((electric$ adj (stimulation or muscle)).tw.
23. electrostimulation.tw.
24. electroanalgesia.tw.
25. (tens or altens).tw.
26. electroacupuncture.tw.
27. neuromusc$ electric$.tw.
28. (high volt or pulsed or current).tw.
29. (electromagnetic or electrotherap$).tw.
30. iontophoresis.tw.
31. or/20-30
32. knee.sh,tw.
33. exp knee joint/
34. osteoarthritis/
35. osteoarthr$.tw.
36. (32 or 33) and (34 or 35)
37. 31 and 36
38. animal/ not (human/ and animal/)
39. 37 not 38
40. randomized controlled trial.pt.
41. controlled clinical trials/
42. exp cross-sectional studies/
43. controlled clinical trial.pt.
44. cross-section$.tw.
45. prospective.tw.
46. retrospective.tw.
47. exp cohort studies/
48. exp case-control studies/
49. random$.tw.
50. control$.tw.
51. (compare or comparative).tw.
52. comparative studies/
53. experiment$.tw.
54. or/40-53
56. 39 and 54

limits: abstract, humans, English

Rheumatoid Arthritis in the Hand (Jan 2003 – Aug 2009)
1. exp osteoarthritis/
2. osteoarthritis.tw.
3. osteoarthrosis.tw.
4. degenerative arthritis.tw.
5. exp arthritis, rheumatoid/
6. rheumatoid arthritis.tw.
7. rheumatism.tw.
8. arthritis, juvenile rheumatoid/
9. caplan's syndrome.tw.
10. felty's syndrome.tw.
11. rheumatoid.tw.
12. ankylosing spondylitis.tw.
13. arthrosis.tw.
14. sjogren$.tw.
15. or/1-14
16. exp electric stimulation therapy/
17. ((electric$ adj nerve) or therapy).tw.
18. electrostimulation.tw.
19. electroanalgesia.tw.
20. (tens or altens).tw.
21. electroacupuncture.tw.
22. (high volt or pulsed or current).tw.
23. (electromagnetic or electrotherap$).tw.
24. clinical trial.pt.
25. randomized controlled trial.pt.
26. tu.fs.
27. dt.fs.
28. random$.tw.
29. placebo$.tw.
30. ((sing$ or doubl$ or tripl$) adj (masked or blind$)).
31. sham.tw.
32. or/24-31
33. 23 and 32
limits: abstract, humans, English

Neck disorders (Jan 2003 – Aug 2009)
1.neck/ or neck muscles/ or exp cervical plexus/ or exp cervical vertebrae/ or Atlanto-Axial Joint/ or atlanto-occipital joint/ or axis/ or atlas/ or spinal nerve roots/ or exp brachial plexus/
2.(odontoid or cervical or occip: or atlant:).tw.
3.1 or 2
4.exp arthritis/ or exp myofascial pain syndromes/ or fibromyalgia/ or spondylitis/ or exp spinal osteophytosis/ or spondylolisthesis/
5.exp headache/ and cervic:.tw.
6.whiplash injuries/ or cervical rib syndrome/ or torticollis/ or cervico-brachial neuralgia.ti,ab,sh. or exp radiculitis/ or polyradiculitis/
or polyradiculoneuritis/ or thoracic outlet syndrome/
7.(monoradicul: or monoradicl:).tw.
8.4 or 5 or 6 or 7

9.random:.ti,ab,sh.
10.randomized controlled trial.pt.
11.Double-Blind Method/
12.single blind method/
13.placebos/
14.clinical trial.pt.
15.exp clinical trials/
16.controlled clinical trial.pt.
17.(clin$ adj25 trial$).ti,ab.
18.((singl$ or doubl$ or trebl$) adj25 (blind$ or mask$)).ti,ab.
19.placebo$.ti,ab.
20.or/9-19
21.exp combined modality therapy/ or exp electric stimulation therapy/ or Transcutaneous Electric Nerve Stimulation/ or exp rehabilitation/
or ultrasonic therapy/ or exp phototherapy/ or lasers/ or exp physical therapy/
22.exp arthritis/rh,th or expmyofascial pain syndromes/rh,th or fibromyalgia/rh,th or spondylitis/rh,th or exp spinal osteophytosis/rh,thor spondylosis/rh,th or spondylolisthesis/rh,th
23.exp headache/rh,th and cervic:.tw.
24.whiplash injuries/rh,th or cervical rib syndrome/rh,th or thoracic outlet syndrome/rh,th or torticollis/rh,th or cervico-brachial neuralgia/rh,th or exp radiculitis/rh,th or polyradiculitis/rh,th or polyradiculoneuritis/rh,th
25.or/22-24
26.3 and 8 and 21
27.3 and 25
28.26 or 27
29.20 and 28
limits: abstract, humans, English

Post-stroke Shoulder Pain (Jan 1998 – Aug 2009)
1. electric stimulation/
2. electric stimulation therapy/
3. transcutaneous electric nerve stimulation/
4. electric$ stimulation.tw
5. neuromuscular stimulation.tw
6. (FES or TENS or ES).tw
7. 1 or 2 or 3 or 4 or 5 or 6
8. exp cerebrovascular disorders/
9. cerebrovasc$.tw
10. stroke$.tw
11. hemiplegia/
12. (hemipleg$ or hemipar$).tw
13. 8 or 9 or 10 or 11 or 12
14. arm/
15. shoulder/
16. shoulder joint/
17. (arm$ or shoulder$ or upper limb$ or upper extremity$).tw
18. 14 or 15 or 16 or 17
19. pain/
20. pain$.tw
21. 19 or 20
22. 7 and 13 and 18 and 21
limits: abstract, humans, English

Chronic Headache (Nov 2002 – Aug 2009)
1. randomized controlled trial.pt.
2. controlled clinical trial.pt.
3. randomized controlled trials.sh.
4. random allocation.sh.
5. double blind method.sh.
6. single-blind method.sh.
7. or/1-6
8. (animal not human).sh.
9. 7 not 8
10. clinical trial.pt.
11. exp clinical trials/
12. (clin$ adj25 trial$).ti,ab.
13. ((singl$ or doubl$ or trebl$ or tripl$) adj25 (blind$ or mask$)).ti,ab.
14. placebos.sh.
15. placebo$.ti,ab.
16. random$.ti,ab.
17. research design.sh.
18. or/10-17
19. 18 not 8
20. 19 not 9
21. comparative study.sh.
22. exp evaluation studies/
23. follow up studies.sh.
24. prospective studies.sh.
25. (control$ or prospectiv$ or volunteer$).ti,ab.
26. or/21-25
27. 26 not 8
28. 26 not (9 or 20)
29. 9 or 20 or 28
30. exp headache/
31. exp physical therapy/
32. transcutaneous electric nerve stimulation/
33. interferential therapy.ti,ab.
34. “biofeedback (psychology)”/feedback/ph
35. manipulation, spinal.sh.
36. chiropractic.sh.
37. osteopathic medicine.sh.
38. heat/tu
39. ultrasonic therapy.sh.
40. electromagnetic therapy.ti,ab.
41. microcurrent.ti,ab.
42. laser therapy.ti,ab.
43. lasers/tu
44. myofascial pain syndromes/th
45. traction.sh.
46. or/31-45
47. 30 and 46
48. 29 and 47
limits: abstract, humans, English

EMBASE

Acute Pain (Aug 2008 – Aug 2009)
1. exp PAIN/
2. Pain Assessment/
3. Pain Threshold/
4. Pain Clinic/
5. Myofascial Pain/
6. HYPERALGESIA/
7. exp "Headache and Facial Pain"/
8. (toothache$ or tooth-ache$ or ear-ache$ or earache$ or sciatic$ or neuralgi$ or migraine$ or headache$ or neuralgi$ or cephalalgi$ or metatarsalgia$ or bursitis or hyperalg$).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name]
9. pain$.ti.
10. pain$.ab.
11. exp Angina Pectoris/
12. angina.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name]
13. METATARSALGIA/
14. or/1-13
15. exp Transcutaneous Nerve Stimulation/
16. "TENS".ti.
17. "TENS".ab.
18. "TNS".ti.
19. "TNS".ab.
20. "ENS".ti.
21. "ENS".ab.
22. ("transcutaneous electric$ nerve stimulation" or "transcutaneous nerve stimulation").mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name]
23. ("electric$ nerve stimulation" or "electrostimulation therap$" or "electro-stimulation therap$").mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name]
24. ("electric$ nerve therap$" or electroanalgesi$).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name]
25. transcutaneous electric$ stimulation.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name]
26. TES.ti,ab.
27. or/15-26
28. 14 and 27
29. random$.ti,ab.
30. factorial$.ti,ab.
31. (crossover$ or cross over$ or cross-over$).ti,ab.
32. placebo$.ti,ab.
33. (doubl$ adj blind$).ti,ab.
34. (singl$ adj blind$).ti,ab.
35. assign$.ti,ab.
36. allocat$.ti,ab.
37. volunteer$.ti,ab.
38. CROSSOVER PROCEDURE.sh.
39. DOUBLE-BLIND PROCEDURE.sh.

40. RANDOMIZED CONTROLLED TRIAL.sh.
41. SINGLE BLIND PROCEDURE.sh.
42. or/29-41
43. ANIMAL/ or NONHUMAN/ or ANIMAL EXPERIMENT/
44. HUMAN/
45. 44 and 43
46. 43 not 45
47. 42 not 46
48. 28 and 47
limits: abstract, human, English

Primary Dysmenorrhea (Aug 2001 - Aug 2009)
1 exp Menstruation disorders/, exp Menstruation disorders/
2 Pelvic pain/
3 (pelvic adj5 pain).tw.
4 Dysmenorrhea/
5 dysmenorrh$.tw.
6 (painful adj5 menstrua$).tw.
7 (painful adj5 period$).tw.
8 menstrual disorder.tw.
9 or/1-8
10 Transcutaneous electric nerve stimulation/
11 transcutaneous electrical nerve stimulation.tw.
12 transcutaneous nerve stimulation.tw.
13 nerve stimulation.tw.
14 TENS.tw.
15 or/10-14
16 9 and 15
limits: abstract, human, English

Chronic Pain (Apr 2008 - Aug 2009)
Search strategy not provided in review, therefore the following strategy was used.

1 “Clinical Trial” [publication type]
2 randomized [tiab]
3 placebo [tiab]
4 randomly [tiab]
5 trial [tiab]
6 groups [tiab]
7 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7
8 chronic [tiab]
9 pain [tiab]
10 #8 OR #9
11 Transcutaneous Electric Nerve Stimulation [mesh]
12 TENS [tiab]
13 TNS [tiab]
14 “transcutaneous electric$ nerve stimulation”
15 “transcutaneous nerve stimulation”
16 “electric$ nerve stimulation”
17 “electric$ neuromodulation”
18 “percutaneous neuromodulation”

19 #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18
20 #7 AND #10 AND #19
limits: abstract, humans, English

Chronic Low Back Pain (Jan 2007- Aug 2009)
1 exp "Clinical Trial [Publication Type]"/
2 randomized.ab,ti.
3 placebo.ab,ti.
4 dt.fs.
5 randomly.ab,ti.
6 trial.ab,ti.
7 groups.ab,ti.
8 or/1-7
9 Animals/
10 Humans/
11 9 not (9 and 10)
12 8 not 11
13 dorsalgia.ti,ab.
14 exp Back Pain/
15 backache.ti,ab.
16 (lumbar adj pain).ti,ab.
17 coccyx.ti,ab.
18 coccydynia.ti,ab.
19 sciatica.ti,ab.
20 sciatica/
21 spondylosis.ti,ab.
22 lumbago.ti,ab.
23 exp Low Back Pain/
24 low back pain.mp.
25 or/13-24
26 Transcutaneous Electric Nerve Stimulation/
27 TENS.mp.
28 ALTENS.mp.
29 transcutaneous nerve stimulation.mp.
30 TNS.mp.
31 transcutaneous electrical neurostimulation.mp.
32 TENMS.mp.
33 exp Electroacupuncture/
34 transdermal electrical stimulation.mp.
35 peripheral conditioning stimulation.mp.
36 percutaneous neural stimulation.mp.
37 microamperage electrical stimulation.mp.
38 cranial electrotherapy stimulation.mp.
39 transcutaneous cranial electrical stimulation.mp.
40 transabdominal neurostimulation.mp.
41 exp Electric Stimulation Therapy/
42 exp Electric Stimulation/
43 electroanalgesia.mp.
44 electrotherapy.mp.
45 or/26-44
46 12 and 25 and 45

limits: abstract, humans, English

Cancer Pain (April 2008 – Aug 2009)
1. TRANSCUTANEOUS ADJ ELECTRIC ADJ NERVE ADJ STIMULATION
2. TRANSCUTANEOUS-NERVE-STIMULATION.DE.
3. TNS
4. PERCUTANEOUS ADJ ELECTRIC ADJ NERVE ADJ STIMULATION
5. ELECTROSTIMULATION.W..DE.
6. ELECTRIC ADJ STIMULATION ADJ THERAPY
7. ELECTROSTIMULATION-THERAPY.DE. OR NERVE-STIMULATION#.DE.
8. ELECTRIC ADJ STIMULATION
9. ELECTROANALGESI$
10. ELECTROANALGESIA.W..DE.
11. ELECTROTHERA$
12. ELECTROMAGNETI$
13. INTERFERENTIAL
14. REBOX
15. CODETRON
16. LIKON
17. 1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13 OR 14 OR 15 OR 16
18. CANCER
19. NEOPLASM#.W..DE.
20. TUMOUR
21. TUMOR
22. ONCOLO$
23. CANCER-PAIN.DE.
24. CARCINOMA
25. MALIGNANT
26. MALIGNANCY
27. MALIGNANT-NEOPLASTIC-DISEASE#.DE.
28. 18 OR 19 OR 20 OR 21 OR 22 OR 23 OR 24 OR 25 OR 26 OR 27
29. PAIN
30. PAIN#.W..DE.
31. PAIN ADJ MEASUREMENT
32. PAIN-ASSESSMENT#.DE.
33. PAIN ADJ SCALE
34. 29 OR 30 OR 31 OR 32 OR 33
35. CLINICAL-TRIAL#
36. META-ANALYSIS.DE.
37. CLINICAL ADJ TRIAL
38. CONTROLLED ADJ CLINICAL ADJ TRIAL
39. RANDOMISED ADJ CONTROLLED ADJ TRIAL
40. META-ANALYSIS
41. EVIDENCE-BASED-PRACTICE#.DE.
42. EVALUATION
43. PROSPECTIVE
44. RANDOM ADJ ALLOCATION
45. MEDICAL-RESEARCH#.DE.
46. CLINICAL ADJ RESEARCH
47. CLINICAL-RESEARCH.DE.
48. 35 OR 36 OR 37 OR 38 OR 39 OR 40 OR 41 OR 42 OR 43 OR 44 OR 45 OR 46 OR 47

49. 17 AND 28 AND 34
50. 48 AND 49
51. ADULT# OR AGED.DE.
52. 50 AND 51
limits: abstract, human, English

Osteoarthritis of the Knee (Jan 1999 - Aug 2009)
1. pain.tw,hw.
2. activities of daily living/
3. (joint$ adj4 (mobility or flexibility)).tw.
4. (return$ adj3 (work or leisure)).tw.
5. (function$ adj2 (status or abilit$)).tw.
6. (stiffness or swelling or swollen or tender).tw.
7. (flexion or extension or abduction or adduction).tw.
8. range of motion, articular/
9. (range adj2 motion).tw.s
10. (strength or power).tw.
11. (grip$ or force or rotation).tw.
12. (dynamomet$ or goniomet$).tw.
13. absenteeism/ or absenteeism.tw.
14. (sick leave or sick day$ or absence).tw.
15. sick leave/
16. (disabilit$ or (work$ adj compensation)).tw.
17. cost$.tw.
18. exp economics/ or ec.fs.
19. or/1-18
20. exp electric stimulation therapy/
21. ((electric$ adj nerve) or therapy).tw.
22. ((electric$ adj (stimulation or muscle)).tw.
23. electrostimulation.tw.
24. electroanalgesia.tw.
25. (tens or altens).tw.
26. electroacupuncture.tw.
27. neuromusc$ electric$.tw.
28. (high volt or pulsed or current).tw.
29. (electromagnetic or electrotherap$).tw.
30. iontophoresis.tw.
31. or/20-30
32. knee.sh,tw.
33. exp knee joint/
34. osteoarthritis/
35. osteoarthr$.tw.
36. (32 or 33) and (34 or 35)
37. 31 and 36
38. animal/ not (human/ and animal/)
39. 37 not 38
40. randomized controlled trial.pt.
41. controlled clinical trials/
42. exp cross-sectional studies/
43. controlled clinical trial.pt.
44. cross-section$.tw.

45. prospective.tw.
46. retrospective.tw.
47. exp cohort studies/
48. exp case-control studies/
49. random$.tw..
50. (compare or comparative).tw.
51. comparative studies/
52. experiment$.tw.
53. or/40-52
54. 39 and 53
limits: abstract, humans, English

Rheumatoid Arthritis in the Hand (Jan 2003 – Aug 2009)
1. exp osteoarthritis/
2. osteoarthritis.tw.
3. osteoarthrosis.tw.
4. degenerative arthritis.tw.
5. exp arthritis, rheumatoid/
6. rheumatoid arthritis.tw.
7. rheumatism.tw.
8. arthritis, juvenile rheumatoid/
9. caplan's syndrome.tw.
10. felty's syndrome.tw.
11. rheumatoid.tw.
12. ankylosing spondylitis.tw.
13. arthrosis.tw.
14. sjogren$.tw.
15. or/1-14
16. exp electric stimulation therapy/
17. ((electric$ adj nerve) or therapy).tw.
18. electrostimulation.tw.
19. electroanalgesia.tw.
20. (tens or altens).tw.
21. electroacupuncture.tw.
22. (high volt or pulsed or current).tw.
23. (electromagnetic or electrotherap$).tw.
24. clinical trial.pt.
25. randomized controlled trial.pt.
26. tu.fs.
27. random$.tw.
28. placebo$.tw.
29. ((sing$ or doubl$ or tripl$) adj (masked or blind$)).
30. sham.tw.
31. or/24-31
32.15 and 31
limits: abstract, human, English

Neck disorders (Jan 2003 – Aug 2009)
1.neck/ or neck muscles/ or exp cervical plexus/ or exp cervical vertebrae/ or Atlanto-Axial Joint/ or atlanto-occipital joint/ or axis/ or atlas/ or spinal nerve roots/ or exp brachial plexus/
2.(odontoid or cervical or occip: or atlant:).tw.

3.1 or 2
4.exp arthritis/ or exp myofascial pain syndromes/ or fibromyalgia/ or spondylitis/ or exp spinal osteophytosis/ or spondylolisthesis/
5.exp headache/ and cervic:.tw.
6.whiplash injuries/ or cervical rib syndrome/ or torticollis/ or cervico-brachial neuralgia.ti,ab,sh. or exp radiculitis/ or polyradiculitis/ or polyradiculoneuritis/ or thoracic outlet syndrome/
7.(monoradicul: or monoradicl:).tw.
8.4 or 5 or 6 or 7
9.random:.ti,ab,sh.
10.randomized controlled trial.pt.
11.Double-Blind Method/
12.single blind method/
13.placebos/
14.clinical trial.pt.
15.exp clinical trials/
16.controlled clinical trial.pt.
17.(clin$ adj25 trial$).ti,ab.
18.((singl$ or doubl$ or trebl$) adj25 (blind$ or mask$)).ti,ab.
19.placebo$.ti,ab.
20.or/9-19
21.exp combined modality therapy/ or exp electric stimulation therapy/ or Transcutaneous Electric Nerve Stimulation/ or exp rehabilitation/ or ultrasonic therapy/ or exp phototherapy/ or lasers/ or exp physical therapy/
22.exp arthritis/rh,th or expmyofascial pain syndromes/rh,th or fibromyalgia/rh,th or spondylitis/rh,th or exp spinal osteophytosis/rh,thor spondylosis/rh,th or spondylolisthesis/rh,th
23.exp headache/rh,th and cervic:.tw.
24.whiplash injuries/rh,th or cervical rib syndrome/rh,th or thoracic outlet syndrome/rh,th or torticollis/rh,th or cervico-brachial neuralgia/rh,th or exp radiculitis/rh,th or polyradiculitis/rh,th or polyradiculoneuritis/rh,th
25.or/22-24
26.3 and 8 and 20
27.3 and 25
28.26 or 27
29.20 and 28
Limits: abstract, human, English

Post-stroke Shoulder Pain (Jan 1998 – Aug 2009)
1. electrostimulation/
2. electrostimulation therapy/
3. nerve stimulation/
4. transcutaneous nerve stimulation/
5. electric$ stimulation.tw
6. neuromuscular stimulation.tw
7. (FES or TENS or ES).tw
8. 1 or 2 or 3 or 4 or 5 or 6 or 7
9. exp cerebrovascular disease/
10. hemiplegia/
11. hemiparesis/
12. (cerebrovasc$ or stroke$ or hemipar$ or hemipleg$).tw
13. 9 or 10 or 11 or 12
14. arm/
15. arm movement/
16. arm muscle/

17. shoulder/
18. shoulder pain/
19. shoulder injury/
20. shoulder girdle/
21. shoulder hand syndrome/
22. frozen shoulder/
23. (arm$ or shoulder$ or upper limb$ or upper extremity$).tw
24. 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23
25. pain/
26. pain$.tw
27. 25 or 26
28. 8 and 13 and 24 and 27

Limits: abstract, human, English

Chronic Headache (Nov 2002 – Aug 2009)

1. randomized controlled trial.pt.
2. controlled clinical trial.pt.
3. randomized controlled trials.sh.
4. random allocation.sh.
5. double blind method.sh.
6. single-blind method.sh.
7. or/1-6
8. (animal not human).sh.
9. 7 not 8
10. clinical trial.pt.
11. exp clinical trials/
12. (clin$ adj25 trial$).ti,ab.
13. ((singl$ or doubl$ or trebl$ or tripl$) adj25 (blind$ or mask$)).ti,ab.
14. placebos.sh.
15. placebo$.ti,ab.
16. random$.ti,ab.
17. research design.sh.
18. or/10-17
19. 18 not 8
20. 19 not 9
21. comparative study.sh.
22. exp evaluation studies/
23. follow up studies.sh.
24. prospective studies.sh.
25. (control$ or prospectiv$ or volunteer$).ti,ab.
26. or/21-25
27. 26 not 8
28. 26 not (9 or 20)
29. 9 or 20 or 28
30. exp headache/
31. exp physical therapy/
32. transcutaneous electric nerve stimulation/
33. interferential therapy.ti,ab.
34. “biofeedback (psychology)”/feedback/ph
35. manipulation, spinal.sh.
36. chiropractic.sh.

37. osteopathic medicine.sh.
38. heat/tu
39. ultrasonic therapy.sh.
40. electromagnetic therapy.ti,ab.
41. microcurrent.ti,ab.
42. laser therapy.ti,ab.
43. lasers/tu
44. myofascial pain syndromes/th
45. traction.sh.
46. or/31-45
47. 30 and 46
48. 29 and 47

Note: The Cochrane Review on labor pain (Dowswell et al. 2009) did not provide a search strategy. Since this review was published so recently, however, an updated search was not deemed necessary.

APPENDIX B: LEVEL OF EVIDENCE DETERMINATION

Methods for critical appraisal and level of evidence assessment

The method used for assessing the quality of evidence of individual studies as well as the overall quality of evidence incorporates aspects of rating scheme developed by the Oxford Centre for Evidence-based Medicine, [Phillips] precepts outlined by the Grades of Recommendation Assessment, Development and Evaluation (GRADE) Working Group [Atkins, 2004] and recommendations made by the Agency for Healthcare Research and Quality (AHRQ) [West].
Taking into account features of methodological quality and important sources of bias combines epidemiologic principles with characteristics of study design.

Procedures for determining adherence to level of evidence (LoE) criteria

Each study was rated against pre-set criteria that resulted in an evidence rating (Level of Evidence I, II, III, or IV) and presented in a table. For therapeutic articles, the criteria are listed in the Table below and an example is given. All criteria met are marked. A blank for the criterion indicates that the criterion was not met, could not be determined or was not reported by the author.

Table B.1 Definition of the different levels of evidence for articles on therapy.

Table B.1. 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
II	Moderate or Poor quality RCT	• Violation of any of the criteria for 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	

*Reliable data are data such as mortality or reoperation.
†Authors must provide a description of robust baseline characteristics, and control for those that are unequally distributed between treatment groups.

Table B.2 Example of methods evaluation for articles on therapy.

Methodological Principle	Author 1	Author 2	Author 3	Author 4
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	**I**	**II**	**III**	**IV**

* applies to randomized controlled trials only.

Table B.3 Assessment checklist for HTAs, systematic reviews and meta-analyses.

	Example
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
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	NA
• Missing data handled appropriately	
• Effect sizes pooled appropriately	■

• Sensitivity analysis conducted	
• Publication bias explored	
Potential conflict of interest stated	

REPORT TYPE
The type and purpose of the report influence the extent to which some of the factors listed above are applicable. For instance, for some purposes, quantitative analysis and statistical pooling may not be possible, necessary or appropriate.

Health Technology Assessments (HTAs) and similar reports are those that systematically evaluate the effectiveness, safety, cost implications and other properties of technology use (frequently therapeutic or diagnostic technologies) in health care, generally with respect to competing alternatives. HTA methods generally include formal systematic search for and critical appraisal of medical literatures and may include meta-analytic techniques for combining data across studies. HTAs and similar reports are frequently done by governmental agencies and/or commissioned by such agencies from private vendors. The primary purpose is to advise or inform technology-related decision and policy-making in a variety of settings, including individual (e.g. patient and/or provider) and institutional (provider organizations, health plans, government agencies) on local, regional, national or international levels.

Systematic review is a general term used to describe focused summaries of medical literature to address specific clinical questions using explicit strategies for literature search, inclusions and exclusions of studies and documentation of processes used to find and summarize data from the medical literature. Systematic reviews may or may not include formal meta-analysis and pooling of data.

Meta-analysis is a term used for systematic reviews which use quantitative, statistical methods to pool data to summarize results across studies. A systematic review generally forms the basis of meta-analysis in that a formally systematic approach to finding and selecting relevant studies for summarization is done. Pooling of data across studies may enhance statistical power to detect differences between groups. The quality of the studies to be pooled and potential for bias based on methodological flaws in individual studies needs to be considered. Methods for pooling studies (or individual patient data from a number of studies) should be stated and appropriate for the types of data and studies from which they come. Heterogeneity across studies can compromise the credibility of the pooled estimate. Heterogeneity can be related to clinical, patient or study characteristics which may or may not manifest in statistical heterogeneity. Formal evaluation and exploration of statistical heterogeneity should be done using accepted methods and modeling done accordingly (e.g. use of random effects model instead of fixed model). In evidence-based medicine, meta-analyses of the highest quality studies (usually RCTs) is considered to the highest level of evidence, however, limitations of meta-analysis should also be considered.

Pooled analyses frequently combine outcomes from individual patients enrolled in primary studies; the patient is the unit of analysis. These analyses may not be part of a complete systematic review of the literature. As with meta-analyses, tests for homogeneity should be done and the basis of pooling should be well described.

CRITERIA:

1. **Purpose, aim, study (or key) questions** and/or hypothesis for the report or analysis should be stated clearly.

2. **The literature search** should be described including timing of the search, data sources searched and search strategies used.

3. **Inclusion and exclusion criteria** for include studies should be stated and relevant to the purpose and questions to be addressed in the report and consistent with accepted methods for conduct of the type of report.
4. **Characteristics of included studies** should be given with regard to study design, populations studied and technologies applied as relevant to the report's purpose and aims.

5. **Quality of included studies** should be formally assessed using a specified system for evaluation that takes into account study design, potential sources of bias, methodological limitations, statistically power and use of appropriate analyses (e.g. controlling for confounding), usually leading to an overall score, classification or grade of evidence.

6. **The Level of Evidence (LoE)** of individual studies included should be the highest possible based on the primary focus of the report. Spectrum Research's LoE criteria are described below. If all included studies are RCTs (randomized controlled trials), the LoE using Spectrum Research's approach is either I or II. For trials of surgery or other interventions where clinician and/or patients are not blinded, the LoE is often II, since there is the opportunity for bias in assessment by the clinician and/or bias in patient response. Whether this criterion is met depends on the primary outcome and whether it could have been assessed in a blinded fashion. Sub-analyses of RCTS are considered LoE II/III since randomization is generally not preserved. Registry studies are primarily retrospective cohort studies and subject to bias from a variety of sources and are classified as LoE III.

7. **Qualitative analysis:** Some reports may primarily provide qualitative assessment of included studies. Systematic reviews and meta-analyses should incorporate most of these components. The extent to which the following criteria are met provides some indication of the overall quality of the assessment:

   - **Critical appraisal of included studies** – The report should describe a formal method of evaluating individual quality with regard to study design, methodological issues and potential for bias, such as the LoE system described below. A "grade" or other classification of study quality should be described and applied across studies.
   - **Evaluation of estimate magnitude and direction:** The report should accurately interpret and describe these, including statistical significance and any statistical adjustments to effect size estimates.
   - **Estimate consistency**: Reports should describe the general patterns of effect size estimates across studies and how consistent they are. Reports should describe if estimates from different studies have the same general direction and magnitude across studies or not.
   - **Estimate stability**: Reports should comment on the general stability of estimates, based in consideration of things like confidence intervals, effects of missing data, study sample size, confounding and other factors which may influence estimate stability.
   - Consideration of the **overall scientific quality** of the evidence for a specific question: Do the report's conclusions consider the overall strength of evidence based on the scientific quality of the studies, the consistency, direction and magnitude of the estimates used to formulate the conclusions?

8. **Quantitative analysis:** This involves the statistical combining and evaluation of data from multiple studies and applies to situations where meta-analysis is done.

   - **Pooling** of data may or may not be appropriate depending on the types of studies and data available. Various methods for pooling data are possible. The report should adequately describe how pooling

was done and methods used to create summary estimates should be appropriate to the data, included studies and consideration of factors such as clinical and statistical heterogeneity. Methods for study weighting and modeling of pooled estimates should be described.

  - Formal meta-analysis is a structured process with specific types of methodologies for combining data, weighting studies, modeling and assessing heterogeneity across studies in order to arrive at pooled estimates of effect size.
  - Not all reports that pool data across studies are true meta-analyses from a methodological perspective.

- **Evaluation of heterogeneity**: Description of how heterogeneity was evaluated should be consistent with the type of analysis and modeling done to pool the data and specific criteria for determining heterogeneity should be described and applied. The results of heterogeneity evaluations should be stated.
- **Exploration of heterogeneity if present**: If there is significant heterogeneity present, a description of possible sources and methods used to explore it should be described and the results reported.
- **Missing data:** Does the report describe missing data, how it was handled and the extent to which it may influence estimate stability, which may in part be done with sensitivity analysis
- **Sensitivity analysis:** The report should explore the stability of estimates using appropriate sensitivity analyses, including around missing data or areas of heterogeneity. Exploration of publication bias should be described as appropriate.

9. **Potential conflicts of interest:** Is the source of funding for the report stated and/or is there information on potential conflicts of interest for authors presented?

DETERMINATION OF OVERALL STRENGTH OF EVIDENCE

Following the assessment of the quality of each individual study included in the report, an overall "strength of evidence for the relevant question or topic is determined. Methods for determining the overall strength of evidence for diagnostic studies are variable across the literature and are most applicable to evaluation of therapeutic studies.

SRI's method incorporates the primary domains of quality (LoE), quantity of studies and consistency of results across studies as described by AHRQ [West].

The following definitions are used by SRI to determine whether or not the body of evidence meets the criteria for each domain:

Domain	Definition/Criterion
Quality	• At least 80% of the studies are LoE I or II
Quantity	• There are at least three studies that are adequately powered to answer the study question
Consistency	• Study results would lead to similar conclusion (similar values, in the same direction) in at least 70% of the studies

Based on the criteria described above, the possible scenarios that would be encountered are described below. Each scenario is ranked according to the impact that future research is likely to have on both the overall

estimates of an effect and the confidence in the estimate. This ranking describes the overall “Strength of Evidence” (SoE) for the body of literature on a specific topic. The method and descriptions of overall strength are adapted for diagnostic studies from system described by the GRADE Working Group [Atkins] for the development of clinical guidelines.

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	-	+	-
			-	-	+
			-	-	-

Assessment of Economic Studies

Full formal economic analyses evaluate both costs and clinical outcomes of two or more alternative interventions. The four primary types are cost minimization analysis (CMA), cost-utility analysis (CUA), cost-effectiveness analysis (CEA), and cost-benefit analyses (CBA). Each employs different methodologies, potentially complicating critical appraisal, but some common criteria can be assessed across studies.

No standard, universally accepted method of critical appraisal of economic analyses is currently in use. A number of checklists [Canadian, BMJ, AMA] are available to facilitate critique of such studies. The Quality of Health Economic Studies (QHES) instrument developed by Ofman, et al.[1] QHES embodies the primary components relevant for critical appraisal of economic studies. It also incorporates a weighted scoring process and which was used as one factor to assess included economic studies. This tool has not yet undergone extensive evaluation for broader use but provides a valuable starting point for critique.

In addition to assessment of criteria in the QHES, other factors are important in critical appraisal of studies from an epidemiologic perspective to assist in evaluation of generalizability and potential sources of study bias.

Such factors include:

- Are the interventions applied to similar populations (eg, with respect to age, gender, medical conditions, etc)? To what extent are the populations for each intervention comparable and are differences considered or accounted for? To what extent are population characteristics consistent with “real world” applications of the comparators?
- Are the sample sizes adequate so as to provide a reasonable representation of individuals to whom the technology would be applied?
- What types of studies form the basis for the data used in the analyses? Data (eg, complication rates) from randomized controlled trials or well-conducted, methodologically rigorous cohort studies for data collection are generally of highest quality compared with case series or studies with historical cohorts.

- Were the interventions applied in a comparable manner (eg, similar protocols, follow-up procedures, evaluation of outcomes, etc)?
- How were the data and/or patients selected or sampled (eg, a random selection of claims for the intervention from a given year/source or all claims)? What specific inclusion/exclusion criteria or processes were used?
- Were the outcomes and consequences of the interventions being compared comparable for each? (e.g., were all of the relevant consequences/complications for each intervention considered or do they primarily reflect those for one intervention?)

Assessment of the overall strength of evidence for formal economic analyses does not appear to be documented in the literature. For the purposes of this HTA, overall strength was determined by:

- Quality of the individual studies: Where the majority of quality indicators described in the QHES met and were the methods related to patient/claim selection, patient population considerations and other factors listed above consistent with a high quality design?
- Number of formal analyses (3 or more).
- Consistency of findings and conclusions from analyses across studies.

APPENDIX C: INCLUDED COCHRANE REVIEWS: CHARACTERISTICS AND OUTCOMES

ACUTE PAIN

Acute Pain (Walsh 2009)[2]

Study Types	RCTs, crossover and parallel designs
Intervention(s)	• Conventional TENS (high frequency) • ALTENS (low frequency)
Comparator(s)	• Placebo (sham) TENS • Control (no treatment) • Pharmacologic treatment
Participant Characteristics	• Sex of participants given in all but two studies: 308 males and 465 females • Included only studies of adults (16 years+; range 11-81 years); excluded from analyses two studies with mix adults and children
Inclusion Criteria	1) Diagnosis of acute pain (<12 weeks) 2) Included: procedural pain (e.g. cervical laser treatment), venipuncture, screening flexible sigmoidoscopy and non-procedural pain (rib fractures, angina, headache, back pain) 3) Postpartum pain studies included if pain studied was due to episiotomy or Caesarean section (not uterine contractions alone)
Exclusion Criteria	1) Pain due to uterine contractions from labor, dental procedures, primary dysmenorrhea 2) Percutaneous electrical nerve stimulation (PENS), neuromuscular electrical stimulations (NMES) devices, and interferential current devices 3) Treatment at intensities reported as 'barely perceptible', 'faint or mild' 3) Concomitant pharmacologic or non-pharmacologic treatments 4) Studies of experimental pain, case reports, clinical observations, and letters, abstracts, reviews (unless they provided additional information from published RCTs that met the criteria)
TENS Device	• TENS had to be delivered using at least 2 electrodes
Electrodes	• TENS electrodes had to be placed at site pain or over nerve bundles proximal to site of pain
Treatment Characteristics (frequency, intensity, duration)	• Included any frequency or duration; self- or therapist-applied • TENS had to be administered at an intensity strong enough to produce paresthesia felt by the patient; ALTENS had to be delivered at strong intensities to generate muscle twitches • Most included studies used high electrical pulse frequency (51Hz-160Hz), applied at the site of pain • In 7 of the included studies, single TENS treatments were applied; application time varied, if reported • In non-procedural studies, TENS typically used for only a few days
# Identified Studies	1479
# Excluded Studies	116 (from narrowed down group of identified studies)
# Included Studies	12

Total N	919
Outcomes	• Pain intensity assessed using standard pain scales/questionnaires (visual analog scale, VAS; numerical rating scale, NRS; McGill Pain Questionnaire (MPQ); verbal scale • Pain relief (poor/good/excellent) • Additional measures included measure of TENS discomfort using 5-point verbal scale, overall impression with TENS using a four-point categorical scale, and a questionnaire on their experience. • Information also sought on level of compliance with intervention, the magnitude, and duration of effect • Adverse events
Findings	*TENS vs. placebo TENS*: • >50% pain relief post-treatment between high- or low-frequency TENS and placebo TENS (VAS: RR 1.92, 95% CI 0.74, 4.98 and PRI: RR, 2.86, 95% CI 0.84, 9.71) • No difference in pain intensity (weighted mean difference) during procedure (-0.27, 95% CI -0.77, 0.23) or post-treatment (-1.53, 95% CI -3.37, 0.31). • Using same outcome measure, a study reported significant decrease in pain VAS after 2 days treatment (-2.44, 95% CI -3.85, =1.03) • No difference in overall impression using categorical scale (excellent/good; RR 1.29, 95% CI 0.65, 2.54) *TENS vs. no treatment control*: • No difference in pain during flexible sigmoidoscopy using NRS *Conventional TENS (100Hz) versus ALTENS (2Hz)*: • No difference in reporting of >50% pain reduction post-treatment using VAS
Adverse Effects	In studies that reported them (n=8): • Adverse effects were reported in both TENS and comparison groups: nausea, shoulder pain, bradycardia and dizziness. • 97% (29/30) in TENS and 20% (6/30) of participants in placebo group reported pain, burning, tingling at electrode site. • Most participants receiving low-frequency TENS found muscle twitches to be uncomfortable. • 3 studies reported no adverse events

LABOR PAIN

Dowswell (2009)[3]

Study Types	RCTs
Intervention(s)	• Conventional (high-frequency) TENS • Acupuncture-like (low-frequency) TENS
Comparator(s)	• Placebo TENS • Control (no treatment; routine care) • Pharmacologic treatment
Participant Characteristics	• Detailed descriptions not provided
Inclusion Criteria	1) Acute labor pain 2) Included studies varied with respect to their inclusion/exclusion criteria (e.g. women undergoing induction, use of oxytocin, analgesia prior to entry into trial)

Exclusion Criteria	1) Studies that did not focus on use of TENS during labor (e.g. pain after C-section, effects on strength of uterine contractions during labor induction) 2) Methodological reasons (e.g. non-random allocation)
TENS Device	• Details not provided; varied across studies
Electrodes	• Location of stimulation: lower back (n=15), acupuncture points (n=2), Limoge currents to the cranium (n=2)
Treatment Characteristics (frequency, intensity, duration)	• Details not provided; varied across studies
# Identified Studies	25
# Excluded Studies	6
# Included Studies	19
Total N	1671
Outcomes	• Pain intensity in labor assessed using VAS, validated questionnaire, or dichotomous variable (has/has not severe pain) • Patient satisfaction • Additional secondary outcomes related to delivery and fetal neonate characteristics • Adverse effects

Findings	• Comparators used (number of studies): placebo TENS (n=10); no intervention/routine care (n=5); pharmacologic analgesics (n=2); three arms (TENS vs. tramadol vs. routine; TENS vs. control vs. pethidine; n=2) • Various co-interventions were used (epidural, other analgesia on request); in only 2 studies did the women receive no analgesics other than study interventions *TENS vs. placebo or usual care* (n=14; 1256 women): • Severe pain during labour was not statistical different (RR 0.77, 95% CI 0.60-1.00, *p*=0.05) for women receiving TENS (to the back) versus placebo or routine care. • Women receiving TENS at acupuncture points were less likely to report having severe pain than controls (RR 0.41, 95% CI 0.32-0.55) • TENS to the back using VAS to measure women's pain in labor, was not statistically different between groups (standardized mean difference (SMD) -0.16, 95% CI -0.39 to 0.07) • Satisfaction with pain relief in labor did not differ between treatment and placebo or control (RR 1.25, 95%CI 0.98-1.60) • One study examining TENS to acupuncture points; TENS group more satisfied with pain relief compared to control group (RR 4.10, 95% CI 1.81-9.29) • TENS group was more likely to be willing to use TENS again in a future labor compared to sham group (RR 1.54 95% CI 1.31 to 1.80) • While 63% of women in the active TENS group would use TENS again, 41% using inactive devices reported that they too would be willing to use TENS in a future labor (unweighted percentages) • TENS versus placebo TENS to acupuncture points similarly reported that women in the active TENS group would be more likely to express a willingness to use TENS again (RR 1.45 95%CI 1.18 to 1.79). • No differences in duration of either 1st or 2nd stages of labor or in numbers of women undergoing C-section or assisted vaginal deliveries, except for TENS at acupuncture points (assisted vaginal: RR 4.50, 95% CI 1.02-19.79) • There was no difference in number of women receiving epidural for control groups compared to TENS applied to the back or acupuncture points *TENS vs. pharmacologic analgesia*: • There was no significant difference between groups in satisfaction with pain relief in labor (RR 0.95, 95% CI 0.80-1.13) • No women in either TENS or control groups had C-section and 2 in tramadol group had assisted deliveries. • No evidence of difference in duration of labor. *TENS as an adjunct to epidural analgesia*; applied to back or cranium: • TENS to the back as an adjunct to epidural analgesia, with pain scores measured at 60 minutes after insertion of the epidural, was not significantly different from control (mean difference (MD) 0.23, 95% CI -8.71 to 9.16). • The study examining cranial TENS with epidural compared to epidural alone also revealed no significant differences in pain scores between groups. • No difference between groups in number of women undergoing caesarean section or having assisted deliveries.
Adverse Effects	• No adverse events were reported

Primary Dysmenorrhea (Proctor 2002)[4]

Study Types	RCTs
Intervention(s)	• Conventional TENS (high frequency; HFTENS) • ALTENS (low frequency; LFTENS) • Acupuncture (not evaluated here)
Comparator(s)	• Placebo (sham) TENS • Control (no treatment) • Pharmacologic treatment
Participant Characteristics	Women of reproductive age; average reported mean age 25.3 years, range 15-38 years
Inclusion Criteria	1) Women of reproductive age 2) Moderate to severe dysmenorrheal (severe/incapacitating pain for at least one day of menses) in >50% of menstrual cycles
Exclusion Criteria	1) Women with secondary dysmenorrhea (i.e. associated with identifiable pelvic pathology) 2) Women with dysmenorrheal due to presence of an intrauterine device (IUD) 3) Women with mild or infrequent dysmenorrhea 4) Inappropriate comparator
TENS Device	• Self- and physician-administered treatments
Electrodes	• Self-administered TENS electrodes tended to place electrodes on the painful areas • Physician-administered TENS electrodes more likely to be placed on meridian points
Treatment Characteristics (frequency, intensity, duration)	• The frequency of HFTENS and LFTENS ranged from 50-100 Hz and 1-5 Hz, respectively, across studies • The pulse width ranged from 40 µsec to 250 µsec across studies • The intensity of HFTENS treatments was reported to be 40-50 mA or was described as “comfortable tingling”, “low intensity – below threshold”, and “comfortable” • The intensity of LFTENS was reported as “highest tolerable”, “high, muscle contractions produced”, “to tolerance level, with visible muscle contractions”, “increased to tolerance”, and “to tolerance level with minimum of palpable contractions • Differences in treatment schedules across studies; many scheduled during menses, while others used preemptively and can be used at any time during the menstrual cycle
# Identified Studies	10
# Excluded Studies	3
# Included Studies	7
Total N	213

Outcomes	• Pain intensity/relief (VAS, other scales, dichotomous scale) • Analgesic consumption (measured as a ratio of women requiring analgesics additional to their assigned treatment) • Restriction of daily life activities (measured as a ratio of women who report activity restriction) • Absence from work or school (measured as a ratio of women who reporting absences from work or school) • Adverse effects (incidence and type of side effects)

Findings

HFTENS vs placebo:

- Pain relief reported as a dichotomous variable: OR 7.2 (95% CI 3.1, 16.5) in favor of HFTENS.
- Pain relief measured with a VAS: WMD 45.0 (95% CI 22.5, 67.5) in favor of high frequency TENS.
- One trial (not included in meta-analysis) reported no difference between high frequency TENS and placebo TENS in pain relief.
- No significant difference in the number of women needing additional analgesics between high frequency and placebo TENS (OR 0.3, 95% CI 0.1, 1.1).
- No significant difference in the number of analgesic tablets taken between the two groups (WMD 0.1, 95% CI -2.1, 2.4).
- No significant difference between HF and placebo TENS in absence from work or school, reported as the number of lost hours per menstrual cycle (WMD 0.04, 95% CI -0.4, 0.5).

LFTENS vs. placebo:

- There were four studies comparing the use of LFTENS with placebo TENS and two studies comparing LFTENS with a placebo pill.
- Overall results suggest no significant difference between LFTENS and placebo TENS or a placebo pill for pain relief. For pain relief reported as a dichotomous variable the OR was 1.3 (95% CI 0.4, 4.1) when comparing LFTENS and placebo TENS (2 trials); and the OR was 2.9 (95% CI 0.4, 24.4) when comparing low frequency TENS and placebo pill (1 trial).
- When pain relief was measured using a VAS the WMD was 24.1 (95% CI -2.9, 51.1; 1 trial).
- Two trials could not be included in the meta-analysis due to the form results were reported in but they are included as descriptive data. One trial comparing low frequency TENS and placebo TENS reported a significant difference between low frequency TENS and placebo TENS in pain relief ($p<0.05$); the other trial showed that low frequency TENS is more effective at reducing pain than a placebo pill ($p<0.05$).
- One trial reported the number of tablets of additional analgesic used, the LFTENS group used significantly less than the placebo TENS group (WMD –3.1, 95% CI -5.5, -0.7).
- Another trial reported no significant difference between the two groups for absence from work or school (WMD -0.2, 95% CI -.6, 0.2).

HFTENS vs. LFTENS:

- There were three studies that compared HFTENS to LFTENS.
- For pain relief reported as a dichotomous variable the OR was 3.9 (95% CI 1.1, 13.0) in favor of HFTENS (1 trial).
- When pain relief was measured with a VAS the WMD was 20.9 (95% CI -4.4, 46.1) showing no significant difference between the two types of TENS but a trend towards HFTENS as achieving more pain relief (1 trial).
- One trial could not be included in the meta-analysis due to the form results were reported in was included as descriptive data, it found LFTENS to be more likely to reduce pain than HFTENS.
- There was a significant difference in favor of LFTENS for the number of analgesic tablets taken in addition to TENS treatment (WMD 3.2, 95%CI 0.5, 5.9).
- There was no significant difference between the two groups for the outcome of absence from work or school (WMD 0.2, 95% CI -0.2, 0.6).

TENS vs. medical treatment:

- 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 pain relief reported as a dichotomous variable ibuprofen proved to be significantly better at reducing pain (OR 0.3, 95% CI 0.1, 0.8). This trial also reported no significant difference between the two treatments for additional use of analgesics (OR 0.4, 95% CI 0.1, 1.4).
- Another trial compared high frequency/high intensity TENS with naproxen (a nonsteroidal anti-inflammatory). For the outcome of

Adverse Effects	• Only one of the trials comparing HFTENS to placebo reported any adverse effects associated with treatment. 4/32 women using high frequency TENS experienced muscle vibrations, tightness, headaches after use, and slight redness or burning of the skin (OR 8.2, 95% CI 1.1, 60.9). There were no reported adverse effects from placebo TENS. • Only one trial comparing LFTENS to placebo reported any information on adverse effects, and found there were none in either the TENS or the placebo pill group. • There was a significant difference between HFTENS and naproxen in the number of adverse effects experienced by participants (OR 26.7, 95% CI 5.5, 130.9). 10/12 women in the TENS group experienced pain from the treatment while no adverse effects were reported by those taking ibuprofen. 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.

Chronic Pain (Nnoaham 2008)[5]

Study Types	RCTs
Intervention(s)	• Conventional TENS (high frequency; HFTENS) • ALTENS (low frequency; LFTENS)
Comparator(s)	• Placebo (sham) TENS • Control (no treatment)
Participant Characteristics	• Patients with rheumatoid arthritis, osteoarthritis, pancreatitis, myofascial pain, diabetic neuropathy and low back pain
Inclusion Criteria	1) Adult patients with chronic pain of at least 3 months
Exclusion Criteria	1) Patients with chronic pain conditions associated with acute episodes (angina, headache and migraine, and dysmenorrhea) 2) Studies where TENS was used under experimental pain conditions 3) Studies that did not use a conventional battery operated portable TENS device, with two or more standard electrodes that were directly applied to the skin 4) Excluded studies that compared TENS in combination with another intervention (e.g. oral analgesic) 5) Studies that did not include subjective measures of either pain intensity, or pain relief as part of the overall assessment of efficacy before and after treatment with TENS
TENS Device	• Conventional battery-operated portable TENS device
Electrodes	• Two or more standard electrodes • Considerable variation in the site of stimulation and electrode placement across studies
Treatment Characteristics (frequency, intensity, duration)	• In 15/25 studies, investigators administered a single TENS dose, repeated single dose, or multiple dose treatments (10-60 min) • In 10/25 studies, TENS was self-administered; treatments ranged from 20 min for a single treatment to up to 168 hours given as 30-60 min stimulation per treatment, over two periods of two weeks separated by a one-week washout period
# Identified Studies	124

# Excluded Studies	99
# Included Studies	25
Total N	1281
Outcomes	• All studies included at least one measure of pain intensity prior to administration of the study treatments (i.e. baseline pain); post-treatment evaluations were made at varying time points after treatment, depending on the total duration of the study period • VAS was using in 16/25 studies to assess pain intensity • Patient satisfaction
Findings	*Active TENS vs. sham TENS:* • 17/25 studies compared active TENS to sham TENS • 5/7 studies examining single dose TENS reported a positive analgesic effect in favor of active TENS for at least one of post-treatment assessments; 2/7 studies found no difference at any time point. • For multiple dose comparisons, 8/15 studies reported a positive analgesic effect in favor of the active TENS treatment for at least one of the post-treatment assessments. • 4/15 studies provided long-term data, with one of these reporting improvement with active TENS at the one-to-four week post- treatment evaluation, and the other three failed to find any difference 2.5 months and >6 months after treatment. *HFTENS vs. LFTENS:* • 2/7 studies made direct comparisons between HFTENS and LFTENS (ALTENS) • Only 1 study observed a difference between different forms of TENS stimulation - a crossover design, with reported marked improvement after ten minutes of stimulation with HFTENS and train TENS, but not for LFTENS • 7/9 studies directly comparing HFTENS vs. LFTENS found no difference in analgesic outcomes, 1/9 reported difference in favor of HFTENS and another 1/9 reported in favor of LFTENS
Adverse Effects	• Methods to detect or report adverse events were detailed for only one study (used overall patient global assessment as index of efficacy vs. side effects and dichotomous data for skin irritation, adherence problems of electrodes and difficulty attaching electrodes) but found no difference in the occurrence of these effects between the groups. • Three studies reported dichotomous data on adverse events attributed to TENS in their results or discussion (one skin rash with HFTENS, another burning over electrode site with LFTENS). • Another study mentioned presence of skin irritation in some patients treated with HFTENS and low frequency ALTENS, but the authors did not specify how many patients were affected. • Three studies made clear statement that none of the patients experienced any adverse events

Chronic Low Back Pain (Khadilkar 2007)[6]

Study Types	RCTs
Intervention(s)	• Conventional (high frequency, HF) TENS • ALTENS (low frequency, LF) TENS
Comparator(s)	• Placebo (sham) TENS

Participant Characteristics	Adults (ages 18+ years; reported means 28-51 years)
Inclusion Criteria	1) Chronic low back pain (LBP) of at least 3 months duration 2) Back pain localized between the inferior gluteal fold and the costal margin
Exclusion Criteria	1) Experimental or control groups received electroacupuncture or percutaneous electrical nerve stimulation (PENS) 2) Only accepted placebo/sham TENS for the control group and excluded head-to-head comparisons of TENS with other active treatment modalities; use of co-interventions assigned equally to both experimental and control groups was permitted 3) Non-standard TENS devices (e.g. Nu-wave) 4) Studies with <5 patients per treatment group 5) Patients with malignancy, infection, fracture, inflammatory disorder, neurologic syndrome 6) Patients with symptoms and signs of sciatica or a prior history of back surgery were not specifically excluded, but had to represent a minority of the study sample to qualify for selection 7) Studies that reported on a mix of chronic and acute (<6 weeks) or subacute (6-12 weeks) back pain, unless data were presented separately for chronic low back pain 8) Similarly, studies including a mix of LBP and middle or upper back pain 9) Restrictions on use of medications were not applied in most studies, but one had patients discontinue medication use and physiotherapy two weeks before the start of the trial and another excluded patients with concomitant physiotherapy or chiropractic therapy 10) Two studies included patients with prior back surgery (10% and 18% of total samples) or sciatica.
TENS Device	Standard TENS devices
Electrodes	• Two to four electrodes places over the area of maximal pain or within the same dermatome • Could be moved by per patient preference or as necessary to maximize pain relief in two studies
Treatment Characteristics (frequency, intensity, duration)	• Treatments ranged from 2-4 weeks with daily sessions ranging from 20 min to 3 hours per day • Self-administered at home (n=2) or by therapist in clinic setting (n=2) • Precise stimulation parameters reported in all but one of the included studies
# Identified Studies	47
# Excluded Studies	43
# Included Studies	4
Total N	585
Outcomes	• Pain intensity • Analgesic consumption • Patient satisfaction • Functional/mechanical evaluation • Only one of the included studies examined long-term data (two-week and two-month follow-up) but did not report on long-term follow-up outcomes

Findings	• Pain intensity was assessed using VAS in 3 out of 4 of included studies. • Statistically insignificant and clinically unimportant benefits were observed with 2 and 4 weeks of treatment. Both assigned conventional TENS, but allowed patients choice of switching to ALTENS at midway point of the four-week trial (at which point improvement not statistically significant). • Statistically significant and clinically important benefits with respect to reduction of pain were reported in another study of conventional TENS (MD 21.80; 95% CI -33.08, -10.52). • Differences in functional status using the Oswestry Disbility Index (ODI) and LBP Outcome scale (LBPOS; n=1) and Roland-Morris Disability Questionnaire (R-MDQ; n=1) were not significant or clinically important. ▪ There were no difference in functional status between ALTENS and placebo using the LBPOS (n=1) or R-MDQ (n=1) ▪ Significant improvements were found with the ODI (MD -6.07; 95% CI -10.52, 1.62), but these were clinically unimportant. • Generic health status was assessed using a modified Sickness Impact Profile (n=1) and short form-36 (SF-36; n=1) ▪ The larger study showed no significant benefits for TENS with the modified SIP ▪ Other study showed significant benefits for TENS on 4/8 subsections of SF-36 (physical role limitations, emotional role limitations, general mental health, vitality) and for ALTENS on just 2/8 subsections (emotional role limitations, general mental health) • Significant improvement in activity pain (n=1) after treatment with conventional TENS (MD -17.20; 95%CI - 27.38, -7.02) or ALTENS (MD -12.50; 95% CI -24.47, -0.53). However, the outcome was not clinically relevant. • No differences in self-rated activity or on McGill Activity Scale • Work status was assessed using the McGill Work Scale (n=1); no difference was observed between TENS and placebo. • Other physical outcomes were measured, but the only significant results were observed with the isometric dead-lift test, which seemed to improve with ALTENS relative to placebo. • No differences reported for use of medical services or the Zung depression scale. • Studies that separately compared conventional TENS and ALTENS to placebo showed similar results for either on most outcomes (differences in isometric dead-lift test, two subsections of SF-36, and activity pain).
Adverse Effects	• Only one of the four included studies reported on adverse effects. • In this study, minor skin irritation was reported for $^{1}/_{3}$ participants at the site of electrode placement; observed equally in TENS and placebo groups. • One placebo participant withdrew from study after developing severe dermatitis four days after start of therapy.

Rheumatoid Arthritis (RA) of the Hand (Brosseau 2003)[7]

Study Types	RCTs (quasi-randomized allowed)
Intervention(s)	• Conventional TENS (C-TENS) • Acupuncture-like (ALTENS)
Comparator(s)	• Placebo (sham) TENS
Participant Characteristics	Adults (ages 18+ years)

Inclusion Criteria	1) Clinical and/or radiologic confirmation of rheumatoid arthritis (RA) of the hand (one or both hands affected) that required pharmaceutical intervention
Exclusion Criteria	1) Studies with patients who were post-surgical 2) Studies that did not examine RA 3) Studies of small sample size (e.g. 2 subjects per group)
TENS Device	
Electrodes	• Included studies with variations in electrode placement
Treatment Characteristics (frequency, intensity, duration)	• Included TENS with different modes of stimulation, pulse frequencies, length of stimulation, time and frequency of stimulation
# Identified Studies	9
# Excluded Studies	6
# Included Studies	3
Total N	78
Outcomes	• Pain intensity (at rest and grip pain) • Number of tender/swollen joints • Patient satisfaction • Functional/mechanical evaluation

Findings	*ALTENS vs. placebo (n=1):* • There was a significantly different, clinically relevant benefit of ALTENS treatment on 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 VAS scale; (Weighted mean difference (WMD) = -59.50, 95% CI -76.58, -42.42; p<0.00001). • Grip pain scores were not significantly different between the ALTENS and placebo groups at the end of 3 weeks of treatment (WMD = -12.00 VAS 100mm, 95% CI -29.90, 5.90; p=0.19); these results also did not demonstrate any clinical benefit of treatment on grip pain. • Administration of 15 minutes of ALTENS once weekly, over 3 consecutive weeks, improved muscle power scores by a relative difference of 55% and work scores by a relative difference of 5%, absolute benefit of 0.98, 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). *C-TENS and ALTENS vs. placebo (n=1):* • No significant difference was found between C-TENS and ALTENS (data not shown), or C-TENS application (one treatment of 20 minutes duration) compared with placebo on the decrease in mean scores for intensity of pain while resting (WMD = -0.20 VAS 10mm, 95% CI: -4.05,3.65; p=0.9) or intensity of pain while gripping (WMD = 0.70 VAS 10mm, 95% CI: -4.11,5.51; p=0.8). • There was no significant difference between C-TENS and placebo on 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=0.5). • Joint tenderness scores showed no clinical benefit from C-TENS treatment over placebo (relative difference in change from baseline = 0%), although there was a statistically significant reduction in joint tenderness scores (WMD = - 20.00 (22 point score), 95% CI: -33.79,-6.21; p=0.004). *C-TENS vs. ALTENS (n=1):* • Treatments were given for 5 minutes, once a day, for 15 days. • At the end of 15 days of treatment, there was a statistically significant difference (WMD = -6.43 (number of participants improved), 95% CI: 0.67,61.47; p=0.11) between the two types of TENS 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.
Adverse Effects	• Not reported in any of the included studies

Osteoarthritis of the Knee (Osiri 2000)[8]

Study Types	RCTs (quasi-randomized allowed)
Intervention(s)	• Conventional TENS • Acupuncture-like TENS (ALTENS)

Comparator(s)	• Placebo (sham) TENS • Electroacupuncture (not evaluated here) • Non-pharmacologic interventions
Participant Characteristics	Adults (age 18+ years)
Inclusion Criteria	1) Clinical and/or radiological confirmation of OA of the knee
Exclusion Criteria	1) Studies with follow-up of <1 year 2) No surgical intervention of the knee
TENS Device	• Wide variety of devices used; not described.
Electrodes	• Included studies varied with respect to electrode placement
Treatment Characteristics (frequency, intensity, duration)	• TENS application protocols were markedly diverse; differences included modes of stimulation, optimal stimulation levels, pulse frequencies, lengths of stimulation time and how often TENS was applied. • Length of duration of TENS application ranged from 20-60 minutes and the length of the experimental intervention period varied from one treatment session to six-week sessions. • Strong burst (and burst mode) TENS used in two studies.
# Identified Studies	210
# Excluded Studies	2
# Included Studies	7
Total N	294
Outcomes	• Pain intensity • Patient satisfaction • Functional/mechanical evaluation

Findings	*TENS and/or ALTENS vs. placebo:* • When the combined efficacies of TENS and ALTENS were compared to placebo and expressed as standardized mean difference (SMD) with 95% confidence intervals (CI), pain relief, measured using a visual analogue scale (VAS), improved significantly in the treatment group (SMD -0.448 VAS, 95% CI: -0.703 to -0.192). • If only the studies of TENS application compared to placebo were analyzed, pain measured on a VAS was still significantly less in the TENS group (SMD -0.38 VAS, 95% CI: -0.655 to -0.104); this analysis still showed heterogeneity. • 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 • The number of participants reporting pain improvement was significantly different between the TENS treated group and placebo group (RR 2.41, 95% CI: 1.58 to 3.69)]. After they finished their courses of TENS treatment, the participants in this group still did better than those in the placebo group regarding pain improvement as shown in follow up studies (RR 2.7, 95% CI: 0.94 to 7.72)]. However, heterogeneity existed in this analysis, which may be explained by the result from one study being significant while the other was not. • Reviewers did separate analysis of one study of two different kinds of TENS applications compared to placebo. After one application, pain relief with HFTENS application was significantly better than placebo (WMD -2.1 cm, 95% CI: - 4.115 to -0.085) while the difference in pain relief between strong burst mode TENS and placebo did not reach a significant level (WMD -1.6 cm, 95% CI: -3.209 to 0.009). • No heterogeneity was found within each mode of TENS setting, however, pain relief by strong burst mode TENS and ALTENS was approximately two times better than with HFTENS. • When analyses were restricted to high quality studies, pain relief for strong burst mode TENS was compared to placebo in another analysis was (SMD -0.72, 95% CI: -1.183 to -0.256), when ALTENS compared to placebo was (SMD - 0.745, 95% CI: -1.32 to -0.17), and when HFTENS was compared to placebo was (SMD -0.332, 95% CI: -0.648 to - 0.016). • Heterogeneity was observed in analyses of repeated TENS applications; pain relief was not significant in the study with single TENS application (SMD -0.324 cm, 95% CI -0.645 to -0.003). • The efficacy of TENS for pain relief in studies with intervention periods less than four weeks was not significantly different from placebo (SMD -0.288, 95% CI: -0.585 to 0.009), while TENS application for at least four weeks showed a significant efficacy in pain relief compared to placebo (SMD -0.85, 95% CI: -1.527 to -0.174).
Adverse Effects	• None reported in the included studies

Cancer Pain (Robb 2008)[9]

Study Types	RCTs
Intervention(s)	• Conventional TENS • Acupuncture-like TENS (ALTENS)

Comparator(s)	• Placebo (sham) TENS • Control (no treatment) • Transcutaneous Spinal Electroanalgesia (TSE) and sham TSE
Participant Characteristics	Adults (age 18+ years)
Inclusion Criteria	1) Cancer-related pain, unspecified or persistent cancer treatment-related pain, or both 2) Minimum of 3 months after any cancer treatment had been completed
Exclusion Criteria	1) TENS delivered at intensities described as “barely perceptible” or “mild” 2) Percutaneous stimulation 3) Not a review exclusion, but both of the included studies had excluded patients who previously used TENS
TENS Device	• Considered conventional TENS as a device that delivered monophasic or biphasic pulsed electrical currents in mA range. • Included neuromuscular electrical stimulation (NMES) and interferential current (IFC) therapy devices provided that a “strong but comfortable” electrical sensation was produced.
Electrodes	• Electrodes placed either in an area of pain where sensation is present or over nerve bundles proximal to the site of pain • No minimum number of electrodes
Treatment Characteristics (frequency, intensity, duration)	• TENS delivered at a “strong but comfortable” electrical sensation; allowed for any parameters of treatment (frequency, duration) resulting in this.
# Identified Studies	37
# Excluded Studies	35
# Included Studies	2
Total N	64
Outcomes	• Pain intensity • Analgesic consumption • Patient satisfaction • Functional/mechanical evaluation

Findings	• Two included studies were heterogeneous with respect to study population, sample size, study design, methodological quality, mode of TENS, treatment duration, method of administration and outcome measures used. • One study used treatment for three weeks duration of each intervention with participants also self-treating at home as needed. • Other study investigated acupuncture-like TENS for cancer pain or nausea and vomiting, or both, in 15 terminally ill participants. The investigators administered TENS for 30 minutes daily for five days. *TENS vs. TSE and sham TSE:* • There were no significant differences in pain relief scores between TENS or sham TSE (n=1). • There were no differences in any other outcome except for one dimension of a patient satisfaction questionnaire where TENS was considered more effective than TSE. • 26/41 women (63%) who completed the study decided to continue with a device on completion of the trial and of these, the majority (n =13) decided to continue with TENS, as opposed to sham TSE (n = 6). • The majority of the women continuing with TENS were still using it to good effect at three months (n = 14) and 12 months (n = 10), with those using sham TSE to good effect at three months and 12 months, n = 4 and n = 2 respectively. • Overall, TENS appeared to be well tolerated, women found TENS easy to use and few reported difficulties with electrode placement. *ALTENS vs. sham ALTENS:* • No significant differences were observed between ALTENS and sham ALTENS. • This study only included 5 participants randomized to each of the three study arms, and only 13 participants completed the study.
Adverse Effects	• Adverse events were monitored and described as 'minimal'

Neck Disorders (Kroeling 2005)[10]

Study Types	RCTs (quasi-randomized allowed)
Intervention(s)	• Conventional TENS • Interferential (IFC) Therapy • Also evaluated other forms of electrostimulation, including galvanic current and electromagnetic fields (not evaluated in the current assessment)
Comparator(s)	• Placebo (sham) TENS • Control (no treatment)
Participant Characteristics	Adults (ages 18+ years)
Inclusion Criteria	1) Patients with mechanical neck disorders (MND) 2) Included both acute (<30 days) and chronic (longer than 90 days) patients 3) Mechanical neck disorders (MND), including whiplash associated disorders (WAD), myofascial neck pain, and degenerative changes 4) Neck disorder with headache (NDH) 5) Neck disorders with radicular findings (NDR)

Exclusion Criteria	1) Studies that investigated neck disorders with definite or possible long tract signs, neck pain caused by other pathological entities 2) Headache that was not of cervical origin but was associated with the neck, co-existing headache when either the neck pain was not dominant or the headache was not provoked by neck movements, or sustained neck postures, or 'mixed' headache. 3) Other forms of high frequency electromagnetic fields, like short wave diathermy, microwave, ultrasound and infrared light because their purpose is to cause therapeutic heat 4) Electroacupuncture 5) Excluded studies if the participants did not meet their definition or they were unable to extract or split useful data
TENS Device	• Not described
Electrodes	• Not described
Treatment Characteristics (frequency, intensity, duration)	• Frequencies of 60 Hz and 80 Hz for two eligible TENS comparisons • One study used a single application of TENS for 20 minutes, while the other study applied TENS with collar for three sessions of 15 minutes each over a week. • Interferential (diadynamic) current was set at 50 Hz, sinusoidal half-wave, LP mode on 3 trigger points for 4 minutes each for 5 consecutive days.
# Identified Studies	15
# Excluded Studies	4
# Included Studies	11
Total N	525
Outcomes	• Pain relief • Patient satisfaction • Functional/mechanical evaluation

Findings	• Five studies examined TENS: TENS vs. placebo (n=1), TENS vs. placebo and other treatments (n=1), TENS vs. other treatments (n=3) *TENS (single treatment, 60 Hz, 20 min) vs. placebo vs. electrical muscle stimulation (EMS) (n=1):* • Included patients with chronic trigger points (trapezius muscle) • Baseline VAS not reported • Reported a significant decrease in pain intensity and trigger point tenderness for those receiving TENS compared to placebo treatment and EMS (10Hz). Pain intensity (% changes): ▪ TENS vs. placebo (SMD -2.60, 95% CI -3.48 to -1.71) Pressure pain threshold (% changes): ▪ TENS vs. placebo (SMD -1.43, 95% CI -2.15 to -0.71) *TENS plus collar (80 Hz, three 15-minute sessions over one week) vs. manual therapy plus collar or collar use alone (n=1)*: • No significant difference in pain relief was found between the three groups of participants with acute MND in this low quality trial; small N's for each of the comparisons. Pain intensity (% changes): ▪ TENS vs. mobilization (SMD -0.04, 95% CI -0.92 to 0.83) ▪ TENS vs. control (collar) (SMD -0.50, 95% CI -1.39 to 0.39). *Microamperage TENS vs. placebo (n=1):* • One study examined 'microamperage TENS', including patients with trigger points in the neck and shoulder region • This unusual (subliminal) form of TENS was not evaluated in the current assessment. *Multimodal Interventions* • Two trials included TENS within a multimodal care framework, therefore it was not possible to delineate the effects of TENS. *Interferential (diadynamic) current therapy vs. placebo (n=1)* • No statistically significant differences between groups in pain intensity (RR 0.69, 95% CI 0.39, 1.24) or patient-rated improvement on a 5-point scale (RR 0.71, 95% CI 0.45, 1.32).
Adverse Effects	• Not reported

Post-stroke Shoulder Pain (Price 2000)[11]

Study Types	RCTs (quasi-randomized allowed)
Intervention(s)	• Functional electrical stimulation (FES) • TENS (low and high intensity) • Low frequency TENS
Comparator(s)	• Placebo • Control
Participant Characteristics	Mean age 66-72 years across studies

Inclusion Criteria	1) Participants required to have a loss of motor function in the upper limb, although the definition of this varied across studies (shoulder subluxation found in 5-40% of participants).
Exclusion Criteria	1) TENS included as part of multimodal treatment 2) Studies including patients with other causes for their neurologic injury 3) Invasive (e.g. percutaneous) electrostimulation techniques
TENS Device	• Not described
Electrodes	• Electrode placement was commonly over supraspinatus and posterior deltoid, however one study placed electrodes over the most painful points and in another study, 20% of subjects only received stimulation on the wrist extensors (these patients did not have shoulder girdle weakness)
Treatment Characteristics (frequency, intensity, duration)	• Varied; three studies used stimulation at intensities intended to cause muscle contraction and one used set intensity at the sensory threshold level. • Treatment programs lasted 4-12 weeks • All subjects received 'conventional' physiotherapy according to clinical need
# Identified Studies	22
# Excluded Studies	16
# Included Studies	4
Total N	170
Outcomes	• Pain intensity (pain rating scale as general assessment of pain, new reports of shoulder pain, change from baseline) • Proportion of subjects with shoulder pain • Functional/mechanical evaluation • In all studies, outcome measures were made at the end of the intervention period and at a later stage. • The second set of measures were at different time intervals (8 weeks to 3 years), represented a variable number of survivors, and were taken after un-blinding. Therefore, the authors felt it was unreliable to combine them and they were not included in the review.

Findings	• Time between stroke and recruitment varied across each of the four included studies: <48 hours, average of 16.5 days, average of 12 weeks, and average of 8.7 months. • Varied whether studies were of treatment versus prevention of shoulder pain: clearly treatment (n=1), pain not recorded at baseline (n=1), mixed treatment and prevention population, predominantly without pain at entry (n=2). • New reports of shoulder pain (n=2), only secondary outcome measure in these studies: no significant change in pain incidence after ES treatment compared to control (OR 0.64, 95% CI 0.19-2.14). • Pain intensity rating change from baseline (n=1): In one study, mean change in pain level in favor of ES vs. control [SMD: 0.71 (95% CI 0.06, 1.35)], however, there were greater initial levels of pain in the treatment group (n=1). Used a 0-4 verbal pain rating scale. • In another study, TENS was no better than control at relieving pain [SMD: 0.44 (95% CI -1.05, 0.16)] (n=1). Used a 0-100 VAS. • One study found that there was a global reduction in lateral rotation for most subjects during the study (hence the negative mean change), but the development of restriction was still more marked in the control group. • Another study compared the passive humeral lateral rotation (PHLR) difference between left and right sides within each subject, demonstrating markedly less restriction on the side affected by stroke in the treatment group.
Adverse Effects	• None reported

APPENDIX D: NEW RCTS EXAMINING TENS FOR PAIN

D.1 ACUTE PAIN

Labor Pain (Borup 2009)[12]

Type of study	RCT, randomization performed by a computer-controlled "voice response system"; needed unique civil registration number in the log before allocation code was given.
Intervention(s)	• TENS, n=144 • Acupuncture, n=314 (not examined in this assessment, but primary intervention of the study) * Supplementary conventional analgesics were provided on request (those allowed for controls)
Comparator(s)	• Control, n=149 ▪ Traditional analgesics; women could choose sterile water papules, NO2, warm tub bath, pethidine, or epidural analgesia
Inclusion criteria	1) Healthy, Danish-speaking women in labor with normal singleton pregnancy 2) Giving birth at term (37-42 completed wks) 3) Fetus in cephalic presentation
Exclusion criteria	1) Women with medical diseases 2) Women with complicated pregnancies 3) Women who already received analgesics during labor.
Demographics	• 607 women enrolled out of an estimated 6.232 eligible. • Enrolled women were similar to the entire group of eligible women on all available parameters (age, start of delivery, blood loss, umbilical cord pH, and Apgar score at 5 min), except for parity. • More nulliparous women were among the participants than non-participants (75% vs. 46%).
Withdrawals/dropouts	• 517/607 (85%) women randomized to the study completed the treatment and 490/517 (95%; 81% of all women randomized) returned the questionnaire on birth experience and satisfaction with pain relief. • Significant difference were found between women who completed treatment compared to those who did not with respect to: ▪ Duration of labor (289 vs. 365 min, p=0.012) ▪ Mode of delivery (8% spontaneous vs. 61%, p<0.001) ▪ Use of pethidine (1.7% vs. 5.6%, p=0.026) and epidural analgesia (15.7% vs. 30.0%, p=0.001).
Device/manufacturer	TENS 120Z unit (ITO CO. LTD. 33-3; Toyotama-Minami, Nerima-ku, Tokyo, Japan)
Where applied	Delivery room
Applied by	Midwives

Electrodes	• 2-4 electrodes placed on the skin of the lower back
Waveform	• Not described
Frequency	• Not described
Pulse amplitude/intensity	• Intensity of stimulation could be adjusted by the woman or the midwife
Pulse duration	• Set in constant mode, initially with a pulse width of 60 µsec and a pulse rate of 100 pulses/sec
Duration & frequency of treatment	• Treatment lasted from 20-45 minutes and could be repeated.
Pain outcome	• Primary outcomes: ▪ Need for pharmacological and invasive method ▪ Experience of pain (assessed using a linear 10-cm VAS) ▪ Birth experience. • 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. • Secondary outcomes: ▪ Duration of labor from randomization until birth ▪ Use of oxytocin ▪ Mode of delivery ▪ Post-partum hemorrhage ▪ Apgar score, ▪ Umbilical cord blood pH level.

Statistical Analysis	• Non-significant trend of fewer women in the TENS group having epidural compared to control group (16% vs. 22%, respectively). • No significant differences found in pain scores between TENS and control at any point during labor, or covering the entire delivery obtained 2 hours after delivery [mean 7.7 (8.0) and 7.8 (8.1), respectively]. • Mean differences in pain scores for the TENS and control groups were 1.1 and 0.7, respectively (p=0.217 across all three groups). • In the TENS group, 34% of women reported TENS gave some or substantial pain relief, 23% that it had a somewhat calming effect, and 84% that it had no side effects. • When asked if they would use TENS again for a future delivery, 18% answered positively, 66% negatively, and 16% did not know. • No significant differences with respect to duration of labor (p=0.485) and restricting to deliveries lasting 1-10 hrs did not change the result (p=0.700). • No differences in blood loss, mode of delivery, and Apgar score. Restricting analyses to 517 women who completed treatment did not substantially alter the results.
Adverse effects	• No signs of serious or prolonged side effects were reported.

Primary Dysmenorrhea (Tugay 2007)[13]

Type of study	RCT
Intervention(s)	• TENS, n=17
Comparator(s)	• Interferential Current (IFC) Therapy, n=15
Inclusion criteria	1) Diagnosis of primary dysmenorrhea, according to history, physical examination, and ultrasound findings
Exclusion criteria	• None described
Demographics	• Student volunteers from the school • Mean age: 21.4 ± 1.7 years (TENS: 21.3 ± 1.9 years vs. IFC: 21.4 ± 1.6 years)
Withdrawals/dropouts	• 32/34 (94%) participants completed follow-up
Device/manufacturer	• TENS device (ITO Model 120Z, two-channel) • IFC: Electronica Pagani ET20 I Rolandserie (Paderno Dugnano, Italy)
Where applied	Clinic at school of physical therapy and rehabilitation

Applied by	• TENS and IFC each applied by two different physiotherapists
Electrodes	• TENS: Applied to the proximal margin of the low back area and to the proximal of the gluteal region laterally • IFC: Polar stimulation with four vacuum electrodes; applied in teh same position and regions as TENS
Waveform	• Not described
Frequency	• TENS: 120 Hz (conventional; high frequency) • IFC: 0-100 and 90-100 pulses/sec (10 min each) to increase circulation and have a sedative effect, respectively
Pulse amplitude/intensity	• Intensity of current was increased up to tolerated level without producing any contraction (both TENS and IFC)
Pulse duration	• TENS: 100 µsec
Duration & frequency of treatment	• 20 minutes applied at the time of menstrual complaints, without taking analgesics (both TENS and IFC)
Pain outcome	• 100-mm VAS of menstrual pain, referred lower limb pain, and low back pain were recorded before treatment, and immediately, 8 hours, and 24 hours after treatment • Physical characteristics, years since menarche, length of menstrual cycle (days), and duration of menstruation (days) were also recorded.
Statistical Analysis	• TENS and IFC groups were similar in terms of age, BMI, time since menarche, length of menstrual cycle, and duration of menstruation (all $p>0.05$). • Pain intensities of the evaluated parameters decreased beginning from just after the applications in both groups ($P<0.05$). • Intensity of referring low back pain in the first three measurement times was different between the TENS and IFC groups ($P<0.05$), but this difference is thought to be due to the baseline values of the groups. • Reductions in menstrual pain, referred lower limb pain, and low back pain at each measurement were significant in both treatment groups ($P<0.05$). • 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 indicate that IFC and TENS are both effective in reducing menstrual pain, referred lower limb pain, and low back pain, which are the common symptoms of dysmenorrhea. • However, the interpretation of these results must be considered in light of limitations in the design of the study, particularly the absence of either untreated or placebo control groups. • Randomization did not make the groups homogeneous with respect to baseline pain intensities.
Adverse effects	•.None observed

D.2 CHRONIC PAIN

Chronic Low Back Pain (Kofotolis 2008)[14]

Type of study	Randomized, sequential allocation
Intervention(s)	• TENS (low frequency), n=23 • TENS (low frequency) + rhythmic stabilization, n=23
Comparator(s)	• Placebo TENS, n=23 • Control (rhythmic stabilization alone), n=23
Inclusion criteria	At least one of the following complaints: 1) LBP during and/or after activity 2) LBP during and/or after sitting 3) LBP during climbing stairs
Exclusion criteria	1) History of surgery or sciatica 2) Spinal abnormalities demonstrated through radiographs (i.e. presence of spondulolysis or spondylolisthesis 3) Lumbar scoliosis >10 degrees 4) Other injuries of the trunk, muscle/tendon ruptures 5) Excluded participants with prior experiences with either TENS or rhythmic stabilization
Demographics	• All females, mean age (SD): 40.5 (6.7) years
Withdrawals/dropouts	• 88/92 (96%) of included women provided two-month follow-up data
Device/manufacturer	• TENS unit 120Z (ITO, Tokyo, Japan) • Sham units (indicator lamp lit up when switched on, but internal circuit was disconnected)
Where applied	Patient rehabilitation clinic
Applied by	Physical therapist
Electrodes	• 4 rubber electrodes (2 cm x 3 cm) from a dual channel TENS unit were placed with aqueous gel • Electrodes were applied on the fascia thoracolumbaliis and approximately 10 cm proximal to this, along the midline of the muscle (i.e. directly over the site of pain).
Waveform	• Not described
Frequency	• 4 Hz
Pulse amplitude/intensity	• “strong but comfortable level of stimulation”
Pulse duration	• 200 µsec
Duration & frequency of treatment	• 40-45 min while resting in a prone position • 5 times/week for 4 weeks

Pain outcome	• Data on functional disability, pain intensity, trunk extension range of motion, dynamic endurance of trunk flexion and static endurance of trunk extension were assessed prior to, immediately after, four weeks and eight weeks post-intervention. • A validated structured questionnaire was completed at the initial phase of the study. • The intensity of the low back pain symptoms was assessed using the Borg verbal rating pain scale. Subjects were required to rate their pain level from 0 ('normal') up to 10 ('emergency'). • Pain symptoms were monitored during each testing session as well as throughout the training period. • The degree of functional impairment was assessed using the Oswestry Low Back Pain Disability Questionnaire. This is a 10-item scale where each item has six ranked detractors scored from 0 to 5 yielding a maximal score of 50. The first section is a pain-related scale whereas the other sections deal with various daily activities relevant to low back disability. • Physical activity at work and during leisure time was graded according to the frequency and the intensity of exercise. • Also recorded: range of motion for total trunk extension (T12–S2) and flexion using the flexicurve technique; dynamic flexion endurance; static endurance; and rate of exercise (not described in this assessment).
Statistical Analysis	• TENS participants were similar to placebo participants ($p>0.05$) with respect to basic characteristics of age, height, body mass index, time since first onset (years), current duration (weeks), Borg Pain Intensity Scale, and Oswestry Index (% /100). • Oswestry Index scores and back pain severity scores were similar between TENS and placebo participants ($p>0.05$; assessed pre-treatment, immediately after treatment, 4 weeks post-treatment, and 8 weeks post-treatment). * Only looked at TENS versus placebo comparisons since these were the focus of the Cochrane Review on chronic LBP.
Adverse effects	• None reported

Chronic Low Back Pain (Itoh 2009)[15]

Type of study	RCT

Intervention(s)	• TENS • TENS + acupuncture (the acupuncture therapies will not be discussed in this report).
Comparator(s)	• Acupuncture • Control (topical poultice as needed)
Inclusion criteria	1) Lumbar or lumbosacral low back pain for at least 6 months 2) No radiation of low back pain 3) Normal neurological findings of lumbosacral nerve, including deep tendon reflexes, plantar response, voluntary muscle action, straight leg raising, and sensory function 4) Not receiving acupuncture treatment for more than 6 months
Exclusion criteria	1) Major trauma or systemic disease 2) Receiving conflicting or ongoing co-interventions (patients under drug treatment were included if there had been no change in medicine and its dosage for one month or longer
Demographics	12/32 (32%) participants male; aged 61-81 years
Withdrawals/dropouts	• 81% of randomized participants completed follow-up and were included in the analyses. • All patients lost to follow-up did so because they discontinued use of their assigned treatment; among the treatment groups, 25% discontinued use of TENS and acupuncture + TENS and 12% discontinued use of acupuncture or control. • All patients lost to follow-up were reported to discontinue therapy because they had not responded to their respective treatment; one patient in the acupuncture + TENS group also reported a deterioration in symptoms.
Device/manufacturer	• Single-channel portable TENS unit (model HV-F300, OMRON Healthcare Ltd. Japan)
Where applied	• Not explicitly reported, but treatment and assessment appear to have taken place in a hospital or clinic setting
Applied by	
Electrodes	• Two electrodes placed over the affected area of LBP on the point with the most tenderness and the near side of the point.
Waveform	• Sinusoidal waves
Frequency	• TENS unit sends a premixed amplitude-modulated frequency of 122 Hz.
Pulse amplitude/intensity	• Adjusted so that a tingling sensation 2-3 times the subject's sensory threshold was produced.

Pulse duration	
Duration & frequency of treatment	• 15 minute session
Pain outcome	Primary outcome measures were: • pain intensity, quantified with a 100-mm VAS • pain disability measured with the Roland Morris Questionnaire (RDQ, 0-24 points) • VAS scores measured immediately prior to first treatment and subsequently at 1, 2, 3, 4, 5, and 10 weeks after the first treatment. • RDQ scores were measured immediately prior to first treatment and subsequently 5 and 10 weeks after the first treatment
Statistical Analysis	• Mean VAS scores decreased in all groups during treatment, but the exact time course differed between groups. • Differences between pre-treatment and 5-week VAS scores were not significant in either the TENS or control group. • VAS score was not significantly differeent between the TENS and control groups after 5 weeks of treatment (mean (standard deviation): 53.2 (25.1) and 53.1 (27.9), respectively). • The RDQ scores decreased in all groups during treatment, but were not statistically significant for either the TENS or control group. • By the end of the 5th week, patients in the TENS group reported lower RDQ scores than the control group (mean (SD): 6.2 (3.4) vs. 7.3 (4.6), respectively), but the difference was not statistically significant.
Adverse effects	• The only reported adverse affect reported was for the patient who dropped out of the study with a deterioration of symptoms

Osteoarthritis of the knee (Paker 2006)[16]

Type of study	RCT
Intervention(s)	• TENS (conventional; high frequency), n=27
Comparator(s)	• Hyaluronic acid (HA) injection, n=25
Inclusion criteria	1) Willingness to participate 2) Aged 40-80 years 3) Radiographic evidence of Kellgren and Lawrence grade II or III OA of the knee 4) Patients were ambulatory and reported symptomatic disease for >1 year 5) Patients had not received previous intra-articular HA injections at any time and no intra-articular corticosteroid injections over the previous 3 months 6) Before study began, patients underwent a 2-week washout period for analgesic and NSAID drugs
Exclusion criteria	1) Patients taking oral glucosamine or chondroitin supplements (acetaminophen adjuvant medication was allowed during the study, if needed) 2) Pregnancy or lactation 3) Inflammatory arthritis 4) Previous fracture around the knee 5) Knee arthroscopy or knee replacement surgery 6) Significant comorbidity (renal, hepatic, or heart disease) 7) Bird hypersensitivity or egg allergy
Demographics	• Patients in the TENS group were significantly younger than those in the Hylan group (mean, 54.2 vs. 64.0, respectively; p<0.0001). • Patients were similar with respect to other baseline characteristics of height, weight, duration of disease, WOMAC pain score, WOMAC stiffness score, Lequesne score, and SF-36 score (all p>0.05).
Withdrawals/dropouts	• 52/60 (87%) enrolled patients completed the follow-up period • TENS group: 3 patients withdrew from the study (1 underwent arthroscopic knee surgery because of a traumatic lesion of the meniscus, 1 experienced worsening of knee pain after treatment began, and 1 disagreed with the treatment protocol). • HA group: 5 patients dropped out (3 lost to follow-up because they moved to another city, 2 did not complete the study because their knee pain subsided).
Device/manufacturer	• Intelect 340 Combo [Stim] (Chattanooga Group, Docklands, Victoria, Australia)
Where applied	Clinic
Applied by	• All TENS applied by a single therapist
Electrodes	• Applied to knees (no other details provided)
Waveform	• Not described
Frequency	• 150 Hz
Pulse amplitude/intensity	• Not described
Pulse duration	• Not described

Duration & frequency of treatment	• 20 minutes applied at a time, 5 times/week for 3 weeks
Pain outcome	• Patients were assessed by an independent, blinded investigator at baseline and at 1, 3, and 6 months after the study was begun. • The WOMAC, Lequesne Index, and SF-36 were used to assess pain, functional status, and QOL. ▪ 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. ▪ WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index; self-administered test that yields summary scores for pain, stiffness, and level of physical function limitation. Reliable and valid outcome measure for use in evaluation of patients with hip or knee OA. In this study, pain and functional status were assessed on a 5-point scale (1, no difficulty; 2, mild; 3, moderate; 4, severe; 5, very severe). ▪ Short Form-36 (SF-36): 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. May be completed as a self-assessment questionnaire.
Statistical Analysis	• During the first month of the study, the TENS group experienced greater pain relief than the HA injection group (52.5% vs. 46.8%, respectively). • WOMAC physical function limitation scores decreased in both groups after therapy was provided (P<.0001); this decline continued throughout the study. • The injection group, however, exhibited a statistically significant improvement at the 6th month compared with the TENS group (P<.05). • WOMAC stiffness decreased in the TENS group during the first month (P<.007)—a benefit that continued throughout the study. • The injection group, however, showed significantly greater improvement at the 6th month compared with the TENS group (P<.05). • No significant difference in stiffness was observed between groups during the 6-month follow-up. • Mean Lequesne functional scores and total scores were low in both groups at baseline and 6 months later. • Scores of patients in the TENS group were significantly lower after therapy than at baseline (P<.05), but HA group scores were similar to TENS group scores at 6-month follow-up. • No significant difference in SF-36 scores was noted after treatment in both groups.
Adverse effects	• Not reported

Osteoarthritis of the knee (Kang 2007)[17]

Type of study	RCT
Intervention(s)	• Percutaneous neuromodulation therapy (PNT), n=35
Comparator(s)	• Placebo, n=28
Inclusion criteria	1) Knee pain secondary to osteoarthritis 2) Adults (aged 18-85 years) 3) VAS >30 mm (prior to treatment) 4) Ability to understand and cooperate with the study procedures.
Exclusion criteria	1) Any patient with an allergy or intolerance to adhesive materials 2) Surgical intervention or injection of a corticosteroid or viscosupplement within the prior 30 days of treatment of the painful knee or its underlying etiology 3) History of substance abuse or dependence within the past 6 months 4) History of pacemaker use 5) Existence of implantable electronic devices 6) Any clinical evidence of cardiovascular, pulmonary, renal, psychological, hepatic, neurological, hematologic or endocrine abnormalities 7) Having received an investigational drug or device in the past 30 days
Demographics	• Males: 28% of population (31% PNT vs. 25% placebo) • Mean age (range), PNT: 55.3 (34-83) years vs. placebo: 58.2 (28-80) years
Withdrawals/dropouts	• 63/70 (90%) patients completed follow-up
Device/manufacturer	• Deepwave® (Biowave Corp, Norwalk, CT)
Where applied	Clinic
Applied by	• Not described, (likely clinic therapist)
Electrodes	• Applied to knees (no other details provided)
Waveform	• Not described
Frequency	• Not described
Pulse amplitude/intensity	• PNT group instructed to tell examiner when they had achieved the highest tolerable intensity. • The intensity leyels then were reassessed and increased as tolerated by the patient after 5, 10, and 15 minutes from initiation of the treatment session. The mean intensity levels for the live group were 16%. 19%, 21%. and 23% at the 0-, 5- (10-. and 15-minute time points, respectively).
Pulse duration	• Not described
Duration & frequency of treatment	• 20 minutes applied at a time, 5 times/week for 3 weeks

Pain outcome	• VAS (100 mm) was used to determine pre- and post-treatment pain levels (immediate, 6 hours, 24 hours, and 48 hours); end-points of 'no pain' and 'worst pain imaginable'. • The WOMAC questionnaire: completed by the tester pre-treatment and immediately after treatment; completed by the patient at 6, 24, and 48 hours post-treatment and mailed back to the investigator. • Patient-perceived overall improvement (0% to 100%) recorded at immediate, 6-, and 24-hour time points. • In addition to the above measures, patients were also asked at 48 hours to report follow-up knee surgery and subjective questions regarding pain control and relief. • A one-week phone survey was used to collect information on adverse effects and medication use.
Statistical Analysis	• Pain intensity difference (PID; defined as the difference in VAS pre- and post-treatment) greater immediately post-treatment for the PNT group than the placebo group ($p<0.04$), 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). • Similar results were obtained when summed PID (cumulative across time points) was compared between the groups. • Median PID (across all time periods) groups: PNT group showed greater reductions (14.5 mm vs. 6.5 mm, $p<0.01$). • There were no significant differences in raw VAS scores between the PNT and placebo groups at any time point. • A significantly greater proportion of the TENS group reported their pain control positively (measured categorically as 'none', 'poor', 'fair', 'well', and 'complete') at 48 hours post-treatment ('well' or 'complete' for 35% PNT and 7% placebo groups; $p=0.04$). • When asked to grade their pain relief on a 0%- 100% scale at 48 hours post-treatment, the PNT group reported significantly greater pain relief (42%) than the placebo group (11%) ($p=0.01$). Similar results were obtained patients rated their satisfaction with treatment. • At one-week follow-up, 77% of PNT patients and 11% of placebo patients reported satisfaction levels of 'good', 'very good', or 'excellent'. • 54% of patients in the PNT group, compared to 0% in the placebo group, reported significantly less medication use at the one-week follow-up. • At 48-hours post-treatment, the PNT group demonstrated greater in improvement in the WOMAC category of stiffness ($p=0.03$), but not pain ($p=0.15$) or function ($p=0.05$).
Adverse effects	• There were no differences in comfort or occurrence of adverse events between the PNT and sham PNT groups ($p>0.05$). Only 3 patients experienced pain/pressure/tingling (1 PNT, 2 sham) and only 1 patient in the PNT group experienced skin irritation.

APPENDIX E. EXCLUDED REVIEWS AND STUDIES

E.1 EXCLUDED REVIEW

Chronic Headache (Brønfort 2004)[18]

Study Types	RCTs (quasi-randomized allowed)
Intervention(s)	• TENS in combination with other treatments
Comparator(s)	• Biofeedback • Relaxation • Other non-invasive treatments
Participants Characteristics	Ages 12-78 years
Inclusion Criteria	1) Migraine, cluster, tension-type, cervicogenic, a mix of migraine and tension-type, and post-traumatic headache 2) In addition to TENS, also included other non-invasive treatments: electromagnetic therapy, microcurrent, ultrasound, laser, exercise, spinal manipulation or mobilization, massager, reflexology, stretching, and trigger-point therapy
Exclusion Criteria	1) Studies of acupuncture and psychological interventions such as biofeedback and relaxation (could be comparators)
# Included Studies	22
Total N	2628
Reason for exclusion	• This review included studies of many types of interventions. • TENS was only examined in two studies as part of multimodal treatments, without appropriate comparators.

E.2 EXCLUDED STUDIES

First Author (Year)	Condition	Reason(s) for Exclusion:
Acute Pain		
Cipriano (2008)[19]	Cardiac surgery	• No measure of analgesic consumption
Chronic Pain		
Lofgren (2009)[20]	Fibromyalgia	• Inappropriate comparison group
Selfe (2008)[21]	Osteoarthritis of the knee	• Used a non-standard TENS device that was either held stationary of moved along the skin in sweeping motions

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