IN THE COURT OF COMMON PLEAS
SUMMIT COUNTY, OHIO

MEMBER WILLIAMS, et al., Plaintiffs, vs. KISLING, NESTICO & REDICK, LLC, *et al.*, Defendants.	Case No. CV-2016-09-3928 Judge James A. Brogan **Notice of Filing Volume VI of Exhibits to the Deposition of Defendant Sam Ghoubrial**

Plaintiffs hereby give notice of filing Volume VI of exhibits to the deposition of Defendant Sam Ghoubrial, taken on April 9, 2019.

Respectfully submitted,

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Subacute and chronic low back pain: Nonpharmacologic and pharmacologic treatment

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INTRODUCTION

Up to 84 percent of adults have low back pain at some time in their lives [1,2]. The long-term outcome of low back pain is generally favorable. In one prospective study, 90 percent of patients with low back pain seen initially in primary care did not seek care after three months [3]. However, symptoms may not completely resolve even among persons who no longer seek care. Given how common low back pain is, persistent symptoms affect millions of individuals. Subacute low back pain is commonly defined as back pain lasting between 4 and 12 weeks and chronic low back pain as pain that persists for 12 or more weeks.

The initial evaluation of patients with low back pain, regardless of its duration, includes history taking and a targeted physical examination focusing on neurologic screening to exclude serious underlying pathology (eg, malignancy, infection, or cauda equina syndrome). On the basis of this evaluation, patients are triaged into broad diagnostic categories that include nonspecific low back pain, radiculopathy, or other specific pathology (eg, spinal stenosis, ankylosing spondylitis, and vertebral compression fracture) [4-6]. (See "Evaluation of low back pain in adults".)

Most patients (>85 percent) who are seen in primary care have "nonspecific low back pain," which

is low back pain that cannot reliably be attributed to a specific disease or spinal pathology [7]. Rapid improvement in pain and disability and return to work are the norm in the first month [8]. Patients who do not improve within four weeks of the onset of low back symptoms should be reevaluated and may require further diagnostic testing to identify a specific cause for their symptoms. (See "Evaluation of low back pain in adults", section on 'Risk assessment subacute back pain' and "Evaluation of low back pain in adults", section on 'Risk assessment chronic back pain'.)

Despite persistent pain, patients with subacute symptoms still have a favorable prognosis. For patients whose symptoms persist beyond three months, however, the goal of treatment moves from "cure" to controlling pain, maintaining function, and preventing disability. Factors associated with development of chronic disability include preexisting psychologic conditions, other types of chronic pain, job dissatisfaction or stress, and dispute over compensation issues [9]. Effective methods for reducing the risk of progression to chronic pain have not been definitively identified [10,11].

It is likely that many patients with chronic low back pain are not receiving evidence-based care. One survey of households in North Carolina, for example, identified 732 adults with chronic low back pain [12]. Responses indicated overutilization of unproven interventions (traction, corsets), high use of second-line medications (opioids and muscle relaxants), and underutilization of exercise therapy and, for patients with depression, antidepressants.

A glossary of terms used in the discussion of low back pain is presented in the table (table 1). Criteria used in this review to classify magnitude of benefits for the most commonly reported outcomes (pain relief or improvement in function) are presented in the table (table 2).

Relatively few randomized trials have evaluated patients specifically with subacute low back pain [13], sciatica, or spinal stenosis [14,15]. Results from trials evaluating mixed populations (subacute with either acute or chronic patients) are commonly applied to both groups. This topic presents recommendations for initial management of patients with subacute and chronic low back pain. Interventional and surgical therapies for subacute and chronic low back pain and treatment recommendations for acute low back pain are discussed separately. (See "Subacute and chronic low back pain: Nonsurgical interventional treatment" and "Subacute and chronic low back pain: Surgical treatment" and "Treatment of acute low back pain".)

A summary of the multiple interventions for subacute and chronic low back pain discussed in these topics is presented in the tables (table 3 and table 4 and table 5 and table 6).

GENERAL APPROACH TO CARE

Overview — All patients with subacute and chronic low back pain should receive advice on self-care and instruction on the importance of maintaining activity as tolerated (see 'Self-care advice' below). We generally advise nonpharmacologic therapy initially and favor "active" interventions that are movement-based and/or address psychosocial contributors to pain. These include exercise, cognitive behavioral therapy (CBT), tai chi, yoga, other relaxation techniques (mindfulness-based stress reduction [MBSR], biofeedback, and progressive relaxation), and multidisciplinary rehabilitation. An emphasis on active therapies is consistent with a biopsychosocial approach to pain, engages patients in their care, and more directly aims to improve function, not just reduce pain. More "passive" interventions, such as acupuncture or spinal manipulation, can be used as adjunctive treatments during symptom flares.

For patients with subacute low back pain who have a high likelihood of spontaneous remission, self-care interventions and patient education may be sufficient. In persons with more severe symptoms who have risk factors for chronicity or who are not improving with self-care and education, short-term interventions such as superficial heat, massage, exercise therapy, spinal manipulation, or acupuncture may be considered. The choice among these interventions also depends on patient preference and their cost and accessibility; there are no data demonstrating superiority of one over another [6]. The STarT Back randomized trial showed that a risk-stratified approach in which patients with risk factors for chronicity received more intensive CBT-based exercise therapy was more effective than usual care [16]. (See 'Activity and physical treatments' below and 'Psychologic interventions' below and 'Physical modalities' below.)

Pharmacologic therapy is reasonable for those who have inadequate symptom control with nonpharmacologic measures. For patients with subacute low back pain who warrant pharmacologic therapy, a nonsteroidal antiinflammatory drug (NSAID) with or without a nonbenzodiazepine skeletal muscle relaxant is preferred over acetaminophen. For patients with chronic low back pain who have had an inadequate response to nonpharmacologic therapy, we suggest an NSAID as initial therapy and tramadol or duloxetine as second-line therapy. (See

'Pharmacologic therapies' below.)

Given the limited benefits and serious harms associated with opioids, clinicians should consider opioids as an option only in patients who have not responded to these management approaches and if the potential benefits outweigh the risks. (See 'Use of opioids' below.)

This approach is consistent with the 2017 updated guideline from the American College of Physicians for the management of acute, subacute, and chronic low back pain [17].

Self-care advice — All patients with low back pain, regardless of duration or severity, should be instructed in self-care techniques. Initial advice should stress the importance of maintaining activity as tolerated [6]. Patients who require a period of bedrest to relieve severe symptoms should be encouraged to return to normal activities as soon as possible.

A systematic review of randomized trials found that bedrest did not improve either function or pain, compared with usual activity, for patients with sciatica [18]. Advice to remain active was as effective as "standard" physical therapy (any combination of exercises, mobilization and/or manipulation, superficial heat or cold, and advice) for improvement in function in a randomized trial [19]. However, patients randomly assigned to physical therapy were more likely to report a perceived benefit than those receiving activity advice.

Self-care education books based on evidence-based guidelines (such as The Back Book [20]) are an inexpensive method for supplementing clinician-provided back information and advice [21]. Several randomized trials have shown self-care education books to be similar in effectiveness, or only slightly inferior, to interventions with higher direct costs, such as supervised exercise, massage, acupuncture, and spinal manipulation [18,22-24].

Bed mattress choice — Evidence regarding how bed mattress choice impacts back pain is limited. A medium-firm mattress may be the preferred mattress choice for patients with chronic back pain, based on findings from a European randomized trial (n = 313) in which patients randomly assigned to a firm mattress, compared with a medium-firm mattress, were less likely to experience improvement in pain-related disability at 90 days (68 versus 82 percent) [25]. The medium-firm mattress was superior to a firm mattress for improvement of pain while lying in bed (odds ratio [OR] 2.36, 95% CI 1.13-4.93) and pain-related disability (OR 2.10, 95% CI 1.24-3.56).

Although these results suggest providers should not recommend a firm mattress for chronic low back pain, the firmness rating scale was a European standard, and the term "medium-firm" may mean different things to different manufacturers in different countries.

Another randomized study comparing back conforming mattresses (waterbed and foam) with a firm mattress suggested less pain and improved sleep for the conforming mattresses, with higher dropout rates for patients assigned to the firm mattress [26].

Lumbar supports — There is no compelling evidence that lumbar supports are effective in patients with chronic low back pain. A systematic review of eight trials for the use of lumbar supports in the treatment of low back pain found overall poor study quality, inadequate randomization, and generally low compliance with the intervention [27]. The conclusion was that there was conflicting evidence whether lumbar supports used as supplements to other treatments were effective in the treatment of low back pain. A French multicenter open-label randomized trial published subsequent to the systematic review found that use of an elastic belt in patients with subacute low back pain modestly reduced the need for pain medication and improved functional status at 30 and 90 days [28]. However, longer-term outcomes are unknown, and if use of a belt leads to avoidance behaviors by reinforcing awareness of a "back problem" and activity restriction, it may discourage exercise participation. Thus, while lumbar supports are not routinely recommended, they may provide some benefit for patients with subacute low back pain who are actively engaged in recommended therapies, such as exercise, and who will remain active.

ACTIVITY AND PHYSICAL TREATMENTS

In addition to self-care instruction, all patients with subacute and chronic low back pain should be advised to remain as active as possible and to incorporate physical therapies into their treatment plan.

Exercise therapy — A number of different types of exercise are commonly used in patients with subacute or chronic low back pain. Exercise programs include motor control exercise (also known as specific stabilization exercise), core strengthening (eg, abdominal and trunk extensor), flexion/extension movements, directional preference, general physical fitness, aerobic exercise, mind-body exercises (eg, yoga and Pilates), and functional restoration programs. Most exercise

programs appear to be similarly effective, though a systematic review found that motor control exercise was associated with slightly less pain intensity and better function than general exercise [29]. Exercise therapy is safe, readily available, helps alleviate pain symptoms, and improves functionality. (See "Exercise-based therapy for low back pain".)

Spinal manipulation — Spinal manipulation is a form of manual therapy that involves the movement of a joint beyond its usual end range of motion, but not past its anatomic range of motion (termed the "paraphysiologic zone"). Loads are applied to the spine using short- or long-lever methods. Short-lever high-velocity movement of the joint is frequently accompanied by an audible cracking or popping sound. Spinal manipulation is most commonly associated with chiropractic providers, but is also performed by other providers, including osteopathic clinicians and physical therapists. (See "Spinal manipulation in the treatment of musculoskeletal pain", section on 'Types of manipulation'.)

A 2011 meta-analysis including 26 randomized trials in patients with chronic low back pain compared spinal manipulation with multiple treatments (general practitioner care, analgesics, physical therapy, exercises, or back school, massage, ultrasound, transcutaneous muscle stimulation, and attending a pain clinic) [30]. Spinal manipulation had small short-term effects on reducing pain and improving functional status compared with other interventions. Subsequent randomized trials support the finding of short-term benefits of spinal manipulation in patients with subacute and chronic low back pain [31,32]. A randomized trial of 192 patients with subacute and chronic back-related leg pain evaluated home exercise and advice with or without spinal manipulative therapy [32]. Spinal manipulation modestly improved leg pain at 12 weeks but not at 52 weeks. Another randomized trial in 107 adults with acute and subacute low back pain found that compared with usual care, manual spinal manipulation improved self-reported short-term disability and pain scores [33].

Serious adverse events following lumbar spinal manipulation (such as worsening lumbar disc herniation or cauda equina syndrome) are rare. (See "Spinal manipulation in the treatment of musculoskeletal pain", section on 'Risks of spinal manipulation'.)

Acupuncture — Acupuncture is an intervention consisting of the insertion of needles at specific predetermined acupuncture points. Evidence on the efficacy of acupuncture versus sham acupuncture is inconsistent. Systematic reviews found acupuncture moderately more effective than

no treatment for short-term (<3 months) pain relief and improvement in function, and more effective than sham acupuncture for pain relief, but not for improvement in function [34,35]. However, two well-blinded trials not included in the systematic reviews found no difference between acupuncture and sham acupuncture for either pain or function [36,37], although a subsequent meta-analysis including these studies still found that acupuncture reduced pain compared with sham and improved function compared with no intervention [38]. It is unclear if the effectiveness of sham acupuncture derives from some attribute of superficial needling or is solely a placebo effect. Acupuncture is likely to be most beneficial in patients who have high expectations of benefit [39]. (See "Acupuncture", section on 'Low back pain'.)

Massage — Interpretation of studies to evaluate the effectiveness of massage therapy in chronic low back pain is hampered by differences in the comparator interventions, types of massage, and duration and frequency of massage sessions. A systematic review including 25 trials found limited evidence for short-term benefits of massage. When compared with inactive controls, there was evidence of short-term improvement in symptoms for subacute and chronic low back pain, but no long-term benefits [40].

For example, one large randomized trial in 579 patients with chronic or recurrent low back pain found that six sessions of massage therapy, with or without a minimal exercise intervention, reduced disability and pain at three months compared with usual care, but benefits were not sustained at 12 months [41]. Another trial in 401 patients with chronic, nonspecific low back pain found that 10 sessions of massage therapy reduced disability and pain at 10 weeks compared with usual care [42]. The benefits waned over time with no clinically meaningful difference at 12 months' follow-up.

PSYCHOLOGIC INTERVENTIONS

These interventions are designed to address the negative psychologic impact of persistent pain, although yoga also involves movement that can directly affect pain and function.

Cognitive behavioral therapy — A variety of psychologic approaches to patients with chronic low back pain have been evaluated. A systematic review found cognitive behavioral therapy (CBT) superior to waitlist control for short-term pain relief, although there were no differences in function

[43]. Results were less conclusive for other types of psychologic intervention [44]. In a subsequent, 12-month randomized trial in patients with subacute or chronic low back pain, those randomly assigned to group CBT reported less pain and disability compared with no further treatment [45].

Mind-body interventions — Mind-body interventions, such as meditation and mindfulness techniques, have been evaluated for the treatment of chronic low back pain. Such interventions often incorporate cognitive behavioral principles and may include a movement component (eg, tai chi, yoga). There is some evidence that these interventions may be effective, but more research is needed to define optimal approaches.

Mindfulness-based stress reduction is a mind-body intervention that can be administered in group settings by laypersons. In a meta-analysis of seven randomized controlled trials involving 864 patients with low back pain, mindfulness-based stress reduction (MBSR) was associated with modest short-term improvements in pain intensity (mean difference [MD] -0.96 point on an 11-point numerical rating scale; 95% CI, -1.64 to -0.34) and physical functioning (MD 2.50 on SF-36 physical functioning subscale; 95% CI, 0.90 to 4.10) compared with usual care [46]. There were no serious adverse events reported.

As an example, in one of the trials included in the meta-analysis, among 342 adults with chronic low back pain, MBSR or CBT (training to change pain-related thoughts and behaviors) were more likely to have clinically meaningful improvement in self-reported function (MBSR, 60.5 percent; CBT, 57.7 percent; usual care, 44.1 percent) and pain bothersomeness (MBSR, 43.6 percent; CBT, 44.9 percent; usual care, 26.6 percent) [47]. There were no differences between the MBSR and CBT groups.

Yoga for low back pain is discussed elsewhere. (See "Exercise-based therapy for low back pain", section on 'Yoga'.)

EDUCATIONAL AND COMBINED INTERVENTIONS

Education — A number of educational interventions have been evaluated for chronic low back, including self-care advice and written booklets (see 'Self-care advice' above). Evidence on the effectiveness of more intensive, individualized educational interventions is limited. A systematic review identified no trials of individual education versus no education, although it included three

trials that found no differences between individual education and non-educational interventions (exercise therapy, yoga, or back school) in pain or function [48]. Data on the comparative effectiveness of different educational approaches or content are also limited. A 2011 systematic review and meta-analysis of pain neurophysiology education, also known as pain neuroscience education (ie, education that focuses on the neurophysiology of pain, including psychosocial contributors) identified two randomized controlled trials (n = 122) that met inclusion criteria [49]. The meta-analysis found that pain neurophysiology education was slightly more effective at improving short-term pain (difference of about 5 points on a 0 to 100 point pain scale) than education that focused on biomechanical aspects of pain. Education was provided by trained physical therapists. Independent validation of these results is needed, as both small trials in the meta-analysis were conducted by the same group that published the pain neurophysiology education manual. A subsequent small trial also found that pain neurophysiology education combined with exercise therapy was beneficial for reducing pain intensity and improving function compared with exercise therapy alone [50], but more rigorous trials are need to confirm the efficacy of this intervention.

Back school — Back school is an intervention originally developed in Sweden consisting of education and a skill program including exercise therapy. Generally, lessons are provided to groups of patients and supervised by a physical therapist or other therapist trained in back rehabilitation, although the content of back school interventions vary and back school based on the traditional Swedish approach is not widely available in the United States. Back school may be a reasonable therapeutic option in patients with subacute or chronic low back pain who are interested in it, but there is limited evidence supporting its effectiveness. There is overlap between back school and group exercise, educational interventions, and multidisciplinary rehabilitation.

A 2017 meta-analysis found very low-quality evidence that back school was modestly more effective than no treatment for short-term pain control (six trials; mean difference [MD] -6.10 on 0-100 point scales, 95% CI -10.18 to -2.01) and reducing short-term disability (three trials; MD -3.38 on 0-100 scales, 95% CI -6.70 to -0.05), but these effects were not seen in intermediate- or long-term follow-up [51]. In addition, back school was no more effective for pain control than medical care, passive physiotherapy, or exercise in intermediate- or long-term follow-up.

Multidisciplinary (interdisciplinary) rehabilitation — Multidisciplinary, or interdisciplinary, rehabilitation combines physical, vocational, educational, and/or behavioral components provided

by multiple health care professionals. Intensity and content of interdisciplinary therapy vary widely. These programs combine graded exercise therapy with a psychosocial approach, generally involving a psychologist. Multidisciplinary therapy can be similar to functional restoration programs which often focus on occupational aspects of rehabilitation; both approaches emphasize functional improvement and typically utilize a multidisciplinary approach with a strong psychological component.

A systematic review of 41 trials found multidisciplinary rehabilitation that included a physical component with a psychological component and/or a social/work-targeted component delivered by clinicians with different professional backgrounds was associated with larger improvements in pain and function than usual care or non-multidisciplinary physical treatments (eg, exercise therapy, physical modalities, manual therapy, education) [52]. Differences were about 0.5 points on a 0 to 10 point pain scale and 1.5 points on the Roland Morris functional scale. Multidisciplinary treatment also increased the likelihood of return to work compared with non-multidisciplinary physical treatments (odds ratio [OR] 1.87, 95% CI 0.73 to 1.47). There was no clear effect of intervention intensity on effectiveness of multidisciplinary rehabilitation.

Patients are more likely to benefit from multidisciplinary rehabilitation and functional restoration if they are highly motivated, as the regimens can be intensive (eg, >20 hours per week). The high cost of the more intensive programs limit their applicability; they may be most appropriate for patients who do not respond to single interventions or as an alternative to surgery. We advise referring clinicians be familiar with outcomes for specific programs, given the cost and heterogeneity of quality among programs [53].

Multidisciplinary programs may not be available in many communities. They are usually practiced in pain clinics or rehabilitation centers. It is uncertain whether providing the components of multidisciplinary rehabilitation outside of a formal program is as effective as a coordinated program. If not available, the primary care clinician may be left the task of coordinating a collaborative arrangement between the various specialists, for which the logistics are burdensome. Primary care clinicians may need to develop and coordinate an individualized care program, involving a physical or occupational therapist, a behavioral psychologist experienced in patients with musculoskeletal symptoms, and a rehabilitation or occupational clinician.

Functional restoration — Functional restoration, also known as work hardening, work

conditioning, or physical conditioning involves simulated or actual work tests in a supervised environment to improve strength, endurance, flexibility, and fitness [54]. This can be used for patients with subacute and chronic low back pain and for injured workers. (See "Exercise-based therapy for low back pain", section on 'Graded activities exercise/back boot camp/functional restoration'.)

PHYSICAL MODALITIES

A large number of physical modalities, in addition to the physical treatments already discussed, have been used in patients with chronic low back pain. For most of these modalities, there is little evidence of benefit from randomized, controlled studies [55], although patient expectations of benefit and placebo effects may play a role in their therapeutic value [39]. (See 'Activity and physical treatments' above.)

- **Interferential therapy** – Interferential therapy is the superficial application of a medium-frequency alternating current, modulated to produce low frequencies up to 150 Hz. There is no convincing evidence from three trials that interferential therapy is effective for chronic low back pain [56-58].

- **Low-level laser therapy** – Low-level laser therapy, used by some physical therapists, is provided as a single wavelength of light, between 632 and 904 nm, directed at the area of discomfort. For chronic low back pain or back pain of unspecified duration, four trials found laser therapy superior to sham therapy for pain relief and improvement in function up to one year following treatment [59-62]. However, another trial found no difference between laser and sham in patients also receiving exercise [63]. Another trial found no differences between laser, exercise, and the combination of laser plus exercise [64].

  A systematic review found some evidence of short-term benefit in relief of low back pain, compared with sham therapy, but protocols for treatment dose, duration, and wavelength were inconsistent [65]. The review concluded that data were insufficient to draw conclusions regarding effectiveness.

- **Ultrasound** – Despite being widely used for the treatment of many musculoskeletal pain syndromes, few studies have evaluated ultrasound. It is usually performed in combination with

other physical therapy modalities, and its beneficial effect is thought to be due to heating of deep tissues. For chronic low back pain, two small (n = 10 and n = 36) trials reported inconsistent results for ultrasound versus sham ultrasound, with the larger trial reporting no differences [66,67]. A systematic review concluded that ultrasound is ineffective in the treatment of chronic low back pain [68].

- **Shortwave diathermy** – Shortwave diathermy is the elevation of the temperature of deep tissues by application of shortwave electromagnetic radiation with a frequency range from 10 to 100 MHz. Two trials found no differences between shortwave diathermy and sham diathermy manipulation for chronic low back pain [69,70].

- **Traction** – Traction involves drawing or pulling in order to stretch the lumbar spine. A variety of methods are used and typically involve a harness around the lower rib cage and around the iliac crest, the pulling action performed via free weights and a pulley, motorized equipment, inversion techniques, or an overhead harness.

  For mixed-duration low back pain with or without sciatica, a systematic review found no convincing evidence from nine trials that continuous or intermittent traction is more effective than placebo, sham, or no treatment [71]. Although autotraction was more effective than placebo, sham, or no treatment in patients with sciatica, it was only evaluated in two trials with methodologic shortcomings.

- **Transcutaneous electrical nerve stimulation** – Transcutaneous electrical nerve stimulation (TENS) refers to the use of a small battery-operated device to provide continuous electrical impulses via surface electrodes, with the goal of providing symptomatic relief by modifying pain perception. A meta-analysis of nine trials comparing TENS with sham, placebo, or pharmacologic therapy found no improvement in lower back pain scores [72].

- **Percutaneous electrical nerve stimulation** – Percutaneous electrical nerve stimulation (PENS) involves insertion of acupuncture-like needles and applying low-level electrical stimulation. The insertion points target dermatomal levels for local pathology, rather than acupuncture points.

  Although several trials found PENS moderately to substantially superior to sham PENS for pain relief, effects on function were inconsistent, all trials had methodologic shortcomings, and

some trials only measured outcomes at the end of a two-week course of treatment [73-76]. PENS is not widely available in the United States.

PHARMACOLOGIC THERAPIES

Medications are commonly used for patients with low back pain. Most evidence of efficacy comes from short-term trials, so the relative benefits and safety of use for prolonged periods in patients with subacute and chronic pain is uncertain. Thus, limiting the duration of use for most medications is reasonable.

We recommend a nonsteroidal antiinflammatory drug (NSAID) for most patients with subacute or chronic back pain in whom medication is indicated. Representative data from two national databases in the United States, in which data from nearly 24,000 visits for spine disorders were analyzed (representative of approximately 440 million visits), found that use of NSAIDs and acetaminophen decreased between 2000 and 2010 (from 37 to 29 percent), while use of opioids increased (from 19 to 29 percent) [77].

Initial therapy — We suggest a short course of NSAIDs for an acute exacerbation of subacute or chronic low back pain. Acetaminophen may be a reasonable alternative in patients with a contraindication to NSAIDs, although evidence of its efficacy is limited.

A systematic review of randomized trials found that, compared with placebo, nonsteroidal medications are slightly more effective for pain relief and function in patients with chronic low back pain [78]. Systematic reviews of patients with osteoarthritis (not limited to the back) consistently found acetaminophen slightly inferior to NSAIDs for pain relief [79-82]. A 2016 Cochrane review concluded that there was high-quality evidence that acetaminophen showed no benefit compared with placebo in acute low back pain; there were no trials evaluating the effectiveness of oral acetaminophen versus placebo for subacute or chronic low back pain [83].

NSAIDs are associated with well-known gastrointestinal and renal side effects. Additionally, exposure to cyclooxygenase (COX)-2 selective inhibitors is associated with an increased risk of myocardial infarction [84]. Cardiovascular and gastrointestinal risk factors should be assessed before prescribing NSAIDs, and the lowest effective dose should be prescribed for the shortest period necessary. (See "Nonselective NSAIDs: Overview of adverse effects".)

Acetaminophen overdose can lead to severe hepatotoxicity and is the most common cause of acute liver failure in the United States [85]. Other possible adverse effects that have been associated with acetaminophen include chronic kidney disease, hypertension, and peptic ulcer disease. (See "Acetaminophen (paracetamol) poisoning in adults: Pathophysiology, presentation, and diagnosis" and "Epidemiology and pathogenesis of analgesic-related chronic kidney disease", section on 'Acetaminophen' and "Unusual causes of peptic ulcer disease", section on 'Acetaminophen' and "NSAIDs and acetaminophen: Effects on blood pressure and hypertension", section on 'Effects of acetaminophen on blood pressure'.)

Second-line therapy

Subacute low back pain — For patients who have subacute low back pain that does not respond to initial pharmacotherapy, we suggest the addition of a short course of nonbenzodiazepine muscle relaxant. In patients who cannot tolerate or have contraindications to muscle relaxants, combining NSAIDs and acetaminophen is an option, although there are few data to support the use of this combination.

A systematic review found insufficient evidence to determine whether skeletal muscle relaxants are effective for subacute or chronic low back pain [86]. In the only trial evaluating efficacy of a skeletal muscle relaxant available in the United States, there was no difference in short-term reduction of muscle spasm between cyclobenzaprine and placebo [87]. Pain relief and improvement in function were not reported in this trial. Two other trials evaluated flupirtine and tolperisone, which are not available in the United States. Both medications were more effective than placebo. The systematic review also found skeletal muscle relaxants associated with more central nervous system adverse events (primarily sedation) than placebo (relative risk [RR] 2.04, 95% CI 1.23-3.37) [86]. The skeletal muscle relaxant carisoprodol is classified as a controlled substance by the US Drug Enforcement Agency (DEA) because it is metabolized to meprobamate, a substance with abuse and addiction potential.

Chronic low back pain — We suggest tramadol or duloxetine as second-line therapy for patients with chronic low back pain that does not respond to NSAID therapy [17].

Tramadol is a dual mechanism drug that has weak affinity for the opioid receptor and is also a norepinephrine reuptake inhibitor. Tramadol may have a lower risk of constipation and dependence

than conventional opioids but carries a risk of serotonin syndrome, especially when combined with other serotonergic agents [88,89].

Three randomized trials found duloxetine more effective than placebo for low back pain [90-92]. However, all trials were sponsored by the drug manufacturer, differences were small (<1 point on 0 to 10 pain or function scales), and patients were more likely to discontinue duloxetine compared with placebo due to adverse effects. Duloxetine was approved by the US Food and Drug Administration (FDA) in 2012 for treatment of low back pain.

Short-term use of skeletal muscle relaxants may be considered as adjunctive therapy in patients with acute exacerbations of chronic low back pain [86], but there are insufficient data to recommend their use for chronic stable low back pain. The lack of clear benefit, the well-known side effects affecting the central nervous system, and the potential for dependence with some skeletal muscle relaxants suggest that this class of medication should not be recommended for prolonged use.

Use of opioids — Opioids may be appropriate for short-term use in selected patients with severe acute exacerbations of low back pain but should not be used routinely and should be used with caution for long-term treatment of patients with chronic back pain [93]. Opioid use should be monitored closely and restricted to patients not highly vulnerable to drug dependence, abuse, or addiction. (See "Overview of the treatment of chronic non-cancer pain".)

Systematic reviews and meta-analyses of opioid use specifically for chronic back pain identified few high-quality or long-term trials [94-96]. Compared with placebo, opioids had short-term efficacy for the relief of pain and improvement of function, but the degree of improvement in pain and function was modest and of questionable clinical significance. Very few trials compared opioids with NSAIDs or antidepressants; in those trials, no difference was seen in pain or function.

The first long-term (one year) randomized trial of an opioid versus nonopioid medication strategy for chronic low back pain and osteoarthritis included 240 patients from Veterans Affairs primary care clinics with moderate to severe chronic back pain or hip or knee osteoarthritis [97]. Improvement in pain-related function was no different in opioid-treated patients compared with nonopioid-treated patients, while pain intensity was slightly better in nonopioid-treated patients. Patients treated with opioids experienced more side effects.

Studies of the use of opioids for chronic and subacute low back pain rarely quantify the risk of important adverse events, such as abuse or addiction, and typically excluded patients at higher risk for these types of adverse events. One systematic review found aberrant drug-taking behaviors in up to 24 percent of patients receiving opioids for low back pain, but most studies had important methodologic shortcomings, including poorly described or validated methods for identifying aberrant drug-related behaviors [94]. The use of opioids for patients with low back symptoms increased in the United States between 2000 and 2010 [77].

Other drugs

Antidepressants — Duloxetine, a serotonin-norepinephrine reuptake inhibitor, is a reasonable adjunctive option for patients with chronic back pain who do not respond to initial pharmacotherapeutic interventions (see 'Chronic low back pain' above). Otherwise, the role of antidepressants for the treatment of back pain is limited. Although tricyclic antidepressants have been used to treat various other chronic pain syndromes (see "Overview of the treatment of chronic non-cancer pain"), their small and inconsistent benefits in studies of back pain do not outweigh their known side effects (most commonly drowsiness, dry mouth, and dizziness).

Meta-analyses evaluating the effect of antidepressant therapy versus placebo for short-term therapy (eight weeks or less) in patients with nonspecific back pain have led to conflicting results [98-100]. Longer-term trials of antidepressants for chronic low back pain are not available. Use of antidepressants was slightly more effective than placebo for low back pain in two meta-analyses [98,99], with an estimated standard mean difference [MD] of 0.41 (95% CI 0.22-0.61) for pain relief but no difference for activities of daily living [98]. Use of tricyclic antidepressants, but not selective serotonin reuptake inhibitors (SSRIs) or trazodone, was associated with improvement. Another meta-analysis (which differed from the earlier studies in the selection criteria used, trials included, and methods for analyzing results) found no difference between antidepressant (primarily tricyclic antidepressants) and placebo treatment for relief of pain or depression and no difference between types of antidepressants [100].

It is important to be aware that depression is common in patients with chronic low back pain, and clinicians should assess for and treat depression appropriately [101]. (See "Evaluation of chronic pain in adults", section on 'Psychiatric comorbidity' and "Unipolar major depression in adults: Choosing initial treatment".)

Benzodiazepines — Benzodiazepines are often used as skeletal muscle relaxants, although not approved by the FDA for this indication. Data on effectiveness of benzodiazepines for subacute or chronic low back pain are limited. A systematic review identified three trials of benzodiazepines, but two evaluated a benzodiazepine not available in the United States (tetrazepam) [86]. Both trials found tetrazepam more effective than placebo for short-term pain intensity (pooled RR 0.82, 95% CI 0.72-0.94 after five to seven days and RR 0.71, 0.54-0.93) and overall improvement (pooled RR 0.63, 0.42-0.97). The only trial evaluating a benzodiazepine available in the United States found no difference between diazepam and placebo for muscle spasm [87]. Because of limited evidence on efficacy and potential for addiction and abuse, benzodiazepines should not be used for long-term treatment of chronic low back pain, although a short course may be indicated for acute exacerbations of chronic low back pain in patients less vulnerable to abuse and addiction. The combination of benzodiazepines and opioids should be avoided whenever possible, as this combination is associated with a marked increase in risk of overdose compared with an opioid alone [102,103].

Antiepileptic medications — Despite the common use of antiepileptic medications for symptomatic treatment of patients with subacute or chronic low back pain, evidence supporting their use is limited.

Agents that have been investigated include gabapentinoids and topiramate:

- Gabapentinoids – In a 2017 meta-analysis of eight randomized control trials evaluating gabapentinoids (gabapentin or pregabalin) for the treatment of chronic low back pain, gabapentin showed nonsignificant minimal improvement of pain compared with placebo (three studies; n = 185; MD -0.22 on a 0 to 10 scale, 95% CI -0.07 to 0.5; very low-quality evidence) [104]. Pregabalin was slightly less effective than other analgesics (amitriptyline, celecoxib, or tramadol/acetaminophen) (three studies; n = 332; MD 0.42 on a 0 to 10 scale, 95% CI 0.20 to 0.64; very low-quality evidence), and its use as adjuvant therapy (added to other medications) in other studies did not show benefit. Gabapentin was associated with an increased risk of side effects, including dizziness, fatigue, difficulties with mentation, and visual disturbances, compared with placebo.

  For chronic radiculopathy, two trials of gabapentin [105,106] and one trial of pregabalin [107] showed only small or unclear effects on pain, which may be offset by their side effects. For

spinal stenosis, one small (n = 55) randomized trial added gabapentin, titrated to 2400 mg/day, to a regimen of supervised exercise therapy, lumbar supports, and NSAIDs in patients with pseudoclaudication and spinal stenosis on computed tomography (CT) or magnetic resonance imaging (MRI) [108]. Patients who took gabapentin had moderately improved mean pain scores at four months (2.9 versus 4.7 on a 0 to 10 scale). Another small (n = 26) randomized trial of patients with neurogenic claudication compared pregabalin titrated to 150 mg twice daily with an active placebo (diphenhydramine). There were no differences in function, pain with ambulation, walking distance, or the Swiss Spinal Stenosis Questionnaire after 10 days [109].

- Topiramate – One trial found topiramate moderately superior to placebo for pain relief and slightly superior for functional improvement in patients with nonradicular chronic low back pain [110]. In another trial, topiramate modestly improved pain in patients with chronic radiculopathy; however, it caused frequent side effects, and many patients dropped out of the trial [111].

Glucosamine — Glucosamine has been extensively studied and is widely used to treat osteoarthritis, particularly of the knee and hip. However, there are little data to support its use for low back pain. In a six-month randomized trial of 250 patients with chronic low back pain and degenerative lumbar osteoarthritis, there were no differences in pain or quality-of-life scores between the glucosamine sulfate (1500 mg daily) and placebo arms [112]. The use of glucosamine for the treatment of knee osteoarthritis is discussed elsewhere. (See "Management of knee osteoarthritis", section on 'Glucosamine and chondroitin'.)

Herbal therapies — The role of herbal medications in the management of low back pain is uncertain. A 2014 systematic review evaluated randomized trials of herbal therapies in patients with acute, subacute, and chronic low back pain. The review found that compared with placebo, the evidence for effectiveness was the best for topical *Capsicum frutescens* (cayenne), with some evidence for oral *Harpagophytum procumbens* (Devil's claw), oral *Salix alba* (white willow bark), topical *Symphytum officinale* (comfrey root extract), and topical lavender essential oil [113]. However, there were methodologic limitations to the trials, outcomes assessed were short-term, and it is not clear how these treatments compare with over-the-counter medications such as NSAIDs or acetaminophen. Additionally, herbal medications may interact with other medications and may contain impurities, and some have significant adverse effects. Patients should be asked

about what nonprescription and herbal medications they are taking for their pain, and this information should be recorded in the medical record. Use and effects of herbal medicines are discussed in more detail separately. (See "Overview of herbal medicine and dietary supplements".)

Anti-TNF-alpha therapy — Systemic anti-tumor necrosis factor (TNF)-alpha therapy, which is primarily used in the treatment of inflammatory rheumatologic and bowel disease, does not appear to have a role for patients with chronic low back pain. This was suggested in the FIRST II trial (n = 40), which found no differences in pain or functional outcomes between a single intravenous infusion of infliximab or saline infusion at three-month and one-year follow-up [114,115]. Epidural and intradiscal injections of anti-TNF-alpha therapy have also been evaluated. (See "Subacute and chronic low back pain: Nonsurgical interventional treatment", section on 'Intradiscal injection'.)

OPTIMIZING THERAPY

There are no trials evaluating optimal sequencing of therapies, and there is no evidence that care directed by one spine provider specialty is superior to other specialties or primary care providers. Decision tools and other methods for individualizing therapy are in early stages of development and may not be practical for use in primary care settings [116].

Patient expectations of benefit from a treatment should be taken into consideration when choosing interventions, as they appear to influence outcomes. Other factors to consider when choosing among therapies include cost, convenience, and availability of skilled providers for specific therapies. Clinicians should avoid interventions not proven effective, as a number of nonpharmacologic therapies are supported by at least fair evidence of moderate benefits.

PREVENTION

There are insufficient data to recommend the use of specific interventions for primary prevention of low back pain [117]. Primary prevention is a challenge due to the limited inability to predict a person's likelihood of developing low back pain. However, exercise therapy may have a role in secondary prevention, particularly for those predisposed to having recurrent low back pain. (See "Exercise-based therapy for low back pain", section on 'Exercise for prevention of low back pain'.)

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Lower spine disorders".)

INFORMATION FOR PATIENTS

UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

- Basics topic (see "Patient education: Low back pain in adults (The Basics)")
- Beyond the Basics topic (see "Patient education: Low back pain in adults (Beyond the Basics)")

SUMMARY AND RECOMMENDATIONS

- Most patients who are seen in primary care have "nonspecific low back pain." Rapid improvement in pain and disability and return to work are the norm in the first month. Subacute low back pain is commonly defined as back pain lasting between 4 and 12 weeks and chronic low back pain as pain that persists for 12 or more weeks. (See 'Introduction' above.)
- We advise all patients on self-care and ideally provide evidence-based information to

supplement verbal advice. We suggest that patients remain active and limit bedrest (**Grade 2B**). We suggest not advising patients to switch to a very firm mattress or other surface (**Grade 2B**), and we suggest not advising routine use of lumbar supports (**Grade 2C**). (See 'Self-care advice' above and 'Bed mattress choice' above and 'Lumbar supports' above.)

- We generally emphasize nonpharmacologic therapy (see 'Overview' above):
  - For patients with chronic low back pain, we suggest "active" interventions that are movement-based and/or address psychosocial contributors to pain rather than passive interventions (**Grade 2C**). We suggest home or supervised exercise therapy (including an individualized regimen for motivated patients) (**Grade 2B**). A trial of cognitive behavioral therapy, mind-body interventions, and relaxation techniques can be used in addition to or as equally effective alternatives to exercise therapy. For patients who do not respond to such active interventions, we suggest a trial of spinal manipulation or acupuncture (**Grade 2B**). The choice among these interventions also depends upon patient preference and their cost and accessibility; there are no data demonstrating superiority of one over another. (See 'Activity and physical treatments' above and 'Psychologic interventions' above and 'Physical modalities' above.)
  - For patients who are more severely impaired by their back pain, we suggest functional restoration or multidisciplinary rehabilitation (**Grade 2B**). (See 'Multidisciplinary (interdisciplinary) rehabilitation' above and 'Functional restoration' above.)
  - For patients with subacute low back pain, short-term interventions such as superficial heat, massage, exercise therapy, spinal manipulation, or acupuncture may be adequate because of the high likelihood of spontaneous remission (see "Treatment of acute low back pain", section on 'Nonpharmacologic therapies'). Should their pain persist beyond 12 weeks, we manage them as patients with chronic low back pain.
- We suggest **not** using the following modalities for low back pain: interferential therapy, low-level laser therapy, shortwave diathermy, traction, transcutaneous electrical nerve stimulation (TENS), ultrasound, or percutaneous electrical nerve stimulation (PENS) (**Grade 2B**). (See 'Physical modalities' above.)
- For patients with subacute or chronic low back pain in whom nonpharmacologic approaches

are insufficient to control pain, we suggest a nonsteroidal antiinflammatory drug (NSAID) rather than acetaminophen (**Grade 2B**). For patients with subacute low back pain who have had an inadequate response to NSAIDs, we suggest the addition of a nonbenzodiazepine skeletal muscle relaxant (**Grade 2C**). For patients with chronic low back pain who have had an inadequate response to NSAIDs, we suggest tramadol or duloxetine as an alternative treatment (**Grade 2B**). (See 'Pharmacologic therapies' above.)

- We suggest prescribing opioids for chronic low back pain only for short-term use in patients with low risk for drug abuse who are experiencing severe acute exacerbations of back pain (**Grade 2C**). Rarely, opioids may also be appropriate for severely disabled patients with chronic low back pain who do not respond to other measures and who are assessed to have a low risk for drug abuse. (See 'Use of opioids' above.)

- We suggest **not** using benzodiazepines or other skeletal muscle relaxants for chronic low back pain (**Grade 2C**). We suggest **not** treating patients for chronic low back pain with antiepileptic medications (**Grade 2C**). (See 'Other drugs' above.)

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GRAPHICS

Glossary of low back pain terms

Acupuncture	An intervention consisting of the insertion of needles at specific acupuncture points.
Artificial disc replacement	Replacement of a degenerated vertebral disc with an artificial (prosthetic) disc.
Back school	An intervention consisting of an education and a skills program, including exercise therapy, in which all lessons are given to groups of patients and supervised by a paramedical therapist or medical specialist.
Biofeedback	The use of auditory and visual signals reflecting muscle tension or activity in order to inhibit or reduce the muscle activity.
Brief educational interventions	Individualized assessment and education about low back pain problems without supervised exercise therapy or other specific interventions.
Chemonucleolysis	Treatment of herniated discs with intradiscal injections of an enzyme extracted from papaya (chymopapain). Chymopapain acts by digesting the jelly-like inner portion of the disc known as the nucleus pulposus, while at the same time, leaving the outer portion, the annulus fibrosis, essentially intact. Collagenase (which may be less likely to induce an allergic reaction) has also been used.
Cognitive behavioral therapy	An intervention that involves working with cognitions to change emotions, thoughts, and behaviors.
Discectomy	Removal of all or parts of an intervertebral disc in order to relieve pressure on adjacent nerve roots.
Epidural steroid injection	An intervention that involves the administration of steroids in the space between the dura and the spine via a catheter. Epidural injections can be performed by the translaminar approach (via the interlaminar space in the spine), the transforaminal approach (through the neuroforamen ventral to the nerve root), or the caudal approach (through the sacral hiatus at the sacral canal).
Exercise therapy	A supervised exercise program or formal home exercise regimen, ranging from programs aimed at general physical fitness or aerobic exercise to programs aimed at muscle strengthening, flexibility, stretching, or different combinations of these elements.
Facet joint injection	Injection of a glucocorticoid into the facet joints in order to reduce inflammation and/or swelling.
Functional restoration (also referred to as work hardening or work conditioning)	An intervention that involves simulated or actual work tests in a supervised environment in order to enhance job performance skills and improve strength, endurance, flexibility, and cardiovascular fitness in injured workers.
Fusion surgery	A surgical procedure that unites (fuses) two or more vertebra together. The goal behind fusion surgery is to restrict spinal motion in order to relieve symptoms. A variety of spinal fusion techniques are practiced. All involve the placement of a bone graft between the vertebrae. In addition, fusion can be performed with or without the use of supplemental hardware (instrumentation), such as plates, screws, or cages that serve as an internal splint while the bone graft heals.
Interdisciplinary	An intervention that combines and coordinates physical, vocational, and behavioral

therapy (also referred to as multidisciplinary therapy)	components and is provided by multiple healthcare professionals with different clinical backgrounds. The intensity and content of interdisciplinary therapy varies widely.
Interferential therapy	The superficial application of a medium frequency alternating current modulated to produce low frequencies up to 150 Hz.
Intradiscal glucocorticoid injection	Injection of a glucocorticoid directly into a lumbar disc in order to reduce swelling and inflammation.
Intradiscal electrothermal therapy (IDET)	An intervention involving the placement of an electrode into the intervertebral disc in patients with presumed discogenic back pain. The catheter is slowly heated and kept at a predetermined temperature for a predetermined time in order to coagulate and shrink adjacent tissues.
Laminectomy	Removal of the vertebral lamina in order to relieve pressure on the spinal cord or nerve roots.
Local injections	Injections into the soft tissues surrounding the back with a local anesthetic, sometimes with a glucocorticoid. A variety of target sites have been proposed, including tender points and various anatomic sites.
Low-level laser therapy (LLLT)	The superficial application of lasers at wavelengths between 632 and 904 nm. Optimal treatment parameters (wavelength, dose, dose-intensity) are uncertain.
Massage	Soft tissue manipulation using the hands or a mechanical device through a variety of specific methods.
Medial branch block	Injection of a local anesthetic (with or without a glucocorticoid) into the area of the nerve innervating the facet joint. Medial branch blocks may be used diagnostically (to determine whether the facet joint is the source of back pain) or therapeutically.
Percutaneous electrical nerve stimulation (PENS)	An intervention involving the insertion of acupuncture-like needles and applying low-level electrical stimulation. It differs from electroacupuncture in that the insertion points target dermatomal levels for local pathology, rather than acupuncture points.
Percutaneous intradiscal radiofrequency thermocoagulation (PIRFT)	An intervention similar to IDET, this intervention involves insertion of an electrode or catheter into the intervertebral disc. Unlike IDET, the electrode or catheter itself does not become hot. Instead, heat is generated in surrounding tissues by an alternating radiofrequency current.
Progressive relaxation	A technique that involves the deliberate tensing and relaxation of muscles, in order to facilitate the recognition and release of muscle tension.
Provocative discography	A procedure involving injection of radiographic contrast material into the nucleus of an intervertebral disc, which may elicit pain. It is most commonly performed in patients with chronic low back pain in order to help identify those who are more likely to benefit from interventional procedures intended to treat "discogenic" back pain.
Radiofrequency denervation	Destruction of nerves using heat generated by a radiofrequency current. It involves the placement of a catheter or electrode near or in the target nerve. Once the position of the catheter is confirmed by fluoroscopy, a radiofrequency current is applied in order to heat and coagulate adjacent tissues, including the target nerve.
Sacroiliac joint injection	Injection of glucocorticoid into the area near the sacroiliac joint, in order to reduce inflammation and/or swelling.

Shortwave diathermy	Therapeutic elevation of the temperature of deep tissues by application of shortwave electromagnetic radiation with a frequency range from 10 to 100 MHz.
Spinal manipulation	Manual therapy in which loads are applied to the spine using short- or long-lever methods. High velocity thrusts are applied to a spinal joint beyond its restricted range of movement. Spinal mobilization, or low velocity, passive movements within or at the limit of joint range, is often used in conjunction with spinal manipulation.
Transcutaneous electrical nerve stimulation (TENS)	Use of a small battery-operated device to provide continuous electrical impulses via surface electrodes, with the goal of providing symptomatic relief by modifying pain perception.
Yoga	An intervention distinguished from traditional exercise therapy by the utilization of specific body positions, breathing techniques, and emphasis on mental focus. Many styles of yoga are practiced, each emphasizing different postures and techniques.

Graphic 79662 Version 2.0

Definitions for estimating magnitude of effects

Size of effect	Definition
Small/slight	**Pain scales:** Mean 5 to 10 mm improvement on a 100 mm visual analogue scale (VAS), or equivalent
	Back-specific functional status: Mean 5 to 10 mm improvement on the Oswestry Disability Index (ODI), 1 to 2 points on the Roland-Morris Disability Questionnaire (RDQ), or equivalent
	All outcomes: Standardized mean difference (SMD) 0.2 to 0.5
Moderate	**Pain scales:** Mean 10 to 20 mm improvement on a 100 mm VAS, or equivalent
	Back-specific functional status: Mean 10 to 20 mm improvement on the ODI, 2 to 5 points on the RDQ, or equivalent
	All outcomes: SMD 0.5 to 0.8
Large/substantial	**Pain scales:** Mean >20 mm improvement on a 100 mm VAS, or equivalent
	Back-specific functional status: Mean >20 mm improvement on the ODI, >5 points on the RDQ, or equivalent
	All outcomes: SMD >0.8

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Medications for subacute or chronic low back pain

Drug	Net benefit*	Graded recommendation¶	Comments
Acetaminophen	Small to none	Suggested as alternative therapy in patients who cannot tolerate NSAIDs, although evidence of efficacy is lacking **(2C)**	Asymptomatic increased liver function tests at therapeutic doses
Antiepileptic drugs	Unable to estimate	Suggest not using **(2C)**	Gabapentin, pregabalin, and topiramate evaluated in short-term trials, primarily in patients with radiculopathy
Benzodiazepines	Unable to estimate	Suggest not using **(2C)**	
Duloxetine	Small	Suggested as alternative regimen for patients with chronic low back pain who do not respond to NSAIDs **(2B)**	
Nonbenzodiazepine skeletal muscle relaxants	Unable to estimate	Suggested as adjunctive therapy for patients with subacute low back pain who to not respond to NSAIDs **(2C)**	Cyclobenzaprine is most the commonly prescribed drug
NSAIDs	Moderate	Suggested as first-line therapy **(2B)**	May cause serious gastrointestinal and cardiovascular adverse events Insufficient evidence to judge benefits and harms of aspirin or celecoxib for low back pain
Opioids	Unable to estimate	Suggest not using as first-line therapy **(2C)**	No reliable data on risks of abuse or addiction
Tramadol	Small to moderate	Suggested as alternative therapy for patients with chronic low back pain who do not respond to NSAIDs **(2B)**	
Tricyclic antidepressants	Unable to estimate	Suggest not using **(2C)**	

NSAIDs: nonsteroidal antiinflammatory drugs.

* Based on evidence showing medication is more effective than placebo, and/or evidence showing medication is at least as effective as other medications or interventions thought to be effective, for one or more of the following outcomes: pain, functional status, or work status. Versus placebo, small benefit defined as 5 to 10 points on a 100-point Visual Analogue Scale (VAS) for pain (or equivalent), 1 to 2 points on the Roland Morris Disability Questionnaire (RDQ), 10 to 20 points on the Oswestry Disability Index (ODI), or a standardized mean difference (SMD) of 0.2 to 0.5. Moderate benefit defined as 10 to 20 points on a VAS for pain, 2 to 5 points on the RDQ, 10 to 20 points on the ODI, or a SMD of 0.5 to 0.8. Large benefit defined as >20 points on a 100-point VAS for pain; >5 points on the RDQ, >20 points on the

ODI, or a SMD of >0.8.

¶ Grading:

1A - Strong recommendation. High-quality evidence. Strong recommendation, can apply to most patients in most circumstances without reservation.

1B - Strong recommendation. Moderate-quality evidence. Strong recommendation, likely to apply to most patients.

1C - Strong recommendation. Low-quality evidence. Relatively strong recommendation; might change when higher quality evidence becomes available.

2A - Weak recommendation. High-quality evidence. Weak recommendation, best action may differ depending on circumstances or patients or societal values.

2B - Weak recommendation. Moderate-quality evidence. Weak recommendation, alternative approaches likely to be better for some patients under some circumstances.

2C - Weak recommendation. Low-quality evidence. Very weak recommendation; other alternatives may be equally reasonable.

§ Due to safety profile.

Graphic 72902 Version 7.0

Nonpharmacologic therapies for subacute or chronic low back pain

Intervention	Net benefit*	Graded recommendation ¶	Comments
Acupuncture	Moderate	Suggested **(2B)**	Efficacy of acupuncture versus sham acupuncture inconsistent
Cognitive behavioral therapy	Moderate	Suggested **(2B)**	
Exercise therapy	Moderate	Suggested **(2B)**	
Functional restoration	Moderate	Suggested **(2B)**	
Interdisciplinary rehabilitation	Moderate	Suggested **(2B)**	More intense interdisciplinary rehabilitation more effective than less intense interdisciplinary rehabilitation
Interferential therapy	Unable to estimate	Suggest not using **(2B)**	
Low-level laser therapy	Unable to estimate	Suggest not using **(2B)**	Trials evaluated different types and intensity of laser, with inconsistent findings
Lumbar supports	Unable to estimate	Suggest not using **(2C)**	
Massage therapy	Unable to estimate	Suggested not using **(2B)**	Some trials evaluated minimal or light massage techniques
Mindfulness-based stress reduction	Moderate	Suggested **(2B)**	
Percutaneous electrical nerve stimulation	Unable to estimate	Suggest not using **(2B)**	
Shortwave diathermy	Not effective	Suggest not using **(2B)**	
Spinal manipulation	Moderate	Suggested **(2B)**	
Traction	Not effective (for continuous traction)	Suggest not using **(2B)**	
Transcutaneous electrical nerve stimulation	Unable to estimate	Suggest not using **(2B)**	
Ultrasound	Unable to estimate	Suggest not using **(2B)**	
Yoga	Moderate (for Viniyoga)	Suggested **(2B)**	Insufficient evidence to judge non-Viniyoga techniques

* Based on evidence showing medication is more effective than placebo, and/or evidence showing medication is at least as effective as other medications or interventions thought to be effective, for one or more of the following outcomes: pain, functional status, or work status. Versus placebo, small benefit defined as 5 to 10 points on a 100-point Visual

Analogue Scale (VAS) for pain (or equivalent), 1 to 2 points on the Roland Morris Disability Questionnaire (RDQ), 10 to 20 points on the Oswestry Disability Index (ODI), or a standardized mean difference (SMD) of 0.2 to 0.5. Moderate benefit defined as 10 to 20 points on a VAS for pain, 2 to 5 points on the RDQ, 10 to 20 points on the ODI, or a SMD of 0.5 to 0.8. Large benefit defined as >20 points on a 100-point VAS for pain; >5 points on the RDQ, >20 points on the ODI, or a SMD of >0.8.

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Interventional therapies for low back pain

Intervention	Population	Net benefit*	Graded recommendation ¶	Comments
Epidural steroid injection	Sciatica or prolapsed lumbar disc with radiculopathy	Moderate (short-term only)	Suggested **(2B)**	Some higher-quality trials found no benefits.
Intradiscal corticosteroid injection	Sciatica or prolapsed lumbar disc with radiculopathy	No effect (versus chemonucleolysis)	Suggest not using **(2C)**	
Local injections	Sciatica or prolapsed lumbar disc with radiculopathy	Unable to determine	Suggest not using **(2C)**	
Radiofrequency denervation	Sciatica or prolapsed lumbar disc with radiculopathy	Unable to determine	Suggest not using **(2C)**	
Facet joint (intraarticular) injection	Presumed facet joint pain	No effect	Suggest not using **(2C)**	
Medial branch block (therapeutic)	Presumed facet joint pain	Unable to determine	Suggest not using **(2C)**	
Radiofrequency denervation	Presumed facet joint pain	Unable to determine	Suggest not using **(2C)**	
Intradiscal corticosteroid injection	Presumed discogenic low back pain	No effect	Suggest not using **(2C)**	
Intradiscal electrothermal therapy	Presumed discogenic low back pain	Unable to determine	Suggest not using **(2B)**	
Intradiscal anti-TNF injections	Presumed discogenic low back pain	No effect	Suggest not using **(2C)**	
Intradiscal methylene blue injection	Presumed discogenic low back pain	Unable to determine	Suggest not using **(2C)**	
Percutaneous intradiscal radiofrequency thermocoagulation	Presumed discogenic low back pain	No effect	Suggest not using **(2B)**	
Radiofrequency denervation	Presumed discogenic low back	Unable to determine	Suggest not using **(2C)**	

	pain			
Epidural steroid injection	Spinal stenosis	No effect	Suggest not using **(2C)**	
Epidural steroid injection	Nonspecific low back pain	Unable to determine	Suggest not using **(2C)**	
Botulinum toxin injection	Nonspecific low back pain	Moderate (short-term only)	Suggest not using **(2C)**	
Local injections	Nonspecific low back pain	Unable to determine	Suggest not using **(2C)**	Interventions varied substantially between trials. No higher-quality trials, all trials had small sample sizes.
Prolotherapy	Nonspecific low back pain	No effect	Suggest not using **(2B)**	

TNF: tumor necrosis factor.

* Based on evidence showing medication is more effective than placebo, and/or evidence showing medication is at least as effective as other medications or interventions thought to be effective, for one or more of the following outcomes: pain, functional status, or work status. Versus placebo, small benefit defined as 5 to 10 points on a 100-point Visual Analogue Scale (VAS) for pain (or equivalent), 1 to 2 points on the Roland Morris Disability Questionnaire (RDQ), 10 to 20 points on the Oswestry Disability Index (ODI), or a standardized mean difference (SMD) of 0.2 to 0.5. Moderate benefit defined as 10 to 20 points on a VAS for pain, 2 to 5 points on the RDQ, 10 to 20 points on the ODI, or a SMD of 0.5 to 0.8. Large benefit defined as >20 points on a 100-point VAS for pain; >5 points on the RDQ, >20 points on the ODI, or a SMD of >0.8.

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Graphic 77165 Version 7.0

Surgery for chronic low back pain (excluding spinal stenosis)

Intervention	Population	Net benefit*	Graded recommendation ¶	Comments
Interbody fusion	Nonspecific low back pain or degenerative disc disease with presumed discogenic low back pain	Moderate versus standard physical therapy supplemented by other nonsurgical therapies, no benefit versus intensive rehabilitation	Suggested (for highly selected patient population) **(2B)**	Inconsistency between trials may be related to use of different comparator interventions.
Artificial disc replacement	Nonspecific low back pain or degenerative disc disease with presumed discogenic low back pain	No evidence	Suggest not performing **(2C)**	One trial found Charite artificial disc noninferior to fusion and one trial found Prodisc-L artificial disc superior to fusion.
Standard open discectomy or microdiscectomy	Lumbar disc prolapse with radiculopathy	Moderate	Suggested **(2B)**	In largest trial, 40 to 55% crossover in both arms; on-treatment analysis consistent with other trials. Benefits associated with surgery attenuated with longer-term follow-up.

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Graphic 63348 Version 2.0

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Conflict of interest policy

Overview of soft tissue rheumatic disorders

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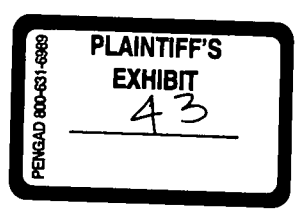
INTRODUCTION

Soft tissue rheumatic disorders refer to nonsystemic, focal pathologic syndromes involving the periarticular tissues, including muscle, tendon, ligament, fascia, aponeurosis, retinaculum, bursa, and subcutaneous tissue. These disorders are extremely common. The archaic term "rheumatism" is sometimes used to refer to these manifestations.

Although soft tissue rheumatic disorders refer to nonarticular pain, patients often attribute their symptoms to nearby joints. Thus, when patients complain of hip pain, the cause is often not pain in the joint itself, but rather in the "hip region": the groin, buttock, upper lateral thigh, greater trochanteric area, and iliac crest. Similarly, complaints of elbow, wrist, knee, and shoulder pain frequently mean pain in the general region of those joints, and may reflect soft tissue conditions such as epicondylitis, tenosynovitis, and bursitis.

Soft tissue disorders may be divided into several broad categories and include:

- Tendinitis
- Enthesitis
- Fasciitis
- Bursitis



- Structural disorders
- Neurovascular entrapment disorders
- Complex regional pain syndromes (CRPS)
- Myofascial pain syndrome
- Generalized pain disorders

Many of these disorders occur in the absence of systemic disease, and some are a consequence of chronic repetitive low-grade trauma and overuse. Many are self-limiting and respond to conservative measures.

This topic will provide a brief overview of the soft tissue rheumatic disorders. A general discussion on the approach to the patient with these disorders is also included. More detailed discussions of these disorders are presented separately. (See appropriate topic reviews.)

SPECIFIC SYNDROMES

Tendinitis — Tendinitis (or tendonitis) is a clinical and pathologic disorder with common features of local pain and dysfunction, inflammation, and degeneration. Tendinitis often results from overuse or a sports injury but may also be due to inflammatory rheumatic diseases or metabolic disturbances such as calcium apatite deposition. Tendinitis and tendon rupture have also been associated with the use of fluoroquinolone antibiotics and statins [1-3].

Tendinitis, tendinosis, and tendinopathy are some of the terms used to characterize acute or chronic tendon pain. The term tendinitis can be confusing because inflammation is often not seen on histopathology, and the other terms may be more appropriate. For the purposes of this discussion, we will use the common term tendinitis. A more detailed discussion on terminology is included elsewhere. (See "Overview of overuse (persistent) tendinopathy", section on 'Pathology and terminology'.)

Common sites of tendinitis include supraspinatus tendinitis of the shoulder (rotator cuff tendinopathy), lateral and medial epicondylitis (tennis and golfer's elbow), bicipital tendinitis, Achilles tendinopathy, and flexor carpi radialis and flexor carpi ulnaris tendinitis. (See "Rotator cuff tendinopathy" and "Epicondylitis (tennis and golf elbow)" and "Biceps tendinopathy and tendon rupture" and "Achilles tendinopathy and tendon rupture".)

Enthesitis — The enthesis is the site of insertion of ligaments, tendons, joint capsules, and fascia to bone (figure 1). These areas are highly vascular and are susceptible to bacterial and antigen deposition [4]. Enthesitis is often seen in spondyloarthropathies; common sites are the insertion of the plantar fascia and the Achilles tendon region (see "Clinical manifestations and diagnosis of peripheral spondyloarthritis in adults", section on 'Musculoskeletal features'). Ultrasonography is helpful for delineation [5,6]. (See "Musculoskeletal ultrasonography: Clinical applications", section on 'Enthesitis'.)

Fasciitis — Fasciitis includes Dupuytren's palmar contracture, fascia lata fasciitis, and plantar fasciitis. They have discrete and disparate pathologies which include proliferation and degeneration of fascia. These disorders are discussed in more detail separately, as are other forms of fasciitis that have more systemic involvement, including necrotizing fasciitis and eosinophilic fasciitis (see "Dupuytren's contracture" and "Evaluation of the adult with hip pain" and "Plantar fasciitis" and "Necrotizing soft tissue infections" and "Eosinophilic fasciitis"). Magnetic resonance imaging (MRI) is often in useful in identifying these conditions.

Bursitis — Bursitis is inflammation of the small fluid-filled pads, called bursae, that act as cushions between the bones and adjacent tendons and muscles, protecting the soft tissues from underlying bony prominences. Bursitis may result from direct trauma, repetitive injury, or infection, or it may be a manifestation of a systemic disease such as rheumatoid arthritis or gout. A diagnosis of bursitis is based on the findings of exquisite local tenderness at bursal sites, pain on motion and at rest, and sometimes associated regional loss of active movement. Swelling may be evident when bursitis occurs close to the body surface (eg, bunion or prepatellar bursitis) [7]. (See "Bursitis: An overview of clinical manifestations, diagnosis, and management".)

Structural disorders — Musculoskeletal structural disorders are relatively common. In healthy young adults, for example, one study found that a total of 158 separate congenital, developmental, and acquired abnormalities were detected in 73 percent of 127 medical students [8]. Findings included decreased joint range of motion and articular laxity, as well as synovitis, tendinitis, and bursitis. Participants in contact sports had the highest prevalence. (See "Joint hypermobility syndrome", section on 'Epidemiology'.)

Subtle disorders often contribute significantly to pain syndromes in the lower extremity. "Miserable malalignment syndrome" is a term used to describe a combination of malalignments of the leg that

include excess femoral anteversion with internal rotation of the hip, genu valgus, squinting patellae, external tibial torsion, and flat feet. Affected individuals are predisposed to overuse injuries and are often advised to avoid sports such as long-distance running. Structural disorders frequently contribute to injury in sports participants. (See "Overview of running injuries of the lower extremity".)

Body asymmetry is a common cause of many regional pain disorders. When one side of the face is smaller, for example, temporomandibular joint dysfunction is more common (picture 1). The rest of the ipsilateral body may also be small in such patients, sometimes resulting in a scapulothoracic syndrome related to scoliosis or back pain in association with a short leg or an underdeveloped buttock.

Neurovascular entrapment — Neurovascular entrapment disorders may occur within the spinal canal (foraminal or central spinal stenosis) or nerve root, or along the course of a peripheral nerve. The peripheral sites most commonly affected are compression of the median nerve at the wrist (carpal tunnel syndrome), compression of the ulnar nerve at the cubital tunnel, and compression of the tibial nerve at the tarsal tunnel. Less commonly, the lateral femoral cutaneous nerve in entrapped under the inguinal ligament (meralgia paresthetica). (See "Overview of upper extremity peripheral nerve syndromes" and "Carpal tunnel syndrome: Clinical manifestations and diagnosis" and "Overview of lower extremity peripheral nerve syndromes" and "Meralgia paresthetica (lateral femoral cutaneous nerve entrapment)".)

The diagnostic triad of peripheral neurovascular entrapment includes:

- A sensation of swelling and pain in the involved region
- Paresthesias distal to the site of entrapment
- Muscle weakness in advanced cases

Tapping over an involved peripheral nerve (eg, Tinel sign in carpal tunnel syndrome) or compression with an inflated blood pressure cuff proximal to the nerve may produce a sensation of electric shock and therefore aid in the diagnosis.

Complex regional pain syndromes — The complex regional pain syndrome (CRPS) may be related to nerve injury, other trauma, surgery, or a vascular event such as myocardial infarction or stroke, or there may be no obvious triggering event. Alternative names include reflex sympathetic

dystrophy (RSD), algodystrophy, causalgia, and shoulder-hand syndrome. It was renamed by a consensus development conference in 1995 as CRPS [9]. It is usually characterized clinically by exquisite burning pain, edema, allodynia, abnormal sudomotor activity, and hyperesthesia in the limb, which may feel cold or hot and may change color, and by local bone demineralization.

Two types of CRPS have been recognized:

- CRPS type I (formerly termed RSD) – Refers to patients without a definable nerve lesion
- CRPS type II (formerly termed causalgia) – Refers to patients with a definable nerve lesion

The causes, clinical features, diagnosis, prevention, and treatment of CRPS (RSD and causalgia) are presented separately. (See "Complex regional pain syndrome in adults: Pathogenesis, clinical manifestations, and diagnosis" and "Complex regional pain syndrome in adults: Prevention and management".)

Myofascial pain syndrome — Myofascial pain syndrome (MPS) is a regional pain disorder caused by the presence of trigger points within muscles or their fascia (figure 2) [10,11]. It has been described as "hyperirritable spots, usually within a taut band of skeletal muscle or in the muscle's fascia that is painful on compression and can give rise to characteristic referred pain, tenderness, and autonomic phenomena" [12]. MPS shares some similar features with fibromyalgia which are discussed separately (table 1). (See "Differential diagnosis of fibromyalgia", section on 'Myofascial pain syndromes'.)

MPS is a relatively common source of chronic pain in the general population. The lack of universally accepted diagnostic criteria has resulted in variable estimates from epidemiologic studies, and most of the available data pertain to musculoskeletal pain in general. One study that estimated the prevalence of myofascial pain in a general internal medicine practice found that the primary complaint of 30 percent of patients was due to myofascial pain [13].

The pain of MPS is of a deep aching quality, occasionally accompanied by a sensation of burning or stinging. The pain often occurs in just one anatomic region, and patients often complain of restricted active movement in that area.

Myofascial trigger points (MTP) are the characteristic findings on physical exam. One or more trigger (pain) points will be found if the examiner gains familiarity with the likely point locations for

each body region (figure 3A-B). Trigger points often feel indurated to palpation, and palpation reproduces the pain in the "target zone," often at some distance away. Trigger points may result from acute trauma, repeated minor microtrauma of daily living, or the chronic strain of sedentary work or living habits. Thus, evaluation of such patients with myofascial pain should include inquiry into activities and habits of movement. Patients with whiplash-associated myofascial pain have a higher prevalence of trigger points along the semispinalis capitis muscle than at other sites in the neck, jaw, and upper shoulder [14]. (See "Overview of joint protection".)

MPS may include other common regional pain disorders such as tension headaches, idiopathic low back and cervical strain disorders, repetitive strain syndromes, occupational overuse syndrome, cumulative trauma disorder, work-related musculoskeletal disorder, and temporomandibular joint (TMJ) syndrome [15-18]. In the head and neck, the pain may be associated with unexplained dizziness and with neurocognitive disturbances. The etiology of these complaints is not understood, although some neurovestibular abnormalities are often found in patients with TMJ and myofascial pain of the head. These poorly understood pain disorders are also associated with fatigue, sleep abnormalities, and mood disturbances, which may also be observed with fibromyalgia (see "Clinical manifestations and diagnosis of fibromyalgia in adults", section on 'Symptoms'). Chronic, unexplained pelvic and urethral pain, sometimes termed the female urethral syndrome, is often considered to be a variation of myofascial pain.

Many clinicians are skeptical about the existence of trigger points. Confusion also arises when differentiating trigger points from the tender points of fibromyalgia (figure 4). Fibromyalgia tender points are said to differ in that they typically are not indurated and occur in tissues other than muscle (table 1). However, some find little difference in the tender point and trigger point examination in patients with fibromyalgia and MPS. A number of reports have questioned the reliability of the tender point evaluation, and they have been eliminated from revised American College of Rheumatology (ACR) diagnostic criteria for fibromyalgia [19,20]. (See "Clinical manifestations and diagnosis of fibromyalgia in adults".)

Myofascial pain is generally treated similarly to fibromyalgia (see "Initial treatment of fibromyalgia in adults"). However, myofascial pain also responds well to local treatments such as application of a cold spray and passive stretch of the involved muscle. Trigger point injections, using dry needling, saline, or botulinum toxin, have been effective in clinical trials for the treatment of myofascial pain [16,17,21].

Generalized pain disorders — Generalized pain disorders include the hypermobility syndrome, fibromyalgia, and somatoform disorders. These disorders all may cause widespread pain and in some cases disability.

- The hypermobility syndrome results from loss of muscle tone in a person with joint laxity. Widespread arthralgias and a sensation of joint swelling (without objective physical signs of swelling) that lasts for hours rather than days are typical of this disorder. (See "Joint hypermobility syndrome".)

- Fibromyalgia is a clinical syndrome marked by widespread pain, fatigue, and is often associated with a variety of other symptoms. There is often overlap of fibromyalgia with chronic fatigue syndrome (CFS), also known as myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) (table 2). (See "Clinical manifestations and diagnosis of fibromyalgia in adults".)

GENERAL INITIAL APPROACH

Six points of management can often be initiated during the first visit in a patient with a suspected soft tissue rheumatic disorder, even before the results of appropriate laboratory or radiologic tests are available:

- Exclude systemic disease
- Eliminate aggravating factors
- Explain the illness
- Provide self-help strategies
- Provide pain relief
- Explain prognosis

Exclude systemic disease — Systemic rheumatic diseases such as rheumatoid arthritis and other disorders such as diabetes mellitus, thyroid dysfunction, occult neoplasm, and drug reactions should be considered and excluded, if possible, in patients presenting with a suspected soft tissue rheumatic disorder. Such concurrent disorders are common. In a classic study, nearly 300 patients with work-related carpal tunnel syndrome underwent a systematic search for concurrent medical diseases. One hundred and nine separate atraumatic illnesses (principally hypothyroidism,

diabetes mellitus, and various arthropathies) capable of causing arm pain or carpal tunnel syndrome were diagnosed. Nearly 70 percent of these conditions would have been missed if only record reviews and patient histories had been utilized [22].

The extent of the work-up is dependent upon the diagnosis. As an example, a patient with tendinitis or bursitis following a cumulative movement strain is not likely to benefit from radiologic or laboratory studies. By contrast, a patient presenting with enthesitis of the Achilles tendon and inflammatory back pain who is under the age of 40 may require additional studies to evaluate for ankylosing spondylitis. (See "Diagnosis and differential diagnosis of axial spondyloarthritis (ankylosing spondylitis and nonradiographic axial spondyloarthritis) in adults" and "Diagnosis and differential diagnosis of rheumatoid arthritis".)

Treatment can, in many cases, be initiated prior to receiving the test results. Furthermore, plain film radiographs or other imaging studies can often be deferred until a later visit if they are not likely to change initial management.

Eliminate aggravating factors — Events and activities preceding the pain state must be reviewed in order to recognize aggravating activities that can cause recurrences. (See "Overview of joint protection".)

- Improper resting, sitting, or working positions are common precipitating factors.
- Strain resulting from job performance, a new hobby, or repetitive tiring tasks should be recognized and modified.
- Strain resulting from structural disorders (eg, flat feet or heavy pendulous breasts) can also be altered with appropriate instructions.
- Psychosocial factors that might influence outcome including drug dependency, interpersonal relationships, and other stressors should be investigated.

Joint protection advice should be provided. (See appropriate topic reviews for the different joints.)

Explain the illness — Patients may be reassured when they are told that they have a soft tissue rheumatic disorder rather than more serious illnesses such as systemic lupus erythematosus or rheumatoid arthritis. In addition, validation that their problem is "real" (eg, in patients with

myofascial pain syndrome [MPS] or fibromyalgia) often relieves anxiety. (See "Initial treatment of fibromyalgia in adults".)

Explain self-help strategies — At-home physical therapy and exercises should be outlined on the first visit, if appropriate (see appropriate topic reviews for rehabilitation programs for the head and neck, upper limb, and lower limb). A good plan is to have the patient enroll in a program that combines an aerobic, strength training, and stretching program.

Pain relief — Pain may promote muscle spasm, leading to a vicious cycle of increased pain and spasm. In addition, the self-help therapy program is more effective and results are obtained more quickly when adequate pain relief is achieved.

Acute injuries should be treated with the RICE regimen:

- Rest
- Ice
- Compression of injured tissue
- Elevation

Despite the paucity of adequate controlled clinical studies, heat and cold modalities have been used for many years in the treatment of musculoskeletal disorders [23]. Heat can readily be applied by hot packs or hot water bottles and can increase the threshold for pain, produce analgesia by acting on free nerve endings, and decrease muscle spasm. A review of the effects of superficial heat on low back pain showed moderate evidence for heat therapy providing a small short-term reduction in pain and disability [24]. It is not at all clear that heat should be used to treat patients with inflammatory diseases. Heat is not indicated in acute arthritis, since it contributes to increased inflammation and pain, but may be helpful for some patients with moderate joint inflammation, where it may reduce pain and muscle spasm. Ice is sometimes useful to control pain and swelling because it induces vasoconstriction of superficial and intra-articular tissues, reduces local metabolism, and slows nerve conduction. It may be applied using cold packs, ice baths, and vapocoolant sprays [25].

In addition to the RICE regimen, other simple, frequently used measures include use of oral or topical nonsteroidal antiinflammatory drugs (NSAIDs), and other topical applications with agents such as lidocaine or capsaicin (table 3) [26,27].

If simple measures have not sufficed, injecting the affected area with a long-acting glucocorticoid-local anesthetic mixture can be effective in bursitis, tendinitis, carpal tunnel syndrome, or MPS. (See appropriate topic reviews for description of the injection technique in the different disorders.)

The use of diagnostic ultrasound promises to greatly improve our diagnostic accuracy and broaden our understanding of soft tissue rheumatic disorders [28]. Ultrasonography should also afford greater precision in defining sites to be injected with glucocorticoids [29,30].

Acupuncture is another method that is employed to relieve pain. Its clinical value varies and seems to be based on the condition being treated and the specific methodology employed. (See "Acupuncture".)

Since it is not at all clear that botulinum toxin injections are clearly superior to the injection of less costly agents, we do not recommend using botulinum toxin for tender or trigger point injections. Several studies suggest that botulinum toxin type A may provide pain relief in MPS [31-33], while others have found an analgesic effect similar to injection of glucocorticoids [33] or saline [34] and less than or similar to that of lidocaine [35,36]. (See "Overview of the treatment of chronic non-cancer pain".)

Explain prognosis — Most soft tissue rheumatic pain disorders are of short duration and the time until improvement becomes evident can be projected. Relief from carpal tunnel syndrome, bursitis, or tendinitis may require only a few days, while symptoms due to hypermobility syndrome or disorders of other structural deficits may require several months before moderate or great improvement is seen.

The expected clinical course should be explained to the patient at the initial visit if possible. Patients should also understand that this course is dependent upon the performance of the self-help program, and that their response to the program may impact the diagnosis.

SUMMARY AND RECOMMENDATIONS

- Soft tissue rheumatic disorders refer to nonsystemic, focal pathologic syndromes involving the periarticular tissues, including muscle, tendon, ligament, fascia, aponeurosis, retinaculum, bursa, and subcutaneous tissue. These disorders are extremely common. (See 'Introduction'

above.)

- Soft tissue disorders may be divided into several broad categories and include tendinitis, enthesitis, fasciitis, bursitis, structural disorders, neurovascular entrapment disorders, complex regional pain syndromes (CRPS), and myofascial pain syndrome (MPS). Many of these disorders occur in the absence of systemic disease, and some are a consequence of chronic repetitive low grade trauma and overuse. Many are self-limiting and respond to conservative measures. (See 'Specific syndromes' above.)

  - Tendinitis (or tendonitis), which often results from overuse, is a disorder with common features of local pain and dysfunction, inflammation, and degeneration.

  - Enthesitis, which is an inflammation of the site of the insertion of the tendon to the bone, is often seen in spondyloarthropathies. Common sites are the insertion of the plantar fascia and the Achilles tendon region. (See 'Enthesitis' above.)

  - Bursitis is inflammation of the small fluid-filled pads, called bursae, which provide a cushion between bones and tendons and/or muscles around a joint. Bursitis may result from direct trauma or repetitive injury, infection, or it may be a manifestation of a systemic disease such as rheumatoid arthritis or gout. (See 'Bursitis' above and "Bursitis: An overview of clinical manifestations, diagnosis, and management".)

  - Musculoskeletal structural disorders are relatively common, sometimes subtle, and often contribute to pain syndromes and to injury in sports participants. Body asymmetry is a common cause for many regional pain disorders. (See 'Structural disorders' above.)

  - Neurovascular entrapment disorders may occur within the spinal canal (foraminal or central spinal stenosis) or along the course of a peripheral nerve. The diagnostic triad of peripheral neurovascular entrapment includes a sensation of swelling and pain in the involved region, paresthesias distal to the site of entrapment, and weakness. (See 'Neurovascular entrapment' above.)

  - A diagnosis of CRPS requires the presence of regional pain and sensory changes usually following a noxious event, often far from the involved site. The pain is of a severity greater than that expected from the inciting injury and is associated with characteristic clinical

findings. (See 'Complex regional pain syndromes' above and "Complex regional pain syndrome in adults: Pathogenesis, clinical manifestations, and diagnosis" and "Complex regional pain syndrome in adults: Prevention and management".)

- In MPS, hyperirritable spots, often in just one body region, usually within a taut band of skeletal muscle or in the muscle's fascia, can give rise to characteristic referred pain. There are usually one or more trigger (pain) points; these are typically indurated and painful on compression. Myofascial trigger points may result from acute trauma, repeated minor microtrauma of daily living, or from a chronic strain of sedentary work or living habits. (See 'Myofascial pain syndrome' above and "Differential diagnosis of fibromyalgia", section on 'Myofascial pain syndromes'.)

- Six points of management can often be initiated during the first visit in a patient with a suspected soft tissue rheumatic disorder, even before the results of appropriate laboratory or radiologic tests are available. These are excluding systemic disease, eliminating aggravating factors, explaining the illness, explaining self-help strategies, providing pain relief, and explaining the prognosis. (See 'General initial approach' above.)

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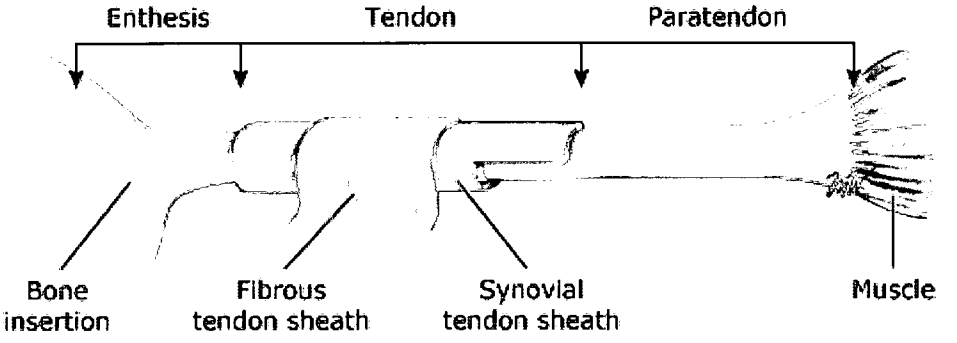
Topic 7757 Version 18.0

GRAPHICS

Tendon anatomy

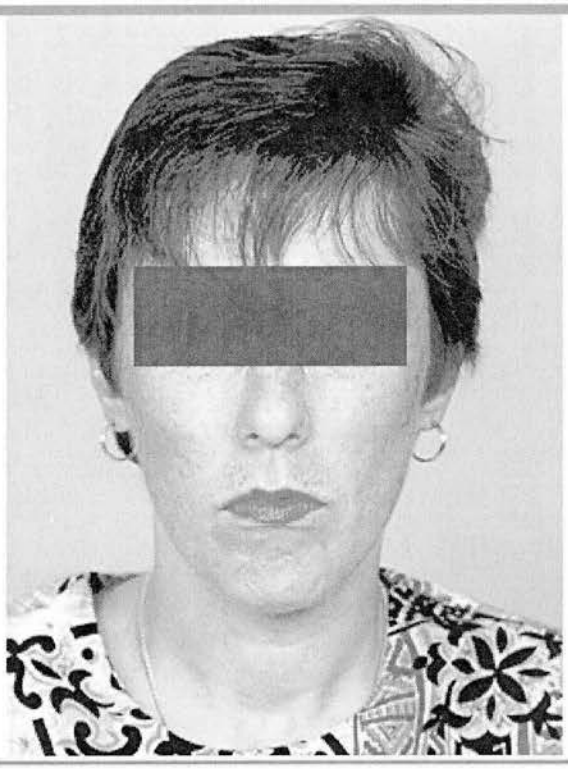


Tendon sheaths, like bursae, develop in response to motion as tendons pull and transmit power. The visceral sheath has a flat synovial lining, and the parietal layer has vesicular and granular patches. There is no basement membrane, only a fatty or collagenous connective tissue. Tendon healing is facilitated by an intact tendon sheath. Snapping or triggering of joint movement can be due to nodular enlargement of the tendon, stenosis of the sheath, or both. Enthesitis involves the area of the tendon that inserts into bone, tendinitis typically involves the area of the tendon closer to the enthesis, peritendonitis involves the area that inserts into muscle, and tenosynovitis represents inflammation of the tendon and its enveloping sheath.

Modified with permission from: Sheon RP, Moskowitz RW, Goldberg VM. Soft Tissue Rheumatic Pain: Recognition, Management, Prevention, 3rd ed, Williams & Wilkins, Baltimore 1996.

Graphic 62565 Version 3.0

Facial asymmetry



The left side of this patient's face is smaller than the right. Temporomandibular joint dysfunction is more common in patients with facial asymmetry. Other associated features may include scoliosis and a short leg.

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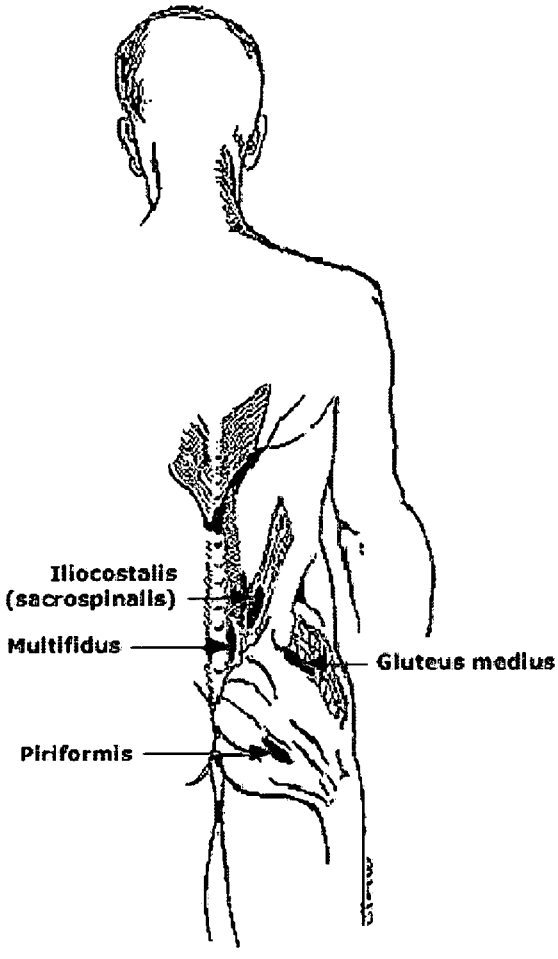
Graphic 64450 Version 3.0

Trigger points in myofascial pain syndrome



Patients with myofascial pain syndrome have tenderness within the affected muscle and soft tissue. Trigger points arising in the erector spinae muscles, the gluteal fascia, and the presacral fascia are common.

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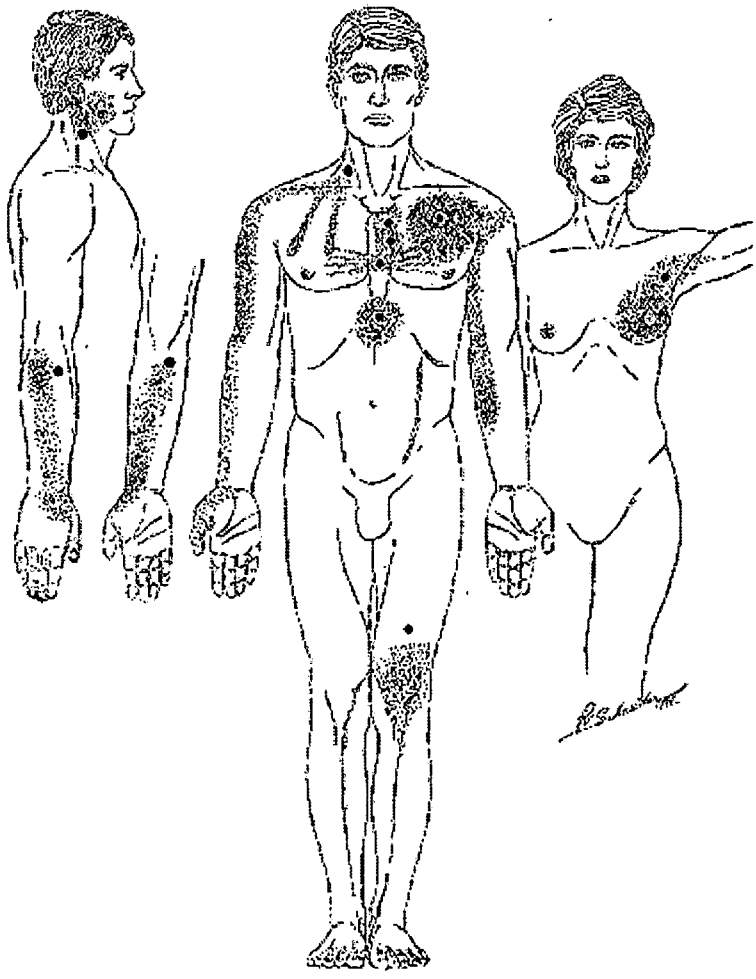
Graphic 81019 Version 2.0

Clinical features of fibromyalgia versus myofascial pain

Variable	Fibromyalgia	Myofascial pain
Pain	Generalized	Localized
Examination	Tender points	Trigger points
Fatigue	Prominent	Data unknown
Gender	90 percent female	Data unknown
Course	Chronic	May be self-limited

Graphic 81771 Version 4.0

Anterior trigger points associated with the myofascial pain syndrome



Palpation of a trigger point (black dots) in patients with the myofascial pain syndrome may cause pain at a distant point. This zone of reference (gray area) is usually quite characteristic for each trigger point.

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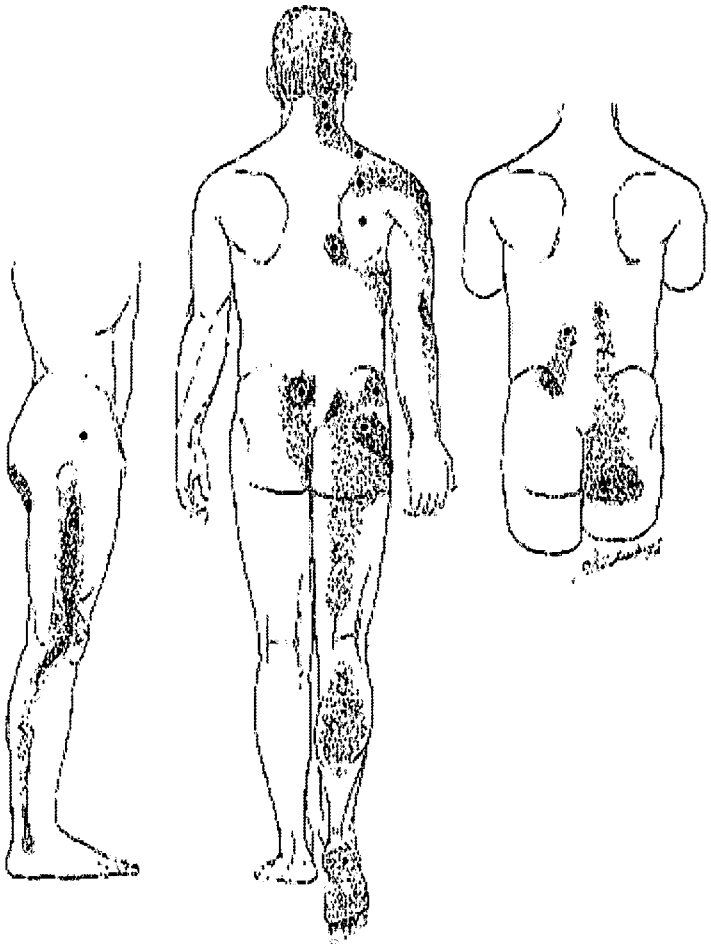
Graphic 66839 Version 1.0

Posterior trigger points associated with the myofascial pain syndrome



Trigger points and zones of reference are also present posteriorly in patients with the myofascial pain syndrome.

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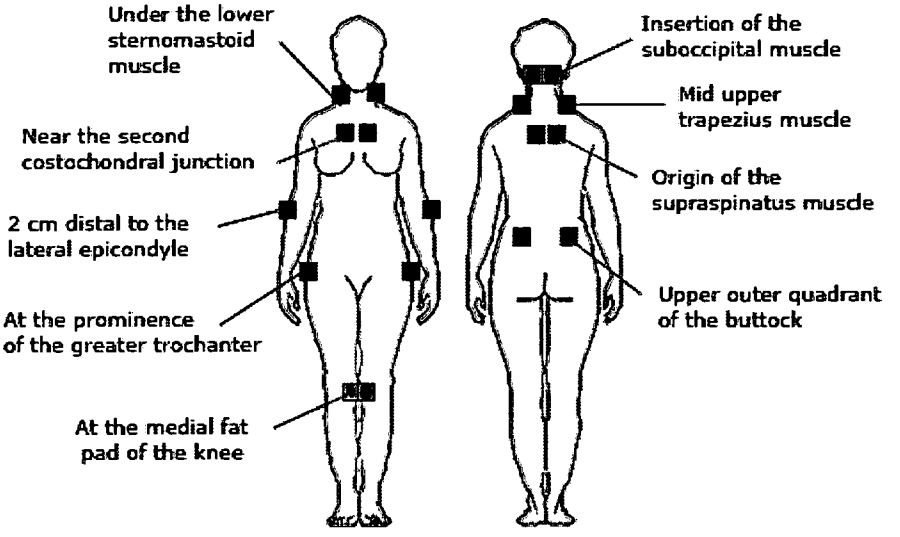
Graphic 79295 Version 1.0

Tender points in fibromyalgia



The 18 "tender points" important for the diagnosis of fibromyalgia. Note the bilateral symmetry of the labeled regions. Tenderness on palpation of at least 11 of these sites in a patient with at least a three-month history of diffuse musculoskeletal pain is recommended as a diagnostic standard for fibromyalgia.

Adapted from: Goldenberg DL. Diagnostic and therapeutic challenges of fibromyalgia. Hosp Pract (Off Ed) 1989; 24:39.

Graphic 77950 Version 3.0

Clinical similarities between fibromyalgia and chronic fatigue syndrome (CFS)

80 to 90% women, usual ages 20 to 55 years
Myalgias and fatigue in more than 90%
Associated common symptoms
Neurocognitive and mood disturbances
Headaches
Sleep disturbances
No identifiable cause
Testing is normal
Physical examination usually normal except for tender points which are required for diagnosis of fibromyalgia and present in most patients with chronic fatigue
Normal laboratory and radiologic tests
Chronic symptoms, no highly effective therapy

Graphic 56019 Version 6.0

Topical analgesics for treatment of superficial painful conditions

Topical analgesic	Usual dose (adult)	Characteristics
Topical nonsteroidal antiinflammatory drugs (NSAIDs)*		
Diclofenac topical gel (1%)	Knees: Rub in 4 g of gel to affected knee(s) three to four times daily. Hands: Rub in 2 g of gel to affected joint(s) three to four times daily. Maximum 16 g per joint per day; 32 g total per day.	Applies to all topically administered NSAIDs: ▪ Useful for treatment of musculoskeletal pain and osteoarthritis of superficial joints (eg, wrist, knee, hand) in combination with acetaminophen and/or tramadol, or as an alternative to systemic therapy ▪ Minimal systemic absorption ▪ Safety data are reassuring despite label warnings on United States products ▪ Local skin reactions include rash, itch, or burning (some products contain propylene glycol, a potential irritant and rarely an allergen) ▪ Refer to topic review on initial pharmacologic therapy of osteoarthritis
Diclofenac topical solution drops (1.5%)	Knees: Rub in 40 drops to affected knee(s) up to four times daily.	
Diclofenac topical solution pump (2%)	Knees: Rub in two pump actions to affected knee(s) up to two times daily.	
Ibuprofen topical gel (5, 10%); not available in United States	Knees or hands: Rub in dose (depends on joint size and location) up to four times daily; refer to product-specific information for detail.	
Ketoprofen topical gel (2.5%); not available in United States	Knees or hands: Rub in 2 to 4 g of gel two to four times daily (maximum 15 g of gel per day); refer to product-specific information for detail.	
Topical capsaicin¶		
Capsaicin creams, gels, liquids, or lotions (0.025 to 0.1%)	Rub in a small amount (pea sized) one to four times daily; the preparation most often studied in osteoarthritis was 0.025% cream.	▪ Useful for treatment of osteoarthritis pain and postherpetic neuralgia as an adjunct or alternative to systemic analgesics ▪ Local irritation may be intolerable ▪ Refer to topic review on initial pharmacologic therapy of osteoarthritis
Capsaicin topical patches (0.025 to 0.05%)	Apply one patch to affected area for up to eight hours (maximum four patches per day).	
Capsaicin topical patch (high concentration 8%)	Postherpetic neuralgia (single treatment): Apply up to four patches to the most painful area for 60 minutes. Treatment may be repeated after three months.	▪ Potential option for local pain relief in postherpetic neuralgia ▪ High-concentration patch must be administered by a health care professional and monitored for up to two hours after treatment ▪ Pretreatment with a local anesthetic (eg, lidocaine) is necessary ▪ After application, local cooling measures can decrease discomfort ▪ Local pain and irritation may be intolerable ▪ Refer to topic review on postherpetic

		neuralgia
Topical lidocaine		
Lidocaine topical patch (5%)	One to three patches applied for up to 12 hours in any 24-hour period.	▪ Low (3 to 5%) systemic absorption through intact skin ▪ Useful for local relief of pain (eg, due to postherpetic neuralgia) in limited areas of intact skin as an adjunct or alternative to systemic analgesics
Lidocaine topical creams, ointments, and gels (2 to 4%)	Apply a thin film two to four times daily (refer to product-specific instructions).	▪ Useful for local relief of minor superficial skin irritation and pain
Lidocaine topical cream (5%)	Apply a thin film three to four times daily (maximum six times daily).	▪ Useful for local relief of anorectal pain and itching

Topical analgesic therapies are moderately effective and useful in combination with systemic therapies for reducing medication load and side effects, and potentially, as monotherapy for adults with localized pain and contraindications to systemic therapies.

* For patients already on oral NSAIDs, topical therapies are generally not recommended because they are unlikely to provide additional pain relief. Gel measurements from tubes are approximate.
¶ Pain relief usually begins within the first week of treatment, and full effect is seen with regular application over approximately four weeks. Topical capsaicin should not come in contact with mucous membranes, abraded skin, eyes, or genital areas.

Graphic 93846 Version 6.0

Contributor Disclosures

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Contributor disclosures are reviewed for conflicts of interest by the editorial group. When found, these are addressed by vetting through a multi-level review process, and through requirements for references to be provided to support the content. Appropriately referenced content is required of all authors and must conform to UpToDate standards of evidence.

Conflict of interest policy

Anthem.

Clinical UM Guideline

Subject: Trigger Point Injections
Guideline #: CG-SURG-17
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Description

This document addresses trigger point injections and dry needling trigger point stimulation.

Trigger points are small, circumscribed, hyperirritable foci in muscles, often found within a firm or taut band of skeletal muscle. Frequently affected sites include the trapezius, supraspinatus, infraspinatus, teres major, lumbar paraspinals, gluteus and pectoralis muscles. The diagnosis is clinical and depends upon the results of a detailed history and a thorough directed exam. There is no laboratory or imaging test to establish the diagnosis of trigger point pain.

Myofascial pain syndrome is a regional painful muscle condition with a relationship between a specific trigger point and its associated pain region. When myofascial pain syndrome is suspected, injections of local anesthetics with or without steroid into the identified trigger points have been used for myofascial pain management for many years within the medical community. *Dry needling* of a trigger point is a technique for pain treatment in which the pain site is stimulated by insertion of a needle without injection of medication.

Clinical Indications

Medically Necessary:

I. Trigger point injections (TPI) with a local anesthetic with or without steroid are considered **medically necessary** when *all of the* following general and specific criteria are met:

A. General Criteria
   1. There is a regional pain complaint; **and**
   2. A neurological, orthopedic or musculoskeletal system evaluation ,which includes the member's description of pain as it relates to location, quality, severity, duration, timing, context, and modifying factors, followed by a physical examination of associated signs and symptoms; **and**
   3. Conservative therapy (for example, physical or chiropractic therapy, oral analgesia, steroids, relaxants or activity modification) fails or is not feasible; **and**
   4. When necessary to facilitate mobilization and return to activities of daily living, an aggressive regimen of physical therapy or other therapeutic modalities; **and**
   5. The response to therapy must be documented for medical review prior to additional therapy authorizations.

B. Specific Criteria
   1. Pain complaint or altered sensation in the expected distribution of referred pain from a trigger point; **and**
   2. Taut band palpable in an accessible muscle when the trigger point is myofascial; **and**
   3. Exquisite spot tenderness at one point along the length of the taut band when the pain is myofascial; **and**
   4. Some degree of restricted range of motion of the involved muscle or joint, when measurable; **and**
   5. The above specific criteria are associated with at least ONE of the following MINOR CRITERIA:
      a. Reproduction of clinical pain complaint or altered sensation by pressure on the tender spot; **or**
      b. Local response (twitch) elicited by snapping palpation at the tender spot or by needle insertion into the tender spot; **or**
      c. Pain alleviation by elongating (stretching) the muscle or by injecting the tender spot.

II. Trigger point injections (TPI) with a local anesthetic with or without steroid are considered **medically necessary** for the treatment of pain associated with fibromyalgia when the American College of Rheumatology (ACR) diagnostic criteria for fibromyalgia or the ACR Preliminary Diagnostic Criteria for Fibromyalgia and Measurement of Symptom Severity criteria are met.

A. Based on the 1990 ACR diagnostic criteria for fibromyalgia, the following criteria must be met:
   1. History of widespread pain for at least 3 months. To be considered wide spread, the pain must be present on both right and left sides and both above and below the waist. In addition axial skeletal pain (cervical spine or anterior chest or thoracic spine or low back) must be present. In this definition, shoulder and

buttock pain is considered as pain for each involved side. "Low back pain" is considered lower segment pain; **and**

2. Pain, on digital palpation, must be present in at least 11 of the following 18 sites:
    a. Occiput: bilateral, at the suboccipital muscle insertions;
    b. Low cervical: bilateral, at the anterior aspects of the intertransverse spaces at C5-C7;
    c. Trapezius: bilateral, at the midpoint of the upper border;
    d. Supraspinatus: bilateral, at origins, above the scapula spine near the medial border;
    e. Second rib: bilateral, at the second costochondral junctions, just lateral to the junctions on upper surfaces; .
    f. Lateral epicondyle: bilateral, 2 cm distal to the epicondyles;
    g. Gluteal: bilateral, in upper outer quadrants of buttocks in anterior fold of muscle;
    h. Greater trochanter: bilateral, posterior to the trochanteric prominence;
    i. Knee: bilateral, at the medial fat pad proximal to the joint line.

or

B. Based on the 2010 ACR Preliminary Diagnostic Criteria for Fibromyalgia and Measurement of Symptom Severity guidelines, the following criteria must be met:
    1. The widespread pain index (WPI) scale score is:
        a. greater than or equal to 7 *and* the symptom severity (SS) scale score is greater than or equal to 5; **or**
        b. the WPI scale score is 3-6 *and* the SS scale score is greater than or equal to 9; **and**
    2. The individual's symptoms have been present at a similar level for a minimum of three (3) months; **and**
    3. The individual does not have a disorder that would otherwise explain the pain.

WPI Scale Score:
The WPI score is determined by noting the number of areas in which the individual has had pain during the last week (the total number of areas in which the individual has had pain). The cumulative score will be between 0 and 19.

Left shoulder girdle	Right lower arm	Left lower leg	Abdomen
Right should girdle	Left hip (buttock, trochanter)	Right lower leg	Upper back
Left upper arm	Right hip (buttock, trochanter)	Left jaw	Lower back
Right upper arm	Left upper leg	Right jaw	Neck
Left lower arm	Right upper leg	Chest	

SSI Scale Score:
The SS scale score is the sum total of the severity of the 3 symptoms (fatigue, feeling unrefreshed upon awaking and symptoms involving cognition) in addition to the extent (severity) of somatic symptoms in general. The final score will range from 0 to 12.

For each of the 3 symptoms (fatigue, feeling unrefreshed upon awaking and symptoms involving cognition), indicate the level of severity over the past week using the following scale:
0 No problem
1 Slight or mild problems, generally mild or sporadic
2 Moderate, considerable problems, frequently present and/or at a moderate level
3 Severe: pervasive, constant, life-disturbing problems

Giving consideration to somatic symptoms in general, indicate whether the individual has:*
0 No symptoms
1 A few symptoms
2 A moderate number of symptoms
3 A great number of symptoms

*Somatic symptoms may include any of the following: irritable bowel syndrome, muscle pain, fatigue/tiredness, thinking or remembering problem, muscle weakness, headache, pain/cramps in the abdomen, dizziness, numbness/tingling, insomnia, depression, constipation, pain in the upper abdomen, nausea, nervousness, chest pain, blurred vision, fever, diarrhea, itching, wheezing, dry mouth, Raynaud's phenomenon, hives/welts, ringing in ears, vomiting, heartburn, oral ulcers, loss of/change in taste, seizures, dry eyes, loss of appetite, shortness of breath, rash, sun sensitivity, hearing difficulties, easy bruising, hair loss, frequent urination, painful urination, and bladder spasms.

III. The following schedule for trigger point injections is considered **medically necessary** when the previous criteria are met:

A. In the diagnostic or stabilization phase, individuals may receive injections at intervals of no sooner than one week and preferably two weeks. The number of trigger point injections should be limited to no more than four (4)

times per year for the diagnostic or stabilization phase.

B. In the treatment or therapeutic phase, trigger point injections should continue only if the previous diagnostic injections provided pain relief and the frequency should be two (2) months or longer between each injection. The previous injections should have provided at least greater than 50% relief of pain for a period of at least six (6) weeks. The injections should be repeated only as necessary based on the medical necessity criteria (see above) and these should be limited to a maximum of six (6) times for local anesthetic and steroid injections.
C. Under unusual circumstances such as a recurrent injury or cervicogenic headache, trigger point injections may be repeated at intervals of six (6) weeks after stabilization in the treatment phase.

Not Medically Necessary:

I. Trigger point injections are considered **not medically necessary** in the presence of:
   A. Systemic infections; **or**
   B. Bleeding tendencies (including individuals undergoing anticoagulation therapy); **or**
   C. Other concomitant unstable medical conditions.
II. "Dry needling" trigger point stimulation is considered **not medically necessary.**

Coding

The following codes for treatments and procedures applicable to this guideline are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

CPT

20552	Injection(s); single or multiple trigger point(s), 1 or 2 muscle(s)
20553	Injection(s); single or multiple trigger point(s), 3 or more muscles
20999	Unlisted procedure, musculoskeletal system, general [when specified as dry needling]

ICD-10 Diagnosis

All diagnoses

Discussion/General Information

A 1990 guideline produced by the American College of Rheumatology (ACR) based the diagnosis of fibromyalgia on the physical examination (presence of at least 11 of 18 specified tender points) and the presence of widespread pain (axial, left and right-sided pain, as well as upper and lower segment). Several objections to these criteria appeared over time. These included the fact that most physicians do not perform technically correct tender point examinations. Researchers discovered that symptoms not considered in the 1990 guideline are consistently associated with the syndrome. In 2010, the ACR published the Preliminary Diagnostic Criteria for Fibromyalgia and Measurement of Symptom Severity diagnostic criteria which do not require a physical or tender point examination.

A component of the 2010 criteria is the fibromyalgia symptom severity (SS) scale which permits the evaluation of the severity of fibromyalgia symptom in individuals with current or previous fibromyalgia, and in those to whom the criteria have not been applied. It is considered to be especially useful in the longitudinal evaluation of individuals with marked symptom variability (Wolfe, 1990; Wolfe, 2010).

Although not supported by rigorous randomized controlled trials (Cummings 2001), trigger point injections with a local anesthetic with or without a steroid are considered an accepted therapy for pain associated with myofascial pain syndrome or fibromyalgia.

In a Cochrane review, Peloso and colleagues (2011) examined the effects of medication and injections on primary outcomes (for example, pain) for adults with mechanical neck disorders and whiplash. In their data analysis, they found that lidocaine injection into myofascial trigger points appears effective in two trials.

In another Cochrane review, Staal and colleagues (2011) performed a data analysis to determine if injection therapy is more effective than placebo or other treatments for individuals with subacute or chronic low-back pain. Based on these results, the review authors concluded that there is no strong evidence for or against the use of any type of injection therapy for individuals with subacute or chronic low-back pain.

Kim and colleagues (2012) evaluated the therapeutic effectiveness of trigger point injections into the muscles around the groin in males with clinically diagnosed chronic prostatitis (CP) and chronic pelvic pain syndrome (CPPS). In addition, the researchers attempted to determine which muscle was the cause of groin pain by using ultrasound guidance during the injection. Twenty-one (21) participants ranging in ages from 20 to 61 years met the inclusion criteria. The NIH-CPSI score and the visual analog scales for pain (VAS) were the main outcome measurements. Trigger point injections were performed in all affected muscles at 1-week intervals. Additional injections were not considered if the participants were satisfied with the reduction in discomfort or the severity of pain, or if the individual did not want another injection for other reasons. No other therapies (such as physical therapy or medications) were allowed during the study period. However, self-exercise and behavior correction were allowed to avoid early recurrence of pain after trigger point injections. Of the 21 participants, all completed the treatment schedule and attended a follow-up. Fourteen participants (66.7%) received one trigger point injection, 6 participants (28.6%) received two injections at an interval of 1 week, and 1 subject (4.7%) received a total of three injections at the same interval. Nineteen of the 21 participants reported improvement of symptoms enough to not need further treatment, while 2 subjects did not complete the injection treatment for personal reasons. With all of the subjects, the VAS and NIH-CPSI scores decreased compared with the baseline scores. The participants did not report any complications related to the injections or serious adverse events attributable to the treatment. The authors concluded that US-guided trigger point injections of the iliopsoas, hip adductor, and abdominal muscles are safe and effective for CP/CPPS groin pain which is believed to originate from muscles. The iliopsoas muscle was affected in all of the participants in this study. The authors acknowledged that limitations of this study include its small size and short follow-up time.

There is little evidence to support dry needling. A Cochrane assessment of dry needling for lower back pain found that while dry-needling may be a useful adjunct to other therapies, most of the limited number of studies available were of low methodological quality and small sample size (Furlan, 2000).

Karakurum and colleagues (2001) studied dry needling for tension type headaches (TTH). Fifteen participants with TTH received intramuscular dry needle insertions into six designated trigger points, while 15 controls received sham dry needle subcutaneous insertions. Results showed significant improvement of mean headache indices after treatment, both in the treatment group and in the placebo group, but the difference between the two groups was not statistically significant. In the treatment group, neck tenderness and range of motion improved, while there was no significant improvement in the sham placebo group. However, the number of participants treated was too small for this difference to be statistically significant. The authors concluded that more and larger controlled, comparative trials were needed to show whether the dry-needle technique is effective in the treatment of TTH.

Irnich and colleagues (2002) compared the effects of dry needling and acupuncture at distant points in chronic neck pain using a randomized, double-blind, sham controlled cross-over trial. Thirty-six participants were included in the prospective trial. Although an assessment of change revealed acupuncture was superior to both sham and dry needling, there was no difference between dry needling and sham control ($p=0.8$).

In 2017, De Meulemeester and colleagues reported the results of a randomized controlled trial evaluating 42 individuals with myofascial neck and/or shoulder pain. Study participants were assigned to receive 4 sessions of dry needling ($n=20$) or manual pressure ($n=22$). All participants were evaluated with the Neck Disability Index, general numeric rating scale, pressure pain threshold, and muscle characteristics before and after treatment. The primary outcome measure was the Neck Disability Index. All subjects were evaluated after 4 treatments and again after 3 months. There were no significant differences in NDI scores between the dry needling cohort and the manual pressure cohort at either follow-up point ($p>0.05$).

Kamanlia and colleagues (2005) reported a prospective single-blind study comparing trigger point injection for myofascial pain syndrome using lidocaine injection, botulinum toxin type A (BTX-A) injection and dry needling. Twenty-nine participants were randomized to three groups of near equal size. A variety of outcome measures were used including pain scores, trigger point pain pressure threshold (PPT), visual analog scales for pain (VAS), the Hamilton depression score and quality of life (QOL) assessments using the Nottingham Health Profile (NHP). While pain pressure thresholds and pain scores improved in all three groups, the pain pressure threshold values were significantly higher in the lidocaine group than in the dry needle group. VAS did not change in the dry needle group, but did decrease in the lidocaine injection and BTX-A injected groups. QOL scores by NHP improved in the lidocaine and BTX-A groups but not in the dry needle group. The limitations of this study include its small size and the lack of an untreated or sham control group.

In 2009, Tough and colleagues published a systematic review and meta-analysis of randomized controlled trials addressing dry needling in the management of myofascial trigger point pain. A meta-analysis was performed on four studies of 134 participants that included a placebo control. This

analysis concluded that dry needling was not superior to placebo. Other randomized studies reported conflicting findings. The authors concluded the limited sample size and poor quality of these studies highlights and supports the need for large scale, good quality placebo controlled trials in this area.

Brennan and colleagues (2017) reported the results of a randomized and partially blinded trial that investigated if the administration of dry needling is noninferior to cortisone injection in reducing lateral hip pain and improving function in subjects with greater trochanteric pain syndrome (also known greater trochanteric or subgluteal bursitis). A total of 50 individuals, all with greater trochanteric pain syndrome were included in the study. Participants were randomly assigned to receive either cortisone injection (n=25 hips) or dry needling (n=25 hips). Treatments were provided over a period of 6 weeks, and clinical outcomes were assessed at baseline and at 1, 3, and 6 weeks. The primary outcome measure was pain measurement (0-10 rating scale). The secondary and tertiary outcome measures were the Patient-Specific Functional Scale (0-10) and pain medication intake, respectively. Baseline characteristics were similar for both groups. A noninferiority test for a repeated-measures design for pain and averaged function scores at 6 weeks (with a noninferiority margin of 1.5 for both outcomes) suggested that dry needling was noninferior to cortisone injection (both, P<.01). Medication usage (P = .74) was similar between groups at the same time point. The authors concluded that dry needling is a noninferior treatment alternative to cortisone injections in individuals with greater trochanteric pain syndrome. Limitations of this study include but are not necessarily limited to the lack of a sham control group and its small size.

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History

Status	Date	Action
Reviewed	05/03/2018	Medical Policy & Technology Assessment Committee (MPTAC) review. The document header wording updated from "Current Effective Date" to "Publish Date." Updated review date, Rationale, References and History sections.
Revised	05/04/2017	MPTAC review. Updated formatting in the Clinical Indications section. In the Not Medically Necessary statement, inserted the word "or" after bullets IA and IB. Updated review date, Coding, and History sections.
Reviewed	05/5/2016	MPTAC review. Updated review date, References and History sections.
	01/01/2016	Updated Coding section with 01/01/2016 descriptor change for CPT 20553; removed ICD-9 codes.
Revised	05/07/2015	MPTAC review. Expanded the medically necessary criteria for trigger point injections for individuals with fibromyalgia to include the 2010 ACR criteria. Updated review date, Discussion/General Information, References and History sections.
Reviewed	05/15/2014	MPTAC review. Updated References section.
Reviewed	05/09/2013	MPTAC review. Updated Discussion/General Information and References sections.
Reviewed	05/10/2012	MPTAC review. Discussion and References sections updated.
Reviewed	05/19/2011	MPTAC review. References and Coding sections updated.
Reviewed	05/13/2010	MPTAC review. References section updated.
Reviewed	05/21/2009	MPTAC review. Discussion and References sections updated. Place of service removed.
Reviewed	05/15/2008	MPTAC review. References section updated.
Revised	05/17/2007	MPTAC review. Guideline revised to address dry needling. Background, Coding, and References section updated.

Reviewed	12/07/2006	MPTAC review. References section updated.
Revised	12/01/2005	MPTAC review. Revision based on Pre-merger Anthem and Pre-merger WellPoint Harmonization.

Pre-Merger Organizations	Last Review Date	Document Number	Title
Anthem, Inc.			None
Anthem BCBS			None
WellPoint Health Networks, Inc.	12/02/2004	Guideline	Regional Anesthesia/Pain Management for Chronic Neck, Back and Myofascial Pain

Medical Coverage Policy

Effective Date..... 7/15/2018
Next Review Date..... 6/15/2019
Coverage Policy Number..... 0139

Minimally Invasive Intradiscal/ Annular Procedures and Trigger Point Injections

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INSTRUCTIONS FOR USE
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Coverage Policy

INJECTION THERAPY: TRIGGER POINT

Diagnostic/Stabilization Phase
Trigger-point injection(s) of anesthetic and/or corticosteroid (CPT codes 20552, 20553) for diagnosis/stabilization of subacute or chronic back, or neck pain, or subacute or chronic myofascial pain syndrome is considered medically necessary when pain has persisted despite appropriate conservative treatment, including pharmacological therapy, physical therapy, and/or a home exercise program.

A maximum of four injection sessions for diagnosis and stabilization may be performed at minimum intervals of one week when provided to determine whether injections provide therapeutic benefit.

Therapeutic Phase

Therapeutic trigger-point injections of anesthetic and/or corticosteroid (CPT codes 20552, 20553) are considered medically necessary when prior diagnostic/stabilization injections resulted in a beneficial clinical response (e.g., improvement in pain, functioning, activity tolerance) and BOTH of the following criteria are met:

- subacute or chronic back pain, neck pain, or myofascial pain syndrome persists
- injections are provided in conjunction with an active treatment program, which may include pain management, physical therapy, and/or a home exercise program

A maximum of six treatment sessions for injection of the same muscle may be performed at a minimum interval of two months, if the preceding therapeutic injection resulted in more than 50% relief for at least six weeks.

Long-term repeated or maintenance therapeutic trigger point injections for any indication are considered experimental, investigational or unproven. Repeat therapeutic trigger point injections provided for 12 months or longer may result in medical necessity review.

When performed for any indication each of the following is considered experimental, investigational, or unproven:

- dry needling of trigger points (CPT Code 64999)
- ultrasound guidance (CPT code 76942) for trigger point injections

INJECTION THERAPY: INTRADISCAL STEROID INJECTION

Intradiscal steroid injection for the treatment of acute, subacute, or chronic back or neck pain is considered experimental, investigational, or unproven.

PERCUTANEOUS AND ENDOSCOPIC LAMINECTOMY AND DISC DECOMPRESSION PROCEDURES of the CERVICAL, THORACIC, OR LUMBAR SPINE

A percutaneous or endoscopic laminectomy or disc decompression procedure, including but not limited to ANY of the following, is considered experimental, investigational or unproven:

- automated percutaneous lumbar discectomy (APLD)/automated percutaneous nucleotomy (CPT code 62287 , HCPCS code C2614)
- endoscopic anterior spinal surgery/Yeung endoscopic spinal system (YESS)/percutaneous endoscopic diskectomy (PELD)/arthroscopic microdiscectomy, selective endoscopic discectomy (SED) (CPT code 62287)
- endoscopic disc decompression ablation, or annular modulation using the DiscFX™ System (CPT codes 22899, 62380, 64999)
- percutaneous laminotomy/laminectomy, percutaneous spinal decompression (e.g., mild® procedure) (CPT codes 0274T, 0275T)
- percutaneous laser discectomy /decompression, laser-assisted disc decompression (LADD) (CPT code 62287), targeted percutaneous laser disc decompression (targeted PLDD)(CPT code 62287)
- endoscopic, anterior cervical disc decompression (e.g., Cervical Deuk Laser Disc Repair) (CPT code 22899)

THERMAL INTRADISCAL PROCEDURES

Each of the following procedures is considered experimental, investigational or unproven:

- intervertebral disc biacuplasty (CPT code 22899)
- intradiscal electrothermal annuloplasty (e.g., intradiscal electrothermal therapy [IDET™]) (CPT codes 22526, 22527)
- percutaneous intradiscal radiofrequency thermocoagulation (PIRFT), intradiscal radiofrequency thermomodulation or percutaneous radiofrequency thermomodulation (CPT code 22899, HCPCS code S2348)
- Coblation® Nucleoplasty™, disc nucleoplasty, decompression nucleoplasty plasma disc decompression, radiofrequency thermocoagulation nucleoplasty (RFTC) (CPT code 62287)
- intraosseous radiofrequency nerve ablation of basivertebral nerve (e.g., INTRACEPT® Intraosseous Nerve Ablation System) (CPT code 64999)
- targeted disc decompression (CPT code 22899)

OTHER PROCEDURES

The following procedures are each considered experimental, investigational or unproven:

- devices for annular repair (e.g., Inclose™ Surgical Mesh System, Xclose™ Tissue Repair System (Anulex Technologies, Inc., Minnetonka, MN)
- epiduroscopy, epidural myeloscopy, epidural spinal endoscopy (CPT code 64999)
- intradiscal injections (e.g., methylene blue, platelet rich plasma, mesenchymal stem cells, tumor necrosis factor [TNF] alpha) and/or paravertebral oxygen/ozone injection
- spinal decompression using Baxano iO-Flex® System (e.g., Baxano Device)

Overview

Management of back pain that is persistent and disabling despite the use of recommended conservative treatment is challenging. Numerous diagnostic and therapeutic injections and other interventional and surgical treatments have therefore been proposed for the treatment back pain. This Coverage Policy addresses injection therapy and other minimally invasive intradiscal and/or annular procedures for treatment of back pain conditions.

General Background

Back pain is a frequent cause of chronic pain and disability, affecting approximately 15% of the U.S. population during their lifetime. Most episodes of low back pain improve substantially within a month without formal medical intervention. In some patients, back pain may be persistent and disabling. Conservative treatment may include pharmacological therapy (e.g., analgesics, anti-inflammatory drugs, muscle relaxants), exercise, spinal manipulation, acupuncture, cognitive-behavioral therapy, and physical therapy. If these measures are unsuccessful, a number of interventional techniques and procedures may be considered that attempt to target specific structures or spinal abnormalities considered to be potential sources of pain, including back muscles and soft tissues, degenerated facet or sacroiliac joints, spinal canal stenosis, and degenerated or herniated intervertebral discs (Chou et al., 2009).

Surgery may be appropriate for medical conditions with remediable underlying pathology (e.g., herniated disc) when confirmed and correlated with imaging findings. There is evidence that surgical discectomy provides significant pain relief in selected patients with lumbar disc prolapse with sciatica that fails to improve with conservative treatment. Discectomy was originally performed in an open operation over the spine called hemilaminectomy, in which the muscles are dissected away from the spine and access to the intervertebral disc is obtained by cutting away a piece of spinal bone (i.e., lamina). This technique remains the treatment of choice in some patients, including those with severe pain or weakness and complicated herniation. Microsurgical discectomy (i.e., microdiscectomy with endoscopic visualization) is a less invasive technique that evolved in an effort to decrease postoperative morbidity and recovery time. Microdiscectomy employs direct visualization but is performed through a smaller (15–25 mm) central incision with the use of an operating microscope. Microdiscectomy outcomes are similar to outcomes seen with open discectomy, and microdiscectomy is

considered the standard treatment by which to compare other minimally invasive therapies. In 2014 the North American Spine Society (NASS) published coverage policy recommendations in support of endoscopic discectomy (with visualization) as an alternative to lumbar discectomy (NASS, 2014). A variety of procedures have been developed as alternatives to open and microsurgical techniques for treatment of back pain related to disc disease (e.g., laser discectomy, percutaneous radiofrequency decompression, disc Nucleoplasty™).

Choosing Wisely: The North American Spine Society (NASS) Choosing Wisely recommendations state when treating low back pain bed rest for more than 48 hours is not recommended; in patients with low back pain, bed rest exceeding 48 hours in duration has not been shown to be of benefit.

Injection Therapy: Trigger Point

Trigger point injection therapy involves the injection of anesthetic or corticosteroids into distinct, focal hyper-irritable spots (i.e., trigger points) located in a tight band of skeletal muscle. Myofascial pain syndrome is a chronic form of muscle pain centered around trigger points. Palpable nodules may be present in the taut band of the muscle which become painful when the tender zone is stimulated. Pain may be perceived at the site of the trigger point or can be referred to other parts of the body, including the back and neck.

Fluoroscopic or computed tomography guidance is performed with other types of injections used to diagnose and treat back and neck pain (e.g., epidural steroid injections, facet joint injections) to identify the surrounding structures and to ensure accurate needle placement to the target area. Guidance has been performed with trigger point injections. Although there are no standard criteria, a common method of identifying a trigger point is through manual examination using a palpation technique; palpating the band leads to a local twitch response (LTR) where contraction of the muscle fibers in the taut band is observed. The diagnostic reliability of this method however is inconsistent. As a result, use of ultrasound has been investigated to identify the trigger point and to visualize the twitch response resulting from the injection. Particularly for deep muscles, such as the lower back, it has been purported the use of ultrasound is clinically useful to identify the LTR and therefore improve the efficacy of the injection (Rha, et al., 2011).Evidence in the published medical literature evaluating the efficacy of adding ultrasound or other guidance to trigger point injections is limited to primarily pilot studies, case reports, case series, case control studies and literature reviews (Khumbare, et al., 2016; Shin, et al., 2014; Shankar, Reddy, 2012; Rha, et al., 2011; Sikdar, et al., 2009; Botwin, et al., 2008; Lewis and Tehan, 1999). Sample populations are small and reported clinical outcomes are inconsistent. A majority of comparative trials compare ultrasound guided trigger point injections to other non-trigger point forms of treatment. While some professional societies have published recommended guidelines for trigger point injections, they do not include the use of guidance for the trigger point injection. In the absence of well-designed comparative clinical trials evaluating the efficacy of trigger point injection with and without guidance, strong evidence based conclusions cannot be made. Further clinical validation is necessary to support improved health outcomes with the use of ultrasound guidance for trigger point injections.

A Cochrane systematic review was conducted to determine if injection therapy is more effective than placebo or other treatments for patients with subacute or chronic low back pain (Staal et al., 2008). This updated review evaluated 18 randomized controlled trials (n=1179) of injection therapy involving epidural, facet or local sites (i.e., tender or trigger points) in patients with non-radicular pain. The injected drugs included corticosteroids, local anesthetics, and a variety of other drugs. Overall, the results indicated that there was no strong evidence for or against the use of any type of injection therapy. The authors concluded that there is insufficient evidence to support the use of injection therapy in subacute and chronic low back pain, but it cannot be ruled out that specific subgroups of patients may respond to a specific type of injection therapy.

Peloso et al. (2007) conducted a Cochrane systematic review to determine the effects of medication and injections on primary outcomes (e.g., pain) for adults with mechanical neck disorders and whiplash. The review evaluated 36 trials that examined the effects of steroid injections, anesthetic agents, psychotropic agents, and NSAIDs. The authors stated that lidocaine injection into myofascial trigger points appeared effective in two trials.

Guidelines on injection therapies, low-back pain, and lumbar fusion published by the American Association of Neurological Surgeons (AANS)/Congress of Neurological Surgeons (Watters, et al., 2014; Resnick et al., 2005), based on a systematic review of studies evaluating trigger point injections, facet joint injections, and epidural steroid injections, concluded that there is conflicting evidence suggesting that the use of local trigger point

injections can be effective for the short-term relief of low-back pain. There are no data to suggest that trigger point injections with either steroids or anesthetics alone provide lasting benefit for patients suffering from chronic low-back pain.

American College of Occupational and Environmental Medicine (ACOEM) evidence-based practice guidelines on low back disorders, updated in 2011, state that trigger and/or tender point injections are not recommended for treatment of acute low back pain because there are other more efficacious treatment strategies available. These injections may be reasonable as second or tertiary options for subacute or chronic low back pain that is not resolving with conservative treatment (e.g., NSAID, progressive aerobic exercises, and other exercises). The guideline states that injections should consist solely of topical anesthetic (e.g., bupivacaine), and that there is no evidence that steroid is required for efficacy of these injections. Repeat injections should be linked to subjective and objective improvements and be a component of an active therapy program. The ACOEM guideline recommends an interval of at least three to four weeks between injections. If the results are unsatisfactory after the first set, the injections may be repeated. If subjective and objective improvements are not seen, further injections are not recommended.

An American Society of Interventional Pain Physicians (ASIPP) Practice Guideline, Interventional Techniques in the Management of Chronic Pain, Part 2.0 (Manchikanti et al., 2001) includes the following recommendations for trigger point injections:

- In the diagnostic or stabilization phase, a patient may receive trigger point injections at intervals of no sooner than one week and preferably two weeks.
- In the treatment or therapeutic phase (after the stabilization is completed), the frequency should be two months or longer between each injection provided that at least >50% relief is obtained for six weeks.
- In the diagnostic or stabilization phase, the number of trigger point injections should be limited to no more than four times per year.
- In the treatment or therapeutic phase, the trigger point injections should be repeated only as necessary judging by the medical necessity criteria and these should be limited to a maximum of six times for local anesthetic and steroid injections.
- Under unusual circumstances with a recurrent injury or cervicogenic headache trigger point injections may be repeated at intervals of six weeks after stabilization in the treatment phase.

Based on the available evidence and specialty society recommendations and guidelines, trigger point injections may be appropriate for selected patients with persistent chronic back, neck or myofascial pain despite appropriate conservative treatment. These injections may provide short-term improvement and allow a determination as to whether conservative treatment will be successful.

Dry Needling of trigger points has been proposed as a treatment of myofascial pain in various parts of the body, including low back pain. Dry-needling involves the insertion of a needle (acupuncture needle or other type of needle) into a trigger point without injecting any medication in an effort to deactivate the trigger point. The needle is not left in place; it is removed and is often followed by stretching exercises.

A Cochrane systematic review of acupuncture and dry needling (Furlan, et al., 2003, updated 2011) concluded that there is insufficient evidence to make any recommendation regarding acupuncture or dry needling for acute low back pain. For chronic low back pain, acupuncture and dry needling may be useful adjuncts to other therapies. Because most studies were of poor methodological quality, however, there is a need for higher quality trials in this area.

There is insufficient evidence in the peer-reviewed published scientific literature to demonstrate the efficacy of dry needling for the treatment of acute or chronic back pain.

Injection Therapy: Intradiscal Steroid

Intradiscal steroid injection, in which glucocorticoids are injected directly into the intervertebral disc under fluoroscopy, has been proposed as a method to reduce the degree of disc herniation and/or produce an inflammatory response.

According to the ACOEM evidence-based practice guidelines on low back disorders (2011) intradiscal steroid injections are not recommended for the management of acute low back pain. The available evidence indicates that intradiscal steroid injections are not effective. There is no quality evidence that these injections improve the natural history of the condition, or that they provide a treatment benefit compared to no treatment or treatment with epidural steroids. In addition, these injections may cause discitis, progression of disc degeneration, and calcification of the intervertebral disc. The guideline also states that intradiscal steroids are moderately not recommended for subacute or chronic low back pain.

The authors of one recent randomized controlled trial (Nguyen, et al., 2018) evaluated intradiscal glucocorticoid injection during discography (n=67) compared with discography alone (n=68) for treatment of chronic low back (Nguyen, et al., 2018). At one month following the injection, pain reduction was higher in the experimental group, however beginning at three months pain scores increased and were higher than that of the control group. At 12 months the groups did not differ in pain intensity and in most secondary outcomes (e.g., pain intensity, activity limitations, and health related quality of life scores). At present, the evidence remains insufficient to determine the safety and efficacy of intradiscal steroid injection for the treatment of back pain.

Percutaneous and Endoscopic Laminectomy and Disc Decompression Procedures of the Cervical, Thoracic, and /or Lumbar Spine

Minimally invasive techniques have been developed which utilize small incisions and employ the use of a multitude of instruments to decompress and/or remove herniated intervertebral disc material under endoscopic or radiologic view. The instruments used for these procedures include arthroscopic instruments, endoscopes, lasers, or other specially designed devices.

Percutaneous Disc Decompression: Percutaneous disc decompression involves surgical procedures performed to relieve pressure at the site of a herniated disc (e.g., chemical, thermal or mechanical). Hayes, Inc. published a technology directory report (Hayes, 2014, reviewed 2016, 2017a, 2018a) evaluating percutaneous disc decompression for cervical disc herniation. A total of 14 studies met inclusion criteria for the review with sample size ranging from 17 to 176 subjects, undergoing five types of PDD interventions (laser, no laser, nucleoplasty, Coblation, and full endoscopic laminotomy) for cervical disc herniation. Follow-up ranged from four weeks to approximately five years. A majority of the studies were limited by lack of controls. Hayes concluded there was insufficient evidence to draw conclusions regarding efficacy of percutaneous disc decompression for cervical disc herniation.

Manchikanti et al. (2013) conducted a systematic review to evaluate the evidence for percutaneous disc decompression (PDD) with Dekompressor in the management of chronic low back and lower extremity pain. The primary outcome was pain relief; secondary outcome measures included functional improvement, improvement of psychological status, opioid intake, and return to work. The authors stated that the evidence of effectiveness is limited, but the procedure may be recommended for patients with persistent pain after failure of other intervention techniques when microdiscectomy is not indicated.

Automated Percutaneous Lumbar Discectomy (APLD)/Automated Percutaneous Nucleotomy: Automated percutaneous lumbar discectomy (APLD), also referred to as automated percutaneous nucleotomy, is a minimally-invasive surgical procedure employing the use of an automated tissue removal instrument and is used for the removal of herniated lumbar intervertebral discs. In this procedure, a cannula is placed in the center of the disc under fluoroscopic guidance using a posterolateral approach. A probe connected to an automated cutting and aspiration device is then introduced through the cannula. The disc is then aspirated until no more nuclear material is obtained. The goal of treatment is to remove herniated disc material that may be pressing on the nerve root resulting in pain and other symptoms (Hayes, 2017).

Hayes, Inc. published a technology directory report (Hayes, 2014, reviewed 2015, 2016, 2017) evaluating automated percutaneous lumbar discectomy (APLD). The authors reviewed 16 peer-reviewed studies, including five comparison and 11 uncontrolled trials. According to the report, although APLD was determined to be a safe procedure that may improve symptoms of herniated disc, the quality of evidence was low and was insufficient to draw conclusions regarding efficacy of APLD for lumbar disc herniation.

A systematic review published by Manchikanti et al. (2013) evaluated the use of automated percutaneous mechanical lumbar discectomy for treatment of contained herniated lumbar discs. The primary outcome was pain relief; secondary outcome measures were functional improvement, improvement of psychological status, opioid intake, and return to work. Nineteen observation studies were included; of the three randomized trials reviewed, none met inclusion criteria for methodological quality assessment. The evidence is limited for automated percutaneous mechanical lumbar discectomy, but the procedure may provide appropriate relief in properly selected patients with contained lumbar disc herniation.

ASIPP 2013 Practice Guidelines for the Management of Chronic Spinal Pain, state that the evidence is limited to fair for APLD, and that the procedure is recommended in select cases.

The North American Spine Society (NASS) published evidence based guidelines for the diagnosis and treatment of lumbar disc herniation (NASS, 2012). Within these guidelines APLD is defined as "a procedure in which a cannula is inserted into the intervertebral disc space, usually with fluoroscopic guidance, and nuclear material is removed without direct visualization by nucleotome, laser or radiofrequency heat. This is an indirect visualization technique using the endoscope and fluoroscopic guidance." NASS recommends APLD as a treatment of lumbar disc herniation with radiculopathy. However, NASS noted the available evidence is poor (C recommendation) and that there is insufficient evidence to recommend for or against APLD compared with open discectomy in the treatment of subjects with lumbar disc herniation and radiculopathy.

American College of Occupational and Environmental Medicine (ACOEM) evidence-based practice guidelines on low back disorders, surgical considerations (2011) states that there is no quality evidence that automated percutaneous discectomy is an effective treatment for any back or radicular pain problem.

Hirsch et al. (2009) conducted a systematic evaluation of the literature to determine the effectiveness of APLD. The primary outcome measure was pain relief; short term effectiveness was defined as significant (>50%) pain relief at six months, and long term effectiveness was defined as significant pain relief at one year. Other outcome measures included functional improvement, improvement in psychological status, and return to work. The authors concluded that this systematic review indicates Level II-2 evidence for APLD; APLD may provide appropriate relief in properly selected patients with contained lumbar disc prolapse. (Level II-2 evidence, as defined by the U.S. Preventive Services Task Force as evidence obtained from well-designed cohort or case-control analytic studies, preferably from more than one center or research group.). The authors acknowledged the paucity of randomized controlled trials in the literature as a limitation.

A Cochrane review of surgery for lumbar disc prolapse, published in 2003 and updated in 2007 (Gibson and Waddell), assessed the effects of available surgical interventions and states that trials of APLD suggest that clinical outcomes are at best fair and certainly worse than microdiscectomy, although the importance of patient selection is acknowledged. The authors stated that there is a need for high-quality randomized controlled trials on APLD and for long-term studies into the effects of surgery on the lifetime natural history of disc disease. The Cochrane review concluded that unless or until better scientific evidence is available, APLD should be regarded as a research technique.

There is insufficient evidence in the peer-reviewed medical literature to support the safety and efficacy of APLD. Results of published studies are inconsistent and do not demonstrate long-term improvement. There is no evidence that APLD is as effective as discectomy/microdiscectomy.

Endoscopic Anterior Spinal Surgery / Yeung Endoscopic Spinal Surgery (YESS)/ Selective Endoscopic Discectomy (SED): The Yeung Endoscopic Spinal System (Richard Wolf Surgical Instrument Corporation) is a specialized endoscope developed for percutaneous spinal endoscopy and discectomy. This endoscope has multi-channel inflow and outflow ports, allowing visualization through one port and suction or other therapeutic services through the working port. The YESS is also used for other spinal procedures, including arthroscopic microdiscectomy, radiofrequency ablation, injection of intraoperative steroids, and laser disc decompression and ablation. Selective Endoscopic Discectomy™ (SED), performed with the YESS endoscope, is used to shrink and remove herniated discs.

Percutaneous Endoscopic Diskectomy (PELD): PELD is a minimally invasive procedure in which indirect access to the herniated disc is made under fluoroscopic guidance using an endoscope and specialized instruments; removal of the disc occurs using laser or other mechanical means. Within a Health Technology Brief document published by Hayes, eight studies were reviewed evaluating safety and efficacy of PELD as treatment of primary lumbar disc herniation were reviewed (Hayes, 2017b). Hayes concluded although overall that the body of evidence was low-quality the evidence consistently suggests PELD performs similarly to other surgical alternatives for decompression when there was failure of conservative management. However, Hayes acknowledged "substantial uncertainty exists due to the overall quality of the body of evidence and additional studies are needed to evaluate comparative effectiveness and determine patient selection criteria when employed for primary disc herniation". In a second Health Technology Brief document Hayes evaluated PELD as treatment of recurrent lumbar disc herniation. A total of six studies were included in the review. According to the report, overall a low quality body of evidence suggests PELD may be inferior to comparison treatments for decreasing back pain and that PELD may have higher recurrence rates than comparison treatments (Hayes, 2018c).

Percutaneous Endoscopic/Arthroscopic Microdiscectomy: Percutaneous endoscopic/arthroscopic microdiscectomy is a procedure that involves the use of an endoscopic or arthroscopic guided approach to removing herniated disc material. The herniated disc is accessed and removed through small incisions using cannulas and other instruments.

Endoscopic Disc Decompression/Ablation/Annular Modulation using Disc-FX™ System (Elliquence LLC, Baldwin, NY): The Disc-FX™ system is a single-use disposable kit used to perform minimally invasive lumbar disc procedures, including endoscopic disc decompression, nucleus ablation and annulus modulation.

There is a steep learning curve for procedures used to access and treat lesions with endoscopic guidance. The purported advantages of endoscopic discectomy or its superiority over microsurgical discectomy have not been demonstrated in the medical literature. There are no prospective controlled clinical trials of the YESS or the Disc FX system, nor are there any prospective studies with long-term follow-up. The efficacy of endoscopic spinal surgery and surgery with the YESS or Disc FX System has not been established in the peer-reviewed medical literature.

Percutaneous Laminotomy/Laminectomy/Percutaneous Spinal Decompression (e.g., mild® Procedure): The mild® Device Kit (Vertos Medical, Inc., Aliso Viejo, CA) received U.S. Food and Drug Administration (FDA) approval on February 4, 2010. The device kit is a set of specialized arthroscopic surgical instruments intended to be used to perform lumbar decompressive procedures for the treatment of various spinal conditions. The mild device is used for image-guided minimally invasive lumbar decompression, referred to as the mild (minimally invasive lumbar decompression) procedure. The procedure is performed under fluoroscopic guidance through a dorsal approach to the spine. The instruments are inserted and positioned on the posterior spinal lamina, to the left or right of the spinous process. The tools are used to cut and remove tissue and bone from the posterior side of the lumbar spine to create a space inside the spine that can help decompress some of the spinal nerves. The mild® procedure has been proposed as a minimally invasive alternative to conservative treatment or surgical decompression for the treatment of lumbar spinal stenosis.

Staats et al. (2016) reported the six month results of a randomized controlled trial comparing the treatment outcomes of the MILD procedure (n=149) and epidural steroid injection (n=153) for lumbar spinal stenosis. Outcomes were measured using ODI, numeric pain rating scale (NPRS), and Zurich Claudication questionnaire. Primary efficacy was the proportion of ODI responders, tested for statistical superiority of the MILD group versus the active control grou with secondary efficacy proportion of NPRS and ZCQ responders using validated MIC thresholds. At 6 months, all primary and secondary efficacy results provided statistically significant evidence that MILD is superior to the active control of epidural steroid injection. The authors are continuing to obtain outcomes extending to two years post procedure. Limitations of the study noted by the authors included lack of blinding and the possibility of a higher non-responder rate versus standard of care in both groups due to restrictions of the study for use of adjunctive therapies.

Hayes, Inc. published a Health Technology Brief evaluating minimally invasive lumbar decompression for lumbar spinal stenosis (Hayes, 2015). One randomized controlled trial, six prospective cohort studies, and two

retrospective studies were included in the review. The average follow-up was 24 months and the range of subjects was reported at 27-78. All subjects had symptomatic lumbar spinal stenosis, and the majority had failed previous nonsurgical conservative therapy for lumbar spinal stenosis. Most subjects were treated bilaterally, at 2 lumbar (L) levels, principally at L4 to L5 and/or L3 to L4. According to the published report the mild procedure was safe over the short-term, relieved pain, reduced disability, and improved quality of life in most subjects. However Hayes acknowledged there is insufficient evidence to support long-term safety and effectiveness.

Chopko (2013) reported two-year outcomes of mild lumbar decompression in the treatment of patients with neurogenic claudication associated lumbar spinal stenosis. The study included 45 of 58 patients included in an earlier analysis of one-year results Of the 13 patients unavailable at two years and not included in the two-year cohort, 3 underwent lumbar spine surgery, one died of unrelated causes, and nine did not respond or withdrew from the study. Outcome measures included the Visual Analog Scale (VAS), Oswestry Disability Index (ODI), and Zurich Claudication Questionnaire (ZCQ). At two years, VAS improved from an average of 7.2 at baseline to a mean of 4.8 ($p<0.0001$); 79% reported an improvement in VAS scores and 29% reported lack of improvement or no improvement. Improvement in physical function and mobility was significant, as measured by the ZCQ and ODI. There were no major adverse events or device-related complications. Limitations of the study include lack of a control group or blinding, and significant numbers of patients lost to follow-up.

Brown (2012) conducted a double-blind randomized study of epidural steroid injections (ESI) vs. the mild procedure in patients with symptomatic lumbar spinal stenosis (n=38). The included patients had painful lower limb neurogenic claudication, with hypertrophic ligamentum flavum as a contributing factor, and had failed conservative treatment. Patients were randomized to the mild procedure (n=21) or ESI (n=17). At six weeks, 76% of the patients in the mild group reported a two point improvement in VAS scores in compared to 35% of patients in the ESI group. There was a significant improvement in Oswestry disability scores in the mild group at six weeks ($p<0.05$), while in the ESI group improvement was not statistically significant. There were no procedure-related or device-related complications in either group. At six weeks, 17 of 21 patients in the ESI group crossed over to the mild procedure. Comparative 12 week outcome data was therefore not available. It is difficult to draw conclusions from this study due to the small number of participants and lack of data on long term outcomes. In addition, patients in the ESI group were treated with a single interlaminar injection; which is generally not typical of ESI treatment.

An observational study conducted by Mekhail et al. (2011) at 11 sites reported one year outcome data on 58 patients treated for spinal stenosis with the mild procedure, with statistically significant improvement in VAS scores and ODI. A single-site case series conducted by Mekhail et al. in 2012 reported 12-month outcomes for 40 consecutive patients treated for spinal stenosis with the mild procedure. There was significant functional improvement and decreased disability as measured by the Pain disability index (PDI), Roland-Morris Disability Questionnaire, walking distance, standing time, and VAS scores.

Deer and Kapurai (2010) published a retrospective review to evaluate the acute safety of the mild procedure. Charts of 90 consecutive patients who underwent the mild procedure for decompression of central lumbar stenosis were reviewed. No major adverse events or complications related to the devices or procedure were reported. There were no incidents of dural puncture or tear, blood transfusion, nerve injury, epidural bleeding or hematoma. Because the review did not include outcome data, no determination as to clinical efficacy can be made. The authors stated that prospective randomized studies have been initiated to collect patient outcomes data regarding post-treatment pain and functional capacity.

Chopka and Caraway (2010) published a preliminary report of MiDAS I (mild Decompression Alternative to Open Surgery, a multi-center prospective case series to evaluate the mild procedure for treatment of symptomatic lumbar spinal stenosis. The procedure was offered as an alternative to surgery or continued medical management. No major device or procedure-related complications were reported. At six weeks, statistically significant reduction of pain as measured by the Visual Analog Scale, Oswestry Disability Index, and Zurich Claudication Questionnaire, and Standard Form -12. (SF-12).

Percutaneous/Laparoscopic Laser Discectomy/Decompression/ Laser-Assisted Decompression (LADD): Laser-assisted discectomy, also called laser-assisted disc decompression (LADD) or laser disc decompression, is a minimally-invasive procedure proposed as an alternative to discectomy/microdiscectomy. It is intended to

provide symptomatic relief of pain cause by a contained herniated intervertebral disc. Laser light energy is used to vaporize part of the nucleus pulposus, resulting in a reduction in intradiscal pressure. Several approaches may be used, depending on the location of the disc and type of laser being used. With one method, a needle is inserted percutaneously into the disc approximately one centimeter (cm) posterior to the disc center, and a flexible optical quartz fiber is threaded through the needle into the disc, delivering laser energy to vaporize and coagulate the nucleus pulposus. In the laparoscopic approach, a trocar is inserted periumbilically and the abdomen is inflated with carbon dioxide. Additional trocars are placed above the pelvic brim. The large and small bowels are retracted, and the iliac bifurcation is identified. The posterior peritoneum is opened and retracted. The L5-S1 interspace is identified and its margins confirmed by x-ray. The annulus of the disc is opened and excised with the neodymium: yttrium-aluminum-garnet (Nd: YAG) laser. Targeted percutaneous laser disc decompression has been described as a PLDD in which the area of laser evaporated nucleus pulposus is closer to the area of disc herniation (middle zone), in contrast to one-third into the intervertebral space (Luo, et al., 2014).

Updated ASIPP Practice Guidelines for the Management of Chronic Spinal Pain (2013) state that the evidence for percutaneous lumbar laser disc decompression is limited.

ACOEM evidence-based practice guidelines on low back disorders, surgical considerations (2011) states that there is no quality evidence that laser discectomy is an effective treatment for any back or radicular pain problem.

A review of the literature published by Schenck et al. (2006) evaluated 16 clinical trials representing a total of 1579 patients. Most were case series with small sample sizes, making interpretation of success rates difficult. Generalization of the results into general clinical practice remains difficult due to different inclusion and exclusion criteria, laser types, and outcome measures as well as the variation in duration of follow-up. These shortcomings prevent a valid comparison to studies evaluating the outcome of conventional surgical treatment for lumbar disc herniation. The authors concluded that well-designed research of sufficient scientific strength comparing percutaneous laser disc decompression to both conventional surgery and conservative management is needed to determine whether this procedure has a role in the treatment of lumbar disc herniation.

A Cochrane systematic review of surgery for lumbar disc prolapse, published in 2003 and updated in 2007 (Gibson and Waddell), assessed the effects of available surgical interventions and states that trials of laser discectomy suggest that clinical outcomes are at best fair and certainly worse than microdiscectomy, although the importance of patient selection is acknowledged. The authors stated that there is a need for high-quality, randomized controlled trials on laser discectomy and for long-term studies into the effects of surgery on the lifetime natural history of disc disease. The Cochrane Review further concluded that unless or until further scientific evidence is available, laser discectomy should be regarded as a research technique.

There is insufficient evidence in the published medical literature to demonstrate the safety, efficacy and long-term outcome of laser discectomy. There are no randomized controlled trials that evaluate laser discectomy and compare this procedure to established treatment methods.

Endoscopic Anterior Cervical Disc Decompression: Cervical Deuk Laser Disc repair is an endoscopic anterior cervical transdiscal surgical procedure under investigation for treatment of symptomatic cervical disc disease (e.g., spondylosis, stenosis, herniations). The repair involves three procedures, a selective partial discectomy, foraminoplasty, and annular debridement. The procedure may be performed as an alternative to anterior cervical discectomy and fusion for treatment of cervical degenerative disc disease. In theory, the endoscopic approach does not require the removal of the intervertebral disc to reach the posterior disc complex, as a result there is no postoperative iatrogenic instability or deformity. In addition, it is not necessary to stabilize the spine with interbody devices, fusion, implants or biologics. At present, evidence in the peer-reviewed published scientific literature is limited to few uncontrolled case series and is insufficient to support the safety and efficacy of endoscopic anterior cervical disc decompression (i.e., Cervical Deuk Laser Disc repair).
There is insufficient evidence in the medical literature to demonstrate the safety and efficacy percutaneous laminotomy/laminectomy approaches, including the mild procedure. Additional well designed trials with long-term outcome data are needed to determine how this procedure compares to available alternative treatments for lumbar stenosis.

Thermal Intradiscal Procedures

Intraosseous Radiofrequency Nerve Ablation: Radiofrequency ablation of intraosseous nerves is an emerging technology intended for treatment of chronic low back pain. Intraosseous nerves are reportedly found within the vertebrae, are referred to as basiverterbal nerves and are present in the basiverterbral foramen. Authors contend the nerves may be a source of intraosseous back pain and that interruption of the nerve pathway using radiofrequency will relieve the associated pain. One device under investigation, The INTERCEPT® System (Relievant MedSystems, Inc, Redwood City, CA) recently received FDA approval for use as a minimally invasive radiofrequency system for treatment of chronic lumbar back pain at one or more levels (i.e., L3 to S1), when back pain is present despite at least six months of conservative care and is accompanied by either Type I or Type 2 Modic changes on MRI (FDA K153272). Evidence in the peer reviewed, published scientific literature evaluating ablation of basiverterbal nerves consists mainly of pilot studies and is insufficient to support safety and efficacy at this time; additional studies are needed to support strong evidence-based conclusions.

Intradiscal Electrothermal Annuloplasty (e.g., intradiscal electrothermal therapy [IDET™]): Intradiscal electrothermal annuloplasty (IEA), also referred to as intradiscal electrothermal therapy (IDET™), intradiscal electrothermal percutaneous annuloplasty, intradiscal thermal annuloplasty, or targeted intradiscal thermal therapy, is a minimally invasive procedure that has been proposed as an alternative to spinal fusion for the treatment of chronic discogenic low back pain. Following a provocative discogram, IEA is performed by inserting a catheter into the annulus and threading a flexible electrode through the catheter and around the inside of the disc, pressing against the posterior edge of the annulus. The electrode is then heated to a temperature of 90° F for up to 17 minutes. Analgesics and/or antibiotics are then injected and the catheter is withdrawn. The heating of the electrode denatures the collagen of the annulus and coagulates the nerve endings, with the ultimate goal of relieving back pain.

Targeted disc decompression is a minimally invasive procedure which involves use of a heat resistant intradiscal catheter. Although similar to IDET in theory, the catheter used in this procedure is a 1.5 cm heating coil, the shrinkage effect and intradiscal pressure changes are generally similar. During targeted disc decompression under fluoroscopic guidance a trocar is inserted to the annulus and advanced to the inner annulus. The intradiscal catheter is pushed forward to the nucleus, and a wire is advanced between the annulus and nucleus. The disc is heated to 90°. The inner part of the disc reaches a target temperature of 60-65° C causing the disc to shrink, and thereby reducing discal pressure. The epidural space is heated to a lower temperature, approximately 30° C. There is a paucity of evidence evaluating clinical outcomes (Adakli, et al., 2015; Schaufele, et al., 2008) and the effectiveness of this method of treatment remains unknown.

A systematic review of percutaneous thermocoagulation intradiscal techniques for discogenic low back pain (Urrutia, et al., 2007) included six studies (283 patients) of IEA and percutaneous intradiscal radiofrequency thermocoagulation (PIRFT). The studies included in the review of IEA consisted of two randomized controlled trials (Freeman and Pauza, discussed above), and two nonrandomized trials. One of the nonrandomized trials assessed the effectiveness of IEA vs. a rehabilitation program consisting of physical therapy, exercise, education and counseling, and the other compared IEA to PIRFT. In both randomized controlled trials that assessed IEA vs. placebo, pain, disability, and quality of life were assessed for six months. There was a small difference in favor of IEA in one study (Pauza), although the difference in disability was clinically irrelevant, while there was no difference in the higher-quality, more recent study (i.e., Freeman). The Freeman study also assessed depression, sitting and work tolerance, medication and neurologic deficit, and found no difference between IEA and placebo. In the nonrandomized trial comparing IEA and a rehabilitation program, the proportion of patients with a ≥ 50% reduction in pain was higher in the IEA group at both 12 and 24 months. The authors concluded that the available evidence does not support the efficacy or effectiveness of percutaneous thermocoagulation intradiscal techniques for the treatment of discogenic low back pain. The authors noted that previous case reports suggested that the procedure might be effective, but these reports, derived from data registries, could not take into account the effect of regression to the mean, the natural history of the condition, the placebo effect, and other potential confounders such as co-interventions and other mechanical and psychosocial factors.

Freeman (2006) conducted a systematic review of the evidence of the efficacy of IEA. The review included 11 prospective cohort studies, five retrospective studies, and two randomized controlled trials. The prospective

cohort studies reported on a total of 256 patients with a mean follow-up of 17.1 months (range 12–28 months). The mean improvement in the VAS for back pain was 3.4 points (range 1.4–6.5), and the mean improvement in ODI was 5.2 points (range 4.0–6.4) The five retrospective studies included 379 patients and reported that between 13 and 23% of patients subsequently underwent surgery for low back pain within the study period. The two randomized controlled trials, Pauza, 2004 and Freeman, 2005, provided inconsistent evidence, as described above. The author concluded that the evidence for efficacy of IEA remains weak and has not passed the standard of scientific proof.

A randomized, double-blind controlled trial was conducted by Freeman et al. (2005) to test the safety and efficacy of IEA compared with placebo for treatment of chronic discogenic low back pain. Patients with one- or two-level symptomatic disc degeneration with posterior or posterolateral annular tears who failed to improve after conservative therapy were considered for the study. Patients were randomized on a 2:1 ratio to IEA (n=38) or a sham procedure (n=19). An independent technician connected the catheter to the generator and delivered electrothermal energy to only the treatment group. Surgeon, patient, and independent outcome assessor were all blinded to the treatment. Low Back Outcome Score (LBOS), Oswestry Disability Index, SF-36, the Zung Depression Index (ZDI) and Modified Somatic Perceptions Questionnaire (MSPQ) were measured at baseline and at six months. Successful outcome was defined as no neurological deficit, improvement in LBOS of greater than seven points, and improvement in SF-36 subsets (i.e., physical function and bodily pain) of greater than one standard deviation. No patient in either group showed improvement of greater than seven points in LBOS or greater than one standard deviation in the specified SF-36 domains. Mean ODI was 41.42 at baseline and 39.77 at six months for the IEA group compared with 40.74 at baseline and 41.58 at six months for the placebo group. There was no significant change in ZDI or MSPQ for either group. The authors concluded that there was no significant benefit from IEA over placebo.

Pauza et al. (2004) conducted a prospective, randomized controlled trial comparing IEA with placebo. Sixty-four patients were randomized to receive IEA or sham treatment. The subjects were not aware of which treatment they received. Outcome tools used were the VAS, the SF-36, and the Oswestry Disability Scale. It is unclear whether the post-procedure outcome examiners were blinded regarding which patients received true IEA. The modest success rates reported in this trial were much less compelling than those from previously published uncontrolled studies. The investigators reported that both groups showed improvement, with mean improvements higher in the active treatment arm. Using the VAS, IEA demonstrated a 2.4-point decrease in the mean pain score. An 11-point decrease was reported in the mean Oswestry score. The baseline disability level of most of the patients was low, and recruitment methods may have led to patient selection bias. The sample size was insufficient to achieve adequate statistical power, and follow-up was limited to six months. In addition, eight patients who dropped out of the study were not included in the data analysis. While the results of this study suggest that IEA may improve outcomes for patients with discogenic low back pain, these methodological flaws make it impossible to draw valid conclusions about the efficacy of this technology.

ASA 2010 Practice Guidelines for Chronic Pain Management states that Thermal intradiscal procedures: intervertebral disc annuloplasty (IDET) may be considered for young, active patients with early single-level degenerative disc disease with well-maintained disc height.

ACOEM evidence-based practice guidelines on low back disorders (2011) states that IDET is not recommended for treatment of acute, subacute, or chronic low back pain or any other back-related disorder.

Updated American Society of Interventional Pain Physicians (ASIPP) Evidence-Based Practice Guidelines in the Management of Chronic Spinal Pain (Manchicanti, et al., 2013).state that the evidence for IDET is limited to fair, and that the procedure may be performed in a select group of patients with discogenic pain non-responsive to conservative modalities, including epidural injections.

The safety, efficacy, and long-term outcomes of intradiscal electrothermal annuloplasty in the treatment of patients with chronic discogenic low back pain have not been established in the published medical literature. This procedure has not been proven to achieve equivalent or improved patient outcomes compared to available and established alternatives. In addition, the long-term effect of thermal coagulation of intervertebral discs has not been determined.

Percutaneous Intradiscal Radiofrequency Thermocoagulation (PIRFT)/ Intradiscal Radiofrequency Thermomodulation/Percutaneous Radiofrequency Thermomodulation: PIRFT may also be referred to as intradiscal radiofrequency thermomodulation or percutaneous radiofrequency thermomodulation. This procedure, used to treat chronic discogenic low back pain, is similar to intradiscal electrothermal therapy (IDET). With IDET, a catheter with a temperature-controlled, thermal-resistive coil is inserted under fluoroscopic guidance into the posterior annular wall of the affected disc, causing annular denervation. With PIRFT, the catheter is placed into the center of the disc rather than the annulus. The mechanism of reported clinical improvement with PIRFT is unclear, since the temperature at the annulus has been found to be well below the temperature required for annular denervation (Davis, 2003). More recently bipolar radiofrequency thermocoagulation has been investigated as treatment of discogenic low back pain (Zhang, et al., 2016). During bipolar radiofrequency thermocoagulation two cannulas are heated simultaneously in contrast to a single cannula as in PIRFT.

Urrutia et al. (2007) conducted a systematic review to evaluate the evidence for the percutaneous thermocoagulation intradiscal techniques IDET and PIRFT in the treatment of discogenic low back pain. Six studies with a total of 283 patients were included. Two randomized controlled trials, including the Barendse trial described below, showed no differences between PIRFT and placebo and between different PIRFT techniques. The authors stated that, although previous case reports and nonrandomized trials suggested positive results, results from randomized clinical trials show that PIRFT is not effective for the treatment of discogenic low back pain.

Barendse et al. (2001) conducted a randomized, double-blind, placebo-controlled trial of PIRFT using the Radionics discTRODE™ RF annuloplasty system. The Radionics system was approved by the U.S. Food and Drug Administration (FDA) through the 510(k) process in October 2000. A total of 28 patients were selected who had a history of at least one year of chronic low back pain, evidence of radiculopathy on neurological examination and a positive response to discography. Patients were randomly assigned to one of two treatment groups. Patients in the radiofrequency group (n=13) received a 90-second 70 degree centigrade (C) lesion of the intervertebral disc. Patients in the control group (n=15) underwent the same procedure but without the use of radiofrequency current. The treating physician and patients were blinded to group assignment. Patients were assessed by a blinded investigator before treatment and eight weeks after treatment. There was no difference between the two groups based on visual analog scores for pain, global perceived effect and the Oswestry disability scale. The treatment was considered a success in one patient in the radiofrequency group and two patients in the control group. The authors concluded that PIRFT is not effective in reducing chronic discogenic low back pain.

Updated American Society of Interventional Pain Physicians (ASIPP) Evidence-Based Practice Guidelines in the Management of Chronic Spinal Pain (Manchicanti, et al., 2013) state that the evidence is limited for discTRODE (PIRFT).

According to the evidence-based clinical practice guideline from the American Pain Society, Interventional Therapies, Surgery, and Interdisciplinary Rehabilitation for Low Back Pain (Chou et al., 2009), the level of evidence for PIRFT is poor. The authors were unable to estimate the net benefit of the procedure in the treatment of patients with nonradicular low back pain.

American College of Occupational and Environmental Medicine (ACOEM) practice guidelines on low back disorders, (2011) states that PIRFT is strongly not recommended for treatment of acute, subacute, or chronic low back pain, particularly including discogenic low back pain.

There is insufficient evidence in the published medical literature to demonstrate the safety, efficacy and long-term outcomes of PIRFT. There is no evidence that this procedure is as effective as established alternatives for the treatment of back pain.

Intervertebral Disc Biacuplasty/Cooled Radiofrequency: The Baylis TransDiscal™ system (Baylis Medical Inc., Montreal Canada) is used to perform intervertebral biacuplasty. The TransDiscal system received FDA approval through the 510(k) process on December 19, 2006. The system is designed to deliver controlled RF energy via two electrodes. Two TransDiscal Probes and the Pain Management Pump Unit, connected to the Baylis Pain Management Generator, work in concert to deliver RF energy. The system is intended to be used to

create RF lesions in nervous tissue, including that which is situated in intervertebral disc material. Separate components of the system had previously received FDA approval; the 2006 approval combined the indications of the predicate devices. (U.S. FDA website).

Intervertebral biacuplasty using the TransDiscal system has been investigated in the treatment of lumbar discogenic pain. The procedure is performed using a bipolar approach in conjunction with internally water-cooled RF probes to coagulate and decompress disc material. Two introducers are placed bilaterally in the posterolateral discs and the TransDiscal probes are then inserted into the introducers. RF energy is applied and directed through the disc between the two probe electrodes. The cooling system is designed to maintain and balance the temperature in each probe, allowing RF energy to be delivered with greater power to heat a larger volume of disc tissue, while avoiding overheating of adjacent tissue.

Desai et al (2016) conducted a prospective randomized clinical trial to compare outcomes of intradiscal biacuplasty and conventional medical management (n=29) with subjects who received conventional medical management alone (n=34). At six months following treatment, subjects were allowed to cross-over to the experiment group and were subsequently followed for an additional six months. The initial experimental group was followed for 12 months. The primary outcome measured was pain level change using VAS with secondary outcomes that included assessments of function, disability, mental health, quality of life and use of opioids. At 12 months post procedure pain reduction, and improvement in function and disability scores were reported to be statistically significant and clinically meaningful in the original experimental group. The authors reported 50% of the cross over group responded to the intervention, with mean outcomes similar to the original group. Daily opioid intake was reduced in both the original and cross-over group. In the authors opinion the study demonstrated long-term effectiveness of intradiscal biacuplasty combined with conventional medical management. Limitations of the study included small sample populations, one-year outcomes, and inconsistent follow-up as reported by the authors.

Kapural et al. (2013) conducted a randomized controlled trial to evaluate transdiscal radiofrequency biacuplasty (IDB) for discogenic lower back pain (n=59). Twenty nine patients were randomized to IDB and 30 to a sham procedure. All had a history of chronic low back pain for longer than six months. The primary outcome measures were physical function, pain, disability, and opioid usage. At six months, there were statistically significant improvements in the treated group compared to the control group in physical function (p=0.129), pain (p=0.006), and disability (p=0.037). There was no significant difference between groups in opioid usage. Limitations of the study include lack of long-term follow-up and small sample size. Of 1894 patients screened, only 59 were included. Kapural et al. (2015) reported in follow-up that the improvements initially reported at 6 months were maintained at nine and 12 months.

Kapural et al. (2008) conducted a pilot study (n=15) of intervertebral disc biacuplasty in the treatment of lumbar discogenic pain. Included patients had a history of chronic low back pain unresponsive to nonoperative care for greater than six months, back pain exceeding leg pain, concordant pain on provocative discography, disc height > 50% of control, and evidence of single-or tow-level degenerative disc disease without evidence of additional changes on MRI. Outcomes were evaluated by questionnaire at one, three and six months. Median VAS pain score decreased from 7 cm at baseline to 4 cm at one month and 3 cm at six months. The Oswestry score improved from 23.3 to 16.5 at one month, with similar results at six months. The SF-36 physical functioning scores improved from 51 to 70 points at six month, and the Bodily Pain score improved from 38 to 54. There was no significant change from baseline in daily opioid use. No procedure-related complications were reported.

Updated ASIPP guideline referenced above (Manchicanti, et al., 2013) state that the evidence for biacuplasty is limited to fair, and that the procedure may be performed in a select group of patients with discogenic pain non-responsive to conservative modalities, including epidural injections.

There is insufficient evidence in the published medical literature to demonstrate the safety, efficacy and long-term outcomes of intervertebral disc biacuplasty.

Coblation® Nucleoplasty™/Disc Nucleoplasty/Decompression Nucleoplasty/Plasma Disc Decompression: Coblation Nucleoplasty, also referred to as disc nucleoplasty, decompression nucleoplasty, or plasma disc decompression, is a minimally invasive technique for decompression of contained herniated discs using the

Arthrocare Perc-D Coblation Spine Wand. The Spine Wand is a bipolar radiofrequency device designed to decompress the disc nucleus with energy and heat. The tip of the wand is slightly curved to allow channeling. Nucleoplasty uses Coblation technology, which generates a low temperature plasma field intended to allow precise ablation with minimal risk of thermal injury. The tip temperature is 50–70 degrees C. A plasma field, a millimicron-thick layer of highly energized particles, causes molecular dissociation of the disc material directly in front of the tip. This creates a channel from the posterolateral annulus to the anteromedial annulus. During withdrawal, the coagulation mode is used. Six separate channels are typically created. The thermal effect is reported to result in denaturization of the Type II collagen, causing shrinkage of the surrounding collagen and widening of the channel (Sharps, et al., 2002; Singh, et al., 2003; Davis, 2003).

Studies evaluating nucleoplasty consist primarily of uncontrolled case series (Sharp and Isaac, 2002; Singh et al., 2003; Bhagia et al., 2006; Cincu, et al., 2015; Ren, et al., 2015, Adakli, et al., 2015). One RCT evaluating percutaneous cervical nucleoplasty (PCN) versus pulsed radiofrequency (PRF) of the dorsal root ganglion for treatment of cervical disc herniation has been published (Halim, et al., 2017). The trial involved 34 patients with radicular pain treated with either PCN (n=17) or PRF (n=17). At three months both groups had significant reduction in pain, although none was superior to other. This study is limited by small sample and short term outcomes; studies evaluating long-term outcomes supporting clinical efficacy are lacking.

A Cochrane review of surgery for lumbar disc prolapse (Gibson and Waddell, 2007) states that, unless or until better scientific evidence is available, Coblation therapy should be regarded as a research technique.

Updated ASIPP Practice Guidelines for the Management of Chronic Spinal Pain (2013) state that the evidence is limited to fair for nucleoplasty, and that the procedure is recommended in select cases.

The evidence-based clinical practice guideline from the American Pain Society, Interventional Therapies, Surgery, and Interdisciplinary Rehabilitation for Low Back Pain (Chou et al., 2009), states that there are no trials evaluating Coblation nucleoplasty. The authors were unable to estimate the net benefit of the procedure in the treatment of patients with back pain, with or without radiculopathy.

ACOEM evidence-based practice guidelines on low back disorders, surgical considerations (2011) state that there is no quality evidence that Coblation therapy is an effective treatment for any back or radicular pain problem.

The safety, efficacy and long-term outcomes of Coblation nucleoplasty have not been demonstrated in the published medical literature. In addition, the long-term consequences of thermal denervation and tissue damage associated with this procedure are unknown.

Other Minimally Invasive Procedures

Baxano iO-Flex® System: The Baxano iO-Flex® System (Baxano, Inc., San Jose, California) is a method of decompression that employs an "inside-out" approach according to the manufacturer. The system consists of a microblade shaver and several accessories which can be used in either minimally invasive or open procedures and according to the manufacturer instead of cutting through healthy pieces of the spine, the iO-Flex® System uses a fine surgical wire to guide the thin iO-Flex® shaver instrument to the location of the overgrown bone and tissue to shave away the stenosis from the inside out. Use of this method is purported to preserve facet joint integrity/lamina, thus maintaining stability and minimizing muscle trauma by allowing decompression of up to 4 nerve roots through a single-point access and unlike traditional rigid instruments used for lumbar decompression the Baxano iO-Flex System utilizes thin flexible instruments. The FDA approvals for these devices suggests the devices are designed for accessing, cutting, and biting soft tissue and bone during surgery involving the spinal column. Nevertheless, evidence in the peer-reviewed scientific literature evaluating these emerging technologies is lacking, therefore evidence based conclusions cannot be made.

Other Intradiscal Injections: Intradiscal oxygen-ozone injection has been proposed as a minimally invasive treatment of lumbar disc herniation. Ozone is reported to be a strong oxidizer that rapidly reacts and oxidizes the proteoglycans in the nucleus pulposus. The procedure is based on the premise that a small reduction in disc volume may result in a significant reduction in pain. The technique is similar to discography and other percutaneous disc procedures. Under image guidance, a needle is positioned into the nucleus pulposus, 1-3 ml

of oxygen/ozone from a medical ozone generator is injected into the disc, and 7-9 ml is injected into the paravertebral muscle surrounding the disc. A pain suppressant (e.g., bupivacaine) and/or corticosteroid may also be injected. Oxygen/ozone injection is primarily practiced in Europe and Asia. No medical ozone generators for use in intradiscal injection have received U.S. Food and Drug Administration (FDA) approval.

A meta-analysis of the effectiveness and safety of ozone treatments for herniated lumbar discs conducted by Steppan et al. (2010) reported a mean improvement of 3.9 for Visual Analog Scale (VAS) and 25.7 for Oswestry Disability Index (ODI). The likelihood for showing improvement on the Modified McNab outcome scale was reported as 79.7%, and the likelihood of complications, 0.064%. It is difficult to draw firm conclusions from this analysis due to the quality of included studies. Of 11 included studies, 9 were retrospective, 2 were prospective, and one consisted of unpublished data. In some studies data required for meta-analysis was not reported, and was estimated by the authors.

There is insufficient evidence in the published medical literature to demonstrate the safety and efficacy of ozone injection or to determine how this treatment compares to other available treatment options for disc herniation. In addition, no medical ozone generators have received FDA approval.

Other agents, such as methylene blue, tumor necrosis factor (TNF)-alpha, mesenchymal stem cells, and platelet rich plasma have been investigated as treatment of chronic back pain, however RCTs are lacking; there is a paucity of evidence in the peer-reviewed published scientific literature (Akeda, et al., 2017; Peng, et al., 2010; Cohen, et al., 2007) and long term outcomes have not yet been evaluated through well-designed studies.

Epiduroscopy/Epidural Myeloscopy/Epidural Spinal Endoscopy: Epiduroscopy, also referred to epidural myeloscopy or epidural spinal endoscopy, is a technique that uses an epiduroscope to visualize the epidural space. It is used in the diagnosis and treatment of intractable low back pain, especially in patients with radiculopathy. Scarring of the epidural space occurs in approximately 50% of patients who have undergone multiple surgeries for back pain. This may lead to formation of epidural fibrosis, adhesions of the nerve root, causing recurrence of pain. In epiduroscopy, a needle is advanced into the sacral canal through which a guide-wire is inserted and advanced. The needle is replaced with an introducer sheath through which an endoscope is inserted. Saline is flushed through the system to expand the sacral space, which can then be examined through the endoscope. Although epiduroscopy may be performed as a diagnostic procedure, it is usually performed in conjunction with the Racz procedure or epidural adhesiolysis. There is no evidence in the published medical literature to support the use of epiduroscopy as a diagnostic procedure. There is no evidence that this invasive technique provides clinically useful information not available with current noninvasive diagnostic methods.

There is insufficient evidence in the published medical literature to support the use of epiduroscopy in the diagnosis or treatment of back pain. There are no published, well-designed, prospective clinical trial of adequate size that evaluates these procedures nor is there information available regarding long-term outcomes. The safety, efficacy and long-term outcomes of these procedures have not been established.

Devices for Annular Repair Following Spinal Surgery: Discectomy procedures involve removal of a bony portion of the vertebral body to access the posterior side of the disc space, and removal of the impinging fragment from the disc. This fragment may be within the wall of the anulus, requiring incision into the anulus to remove it. Sutures may be placed to seal the annular defect to reduce recurrent herniation following discectomy. The Inclose™ Surgical Mesh System and the Xclose™ Tissue Repair System (Anulex Technologies, Inc., Minnetonka, MN) have been proposed for annular repair following discectomy as an alternative method to re-approximate the compromised tissue of the anulus fibrosus. Use of the Xclose system for this indication, however is beyond the scope of the FDA 510 (k) clearance, detailed below.

The Inclose Surgical Mesh System received FDA approval through the 510(k) process on August 18, 2005. According to the 510(k) summary, the device is comprised of a mesh implant and two suture assemblies (anchor bands). The mesh implant is an expandable braided patch that is inserted through the aperture of the tissue defect and affixed to surrounding soft tissue with the anchor bands. The product may be used to support soft tissue where weakness exists, or for the repair of hernias requiring the addition of a reinforcing, or bridging material, such as the repair of groin hernias.

The Xclose Tissue Repair System received FDA approval through the 510(k) process on August 7, 2006. The system is described in the 510(k) summary as consisting of two non-absorbable braided surgical 3-0 suture and T-anchor assemblies connected with a loop of green 2-0 suture. The 2-0 suture loop is used to facilitate tightening, drawing the 3-0 suture assemblies together and re-approximating the tissue. The system is indicated for use in soft tissue approximation for procedures such as general and orthopedic surgery.

There is inadequate evidence to demonstrate the safety and efficacy of these devices or to determine the impact on patient outcomes compared to standard surgical techniques. In addition to the procedures described above, several recently introduced techniques combine established surgical approaches for disc removal with additional procedures for which safety and efficacy has not been established, including radiofrequency, laser or other disc ablation and modulation procedures (e.g., Disc-Fx [Elliquency Innovations, Oceanside NY]), selective endoscopic discectomy (SED).

Use Outside the U.S.
Guidance, National Institute for Health and Clinical Excellence (NICE) (United Kingdom): Interventional procedural guidance issued by NICE for the following procedures states that in view of uncertainty about the efficacy of these procedures each should not be done without special arrangements for consent and for audit or research:

- Automated percutaneous mechanical lumbar discectomy (2005, IPG141)
- Percutaneous endoscopic laser thoracic discectomy (2004, IPG61)
- Percutaneous endoscopic laser cervical discectomy (2009, IPG303)
- Epiduroscopic lumbar discectomy through the sacral hiatus for sciatica (2016, IPG570)
- Percutaneous electrothermal treatment of the intervertebral disc annulus for low back pain and sciatica (2016, IPG544)
- Percutaneous intradiscal radiofrequency treatment of the intervertebral disc nucleus for low back pain (2016, IPG545)
- Percutaneous coblation of the intervertebral disc for low back pain and sciatica (2016, IPG543)

Coding/Billing Information

Note: 1) This list of codes may not be all-inclusive.
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Injection Therapy: Trigger Point

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

CPT®* Codes	Description
20552†	Injection(s); single or multiple trigger point(s), 1 or 2 muscle(s)
20553†	Injection(s); single or multiple trigger point(s), 3 or more muscle(s)

†Note: Considered Experimental/Investigational/Unproven when used to report dry needling of trigger points

ICD-10-CM Diagnosis Codes	Description
M43.8X9	Other specified deforming dorsopathies, site unspecified
M53.80	Other specified dorsopathies, site unspecified
M53.81	Other specified dorsopathies, occipito-atlanto-axial region
M53.82	Other specified dorsopathies, cervical region
M53.83	Other specified dorsopathies, cervicothoracic region

M53.84	Other specified dorsopathies, thoracic region
M53.85	Other specified dorsopathies, thoracolumbar region
M53.9	Dorsopathy, unspecified
M54.2	Cervicalgia
M54.5	Low back pain
M54.6	Pain in thoracic spine
M54.81	Occipital neuralgia
M54.89	Other dorsalgia
M54.9	Dorsalgia, unspecified

Considered Experimental/Investigational/Unproven:

ICD-10-CM Diagnosis Codes	Description
	All other codes

Dry Needling of Trigger Points

Considered Experimental/Investigational/Unproven:

CPT®* Codes	Description
64999	Unlisted procedure, nervous system

ICD-10-CM Diagnosis Codes	Description
	All codes

Ultrasound Guidance for Trigger Point Injections

Considered Experimental/Investigational/Unproven:

CPT®* Codes	Description
76942	Ultrasonic guidance for needle placement (eg, biopsy, aspiration, injection, localization device), imaging supervision and interpretation

ICD-10-CM Diagnosis Codes	Description
	All codes

Injection Therapy: Intradiscal Steroid Injection

Considered Experimental/Investigational/Unproven:

CPT®* Codes	Description
22899	Unlisted procedure, spine
64999	Unlisted procedure, nervous system

ICD-10-CM Diagnosis Codes	Description
	All codes

Percutaneous, Endoscopic Laminectomy, and Disc Decompression Procedures of the Cervical, Thoracic, or Lumbar Spine

Considered Experimental/Investigational/Unproven when used to report automated percutaneous lumbar discectomy (APLD)/automated percutaneous nucleotomy; endoscopic cervical disc decompression; endoscopic anterior spinal surgery/Yeung endoscopic spinal system (YESS)/percutaneous endoscopic diskectomy (PELD)/arthroscopic microdiscectomy, selective endoscopic discectomy (SED); endoscopic disc decompression, ablation, or annular modulation using the DiscFX™ System; percutaneous laminotomy/laminectomy, percutaneous spinal decompression (e.g., mild® procedure); percutaneous laser discectomy /decompression, laser-assisted disc decompression (LADD), targeted percutaneous laser disc decompression (targeted PLDD); endoscopic, anterior cervical disc decompression (e.g., Cervical Deuk Laser Disc Repair):

CPT®* Codes	Description
22899	Unlisted procedure, spine
62287	Decompression procedure, percutaneous, of nucleus pulposus of intervertebral disc, any method utilizing needle based technique to remove disc material under fluoroscopic imaging or other form of indirect visualization, with discography and/or epidural injection(s) at the treated level(s), when performed, single or multiple levels, lumbar
62380	Endoscopic decompression of spinal cord, nerve root(s), including laminotomy, partial facetectomy, foraminotomy, discectomy and/or excision of herniated intervertebral disc, 1 interspace, lumbar
64999	Unlisted procedure, nervous system
0274T	Percutaneous laminotomy/laminectomy (interlaminar approach) for decompression of neural elements, (with or without ligamentous resection, discectomy, facetectomy and/or foraminotomy), any method, under indirect image guidance (eg, fluoroscopic, CT), single or multiple levels, unilateral or bilateral; cervical or thoracic
0275T	Percutaneous laminotomy/laminectomy (interlaminar approach) for decompression of neural elements, (with or without ligamentous resection, discectomy, facetectomy and/or foraminotomy), any method, under indirect image guidance (eg, fluoroscopic, CT), single or multiple levels, unilateral or bilateral; lumbar

HCPCS Codes	Description
C2614	Probe, percutaneous lumbar discectomy

ICD-10-CM Diagnosis Codes	Description
	All codes

Thermal Intradiscal Procedures

Considered Experimental/Investigational/Unproven when used to report intervertebral disc Biacuplast; intradiscal electrothermal annuloplasty (e.g., intradiscal electrothermal therapy [IDET™]); percutaneous intradiscal radiofrequency thermocoagulation (PIRFT), intradiscal radiofrequency thermomodulation or percutaneous radiofrequency thermomodulation; Coblation® Nucleoplasty™, disc nucleoplasty, decompression nucleoplasty plasma disc decompression, radiofrequency thermocoagulation nucleoplasty (RFTC); intraosseous radiofrequency nerve ablation of

basivertebral nerve (e.g., INTRACEPT® Intraosseous Nerve Ablation System); targeted disc decompression:

CPT®* Codes	Description
22526	Percutaneous intradiscal electrothermal annuloplasty, unilateral or bilateral including fluoroscopic guidance; single level
22527	Percutaneous intradiscal electrothermal annuloplasty, unilateral or bilateral including fluoroscopic guidance; 1 or more additional levels (List separately in addition to code for primary procedure)
22899	Unlisted procedure, spine
62287	Decompression procedure, percutaneous, of nucleus pulposus of intervertebral disc, any method utilizing needle based technique to remove disc material under fluoroscopic imaging or other form of indirect visualization, with discography and/or epidural injection(s) at the treated level(s), when performed, single or multiple levels, lumbar
64999	Unlisted procedure, nervous system

HCPCS Codes	Description
S2348	Decompression procedure, percutaneous, of nucleus pulposus of intervertebral disc, using radiofrequency energy, single or multiple levels, lumbar

ICD-10-CM Diagnosis Codes	Description
	All codes

Other Procedures

Considered Experimental/Investigational/Unproven when used to report devices for annular repair (e.g., Inclose™ Surgical Mesh System, Xclose™ Tissue Repair System); epiduroscopy, epidural myeloscopy, epidural spinal endoscopy; intradiscal injections (e.g., methylene blue, platelet rich plasma, mesenchymal stem cells, tumor necrosis factor *TNF) alpha) and/or paravertebral oxygen/ozone injection; spinal decompression using Baxano iO-Flex® System (e.g., Baxano Device):

CPT®* Codes	Description
22899	Unlisted procedure, spine
64999	Unlisted procedure, nervous system

HCPCS Codes	Description
0232T†	Injection(s), platelet rich plasma, any site, including image guidance, harvesting and preparation when performed)

†**Note: Considered Experimental/Investigational/Unproven when used to report platelet rich plasma used in an intradiscal injection.**

ICD-10-CM Diagnosis Codes	Description
	All codes

***Current Procedural Terminology (CPT®) ©2017 American Medical Association: Chicago, IL.**

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Back to Search Results (/medicare-coverage-database/search/search-results.aspx?LCDId=34588&ver=18&CoverageSelection=Local&ArticleType=All&PolicyType=Final&s=All&CptHcpcsCode=20552&bc=gAAAACAAAAAA&)

Local Coverage Determination (LCD): Trigger Points, Local Injections (L34588)

Select the **Print Complete Record**, **Add to Basket** or **Email Record** Buttons to print the record, to add it to your basket or to email the record.
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- Contractor Information

CONTRACTOR NAME	CONTRACT TYPE	CONTRACT NUMBER	JURISDICTION	STATE(S)
Wisconsin Physicians Service Insurance Corporation (/medicare-coverage-database/staticpages/contractor-details.aspx?ContrId=143&ver=1)	MAC - Part A	05101 - MAC A	J - 05	Iowa
Wisconsin Physicians Service Insurance Corporation (/medicare-coverage-database/staticpages/contractor-details.aspx?ContrId=147&ver=1)	MAC - Part B	05102 - MAC B	J - 05	Iowa
Wisconsin Physicians Service Insurance Corporation (/medicare-coverage-database/staticpages/contractor-details.aspx?ContrId=144&ver=1)	MAC - Part A	05201 - MAC A	J - 05	Kansas
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Wisconsin Physicians Service Insurance Corporation (/medicare-coverage-database/staticpages/contractor-details.aspx?ContrId=145&ver=1)	MAC - Part A	05301 - MAC A	J - 05	Missouri - Entire State
Wisconsin Physicians Service Insurance Corporation (/medicare-coverage-database/staticpages/contractor-details.aspx?ContrId=149&ver=1)	MAC - Part B	05302 - MAC B	J - 05	Missouri - Entire State
Wisconsin Physicians Service Insurance Corporation (/medicare-coverage-database/staticpages/contractor-details.aspx?ContrId=146&ver=1)	MAC - Part A	05401 - MAC A	J - 05	Nebraska
Wisconsin Physicians Service Insurance Corporation (/medicare-coverage-database/staticpages/contractor-details.aspx?ContrId=151&ver=1)	MAC - Part B	05402 - MAC B	J - 05	Nebraska
Wisconsin Physicians Service Insurance Corporation (/medicare-coverage-database/staticpages/contractor-	MAC - Part A	05901 - MAC A	J - 05	Alaska Alabama Arkansas Arizona

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details.aspx?ContrId=268&ver=1)				California - Entire State Colorado Connecticut Delaware Florida Georgia Hawaii Iowa Idaho Illinois Indiana Kansas Kentucky Louisiana Massachusetts Maryland Maine Michigan Missouri - Entire State Mississippi Montana North Carolina North Dakota Nebraska New Hampshire New Jersey New Mexico Nevada Ohio Oklahoma Oregon Pennsylvania Rhode Island South Carolina South Dakota Tennessee Texas Utah Virginia Vermont Washington Wisconsin West Virginia Wyoming
Wisconsin Physicians Service Insurance Corporation (/medicare-coverage-database/staticpages/contractor-details.aspx?ContrId=264&ver=1)	MAC - Part A	08101 - MAC A	J - 08	Indiana
Wisconsin Physicians Service Insurance Corporation (/medicare-coverage-database/staticpages/contractor-details.aspx?ContrId=265&ver=1)	MAC - Part B	08102 - MAC B	J - 08	Indiana
Wisconsin Physicians Service Insurance Corporation (/medicare-coverage-database/staticpages/contractor-details.aspx?ContrId=266&ver=1)	MAC - Part A	08201 - MAC A	J - 08	Michigan
Wisconsin Physicians Service Insurance Corporation (/medicare-coverage-database/staticpages/contractor-details.aspx?ContrId=267&ver=1)	MAC - Part B	08202 - MAC B	J - 08	Michigan

- LCD Information

Document Information

LCD ID
L34588

Original ICD-9 LCD ID

LCD Title
Trigger Points, Local Injections

Proposed LCD in Comment Period
N/A

Source Proposed LCD
N/A

AMA CPT / ADA CDT / AHA NUBC Copyright Statement

Original Effective Date
For services performed on or after 10/01/2015

Revision Effective Date
For services performed on or after 10/01/2018

Revision Ending Date
N/A

Retirement Date
N/A

Notice Period Start Date
N/A

Notice Period End Date
N/A

CMS National Coverage Policy

Title XVIII of the Social Security Act, section 1862(a)(1)(A). This section allows coverage and payment for only those services that are considered to be medically reasonable and necessary.

Title XVIII of the Social Security Act, section 1833(e). This section prohibits Medicare payment for any claim which lacks the necessary information to process the claim.

Title XVIII of the Social Security Act, section 1862 (a)(7) excludes routine physical evaluations.

PUB 100-03 *Medicare National Coverage Determinations (NCD) Manual-*
Part 1 Section 30.3 – Acupuncture, 30.3.1 Acupuncture for Fibromyalgia, 30.3.2 Acupuncture for Osteoarthritis.
Part 2 Section 150.7 - Prolotherapy, Joint Sclerotherapy, and Ligamentous Injections with Sclerosing Agents.

Coverage Guidance

Coverage Indications, Limitations, and/or Medical Necessity

Myofascial trigger points are self-sustaining hyper-irritative foci that may occur in any skeletal muscle in response to strain produced by acute or chronic overload. These trigger points produce a referred pain pattern characteristic for that individual muscle. Each pattern becomes part of a single muscle myofascial pain syndrome (MPS); each of these single muscle syndromes is responsive to appropriate treatment. To successfully treat chronic myofascial pain syndrome, each single muscle syndrome needs to be identified along with every perpetuating factor.

There is no laboratory or imaging test for establishing the diagnosis of trigger points; it depends therefore, upon the detailed history and thorough directed examination. The following clinical features are present most consistently and are helpful in making the diagnosis:

1. history of onset and its cause (injury, sprain, etc.);
2. distribution of pain;
3. restriction of movement;
4. mild muscle specific weakness;
5. focal tenderness of a trigger point;
6. palpable taut band of muscle in which trigger point is located;
7. local taut response to snapping palpitation; and
8. reproduction of referred pain pattern upon most sustained mechanical stimulation of the trigger point.

The goal is to identify and treat the cause of the pain and not just the symptom of pain.
After making the diagnosis of myofascial pain syndrome and identifying the trigger point responsible for it, the treatment options are:

1. medical management, including the use of anti-inflammatory agents, tricyclics, etc.;
2. stretch and use of coolant spray followed by hot packs and/or aerobic exercises;
3. application of low intensity ultrasound directed at the trigger point (this approach is used when the trigger point is otherwise inaccessible);
4. deep muscle massage;
5. injection of local anesthetic into the muscle trigger points:
    a. as the initial or the only therapy when a joint movement is mechanically blocked, as is the case of coccygeus muscle, or when a muscle cannot be stretched fully, as is the case of the lateral pterygoid muscle;
    b. as treatment of trigger points that are unresponsive to non-invasive methods of treatment, e.g., use of medications, stretch and spray.

NOTE: For all conditions, the actual area must be reported specifically and must be documented in the medical record. Using a non-specific diagnosis code to support injections of multiple areas of the body, rather than more specific diagnosis codes, may result in denial of payment.

1. Known trigger points may be treated at frequencies necessitated by the nature and the severity of associated symptoms and signs
2. Per national Medicare regulations acupuncture is not a covered service, even if provided for treatment of established trigger point:
    a. Use of acupuncture needles and/or the passage of electrical current through these needles is not a covered service whether the service is rendered by an acupuncturist or any other provider;
    b. providers of acupuncture services should inform the beneficiary that such services will not be covered; and
    c. prolotherapy is not covered by Medicare and cannot be billed under the trigger point injection code.
3. If the service has been provided for a diagnosis that is not listed in the covered diagnosis codes section, the provider must thoroughly document the medical necessity and rationale for providing the service for the unlisted diagnosis in the patient's medical records and this must be provided at the review level for consideration.

The diagnosis codes listed as covered should only be used for purposes of this policy when a trigger point is injected.

Documentation must be maintained noting the anatomic location of the injection site(s).

Summary of Evidence

N/A

Analysis of Evidence
(Rationale for Determination)

N/A

- Coding Information

Bill Type Codes:
Contractors may specify Bill Types to help providers identify those Bill Types typically used to report this service. Absence of a Bill Type does not guarantee that the policy does not apply to that Bill Type. Complete absence of all Bill Types indicates that coverage is not influenced by Bill Type and the policy should be assumed to apply equally to all claims.

N/A

Revenue Codes:
Contractors may specify Revenue Codes to help providers identify those Revenue Codes typically used to report this service. In most instances Revenue Codes are purely advisory. Unless specified in the policy, services reported under other Revenue Codes are equally subject to this coverage determination. Complete absence of all Revenue Codes indicates that coverage is not influenced by Revenue Code and the policy should be assumed to apply equally to all Revenue Codes.

CODE	DESCRIPTION
0360	Operating Room Services - General Classification
0450	Emergency Room - General Classification
049X	Ambulatory Surgical Care - General Classification
050X	Outpatient Services - General Classification
051X	Clinic - General Classification

052X	Freestanding Clinic - General Classification
0761	Specialty Services - Treatment Room
096X	Professional Fees - General Classification

CPT/HCPCS Codes

Group 1 Paragraph:

N/A

Group 1 Codes:

CODE	DESCRIPTION
20552	INJECTION(S); SINGLE OR MULTIPLE TRIGGER POINT(S), 1 OR 2 MUSCLE(S)
20553	INJECTION(S); SINGLE OR MULTIPLE TRIGGER POINT(S), 3 OR MORE MUSCLES

Group 1 Paragraph:

N/A

Group 1 Codes:

CODE	DESCRIPTION
20552	INJECTION(S); SINGLE OR MULTIPLE TRIGGER POINT(S), 1 OR 2 MUSCLE(S)
20553	INJECTION(S); SINGLE OR MULTIPLE TRIGGER POINT(S), 3 OR MORE MUSCLES

ICD-10 Codes that Support Medical Necessity

Group 1 Paragraph:

N/A

Group 1 Codes:

ICD-10 CODE	DESCRIPTION
M46.01	Spinal enthesopathy, occipito-atlanto-axial region
M46.02	Spinal enthesopathy, cervical region
M46.03	Spinal enthesopathy, cervicothoracic region
M46.04	Spinal enthesopathy, thoracic region
M46.05	Spinal enthesopathy, thoracolumbar region
M46.06	Spinal enthesopathy, lumbar region
M46.07	Spinal enthesopathy, lumbosacral region
M46.08	Spinal enthesopathy, sacral and sacrococcygeal region
M46.09	Spinal enthesopathy, multiple sites in spine
M53.82	Other specified dorsopathies, cervical region
M60.811	Other myositis, right shoulder
M60.812	Other myositis, left shoulder
M60.821	Other myositis, right upper arm
M60.822	Other myositis, left upper arm

M60.831	Other myositis, right forearm
M60.832	Other myositis, left forearm
M60.841	Other myositis, right hand
M60.842	Other myositis, left hand
M60.851	Other myositis, right thigh
M60.852	Other myositis, left thigh
M60.861	Other myositis, right lower leg
M60.862	Other myositis, left lower leg
M60.871	Other myositis, right ankle and foot
M60.872	Other myositis, left ankle and foot
M60.88	Other myositis, other site
M60.89	Other myositis, multiple sites
M75.81	Other shoulder lesions, right shoulder
M75.82	Other shoulder lesions, left shoulder
M76.31	Iliotibial band syndrome, right leg
M76.32	Iliotibial band syndrome, left leg
M76.811	Anterior tibial syndrome, right leg
M76.812	Anterior tibial syndrome, left leg
M77.51	Other enthesopathy of right foot
M77.52	Other enthesopathy of left foot
M77.9	Enthesopathy, unspecified
M79.0	Rheumatism, unspecified
M79.11	Myalgia of mastication muscle
M79.12	Myalgia of auxiliary muscles, head and neck
M79.18	Myalgia, other site
M79.7	Fibromyalgia

Group 1 Paragraph:

N/A

Group 1 Codes:

ICD-10 CODE	DESCRIPTION
M46.01	Spinal enthesopathy, occipito-atlanto-axial region
M46.02	Spinal enthesopathy, cervical region
M46.03	Spinal enthesopathy, cervicothoracic region
M46.04	Spinal enthesopathy, thoracic region
M46.05	Spinal enthesopathy, thoracolumbar region
M46.06	Spinal enthesopathy, lumbar region
M46.07	Spinal enthesopathy, lumbosacral region

M46.08	Spinal enthesopathy, sacral and sacrococcygeal region
M46.09	Spinal enthesopathy, multiple sites in spine
M53.82	Other specified dorsopathies, cervical region
M60.811	Other myositis, right shoulder
M60.812	Other myositis, left shoulder
M60.821	Other myositis, right upper arm
M60.822	Other myositis, left upper arm
M60.831	Other myositis, right forearm
M60.832	Other myositis, left forearm
M60.841	Other myositis, right hand
M60.842	Other myositis, left hand
M60.851	Other myositis, right thigh
M60.852	Other myositis, left thigh
M60.861	Other myositis, right lower leg
M60.862	Other myositis, left lower leg
M60.871	Other myositis, right ankle and foot
M60.872	Other myositis, left ankle and foot
M60.88	Other myositis, other site
M60.89	Other myositis, multiple sites
M75.81	Other shoulder lesions, right shoulder
M75.82	Other shoulder lesions, left shoulder
M76.31	Iliotibial band syndrome, right leg
M76.32	Iliotibial band syndrome, left leg
M76.811	Anterior tibial syndrome, right leg
M76.812	Anterior tibial syndrome, left leg
M77.51	Other enthesopathy of right foot
M77.52	Other enthesopathy of left foot
M77.9	Enthesopathy, unspecified
M79.0	Rheumatism, unspecified
M79.11	Myalgia of mastication muscle
M79.12	Myalgia of auxiliary muscles, head and neck
M79.18	Myalgia, other site
M79.7	Fibromyalgia

Showing 1 to 40 of 40 entries in Group 1

First Prev 1 Next Last

ICD-10 Codes that DO NOT Support Medical Necessity
N/A
Additional ICD-10 Information
N/A

Additional ICD-10 Information
N/A

- General Information

Associated Information
Documentation Requirements

1. Documentation of proper evaluation leading to diagnosis of the trigger point.
2. Identification of the affected muscle(s).
3. Documentation of reasons for selecting this therapeutic option.
4. Precise diagnosis code must be used: generalized diagnoses like low back pain, lumbago, etc. will not be covered.
5. Documentation which includes the frequency of injections.
6. Documentation must reflect the medical necessity of providing the service. In a post payment review, the process of making the diagnosis of the trigger point in an individual muscle as detailed in the description section must be documented.
7. If a patient requires more than 4 sets/series of injections during one year, (trigger points in different anatomical locations), a report stating the unusual circumstances and medical necessity for giving the additional injections must accompany the claim for review and individual consideration.

Utilization Guidelines
Repeat trigger point injections may be necessary when there is evidence of persistent pain. Generally, more than three injections of the same trigger point are not indicated. Evidence of partial improvements to the range of motion in any muscle area after an injection, but with persistent significant pain, would justify a repeat injection. The medical record must clearly reflect the medical necessity of the repeat injections.

Only one Trigger Point Injection CPT code can be billed per date of service.

Because the diagnosis code manual does not list "trigger point" or "myofascial pain syndrome," this LCD lists related diagnoses that can reasonably include trigger points and uses "myofascial pain syndrome" to refer to trigger points.

Sources of Information
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Bibliography
N/A

- Revision History Information

REVISION HISTORY DATE	REVISION HISTORY NUMBER	REVISION HISTORY EXPLANATION	REASON(S) FOR CHANGE
10/01/2018	R7	10/01/2018 ICD-10 Codes updates: deleted code M79.1 and added codes M79.11, M79.12, and M79.18 in Group One.	• Revisions Due To ICD-10-CM Code Changes
02/01/2018	R6	02/01/2018 Annual review completed 01/10/2018 with no change in coverage. At this time 21st Century Cures Act will apply to new and revised LCDs that restrict coverage which requires comment and notice. This revision is not a restriction to the coverage determination; and, therefore not all the fields included on the LCD are applicable as noted in this policy.	• Other (- Annual review)
03/01/2017	R5	03/01/2017 Annual review done 02/02/2017. No change in coverage, reformatting, and typographical corrections made.	• Other (Annual review)

03/01/2016	R4	03/01/2016 Annual review no change in coverage, removed CAC information.	• Other (Maintenance annual review)
10/01/2015	R3	10/06/2015 - Due to CMS guidance, we have removed the Jurisdiction 8 Notice and corresponding table from the CMS National Coverage Policy section. No other changes to policy or coverage.	• Other
10/01/2015	R2	05/29/2015 – Annual updates to the Bill Type Codes and Revenue Codes have been reviewed by the Policy Department and are being Approved for public display. No other changes to policy or coverage.	• Other (Annual Bill Type Code and Revenue Code updates.)
10/01/2015	R1	04/01/2015 Annual review no change in coverage updated references.	• Other (Maintenance annual review)

- Associated Documents

Attachments

N/A

Related Local Coverage Documents

N/A

Related National Coverage Documents

NCD(s)
30.3 - Acupuncture (/medicare-coverage-database/details/ncd-details.aspx?
NCDId=11&ncdver=1&LCDId=34588&ver=18&CoverageSelection=Local&ArticleType=All&PolicyType=Final&s=All&CptHcpcsCode=20552&bc=gAAAACAE
30.3.1 - Acupuncture for Fibromyalgia (/medicare-coverage-database/details/ncd-details.aspx?
NCDId=283&ncdver=1&LCDId=34588&ver=18&CoverageSelection=Local&ArticleType=All&PolicyType=Final&s=All&CptHcpcsCode=20552&bc=gAAAACA
30.3.2 - Acupuncture for Osteoarthritis (/medicare-coverage-database/details/ncd-details.aspx?
NCDId=284&ncdver=1&LCDId=34588&ver=18&CoverageSelection=Local&ArticleType=All&PolicyType=Final&s=All&CptHcpcsCode=20552&bc=gAAAACA
150.7 - Prolotherapy, Joint Sclerotherapy, and Ligamentous Injections with Sclerosing Agents (/medicare-coverage-database/details/ncd-details.aspx?
NCDId=15&ncdver=1&LCDId=34588&ver=18&CoverageSelection=Local&ArticleType=All&PolicyType=Final&s=All&CptHcpcsCode=20552&bc=gAAAACAI

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Updated on 09/18/2018 with effective dates 10/01/2018 - N/A
Updated on 01/23/2018 with effective dates 02/01/2018 - 09/30/2018 (/medicare-coverage-database/details/lcd-details.aspx?LCDId=34588&ver=15&CoverageSelection=Local&ArticleType=All&PolicyType=Final&s=All&CptHcpcsCode=20552&bc=gAAAACABAAAA&)
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- Keywords

N/A

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BlueCross BlueShield of Tennessee Medical Policy Manual

Trigger Point Injections

Does not apply to BlueCare

DESCRIPTION

Trigger point injection therapy is used for the treatment of myofascial pain syndrome (MPS). Myofascial pain is a common, non-articular musculoskeletal disorder characterized by symptomatic myofascial trigger points - hard, palpable, localized nodules within taut bands of skeletal muscle that are painful upon compression. MPS is a chronic condition affecting the connective tissue (i.e., fascia) surrounding the muscles; sensitive points in your muscles (trigger points) cause referred pain in seemingly unrelated parts of the body. MPS typically occurs after a muscle has been contracted repetitively. The large upper back muscles are prone to developing myofascial pain, as well as the neck, shoulders, heel and temporomandibular joint.

Treatment options for myofascial pain syndrome include medications, physical therapy and trigger point injections.

Pain that persists for extended periods of time (generally greater than 3 months) and fails to be alleviated with conservative approaches may be treated with injections of local anesthetics, anti-inflammatory drugs, and/or corticosteroid in an attempt to deactivate the trigger point.

Dry needling is a variant of trigger point injection and refers to a procedure in which a fine needle is inserted into the skin and muscle at the site of myofascial pain. The needle may be moved in an up-and-down motion, rotated, and/or left in place for as long as 30 minutes; no medications are given through the needle. Dry needling is not the same as acupuncture.

POLICY

- Trigger point injections with local anesthetics, with or without steroids, are considered ***medically necessary.*** *(Note: No more than four (4) trigger point injection sessions are considered appropriate in a one year period.)*
- Ultrasound guidance of trigger point injections is considered ***not medically necessary.***
- Dry needling for the treatment of trigger points is considered ***investigational.***
- Any device or agent utilized for this procedure must have FDA approval specific to the indication, otherwise it will be considered ***investigational.***

IMPORTANT REMINDERS

- Any specific products referenced in this policy are just examples and are intended for illustrative purposes only. It is not intended to be a recommendation of one product over another, and is not intended to represent a complete listing of all products available. These examples are contained in the parenthetical e.g. statement.
- We develop Medical Policies to provide guidance to Members and Providers. This Medical Policy relates only to the services or supplies described in it. The existence of a Medical Policy is not an authorization, certification, explanation of benefits, or a contract for the service (or supply) that is referenced in the Medical Policy. For a determination of the benefits that a Member is entitled to receive under his or her health plan, the Member's health plan must be reviewed. If there is a conflict between the Medical Policy and a health plan, the express terms of the health plan will govern.

Does not apply to BlueCare

ADDITIONAL INFORMATION

There are limited comparative studies available in peer-reviewed journals to determine efficacy or utility of dry needling in the treatment of trigger points. Palpation remains the standard of care for the diagnosis of trigger points and the technique utilized in the guidance of the injections.

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ORIGINAL EFFECTIVE DATE: 7/14/2012

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Electrical Stimulation for Pain

Clinical Policy Bulletins | Medical Clinical Policy Bulletins

Number: 0011

(Replaces CPBs 12, 335)

Policy

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

Aetna considers TENS experimental and investigational for acute pain (less than 3 months duration) other than post-operative pain. TENS is also considered experimental and investigational for any of the following (not an all-inclusive list) because there is inadequate scientific evidence to support its efficacy for these specific types of pain:

- Acute and chronic headaches,
- Adhesive capsulitis (frozen shoulder),
- Chemotherapy-induced peripheral neuropathy,
- Chronic low back pain,
- Deep abdominal pain,
- Fibromyalgia,
- Hip fracture pain,

Policy History

Last Review

03/15/2019
Effective: 07/31/1995
Next Review: 01/09/2020

Review History

Definitions

Additional Information

PLAINTIFF'S EXHIBIT A8

PENGAD 800-631-6989

- Migraine,
- Musculoskeletal pain in hemophilia,
- Neuropathic pain,
- Pain management in burn persons,
- Pelvic pain,
- Peripheral arterial disease,
- Phantom pain,
- Post-total knee arthroplasty pain,
- Rotator cuff disease (e.g., calcific tendinitis, rotator cuff tendinitis, and subacromial impingement syndrome),
- Stump pain,
- Temporomandibular joint (TMJ) pain

Clinical Policy Bulletin Notes

II. **Note**: When TENS is used for acute post-operative or chronic intractable pain, Aetna considers use of the device medically necessary initially for a trial period of at least 1 month but not to exceed 2 months. The trial period must be monitored by the physician to determine the effectiveness of the TENS unit in modulating the pain. After this 1-month trial period, continued TENS treatment may be considered medically necessary if the treatment significantly alleviates pain and if the attending physician documents that the patient is likely to derive significant therapeutic benefit from continuous use of the unit over a long period of time. The physician's records must document a reevaluation of the member at the end of the trial period, must indicate how often the member used the TENS unit, the typical duration of use each time, and the results. The physician ordering the TENS unit must be the attending physician or a consulting physician for the disease or condition resulting in the need for the TENS unit. If the TENS unit produces incomplete relief, further evaluation with percutaneous electrical nerve stimulation (PENS) may be indicated. This clinical policy is consistent with Medicare DME MAC guidelines.

III. Aetna considers a form-fitting conductive garment medically necessary DME only when it has been approved for marketing by the FDA, has been prescribed by a doctor for delivering TENS for one of the medically necessary indications listed above, and *any* of the following criteria is met:

- The member can not manage without the conductive garment due to the large area or the large number of sites to be stimulated, and the stimulation would have to be delivered so frequently that it is not feasible to use

conventional electrodes, adhesive tapes, and lead wires; *or*

- The member has a medical need for rehabilitation strengthening following an injury where the nerve supply to the muscle is intact; *or*
- The member has a skin problem or other medical conditions that precludes the application of conventional electrodes, adhesive tapes, and lead wires; *or*
- The member requires electrical stimulation beneath a cast to treat disuse atrophy, where the nerve supply to the muscle is intact.

IV. Aetna considers stellate ganglion blockade using TENS experimental and investigational because its clinical value has not been established.

V. Aetna considers interferential stimulation (e.g., RS-4i Sequential Stimulator) experimental and investigational for the reduction of pain and edema and all other indications because its effectiveness has not been established.

VI. Aetna considers percutaneous electrical nerve stimulation (PENS) medically necessary DME for

A. up to a 30-day period for the treatment of members with chronic low back pain secondary to degenerative disc disease when PENS is used as part of a multi-modality rehabilitation program that includes exercise, and
B. the treatment of members with diabetic neuropathy or neuropathic pain who failed to adequately respond to conventional treatments including three or more of the following groups of agents: anti-convulsants (e.g., pregabalin), anti-depressants (e.g., amitriptyline, and duloxetine), opioids (e.g., morphine sulphate and tramadol), and other pharmacological agents (e.g., capsaicin and isosorbide dinitrate spray).

Aetna considers PENS experimental and investigational for the treatment of chronic neck pain, and all other indications because its effectiveness for these indications has not been established.

VII. Aetna considers peripherally implanted nerve stimulators (e.g., StimRouter System) medically necessary DME for treatment of members with intractable neurogenic pain when *all* of the following criteria are met:

- Member has chronic intractable pain, refractory to other methods of treatment (e.g., analgesics, physical therapy, local injection, surgery), *and*

- Member is not addicted to drugs (per American Society of Addiction Medicine guidelines), *and*
- There is no psychological contraindication to peripheral nerve stimulation, *and*;
- There is objective evidence of pathology (e.g., electromyography), *and*;
- Trial of transcutaneous stimulation was successful (resulting in at least a 50 % reduction in pain).

Note: Peripheral nerve stimulation is considered experimental and investigational for post-herpetic neuralgia and all other indications because its effectiveness for these indications has not been established.

VIII. Aetna considers H-WAVE type stimulators experimental and investigational for diabetic peripheral neuropathy and for all other indications including *any* of the following indications because their effectiveness for these indications has not been established.

- To accelerate healing; *or*
- To reduce edema; *or*
- To reduce pain from causes other than chronic diabetic peripheral neuropathy; *or*
- To treat chronic pain due to ischemia.

IX. Aetna considers intramuscular stimulation experimental and investigational for the management of members with soft-tissue or neuropathic pain and all other indications because its effectiveness has not been established.

X. Aetna considers sympathetic therapy (Dynatronics Corporation, Salt Lake City, UT) experimental and investigational since its effectiveness has not been established.

XI. Aetna considers electroceutical therapy (also known as bioelectric nerve block) experimental and investigational for the treatment of acute pain or chronic pain (e.g., back pain, diabetic pain, joint pain, fibromyalgia, headache, and reflex sympathetic dystrophy) or other indications because there is a lack of scientific evidence regarding the effectiveness of this technology.

Note: Other terms used to refer to electroceutical therapy devices include "non-invasive neuron blockade" devices, "electroceutical neuron blockade" devices, and "bioelectric treatment systems."

XII. Aetna considers the Electro-Acuscope Myopulse Therapy System experimental and investigational for the treatment of pain and tissue damage and all other indications because its effectiveness has not been demonstrated in the peer-reviewed scientific literature.

XIII. Aetna considers electrical stimulation of the sacral nerve roots or lumbosacral plexus experimental and investigational for the treatment of chronic pelvic or abdominal pain or other indications because the effectiveness of these interventions has not been established.

XIV. Aetna considers microcurrent electrical nerve stimulation (MENS) therapy (including, but not limited to, Algonix, Alpha-Stim 100, Electro-Myopulse 75L, electro-Lyoscope 85P, KFH Energy, MENS 2000-D, MICROCURRENT or Myopulse 75C) experimental and investigational for the treatment of chronic back pain and all other indications because its effectiveness has not been established.

XV. Aetna considers Scrambler therapy/the Calmare therapy device (also known as transcutaneous electrical modulation pain reprocessing (TEMPR)) experimental and investigational for the treatment of cancer pain, chronic pain, neuropathic pain associated with chemotherapy-induced peripheral neuropathy, post-mastectomy pain, and other indications because of insufficient evidence regarding its effectiveness.

XVI. Aetna considers non-invasive interactive neurostimulation (e.g., the InterX 1000 neurostimulator device experimental and investigational for the treatment of chronic pain and other indications (e.g., ankle fracture, knee osteoarthritis and neck pain) because of insufficient evidence regarding its effectiveness.

XVII. Aetna considers peripherally implanted nerve stimulation (also known as peripheral subcutaneous field stimulation (PSFS) or peripheral nerve field stimulation (PNFS)) experimental and investigational for the treatment of chronic pain and other indications (e.g., angina, notalgia paraesthetica) because of insufficient evidence regarding its effectiveness.

XVIII. Aetna considers electro-therapeutic point stimulation (also known as microcurrent point stimulation) experimental and investigational for the treatment of chronic pain and other indications because of insufficient evidence regarding its effectiveness.

XIX. Aetna considers pulse stimulation (e.g., the P-STIM device) experimental and investigational for the treatment of cervicalgia, cervical radiculopathy, cervical spasm, chronic neck pain, failed back syndrome, lumbago, lumbar muscle spasm, lumbosacral myofasciitis, lumbosacral radiculopathy, osteoarthritis of the knee, post-herpetic neuralgia, or other conditions because its clinical value has not been established.

XX. Aetna considers TENS with low level laser therapy (LLLT) (e.g., the Neurolumen device) for the treatment of Morton's neuroma and all other indications experimental and investigational because its clinical value has not been established.

XXI. Aetna considers non-invasive/no-incision pain procedure (NIP) device experimental and investigational for the treatment of chronic pain (arthritis, cancer pain, cervical pain, fibromyalgia, joint pain, low back pain, migraines, post-operative pain, and sciatica; not an all-inclusive list) and all other conditions (e.g., anxiety, depression and insomnia; not an all-inclusive list) because its clinical value has not been established.

XXII. Aetna considers Electro-Analgesia Treatment (EAT) using the Synaptic electrical stimulator with or without peripheral nerve blocks experimental and investigational for peripheral neuropathy and all other indications.

XXIII. Aetna considers electrotherapy for the treatment of adhesive capsulitis (frozen shoulder) experimental and investigational because its effectiveness of for this indication has not been established.

XXIV. Aetna considers Cefaly transcutaneous electrical stimulator headband experimental and investigational for migraine headache prevention and treatment and all other indications.

XXV. Aetna considers percutaneous neuromodulation therapy (e.g., Vertis PNT, BiowavePRO) experimental and investigational for pain and other indications.

XXVI. Aetna considers the Quell device experimental and investigational for all indications.

XXVII. Aetna considers SENSUS transcutaneous electrical nerve stimulation experimental and investigational for diabetic neuropathy and other indications.

XXVIII. Aetna considers transcutaneous electrical joint stimulation devices/pulsed electrical stimulation (PES) (e.g., the BioniCare device, Jstim 1000) experimental and investigational for the treatment of knee osteoarthritis. Aetna considers pulsed electrical stimulator (PES) experimental and investigational for soft-tissue injuries (e.g., ankle sprain) and all other indications because its effectiveness has not been established.

XXIX. Aetna considers variable muscle stimulators experimental and investigational because their effectiveness has not been established.

XXX. Aetna considers combined high frequency electrical stimulation and peripheral nerve block (also referred to as combination electrochemical therapy, combination electrochemical treatment, or CET) experimental and investigational for all indications. (See CPB 0729 - Diabetic Neuropathy: Selected Treatments (../700_799/0729.html))

XXXI. Aetna considers galvanic stimulation or other types of electrical stimulation for the treatment of peripheral arterial disease experimental and investigational because their effectiveness for this indication has not been established.

XXXII. Aetna considers combination stimulation devices experimental and investigational for all indications:

A. ICS and muscle stimulator (e.g., RS-4i sequential stimulator, EMSI TENS/EMS-14); or
B. TENS with ICS; or
C. TENS with NMES (e.g., Empi Phoenix, QB1 System); or
D. TENS with ultrasound device; or

E. Transcranial direct current stimulation and breathing-controlled electrical stimulation for the treatment of neuropathic pain after spinal cord injury

XXIII. Aetna considers electrical stimulation of the posterior tibial nerve for the treatment of neuropathic pain associated with polyneuropathy experimental and investigational because the effectiveness of this approach has not been established.

XXIV. Aetna considers intravaginal electrical stimulation, percutaneous tibial nerve stimulation, and respiratory-gated auricular vagal afferent nerve stimulation for the treatment of chronic pelvic pain experimental and investigational because the effectiveness of these approaches has not been established.

XXV. Aetna considers reduced impedance non-invasive cortical electrostimulation (RINCE) for the treatment of chronic pain experimental and investigational because its effectiveness has not been established.

XXVI. Aetna considers ultrasound-guided percutaneous stimulation of the femoral nerve for post-operative analgesia following anterior cruciate ligament reconstruction experimental and investigational because the effectiveness of this approach has not been established.

XXVII. Aetna considers ultrasound-guided percutaneous stimulation of the sciatic nerve for post-operative analgesia following ambulatory foot surgery experimental and investigational because the effectiveness of this approach has not been established.

Note: Below is a list of CPBs that address other types of electrical stimulation:

CPB 0175 - High-Frequency Pulsed Electromagnetic Stimulation (../100_199/0175.html)

CPB 0191 - Vagus Nerve Stimulation (../100_199/0191.html)

CPB 0194 - Spinal Cord Stimulation (../100_199/0194.html)

CPB 0208 - Deep Brain Stimulation (../200_299/0208.html)

CPB 0223 - Urinary Incontinence (../200_299/0223.html)

CPB 0302 - Xerostomia: Selected Treatments (../300_399/0302.html)

CPB 0327 - Infertility (../300_399/0327.html) (discusses electroejaculation)

CPB 0343 - Bone Growth Stimulators (../300_399/0343.html)

CPB 0398 - Idiopathic Scoliosis (../300_399/0398.html) (discusses surface electrical muscle stimulation)

CPB 0406 - Tinnitus Treatments (../400_499/0406.html) (discusses the use of TENS)

CPB 0469 - Transcranial Magnetic Stimulation and Cranial Electrical Stimulation (../400_499/0469.html)

CPB 0545 - Electrothermal Arthroscopy (../500_599/0545.html)

CPB 0676 - Electrical Stimulation for Nausea, Vomiting, and Motion Sickness (PrimaBella and ReliefBand) and Other Selected Indications (../600_699/0676.html)

CPB 0677 - Functional Electrical Stimulation and Neuromuscular Electrical Stimulation (../600_699/0677.html)
(for Bell's palsy, cerebral palsy, diaphragmatic pacing, neurogenic bladder, spinal cord injury, and stroke)

CPB 0678 - Gastric Pacing and Gastric Electrical Stimulation (../600_699/0678.html)

CPB 0679 - Levator Syndrome Treatments (../600_699/0679.html)

CPB 0680 - Electrical Stimulation for Chronic Ulcers (../600_699/0680.html)

CPB 0707 - Headaches: Invasive Procedures (../700_799/0707.html) (discusses electrical stimulation of the occipital nerve for occipital neuralgia)

CPB 0729 - Diabetic Neuropathy: Selected Treatments (../700_799/0729.html) (discusses percutaneous electrical stimulation for the treatment of diabetic neuropathy)

Background

The following are brief descriptions of various types of electrical stimulation discussed in this CPB, and a summary of available evidence:

Transcutaneous Electrical Nerve Stimulator (TENS)

A TENS is a device which utilizes electrical current delivered through electrodes placed on the surface of the skin to decrease the patient's perception of pain by inhibiting the transmission of afferent pain nerve impulses and/or stimulating the release of endorphins. A TENS unit must be distinguished from other electrical stimulators (e.g., neuromuscular stimulators) which are used to directly stimulate muscles and/or motor nerves. Transcutaneous electrical nerve stimulation is characterized by biphasic current and selectable parameters such as pulse rate and pulse width. In theory, TENS stimulates sensory nerves to block pain signals; it also stimulates endorphin production to help normalize sympathetic function. Most TENS units produce current of 1 to 80 microampere (mA), 9 V (average), 2 to 1000 Hz, with a pulse width of 250 to 400 microseconds (mS).

Transcutaneous electrical nerve stimulation has been widely used in the treatment of various types of pain. It has been shown that TENS is highly effective in alleviating pain and reducing analgesic medications following cesarean section, orthopedic and thoracic operations as well as mixed surgical procedures (AHCPR, 1992). Moreover, TENS has been found to be beneficial also to those who suffer from acute musculoskeletal pain (Long, 1991). On the other hand, the use of TENS in the treatment of chronic malignant pain is sparse and its effectiveness remains unproven. Studies by Ventafridda and colleagues (1979) reported that of the 159 cancer patients who experienced short-term pain relief with TENS therapy, 58 % of them found the treatment ineffective by day 10, and only 35 % of these subjects continued its use after 1 month. In another group of 37 patients, pain was markedly reduced in 96 % of them during the first 10 days of TENS treatment. However, pain reduction was found only in 33 % of the subjects during the second 10 days, and to only 11 % during the third 10 days. Physical mobility was improved initially in 76 % of patients, but dropped to 19 % by the end of 1 month (Ventafridda et al, 1979). The Canadian Coordinating Office for Health Technology Assessment evaluated the clinical value of TENS in pain management and concluded that there is little evidence of the effectiveness of TENS in treating chronic pain (1995).

On June 8, 2012, the Centers for Medicare & Medicaid Services (CMS) rendered a decision memo for TENS for chronic low back pain. It states that TENS is not reasonable and necessary for the treatment of chronic low back pain. The CMS will only cover TENS if individuals are enrolled in an approved clinical study meeting specific requirements.

The Centers for Medicare & Medicaid Services (2012) has issued a decision memorandum concluding that TENS not reasonable and necessary for the treatment of chronic low back pain. For purposes of the decision memorandum, chronic low back pain was defined as an episode of low back pain that has persisted for three months or longer; and is not a manifestation of a clearly defined and generally recognizable primary disease entity. For example, there are cancers that, through metastatic spread to the spine or pelvis, may elicit pain in the lower back as a symptom; and certain systemic diseases such as rheumatoid arthritis and multiple sclerosis manifest many debilitating symptoms of which low back pain is not the primary focus. The CMS decision memorandum stated that the evidence demonstrates that the use of TENS for chronic low back pain as defined within the scope of this analysis does not produce a clinically meaningful improvement in any of the considered health outcomes The decision memorandum stated that it is apparent that sham (placebo) TENS produces equivalent analgesia as active TENS.

In an evidence-based review, the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology evaluated the effectiveness of TENS in the treatment of pain in neurological disorders (Dubinsky and Miyasaki, 2010). There are conflicting reports of TENS compared to sham TENS in the treatment of chronic low back pain (LBP), with 2 Class II studies showing benefit, while 2 Class I studies and another Class II study not showing benefit. Because the Class I studies are stronger evidence, TENS is established as ineffective for the treatment of chronic LBP. On the other hand, TENS is probably effective in treating painful diabetic neuropathy (2 Class II studies. The authors concluded that: (i) TENS is not recommended for the treatment of chronic LBP (Level A), and (ii) TENS should be considered in the treatment of painful diabetic neuropathy (Level B). They stated that further research into the mechanism of action of TENS is needed, as well as more rigorous studies for determination of efficacy.

Guidelines on treatment of LBP from the National Collaborating Centre for Primary Care (Savigny et al, 2009) found insufficient evidence for the use of TENS in LBP and recommended against its use for that indication.

In a Cochrane review, Mulvey et al (2010) evaluated the analgesic effectiveness of TENS for the treatment of phantom pain and stump pain following amputation in adults. These investigators searched MEDLINE, Cochrane Central Register of Controlled Trials (CENTRAL), EMBASE, PsycINFO, AMED, CINAHL, PEDRO and SPORTDiscus (February 2010). Only randomized controlled trials (RCTs) investigating the use of TENS for the management of phantom pain and stump pain following an amputation in adults were included. Two review authors independently assessed trial quality and extracted data. It was planned that where available and appropriate, data from outcome measures were to be pooled and presented as an overall estimate of the effectiveness of TENS. No RCTs that examined the effectiveness of TENS for the treatment of phantom pain and stump pain in adults were identified by the searches. The authors concluded that there were no RCTs on which to judge the effectiveness of TENS for the management of phantom pain and stump pain. The published literature on TENS for phantom pain and stump pain lacks the methodological rigor and robust reporting needed to confidently assess its effectiveness. They stated that further RCT evidence is needed before such a judgment can be made.

Johnson et al (2015) updated of a Cochrane review published in 2010 on TENS for phantom pain and stump pain following amputation in adults. The authors concluded that there were no RCTs to judge the effectiveness of TENS for the management of phantom pain and stump pain. The published literature on TENS for phantom pain and stump pain lacks the methodological rigor and robust reporting needed to confidently assess its effectiveness. They stated that further RCT evidence is needed before an assessment can be made. Since publication of the original version of this review, these investigators have found no new studies and their conclusions remain unchanged.

Zeng et al (2015) examined the effectiveness of different electrical stimulation (ES) therapies in pain relief of patients with knee osteoarthritis (OA). Electronic databases including MEDLINE, Embase and Cochrane Library were searched through for RCTs comparing any ES therapies with control interventions (sham or blank) or with each other. Bayesian network meta-analysis was used to combine both the direct and indirect evidence on treatment effectiveness. A total of 27 trials and 6 types of ES therapies, including high-frequency TENS (h-TENS), low-frequency TENS (l-TENS), neuromuscular electrical stimulation (NMES), interferential current (IFC), pulsed electrical stimulation (PES), and noninvasive interactive neurostimulation (NIN), were included. Interferential current is the only significantly effective treatment in terms of both pain intensity and change pain score at last follow-up time-point when compared with the control group.

Meanwhile, IFC showed the greatest probability of being the best option among the 6 treatment methods in pain relief. These estimates barely changed in sensitivity analysis. However, the evidence of heterogeneity and the limitation in sample size of some studies could be a potential threat to the validity of results. The authors conclude that IFC seems to be the most promising pain relief treatment for the management of knee OA. However, evidence was limited due to the heterogeneity and small number of included trials. Although the recommendation level of the other ES therapies is either uncertain (h-TENS) or not appropriate (l-TENS, NMES, PES and NIN) for pain relief, it is likely that none of the interventions is dangerous.

Cheing and Luk (2005) examined the clinical effectiveness of high-frequency (HF) TENS for reducing hyper-sensitivity of the hand in patients with neuropathic pain. A total of 19 patients suffering from hand hyper-sensitivity were randomly assigned into either a treatment or a placebo group. A visual analog scale (VAS) and the Downey Hand Center Hand Sensitivity Test were used to measure the tactile tolerance of the hand. Grip strength was assessed by a grip dynamometer. Daily applications of electrical stimulation were provided for 2 weeks. Significantly lower pain scores were found in the treatment group than in the placebo group by day 7 and day 11. The ranking of 10 dowel textures of the Downey Hand Center Hand Sensitivity Test in the treatment group was significantly higher than in the placebo group by day 7 and day 11. However, no significant inter-group difference was found in grip strength.

The Ad hoc Committee of the Croatian Society for Neurovascular Disorders and the Croatian Medical Association's recommendations for neuropathic pain treatment (Demarin et al, 2008) stated that damage to the somatosensory nervous system poses a risk for the development of neuropathic pain. Such an injury to the nervous system results in a series of neurobiological events resulting in sensitization of both the peripheral and central nervous system. The diagnosis of neuropathic pain is based primarily on the history and physical examination finding. Although monotherapy is the ideal approach, rational poly-pharmacy is often pragmatically used. Several classes of drugs are moderately effective, but complete or near-complete relief is unlikely. Anti-depressants and anti-convulsants are most commonly used. Opioid analgesics can provide some relief but are less effective than for nociceptive pain; adverse effects may prevent adequate analgesia. Topical drugs and a lidocaine-containing patch may be effective for peripheral syndromes. Sympathetic blockade is usually ineffective except for some patients with complex regional pain syndrome. TENS was not mentioned as a therapeutic option.

Norrbrink (2009) assessed the short-term effects of HF and low-frequency (LF) TENS for neuropathic pain following spinal cord injury (SCI). A total of 24 patients participated in the study. According to the protocol, 50 % of the patients were assigned to HF (80 Hz) and 50 % to LF (burst of 2 Hz) TENS. Patients were instructed to treat themselves 3 times daily for 2 weeks. After a 2-week wash-out period, patients switched stimulation frequencies and repeated the procedure. Results were calculated on an intent-to-treat basis. No differences between the 2 modes of stimulation were found. On a group level, no effects on pain intensity ratings or ratings of mood, coping with pain, life satisfaction, sleep quality, or psychosocial consequences of pain were seen. However, 29 % of the patients reported a favorable effect from HF and 38 % from LF stimulation on a 5-point global pain-relief scale. Six of the patients (25 %) were, at their request, prescribed TENS stimulators for further treatment at the end of the study. The authors concluded that TENS merits consideration as a complementary treatment in patients with SCI and neuropathic pain. The mild benefits observed -- 29 % of subjects in the HF group and 38 % of subjects in the LF group could be a placebo effect.

Moharic and Burger (2010) examined if TENS improves small fiber function diminished because of painful diabetic neuropathy. A total of 46 patients with painful diabetic neuropathy were treated with TENS 3 consecutive hours a day for 3 weeks. Treatment effect was evaluated with cold, warm, cold pain and heat pain thresholds, vibration perception thresholds and touch perception thresholds. In all patients, thermal-specific and thermal pain sensitivity determination showed quantitative and qualitative abnormalities in all the measured spots. After the TENS therapy, no statistically significant changes in cold, warm, cold pain, heat pain, vibratory perception and touch perception thresholds were observed in the stimulated area. TENS did not alter C, Aδ nor Aβ fiber-mediated perception thresholds. The authors noted that the observed changes at thenar were probably because of central mechanisms. In general, analgesic mechanisms of TENS are likely to be complex.

Jin et al (2010) evaluated the effectiveness of TENS on diabetic peripheral neuropathy (DPN). Randomized controlled trials (RCTs) comparing TENS with routine care, pharmacological interventions or placebo devices on patients with symptomatic DPN, were identified by electronic and manual searches. Studies were selected and available data were extracted independently by 2 investigators. Meta-analysis was performed by RevMan 4.2.8 software. A total of 3 RCTs involving 78 patients were included in this study. The reductions in mean pain score were significantly greater in TENS group than in placebo TENS group in 4 weeks and 6 weeks follow-up [4 weeks, standard mean difference (SMD) -5.37, 95 % confidence interval [CI]: -6.97 to -3.77; 6 weeks, SMD-

1.01, 95 % CI: -2.01 to -0.01)], but not in 12 weeks follow-up [SMD-1.65, 95 % CI: -4.02 to 0.73]. TENS therapy was associated with significantly subjective improvement in overall neuropathic symptoms in 12 weeks follow-up [WMD-0.18, 95 % CI: -0.32 to -0.051]. No TENS-related adverse events were registered in TENS group. The authors concluded that TENS therapy may be an effective and safe strategy in treatment of symptomatic DPN. They stated that due to small sample and short-term treatment duration, large multi-center RCTs are needed to further evaluate the long-term effect of TENS on DPN.

Johnson and Bjordal (2011) stated that the management of neuropathic pain is challenging, with medication being the first-line treatment. Transcutaneous electrical nerve stimulation is a non-invasive, self-administered technique that is used as an adjunct to medication. Clinical experience suggested that TENS is beneficial providing it is administered at a sufficiently strong intensity, close to the site of pain. At present, there are too few RCTs on TENS for neuropathic pain to judge effectiveness. The findings of systematic reviews of TENS for other pain syndromes are inconclusive because trials have a low fidelity associated with inadequate TENS technique and infrequent treatments of insufficient duration. The use of electrode arrays to spatially target stimulation more precisely may improve the efficacy of TENS in the future.

In a systematic review, Abou-Setta (2011) reviewed the benefits and harms of pharmacological and non-pharmacological interventions for managing pain after hip fracture. A total of 25 electronic databases (January 1990 to December 2010), gray literature, trial registries, and reference lists, with no language restrictions were searched. Multiple reviewers independently and in duplicate screened 9,357 citations to identify RCT); non-RCTs; and cohort studies of pain management techniques in older adults after acute hip fracture. Independent, duplicate data extraction and quality assessment were conducted, with discrepancies resolved by consensus or a third reviewer. Data extracted included study characteristics, inclusion and exclusion criteria, participant characteristics, interventions, and outcomes. A total of 83 unique studies (64 RCTs, 5 non-RCTs, and 14 cohort studies) were included that addressed nerve blockade (n = 32), spinal anesthesia (n = 30), systemic analgesia (n = 3), traction (n = 11), multi-modal pain management (n = 2), neurostimulation (n = 2), rehabilitation (n = 1), and complementary and alternative medicine (n = 2). Overall, moderate evidence suggested that nerve blockades are effective for relieving acute pain and reducing delirium. Low-level evidence suggested that pre-operative traction does not reduce acute pain. Evidence was insufficient on the benefits and harms of most interventions, including spinal anesthesia, systemic analgesia, multi-modal pain management, acupressure,

relaxation therapy, TENS, and physical therapy regimens, in managing acute pain. The authors concluded that nerve blockade seems to be effective in reducing acute pain after hip fracture. Sparse data preclude firm conclusions about the relative benefits or harms of many other pain management interventions (including TENS) for patients with hip fracture.

In a Cochrane review, Page et al (2014) examined the available evidence regarding the benefits and harms of electrotherapy modalities, delivered alone or in combination with other interventions, for the treatment of adhesive capsulitis (frozen shoulder). These investigators searched CENTRAL, MEDLINE, EMBASE, CINAHL Plus and the ClinicalTrials.gov and World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP) clinical trials registries up to May 2014, unrestricted by language, and reviewed the reference lists of review articles and retrieved trials to identify any other potentially relevant trials. They included RCTs and controlled clinical trials using a quasi-randomized method of allocation that included adults with adhesive capsulitis and compared any electrotherapy modality to placebo, no treatment, a different electrotherapy modality, or any other intervention. The 2 main questions of the review focused on whether electrotherapy modalities are effective compared to placebo or no treatment, or if they are an effective adjunct to manual therapy or exercise (or both). The main outcomes of interest were participant-reported pain relief of 30 % or greater, overall pain, function, global assessment of treatment success, active shoulder abduction, quality of life, and the number of participants experiencing any adverse event. Two review authors independently selected trials for inclusion, extracted the data, performed a risk of bias assessment, and assessed the quality of the body of evidence for the main outcomes using the GRADE approach. A total of 19 trials (1,249 participants) were included in the review; 4 trials reported using an adequate method of allocation concealment and 6 trials blinded participants and personnel. Only 2 electrotherapy modalities (low-level laser therapy (LLLT) and pulsed electromagnetic field therapy (PEMF)) have been compared to placebo. No trial has compared an electrotherapy modality plus manual therapy and exercise to manual therapy and exercise alone. The 2 main questions of the review were investigated in 9 trials. Low-quality evidence from 1 trial (40 participants) indicated that LLLT for 6 days may result in improvement at 6 days; 81 % (16/20) of participants reported treatment success with LLLT compared with 10 % (2/20) of participants receiving placebo (risk ratio (RR) 8.00, 95 % CI: 2.11 to 30.34; absolute risk difference 70 %, 95 % CI: 48 % to 92 %). No participants in either group reported adverse events. These researchers were uncertain whether PEMF for 2 weeks improved pain or function more than placebo at 2 weeks because of the very low quality evidence from 1 trial (32 participants); 75 % (15/20) of participants reported pain relief of

30 % or more with PEMF compared with 0 % (0/12) of participants receiving placebo (RR 19.19, 95 % CI: 1.25 to 294.21; absolute risk difference 75 %, 95 % CI: 53 % to 97 %). Fifty-five per cent (11/20) of participants reported total recovery of joint function with PEMF compared with 0 % (0/12) of participants receiving placebo (RR 14.24, 95 % CI: 0.91 to 221.75; absolute risk difference 55 %, 95 % CI: 31 to 79). Moderate quality evidence from 1 trial (63 participants) indicated that LLLT plus exercise for 8 weeks probably resulted in greater improvement when measured at the 4th week of treatment, but a similar number of adverse events, compared with placebo plus exercise. The mean pain score at 4 weeks was 51 points with placebo plus exercise, while with LLLT plus exercise the mean pain score was 32 points on a 100-point scale (mean difference (MD) 19 points, 95 % CI: 15 to 23; absolute risk difference 19 %, 95 % CI: 15 % to 23 %). The mean function impairment score was 48 points with placebo plus exercise, while with LLLT plus exercise the mean function impairment score was 36 points on a 100-point scale (MD 12 points, 95 % CI: 6 to 18; absolute risk difference 12 %, 95 % CI: 6 to 18). Mean active abduction was 70 degrees with placebo plus exercise, while with LLLT plus exercise mean active abduction was 79 degrees (MD 9 degrees, 95 % CI: 2 to 16; absolute risk difference 5 %, 95 % CI: 1 % to 9 %). No participants in either group reported adverse events; LLLT's benefits on function were maintained at 4 months. Based on very low quality evidence from 6 trials, these investigators were uncertain whether therapeutic ultrasound, PEMF, continuous short-wave diathermy, Iodex phonophoresis, a combination of Iodex iontophoresis with continuous short-wave diathermy, or a combination of therapeutic ultrasound with TENS were effective adjuncts to exercise. Based on low or very low quality evidence from 12 trials, these researchers were uncertain whether a diverse range of electrotherapy modalities (delivered alone or in combination with manual therapy, exercise, or other active interventions) were more or less effective than other active interventions (e.g., glucocorticoid injection). The authors concluded that based upon low quality evidence from 1 trial, LLLT for 6 days may be more effective than placebo in terms of global treatment success at 6 days. Based upon moderate quality evidence from 1 trial, LLLT plus exercise for 8 weeks may be more effective than exercise alone in terms of pain up to 4 weeks, and function up to 4 months. It is unclear whether PEMF is more or less effective than placebo, or whether other electrotherapy modalities are an effective adjunct to exercise. They stated that further high quality RCTs are needed to establish the benefits and harms of physical therapy interventions (that comprise electrotherapy modalities, manual therapy and exercise, and are reflective of clinical practice) compared to interventions with evidence of benefit (e.g., glucocorticoid injection or arthrographic joint distension).

TENS for Pain Management in Burn Persons

In a pilot study, Perez-Ruvalcaba and colleagues (2015) examined the effect of continuous and intermittent TENS on the perception of pain in patients with burns of different types. This study was conducted in 14 patients (aged 30.9 ± 7.5 years) with 2nd- and 3rd-degree burns of different types. The burn types included electrical, fire/flame, and chemical. All patients received continuous and intermittent TENS sessions 3 times per week for 4 weeks; each session had a duration of 30 minutes. A pair of electrodes were placed around the burn. The primary effectiveness end-point was the perception of pain assessed by a VAS at baseline and at the 30th day. A significant reduction of pain perception was reported (8.0 ± 1.7 versus 1.0 ± 0.5; p = 0.027) by all patients after TENS therapy. There were no reports of adverse events during the intervention period. The authors concluded that TENS could be a potential non-pharmacological therapeutic option for pain management in burn patients. These preliminary findings need to be validated by well-designed studies.

TENS for Peripheral Arterial Disease

Seenan and colleagues (2016) examined the effects of 2 types of TENS on walking distance and measures of pain in patients with peripheral arterial disease (PAD) and intermittent claudication (IC). In a phase IIa clinical trial, a total of 40 participants with PAD and IC completed a graded treadmill test on 2 separate testing occasions. Active TENS was applied to the lower limb on the 1st occasion; and placebo TENS, on the 2nd occasion. Participants were divided into 2 experimental groups: (i) one group received high-frequency TENS; and (ii) (the 2nd group received low-frequency TENS. Measures taken were initial claudication distance, functional claudication distance, and absolute claudication distance. The McGill Pain Questionnaire (MPQ) vocabulary was completed at the end of the intervention, and the MPQ-Pain Rating Index score was calculated. Four participants were excluded from the final analysis because of non-completion of the experimental procedure. Median walking distance increased with high-frequency TENS for all measures ($p < 0.05$, Wilcoxon signed rank test, all measures). Only absolute claudication distance increased significantly with low-frequency TENS compared with placebo (median of 179 to 228; Ws = 39; z = 2.025; p = 0.043; r = 0.48). No difference was observed between reported median MPQ-Pain Rating Index scores: 21.5 with placebo TENS and 21.5 with active TENS (p = 0.41). The authors concluded that TENS applied to the lower limb of the patients with PAD and IC was associated with increased walking distance on a treadmill; but not with any reduction in pain. They stated that TENS may be a useful adjunctive intervention to help increase walking performance in patients with IC.

TENS for Post-Total Knee Arthroplasty Pain

Chughtai and associates (2016) noted that despite technological advances in total knee arthroplasty (TKA), management of post-operative muscle weakness and pain continue to pose challenges for both patients and health care providers. Non-pharmacologic therapies, such as neuromodulation in the form of NMES and TENS, and other modalities, such as cryotherapy and pre-habilitation, have been highlighted as possible adjuncts to standard-of-care pharmacologic management to treat post-operative pain and muscle weakness. These researchers discussed existing evidence for neuromodulation in the treatment of pain and muscular weakness following TKA, and shed light on other non-invasive and potential future modalities. The review of the literature demonstrated that NMES, pre-habilitation, and some specialized exercises are beneficial for post-operative muscle weakness, and TENS, cooling therapies, and compression may help to alleviate post-TKA pain. However, there are no clear guidelines for the use of these modalities. The authors concluded that further studies should be aimed at developing guidelines or delineating indications for neuromodulation and other non-pharmacologic therapies in the management of post-TKA pain and muscle weakness.

TENS for Rotator Cuff Disease

In a Cochrane review, Page and colleagues (2016) synthesized available evidence regarding the benefits and harms of electrotherapy modalities for the treatment of people with rotator cuff disease. These investigators searched the Cochrane Central Register of Controlled Trials (CENTRAL; 2015, Issue 3), Ovid Medline (January 1966 to March 2015), Ovid Embase (January 1980 to March 2015), CINAHL Plus (EBSCOhost, January 1937 to March 2015), ClinicalTrials.gov and the WHO ICTRP clinical trials registries up to March 2015, unrestricted by language, and reviewed the reference lists of review articles and retrieved trials, to identify potentially relevant trials. They included RCTs and quasi-randomized trials, including adults with rotator cuff disease (e.g., calcific tendinitis, rotator cuff tendinitis, and subacromial impingement syndrome), and comparing any electrotherapy modality with placebo, no intervention, a different electrotherapy modality or any other intervention (e.g., glucocorticoid injection). Trials investigating whether electrotherapy modalities were more effective than placebo or no treatment, or were an effective addition to another physical therapy intervention (e.g., manual therapy or exercise) were the main comparisons of interest. Main outcomes of interest were overall pain, function, pain on motion, patient-reported global assessment of treatment success, quality of life and the number of participants experiencing adverse events. Two review

authors independently selected trials for inclusion, extracted the data, performed a risk of bias assessment and assessed the quality of the body of evidence for the main outcomes using the GRADE approach. These researchers included 47 trials (2,388 participants). Most trials (n = 43) included participants with rotator cuff disease without calcification (4 trials included people with calcific tendinitis); 16 (34 %) trials investigated the effect of an electrotherapy modality delivered in isolation. Only 23 % were rated at low risk of allocation bias, and 49 % were rated at low risk of both performance and detection bias (for self-reported outcomes). The trials were heterogeneous in terms of population, intervention and comparator, so none of the data could be combined in a meta-analysis. In 1 trial (61 participants; low quality evidence), pulsed therapeutic ultrasound (US) (3 to 5 times a week for 6 weeks) was compared with placebo (inactive US therapy) for calcific tendinitis. At 6 weeks, the mean reduction in overall pain with placebo was -6.3 points on a 52-point scale, and -14.9 points with US (MD -8.60 points, 95 % CI: -13.48 to -3.72 points; absolute risk difference 17 %, 7 % to 26 % more). Mean improvement in function with placebo was 3.7 points on a 100-point scale, and 17.8 points with US (MD 14.10 points, 95 % CI: 5.39 to 22.81 points; absolute risk difference 14 %, 5 % to 23 % more); 91 % (29/32) of participants reported treatment success with US compared with 52 % (15/29) of participants receiving placebo (RR 1.75, 95 % CI: 1.21 to 2.53; absolute risk difference 39 %, 18 % to 60 % more). Mean improvement in quality of life with placebo was 0.40 points on a 10-point scale, and 2.60 points with US (MD 2.20 points, 95 % CI: 0.91 points to 3.49 points; absolute risk difference 22 %, 9 % to 35 % more). Between-group differences were not important at 9 months. No participant reported adverse events. Therapeutic US produced no clinically important additional benefits when combined with other physical therapy interventions (8 clinically heterogeneous trials, low quality evidence). The authors were uncertain whether there were differences in patient-important outcomes between US and other active interventions (manual therapy, acupuncture, glucocorticoid injection, glucocorticoid injection plus oral tolmetin sodium, or exercise) because the quality of evidence is very low; 2 placebo-controlled trials reported results favoring LLLT up to 3 weeks (low quality evidence), however combining LLLT with other physical therapy interventions produced few additional benefits (10 clinically heterogeneous trials, low quality evidence). These researchers were uncertain whether TENS was more or less effective than glucocorticoid injection with respect to pain, function, global treatment success and active ROM because of the very low quality evidence from a single trial. In other single, small trials, no clinically important benefits of PEMF, MENS, acetic acid iontophoresis and microwave diathermy were observed (low or very low quality evidence). No adverse events of therapeutic US, LLLT, TENS or microwave diathermy were reported by any participants. Adverse events were not measured in any trials investigating the effects of PEMF, MENS

or acetic acid iontophoresis. The authors concluded that based on low quality evidence, therapeutic US may have short-term benefits over placebo in people with calcific tendinitis, and LLLT may have short-term benefits over placebo in people with rotator cuff disease. They stated that further high quality placebo-controlled trials are needed to confirm these results. In contrast, based on low quality evidence, PEMF may not provide clinically relevant benefits over placebo, and therapeutic US, LLLT and PEMF may not provide additional benefits when combined with other physical therapy interventions. The authors were uncertain if TENS is superior to placebo, and whether any electrotherapy modality provides benefits over other active interventions (e.g., glucocorticoid injection) because of the very low quality of the evidence. They stated that practitioners should communicate the uncertainty of these effects and consider other approaches or combinations of treatment. The authors stated that further trials of electrotherapy modalities for rotator cuff disease should be based upon a strong rationale and consideration of whether or not they would alter the conclusions of this review.

Desmeules et al (2016) performed a systematic review on the effectiveness of TENS for the treatment of rotator cuff tendinopathy in adults. A literature search was conducted in 4 databases (CINAHL, Embase, PubMed and PeDRO) for RCTs published from date of inception until April 2015, comparing the effectiveness of TENS for the treatment of rotator cuff tendinopathy with placebo or any other intervention. Risk of bias was evaluated using the Cochrane risk of bias tool; results were summarized qualitatively. A total of 6 studies were included in this review. The mean methodological score was 49 % (standard deviation 16 %), indicating an overall high risk of bias. One placebo-controlled trial reported that a single TENS session provided immediate pain reduction for patients with rotator cuff tendinopathy, but did not follow the participants in the short-, medium- or long-term. Two trials that compared US therapy with TENS reported discrepancy and contradictory results in terms of pain reduction and shoulder ROM. Corticosteroid injections were found to be superior to TENS for pain reduction in the short-term, but the differences were not clinically important. Other studies included in this review concluded that TENS was not superior to heat or pulsed radiofrequency. The authors concluded that due to the limited number of studies and the overall high risk of bias of the studies included in this review, no conclusions can be drawn on the effectiveness of TENS for the treatment of rotator cuff tendinopathy. They stated that more methodologically sound studies are needed to document the effectiveness of TENS; until then, clinicians should prefer other evidence-based rehabilitation interventions proven to be effective to treat patients with rotator cuff tendinopathy.

TENS for Chemotherapy-Induced Peripheral Neuropathy

In a double-blind, randomized and placebo-controlled study, Tonezzer and associates (2017) examined the effects of TENS for reducing the side effects of chemotherapy-induced peripheral neuropathy (CIPN) in cancer patients undergoing chemotherapy with oxaliplatin or paclitaxel. A total of 24 patients were randomly allocated into 2 groups: (i) active or (ii) (placebo stimulation. All patients were evaluated for pain, numbness/tingling, frequency of symptoms, and quality of life. The TENS device was applied daily with modulating frequencies ranging between 7-Hz and 65-Hz in distal limb regions during 3 cycles of chemotherapy (45 days). The other stimulation parameters were: pulse duration of 200 μsec, intensity at the highest tolerable level, and increases in intensity when it diminished. The data showed no difference between active or placebo groups in terms of pain, numbness/tingling, frequency of symptoms or impact on daily life activities. The authors concluded that these results suggested that TENS applied in the frequency variation mode was not proven to be effective to improve the symptoms of CIPN during chemotherapy cycles. There was no worsening of symptoms in subsequent cycles of the onset of symptoms of the disease.

TENS for Fibromyalgia

In a Cochrane review, Johnson and colleagues (2017) evaluated the effectiveness and adverse events of TENS alone or added to usual care (including exercise) compared with placebo (sham) TENS; no treatment; exercise alone; or other treatment including medication, electro-acupuncture, warmth therapy, or hydrotherapy for fibromyalgia in adults. These investigators searched the following electronic databases up to January 18, 2017: CENTRAL (CRSO); Medline (Ovid); Embase (Ovid); CINAHL (EBSCO); PsycINFO (Ovid); LILACS; PEDRO; Web of Science (ISI); AMED (Ovid); and SPORTDiscus (EBSCO). They also searched 3 trial registries. There were no language restrictions. These researchers included RCTs or quasi-randomized trials of TENS treatment for pain associated with fibromyalgia in adults. They included cross-over and parallel-group trial designs. They included studies that evaluated TENS administered using non-invasive techniques at intensities that produced perceptible TENS sensations during stimulation at either the site of pain or over nerve bundles proximal (or near) to the site of pain. The authors included TENS administered as a sole treatment or TENS in combination with other treatments, and TENS given as a single treatment or as a course of treatments. Two review authors independently determined study eligibility by assessing each record and reaching agreement by discussion. A 3rd review author acted as arbiter. These researchers did not anonymize the records of studies before

assessment. Two review authors independently extracted data and assessed risk of bias of included studies before entering information into a "Characteristics of included studies" table. Primary outcomes were participant-reported pain relief from baseline of 30 % or greater or 50 % or greater, and Patient Global Impression of Change (PGIC). These investigators assessed the evidence using GRADE and added "Summary of findings" tables. The authors included 8 studies (7 RCTs, 1 quasi-RCT, 315 adults (299 women), aged 18 to 75 years): 6 used a parallel-group design and 2 used a cross-over design. Sample sizes of intervention arms were 5 to 43 subjects. Two studies, 1 of which was a cross-over design, compared TENS with placebo TENS (82 participants), 1 study compared TENS with no treatment (43 subjects), and 4 studies compared TENS with other treatments (medication (2 studies, 74 participants), electro-acupuncture (1 study, 44 participants), superficial warmth (1 cross-over study, 32 subjects), and hydrotherapy (1 study, 10 participants)). Two studies compared TENS plus exercise with exercise alone (98 participants, 49 per treatment arm). None of the studies measured participant-reported pain relief of 50 % or greater or PGIC. Overall, the studies were at unclear or high risk of bias, and in particular all were at high risk of bias for sample size. Only 1 study (14 participants) measured the primary outcome participant-reported pain relief of 30 % or greater; 30 % achieved 30 % or greater reduction in pain with TENS and exercise compared with 13 % with exercise alone. One study found 10/28 participants reported pain relief of 25 % or greater with TENS compared with 10/24 participants using superficial warmth (42 °C). These researchers judged that statistical pooling was not possible because there were insufficient data and outcomes were not homogeneous. There were no data for the primary outcomes participant-reported pain relief from baseline of 50 % or greater and PGIC. There was a paucity of data for secondary outcomes. One pilot cross-over study of 43 subjects found that the mean (95 % CI) decrease in pain intensity on movement (100-mm VAS) during one 30-min treatment was 11.1 mm (95 % CI: 5.9 to 16.3) for TENS and 2.3 mm (95 % CI: 2.4 to 7.7) for placebo TENS. There were no significant differences between TENS and placebo for pain at rest. One parallel group study of 39 participants found that mean ± standard deviation (SD) pain intensity (100-mm VAS) decreased from 85 ± 20 mm at baseline to 43 ± 20 mm after 1 week of dual-site TENS; decreased from 85 ± 10 mm at baseline to 60 ± 10 mm after single-site TENS; and decreased from 82 ± 20 mm at baseline to 80 ± 20 mm after 1 week of placebo TENS. The authors of 7 studies concluded that TENS relieved pain but the findings of single small studies are unlikely to be correct. One study found clinically important improvements in Fibromyalgia Impact Questionnaire (FIQ) subscales for work performance, fatigue, stiffness, anxiety, and depression for TENS with exercise compared with exercise alone. One study found no additional improvements in FIQ scores when TENS was added to the first 3 weeks of a 12-week supervised exercise

program. No serious adverse events were reported in any of the studies although there were reports of TENS causing minor discomfort in a total of 3 participants. The quality of evidence was very low. These investigators down-graded the GRADE rating mostly due to a lack of data; thus, they had little confidence in the effect estimates where available. The authors concluded that there was insufficient high-quality evidence to support or refute the use of TENS for fibromyalgia. They found a small number of inadequately powered studies with incomplete reporting of methodologies and treatment interventions.

TENS for Musculoskeletal Pain in Hemophilia

Rodriguez-Merchan (2018) noted that musculoskeletal pain treatment is inadequate in many hemophilic patients. Analgesics are used only by 36 % of adult patients. FVIII/FIX intravenous infusion is mainly used to lessen pain, followed in frequency by usage of NSAIDS (primarily COX-2 inhibitors). In about 30 % of patients, pain continues after infusion of F VIII/IX. In acute hemarthroses pain treatment must continue until total disappearance (checked by ultrasonography) and include hematologic treatment, short-term rest of the involved joint, cryotherapy, joint aspiration and analgesic medication (paracetamol in mild pain, metamizole for more intense pain, and in a few precise patients, soft opioids such as codeine or tramadol). In the circumstance of intolerable pain these investigators use morphine hydrochloride either by continual infusion or a patient-controlled analgesia (PCA) pump, determined by the age, mental condition and grade of observance of the patient. Epidural blocks utilizing bupivacaine and fentanyl may be very effective as well. Three main strategies to alleviate chronic musculoskeletal pain secondary to hemophilic arthropathy (joint degeneration) exist: (i) pharmacologic management, (ii) physical medicine and rehabilitation, and (iii) intra-articular injections. As for pharmacologic management, NSAIDs (ibuprofen, diclofenac, celecoxib, robecoxib) are better than paracetamol. The advantages of tramadol or tramadol/paracetamol and non-tramadol opioids are scanty. With respect to physical medicine and rehabilitation, there is insufficient confirmation that a brace has supplementary favorable effect compared with isolated pharmacologic management. Land-based curative exercise and watery exercise have at the minimum a tiny short-run benefit. Curative ultrasound can be helpful (poor quality of evidence). The effectiveness of TENS for pain mitigation has not been proven. Electrical stimulation treatment can procure notable ameliorations. With respect to intra-articular injections, viscosupplementation appears to be a useful method for pain alleviation in the short-run (months). The short-run (weeks) advantage of intra-articular corticosteroids in the treatment of joint pain has been shown.

Interferential Stimulation

Interferential stimulation (IFS) is characterized by 2 alternating-current sine waves of differing frequencies that "work" together to produce an interferential current that is also known as a beat pulse or alternating modulation frequency. One of the 2 currents is usually held at 4,000 Hz, and the other can be held constant or varied over a range of 4,001 to 4;100 Hz. Interferential currents reportedly can stimulate sensory, motor, and pain fibers. Because of the frequency, the interferential wave meets low impedance when crossing the skin to enter the underlying tissue. This deep tissue penetration can be adjusted to stimulate parasympathetic nerve fibers for increased blood flow. According to proponents, interferential stimulation differs from TENS because it allows a deeper penetration of the tissue with more comfort (compliance) and increased circulation.

It has been claimed that IFS is highly effective in reducing: (i) pain and use of pain medications, (ii) edema and inflammation, and (iii) healing time, as well as in improvin range of motion, and activity levels, and quality of life. However, there are very few well designed studies such as randomized, double blind, controlled clinical trials that support such claims. Low (1988) stated that in spite of widespread agreement among physiotherapists that IFS has a marked pain relieving effect, there is a paucity of objective investigations into this analgesic effect. He claimed that both the therapeutic and physiological effects of interferential currents require further investigation. This notion is echoed by Goats (1990) who reported that evidence supporting the use of IFS in the control of edema appears mainly anecdotal. Reitman and Esses (1995) noted that there were no controlled studies proving the effectiveness of IFS. Indergand and Morgan (1995) reported that interferential current applied over the stellate ganglion did not change forearm hemodynamics in asymptomatic individuals. The authors stated that these findings challenged the concept that IFS can block sympathetic vasoconstrictor impulses in peripheral nerves. In a randomized placebo controlled study, Van Der Heijden et al (1999) evaluated the effectiveness of bipolar interferential electrotherapy (ET) and pulsed ultrasound (US) as adjuvants to exercise therapy for soft tissue shoulder disorders (n = 180). Patients with shoulder pain and/or restricted shoulder mobility, because of soft tissue impairment without underlying specific or generalized condition, were randomised to receive: (i) active ET plus active US; (ii) active ET plus dummy US; (iii) dummy ET plus active US; (iv) dummy ET plus dummy US; or (v) no adjuvants. Additionally, they received a maximum of 12 sessions of exercise therapy in 6 weeks. Measurements at baseline, 6 weeks and 3, 6, 9, and 12 months later were blinded for treatment. Outcome measures: recovery, functional status, chief complaint, pain, clinical

status, and range of motion. At the 6th-week, 7 patients (20 %) without adjuvants reported very large improvement (including complete recovery), 17 (23 %) and 16 (22 %) with active and dummy ET, and 19 (26 %) and 14 (19 %) with active and dummy US. These proportions increased to about 40 % at the 3rd-months, but remained virtually stable thereafter. The authors concluded that neither ET nor US proved to be effective as adjuvants to exercise therapy for soft tissue shoulder disorders. Jarit et al (2003) concluded that home IFS may help reduce pain, pain medication taken, and swelling while increasing range of motion in patients undergoing knee surgery. This could result in quicker return to activities of daily living and athletic activities. Drawbacks of this study were as follows: (i) while placebo subjects did consume more medications at all time points, the difference was only at some points, and (ii) a functional assessment scale was not used. The findings of this study need to be validated by further investigation. Furthermore, a technology assessment by the California Technology Assessment Forum (CTAF, 2005) concluded that interferential stimulation does not meet CTAF's assessment criteria.

A review on non-pharmacological therapies (including IFS) for acute and chronic LBP by the American Pain Society and the American College of Physicians (Chou et al, 2007) concluded that therapies with good evidence of moderate efficacy for chronic or sub-acute LBP are cognitive-behavioral therapy, exercise, spinal manipulation, and inter-disciplinary rehabilitation. For acute LBP, the only therapy with good evidence of efficacy is superficial heat.

Guidelines on treatment of LBP from the National Collaborating Centre for Primary Care (Savigny et al, 2009) found insufficient evidence for the use of interferential stimulation in LBP and recommended against its use for that indication.

In a systematic review and meta-analysis, Fuentes et al (2010) analyzed the available information regarding the efficacy of IFS in the management of musculoskeletal pain. Randomized controlled trials were obtained through a computerized search of bibliographic databases (i.e., CINAHL, Cochrane Library, EMBASE, MEDLINE, PEDro, Scopus, and Web of Science) from 1950 to February 8, 2010. Two independent reviewers screened the abstracts found in the databases. Methodological quality was assessed using a compilation of items included in different scales related to rehabilitation research. The mean difference, with 95 % confidence interval (CI), was used to quantify the pooled effect. A chi-square test for heterogeneity was performed. A total of 2,235 articles were found. A total of 20 studies fulfilled the inclusion criteria; 7 articles assessed the use of IFS on joint pain; 9 articles evaluated the use of IFS on muscle pain;

3 articles evaluated its use on soft tissue shoulder pain; and 1 article examined its use on post-operative pain. Three of the 20 studies were considered to be of high methodological quality, 14 studies were considered to be of moderate methodological quality, and 3 studies were considered to be of poor methodological quality. Fourteen studies were included in the meta-analysis. The authors concluded that IFS as a supplement to another intervention seems to be more effective for reducing pain than a control treatment at discharge and more effective than a placebo treatment at the 3-month follow-up. However, it is unknown whether the analgesic effect of IFS is superior to that of the concomitant interventions. Interferential current alone was not significantly better than placebo or other therapy at discharge or follow-up. Results must be considered with caution due to the low number of studies that used IFS alone. In addition, the heterogeneity across studies and methodological limitations prevent conclusive statements regarding analgesic efficacy.

Percutaneous Electrical Nerve Stimulation (PENS)

Percutaneous electrical nerve stimulation uses acupuncture-like needles as electrodes. These needles are placed in the soft tissues or muscles at dermatomal levels corresponding to local pathology (needles are usually inserted above and below and into the central area of pain). A 5-Hz frequency with a pulse width of 0.5 mS is usually used. If relief is not attained within 15 minutes, the frequency may be lowered to 1 Hz. According to PENS proponents, the main advantage of PENS over TENS is that it bypasses the local skin resistance and delivers electrical stimuli at the precisely desired level in close proximity to the nerve endings located in soft tissue, muscle, or periosteum of the involved dermatomes.

Percutaneous electrical nerve stimulation has also been used in the treatment of neck pain; however, there is insufficient evidence to support its effectiveness for this indication. Harris and Susman (2002) stated that the Philadelphia Panel recently formulated evidence-based guidelines for selected rehabilitation interventions in the management of low back, knee, neck, and shoulder pain. The guidelines were developed with the use of a 5-step process: (i) define the intervention, (ii) collect evidence, (iii) synthesize results, (iv) make recommendations based on the research, and (v) grade the strength of the recommendations. Outpatient adults with low back, knee, neck, or shoulder pain without vertebral disk involvement, scoliosis, cancer, or pulmonary, neurological, cardiac, dermatological, or psychiatric conditions were included in the review. To prepare the data, systematic reviews were performed for low back, knee, neck, and shoulder pain. Therapeutic exercise, massage, transcutaneous

electrical nerve stimulation, thermotherapy, ultrasound, electrical stimulation, and combinations of these therapies were included in the literature search. Studies were identified and analyzed based on study type, clinical significance, and statistical significance. The authors concluded that the Philadelphia Panel guidelines recommend continued normal activity for acute, uncomplicated LBP and therapeutic exercise for chronic, subacute, and post-surgical LBP; TENS and exercise for knee osteoarthritis; proprioceptive and therapeutic exercise for chronic neck pain; and the use of therapeutic ultrasound in the treatment of calcific tendonitis of the shoulder.

Weiner and Ernst (2004) reviewed common complementary and alternative treatment modalities for the treatment of persistent musculoskeletal pain in older adults. A critical review of the literature on acupuncture and related modalities, herbal therapies, homeopathy, and spinal manipulation was carried out. Review included 678 cases within 21 randomized trials and 2 systematic reviews of herbal therapies: 798 cases within 2 systematic reviews of homeopathy; 1,059 cases within 1 systematic review of spinal manipulation for LBP, and 419 cases within 4 randomized controlled trials for neck pain. The review of acupuncture and related modalities was based upon a paucity of well-controlled studies combined with the authors' clinical experience. Insufficient experimental evidence exists to recommend the use of traditional Chinese acupuncture over other modalities for older adults with persistent musculoskeletal pain. Promising preliminary evidence exists to support the use of percutaneous electrical nerve stimulation for persistent LBP. The authors noted that while the use of complementary and alternative modalities for the treatment of persistent musculoskeletal pain continues to increase, rigorous clinical trials examining their effectiveness are needed before definitive recommendations regarding the application of these modalities can be made.

A Cochrane review on electrotherapy for mechanical neck disorders (Kroeling et al, 2005) evaluated if electrotherapy relieves pain or improves function/disability in adults with mechanical neck disorders (MND). For the pain outcome, there was limited evidence of benefit, i.e., pulsed electromagnetic field (PEMF) therapy resulted in only immediate post-treatment pain relief for chronic MND and acute whiplash (WAD). Other findings included unclear or conflicting evidence (galvanic current for acute or chronic occipital headache; iontophoresis for acute, subacute WAD; TENS for acute WAD, chronic MND; PEMF for medium- or long-term effects in acute WAD, chronic MND); and limited evidence of no benefit (diadynamic current for reduction of trigger point tenderness in chronic MND, cervicogenic headache; permanent magnets for chronic

MND; electrical muscle stimulation (EMS) for chronic MND). The authors concluded that in pain as well as other outcomes, the evidence for treatment of acute or chronic MND by different forms of electrotherapy is either lacking, limited, or conflicting.

The National Institute for Health and Clinical Excellence's assessment on "Percutaneous electrical nerve stimulation for refractory neuropathic pain" (NICE, 2013) stated that "Current evidence on the safety of percutaneous electrical nerve stimulation (PENS) for refractory neuropathic pain raises no major safety concerns and there is evidence of efficacy in the short term. Therefore this procedure may be used with normal arrangements for clinical governance, consent and audit".

Fraser and Woodbury (2017) stated that fibromyalgia and complex regional pain syndrome (CRPS) are both chronic pain syndromes with pathophysiologic mechanisms related to autonomic nervous system (ANS) dysregulation and central sensitization. Both syndromes are considered difficult to treat with conventional pain therapies. These investigators described a female veteran with fibromyalgia and a male veteran with CRPS, both of whom failed multiple pharmacologic, physical and psychological therapies for pain, but responded to percutaneous electrical neural field stimulation (PENFS) targeted at the auricular branches of the cranial nerves. The authors concluded that while PENFS applied to the body has been previously described for treatment of localized pain, PENFS effects on cranial nerve branches of the ear was not well-known, particularly when used for regional and full-body pain syndromes such as those described here. They stated that PENFS of the ear is a minimally-invasive, non-pharmacologic therapy that could lead to improved quality of life (QOL) and decreased reliance on medication. However, they stated that ffurther research is needed to guide clinical application, particularly in complex pain patients.

Percutaneous Neuromodulation

Percutaneous neuromodulation therapy (PNT) is a variation of PENS, but utilizes different electrical impulses than PENS; it utilizes an alternating low and high frequency current at varying pulse impulses (Washington State Department of Labor and Industries, 2004). The electrical stimulation is delivered via needle-like electrodes which is purported to allow the stimulation to reach the deep tissue. Examples of this type of device include, but may not be limited to, the Vertis PNT System and the BioWavePRO Neuromodulation Pain Therapy System. The Vertis PNT is for treatment of back pain; the BioWavePRO, however, is not limited to the spine but may also be used in other painful areas in the body. These devices are not for home use, but must be used by a healthcare provider,

such as a physician or physical therapist, in a clinic or office setting.

Kang, et al. (2007) reported on a single-blinded pilot randomized controlled trial in 70 patients with knee osteoarthritis who were randomized to a BioWave Deepwave percutaneous neuromodulation device or to sham administered in a clinic over 30 minutes. Seven subjects assigned to sham were lost to followup. Pain intensity difference was the primary measure of efficacy in this trial. Pain intensity difference was defined as the difference in visual analog pain scale noted at pretreatment (baseline) versus the visual analog pain scale noted at each post-treatment period. The active group's pain intensity difference was statitically significantly greater than the sham group's pain intensity difference by 9.5 mm immediately after treatment. The active group's pain intensity difference was also greater than the sham group's pain intensity difference by 5.0 mm, 9.0 mm, and 7.0 mm for the 6-, 24-, and 48-hour post-treatment periods, respectively, although the pain intensity difference was not statistically significant at these time points. Additionally, a nonsignificant trend was noted in improvement of the pain intensity difference in the live group as compared to the sham group 48 hours post-treatment. Limitations of this pilot study include single blinding, lack of testing of adequacy of blinding, and lack of intention-to-treat analysis. The authors concluded: "The results from this pilot phase may be used to design a broader multicenter study that will be powered to provide greater data points leading to broader conclusions as to the treatment efficacy of the percutaneous Deepwave device."

Peripherally Implanted Nerve Stimulation

In this particular treatment, an electrical current is transmitted via an electrode that has been implanted around the selected peripheral nerve. This electrical current purports to block or disrupt the normal transmission of pain signals. The electrodes are connected by a wire to the peripherally implanted neurostimulator (also known as an implantable subcutaneous target stimulator). An external generator (similar to a remote control device) controls the degree of stimulation the individual receives.

In an industry funded study, Deer, et al. (2016) reported on a crossover study of 94 patients with pain of peripheral origin were implanted and then randomized to the treatment with peripheral nerve stimulation (45) or the control group (49). The primary efficacy endpoint was response rate, defined as a 30 percent decrease in a numerical rating scale, with no upward titration in the patient's medication regimen, three months months after randomization to treatment. The investigators reported that patients receiving active stimulation achieved a statistically significantly higher response rate of

38% versus the 10% rate found in the control group ($p = 0.0048$). Improvement in pain was statistically significant between the randomized groups, with the treatment group achieving a mean pain reduction of 27.2% from baseline to month 3 compared to a 2.3% reduction in the control group ($p < 0.0001$). During the partial crossover period, patients again demonstrated statistically significant improvement in pain relief with active stimulation compared to baseline. Further, the treatment group had significantly better improvement than the control group in secondary measures including but not limited to quality of life and satisfaction. Safety, assessed throughout the trial and with follow-up to one year, demonstrated no serious adverse events related to the device. The investigators reported that all device-related adverse events were minor and self-limiting. Additional studies confirming these benefits are needed.

Peripheral Subcutaneous Field Stimulation

Subcutaneous stimulation (peripheral nerve field stimulation/PNFS) is a novel neuromodulation modality that has increased in its utilization during the past decade. It consists of introducing a lead in the subdermal level to stimulate the small nerve fibers in that layer. Unlike other neuromodulation techniques including direct peripheral nerve stimulation, spinal cord stimulation (SCS), or deep brain stimulation, the precise target is not identified. Falco et al (2009) stated that relief of regional, non-appendicular pain, particularly LBP, through SCS has proven challenging. Recently, peripheral nerve stimulation (PNS), also known as PNFS depending on the stimulation area, has demonstrated efficacy for the treatment of well-localized, small areas of pain involving the abdomen, inguinal region, pelvis, face, occipital area, and low back. More widespread application of PNFS has been limited by its narrow field of coverage in a larger group of patients with diffuse or poorly localized pain.

McRoberts and Roche (2010) described a novel approach for the treatment of severe, chronic knee joint pain following total knee arthroplasty utilizing peripheral subcutaneous field stimulation (PSFS) and discussed the role of this treatment modality in patients with symptoms that are refractory to conventional pharmacologic, surgical, and physical therapies. These researchers presented 2 case reports of patients with chronic intractable knee pain where PNS via a permanent neurostimulating implant was introduced successfully. Both patients presented with persistent knee pain, for greater than 1 year, after having had total knee arthroplasty. Their symptoms failed to be alleviated by a variety of interventions including NSAIDS, oral anti-depressants, membrane stabilizers, opioids, physical therapy, surgical revisions, manipulation under anesthesia, local anesthetic patches, and TENS. In each case, direct stimulation of the

knee was achieved utilizing a peripheral nerve stimulator via a peri-articular approach. Neuromodulation daily has produced both significant pain relief and functional improvement. Significant decreases in VAS pain scores and improvement in functional capacity were observed during the stimulation trial and during the follow-up after permanent implantation. The mean VAS score changed dramatically. The authors concluded that introduction of PSFS directly to the painful knee area is a novel and simple procedure that was extremely effective for the relief of pain and may provide a breakthrough in the treatment of chronic intractable knee pain following total knee arthroplasty. The peri-articular approach has several advantages, including only small incisions over the lateral and medial knee, proximal thigh and abdomen resulting in minimal strain on the lead array with flexion and extension contributing to overall stability of this system.

Yakovlev and Resch (2010) presented a case report describing application of PSFS to a patient with chronic intractable atypical facial pain (ATFP) that conventional treatment failed to ameliorate. The patient underwent an uneventful PSFS trial with percutaneous placement of 2 temporary 8-electrode leads (Medtronic Inc, Minneapolis, MN) placed subdermally over the left mandible. After experiencing excellent pain relief over the next 2 days, the patient was implanted with permanent leads and rechargeable generator 2 and a half weeks later and reported sustained pain relief at 12-month follow-up visit. Peripheral subcutaneous field stimulation provides an effective treatment option for patients suffering from chronic ATFP who have failed conservative treatment. The authors concluded that PSFS offers an alternative treatment option to select patients with intractable ATFP.

In a retrospective study, Yakovlev et al (2010) evaluated the effectiveness of PSFS for the treatment of chronic hip pain after total hip arthroplasty (THA) and greater trochanteric bursectomy (GTB). A total of 12 patients with chronic post-operative pain after THA and GTB underwent an uneventful PSFS trial with percutaneous placement of 2 temporary 8-electrode leads positioned in the subcutaneous tissue in the area of greatest pain, parallel to post-operative scar over the affected upper lateral thigh. After experiencing excellent pain relief over the next 2 days, the patients were implanted with permanent leads and rechargeable or non-rechargeable generator 2 to 4 weeks later. They reported sustained pain relief at 12-month follow-up visits. The authors concluded that PSFS provided an effective alternative treatment option for select patients with chronic post-operative pain after THA and GTB who have failed conservative treatment.

Ricciardo et al (2010) presented a case study to exemplify the application of PSFS in the treatment of recalcitrant notalgia paraesthetica. The patient was a 60-year old woman with severe and disabling notalgia paraesthetica. The itch persisted despite the use of several medications -- topical and oral. Following a successful trial of PSFS with a temporary electrode, 2 subcutaneous electrodes were inserted into the affected area with a battery implanted subcutaneously in her right buttock. The patient was reviewed at 5 months post-implantation. She reported a greater than 85 % improvement in her itch. She also reported a major improvement in her quality of life, with particular improvement in her ability to sleep through the night. This case illustrated the possible utilization of PSFS in the treatment of notalgia paraesthetica, which is a common yet poorly understood and treated condition. The authors stated that replication and controlled studies are needed to determine the general applicability of this approach.

Goroszeniuk et al (2012) reported the use of an alternative approach to neuromodulation of anginal pain using subcutaneous leads placed at the site of pain. In this case series, 5 patients with refractory angina received successful treatment with subcutaneous target stimulation -- peripheral subcutaneous field stimulation. This technique was able to provide good analgesia in 2 patients that had had poor pain relief from existing spinal cord stimulators. All 5 patients achieved significant pain relief with a reduction in symptoms and a decrease in the use of pain medication.

Burgher et al (2012) performed a retrospective review of consecutive patients evaluated from August 2009 to December 2010 who had undergone trial of subcutaneous (SQ) PNS with inter-lead stimulation for axial spine pain. Patients proceeding to implant were followed post-operatively with routine clinical visits and a survey form at last follow-up. Ultrasound was used intra-operatively to ensure placement of electrodes at the appropriate depth in patients with larger body mass index. Primary outcome was patient-reported pain relief at last follow-up. Literature review was conducted by searching MEDLINE (1948 to present) and through an unstructured review by the authors. A total of 10 patients underwent trial of SQ PNS and 6 proceeded to permanent implantation; 3 of the 6 (50 %) implanted patients preferred neurostimulation programming that included inter-lead stimulation ("cross-talk"). Average duration of post-operative follow-up was 4.5 months (range of 2 to 9 months). Average patient-reported pain relief at last follow-up was 45 % (range of 20 to 80 %). One patient required re-operation for migration. Patients not proceeding to implant had paresthesia coverage but no analgesia. The authors concluded that SQ PNS is a promising therapy for axial neck and back pain based on a small cohort of patients. Ultrasound was useful to assist with electrode placement at the most appropriate depth beneath the skin. While inter-lead stimulation

has been preferred by patients in published reports, these investigators did not find it clearly influenced pain relief. The authors stated that future investigations should include a randomized, controlled study design, as well as defined implantation technique and neurostimulator programming algorithms.

H-Wave Stimulation

H-Wave stimulation is a form of electrical stimulation that differs from other forms of electrical stimulation in terms of its waveform. The H-wave produces low frequency muscle stimulation and high frequency pain control. H-wave stimulation has been purported for use in pain control for conditions such as complex regional pain syndrome (reflex sympathetic dystrophy), muscle sprains, temporomandibular joint dysfunctions or treatment of diabetic neuropathy.

H-wave stimulation delivers electrical stimulation in the form of milliamperage. H-wave stimulation is intended to emulate the H waveform found in nerve signals (Hoffman Reflex) and therefore enables greater and deeper penetration of a low frequency current, while using significantly less power than other machines. This allegedly makes H-Wave stimulation much safer, less painful and more effective than other forms of electrotherapy to date. The H-wave signal is a bipolar, exponential decaying waveform that supposedly overcomes the disadvantages of other electrotherapy machines. It allows the therapist to apply 2 treatments at the same time: (i) low-frequency muscle stimulation and (ii) high-frequency deep analgesic pain control (a "TENS" effect). **Note**: H-wave stimulation must be distinguished from the H-waves that are a component of electromyography.

The H-wave stimulator (Electronic Waveform Lab, Inc., Huntington Beach, CA) is an electrostimulation device that has been used to reduce pain and swelling associated with a variety of diseases and conditions. In a single-blinded clinical study, Kumar and Marshall (1997) evaluated the effectiveness of H-wave stimulation for the treatment of chronic (greater than 2 months) pain associated with diabetic (type 2) peripheral neuropathy (n = 31). Patients were randomly assigned to: (i) H-wave stimulation, or (ii) sham treatment. The authors reported that H-wave treated patients exhibited greater symptomatic relief than their sham-treated counterparts. Moreover, it has also been shown that H-wave stimulation may be a useful adjunctive modality when combined with pharmacotherapy (e.g., amitriptyline) to augment symptomatic relief in patients with diabetic peripheral neuropathy (Julka et al, 1998; McDowell et al, 1999).

On the other hand, H-wave stimulators have not been shown to be effective in reducing pain from causes other than chronic diabetic peripheral neuropathy, or in reducing edema or swelling. In particular, H-wave stimulation has not been demonstrated to be effective in treating chronic pain due to ischemia. In the study by Kumar and Marshall (1997), patients with significant peripheral vascular disease were excluded from the trial. Furthermore, in a randomized controlled study (n = 112), McDowell et al (1995) reported that H-wave stimulation was not effective in reducing experimental ischemic pain.

A systematic evidence review concluded that H-wave stimulation had a moderate to strong effects in relieving pain, reducing pain medication use and increasing functionality in patients with chronic soft tissue inflammation or neuropathic pain (Blum et al, 2008). A critique of this systematic evidence review by the Centre for Reviews and Dissemination (CRD, 2009) concluded that "it is not possible to determine whether the results of this review are reliable" given its significant methodologic limitations. In particular, very limited details of the included studies were given in the review; in particular it was unclear which studies were randomized, no control interventions were detailed, and there were insufficient details on the outcome measures used. Although a validity assessment was performed, the results were not presented. "Given these omissions, it is difficult to assess either the internal or external validity of the results." The CRD noted that the authors of the systematic evidence review used meta-analysis to combine the results, but different measures of effect appeared to be combined in a single effect size. Insufficient details on the outcome measures used in the included studies meant that it was not possible to determine if this was appropriate or not. The CRD critique noted that, in addition to four authors of the systematic evidence review being independent consultants for Electronic Waveform Lab (the makers of the H-Wave device), 2 authors were members of the research groups responsible for conducting the primary studies.

Intramuscular Stimulation

Intramuscular stimulation can be considered as a variation of acupuncture. It has been claimed to promote long-term relief in chronic neuropathic pain. Intramuscular stimulation utilizes the same sized needles as in acupuncture; they are inserted into the part of a shortened muscle where a nerve may be entrapped. This most often causes some local pain as the needle is re-inserted several times to release the nerve and lengthen the muscle. In general, treatments are administered once or twice weekly for 3 to 6 weeks. However, the clinical value of this invasive procedure has not been validated by randomized controlled studies.

Sympathetic Therapy (Dynatron)

Many chronic pain syndromes/conditions (e.g., peripheral neuropathies and reflex sympathetic dystrophy) are "sympathetically biased" and have no identifiable underlying cause(s).

Sympathetic Therapy is a non-invasive treatment protocol advocated for the symptomatic relief of patients with chronic pain. It is a patented method of delivering electrostimulation via peripheral nerves to create a "special" form of stimulation of the sympathetic nervous system. It incorporates dual interfering waveforms with specific electrode placement on the upper and lower extremities (8 electrodes/treatment). Electrodes are placed bilaterally over dermatomes, thus accessing the autonomic nervous system via the peripheral nervous system.

The treatment plan for Sympathetic Therapy includes clinical treatments followed by home therapy. Electrostimulation is administered by means of the Dynatron STS (a clinical unit) or the Dynatron STS Rx (a home unit). A software program is included with the clinical Dynatron unit to help doctors with electrode placement and to record patient progress. According to the manufacturer, electrostimulation delivered by the Dynatron is different from that provided by TENS. The key difference is in its application -- Dynatron applied within the Sympathetic Therapy protocol supposedly treats systemically while TENS treats transcutaneously at or near the primary pain location. Daily therapy sessions are needed to establish effectiveness of the treatment and to ascertain the most effective protocol for individual patients (20 or more sessions may be needed to complete this process). Each treatment session lasts about 60 mins. If the patient responds to treatment and the optimal protocol has been established, a home Dynatron unit may be prescribed to facilitate treatments over an extended period of time and, in most cases, indefinitely. If necessary, the patient may return to the clinic periodically for a follow-up visit to adjust the protocol or receive additional guidance in administering home therapy.

Guido (2002) reported on the effects of Sympathetic Therapy on 20 patients with chronic pain and peripheral neuropathies. Subjects were treated daily with the Dynatron STS for 28 days. At the beginning of the study, 11 of 15 patients reported being in moderate to severe pain, whereas by the end of treatment, 5 of 15 patients defined their pain as being moderate to severe. For these 15 patients, mean cumulative VAS for multiple locations of pain decreased significantly, from 107.8 to 45.3. (The authors stated, without further explanation, that self-reports of pain severity were unavailable for 5 of the

20 patients.) However, because the study did not include a randomized masked control group, placebo effects and other biases could affect results. In addition, the lack of data on pain severity in a quarter of the patients included in this study may have significantly biased the results. There are no published randomized controlled clinical trials of the effectiveness of Sympathetic Therapy in the management of patients with chronic intractable pain. Randomized controlled trials are needed to ascertain the clinical benefits of this treatment protocol in these patients.

An assessment (2003) conducted by the Washington State Department of Labor and Industries concluded that insufficient evidence exists to determine Dynatron STS' effectiveness in the treatment of chronic pain.

Guidelines on management of chronic pain from the Work Loss Data Institute (2008) considered, but did not recommend, sympathetic therapy for chronic pain.

Electroceutical Therapy

Electroceutical therapy is a noninvasive device that uses a variety of electrical modalities as a proposed treatment for acute and chronic pain. The device is similar to TENS, except electroceutical treatments use higher electrical frequencies, altering the electric current to mimic the human bioelectric system. This therapy may also be referred to as bioelectric nerve block, noninvasive neuron blockade, electroceutical neuron blockade and bioelectric treatment system. An example of this is the Hako-Med Pro Elect DT 2000.

Electroceutical medicine entails the use of various electrical modalities. While certain "low-strength" electrical treatments such as transcutaneous electrical nerve stimulation (TENS) units may be safely used at home, electroceutical treatments use much higher electrical frequencies than TENS units (ranging from 1 to 20,000 Hz compared to 0.5 to 100 Hz used in TENS) and may only be prescribed and administered under the supervision of a healthcare provider experienced in this method of treatment.

Electroceutical therapy, also known as bioelectric nerve block, involves blockade of axonal transmissions. Electroceutical therapy has been used in the management of neuropathic pain (non-malignant pain) as well as pain associated with cancer (malignant pain). According to a manufacturer of an electroceutical nerve block device, the electroceutical treatment approach is based on the non-invasive application of controlled, specific parameter bioelectric impulses. Electrical current is altered via special step-

down transformers into bioelectric impulses, which are designed to mimic the human bioelectric system. Currently, there are 2 distinctive electroceutical classifications: (i) stimulatory class in which repetitive action potentials are induced in excitable cells (depolarization and repolarization activity), and (ii) multi-facilitory class that produces biophysical effects without repetitive action potential propagation. The proper electroceutical class, dosage, regimen duration and anatomical placement of electrodes are determined by the individual patient's diagnosis. Proponents of electroceutical therapy claim that its use has resulted in significant relief of pain and elimination or drastic reductions in patients' pain medication requirements, such that patients are able to resume their daily activities. However, there is a lack of scientific evidence to substantiate these claims. Guidelines from the Work Loss Data Institute (2008) considered, but did not recommend, electroceutical therapy for chronic pain. Well-designed, randomized controlled clinical studies are needed to determine the usefulness of electroceutical therapy in the treatment of patients with acute or chronic pain.

Transcutaneous Electrical Joint Stimulation and Pulsed Electrical Stimulation

Transcutaneous electrical joint stimulation is also known as pulsed electrical stimulation; and the Bionicare device uses this type of electrical stimulation. Zizic et al (1995) evaluated the safety and effectiveness of pulsed electrical stimulation for the treatment of osteoarthritis (OA) of the knee (n = 78). Patients were treated 6 hours/day for 4 weeks. The investigators reported that patients treated with the active devices showed significantly greater improvement than the placebo group for all primary efficacy variables in comparisons of mean change from baseline to the end of treatment. Improvement of greater or equal to 50 % from baseline was shown in at least 1 primary efficacy variable in 50 % of the active device group, in 2 variables in 32 %, and in all 3 variables in 24 %. In the placebo group improvement of greater or equal to 50 % occurred in 36 % for one, 6 % for 2, and 6 % for 3 variables. Mean morning stiffness decreased 20 mins in the active device group and increased 2 mins in the placebo group ($p < 0.05$). No statistically significant differences were observed for tenderness, swelling, or walking time. The authors concluded that improvements in clinical measures for pain and function found in this study suggest that pulsed electrical stimulation is effective for treating OA of the knee. The investigators noted, however, that studies of the durability of results are warranted.

In a Cochrane review on pulsed electric stimulation for the treatment of OA (Hulme et al, 2002), the authors stated that current evidence suggests that electrical stimulation therapy may provide significant improvements for knee OA, but further studies are required to confirm whether the statistically significant results shown in these trials confer clinically significant and durable benefits.

A systematic evidence review by McCarthy et al (2006) concluded that pulsed electromagnetic field therapy is unlikely to benefit patients with knee osteoarthritis. The systematic evidence review identified 5 RCTs of pulsed electromagnetic field therapy for knee osteoarthritis: 2 RCTs scored 5 points for validity, 1 scored 4 and 2 scored 3. The investigators found that none of the individual studies reported a statistically significant difference between treatments for pain. Only 1 study (n = 83) with a low quality score of 3 reported a statistically significant difference between treatments in function (standardized mean difference -0.58, 95 % CI: -1.02 to -0.14). For all studies combined, there was no significant difference between interventions in pain (weighted mean difference -0.66, 95 % CI: -1.67 to 0.35) or function (weighted mean difference -0.70, 95 % CI: -1.92 to 0.52).

Fary and colleagues (2008) stated that OA of the knee is one of the main causes of musculoskeletal disability in the western world. Current available management options provide symptomatic relief (exercise and self-management, medication and surgery) but do not, in general, address the disease process itself. Moreover, adverse effects and complications with some of these interventions (medication and surgery) and the presence of co-morbidities commonly restrict their use. There is clearly a need to investigate treatments that are more widely applicable for symptom management and which may also directly address the disease process itself. The authors described the protocol of a double-blind, randomized, placebo-controlled, repeated measures trial to examine the effectiveness of pulsed electrical stimulation in providing symptomatic relief for people with OA of the knee over 26 weeks. A total of 70 subjects will be recruited and information regarding age, gender, body mass index and medication use will be recorded. The population will be stratified for age, gender and baseline pain levels. Outcome measures will include pain (100 mm VAS and Western Ontario and McMaster Universities Osteoarthritis Index [WOMAC] 3.1), function (WOMAC 3.1), stiffness (WOMAC 3.1), patient global assessment (100 mm VAS) and quality of life (Medical Outcomes Study Short-Form 36 [SF-36]). These outcomes will be measured at baseline, 4, 16 and 26 weeks. Activity levels will be measured at baseline and 16 weeks using accelerometers and the Human Activity Profile questionnaire. A patient global perceived effect scale (11-point Likert) will be completed at 16 and 26 weeks.

In a double-blind, randomized, placebo-controlled, repeated-measures study, Fary et al (2011) determined the effectiveness of subsensory, pulsed electrical stimulation (PES) in the symptomatic management of OA of the knee. A total of 70 participants with clinical and radiographically diagnosed OA of the knee were randomized to either PES or placebo. The primary outcome was change in pain score over 26 weeks measured on a 100-mm VAS. Other measures included pain on the WOMAC, function on the WOMAC, patient's global assessment of disease activity (on a 100-mm VAS), joint stiffness on the WOMAC, quality of life on the SF-36 health survey, physical activity (using the Human Activity Profile and an accelerometer), and global perceived effect (on an 11-point scale). Thirty-four participants were randomized to PES and 36 to placebo. Intent-to-treat analysis showed a statistically significant improvement in VAS pain score over 26 weeks in both groups, but no difference between groups (mean change difference 0.9 mm [95 % CI: -11.7 to 13.4]). Similarly, there were no differences between groups for changes in WOMAC pain, function, and stiffness scores (-5.6 [95 % CI: -14.9 to 3.6], -1.9 [95 % CI: -9.7 to 5.9], and 3.7 [95 % CI: -6.0 to 13.5], respectively), SF-36 physical and mental component summary scores (1.7 [95 % CI: -1.5 to 4.8] and 1.2 [95 % CI: -2.9 to 5.4], respectively), patient's global assessment of disease activity (-2.8 [95 % CI: -13.9 to 8.4]), or activity measures; 56 % of the PES-treated group achieved a clinically relevant 20-mm improvement in VAS pain score at 26 weeks compared with 44 % of controls (12 % [95 % CI: -11 % to 33 %]). The authors concluded that in this sample of subjects with mild-to-moderate symptoms and moderate-to-severe radiographic OA of the knee, 26 weeks of PES was no more effective than placebo.

Mendel et al (2010) noted that high-voltage pulsed current (HVPC), a form of electrical stimulation, is known to curb edema formation in laboratory animals and is commonly applied for ankle sprains, but the clinical effects remain undocumented. In a multi-center, randomized, double-blind, placebo-controlled trial, these investigators examined if, as an adjunct to routine acute and subacute care, subsensory HVPC applied nearly continuously for the first 72 hours after lateral ankle sprains affected time lost to injury. Data were collected at 9 colleges and universities and 1 professional training site. A total of 50 intercollegiate and professional athletes were included in this study. Participants were given near-continuous live or placebo HVPC for 72 hours post-injury in addition to routine acute and subacute care. Main outcome measure was time lost to injury measured from time of injury until declared fit to play. Overall, time lost to injury was not different between treated and control groups ($p = 0.55$). However, grade of injury was a significant factor. Time lost to injury after grade I lateral ankle sprains was greater for athletes receiving live HVPC than for those receiving placebo HVPC ($p = 0.049$), but no

differences were found between groups for grade II sprains (p = 0.079). The authors concluded that application of subsensory HVPC had no clinically meaningful effect on return to play after lateral ankle sprain.

Electro-Acuscope Myopulse

The Electro-Acuscope Myopulse Therapy System is an electronic device that has been used for a wide range of neuromuscular conditions. The Acuscope uses electricity to treat pain by stimulating the nervous system without puncturing the skin. The Myopulse, a companion instrument to the Acuscope, stimulates muscles, tendons and ligaments, reducing spasm, inflammation and strengthening tissue damaged by traumatic injury. This form of therapy purportedly helps the body heal itself by stimulating the supply of blood and oxygen to the involved area. The Electro-Acuscope Myopulse Therapy System has been used in the treatment of pain and many types of tissue damage including swelling, inflammation, and soreness. However there is insufficient scientific evidence to support its effectiveness.

Sacral Nerve Root and Lumbosacral Plexus Stimulation

Electrical stimulation of the sacral nerves (sacral neuromodulation) or lumbosacral plexus has been used for painful conditions resulting from chronic abdominal, pelvic, genital, and anal pain syndromes (Kim, 2004). Specific conditions that have been treated include pain from interstitial cystitis, coccydynia, pyelonephritis, pancreatitis, rectal fugax, and vulvodynia.

Procedures allowing access to sacral and lumbosacral nerves include a retrograde (cephalocaudad) epidural approach and a sacral transforaminal approach. The transforaminal approach is mainly used for the treatment of urge urinary incontinence and urinary retention, while the retrograde approach has been used primarily for the treatment of pelvic pain.

Evidence for sacral nerve root and lumbosacral plexus stimulation is limited to case reports and small case series. Alo and colleagues (1999) reported that lumbar and sacral nerve root stimulation through the retrograde approach resulted in adequate paresthesia and effective pain relief as reflected by VAS scores in 5 patients with chronic pain (e.g., ilioinguinal neuralgia, discogenic LBP, failed back syndrome, and vulvodynia).

These investigators concluded that further clinical trials are needed to assess the safety and long-term success rates of lumbar/sacral nerve root stimulation in the management of patients with chronic pain.

Anterograde sacral nerve root stimulation (SNRS) through the sacral hiatus is another method that has been tried for the treatment of pelvic pain. In a case report study, Falco et al (2003) found that anterograde SNRS provided good pain relief (as indexed by VAS scores) in a patient with chronic pelvic (rectal, coccygeal, and perineal) pain. The authors concluded that further investigation is needed before any conclusions can be rendered regarding the reliability of SNRS in the treatment of theses disorders.

Siegel and colleagues (2001) examined the effectiveness of transforaminal sacral nerve stimulation in patients with chronic intractable pelvic pain. After successful percutaneous trial stimulation, a neuroprosthetic sacral nerve stimulation device was surgically implanted in 10 patients with chronic intractable pelvic pain. Leads were placed in the S3 and S4 foramen in 8 and 2 cases, respectively. Patients were evaluated throughout the study using a patient pain assessment questionnaire on a scale of 0 (absence of pain) to 5 (excruciating pain). Pain was assessed at baseline, during test stimulation, and 1, 3 and 6 months after implantation of surgical lead. An additional long-term assessment was done at a median follow-up of 19 months. Of the 10 patients with the implant, 9 had a decrease in the severity of the worst pain compared to baseline at a median follow-up of 19 months. The number of hours of pain decreased from 13.1 to 6.9 at the same follow-up interval. There was also an average decrease in the rate of pain from 9.7 at baseline to 4.4 on a scale of 10 (always having pain) to 0 (never having pain). At a median of 19 months, 6 of 10 patients reported significant improvement in pelvic pain symptomatology. The authors concluded that these data imply that transforaminal sacral nerve stimulation can have beneficial effects on the severity and frequency of chronic intractable pelvic pain. They further stated that future clinical studies are necessary to determine the long-term effectiveness of this therapy.

The available evidence on sacral nerve root and lumbosacral plexus stimulation is insufficient to draw reliable conclusions about the effect of these interventions on chronic pelvic and abdominal pain.

Microcurrent Therapy

Microcurrent electrical nerve stimulation (MENS) devices are also non-invasive devices in which precise, tightly controlled electrical current is applied to specific points on the body. These specific points correspond with classical acupuncture points. MENS is also referred to as microelectrical therapy (MET) or microelectrical neuro-stimulation. Examples of this type of device include, but may not be limited to, Algonix, Alpha-Stim 100, Electro-Lyoscope 85P, Electro-Myopulse 75L, KFH Energy, MENS 2000-D, MICROCURRENT and Myopulse 75C.

Microcurrent therapy (MCT), also known as low-voltage microampere stimulation, is characterized by sub-sensory current that acts on the body's naturally occurring electrical impulses to decrease pain and facilitate the healing process. It uses microamperage instead of milliamperage to drive its current into the injured site. Microcurrent therapy uses current between 1 and 1,000 microA at a voltage of 10 to 60 V, and a frequency of 0.5 to 100 Hz. It differs from TENS in that it uses a significantly reduced electrical stimulation. While TENS blocks pain, MCT acts on the naturally occurring electrical impulses to decrease pain by stimulating the healing process.

Koopman et al (2009) stated that MCT is a novel treatment for pain syndromes. The MCT patch is hypothesized to produce stimuli that promote tissue healing by facilitating physiologic currents. Solid evidence from randomized clinical trials is lacking. To assess the effectiveness of MCT in treating non-specific, chronic LBP, these researchers conducted a double-blind, randomized, cross-over, pilot trial. A total of 10 succeeding patients presenting with non-specific, chronic LBP were included. Patients started with 2, 9-day baseline period followed by a 5-day treatment periods. During the treatment periods, either a placebo or MCT (verum) patch was randomly assigned. Mean and worst pain scores were evaluated daily by a VAS. Furthermore, analgesic use, side effects, and quality of life were assessed after each period. Differences between the last 4 days of a treatment period and the baseline period were calculated. Differences between verum and placebo periods per patient were compared using paired-t tests. A 20-mm VAS score reduction was considered clinically relevant. The VAS score was lower during verum treatment, with a reduction (95 % CI) of -0.43 (-1.74; 0.89) in mean and -1.07 (-2.85; 0.71) in worst pain. Analgesic use decreased during verum treatment, except for non-steroid anti-inflammatory drug use, which increased. Quality of life improved during verum treatment. However, none of the findings was statistically significant. A positive trend in MCT use for aspecific, chronic LBP was reported. The authors stated that further investigations are needed to evaluate the significance and relevance of these findings.

Furthermore, the American Pain Society's clinical practice guideline on non-surgical interventional therapies for LBP (Chou et al, 2009) concluded that few non-surgical interventional therapies for LBP have been shown to be effective in randomized, placebo-controlled trials.

Zuim et al (2006) evaluated the effect of microcurrent electrical nerve stimulation (MENS) and compared with occlusal splint therapy in temporo-mandibular disorders (TMD) patients with muscle pain. A total of 20 TMD patients were divided into 4 groups. One received occlusal splint therapy and MENS (I); other received splints and placebo MENS (II); the third, only MENS (III) and the last group, placebo MENS (IV). Sensitivity derived from muscle palpation was evaluated using a VAS. Results were submitted to analysis of variance ($p < 0.05$). There was reduction of pain level in all groups: group I (occlusal splint and MENS) had a 47.7 % reduction rate; group II (occlusal splint and placebo MENS), 66.7 %; group III (MENS), 49.7 % and group IV (placebo MENS), 16.5 %. In spite of that, there was no statistical difference (analysis of variance/$p < 0.05$) between MENS and occlusal splint therapy regarding muscle pain reduction in TMD patients after 4 weeks.

In a placebo-controlled, single-blinded, and randomized study, Gossrau et al (2011) evaluated the effect of micro-TENS in reducing neuropathic pain in patients with painful diabetic neuropathy (PDN). A total of 22 diabetic patients have been treated with a micro-TENS therapy and 19 patients have been treated with a placebo therapy. Treatment duration was 4 weeks with 3 therapeutic settings per week. Standardized questionnaires (Pain Disability Index [PDI], neuropathic pain score [NPS], Center for Epidemiologic Studies Depression Scale [CES-D]) were used to assess pain intensity, pain disability, as well as quality of life at baseline at the end of the treatment period and 4 weeks after treatment termination. Patients with a minimum of 30 % reduction in NPS were defined as therapy responders. After 4 weeks of treatment, 6/21 (28.6 %) patients in the verum group versus 10/19 (52.6 %) patients in the placebo group responded to therapy. The median PDI score after 4 weeks of treatment showed a reduction of 23 % in the verum versus 25 % in the placebo group. The differences did not reach statistical significance. The authors concluded that the pain reduction with the applied transcutaneous electrotherapy regimen is not superior to a placebo treatment.

Scrambler Therapy/The Calmare Therapy Device

Scrambler therapy (also known as transcutaneous electrical modulation pain reprocessing) is an electro-cutaneous nerve stimulation device that interferes with pain signal transmission by mixing a "non-pain" information into the nerve fibers. It consists of a multi-processor apparatus capable of simulating 5 artificial neurons that send out signals identified by the central nervous system as "no pain" via the application of surface electrodes on skin in the pain areas.

Marineo (2003) examined the effects of the Scrambler therapy in the treatment of drug-resistant oncological pain of the visceral/neuropathic type. A total of 11 terminal cancer patients (3 pancreas, 4 colon, 4 gastric) suffering from elevated drug resistant visceral pain were included in this study. The trial program was related to the first 10 treatment sessions. Subsequently, each patient continued to receive treatment until death. Pain measures were performed using the VAS before and after each treatment session and accompanied by diary recordings of the duration of analgesia in the hours following each single application. Any variation in pain-killing drug consumption was also recorded. All patients reacted positively to the treatment throughout the whole reference period. Pain intensity showed a significant decrease ($p < 0.001$), accompanied by a gradual rise both in the pain threshold and the duration of analgesia; 9 (81.8 %) of the patients suspended pain-killers within the first 5 applications, while the remaining 2 (18.2 %) considerably reduced the dosage taken prior to Scrambler therapy. No undesirable side effects were observed. Compliance was found to be optimal. The authors concluded that these preliminary results obtained using Scrambler therapy were extremely encouraging, both in terms of enhanced pain control after each treatment session and in view of the possible maintenance of effectiveness over time.

Sabato et al (2005) assessed the effectiveness of the Scrambler therapy in the treatment of neuropathic pain. A total of 226 patients, all suffering from intense drug-resistant neuropathic pain, were recruited for this trial. Inclusion criteria included neuropathic pain, very high baseline VAS. Exclusion criteria included pacemaker users, neurolithic blocks or neurolesive pain control treatment. The treated neuropathic pain syndromes were: failed back surgery syndrome (FBSS), post-herpetic neuralgia (PHN), trigeminal neuralgia, post-surgery nerve lesion neuropathy, pudendal neuropathy, brachial plexus neuropathy, LBP, and others. The trial program entailed 1 to 6 therapy sessions of 5 treatments, each one lasting 30 mins. Pain intensity was evaluated using VAS before and after each treatment. The statistical significance of VAS was measured using the paired t-test. The total results showed 80.09 % of responders (pain relief greater than 50 %), 10.18 % of partially responders (pain relief from 25 % to 49 %) and 9.73 % of no

responders (patients with pain relief less than 24 % or VAS greater than 3). The authors concluded that the Scrambler therapy produced a statistically significant ($p < 0.0001$) pain relief in all treated neuropathies.

In a pilot study, Marineo et al (2012) compared guideline-based drug management with Scrambler therapy. A clinical trial with patients randomized to either guideline-based pharmacological treatment or Scrambler therapy for a cycle of 10 daily sessions was performed. Patients were matched by type of pain including post-surgical neuropathic pain, PHN, or spinal canal stenosis. Primary outcome was change in VAS pain scores at 1 month; secondary outcomes included VAS pain scores at 2 and 3 months, pain medication use, and allodynia. A total of 52 patients were randomized. The mean VAS pain score before treatment was 8.1 points (control) and 8.0 points (Scrambler). At 1 month, the mean VAS score was reduced from 8.1 to 5.8 (-28 %) in the control group, and from 8 to 0.7 points (-91 %) in the Scrambler group ($p < 0.0001$). At 2 and 3 months, the mean pain scores in the control group were 5.7 and 5.9 points, respectively, and 1.4 and 2 points in the Scrambler group, respectively ($p < 0.0001$). More relapses were seen in polyradicular pain than monoradicular pain, but re-treatment and maintenance therapy gave relief. No adverse effects were observed. The authors concluded that in this pilot randomized trial, Scrambler therapy appeared to relieve chronic neuropathic pain better than guideline-based drug management.

In a pilot study, Smith et al (2010) evaluated the impact on chemotherapy-induced peripheral neuropathy (CIPN) associated with the MC5-A Calmare therapy device. A total of 18 patients from 1 center received 1-hour interventions daily over 10 working days. Of 18 patients, 16 were evaluable. The mean age of the patients (4 men and 14 women) was 58.6 years and the duration of CIPN was 3 months to 8 years. The most common drugs used by these subjects were taxanes, platinum, and bortezomib. At the end of the study (day 10), a 20 % reduction in numeric pain scores was achieved in 15 of 16 patients. The pain score fell 59 % from 5.81 +/- 1.11 before treatment to 2.38 +/- 1.82 at the end of 10 days ($p < 0.0001$ by paired t-test). A daily treatment benefit was seen with a strong statistically significant difference between the pre- and post-daily pain scores ($p < 0.001$). Four patients had their CIPN reduced to zero. A repeated-measures analysis using the scores from all 10 days confirmed these results. No toxicity was seen. Some responses have been durable without maintenance. The authors concluded that patient-specific cutaneous electro-stimulation with the MC5-A Calmare device appears to dramatically reduce pain in refractory CIPN patients with no toxicity. They stated that further studies (determining effectiveness compared with sham or placebo treatment, and the need for maintenance therapy) are underway to define the

benefit, mechanisms of action, and optimal schedule. The preliminary findings of this pilot study need to be validated by well-designed studies. There is a phase II clinical trial that examines the effectiveness of the MC5-A Scrambler therapy in reducing peripheral neuropathy caused by chemotherapy.

Ricci et al (2012) evaluated the effectiveness of an innovative neuromodulative approach to the treatment of chronic pain using electrical stimulus integrated with pharmacological support. The MC5-A Calmare is a new device for patient-specific cutaneous electro-stimulation which, by "scrambling" pain information with "no pain" information, aims to reduce the perception of pain intensity. These researchers prospectively treated 73 patients with cancer-related (n = 40) and non-cancer-related (n = 33) pain whose pain management was unsatisfactory. The primary objective of the study was to assess efficacy and tolerability of the device. Pain intensity was assessed daily with a Numerical Rating Scale (NRS) for the duration of treatment (2 weeks) and then on a weekly basis for the 2 weeks of follow-up. Mean pain value at T0 (pre-treatment value) was 6.2 [+/- 2.5 SD], 1.6 (+/- 2.0) ($p < 0.0001$) at T2 (after the 10th day of treatment), and 2.9 (+/- 2.6) ($p < 0.0001$) at T4 (after the second week of follow-up, i.e., 1 month after the beginning of treatment). Response after the second week of treatment showed a clear reduction in pain for both cancer (mean absolute delta of the reduction in NRS value = 4.0) and non-cancer (mean delta = 5.2) patients. The pain score had decreased by 74 % at T2. On the basis of pre-established response criteria, there were 78 % of responders at T2 and 81 % at T4. No side effects were reported. The authors concluded that these preliminary results suggested that cutaneous electro-stimulation with the MC5-A Calmare can be hypothesized as part of a multi-modality approach to the treatment of chronic pain. They stated that further studies on larger numbers of patients are needed to assess its efficacy, to quantify the effects of inter-operator variability, and to compare results obtained from the active device versus those from a sham machine.

Smith and Marineo (2018) noted that post-herpetic neuropathy (PHN) is common, severe, and often refractory to treatment. These investigators treated 10 patients with refractory PHN using Scrambler therapy, a neurocutaneous stimulation device that delivers "non-pain" information with surface electrodes. Scrambler therapy was given as 30-minute sessions daily for 10 days. Pain was recorded before and after treatment. The average pain score rapidly diminished from 7.64 ± 1.46 at baseline to 0.42 ± 0.89 at 1 month, a 95 % reduction, with continued relief at 2 and 3 months. Patients achieved maximum pain relief with less than 5 treatments. The authors concluded that the Scrambler therapy appeared to have a promising effect on PHN, with prompt and continued relief and no side effects. They stated that further research is warranted.

Pachman et al (2014) stated that chemotherapy-induced peripheral neuropathy (CIPN) is a common toxicity associated with multiple chemotherapeutic agents. CIPN may have a detrimental impact on patients' quality of life and functional ability, as well as result in chemotherapy dose reductions. Although symptoms of CIPN can improve with treatment completion, symptoms may persist. Currently, the treatment options for CIPN are quite limited. Duloxetine, a serotonin-norepinephrine reuptake inhibitor, has the most evidence supporting its use in the treatment of CIPN. Other agents with potential benefit for the treatment of established CIPN include gabapentinoids, venlafaxine, tricyclic antidepressants, and a topical gel consisting of the combination of amitriptyline, ketamine, and baclofen; none of these, however, has been proven to be helpful and ongoing/future studies may well show that they are not beneficial. The use of these agents is often based on their efficacy in the treatment of non-CIPN neuropathic pain, but this does not necessarily mean that they will be helpful for CIPN-related symptoms. Other non-pharmacologic interventions including acupuncture and Scrambler therapy are supported by positive preliminary data; however, further larger, placebo-controlled trial data are needed to confirm or refute their effectiveness.

In a double-blinded, randomized controlled trial, Starkweather et al (2015) evaluated the effects of Calmare, a non-invasive neurocutaneous electrical pain intervention, on lower back pain intensity as measured by the "worst" pain score and on pain interference using the Brief Pain Inventory-Short Form, on measures of pain sensitivity assessed by quantitative sensory testing, and on mRNA expression of pain sensitivity genes. A total of 30 participants were randomized to receive up to 10 sessions of Calmare® treatment (n = 15) or a sham treatment (n = 15) using the same device at a non-therapeutic threshold. At 3 weeks after conclusion of treatment, compared with the sham group, the Calmare® group reported a significant decrease in the "worst" pain and interference scores. There were also significant differences in pain sensitivity and differential mRNA expression of 17 pain genes, suggesting that Calmare® can be effective in reducing pain intensity and interference in individuals with persistent low back pain by altering the mechanisms of enhanced pain sensitivity. The authors stated that further study of long-term pain outcomes, particularly functional status, analgesic use and health care utilization, is warranted.

Pachman et al (2015) stated that CIPN, a common side effect of chemotherapy, needs better effective treatments. Preliminary data support the use of Scrambler therapy, a device which treats pain via noninvasive cutaneous electrostimulation, for the treatment of CIPN. The current manuscript reported data from a pilot trial, performed to investigate the effect of Scrambler therapy for the treatment of established CIPN. Eligible patients

had CIPN symptoms of greater than or equal to 1 month duration with tingling and/or pain greater than or equal to 4/10 during the prior week. Patients were treated with Scrambler therapy to the affected area(s) for up to 10 daily 30-min sessions. Symptoms were monitored using a neuropathy questionnaire consisting of numerical analog scales ranging from 0 to 10, daily before therapy as well as weekly for 10 weeks after therapy. Descriptive summary statistics formed the basis of data analysis. A total of 37 patients were enrolled; 25 patients were treated primarily on their lower extremities while 12 were treated primarily on their upper extremities. There was a 53 % reduction in pain score from baseline to day 10; a 44 % reduction in tingling; and a 37 % reduction in numbness. Benefit appeared to last throughout 10 weeks of follow-up. There were no substantial adverse events. The authors concluded that preliminary data support that Scrambler therapy may be effective for the treatment of CIPN; they stated that a prospective placebo-controlled clinical trial should be performed.

In a single-center, case-series study, Notaro et al (2016) examined the effectiveness of Scrambler therapy in reducing cancer pain induced by skeletal and visceral metastases after failure of standard treatments, including pharmacological therapies and radiation therapy. A total of 25 consecutive patients underwent Scrambler therapy individually delivered by MC5-A Calmare for 10 daily sessions each of 30 to 40 mins. Pain was measured by a numeric rating scale at baseline, as well as before and after each treatment session; 100 % of patients reached a pain relief of greater than or equal to 50 %. Pain score was reduced from 8.4 at baseline to 2.9 after treatment, with a mean pain relief of 89 %. The sleeping hours improved from 4.4 ± 1.2 to 7.5 ± 1.1. The duration of pain control by Scrambler therapy was 7.7 ± 5.3 weeks. No adverse events were observed. The authors concluded that Scrambler therapy did not present toxicity and allowed opioids dosage reduction, and it is also a repeatable treatment. They stated that present novel data support that Scrambler therapy appeared to be effective for the treatment of cancer pain; further evaluation in RCTs is needed to confirm these findings.

Majithia et al (2016) evaluated what is known regarding the mechanisms and mechanics of Scrambler therapy and investigated the preliminary data pertaining to the effectiveness of this treatment modality. The PubMed/Medline, SCOPUS, Embase, and Google Scholar databases were searched for all articles published on Scrambler therapy prior to November 2015. All case studies and clinical trials were evaluated and reported in a descriptive manner. To-date, 20 reports, of varying scientific quality, have been published regarding this device; all but 1 small study, published only as an abstract, provided results that appeared positive. The authors concluded that the positive findings from preliminary studies with Scrambler therapy support that this device provides benefit

for patients with refractory pain syndromes. Moreover, they stated that larger, randomized studies are needed to further evaluate the effectiveness of this approach.

Smith and colleagues (2017) stated that chronic post-mastectomy pain (cPMP), including post-lumpectomy pain, is common with no established ways of treatment. These researchers treated 3 consecutive patients referred with cPMP with Scrambler therapy. Treatment was given across the area of pain following the dermatomes for 45 minutes daily, for several consecutive days until relief, and then was repeated as needed. The Scrambler therapy MC5A device synthesized 16 different waveforms that resemble action potentials, delivered to the surface receptors of the c-fibers, to send "non-pain" information along the damaged pathways to reduce central sensitization. All 3 had marked (over 75 %) and sustained (months) reduction of allodynia, hyperalgesia, and pain. All reported marked improvements in their quality of life and normal function. One woman was able to stop chronic opioid use. No side effects were observed. The authors concluded that Scrambler therapy is a promising way to relieve cancer and other types of neuropathic pain, and may be helpful in cPMP. They stated that further prospective clinical trials are needed.

Non-Invasive Interactive Neurostimulation (e.g., the InterX 1000 Neurostimulator Device)

The InterX 1000 neurostimulator appears to be a hand-held, personal device for home use. It delivers interactive, high amplitude, high density stimulation to the cutaneous nerves, activating the body's natural pain relieving mechanisms (segmental and descending inhibition). However, there is insufficient evidence regarding its effectiveness for the treatment of chronic pain.

In a randomized, sham-controlled, pilot study, Selfe et al (2008) examined the effects of non-invasive interactive neurostimulation used as an adjunct to usual care, on pain and other symptoms in adults with OA of the knee. A total of 37 adults with knee OA (based on American College of Rheumatology diagnostic criteria) were included in this study. Subjects received 17 non-invasive interactive neurostimulation (active or sham) sessions over 8 weeks with a week 12 follow-up. Outcome measures included 11-point numeric rating scale for weekly pain; WOMAC, patient global assessment, and SF-36 completed at baseline and weeks 4, 8, and 12. For the main outcome, pain, the differences between the groups over time did not reach statistical significance (all $p > 0.05$). However, a clinically important reduction in pain (defined as a 2-point or 30 % reduction on an 11-point numeric rating scale) was maintained at week 12 by the active non-

invasive interactive neurostimulation group (2.17 points, 34.55 % reduction) but not the sham group (1.63, 26.04 % reduction). Pain improved over time in participants regardless of group membership (numeric rating scale average pain, $p = 0.002$; numeric rating scale worst pain, $p < 0.001$; and WOMAC pain, $p < 0.001$), as did WOMAC function, WOMAC stiffness, and WOMAC total score (all $p < 0.001$). Repeated measures ANOVA revealed a statistically significant difference between the groups over time for the SF-36 Vitality scale, $F (3, 105) = 3.54$, $p = 0.017$. In addition, the active device group improved on the patient global assessment from baseline to week 8 compared to the sham device group, $F (1, 35) = 4.025$, $p = 0.053$. The authors concluded that in this pilot study, clinically important reductions in knee pain were maintained at week 12 in the active, but not the sham, non-invasive interactive neurostimulation group. They stated that further study of this non-invasive therapy is needed.

Gorodetskyi et al (2010) undertook a trial with 60 patients who had undergone operative reduction and internal fixation of bimalleolar, AO type B2 ankle fractures with comminution. Patients were randomized into 2 groups, one of which received post-operative treatment using a non-invasive interactive neurostimulation device (InterX) and the other with a sham device. The trial was designed to test the hypothesis that incorporation of non-invasive interactive neurostimulation into the rehabilitation protocol would result in reduced pain, increased range of motion (ROM), reduced edema, and reduced consumption of pain medication, in comparison with the sham therapy group. Outcome measurements included the patient's subjective assessment of level of pain, ROM, and the extent of edema in the involved ankle, and the use of ketorolac for post-operative control of pain. The authors concluded that these results showed significantly better results in the patients receiving treatment with active neurostimulation (repeated measures analysis of variance, $p < 0.001$).

In a Cochrane review, Lin and colleagues (2012) evaluated the effects of rehabilitation interventions following conservative or surgical treatment of ankle fractures in adults. The authors concluded that there is limited evidence supporting early commencement of weight-bearing and the use of a removable type of immobilization to allow exercise during the immobilization period after surgical fixation. Because of the potential increased risk of adverse events, the patient's ability to comply with the use of a removable type of immobilization to enable controlled exercise is essential. There is little evidence for rehabilitation interventions during the immobilization period after conservative orthopedic management and no evidence for stretching, manual therapy or exercise compared to usual care following the immobilization period. Furthermore, they

stated that small, single studies showed that some electrotherapy modalities may be beneficial. They stated that more clinical trials that are well-designed and adequately-powered are needed to strengthen current evidence.

Teodorczyk-Injeyan et al (2015) evaluated the effect of treatment with a novel non-invasive interactive neurostimulation device (InterX5000) on the production of inflammatory biomarkers in chronic and recurrent mechanical neck pain (NP) syndrome. This study represented pilot biological data from a RCT. A total of 25 NP patients and 14 asymptomatic subjects included for baseline comparison only completed the study. The patients received 6 InterX5000 or placebo treatments within 2 weeks, and pre-treatment and post-treatment blood samples were collected for in-vitro determination of biomarker production. Whole blood cell cultures were activated by lipopolysaccharide or by the combination of lipopolysaccharide and phytohemagglutinin for 24 to 48 hours. The levels of tumor necrosis factor-alpha (TNFα) and its soluble type II receptor (sTNFR II), interleukin (IL) 1, IL-1 receptor antagonist (IL-1RA), IL-6, IL-10, and monocyte chemotactic protein (CCL2/MCP-1) were determined by specific immunoassays. Compared with asymptomatic subjects, baseline production levels of all pro-inflammatory mediators (TNFα, IL-1β, IL-6, and CCL2/MCP-1) were significantly augmented or trended higher ($p = 0.000$ to 0.008) in patients with NP. Of the anti-inflammatory markers, only IL-1RA was significantly elevated ($p = 0.004$). The increase in IL-10 and TNF receptor II levels did not reach statistical significance. Neither InterX5000 nor placebo therapy had any significant effect on the production of the inflammatory mediators over the study period. The authors concluded that this investigation determined that inflammatory cytokine pathways are activated in NP patients but found no evidence that a short course of InterX5000 treatment normalized the production of inflammatory biomarkers.

Electro Therapeutic Point Stimulation

Electro-therapeutic point stimulation (ETPS), also known as microcurrent point stimulation (MPS), employs a non-invasive device to administer low-frequency direct current to acupuncture points, motor/trigger points, and contracted muscle bands. The device (known as called the ETPS 1000) has an enhanced point finder that detects treatment points on the skin and applies brief, concentrated electrical microstimulation in short bursts. This modality/approach combines the principles of acupuncture, massage, physical therapy and microcurrent stimulation. The treatment can be self-administered by the patient at home. There is insufficient peer-reviewed evidence to support the safety and effectiveness of ETPS/MPS.

Aliyev and Geiger (2012) examined the effects of cell-stimulation therapy of lateral epicondylitis with frequency-modulated low-intensity electric current. Patients with lateral epicondylitis were subjected to a 12-week cell-stimulation therapy with low-intensity frequency-modulated electric current in addition to routine therapy. Patients in the control group received the same routine therapy and sham stimulation (the therapeutic apparatus was not energized). The effectiveness of MPS was estimated by comparing medical indices before therapy and at the end of a 12-week therapeutic course using a 10-point pain severity numeric rating scale (NRS) and Roles-Maudsley pain score. The study revealed high therapeutic efficiency of cell-stimulation with low-intensity electric current resulting probably from up-regulation of intracellular transmitters, interleukins, and prostaglandins playing the key role in the regulation of inflammation. The findings of this study need to be validated by well-designed studies with long-term follow-up.

Pulsed Stimulation (e.g., P-Stim)

In a pilot study, Sator-Katzenschlager et al (2003) tested the hypothesis that auricular electro-acupuncture (EA) relieves pain more effectively than conventional manual auricular acupuncture. These researchers studied 21 chronic cervical pain patients without radicular symptoms with insufficient pain relief (VAS greater than 5) treated with standardized analgesic therapy. All patients received disposable acupuncture needles on the dominant side on the following acupuncture points: cervical spine, shen men, and cushion. In 10 patients, needles were continuously stimulated (2-mA constant current, 1 Hz monophasic) by using the electrical point stimulation device P-STIM. In 11 control patients, no electrical stimulation was administered. All needles were withdrawn 48 hrs after insertion. Acupuncture was performed once a week for 6 wks. Patients had to complete a questionnaire assessing pain intensity, psychological well-being, activity, sleep, and demand for rescue medication (lornoxicam and tramadol). The reduction in pain scores was significant in the EA group. Similarly, psychological well-being, activity, and sleep were significantly improved in patients receiving EA, and consumption of rescue medication was significantly less. These results demonstrated that continuous electrical stimulation of auricular acupuncture points by using the new point stimulation device P-STIM improves the treatment of chronic cervical pain in an outpatient population. The authors concluded that continuous electrical stimulation of auricular acupuncture points by using the new point stimulation device P-STIM significantly decreases pain intensity and significantly improves psychological well-being, activity, and sleep in chronic cervical pain patients. This was a pilot study with small number of subjects with short-term follow-up.

In a prospective, randomized, double-blind, controlled study, Sator-Katzenschlager et al (2004) tested the hypothesis that auricular EA relieves pain more effectively than conventional manual auricular acupuncture (CO) in chronic LBP patients with insufficient pain relief (VAS greater than or equal to 5) treated with standardized analgesic therapy. Disposable acupuncture needles were inserted in the auricular acupuncture points 29, 40, and 55 of the dominant side and connected to a newly developed battery-powered miniaturized stimulator worn behind the ear. Patients were randomized into group EA (n = 31) with continuous low-frequency auricular EA (1 Hz biphasic constant current of 2 mA) and group CO (n = 30) without electrical stimulation (sham-EA). Treatment was performed once-weekly for 6 wks, and in each group needles were withdrawn 48 hrs after insertion. During the study period and a 3-month follow-up, patients were asked to complete the McGill questionnaire. Psychological well-being, activity level, quality of sleep, and pain intensity were assessed by means of VAS; moreover, analgesic drug consumption was documented. Pain relief was significantly better in group EA during the study and the follow-up period as compared with group CO. Similarly, psychological well-being, activity, and sleep were significantly improved in group EA versus group CO, the consumption of analgesic rescue medication was less, and more patients returned to full-time employment. Neuropathic pain in particular improved in patients treated with EA. There were no adverse side effects. These results were the first to demonstrate that continuous EA stimulation of auricular acupuncture points improves the treatment of chronic LBP in an out-patient population. The authors concluded that continuous electrical stimulation of auricular acupuncture points using the new point stimulation device P-Stim significantly decreases pain intensity and improves psychological well-being, activity, and sleep in chronic LBP patients. This was a small study with a short-term follow-up.

Sator-Katzenschlager and Michalek-Sauberer (2007) stated that acupuncture is now accepted as a complementary analgesic treatment. Auricular acupuncture is a distinct form of acupuncture. Electrical stimulation of acupoints (EA) increases the effects of acupuncture. Recently, an auricular EA device, the P-Stim, has become available. Clinical studies in outpatients have investigated the P-Stim in chronic musculo-skeletal pain and its use for minor surgery. In chronic cervical or LBP, auricular EA was more effective than conventional auricular acupuncture. The results in acute pain were controversial. Auricular EA reduced pain and remifentanil consumption during oocyte aspiration when compared with conventional auricular acupuncture or a sham treatment. However, after third molar tooth extraction, auricular EA and auricular acupuncture failed

to reduce either postoperative pain or analgesic consumption. The authors concluded that further large-scale studies are needed to evaluate the analgesic efficacy of auricular EA.

Michalek-Sauberer et al (2007) examined the effects of auricular EA on pain and analgesic drug consumption in the first 48 hrs after unilateral mandibular third molar tooth extraction under local anesthesia in a prospective, randomized, double-blind, placebo-controlled study in 149 patients. Patients received either auricular acupuncture with electrical stimulation (AE, n = 76) or without (AA, n = 37) electrical stimulation at an alternating frequency of 2/100 Hz or a sham AE with metal plates instead of needles and no electrical stimulation, no-needle (NN, n = 36) at the AA points 1 (tooth), 55 (Shen men) and 84 (mouth) during the entire study period. Regularly rated pain intensity (5-point verbal rating scale), consumption of acetaminophen 500-mg tablets and additional rescue medication with 500-mg mefenamic acid were assessed. The median fraction of time when pain was rated as moderate or worse (upper and lower quartile): AE: 33 % (12 %, 64 %), AA: 22 % (6 %, 56 %), NN: 30 % (7 %, 53 %) did not differ significantly among the treatment groups. There were no significant differences in mean number of acetaminophen 500-mg tablets (range): AE: 5.2 (0 to 12), AA: 4.6 (0 to 11), NN: 5.4 (0 to 10) or percentage of patients requiring additional mefenamic acid: AE: 19 %, AA: 18 %, NN: 19 %. The authors concluded that neither AE nor AA alone reduce either pain intensity or analgesic consumption in a molar tooth extraction model of acute pain.

Wang (2007) reported the successful treatment of a patient with post-herpetic neuralgia (PHN) using traditional pharmacology in combination with acupuncture. A 13-year old girl developed PHN following a severe attack of varicella zoster. Despite a 1-week course of intravenous acyclovir initiated at the onset of symptoms, the patient developed persistent left facial pain and constant nausea after lesions were healed. A comprehensive pain treatment regimen, consisting of a stellate ganglia block, medications, transcutaneous electrical nerve stimulation and hypnosis, was administered, but the patient did not gain any incremental pain relief. The acupuncture service was consulted to provide assistance with this patient's pain management. A combination of body and auricular acupuncture as well as related techniques, including acupressure and transcutaneous acupoint electrical stimulation, was added to the pain treatment regimen. After 10 complementary acupuncture treatments over a 2-month period, the patient's nausea disappeared. Her left facial pain continued to decline from a maximum of 10 to 0 as assessed by a VAS over a period of 4 months following self-administered treatments of acupressure and transcutaneous acupoint electrical stimulation. The patient was then gradually weaned off all her medications and the

complementary acupuncture treatment. She was discharged from the pediatric pain clinic after 5 months of the combined therapy. The author concluded that acupuncture and its related techniques may be an effective adjunctive treatment for symptoms associated with PHN and deserved further study.

Holzer et al (2011) examined the effects of electrical auricular acupuncture (AA) on post-operative pain in patients undergoing laparoscopy with an emphasis on patient-blinding and the exclusion of therapist-patient interactions. With institutional review board approval and written informed consent, these investigators included 40 female patients undergoing laparoscopy. Patients were randomly assigned to receive AA (shen men, thalamus and 1 segmental organ-specific point) or electrodes only and an electrical stimulation device. All patients received this intervention under general anesthesia guaranteeing patient blinding and excluding therapist-patient interactions. Needles and devices were removed 72 hours post-operatively. Post-operatively, patients received 1,000-mg paracetamol every 6 hours. Additional piritramide was given on demand. A blinded observer obtained the VAS scores at 0, 2, 24, 48, and 72 hours as well as the post-operatively administered doses of piritramide. There was no difference in VAS scores or the consumption of piritramide during the first 72 hours post-operatively between groups (acupuncture versus placebo: 2.32 [1.40 to 3.25] versus 2.62 [1.89 to 3.36] average pain on VAS 0-10; 15.3 [12.0 to 18.6] mg versus 13.9 [10.5 to 17.3] mg piritramide). Values are expressed as mean CI. The authors concluded that the findings of this study showed no reduction in post-operative pain or an opioid sparing effect of auricular acupuncture in women undergoing laparoscopic procedures. Because the authors emphasized blinding of the patients and the exclusion of therapist-patient interactions, this study suggested that electrical auricular acupuncture has no effect on post-operative pain.

In a double-blind, randomized, placebo-controlled, repeated-measures trial, Fary and colleagues (2011) examined the effectiveness of sub-sensory, pulsed electrical stimulation (PES) in the symptomatic management of osteoarthritis (OA) of the knee. A total of 70 participants with clinical and radiographically diagnosed OA of the knee were randomized to either PES or placebo. The primary outcome was change in pain score over 26 weeks measured on a 100-mm VAS. Other measures included pain on the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), function on the WOMAC, patient's global assessment of disease activity (on a 100-mm VAS), joint stiffness on the WOMAC, quality of life on the Medical Outcomes SF-36 health survey, physical activity (using the Human Activity Profile and an accelerometer), and global perceived effect (on an 11-point scale). Thirty-four participants were randomized to PES

and 36 to placebo. Intent-to-treat analysis showed a statistically significant improvement in VAS pain score over 26 weeks in both groups, but no difference between groups (mean change difference 0.9 mm [95 % CI: -11.7 to 13.4]). Similarly, there were no differences between groups for changes in WOMAC pain, function, and stiffness scores (-5.6 [95 % CI: -14.9 to 3.6], -1.9 [95 % CI: -9.7 to 5.9], and 3.7 [95 % CI: -6.0 to 13.5], respectively), SF-36 physical and mental component summary scores (1.7 [95 % CI: -1.5 to 4.8] and 1.2 [95 % CI: -2.9 to 5.4], respectively), patient's global assessment of disease activity (-2.8 [95 % CI: -13.9 to 8.4]), or activity measures; 56 % of the PES-treated group achieved a clinically relevant 20-mm improvement in VAS pain score at 26 weeks compared with 44 % of controls (12 % [95 % CI: -11 5 to 33 %]). The authors concluded that in this sample of subjects with mild-to-moderate symptoms and moderate-to-severe radiographic OA of the knee, 26 weeks of PES was no more effective than placebo.

Neurolumen Device

The Neurolumen is a portable machine that consists of a control unit, 4 wrap assemblies and a battery charger. Each wrap contains 2 laser diodes, 4 light emitting diodes and 1 or 2 electrolytic nerve stimulation gel pads. Once the wraps are in place, the control unit provides up to 30 mins of simultaneous TENS, low-level laser (LLLT) and light-emitting diode (LED) therapy.

However, there is a lack of evidence regarding the effectiveness of the Neurolumen device for the treatment of Morton's neuroma or any other indications. An UpToDate review on "on Peripheral Nerve Tumors" (Gilchrist and Donahue, 2013) states that "Morton neuroma is a subject of controversy regarding its nomenclature, pathology, and appropriate treatment. Abnormalities ascribed to Morton neuroma are typically located between the metatarsals of the third and fourth toes or at the bifurcation of the fourth plantar digital nerve. The lesions look like a traumatic neuroma grossly, and are comprised of degenerated and/or demyelinated axons, vascular hyalinization, and fibrosis. Clinical manifestations can include pain and tenderness, but similar lesions are common in patients who are asymptomatic. Surgical removal is advocated by some authors for those who fail conservative measures, but data are limited regarding the effectiveness of surgical and nonsurgical interventions for Morton neuroma". Furthermore, an UpToDate review on "Overview of running injuries of the lower extremity (Callahan, 2013) does not mention the use of electrical stimulation or laser therapy as therapeutic options for Morton's neuroma.

Non-Invasive/No-Incision Pain Procedure (NIP) Device

According to the FixPain website, the NIP Procedure refers to "Non-Invasive, or No-Incision Pain" Procedure. It is FDA-cleared/certified for various types of chronic pain (arthritis, cancer pain, cervical pain, fibromyalgia, joint pain, low back pain, migraines, post-operative pain, and sciatica) and other conditions (e.g., anxiety, depression and insomnia). The microchip NIP Procedure™ device is placed behind the ear of the patient, the acupuncture in corresponding points and the pulses are transmitted through the stimulating needle. With the help of the NIP Procedure™ device, the patients are receiving continuous treatment for 4 to 5 days. It is recommended that therapies be applied for up to 9 weeks.

However, there is a lack of evidence regarding the effectiveness of the NIP Procedure device for the treatment of chronic pain or any other indications.

Electro-Analgesia Treatment (EAT)

Electro-Analgesia Treatment (EAT) has been described as nerve block injections followed by electrical stimulation administered with the Synaptic device, and has been used as a treatment for diabetic peripheral neuropathy. The combination of nerve block therapy and electrical stimulation is referred to as Electro-Analgesia Treatment or EAT. The manufacturer states that the Synaptic 4000 treatment is controlled by the patient using a joystick.

According to the manufacturer, electrical stimulation with the Synaptic device is different from other forms of electrical stimuation: "The Synaptic technology is unique and stands apart from all other electrical neuro-stimulation devices such as TENS, EMS, functional electrical stimulation (FES), sacral nerve stimulation (SNS), vagus nerve stimulation (VNS), deep brain stimulation (DBS), spinal cord stimulation (SCS) and cochlear and ocular implants." The manufacturer explains: "The frequency range is from 40,000 to 400 Hertz. Conventional modalities have a frequency range of only 500-180 Hertz and begin their activity at the low end of the range increasing to their maximum as controls are elevated. In contrast, Synaptic begins its frequency sweep at the maximum (40,000 Hertz) and as the remote is advanced the frequency decreases to the minimum (400 Hertz). This cycle may be repeated during each of the ten intensity levels."

The manufacturer states that the waveform of the Synaptic is also unique. "Also protected are the A-waveform, the unique mechanism for SEA energy delivery as well as the method of patient-controlled treatment using a joystick. The waveform developed for SEA technology mimics a biological process. It simulates the action potential responsible for producing electrical activity in the neuron using a fast rise time and a slow decay, reproducing the action potential in humans."

There are a lack of peer-reviewed published studies of Electro-Analgesia Treatment or of the Synaptic electrical stimulation device.

Variable Muscle Stimulators (VMS)

Variable muscle stimulators (VMS), like TENS units, produce bi-phasic waves. However, TENS units produce asymmetric bi-phasic waves, whereas VMS units produce symmetrical bi-phasic waves. Unlike TENS, VMS is used to do FES. However, there is a lack of evidence regarding the clinical effectiveness of VMS.

Cefaly

The Cefaly transcutaneous supraorbital nerve stimulator, classified as a transcutaneous electrical nerve stimulator, has an FDA approved indication which is limited to the prophylactic treatment of episodic migraine in individuals 18 years of age or older. Cefaly is a plastic, battery-powered transcutaneous electrical nerve stimulator worn like a headband with reusable self-adhesive electrodes placed on the forehead to cover the supratrochlear and supraorbital nerves (branches of the trigeminal nerve). The device purportedly works through neuromodulatory effects on those nerves, thereby blocking pain signals.

Piquet et al (2011) stated that transcutaneous neurostimulation (TNS) at extra-cephalic sites is a well-known treatment of pain. Thanks to recent technical progress, the Cefaly device now also allows supraorbital TNS. During observational clinical studies, several patients reported decreased vigilance or even sleepiness during a session of supraorbital TNS. These researchers examined in more detail the potential sedative effect of supraorbital TNS, using standardized psychophysical tests in healthy volunteers. They performed a double-blind, cross-over, sham-controlled study on 30 healthy subjects. Subjects underwent a series of 4 vigilance tests (Psychomotor Vigilance Task, Critical Flicker Fusion Frequency, Fatigue Visual Numeric Scale, d2 test). Each subject was tested under 4 different experimental conditions: without the neurostimulation device,

with sham supraorbital TNS, with low frequency supraorbital TNS and with high frequency supraorbital TNS. As judged by the results of 3 tests (Psychomotor Vigilance Task, Critical Flicker Fusion Frequency, Fatigue Visual Numeric Scale) there was a statistically significant ($p < 0.001$) decrease in vigilance and attention during high frequency TNS, while there were no changes during the other experimental conditions. Similarly, performance on the d2 test was impaired during high frequency TNS, but this change was not statistically significant. The authors concluded that supraorbital high frequency TNS applied with the Cefaly device decreased vigilance in healthy volunteers. They stated that additional studies are needed to determine the duration of this effect, the underlying mechanisms and the possible relation with the stimulation parameters. Meanwhile, this effect opened interesting perspectives for the treatment of hyperarousal states and, possibly, insomnia.

In a double-blinded, randomized controlled trial (RCT), Schoenen et al (2013) examined the safety and efficacy of trigeminal neurostimulation with a supraorbital transcutaneous stimulator (Cefaly, STX-Med., Herstal, Belgium) in migraine prevention. This trial was conducted at 5 Belgian tertiary headache clinics. After a 1-month run-in, patients with at least 2 migraine attacks/month were randomized 1:1 to verum ($n = 34$) or sham ($n = 33$) stimulation, and applied the stimulator daily for 20 mins during 3 months. Primary outcome measures were change in monthly migraine days and 50 % responder rate. A total of 67 patients were randomized and included in the intention-to-treat analysis. Between run-in and third month of treatment, the mean number of migraine days decreased significantly in the verum (6.94 versus 4.88; $p = 0.023$), but not in the sham group (6.54 versus 6.22; $p = 0.608$). The 50 % responder rate was significantly greater ($p = 0.023$) in the verum (38.1 %) than in the sham group (12.1 %). Monthly migraine attacks ($p = 0.044$), monthly headache days ($p = 0.041$), and monthly acute anti-migraine drug intake ($p = 0.007$) were also significantly reduced in the verum but not in the sham group. There were no adverse events (AEs) in either group. The authors concluded that supraorbital transcutaneous stimulation with the device used in this trial was safe and effective as a preventive therapy for migraine. The therapeutic gain (26 %) was within the range of those reported for other preventive drug and non-drug anti-migraine treatments. Moreover, they stated that adequate studies are needed to disentangle the precise mode of action. This study provided Class III evidence that treatment with a supraorbital transcutaneous stimulator was safe and effective as a preventive therapy for migraine.

The authors noted that despite methodologic precautions including concealed allocation, partial un-blinding may have occurred in this trial. It was difficult to blind peripheral neurostimulation trials because the effective electrical stimulation produces intense paresthesia. These investigators doubted, however, that un-blinding markedly influenced their results for the following reasons. The sham response was within the range of that found in other trials with neurostimulation devices. Compared to the ONSTIM trial of occipital nerve stimulation, it was even higher for the 50 % responder rate: 6 % in ONSTIM, 12.8 % in PREMICE. Un-blinding could thus have been twice more pronounced in ONSTIM than in PREMICE, if one assumed that it was inversely proportional to the percentage of responders in a sham group. The rather small difference (7.3 %) in compliance rates between verum and sham groups also did not favor massive un-blinding. If this were the case, one would expect a much lower compliance in the sham group. Another possible weakness of this trial appeared when data from the different centers were analyzed: patients in the verum group were on average younger than those in the sham group and the duration of their migraine was somewhat shorter. On post-hoc statistical analyses these researchers were unable, however, to detect an influence of age or of disease duration on treatment outcome. In the ONSTIM trial, the difference in mean age between the effectively stimulated patients and the smaller "ancillary" group was 9 years. Overall, both patient groups in PREMICE were well in the age range of migraine patients included in other trials. These researchers stated that beyond statistics, the question whether the results of the PREMICE trial were clinically relevant merits consideration. Besides the therapeutic gain for 50 % responders, other outcome measures suggested that STS could be of benefit to migraine patients. It decreased significantly consumption of acute anti-migraine drugs, which is a pharmaco-economical advantage. In addition, more than 70 % of effectively stimulated patients were satisfied with the treatment. The patients recruited for PREMICE were not the most disabled migraineurs. Having 4 migraine attacks or 7 migraine days per month, they were similar, however, to those included in topiramate trials and representative of the majority of migraine patients in the general population who are in need of preventive treatment according to international recommendations. Whether STS treatment is effective in patients with more frequent attacks or with chronic migraine remains to be determined.

Russo and Tessitore (2015) noted that transcutaneous supraorbital neurostimulation (tSNS) has been recently found superior to sham stimulation for episodic migraine prevention in a randomized trial. These researchers evaluated both the safety and efficacy of a brief period of tSNS in a group of patients with migraine without aura (MwoA). They enrolled 24 consecutive patients with MwoA experiencing a low frequency

of attacks, which had never taken migraine preventive drugs in the course of their life. Patients performed a high frequency tSNS and were considered "compliant" if they used the tSNS for greater than or equal to 2/3 of the total time expected. For this reason, 4 patients were excluded from the final statistical analysis. Primary outcome measures were the reduction migraine attacks and migraine days per month ($p < 0.05$). Furthermore, these investigators evaluated the percentage of patients having at least 50 % reduction of monthly migraine attacks and migraine days. Secondary outcome measures were the reduction of headache severity during migraine attacks and HIT-6 (Headache Impact Test) rating as well as in monthly intake of rescue medication ($p < 0.05$). Finally, compliance and satisfaction to treatment and potential adverse effects related to tSNS have been evaluated. Between run-in and 2nd month of tSNS treatment, both primary and secondary end-points were met. Indeed, these researchers observed a statistically significant decrease in the frequency of migraine attacks ($p < 0.001$) and migraine days ($p < 0.001$) per month. They also demonstrated at least 50 % reduction of monthly migraine attacks and migraine days in respectively 81 % and 75 % of patients. Furthermore, a statistically significant reduction in average of pain intensity during migraine attacks ($p = 0.002$) and HIT-6 rating ($p < 0.001$) and intake of rescue medication ($p < 0.001$) has been shown. All patients showed good compliance levels and no relevant AEs. The authors concluded that in patients experiencing a low frequency of attacks, significant improvements in multiple migraine severity parameters were observed following a brief period of high frequency tSNS. Thus, tSNS may be considered a valid option for the preventive treatment of migraine attacks in patients who cannot or are not willing to take daily medications, or in whom low migraine frequency and/or intensity would not require pharmacological preventive therapies.

The authors stated that this study had several drawbacks. First, these researchers did not use a tSNS sham device and, therefore, they could not rule-out the possible role of a placebo-effect on primary and secondary outcomes in this study. In particular, several factors may contribute to the remedial efficacy of tSNS in these patients such as alternative form of medical therapy, patients naïve to preventive treatment and observation period limited to no more than 2 months. However, the placebo-effect appeared to have a lower impact in the prophylactic treatment than in the acute treatment of migraine attacks. This could be due to the inherent variability in response measured over a period of months compared with one measured over a period of hours. Moreover, the effective tSNS superiority respect to sham stimulation for the prevention of migraine headaches has been extensively demonstrated in a previous RCT in a large cohort of patients with migraine. Nevertheless, in partial disagreement with these findings, Schoenen and colleagues (2013) did not show statistically significant effect on

migraine attacks at 2 months, although ameliorating effect on migraine severity vanished in sham treated patients and amplified in effectively treated patients at this time of the study. These investigators suggested that a greater migraine severity (i.e., frequency of migraine per month and disease duration) and, probably, previous pharmacological anti-migraine preventive therapies may cause a different impact on pain pathways in the 2 migraine populations and consequent different response to the tSNS treatment. Second, the lack of blinding may weaken the results of the present study. However, empirical evidence showed that although double-blind RCTs are the gold standard for proving efficacy of a therapeutic procedure, they often suffer from lack of generalizability. Therefore, the authors believed that these data, in addition to the previous effectiveness and safety results of double-blind RCTs (Schoenen and colleagues, 2013) could provide additional information which may be useful in everyday clinical practice. Finally, although these findings were consistent with previous studies, the sample size was relatively small (n = 20 available for final analysis). Thys, they stated that further studies are needed to corroborate these findings and to explore tSNS efficacy and tolerability in patients with migraine compared with preventive treatments used in clinical practice.

Magis et al (2017) noted that a recent sham-controlled trial showed that external trigeminal nerve stimulation (eTNS) is effective in episodic migraine (MO) prevention. However, its mechanism of action remains unknown. These researchers performed 18-fluorodeoxyglucose positron emission tomography (FDG-PET) to evaluate brain metabolic changes before and after eTNS in episodic migraineurs. A total of 28 individuals were recruited: 14 with MO and 20 healthy volunteers (HVs). HVs underwent a single FDG-PET, whereas patients were scanned at baseline, directly after a first prolonged session of eTNS (Cefaly) and after 3 months of treatment (uncontrolled study). The frequency of migraine attacks significantly decreased in compliant patients (n = 10). Baseline FDG-PET revealed a significant hypo-metabolism in fronto-temporal areas, especially in the orbito-frontal (OFC) and rostral anterior cingulate cortices (rACC) in MO patients. This hypo-metabolism was reduced after 3 months of eTNS treatment. The authors concluded that the findings of this study suggested that OFC and rACC are hypo-metabolic in MO patients at rest. After a 3-month treatment with eTNS, this hypo-metabolism was reduced and the changes were associated with a significant decrease.

of migraine attack frequency. It is known that neurostimulation can modulate OFC and rACC activity. Like cluster and medication overuse headache, MO appeared to be associated with dysfunction of medial frontal cortex areas involved in affective and cognitive dimensions of pain control. Because this study was under-powered and had no sham arm, these researchers were unable to formally attribute the metabolic changes to

the non-invasive neurostimulation treatment. Nonetheless, the observed effect was likely similar to that found with invasive neurostimulation of peri-cranial nerves, such as pONS. These researchers stated that further trials are needed to confirm these findings.

The authors stated that this study had several drawbacks. Because of the small number of evaluable patients (n = 14), the results must be taken with caution. As discussed, the study design did not allow assessing a direct causal effect of eTNS on brain metabolism since a sham condition is missing. These investigators found sham stimulation for 3 months would be unethical knowing that there is evidence for eTNS efficacy from an RCT. The compliance rate with eTNS therapy was rather low. For preventive drug treatments, adherence varies from 48 % to 94 % between studies. Neurostimulation was more time consuming (20 mins daily in this study), which provoked lower compliance. In the PREMICE trial, patients had a compliance rate of 62 %, while participants renting the eTNS Cefaly device via the internet used it on average 58 % of the recommended time. In this study, the authors considered patients who performed at least 30 % of the sessions as "compliant"; this threshold was chosen on an empirical basis and experience from clinical practice showing that patients may benefit from eTNS with non-daily use of the device. However, the minimal time of use to obtain a clinical improvement in migraine is unknown, and may vary between patients. Although the headache diaries allowed monitoring global intake of acute medications for each patient, they did not allow these researchers to determine the precise proportion of drugs taken within each of the pharmacological classes, analgesics, NSAIDs, triptans, nor its possible change after eTNS. I t is unlikely, however, that such a change would have influenced brain metabolism.

Russo et al (2017) examined the functional re-organization of the pain processing network during trigeminal heat stimulation (THS) after 60 days of eTNS in migraine without aura (MwoA) patients between attacks. Using whole-brain BOLD-fMRI, functional response to THS at 2 different intensities (41 and 51°C) was investigated interictally in 16 adults MwoA patients before and after eTNS with the Cefaly device. These researchers calculated the percentage of patients having at least a 50 % reduction of monthly migraine attacks and migraine days between baseline and the last month of eTNS. Secondary analyses evaluated associations between BOLD signal changes and clinical features of migraine. Before eTNS treatment, there was no difference in BOLD response between MwoA patients and healthy controls (HC) during low-innocuous THS at 41°C, whereas the perigenual part of the right anterior cingulate cortex (ACC) revealed a greater BOLD response to noxious THS at 51°C in MwoA patients when compared to HC. The same area demonstrated a significant reduced

BOLD response induced by the noxious THS in MwoA patients after eTNS ($p = 0.008$). Correlation analyses showed a significant positive correlation between ACC BOLD response to noxious THS before eTNS treatment and the decrease of ACC BOLD response to noxious THS after eTNS. Moreover, a significant negative correlation in the migraine group after eTNS treatment between ACC functional activity changes and both the perceived pain ratings during noxious THS and pre-treatment migraine attack frequency has been found. The authors concluded that the findings of this study suggested that eTNS treatment with the Cefaly® device induced a functional anti-nociceptive modulation in the ACC that is involved in the mechanisms underlying its preventive anti-migraine efficacy. Nevertheless, these researchers stated that further observations to confirm whether the observed fMRI effects of eTNS are both related to clinical improvement and specific to anti-nociceptive modulation in migraine patients are mandatory.

The authors noted that this study had several drawbacks. First, these investigators did not use an eTNS sham device and, therefore, they could not rule out the possible role of a placebo effect in imaging and clinical data. However, the superiority of effective eTNS respect to sham stimulation for the prevention of migraine headaches has already been demonstrated in a randomized, sham-controlled trial. Second, the HC did not undergo eTNS treatment, thus, the authors could not determine if the eTNS-induced changes in ACC activation by THS were specific to migraineurs. By corollary, these researchers could not exclude that these changes could be due to the clinical improvement of patients after eTNS, rather than to the neurostimulation treatment itself.

An UpToDate review on "Preventive treatment of migraine in adults" (Bajwa and Smith, 2018) states that "Transcutaneous nerve stimulation -- Although data are limited, the findings of a controlled trial conducted at 5 tertiary headache centers in Belgium suggest that treatment with a supraorbital transcutaneous electrical nerve stimulator is beneficial for patients with episodic migraine. The trial randomly assigned 69 adults with migraine (with or without aura) to active or sham stimulation for 20 minutes daily for three months. Exclusion criteria included the use of preventive treatment for migraine in the 3 months prior to enrollment. At 3 months of treatment, the responder rate, defined as the percentage of subjects with a ≥ 50 % reduction in migraine days per month, was significantly higher for the active stimulation compared with the sham stimulation group (38.2 versus 12.1 %), as was the mean reduction in monthly migraine days (-2.1 versus +0.3 days). There were no adverse events in either group. Limitations to this trial include small effect size, low patient numbers, and uncertainty in concealing treatment allocation, given that active stimulation causes intense paresthesia. The device used in

this trial is approved for marketing in the United States, Canada, Europe, and several additional countries ... Non-pharmacologic measures that may be beneficial for migraine headache prevention include aerobic exercise, biofeedback, other forms of relaxation training, cognitive-behavioral therapies, acupuncture, and transcutaneous electrical nerve stimulation".

Furthermore, an UpToDate review on "Preventive treatment of migraine in children" (Mack, 2018) does not mention "Cefaly / supraorbital transcutaneous electrical nerve stimulation" as a management option.

Quell Device

A recently FDA cleared device, the Quell device, is the first electrical stimulator to receive approval for use during sleep. The device consists of a band worn around the upper calf to theoretically provide systemic relief of chronic pain and is controlled by an individual's smartphone or tablet.

Combination Therapies

A more recent approach to electrical stimulation has been development of devices that may use a combination of different stimulation modalities, such as combining TENS with ICS, TENS with ultrasound, TENS with low level laser therapy (LLLT) or TENS with neuromuscular stimulation (NMES). Examples of combination devices include, but may not be limited to, the Neurolumen device (combines TENS with LLLT and light-emitting diode (LED) therapy) or the Empi Phoenix and QB1 System (combination TENS with NMES devices).

Additionally, combined ICS and muscle stimulation utilize ICS for pain and muscle stimulation to treat underlying muscle conditions. Examples of this type of device are the RS-4i sequential stimulator and the EMSI TENS/EMS-14.

In combined therapy which consists of high frequency electrical stimulation and peripheral nerve block (also referred to as combination electrochemical therapy, combination electrochemical treatment, or CET), it is purported to treat peripheral neuropathy by first injecting the peripheral nerve with a local anesthetic, followed by a high frequency electrical stimulation.

In a sham-controlled, single-blinded, single-center, cross-over study, Li and co-workers (2018) examined if transcranial direct current stimulation (tDCS) augments the analgesic effect of breathing-controlled electrical stimulation (BCES) in patients with spinal cord injury (SCI) who have chronic neuropathic pain. This trial included 12 participants with incomplete SCI. The treatment protocol included a 20-min tDCS (sham or active), followed by a 20-min BCES to the median nerve on the dominant side. The treatment session with sham or control tDCS was given on different days in a randomized order; VAS was used to assess neuropathic pain at baseline, 10 mins after tDCS, and 10 mins after BCES. Subjects were blinded to the status of tDCS. Of the 12 subjects, 10 completed sessions of both sham and active tDCS, while the other 2 completed only active tDCS and BCES treatment. Of the 12 subjects, 7 showed analgesic effects after active tDCS, while sham tDCS produced some analgesic effects in 4 of 10 subjects. At the group level, there was no difference between active and sham tDCS treatment. All except 1 subject responded positively to BCES in all sessions; VAS score for pain decreased significantly after BCES combined with either active tDCS or sham tDCS treatment. The authors concluded that the immediate analgesic effect of BCES was confirmed. However, this effect was not augmented after 1 session of tDCS treatment.

SENSUS Device

The SENSUS device uses transcutaneous electromagnetic nerve stimulation to purportedly treat individuals with diabetic peripheral neuropathy.

Galvanic Stimulation for Peripheral Arterial Disease

Williams et al (2017) noted that PAD is common and symptoms can be debilitating and lethal. Risk management, exercise, radiological and surgical intervention are all valuable therapies, but morbidity and mortality rates from this disease are increasing. Circulatory enhancement can be achieved using simple medical electronic devices, with claims of minimal adverse side effects. The evidence for these is variable, prompting a review of the available literature. Embase and Medline were interrogated for full text articles in humans and written in English. Any external medical devices used in the management of PAD were included if they had objective outcome data. A total of 31 papers met inclusion criteria, but protocols were heterogeneous. The medical devices reported were intermittent pneumatic compression (IPC), NMES or EMS, and galvanic electrical dressings. In patients with intermittent claudication, IPC devices increase popliteal artery velocity (49 to 70 %) and flow (49 to 84 %). Gastrocnemius EMS increased superficial femoral artery flow by 140 %. Over 4.5 to 6 months IPC increased intermittent

claudication distance (ICD) (97 to 150 %) and absolute walking distance (AWD) (84 to 112 %), with an associated increase in quality of life; NMES of the calf increased ICD and AWD by 82 % and 61 to 150 % at 4 weeks, and 26 % and 34 % at 8 weeks. In patients with critical limb ischemia (CLI), IPC reduced rest pain in 40 to 100 % and was associated with ulcer healing rates of 26 %; IPC had an early limb salvage rate of 58 to 83 % at 1 to 3 months, and 58 to 94 % at 1.5 to 3.5 years. No studies have reported the use of EMS or NMES in the management of CLI. The authors concluded that there is evidence to support the use of IPC in the management of claudication and CLI. There is a building body of literature to support the use of electrical stimulators in PAD, but this is low level to date. Devices may be of special benefit to those with limited exercise capacity, and in non-reconstructable CLI. Moreover, they stated that galvanic stimulation is not recommended.

Electrical Stimulation for the Treatment of Chronic Pelvic Pain

Fuentes-Marquez and colleagues (2018) summarized the available scientific evidence on physiotherapy interventions in the management of chronic pelvic pain (CPP). These researchers carried out a systematic review of RCTs. An electronic search of Medline, CINAHL, and Web of Science databases was performed to identify relevant randomized trials from 2010 to 2016. Manuscripts were included if at least 1 of the comparison groups received a physiotherapy intervention. Studies were assessed in duplicate for data extraction and risk of bias using the Physiotherapy Evidence Database scale PEDro; 8 of the studies screened met the inclusion criteria -- 4 manuscripts studied the effects of electrotherapy including intravaginal electrical stimulation, short wave diathermy, respiratory-gated auricular vagal afferent nerve stimulation, percutaneous tibial nerve stimulation, and sono-electro-magnetic therapy with positive results; 3 studies focused on manual assessing the efficacy of myofascial versus massage therapy in 2 of them and ischemic compression for trigger points. The authors concluded that although physiotherapy interventions showed some beneficial effects, evidence could not support the results. They stated that heterogeneity in terms of population phenotype, methodological quality, interpretation of results, and operational definition resulted in little overall evidence to guide treatment.

Electrical Stimulation of the Posterior Tibial Nerve for the Treatment of Neuropathic Pain associated with Polyneuropathy

Dabby and associates (2018) stated that peripheral neuropathic pain (PNP) is caused by neuronal damage to the peripheral nervous system (PNS) and usually affects the distal extremities. In an open-label study, these researchers examined the effect of short-term

PNS on individuals with PNP due to polyneuropathy. A total of 12 patients (mean age of 63.0 ± 10.0 years, 41.7 % men) with daily bilateral PNP for at least 6 months (mean duration of neuropathic pain of 7.4 ± 7.8 years) received a total of 6 direct electrical stimulation therapies to the posterior tibial nerve at 3 to 4-day intervals; 8 patients completed the study and were included in the efficacy analysis. The average pain at baseline was 36.6 ± 3.80 estimated by the Short-Form McGill Pain Questionnaire. After the last stimulation, pain was significantly reduced by 85.5 % to 4.88 ± 3.1 (p = 0.008); 6 patients (75 %) had over 50 % decrease in pain after the first stimulation therapy and 99.2 % after the final stimulation therapy. The patients also reported statistically significant decreases in pain level (measured by VAS), ranging from 54.85 % to 87.50 % after each of the stimulations as compared to the pain experienced prior to the stimulations. The authors concluded that the procedure was safe without any serious AEs; PNS has shown excellent efficacy and improvement of PNP symptoms. Moreover, they stated that further studies in larger patient populations and longer duration are needed.

The authors stated that this study's drawbacks included its small sample size (n = 8), short duration of treatment (6 months), and 33 % patient drop-out.

Reduced Impedance Non-Invasive Cortical Electrostimulation (RINCE) for the Treatment of Chronic Pain

O'Connell and colleagues (2018) provided an update on the original Cochrane Review published in 2010, Issue 9, and last updated in 2014, Issue 4. Non-invasive brain stimulation techniques aim to induce an electrical stimulation of the brain in an attempt to reduce chronic pain by directly altering brain activity. They include repetitive transcranial magnetic stimulation (rTMS), cranial electrotherapy stimulation (CES), tDCS, transcranial random noise stimulation (tRNS) and reduced impedance non-invasive cortical electrostimulation (RINCE). These investigators evaluated the efficacy of non-invasive cortical stimulation techniques in the treatment of chronic pain. For this update, they searched CENTRAL, Medline, Embase, CINAHL, PsycINFO, LILACS and clinical trials registers from July 2013 to October 2017. Randomized and quasi-randomized studies of rTMS, CES, tDCS, RINCE and tRNS if they employed a sham stimulation control group, recruited patients over the age of 18 years with pain of 3 months' duration or more, and measured pain as an outcome were selected for analysis. Outcomes of interest were pain intensity measured using VAS or NRS, disability, QOL and adverse events (AEs). These investigators included an additional 38 trials (involving 1,225 randomized participants) in this update, making a total of 94 trials in the review (involving 2,983

randomized participants). This update included a total of 42 rTMS studies, 11 CES, 36 tDCS, 2 RINCE and 2 tRNS; 1 study evaluated both rTMS and tDCS. These investigators judged only 4 studies as low-risk of bias across all key criteria. The authors concluded that there is very low-quality evidence that single doses of high-frequency rTMS of the motor cortex and tDCS may have short-term effects on chronic pain and QOL; but multiple sources of bias existed that may have influenced the observed effects. These researchers did not find evidence that low-frequency rTMS, rTMS applied to the dorsolateral prefrontal cortex and CES were effective for reducing pain intensity in chronic pain. They noted that the broad conclusions of this review have not changed substantially for this update. There remains a need for substantially larger, rigorously designed studies, particularly of longer courses of stimulation.

Scrambler Therapy for Neuropathic Pain Associated with Chemotherapy-Induced Peripheral Neuropathy

Tomasello and colleagues (2018) noted that chemotherapy-induced peripheral neuropathy (CIPN) is a common side effect of chemotherapy in need of effective treatment. Preliminary data supported the efficacy of scrambler therapy (ST), a non-invasive cutaneous electrostimulation device, in adults with CIPN. These researchers examined the safety, efficacy, and durability of ST for neuropathic pain in adolescents with CIPN. They studied 9 pediatric patients with cancer and CIPN who received ST for pain control. Each patient received 45-min daily sessions for 10 consecutive days as a first step, but some of them required additional treatment. Pain significantly improved comparing NRS after 10 days of ST (9.22 ± 0.83 versus 2.33 ± 2.34; $p < 0.001$) and at the end of the optimized cycle (EOC) (9.22 ± 0.83 versus 0.11 ± 0.33, $p < 0.001$). The improvement in QOL was significantly reached on pain interference with general activity (8.67 ± 1.66 versus 3.33 ± 2.12, $p < 0.0001$), mood (8.33 ± 3.32 versus 2.78 ± 2.82, $p < 0.0005$), walking ability (10.00 versus 2.78 ± 1.22, $p < 0.0001$), sleep (7.56 ± 2.24 versus 2.67 ± 1.41, $p < 0.001$), and relations with people (7.89 ± 2.03 versus 2.11 ± 2.03, $p < 0.0002$; Lansky score 26.7 ± 13.2 versus 10 days of ST 57.8 ± 13.9, $p < 0.001$; 26.7 ± 13.2 versus EOC 71.1 ± 16.2, $p < 0.001$). The authors concluded that based on these preliminary data, ST could be a good choice for adolescents with CIPN for whom pain control is difficult; ST caused total relief or dramatic reduction in CIPN pain and an improvement in QOL, durable in follow-up. It resulted in no detected side effects, and could be re-trained successfully. Moreover, these researchers stated that further larger studies are needed to confirm these promising preliminary data in pediatric patients with cancer.

Transcutaneous Electrical Nerve Stimulation for the Treatment of Migraine

Tao and colleagues (2018) stated that migraine is now ranked as the 2nd most disabling disorder worldwide reported by the Global Burden of Disease Study 2016. As a non-invasive neuro-stimulation technique, TENS has been applied as an abortive and prophylactic treatment for migraine recently. These investigators conducted this meta-analysis to analyze the safety and effectiveness of TENS on migraineurs. They searched Medline (via PubMed), Embase, the Cochrane Library and the Cochrane Central Register of Controlled Trials to identify RCTs, which compared the effect of TENS with sham TENS on migraineurs. Data were extracted and methodological quality assessed independently by 2 reviewers. Change in the number of monthly headache days, responder rate, painkiller intake, adverse events and satisfaction were extracted as outcome. A total of 4 studies were included in the quantitative analysis with 161 migraine patients in real TENS group and 115 in sham TENS group. These researchers found significant reduction of monthly headache days (SMD: -0.48; 95 % CI: -0.73 to - 0.23; $p < 0.001$) and painkiller intake (SMD: -0.78; 95 % CI: -1.14 to - 0.42; $p < 0.001$). Responder rate (RR: 4.05; 95 % CI: 2.06 to 7.97; $p < 0.001$) and satisfaction (RR: 1.85; 95 % CI: 1.31 to 2.61; $p < 0.001$) were significantly increased compared with sham TENS. The authors concluded that the findings of this meta-analysis suggested that TENS may serve as an effective and well-tolerated alternative for migraineurs. However, they stated that the low quality of evidence prevented them from reaching definitive conclusions; future well-designed RCTs are needed to confirm and update the findings of this analysis.

Transcutaneous Electrical Nerve Stimulation for the Treatment of Chronic Pain Following Ankylosing Spondylitis

Chen and colleagues (2018) examined the effect of TENS for the treatment of patients with chronic pain after ankylosing spondylitis (AS). A total of 72 eligible patients with chronic pain following AS were included. All included patients received exercise and were assigned to a treatment group and a control group equally. In addition, patients in the treatment group also underwent TENS therapy. All patients were treated for a total of 6 weeks. The primary outcome of pain intensity was measured by VAS. The secondary outcomes included degree of functional limitation, as assessed by Bath Ankylosing Spondylitis Functional Index (BASFI); and QOL, as evaluated by Ankylosing Spondylitis Quality of Life (ASQOL) questionnaire. All outcomes were assessed before and after 6 weeks treatment. Furthermore, adverse events were also recorded. After 6-week treatment, patients in the treatment group did not show more promising outcomes in pain

reduction, as measured by VAS (p=0.08); functional evaluation, as evaluated by BASFI (p=0.19); as well as QOL, as assessed by ASQOL (p=0.18), compared with patients in the control group; no AEs occurred in both groups. The authors concluded that this study did not exert encouraging outcomes in patients with chronic pain following AS after 6-week treatment.

Ultrasound-Guided Percutaneous Stimulation off the Sciatic Nerve for Post-Operative Analgesia Following Ambulatory Foot Surgery

Ilfeld and colleagues (2018) noted that percutaneous PNS is an analgesic modality involving the insertion of a lead through an introducing needle followed by the delivery of electric current. This modality has been reported to treat chronic pain as well as post-operative pain the day following knee surgery. However, it remains unknown if this analgesic technique may be used in ambulatory subjects following foot procedures beginning within the recovery room immediately following surgery, and with only short series of patients reported to-date, the only available data are derived from strictly observational studies. In a proof-of-concept study, these researchers examined the feasibility of using percutaneous sciatic nerve PNS to treat post-operative pain following ambulatory foot surgery in the immediate post-operative period and provided the first available data from a randomized controlled study design to provide evidence of analgesic effect. Pre-operatively, an electrical lead (SPRINT; SPR Therapeutics, Inc., Cleveland, OH) was percutaneously inserted posterior to the sciatic nerve between the sub-gluteal region and bifurcation with US-guidance. Following hallux valgus osteotomy, subjects received 5 mins of either stimulation or sham in a randomized, double-masked fashion followed by a 5-min cross-over period and then continuous stimulation until lead removal on post-operative days 14 to 28. During the initial 5-min treatment period, subjects randomized to stimulation (n = 4) experienced a down-ward trajectory in their pain over the 5 mins of treatment, whereas those receiving sham (n = 3) reported no such change until their subsequent 5-min stimulation cross-over. During the subsequent 30 mins of stimulation, pain scores decreased to 52 % of baseline (n = 7); 3 subjects (43 %) used a continuous popliteal nerve block for rescue analgesia during post-operative days 0 to 3. Overall, resting and dynamic pain scores averaged less than 1 on the NRS, and opioid use averaged less than 1 tablet daily with active stimulation. One lead dislodged, 2 fractured during use, and 1 fractured during intentional withdrawal. The authors concluded that this small, pilot, proof-of-concept study demonstrated that percutaneous sciatic nerve PNS was feasible for ambulatory foot surgery and suggested that this modality provided analgesia and decreased opioid requirements following hallux

valgus osteotomy procedures. However, lead dislodgement and fracture were concerns. Moreover, they stated that the findings of this pilot study indicated that a subsequent clinical trial is needed.

The authors stated that this study had several drawbacks. Prior experience with percutaneous PNS in post-operative subjects 6 to 97 days following knee arthroplasty suggested that analgesia onset and peak were nearly instantaneous following the introduction of electrical current. Thus, these researchers designed the current randomized, sham-controlled, cross-over portion of this study with only 5-min treatment periods so that subjects randomized to sham initially would have a minimal duration without supplemental analgesia. However, the results of this trial suggested that for acute pain in the immediate post-operative period maximum PNS-induced analgesia requires far longer than 5 mins: pain scores continued to decrease even as subjects emerged from general anesthesia through the 40-min time-point. Unfortunately, no subsequent pain data were collected until the following day, so the duration for maximum analgesic effect remains to be determined. In contrast, these investigators were aware of a "carryover" effect following PNS so that subjects continued to receive a variable duration and degree of analgesia following electrical current discontinuation, possibly due to sustained modification of supra-spinal pain processing. These researchers knew that this carryover effect would make the data of the 5-min sham period for the group who initially received active current difficult or impossible to interpret. However, to keep the double-masked study design, the authors had no choice but to collect the measurements from this 5-min period. Thus, they included the collected data; but presented them in ghost to indicate the uncertainty of its interpretation.

Ultrasound-Guided Percutaneous Stimulation off the Femoral Nerve for Post-Operative Analgesia Following Anterior Cruciate Ligament Reconstruction

In a prospective, proof-of-concept study, Ilfeld and associates (2018) examined the feasibility of using percutaneous PNS of the femoral nerve to treat pain in the immediate post-operative period following ambulatory anterior cruciate ligament (ACL) reconstruction with a patellar autograft. Pre-operatively, an electrical lead (SPRINT, SPR Therapeutics, Inc., Cleveland, OH) was percutaneously implanted with US-guidance anterior to the femoral nerve caudad to the inguinal crease. Within the recovery room, subjects received 5 mins of either stimulation or sham in a randomized, double-masked fashion followed by a 5-min cross-over period, and then continuous active stimulation until lead removal post-operative day 14 to 28. Statistics were not applied to the data

due to the small sample size of this feasibility study. During the initial 5-min treatment period, subjects randomized to stimulation (n = 5) experienced a slight down-ward trajectory (decrease of 7 %) in their pain over the 5 mins of treatment, while those receiving sham (n = 5) reported a slight up-ward trajectory (increase of 4 %) until their subsequent 5-min stimulation cross-over, during which time they also experienced a slight down-ward trajectory (decrease of 11 % from baseline). A majority of subjects (80 %) used a continuous adductor canal nerve block for rescue analgesia (in addition to stimulation) during post-operative days 1 to 3, after which the median resting and dynamic pain scores remained equal or less than 1.5 on the NRS, respectively, and the median daily opioid consumption was less than 1.0 tablet. The authors concluded that the findings of this proof-of-concept study demonstrated that percutaneous femoral nerve stimulation was feasible for ambulatory knee surgery; and suggested that this modality may be effective in providing analgesia and decreasing opioid requirements following ACL reconstruction. These researchers stated that the results of this pilot study indicated that a subsequent clinical trial is needed.

The authors stated that this study had several drawbacks. First, this proof-of-concept study lacked a control group following the initial 10-min treatment period within the recovery room; and, thus documentation and quantification of analgesia delivery and opioid sparing require additional investigation. Second, the needle could not be withdrawn without deploying the lead. Therefore, instead of withdrawing and re-positioning the needle/lead combination if a first attempt passed the femoral nerve without the desired response, an entirely new lead had to be implanted at a different trajectory. This obviously added greatly to both the required attempts and overall procedure duration since multiple implantation kits and leads had to be prepared. Lastly, these researchers were aware of a "carryover" effect following PNS so that subjects continued to receive a variable duration and degree of analgesia following electrical current discontinuation, possibly due to sustained modification of supra-spinal pain processing. They knew that this carryover effect would make the data of the 5-min sham period for the group which initially received active current difficult or impossible to interpret. However, to keep the double-masked study design, the authors had no choice but to collect the measurements from this 5-min period. Thus, they included the collected data but presented them in ghost to indicate the uncertainty of its interpretation.

Appendix

TENS Unit Supplies

- A 4-lead TENS unit may be used with either 2 leads or 4 leads, depending on the characteristics of the member's pain. If it is ordered for use with 4 leads, the medical record must document why 2 leads are insufficient to meet the member's needs.
- If 2 TENS leads are medically necessary, then a maximum of 1 unit of a TENS supply allowance (HCPCS Code A4595) would be considered medically necessary per month; if 4 TENS leads are necessary, a maximum of 2 units per month would be considered medically necessary. If the use of the TENS unit is less than daily, medical necessity of the TENS supply allowance is reduced proportionally. Note: A TENS supply allowance (HCPCS code A4595) includes electrodes (any type), conductive paste or gel (if needed, depending on the type of electrode), tape or other adhesive (if needed, depending on the type of electrode), adhesive remover, skin preparation materials, batteries (9 volt or AA, single use or rechargeable), and a battery charger (if rechargeable batteries are used).
- Replacement of lead wires more often than every 12 months is rarely medically necessary.

For ongoing supplies and rental DME items, in addition to information described above that justifies the initial provision of the item(s) and/or supplies, there must be information in the member's medical record to support that the item continues to be used by the member and remains medically necessary.

CPT Codes / HCPCS Codes / ICD-10 Codes

Information in the [brackets] below has been added for clarification purposes. Codes requiring a 7th character are represented by "+":

Code	Code Description
Transcutaneous Electrical Nerve Stimulators (TENS):	
CPT codes covered if selection criteria are met:	
64550	Application of surface (transcutaneous) neurostimulator
Other CPT codes related to the CPB:	
97014	Application of a modality to 1 or more areas; electrical stimulation (unattended)
97032	Application of a modality to one or more areas; electrical stimulation, (manual), each 15 minutes

HCPCS codes covered if selection criteria are met:	
A4556	Electrodes (e.g., apnea monitor), per pair
A4557	Lead wires (e.g., apnea monitor), per pair
A4558	Conductive gel or paste, for use with electrical device (e.g., TENS, NMES), per oz.
A4595	Electrical stimulator supplies, 2 lead, per month, (e.g. TENS, NMES)
E0720	Transcutaneous electrical nerve stimulation (TENS) device, 2 lead, localized stimulation [not covered for Sensus]
E0730	Transcutaneous electrical nerve stimulation (TENS) device, 4 or more leads, for multiple nerve stimulation [not covered for Sensus]
hyphen ICD-only">hyphen10 codes covered if selection criteria are met:	
G89.18	hyphen Other acute postprocedural pain [not covered for post-only">hyphentotal knee arthroplasty pain]
hyphen G89.21 -only">hyphen G89.29	Chronic pain
G89.4	Chronic pain syndrome
hyphen ICD-only">hyphen10 codes not covered for indications listed in the hyphen CPB (not all-only">hypheninclusive):	
hyphen E08.40 -only">hyphen E08.42	Diabetes mellitus due to underlying condition with diabetic neuropathy, unspecified, mononeuropathy, and polyneuropathy [not covered for SENSUS]
hyphen E09.40 -only">hyphen E09.42	Drug or chemical induced diabetes mellitus with neurological complications with diabetic neuropathy unspecified, mononeuropathy, and polyneuropathy [not covered for SENSUS]
hyphen E10.40 -only">hyphen E10.42	Type 1 diabetes mellitus with diabetic neuropathy, unspecified, mononeuropathy, and polyneuropathy [not covered for SENSUS]
hyphen E11.40 -only">hyphen E11.42	Type 2 diabetes mellitus with diabetic neuropathy, unspecified, mononeuropathy, and polyneuropathy [not covered for SENSUS]
hyphen E13.40 -only">hyphen E13.42	Other specified diabetes mellitus with diabetic neuropathy, unspecified, mononeuropathy, and polyneuropathy [not covered for SENSUS]

hyphen G43.001 -only">hyphen G43.919	Migraine
hyphen G44.001 -only">hyphen G44.89	Other headache syndromes
G62.0	hyphen Drug-only">hypheninduced polyneuropathy hyphen [chemotherapy-only">hypheninduced peripheral neuropathy]
G54.6	Phantom limb syndrome with pain
G89.11	Acute pain due to trauma [hip fractures]
I73.9	Peripheral vascular disease, unspecified
hyphen M26.602 -only">hyphen M26.609	Temporomandibular joint disorders
hyphen M54.40 -only">hyphen M54.5	Lumbago
hyphen M75.00 -only">hyphen M75.02	Adhesive capsulitis of shoulder
hyphen M75.30 -only">hyphen M75.32	Calcific tendinitis of shoulder
hyphen M75.40 -only">hyphen M75.42	Impingement syndrome of shoulder
hyphen M75.50 -only">hyphen M75.52	Bursitis of shoulder [rotator cuff tendinitis]
M79.7	Fibromyalgia
hyphen N94.0 -only">hyphen N94.9	Pain and other conditions associated with female genital organs and menstrual cycle

hyphen R10.0 -only">hyphen R10.13 hyphen R10.30 -only">hyphen R10.33	Abdominal pain
R51	Headache
T20.00xA – T32.99	Burns and corrosions
T87.9	Unspecified complications of amputation stump [stump pain]
***hyphen Form-only">hyphenfitting Conductive Garment*:**	
HCPCS codes covered if selection criteria are met:	
E0731	hyphen Form-only">hyphenfitting conductive garment for delivery of TENS or NMES (with conductive fibers separated from the patient's skin by layers of fabric)
hyphen ICD-only">hyphen10 codes covered if selection criteria are met (not hyphen all-only">hypheninclusive):	
hyphen M62.50 -only">hyphen M62.59	Muscular wasting and atrophy, not elsewhere classified
M62.84	Sarcopenia
***Interferential Stimulation*:**	
No specific codes	
HCPCS codes not covered for indications listed in the CPB:	
S8130	Interferential current stimulator, 2 channel
S8131	Interferential current stimulator, 4 channel
***Percutaneous Electrical Nerve Stimulation (PENS)*:**	
CPT codes covered if selection criteria are met:	
hyphen *Percutaneous Electrical Nerve Stimulation (PENS)* -only">hyphen no specific code:	
Other CPT codes related to the CPB:	
76942	Ultrasonic guidance for needle placement(eg, biopsy, aspiration, injection, localization device), imaging supervision and interpretation
76998	Ultrasonic guidance, intraoperative
Other HCPCS codes related to the CPB:	
S8930	Electrical stimulation of auricular acupuncture points; each 15 hyphen minutes of personal one-only">hyphenon one contact with the patient
hyphen ICD-only">hyphen10 codes covered if selection criteria are met:	

hyphen G56.00 -only">hyphen G58.9	Mononeuropathies of upper and lower limbs
hyphen M51.04 -only">hyphen M51.06	Thoracic, thoracolumbar and lumbosacral intervertebral disc disorders with myelopathy
hyphen M51.24 -only">hyphen M51.37	Other thoracic, thoracolumbar and lumbosacral intervertebral disc displacement and degeneration
hyphen M54.10 -only">hyphen M54.18	Radiculopathy
hyphen M54.30 -only">hyphen M54.32	Sciatica
hyphen M54.40 -only">hyphen M54.42	Lumbago with sciatica
M54.5	Low back pain [lumbago]
M54.6	Pain in thoracic spine
M79.2	Neuralgia and neuritis, unspecified [neuropathic pain]
M96.1	Postlaminectomy syndrome, lumbar region
hyphen ICD-only">hyphen10 codes not covered for indications listed in the CPB:	
G89.18	Other acute postprocedural pain
hyphen M47.11 -only">hyphen M47.13 hyphen M47.811 -only">hyphen M47.813	Cervical spondylosis [with or without myelopathy]
hyphen M48.01 -only">hyphen M48.03	Spinal stenosis [cervical region]
hyphen M50.00	Cervical disc disorder with myelopathy

-only">hyphen M50.03	
hyphen M50.20 -only">hyphen M50.23	Other cervical disc displacement
hyphen M50.30 -only">hyphen M50.33	Other cervical disc degeneration
hyphen M50.80 -only">hyphen M50.83	Other cervical disc disorders
hyphen M50.90 -only">hyphen M50.93	Cervical disc disorder, unspecified
M96.1	Postlaminectomy syndrome, not elsewhere classified [cervical region]
***Scrambler Therapy/Calmare Therapy Device*:**	
hyphen CPT codes not covered for indications listed in the CPB (not all-only">hypheninclusive):	
0278T	Trancutaneous electrical modulation pain reprocessing (eg, scrambler therapy), each treatment session (includes placement of electrodes) [Calmare therapy device]
hyphen ICD-only">hyphen10 codes not covered for indications listed in the hyphen CPB (not all-only">hypheninclusive):	
G62.0	hyphen Drug-only">hypheninduced polyneuropathy hyphen [chemotherapy-only">hypheninduced peripheral neuropathy]
hyphen G89.21 -only">hyphen G89.29	Chronic pain
G89.3	Neoplasm related pain (acute) (chronic)
M79.2	Neuralgia and neuritis, unspecified [neuropathic pain]
***hyphen Non-only">hyphenInvasive Interactive Neurostimulation*:**	
No specific code	

hyphen ICD-only">hyphen10 codes not covered for indications listed in the CPB:	
hyphen M17.0 -only">hyphen M17.9	Osteoarthritis of knee
M54.2	Cervicalgia
hyphen M84.471 -only">hyphen M84.473	Pathological fracture, left, right, or unspecified ankle
***Peripheral Subcutaneous Field Stimulation*:**	
CPT codes not covered for indications listed in the CPB:	
0282T	Percutaneous or open implantation of neurostimulator electrode array(s), subcutaneous (peripheral subcutaneous filed stimulation), including imaging guidance, when performed, cervical, thoracic or lumbar; for trial, including removal at the conclusion of trial period
0283T	permanent, with implantation of a pulse generator
0284T	Revision or removal of pulse generator or electrodes, including imaging guidance, when performed, including addition of new electrodes, when performed
0285T	Electronic analysis of implanted peripheral subcutaneous field stimulation pulse generator, with reprogramming when performed
hyphen ICD-only">hyphen10 codes not covered for indications listed in the CPB:	
I20.0	Unstable angina
hyphen I20.1 -only">hyphen I20.09	Angina pectoris
hyphen R20.0 -only">hyphen R20.9	Disturbances of skin sensation
***Peripherally Implanted Nerve Stimulators*:**	
CPT codes covered if selection criteria are met:	
64568	Incision for implantation of cranial nerve (eg, vagus nerve) neurostimulator electrode array and pulse generator
64575	peripheral nerve (excludes sacral nerve)

64585	Revision or removal of peripheral neurostimulator electrodes
64590	Insertion or replacement of peripheral or gastric neurostimulator pulse generator or receiver, direct or inductive coupling
64595	Revision or removal of peripheral or gastric neurostimulator pulse generator or receiver
Other CPT codes related to the CPB:	
hyphen 95860 -only">hyphen 95872	Electromyography
95937	Neuromuscular junction testing (repetitive stimulation, paired stimuli), each nerve, any 1 method
HCPCS codes covered if selection criteria are met:	
L8680	Implantable neurostimulator electrode, each
L8681	Patient programmer (external) for use with implantable programmable neurostimulator pulse generator, replacement only
L8682	Implantable neurostimulator radiofrequency receiver
L8683	Radiofrequency transmitter (external) for use with implantable neurostimulator radiofrequency receiver
L8685	Implantable neurostimulator pulse generator, single array, rechargeable, includes extension
L8686	Implantable neurostimulator pulse generator, single array, hyphen non-only">hyphenrechargeable, includes extension
L8687	Implantable neurostimulator pulse generator, dual array, rechargeable, includes extension
L8688	Implantable neurostimulator pulse generator, dual array, hyphen non-only">hyphenrechargeable, includes extension
L8689	External recharging system for battery (internal) for use with implantable neurostimulator, replacement only
L8695	External recharging system for battery (external) for use with implantable neurostimulator, replacement only
hyphen ICD-only">hyphen10 codes covered if selection criteria are met:	
hyphen G56.00 -only">hyphen G59	Mononeuropathies
hyphen G90.50	Complex regional pain syndrome I (CRPS I)

-only">hyphen G90.59	
hyphen S14.101S -only">hyphen S14.159S hyphen S14.2xxS -only">hyphen S14.9xxS hyphen S24.101S -only">hyphen S24.159S hyphen S24.2xxS -only">hyphen S24.9xxS hyphen S34.101S -only">hyphen S34.139S hyphen S34.21xS -only">hyphen S34.9xxS hyphen S44.8x1S -only">hyphen S44.92xS hyphen S54.8x1S -only">hyphen S54.92xS hyphen S64.8x1S -only">hyphen S64.92xS hyphen S74.8x1S -only">hyphen S74.92xS hyphen S84.801S -only">hyphen S84.92xS hyphen S94.8x1S -only">hyphen	Spinal cord injury, injury to nerve root(s), spinal plexus(s), and other nerves of trunk, injury to peripheral nerve of shoulder girdle and upper limb, or injury to peripheral nerve of pelvic girdle and lower limb, sequela

S94.92xS	
hyphen S14.2xx+ -only">hyphen S14.9xx+ hyphen S24.101+ -only">hyphen S24.159+ hyphen S24.2xx+ -only">hyphen S24.9xx+ hyphen S34.101+ -only">hyphen S34.139+ hyphen S34.21x+ -only">hyphen S34.9xx+ hyphen S44.8x1+ -only">hyphen S44.92x+ hyphen S54.8x1+ -only">hyphen S54.92x+ hyphen S64.8x1+ -only">hyphen S64.92x+ hyphen S74.8x1+ -only">hyphen S74.92x+ hyphen S84.801+ -only">hyphen S84.92x+ hyphen S94.8x1+ -only">hyphen S94.92x+	Injury to nerve roots and spinal plexus, injury to other nerve(s) of trunk, excluding shoulder and pelvic girdles, injury to peripheral nerve(s) of shoulder girdle and upper limb, or injury to peripheral nerve(s) of pelvic girdle and lower limb
hyphen	**ICD-only">hyphen10 codes not covered for indications listed in the CPB:**
B02.23	Postherpetic polyneuropathy

hyphen F11.90 -only">hyphen F19.99	Drug dependence disorders
R10.2	Pelvic and perineal pain
hyphen H-only">hyphenWave Type Stimulators:	
HCPCS codes not covered if selection criteria are met:	
E0745	hyphen Neuromuscular stimulator; electronic shock unit [H-only">hyphenWave stimulator]
hyphen ICD-only">hyphen10 codes not covered for indications listed in the hyphen CPB (not all-only">hypheninclusive):	
E08.49, E09.49, E10.49, E11.49, E13.49	Diabetes mellitus with other diabetic neurological complication
Intramuscular stimulation:	
CPT codes not covered for indications listed in the CPB:	
64565	Percutaneous implantation of neurostimulator electrodes; neuromuscular
64580	Incision for implantation of neurostimulator electrodes; neuromuscular
hyphen ICD-only">hyphen10 codes not covered for indications listed in the hyphen CPB (not all-only">hypheninclusive):	
hyphen M25.50 -only">hyphen M25.579	Pain in joint
M54.10	Radiculopathy [radiculitis]
hyphen M60.80 -only">hyphen M60.9	Other and unspecified myositis
hyphen M79.10 -only">hyphen M79.18	Myalgia
M79.2	Neuralgia and neuritis, unspecified
Sympathetic Therapy :	
No specific codes	
Electroceutical Therapy:	

No specific codes	
Transcutaneous electrical joint stimulation devices (BioniCare):	
HCPCS codes not covered for indications listed in the CPB:	
E0762	Transcutaneous electrical joint stimulation device system, includes all accessories
hyphen ICD-only">hyphen10 codes not covered for indications listed in the hyphen CPB (not all-only">hypheninclusive):	
hyphen S93.401+ -only">hyphen S93.499+	Sprain of ankle
hyphen Electro-only">hyphenAcuscope Myopulse Therapy:	
No specific codes	
Electrical stimulation of sacral roots or lumbosacral plexus:	
CPT codes not covered for indications listed in the CPB:	
64555	Percutaneous implantation of neurostimulator electrodes; peripheral nerve (excludes sacral nerve)
64561	sacral nerve (transforaminal placement) including image guidance, if performed
64575	Incision for implantation of neurostimulator electrodes; peripheral nerve (excludes sacral nerve)
64581	sacral nerve (transforaminal placement)
hyphen ICD-only">hyphen10 codes not covered for indications listed in the hyphen CPB (not all-only">hypheninclusive):	
hyphen R10.0 -only">hyphen R10.13 hyphen R10.30 -only">hyphen R10.33	Abdominal pain
hyphen R10.811 -only">hyphen R10.829	Abdominal tenderness
R19.8	Other specified symptoms and signs involving the digestive system and abdomen
Microcurrent Therapy:	
No specific codes	
hyphen ICD-only">hyphen10 codes not covered for indications listed in the hyphen CPB (not all-only">hypheninclusive):	

M54.5	Low back pain [lumbago]
M54.9	Dorsalgia, unspecified
***hyphen Pulse Stimulation [P-only">hyphenStim]*:**	
hyphen HCPCS codes not covered for indications listed in the CPB (not all-only">hypheninclusive):	
S8930	Electrical stimulation of auricular acupuncture points; each 15 hyphen hyphen minutes of personal one-only">hyphenon-only">hyphenone contact with the patient hyphen [P-only">hyphenSTIM device]
hyphen ICD-only">hyphen10 codes not covered for indications listed in the hyphen CPB (not all-only">hypheninclusive):	
hyphen B02.21 -only">hyphen B02.29	Zoster with other nervous system involvement
hyphen M17.0 -only">hyphen M17.9	Osteoarthritis of knee
hyphen M51.14 -only">hyphen M54.17	Thoracic, thoracolumbar and lumbosacral intervertebral disc disorders with radiculopathy
hyphen M54.10 -only">hyphen M54.2	Radiculopathy
M54.5	Low back pain
M62.830	Muscle spasm of back [cervical, lumbar]
M96.1	Post laminectomy syndrome [failed back]
***Neurolumen device*:**	
No specific code	
hyphen ICD-only">hyphen10 codes not covered for indications listed in the hyphen CPB (not all-only">hypheninclusive):	
E08.40, E08.42, E09.40, E09.42, E10.40, E10.42, E11.40, E11.42, E13.40, E13.42	Polyneuropathy in diabetes

hyphen G57.60 -only">hyphen G57.63	Lesion of plantar nerve [Morton's neuroma]
hyphen G60.0 -only">hyphen G60.9	Hereditary and idiopathic neuropathy
hyphen hyphen	***Non-only">hypheninvasive/no-only">hyphenincision pain procedure (NIP) device:***
No specific code	
hyphen ICD-only">hyphen10 codes not covered for indications listed in the hyphen CPB (not all-only">hypheninclusive):	
F32.9	Major depressive disorder, single episode, unspecified
F41.9	Anxiety disorder, unspecified
hyphen G43.001 -only">hyphen G43.919	Migraine
hyphen G47.00 -only">hyphen G47.09	Insomnia
G89.18	Other acute postprocedural pain
G89.3	Neoplasm related pain (acute) (chronic)
hyphen M12.00 -only">hyphen M12.9	Other and unspecified arthropathy
hyphen M25.50 -only">hyphen M25.579	Pain in joint
M54.2	Cervicalgia
hyphen M54.30 -only">hyphenM54.5	Sciatica and low back pain
hyphen M60.80 -only">hyphen M60.9	Myositis
hyphen M79.10	Myalgia

-only">hyphen M78.18	
***hyphen Electro-only">hyphenAnalgesia Treatment (EAT) using the Synaptic electrical stimulator*:**	
No specific code	
Other CPT codes related to the CPB:	
64450	Injection, anesthetic agent, other peripheral nerve or branch
hyphen ICD-only">hyphen10 codes not covered for indications listed in the CPB (not all inclusive):	
E08.40, E08.42, E09.40, E09.42, E10.40, E10.42, E11.40, E11.42, E13.40, E13.42	Polyneuropathy in diabetes
G60.0	Hereditary motor and sensory neuropathy
G60.8	Other hereditary and idiopathic neuropathies
***Cefaly transcutaneous electrical stimulator headband*:**	
hyphen ICD-only">hyphen10 codes not covered for indications listed in the CPB (not all inclusive):	
hyphen G43.001 -only">hyphen G43.919	Migraines
***Percutaneous neuromodulation therapy*:**	
No specific code	
hyphen ICD-only">hyphen10 codes not covered for indications listed in the CPB (not all inclusive):	
hyphen G89.0 -only">hyphen G89.4	Pain, not elsewhere classified
***Variable Neuromuscular Stimulation – see CPB 677*:**	
***The Quell device*:**	
No specific code	
***Combination electrochemical therapy/treatment (CET)*:**	
No specific code	
***Galvanic stimulation and other types of electrical stimulation*:**	
CPT codes not covered for indications listed in the CPB:	
97014	Application of a modality to 1 or more areas; electrical stimulation

	(unattended)
97032	Application of a modality to one or more areas; electrical stimulation, (manual), each 15 minutes
hyphen HCPCS codes not covered for indications listed in the CPB (not all-only">hypheninclusive):	
E0745	Neuromuscular stimulator, electronic shock unit
hyphen ICD-only">hyphen10 codes not covered for indications listed in the CPB (not all inclusive):	
I73.9	Peripheral vascular disease, unspecified
***hyphen Combined transcranial direct current stimulation and breathing-only">hyphencontrolled electrical stimulation*:**	
No specific code	
hyphen ICD-only">hyphen10 codes not covered for indications listed in the CPB (not all inclusive):	
M79.2	Neuralgia and neuritis, unspecified
hyphen S14.101A -only">hyphen S14.159S, S24.101A hyphen -only">hyphen S24.159S, S34.101A hyphen -only">hyphen S34.139S	Spinal cord injury
***Electrical stimulation of posterior tibial nerve*:**	
CPT codes not covered for indications listed in the CPB:	
64566	Posterior tibial neurostimulation, percutaneous needle electrode, single treatment, includes programming
hyphen ICD-only">hyphen10 codes not covered for indications listed in the CPB (not all inclusive):	
hyphen G61.0 -only">hyphen G63	Inflammatory polyneuropathy
M79.2	Neuralgia and neuritis, unspecified [neuropathic pain associated with polyneuropathy]
R10.2	Pelvic and perineal pain
***Intravaginal electrical stimulation*:**	

No specific code	
hyphen ICD-only">hyphen10 codes not covered for indications listed in the CPB (not all inclusive):	
R10.2	Pelvic and perineal pain
hyphen Reduced impedance non-only">hypheninvasive cortical electrostimulation (RINCE):	
No specific code	
hyphen ICD-only">hyphen10 codes not covered for indications listed in the hyphen CPB (not all-only">hypheninclusive):	
hyphen G89.21 -only">hyphen G89.29	Chronic pain
G89.4	Chronic pain syndrome

The above policy is based on the following references:

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IN THE COURT OF COMMON PLEAS
SUMMIT COUNTY, OHIO

MEMBER WILLIAMS, *et al.*, Plaintiffs, vs. KISLING, NESTICO & REDICK, LLC, *et al.*, Defendants.	Case No. 2016-CV-09-3928 Judge James A. Brogan **SUPPLEMENTAL ANSWERS OF DEFENDANT SAM N. GHOUBRIAL, M.D. TO PLAINTIFF MONIQUE NORRIS'S FIRST SET OF INTERROGATORIES**

Now comes Defendant, Sam N. Ghoubrial, M.D., by and through counsel, and for his Supplemental Answers and Objections to Plaintiff Monique Norris's First Set of Interrogatories, states as follows:

GENERAL OBJECTIONS

Defendant objects to Plaintiff's Interrogatories and Document Requests to the extent they seek information protected by the attorney-client privilege, work product doctrine, the joint defense and common interest privilege, and other applicable privileges and rules. Specifically, some of Plaintiff's Interrogatories and Document Requests seek information regarding the care and treatment of Defendant's patients in violation of the physician-patient privilege and/or HIPAA.

Defendant Objects to the "Instructions" and "Definitions" preceding Plaintiff's Interrogatories and Document Requests on the grounds they are vague, ambiguous, seek irrelevant information not reasonably calculated to lead to the discovery of admissible evidence, and see to impose obligations on Defendant that are greater than,

or inconsistent with, those obligations imposed by the Ohio Rules of Civil Procedure. Defendant will respond to Plaintiff's Interrogatories and Document Requests in accordance with his obligations under the Ohio Rules of Civil Procedure.

Defendant Objects to the extent there are no date limitations on these Interrogatories and Document Requests, which make them overly broad and unduly burdensome.

Defendant objects to the extent the Interrogatories and Document Requests are based on illegally obtained documents. Plaintiff should not be able to take advantage of the illegally obtained documents. See *Raymond v. Spirit AeroSystems Holdings, Inc.*, Case No. 16-1282-JTM-GEB-, 2017 U.S. Dist. LEXIS 101926 (D. Kan. June 30, 2017).

Defendant objects to Plaintiff's submission of more than forty (40) Interrogatories without leave of Court in violation of Civ. R. 33(A). Defendant will only respond to the first forty (40) Interrogatories consistent with Civ. R. 33(A). Currently, Plaintiff has exceeded the maximum number of Interrogatories permitted by Rule.

Defendant objects to the Interrogatories and Document Requests to the extent they are not related to class certification or matters the "overlap" with issues relate to class certification.

Defendant denies all allegations or statements in the Interrogatories and Document Requests, except as expressly admitted herein.

These "General Objections" are applicable to and incorporated in each of Defendant's responses to Interrogatories and Document Requests. All Defendant's responses are made subject to and without waiving these objections. Failing to state a specific objection to a particular Interrogatory or Document Request should not be

construed as a waiver of these General Objections.

Defendant reserves the right to amend or supplement his responses to these Interrogatories and Document Requests.

Defendant's discovery responses are made without waiver of, and with preservation of:

All questions are to competency, relevancy, materiality, privilege, and admissibility of the responses and subject matter thereof as evidence for any purpose in any further proceedings in this action or any other action;

The right to object to the use of any such responses or the subject matter thereof, on any ground in any further proceedings of this action and in any other action;

The right to object on any ground at any time to a demand or request for a further response to the requests or other discovery involving or relating to the subject matter of the Interrogatories and Document Requests herein responded to;

The right to revise, correct, add to, supplement, or clarify any of the responses contained herein and to provide information and produce evidence of any subsequently discovered facts;

The right to assert additional privileges; and

The right to assert the attorney-client privilege, attorney work product doctrine, or other such privilege as to the discovery produced or the information obtained therefrom, for any purpose in any further proceeding in this action and in any other action.

Interrogatories

1. Identify all agreements and/or arrangements, written or otherwise, formal or informal, regarding, relating to, or involving referrals of clients and/or patients between you and KNR including by identifying the terms of each agreement.

RESPONSE:

Objection. This interrogatory is not reasonably calculated to lead to the discovery of admissible evidence, it contains vague and undefined terms, and it is not related to class certification, nor does the information sought "overlap" with any issues related to class certification. **Further answering, and without waiving said objections, there are no "agreements" or "arrangements, written or otherwise, formal or informal" regarding referrals of patients between Defendant and KNR. There is no referral agreement of any kind between KNR and Dr. Ghoubrial.**

2. Identify all persons, corporations, or business entities through which you have treated KNR clients, billed KNR clients for your services, or to which KNR clients have paid for your services, including by listing all known employees and owners of each entity, and the percentage of ownership of each such owner identified.

RESPONSE:

Objection. This interrogatory is not reasonably calculated to lead to the discovery of admissible evidence, it contains vague and undefined terms, and it is not related to class certification, nor does the information sought "overlap" with any issues related to class certification. **Further answering, and without waiving said objections, Sam Ghoubrial, MD, Inc. bills for its treatment through Clearwater Billing Services, LLC.**

3. Identify the purpose of your affiliation with or incorporation of all of the persons or entities you identify in your response to Interrogatory No. 2 above.

RESPONSE:

Objection. This interrogatory is not reasonably calculated to lead to the discovery of admissible evidence, it contains vague and undefined terms, and it is not related to class certification, nor does the information sought "overlap" with any issues related to class certification. **Further answering, and without waiving said objections, the medical practice simply bills through a separate entity.**

4. To the extent you have not already done so above, identify the purpose of your affiliation with or incorporation of Clearwater Billing Services, LLC, Hanchrist LLC, and TPI Airways LLC, including by listing all known employees and owners of each entity, and the percentage of ownership of each such owner identified.

RESPONSE:

Objection. This interrogatory is not reasonably calculated to lead to the discovery of admissible evidence, it contains vague and undefined terms, and it is not related to class certification, nor does the information sought "overlap" with any issues related to class certification. **Further answering, see response to Interrogatory No. 3.**

5. Identify the circumstances by which you first entered into any referral agreement or arrangement with KNR.

RESPONSE:

Objection. This interrogatory is not reasonably calculated to lead to the discovery of admissible evidence, it contains vague and undefined terms, and it is not related to class certification, nor does the information sought "overlap" with any issues related to class certification. Further, this interrogatory assumes facts not in evidence. **Further answering, and without waiving said objection, there is no referral agreement or arraignment with KNR, see response to Interrogatory No. 1.**

6. Identify the circumstances by which you first began treating KNR clients.

RESPONSE:

Objection. This interrogatory is not reasonably calculated to lead to the discovery of admissible evidence, it contains vague and undefined terms, and it is not related to class certification, nor does the information sought "overlap" with any issues related to class certification. **Further answering, and without waiving said objections, I do not recall how the first KNR client ended up in my care.**

7. Identify all terms under which you have agreed to treat KNR clients.

RESPONSE:

Objection. This interrogatory is not reasonably calculated to lead to the discovery of admissible evidence, it contains vague and undefined terms, and it is not related to class certification, nor does the information sought "overlap" with any issues related to class certification. **Further answering, and without said objections, there were no specific "terms" under which I agree to treat KNR clients. I treated all PI clinic patients sent to me the same way regardless of how they came into my care.**

8. Identify in detail any representation made by KNR to you relating to any legal or ethical issues raised by any referral agreement and/or arrangement between KNR and you, including any representation by KNR that a referral agreement and/or arrangement between KNR and you was legal and/or ethical.

RESPONSE:

Objection. This interrogatory is not reasonably calculated to lead to the discovery of admissible evidence, it contains vague and undefined terms, and it is not related to class certification, nor does the information sought "overlap" with any issues related to class certification. **Further answering, and without waiving said objections, no such representations were ever made, there was never any referral agreement with KNR, see response to Interrogatory No. 1.**

9. Identify any other law firm with whom you have a referral agreement and terms of each such agreement.

RESPONSE:

Objection. This interrogatory is not reasonably calculated to lead to the discovery of admissible evidence, it contains vague and undefined terms, and it is not related to class certification, nor does the information sought "overlap" with any issues related to class certification. **Further answering, and without waiving said objections, I have no referral agreements or arrangements with any law firm, see response to Interrogatory No. 1.**

10. Identify any other law firm from whom you have received patient referrals in the last 8 years.

RESPONSE:

Objection. This interrogatory is not reasonably calculated to lead to the discovery of admissible evidence, it contains vague and undefined terms, and it is not related to class certification, nor does the information sought "overlap" with any issues related to class certification.

11. Identify the number of KNR clients you have treated whose payment for your services was deducted from the clients' KNR settlement.

RESPONSE:

Objection. This interrogatory is not reasonably calculated to lead to the discovery of admissible evidence, it contains vague and undefined terms, and it is not related to class certification, nor does the information sought "overlap" with any issues related to class certification. Further objecting this Interrogatory is overly broad, unduly burdensome and directed to the wrong Defendant.

12. Identify each and every form that you have used in treating KNR clients whose payment for your services was deducted from the clients' KNR settlement, including all releases, lien forms, reservations of rights, informed consent forms, disclosures (including of your financial interest in any aspect of the clients' treatment), and requests for patient information. Please also identify the time period during which each form was used.

RESPONSE:

Objection. This interrogatory is not reasonably calculated to lead to the discovery of admissible evidence, it contains vague and undefined terms, and it is not related to class certification, nor does the information sought "overlap" with any issues related to class certification. Further objecting, this Interrogatory is overly broad, unduly burdensome and directed to the wrong Defendant.

13. Identify each and every facility or location where you have treated KNR clients whose payment for your services was deducted from the clients' KNR settlement, including by identifying the address and owner of each facility or location.

RESPONSE:

Objection. This interrogatory is not reasonably calculated to lead to the discovery of admissible evidence, it contains vague and undefined terms, and it is not related to class certification, nor does the information sought "overlap" with any issues related to class certification. **Further answering, and without waiving said objections, I have treated KNR clients at my Wadsworth office, at my Arlington Road and Brown Street facilities, Akron Square Chiropractic, Town & Country Chiropractic, and potentially other clinics I cannot recall.**

14. Identify all agreements, formal or informal, that you have entered regarding your use of facilities or locations identified in your response to Interrogatory No. 13 including by identifying the terms of and parties to each agreement.

RESPONSE:

Objection. This interrogatory is not reasonably calculated to lead to the discovery of admissible evidence, it contains vague and undefined terms, and it is not related to class certification, nor does the information sought "overlap" with any issues related to class certification. **Further answering, and without waiving said objections, there are no such agreements, either formal or informal.**

15. Identify the circumstances that led to your treating KNR clients at each of the facilities or locations identified in your response to Interrogatory No. 13.

RESPONSE:

Objection. This interrogatory is not reasonably calculated to lead to the discovery of admissible evidence, it contains vague and undefined terms, and it is not related to class certification, nor does the information sought "overlap" with any issues related to class certification.

16. Identify each and every type of medical supply that you have sold or distributed to KNR clients and were reimbursed or paid for the supplies from the KNR clients' settlement proceeds, including TENS units and orthopedic braces.

RESPONSE:

Objection. This interrogatory is not reasonably calculated to lead to the discovery of admissible evidence, it contains vague and undefined terms, and it is not related to class certification, nor does the information sought "overlap" with any issues related to class certification. Further objecting, this Interrogatory is overly broad, unduly burdensome and virtually impossible to answer with any certainty. This Interrogatory also improperly seeks proprietary business information as we as information protected by the physician-patient privilege, HIPAA and related laws. **Further answering, and without waiving said objections, I have provided TENS Units, various injections, and medical braces to patients based on individual needs.**

17. Identify the cost you paid and the amount that you charged KNR clients for each medical supply that you identified in your response to Interrogatory No. 16. To the extent these amounts changed over time, please identify the cost and amount charged for each relevant time period. In responding to this interrogatory, please do not account for any discount or write-off that any particular KNR client might have received on any occasion, but rather the price initially billed to the client regardless of whether that price was eventually discounted or written down in settling the client's claim.

RESPONSE:

Objection. This interrogatory is not reasonably calculated to lead to the discovery of admissible evidence, it contains vague and undefined terms, and it is not related to class certification, nor does the information sought "overlap" with any issues related to class certification. **Further answering, and without waiving said objections, see documents produced in response to Plaintiffs' Request for Production of Documents.**

18. Identify the quantity of each medical supply identified in your response to Interrogatory No. 16 above that you have sold or distributed to KNR clients.

RESPONSE:

Objection. This interrogatory is not reasonably calculated to lead to the discovery of admissible evidence, it contains vague and undefined terms, and it is not related to class certification, nor does the information sought "overlap" with any issues related to class certification. **Further answering, there is no way identify the amount of each medical supply without reviewing each individual patient chart. Every patient was treated based on their individual medical needs. See Charts produced per HIPAA releases.**

19. Identify the number of KNR clients to whom you have sold or distributed the medical supplies described in your response to Interrogatory No. 16, above.

RESPONSE:

Objection. This interrogatory is not reasonably calculated to lead to the discovery of admissible evidence, it contains vague and undefined terms, and it is not related to class certification, nor does the information sought "overlap" with any issues related to class certification. **Further answering, and without waiving said objections, see documents produced in response to Plaintiffs' Request for Production of Documents, see response to Interrogatory No. 17.**

20. Identify all costs associated with your distribution and sale of each medical supply that you identified in your response to Interrogatory No. 16.

RESPONSE:

Objection. This interrogatory is not reasonably calculated to lead to the discovery of admissible evidence, it contains vague and undefined terms, and it is not related to class certification, nor does the information sought "overlap" with any issues related to class certification. **Further answering; see response to Interrogatory Nos. 17, 18.**

21. Identify each and every type of injection that you have administered to KNR clients for which you were paid or reimbursed from the KNR clients' settlement proceeds, including all "trigger point" injections and all injections of corticosteroids or Buvipacaine (Marcaine).

RESPONSE:

Objection. This interrogatory is not reasonably calculated to lead to the discovery of admissible evidence, it contains vague and undefined terms, and it is not related to class certification, nor does the information sought "overlap" with any issues related to class certification. **Further objecting, this Interrogatory**

seeks information protected by the physician-patient privilege, HIPAA and related laws. Moreover, this Interrogatory is not limited to any specific period of time and requests that Defendant review thousands of records to accurately respond; see response to Interrogatory Nos. 17, 18.

22. Identify the cost you paid and the amount that you charged KNR clients for each type of injection identified in your response to Interrogatory No. 21 above. To the extent these amounts changed over time, please identify the cost and amount charged for each relevant time period. In responding to this interrogatory, please do not account for any discount or write-off that any particular KNR client might have received on any occasion, but rather the price initially billed to the client for each injection regardless of whether that price was eventually discounted or written down in settling the client's claim.

RESPONSE:

Objection. This interrogatory is not reasonably calculated to lead to the discovery of admissible evidence, it contains vague and undefined terms, and it is not related to class certification, nor does the information sought "overlap" with any issues related to class certification. Further objecting, this Interrogatory seeks information protected by the physician-patient privilege, HIPAA and related laws. **Further answering; see response to Interrogatory Nos. 17, 18.**

23. Identify the quantity of each type of injection identified in your response to Interrogatory No. 21 above that you have administered to KNR clients.

RESPONSE:

Objection. This interrogatory is not reasonably calculated to lead to the discovery of admissible evidence, it contains vague and undefined terms, and it is not related to class certification, nor does the information sought "overlap" with any issues related to class certification. **Further answering, and without waiving said objections, see response to Interrogatory Nos. 17, 18.**

24. Identify the number of KNR clients to whom you have administered the injections identified in your response to Interrogatory No. 21, above.

RESPONSE:

Objection. This interrogatory is not reasonably calculated to lead to the discovery of admissible evidence, it contains vague and undefined terms, and it is not related to class certification, nor does the information sought "overlap" with any issues related to class certification. Further answering, and without waiving said objections, see response to Interrogatory Nos. 17, 18.

25. Identify all costs associated with your administration of the injections identified in your response to Interrogatory No. 21, above.

RESPONSE:

Objection. This interrogatory is not reasonably calculated to lead to the discovery of admissible evidence, it contains vague and undefined terms, and it is not related to class certification, nor does the information sought "overlap" with any issues related to class certification. Further answering, and without waiving said objections, see response to Interrogatory Nos. 17, 18.

26. Identify all evidence-based studies, medical research, or surveys of which you are aware that supports or informs your treatment of KNR clients with injections.

RESPONSE:

Objection. This interrogatory is not reasonably calculated to lead to the discovery of admissible evidence, it contains vague and undefined terms, and it is not related to class certification, nor does the information sought "overlap" with any issues related to class certification. **Further answering, and without waiving said objections, this Defendant relies upon his education, training, experience and professional judgment in treating patients.**

27. Identify all evidence-based studies, medical research, or surveys of which you are aware that supports or informs your treatment of KNR clients with TENS units.

RESPONSE:

Objection. This interrogatory is not reasonably calculated to lead to the discovery of admissible evidence, it contains vague and undefined terms, and it is not related to class certification, nor does the information sought "overlap" with any issues related to class certification. **Further answering, and without waiving said objections, this Defendant relies upon his education, training, experience and professional judgment in treating patients.**

28. Identify all published guidelines or standards of which you are aware that support or inform your treatment of KNR clients with injections.

RESPONSE:

Objection. This interrogatory is not reasonably calculated to lead to the discovery of admissible evidence, it contains vague and undefined terms, and it

is not related to class certification, nor does the information sought "overlap" with any issues related to class certification. **Further answering, and without waiving said objections, this Defendant relies upon his education, training, experience and professional judgment in treating patients.**

29. Identify all published guidelines or standards of which you are aware that support or inform your treatment of KNR clients with TENS units.

RESPONSE:

Objection. This interrogatory is not reasonably calculated to lead to the discovery of admissible evidence, it contains vague and undefined terms, and it is not related to class certification, nor does the information sought "overlap" with any issues related to class certification. **Further answering, and without waiving said objections, this Defendant relies upon his education, training, experience and professional judgment in treating patients.**

30. Identify all training that you've received to provide treatment for acute pain resulting from automobile accidents.

RESPONSE:

Objection. This interrogatory is not reasonably calculated to lead to the discovery of admissible evidence, it contains vague and undefined terms, and it is not related to class certification, nor does the information sought "overlap" with any issues related to class certification.

31. Identify all modalities of which you are aware for treating acute pain resulting from automobile accidents that are less invasive than the administration of injections.

RESPONSE:

Objection. This interrogatory is not reasonably calculated to lead to the discovery of admissible evidence, it contains vague and undefined terms, and it is not related to class certification, nor does the information sought "overlap" with any issues related to class certification. **Further answering, and without waiving said objections, see all modalities provided by the various chiropractors that refer their patients to me for further treatment.**

32. Identify all modalities of which you are aware for treating acute pain resulting from automobile accidents that are less expensive than the administration of injections.

RESPONSE:

Objection. This interrogatory is not reasonably calculated to lead to the discovery of admissible evidence, it contains vague and undefined terms, and it is not related to class certification, nor does the information sought "overlap" with any issues related to class certification. **Further answering, and without waiving said objections, see all modalities provided by the various chiropractors that refer their patients to me for further treatment.**

33. Identify any complaints received from KNR clients regarding TENS units, orthopedic braces, other medical supplies, or injections, including the nature of the complaint, the date of the complaint, and your response to the complaint.

RESPONSE:

Objection. This interrogatory is not reasonably calculated to lead to the discovery of admissible evidence, it contains vague and undefined terms, and it is not related to class certification, nor does the information sought "overlap" with any issues related to class certification. Further objecting, this Interrogatory seeks information protected by the physician-patient privilege, HIPAA and related laws, and is not limited to any specific time period. **Further answering, and without waiving said objections, none that I'm aware of.**

34. Identify any expense advanced by KNR and/or received by you, including travel, lodging, or meals or entertainment, not related to a specific patient.

RESPONSE:

Objection. This interrogatory is not reasonably calculated to lead to the discovery of admissible evidence, it contains vague and undefined terms, and it is not related to class certification, nor does the information sought "overlap" with any issues related to class certification. **Further answering, and without waiving said objections, none.**

35. Identify all persons—including their true, full and correct names, employers, positions, supervisors, and present addresses and phone numbers—who is now or at any time was responsible for developing or maintaining your relationship with KNR.

RESPONSE:

Objection. This interrogatory is not reasonably calculated to lead to the discovery of admissible evidence, it contains vague and undefined terms, and it is not related to class certification, nor does the information sought "overlap" with

any issues related to class certification. **Further answering, and without waiving said objection, no one other than myself, see response to Interrogatory No. 1.**

36. Identify all persons—including their true, full and correct names, employers, positions, supervisors, and present addresses and phone numbers—employed by you as a biller or coder from 2010-present.

RESPONSE:

Objection. This interrogatory is not reasonably calculated to lead to the discovery of admissible evidence, it contains vague and undefined terms, and it is not related to class certification, nor does the information sought "overlap" with any issues related to class certification. **Further answering, and without waiving said objections, Erin Elefrtiz, Clearwater Billing Services. Ms. Elefritz can be reached through undersigned counsel.**

37. Identify all billing or treatment codes relating to treatment provided to KNR clients, including your providing TENS units, orthopedic braces, other medical supplies, or administering injections to KNR clients.

RESPONSE:

Objection. This interrogatory is not reasonably calculated to lead to the discovery of admissible evidence, it contains vague and undefined terms, and it is not related to class certification, nor does the information sought "overlap" with any issues related to class certification. Further objecting, this Interrogatory is overly broad, unduly burdensome and not reasonably limited in time period or scope. **Further answering, and without waiving said objections, see billing codes list, produced in response to Plaintiffs' Request for Production of Documents.**

38. Identify all disclosures made to Monique Norris regarding the cost of the TENS unit provided to her, and how you would receive payment for the treatment you provided to her.

RESPONSE:

Objection. Interrogatory assumes facts not in evidence. Specifically, this Interrogatory assumes a physician is required to disclose to his or her patients the costs associated with care and how, if at all, the physician is reimbursed for the care and treatment provided. No such requirement exists. **Further answering, and without waiving said objections, Plaintiff Norris, like the vast majority of patients, never asked a single question regarding the costs of the treatment being provided and/or how that treatment would be reimbursed. Had she asked she would have been so informed.**

39. Identify the purpose for your attendance on the trip to Cancun discussed in Paragraph 50 of the Fourth Amended Complaint.

RESPONSE:

Objection. This interrogatory is not reasonably calculated to lead to the discovery of admissible evidence, it contains vague and undefined terms, and it is not related to class certification, nor does the information sought "overlap" with any issues related to class certification. **Further answering, and without waiving said objections, there was no "purpose" other than a vacation with friends.**

40. Identify all expenses you incurred from 2011 to the present relating to transporting yourself, your employees, or KNR clients to facilitate the treatment of KNR clients.

RESPONSE:

Objection. This interrogatory is not reasonably calculated to lead to the discovery of admissible evidence, it contains vague and undefined terms, and it is not related to class certification, nor does the information sought "overlap" with any issues related to class certification. Further objecting, this Interrogatory exceeds the amount permitted by Civ. R. 33(A) without leave of court.

41. State, with as much particularity as possible from the date of the first referral by KNR to you, what percentage of your yearly gross business revenue was and/or is attributable to referrals from KNR.

RESPONSE:

Objection. This interrogatory is not reasonably calculated to lead to the discovery of admissible evidence, it contains vague and undefined terms, and it is not related to class certification, nor does the information sought "overlap" with any issues related to class certification. Further objecting, this Interrogatory exceeds the amount permitted by Civ. R. 33(A) without leave of court.

42. Identify the reasons why you do not accept payment from Medicare or any health-insurance organization for the work you perform on behalf of KNR clients.

RESPONSE:

Objection. This interrogatory is not reasonably calculated to lead to the discovery of admissible evidence, it contains vague and undefined terms, and it is not related to class certification, nor does the information sought "overlap" with any issues related to class certification. **Further answering, and without waiving said objections, it is a business decision based on experience so I**

am compensated for the services I provide..

43. Identify all laws and regulations of which you are aware pertaining to doctors' or doctors' offices' maintenance of patient treatment and billing records in the state of Ohio.

RESPONSE:

Objection. This interrogatory is not reasonably calculated to lead to the discovery of admissible evidence, it contains vague and undefined terms, and it is not related to class certification, nor does the information sought "overlap" with any issues related to class certification. Further objecting, this Interrogatory exceeds the amount permitted by Civ. R. 33(A) without leave of court.

44. Identify all document retention policies maintained by you and every entity through which you have treated KNR clients, including with respect to the maintenance of patient treatment and billing records, including by identifying the terms of each policy.

RESPONSE:

Objection. This interrogatory is not reasonably calculated to lead to the discovery of admissible evidence, it contains vague and undefined terms, and it is not related to class certification, nor does the information sought "overlap" with any issues related to class certification. Further objecting, this Interrogatory exceeds the amount permitted by Civ. R. 33(A) without leave of court.

45. Identify the reasons why you obtained, procured, or assisted in obtaining or procuring insurance coverage on behalf of Tritec.

RESPONSE:

Objection. This interrogatory is not reasonably calculated to lead to the discovery of admissible evidence, it contains vague and undefined terms, and it is not related to class certification, nor does the information sought "overlap" with any issues related to class certification. Further objecting, this Interrogatory exceeds the amount permitted by Civ. R. 33(A) without leave of court.

46. If your response to any Request for Admission is anything but an unqualified admission, identify the basis for your qualification or denial of each such request.

RESPONSE:

Objection. This interrogatory is not reasonably calculated to lead to the discovery of admissible evidence, it contains vague and undefined terms,

and it is not related to class certification, nor does the information sought "overlap" with any issues related to class certification. Further objecting, this Interrogatory exceeds the amount permitted by Civ. R. 33(A) without leave of court.

47. Identify every person who participated in the preparation of these responses and each Defendant's responses to the Requests for Admission and Requests for Production of Documents, including their true, full and correct names, employers, positions, supervisors, and present addresses and phone numbers, the specific discovery requests to which each person's participation pertained, and each task that each person performed in preparing the responses.

RESPONSE:

Objection. This interrogatory is not reasonably calculated to lead to the discovery of admissible evidence, it contains vague and undefined terms, and it is not related to class certification, nor does the information sought "overlap" with any issues related to class certification. Further objecting, this Interrogatory exceeds the amount permitted by Civ. R. 33(A) without leave of court.

AS TO OBJECTIONS

/s/ Bradley J. Barmen

Respectfully submitted,

/s/ Bradley J. Barmen
Bradley J. Barmen (0076515)
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Attorney for Defendant
Sam N. Ghoubrial, M.D.

CERTIFICATE OF SERVICE

I hereby certify that a copy of the foregoing Supplemental Answers of Sam Ghoubrial to Plaintiff's First Set of Interrogatories has been served this 1st day of April, 2019 upon the following:

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Counsel for Defendants Kisling, Nestico
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/s/ Bradley J. Barmen
Bradley J. Barmen (0076515)
Attorney for Defendant
Sam N. Ghoubrial, M.D.

IN THE COURT OF COMMON PLEAS
SUMMIT COUNTY, OHIO

MEMBER WILLIAMS, *et al.*, Plaintiffs, vs. KISLING, NESTICO & REDICK, LLC, *et al.*, Defendants.	Case No. 2016-CV-09-3928 Judge James A. Brogan **DEFENDANT SAM N. GHOUBRIAL, M.D.'S ANSWERS TO PLAINTIFF MONIQUE NORRIS'S FIRST SET OF REQUESTS FOR ADMISSION**

Now comes Defendant, Sam N. Ghoubrial, M.D., by and through counsel, and for his Responses to Plaintiff Monique Norris's First Set of Requests for Admission, states as follows:

Requests for Admission

1. Admit that you entered into an agreement with KNR relating to referrals.

RESPONSE:

Deny

2. Admit that you do not accept payment from any health-insurance organization for the work you perform on behalf of KNR clients.

RESPONSE:

Defendant Admits he does not accept payment from health-insurance organizations for any patient injured in a motor vehicle accident. This is practice-wide and not limited to KNR clients.

3. Admit that you accept payment from health-insurance organizations for the work you perform on behalf of patients who are not KNR clients.

RESPONSE:

Deny. Defendant does not accept payment form health-insurance organizations for any patient injured in a motor vehicle accident.

PLAINTIFF'S EXHIBIT 50

PENGAD 800-631-6989

4. Admit that you purchased TENS units from Tritec for a price of $27.50 per TENS unit.

RESPONSE:

Objection. Can neither admit nor deny. Request for Admission No. 4 seeks proprietary business information protected from disclosure.

5. Admit that you sold the TENS units described in Request for Admission #4 to KNR clients for a price of $500 per TENS unit.

RESPONSE:

Defendant admits the charge to all patients injured in motor vehicle accidents for a TENS unit is $500. This is the standard charge and is not limited to KNR clients who are charged the same amount as all other motor vehicle accident patients.

6. Admit that when you provided TENS units to KNR clients, you never disclosed the amount of the profit that you would receive for each TENS unit for which a KNR client was ultimately charged from their lawsuit proceeds.

RESPONSE:

Deny as written.

7. Admit that when you provided TENS units to KNR clients, you never disclosed that the client could obtain the same device at a lower price than what you would ultimately collect from the KNR clients' lawsuit proceeds.

RESPONSE:

Deny as written.

8. Admit that you own Clearwater Billing Services, LLC.

RESPONSE:

Admit.

9. Admit that you operate, control, and direct the operations of Clearwater Billing Services, LLC.

RESPONSE:

Objection. Request for Admission No. 9 seeks a legal conclusion. Without waiving said objection, admit.

10. Admit that you billed KNR clients through Clearwater Billing Services, LLC.

RESPONSE:

Defendant admits he billed all patients injured in motor vehicle accidents trough Clearwater Billing Services, LLC.

11. Admit that you own Hanchrist, LLC.

RESPONSE:

Deny.

12. Admit that you operate, control, and direct the operations of Hanchrist, LLC.

RESPONSE:

Deny.

13. Admit that you billed or treated KNR clients through Hanchrist, LLC.

RESPONSE:

Deny.

14. Admit that you own TPI Airways, LLC

RESPONSE:

Deny.

15. Admit that you operate, control, and direct the operations of TPI Airways, LLC.

RESPONSE:

Deny.

16. Admit that you have retained the records of your treatment and billing of every KNR client that you have treated since 2010.

RESPONSE:

Defendant admits he has retained records of treatment and billing of all patients consistent with his professional requirements.

17. Admit that you are required by Ohio law to have retained the records of your treatment and billing of every KNR client that you have treated since 2010.

RESPONSE:

Objection. Request for Admission No. 17 seeks a legal conclusion. Further answering, and without waiving said objection, Defendant admits he has retained records of treatment and billing of all patients consistent with his professional requirements.

18. Admit that you are required by federal law to have retained the records of your treatment and billing of every KNR client that you have treated since 2010.

RESPONSE:

Objection. Request for Admission No. 18 seeks a legal conclusion. Further answering, and without waiving said objection, Defendant admits he has retained records of treatment and billing of all patients consistent with his professional requirements.

19. Admit that you traveled by airplanes owned by TPI Airways, LLC to treat KNR clients at various locations throughout the state of Ohio, including at the locations identified in your response to Interrogatory No. 13.

RESPONSE:

Deny.

20. Admit that you do not receive compensation for services rendered to KNR clients if KNR does not obtain a settlement, verdict, or judgment on the particular client's behalf.

RESPONSE:

Deny as written. All such situations are handled on a case-by-case basis and there is no separate policy for KNR clients.

21. Admit that you obtained, procured, or assisted in obtaining or procuring insurance coverage on behalf of Tritec.

RESPONSE:

Deny.

22. Admit that Richard Gunning and Lisa Esterle are your employees who are employed on an at-will basis.

RESPONSE:

Admit that Richard Gunning and Lisa Esterle are employees. Deny that Lisa Esterle is an employee at will.

23. Admit that you have never used the Ohio Automated RX Reporting System (OARRS) to assess whether a KNR client had previously been prescribed controlled substances.

RESPONSE:

Deny.

AS TO ALL OBJECTIONS.

Bradley J. Barmen

Respectfully submitted,

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Attorney for Defendant
Sam N. Ghoubrial, M.D.

CERTIFICATE OF SERVICE

I hereby certify that a copy of the foregoing Responses to Plaintiff's First Set of Requests for Admission, has been served this 4th day of December, 2018 upon the following:

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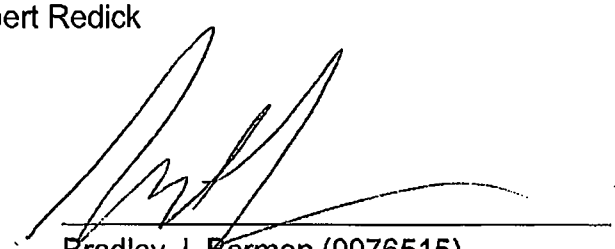
Counsel for Defendants Kisling, Nestico
& Redick, LLC, Alberto R. Nestico and Robert Redick



Bradley J. Barmen (0076515)
Attorney for Defendant
Sam N. Ghoubrial, M.D.

IN THE COURT OF COMMON PLEAS
SUMMIT COUNTY, OHIO

MEMBER WILLIAMS, *et al.*, Plaintiffs, vs. KISLING, NESTICO & REDICK, LLC, *et al.*, Defendants.	Case No. 2016-CV-09-3928 Judge James A. Brogan **SUPPLEMENTAL RESPONSES OF DEFENDANT SAM N. GHOUBRIAL, M.D. TO PLAINTIFF MONIQUE NORRI'S FIRST SET OF REQUESTS FOR PRODUCTION OF DOCUMENTS**

Now comes Defendant, Sam N. Ghoubrial, M.D., by and through counsel, and for his Supplemental Responses to Plaintiff Monique Norris's First Set of Requests for Production of Documents, states as follows:

GENERAL OBJECTIONS

Defendant objects to Plaintiff's Interrogatories and Document Requests to the extent they seek information protected by the attorney-client privilege, work product doctrine, the joint defense and common interest privilege, and other applicable privileges and rules. Specifically, some of Plaintiff's Interrogatories and Document Requests seek information regarding the care and treatment of Defendant's patients in violation of the physician-patient privilege and/or HIPAA.

Defendant Objects to the "Instructions" and "Definitions" preceding Plaintiff's Interrogatories and Document Requests on the grounds they are vague, ambiguous, seek irrelevant information not reasonably calculated to lead to the discovery of admissible evidence, and see to impose obligations on Defendant that are greater than, or inconsistent with, those obligations imposed by the Ohio Rules of Civil Procedure.

Defendant will respond to Plaintiff's Interrogatories and Document Requests in accordance with his obligations under the Ohio Rules of Civil Procedure.

Defendant Objects to the extent there are no date limitations on these Interrogatories and Document Requests, which make them overly broad and unduly burdensome.

Defendant objects to the extent the Interrogatories and Document Requests are based on illegally obtained documents. Plaintiff should not be able to take advantage of the illegally obtained documents. See *Raymond v. Spirit AeroSystems Holdings, Inc.*, Case No. 16-1282-JTM-GEB-, 2017 U.S. Dist. LEXIS 101926 (D. Kan. June 30, 2017).

Defendant objects to Plaintiff's submission of more than forty (40) Interrogatories without leave of Court in violation of Civ. R. 33(A). Defendant will only respond to the first forty (40) Interrogatories consistent with Civ. R. 33(A). Currently, Plaintiff has exceeded the maximum number of Interrogatories permitted by Rule.

Defendant objects to the Interrogatories and Document Requests to the extent they are not related to class certification or matters the "overlap" with issues relate to class certification.

Defendant denies all allegations or statements in the Interrogatories and Document Requests, except as expressly admitted herein.

These "General Objections" are applicable to and incorporated in each of Defendant's responses to Interrogatories and Document Requests. All Defendant's responses are made subject to and without waiving these objections. Failing to state a specific objection to a particular Interrogatory or Document Request should not be construed as a waiver of these General Objections.

Defendant reserves the right to amend or supplement his responses to these Interrogatories and Document Requests.

Defendant's discovery responses are made without waiver of, and with preservation of:

All questions are to competency, relevancy, materiality, privilege, and admissibility of the responses and subject matter thereof as evidence for any purpose in any further proceedings in this action or any other action;

The right to object to the use of any such responses or the subject matter thereof, on any ground in any further proceedings of this action and in any other action;

The right to object on any ground at any time to a demand or request for a further response to the requests or other discovery involving or relating to the subject matter of the Interrogatories and Document Requests herein responded to;

The right to revise, correct, add to, supplement, or clarify any of the responses contained herein and to provide information and produce evidence of any subsequently discovered facts;

The right to assert additional privileges; and

The right to assert the attorney-client privilege, attorney work product doctrine, or other such privilege as to the discovery produced or the information obtained therefrom, for any purpose in any further proceeding in this action and in any other action.

Requests for Production of Documents

Please produce the following documents:

1. All documents reflecting the number of referrals between you and KNR over any period of time, where such documents *do not* relate or refer to a specific patient.

   RESPONSE:

   Objection. This Request is not reasonably calculated to lead to the discovery of admissible evidence, it contains vague and undefined terms, and it is not related to class certification, nor does the information sought "overlap" with any issues related to class certification. In addition, this Request is not reasonably limited to any specific time period and is therefore overly broad and unduly burdensome. Further answering, and without waiving said objections, none.

2. All documents reflecting any agreement, arrangement, or understanding with KNR concerning KNR's referral of clients to you.

   RESPONSE:

   Objection. This Request is not reasonably calculated to lead to the discovery of admissible evidence, it contains vague and undefined terms, and it is not related to class certification, nor does the information sought "overlap" with any issues related to class certification. In addition, this Request is not reasonably limited to any specific time period and is therefore overly broad and unduly burdensome. **Further answering, and without waiving said objections, Defendant is not in possession of any responsive documents as no referral agreement or arrangement exists.**

3. All documents reflecting any payment made between KNR and you, *not associated* with medical services provided for a *specific* KNR client.

   RESPONSE:

   Objection. This Request is not reasonably calculated to lead to the discovery of admissible evidence, it contains vague and undefined terms, and it is not related to class certification, nor does the information sought "overlap" with any issues related to class certification. In addition, this Request is not reasonably limited to any specific time period and is therefore overly broad and unduly burdensome. **Further answering, and without waiving said objections, Defendant is not in possession of any responsive documents as there have been no payments**

from KNR not associated with medical treatment provided.

4. All documents reflecting solicitations or communications to you asking, suggesting, urging or incentivizing any referral agreement and/or arrangement with KNR.

RESPONSE:

Objection. This Request is not reasonably calculated to lead to the discovery of admissible evidence, it contains vague and undefined terms, and it is not related to class certification, nor does the information sought "overlap" with any issues related to class certification. In addition, this Request is not reasonably limited to any specific time period and is therefore overly broad and unduly burdensome. Further answering, and without waiving said objections, none.

5. All documents reflecting policies, procedures, or guidance on how to treat or bill KNR clients.

RESPONSE:

Objection. This Request is not reasonably calculated to lead to the discovery of admissible evidence, it contains vague and undefined terms, and it is not related to class certification, nor does the information sought "overlap" with any issues related to class certification. In addition, this Request is not reasonably limited to any specific time period and is therefore overly broad and unduly burdensome. **Further answering, and without waiving said objections, see Employee Handbook, attached.**

6. All documents reflecting policies, procedures, or guidance on how to process new patients.

RESPONSE:

Objection. This Request is not reasonably calculated to lead to the discovery of admissible evidence, it contains vague and undefined terms, and it is not related to class certification, nor does the information sought "overlap" with any issues related to class certification. In addition, this Request is not reasonably limited to any specific time period and is therefore overly broad and unduly burdensome. **Further answering, and without waiving said objections, see Employee Handbook, attached. Defendant uses a standard intake form for all new patients. See Charts provided pursuant to HIPAA releases.**

7. All documents that you presented to KNR clients relating to any lien on any settlement, judgment, or verdict obtained by KNR.

RESPONSE:

Objection. This Request is not reasonably calculated to lead to the discovery of admissible evidence, it contains vague and undefined terms, and it is not related to class certification, nor does the information sought "overlap" with any issues related to class certification. In addition, this Request is not reasonably limited to any specific time period and is therefore overly broad and unduly burdensome. **Further answering, and without waiving said objections, see LOPs already in Plaintiffs' possession.**

8. All documents relating to billing codes used for medical supplies or services provided to KNR clients, including TENS units, orthopedic braces, and/or trigger-point injections.

RESPONSE:

Objection. This Request is not reasonably calculated to lead to the discovery of admissible evidence, it contains vague and undefined terms, and it is not related to class certification, nor does the information sought "overlap" with any issues related to class certification. In addition, this Request may seek proprietary business information and is not reasonably limited to any specific time period and is therefore overly broad and unduly burdensome. **Further answering, and without waiving said objections, see CPT Billing Codes, attached.**

9. All documents relating to your purchasing, procuring, or obtaining TENS units and orthopedic braces from Tritec.

RESPONSE:

Objection. This Request is not reasonably calculated to lead to the discovery of admissible evidence, it contains vague and undefined terms, and it is not related to class certification, nor does the information sought "overlap" with any issues related to class certification. In addition, this Request is not reasonably limited to any specific time period and is therefore overly broad and unduly burdensome. Further answering, and without waiving said objections, see Tritec Invoice No. 4941, attached.

10. All documents relating to your making financial disclosures to, or obtaining consent pertaining to financial disclosures from, KNR clients.

RESPONSE:

Objection. This Request is not reasonably calculated to lead to the discovery of admissible evidence, it contains vague and undefined terms, and it is not related to class certification, nor does the information sought "overlap" with any issues related to class certification. In addition, this Request is not reasonably limited to any specific time period and is therefore overly broad and unduly burdensome. Further answering, and without waiving said objections, none.

11. All documents relating to the existence of a quota, goal, metric, or expectation of any person employed by you for the administration of trigger-point injections to KNR clients.

RESPONSE:

Objection. This Request is not reasonably calculated to lead to the discovery of admissible evidence, it contains vague and undefined terms, and it is not related to class certification, nor does the information sought "overlap" with any issues related to class certification. In addition, this Request is not reasonably limited to any specific time period and is therefore overly broad and unduly burdensome. **Further answering, and without waiving said objections, Defendant is not in possession of any responsive documents as no such quotas, goals, or metrics exist..**

12. All documents regarding billing procedures, processes, or policies relating to treating patients who are not KNR clients.

RESPONSE:

Objection. This Request is not reasonably calculated to lead to the discovery of admissible evidence, it contains vague and undefined terms, and it is not related to class certification, nor does the information sought "overlap" with any issues related to class certification. In addition, this Request is not reasonably limited to any specific time period and is therefore overly broad and unduly burdensome. Further answering, and without waiving said objections, see Employee Handbook, attached

13. All documents relating to your operation, control, or direction of Clearwater Billing Services, LLC and any other entity identified in your response to Interrogatory Nos. 2 and 4.

RESPONSE:

Objection. This Request is not reasonably calculated to lead to the discovery of admissible evidence, it contains vague and undefined terms, and it is not related to class certification, nor does the information sought "overlap" with any issues related to class certification. In addition, this Request is not reasonably limited to any specific time period and is therefore overly broad and unduly burdensome. Further answering, and without waiving said objections, see Ohio Secretary of States website for public information equally available to Plaintiffs.

14. All documents relating to Monique Norris, including all patient ledgers, billing records, and any record of financial disclosures made to Ms. Norris.

RESPONSE:

Objection. This Request is not reasonably calculated to lead to the discovery of admissible evidence, it contains vague and undefined terms, and it is not related to class certification, nor does the information sought "overlap" with any issues related to class certification. In addition, this Request is not reasonably limited to any specific time period and is therefore overly broad and unduly burdensome. **Further answering, and without waiving said objections, Monique Norris' entire chart, including billing records, has already been produced and is in Plaintiffs' possession**

15. All documents regarding the circumstances under which you accept or do not accept insurance from patients.

RESPONSE:

Objection. This Request is not reasonably calculated to lead to the discovery of admissible evidence, it contains vague and undefined terms, and it is not related to class certification, nor does the information sought "overlap" with any issues related to class certification. In addition, this Request is not reasonably limited to any specific time period and is therefore overly broad and unduly burdensome. Further answering, and without waiving said objections, Defendant is not in possession of any responsive documents.

16. All documents that you use to train your employees, including any manuals, handbooks, memos, or new-employee guides.

RESPONSE:

Objection. This Request is not reasonably calculated to lead to the discovery of admissible evidence, it contains vague and undefined terms, and it is not related to class certification, nor does the information sought "overlap" with any issues related to class certification. In addition, this Request is not reasonably limited to any specific time period and is therefore overly broad and unduly burdensome. **Further answering, and without waiving said objections, see Employee Handbook, attached**

17. All documents reflecting fee agreements that are associated with KNR and/or that KNR provided to your office.

RESPONSE:

Objection. This Request is not reasonably calculated to lead to the discovery of admissible evidence, it contains vague and undefined terms, and it is not related to class certification, nor does the information sought "overlap" with any issues related to class certification. In addition, this Request is not reasonably limited to any specific time period and is therefore overly broad and unduly burdensome. **Further answering, and without waiving said objections, Defendant is not possession of any responsive documents. See Response to Interrogatory No. 1**

18. All documents reflecting communications between you and any person at Tritec relating to obtaining TENS units or orthopedic braces for KNR clients, where such documents are not related to any *specific* KNR client.

RESPONSE:

Objection. This Request is not reasonably calculated to lead to the discovery of admissible evidence, it contains vague and undefined terms, and it is not related to class certification, nor does the information sought "overlap" with any issues related to class certification. In addition, this Request is not reasonably limited to any specific time period and is therefore overly broad and unduly burdensome. **Further answering, and without waiving said objections, see Tritec Invoice No. 4941, attached.**

19. All documents relating to your ownership and affiliation with TPI Airways LLC

RESPONSE:

Objection. This Request is not reasonably calculated to lead to the discovery of admissible evidence, it contains vague and undefined terms, and it is not related to class certification, nor does the information sought "overlap" with any issues related to class certification. In addition, this Request is not reasonably limited to any specific time period and is therefore overly broad and unduly burdensome. **Further answering, and without waiving said objections, Defendant is not in possession of any responsive documents and any responsive documents would be equally available to Plaintiffs' on the Ohio Secretary of State website.**

20. All documents relating to arranging, planning, or contracting for transportation services for the purpose of treating KNR clients outside of your office(s), including the flight manifests for all flights that you took to treat KNR clients, including at the locations listed in your response to Interrogatory No. 13.

RESPONSE:

Objection. This Request is not reasonably calculated to lead to the discovery of admissible evidence, it contains vague and undefined terms, and it is not related to class certification, nor does the information sought "overlap" with any issues related to class certification. In addition, this Request is not reasonably limited to any specific time period and is therefore overly broad and unduly burdensome. Further answering, and without waiving said objections, none.

21. All documents reflecting or consisting of a summary of the revenues and expenses for TPI Airways

RESPONSE:

Objection. This Request is not reasonably calculated to lead to the discovery of admissible evidence, it contains vague and undefined terms, and it is not related to class certification, nor does the information sought "overlap" with any issues related to class certification. In addition, this Request is not reasonably limited to any specific time period and is therefore overly broad and unduly burdensome. Further answering, and without waiving said objections, none.

22. All documents reflecting communication with KNR relating to trips, retreats, vacations, or that you have attended with KNR employees or representatives.

RESPONSE:

Objection. This Request is not reasonably calculated to lead to the discovery of admissible evidence, it contains vague and undefined terms, and it is not related to class certification, nor does the information sought "overlap" with any issues related to class certification. In addition, this Request is not reasonably limited to any specific time period and is therefore overly broad and unduly burdensome. **Further answering, and without waiving said objections, Defendant is not in possession of any responsive documents and any documents responsive to this Request have already been produced by Co-Defendant KNR.**

23. All documents supporting or relating to your response to any Interrogatory served by Plaintiffs in this lawsuit, including all documents consisting of or relating to the agreements or terms referenced in any Interrogatory, the forms referenced in Interrogatory No. 12, the studies, research, and surveys referenced in Interrogatory Nos. 25 and 26, the guidelines or standards referenced in Interrogatory Nos. 27 and 28, the patient complaints referenced in Interrogatory No. 32, the expenses referenced in Interrogatory No. 33, and the document retention policies referenced in Interrogatory No. 43.

RESPONSE:

Objection. This Request is not reasonably calculated to lead to the discovery of admissible evidence, it contains vague and undefined terms, and it is not related to class certification, nor does the information sought "overlap" with any issues related to class certification. In addition, this Request is not reasonably limited to any specific time period and is therefore overly broad and unduly burdensome. Further answering, and without waiving said objections, none.

24. All documents supporting the truth of your denial of any Request for Admission served by Plaintiffs in this lawsuit.

RESPONSE:

Objection. This Request is not reasonably calculated to lead to the discovery of admissible evidence, it contains vague and undefined terms, and it is not related to class certification, nor does the information sought "overlap" with any issues related to class certification. In addition, this Request is not reasonably limited to any specific time period and is therefore overly broad and unduly burdensome. **Further answering, and without waiving said objections, Defendant is not in possession of any responsive documents not already produced by the Parties to this action.**

25. All insurance policies that do or could provide coverage for the defense or payment of the claims at issue in this lawsuit, and documents sufficient to determine the full extent of any such coverage.

RESPONSE:

Objection. This Request is not reasonably calculated to lead to the discovery of admissible evidence, it contains vague and undefined terms, and it is not related to class certification, nor does the information sought "overlap" with any issues related to class certification. **Further answering, and without waiving said objections, Defendant is not in possession of any responsive documents considering Plaintiffs' unsupported contention the claims asserted against Dr. Ghoubrial sound in fraud and not medical malpractice.**

26. All contracts or employment agreements with Richard Gunning, M.D., Joshua Jones, M.D., and Lisa Esterle, D.O.

RESPONSE:

Objection. This Request is not reasonably calculated to lead to the discovery of admissible evidence, it contains vague and undefined terms, and it is not related to class certification, nor does the information sought "overlap" with any issues related to class certification. In addition, this Request seeks proprietary information. **Further answering and without waiving said objections, the current contract for Dr. Esterle and the last contract for Dr. Jones are being produced subject to the Stipulate Protective Order in place and are attached. Dr. Gunning does not have an employment contract.**

27. All employment manuals, handbooks, or job descriptions pertaining to your employment of Richard Gunning, M.D., Joshua Jones, M.D., and Lisa Esterle, D.O.

RESPONSE:

Objection. This Request is not reasonably calculated to lead to the discovery of admissible evidence, it contains vague and undefined terms, and it is not related to class certification, nor does the information sought "overlap" with any issues related to class certification. In addition, this Request is not reasonably limited to any specific time period and is therefore overly broad and unduly burdensome. **Further answering, and without waiving said objections, Defendant is not in possession of any responsive documents.**

28. Records reflecting each and every instance where you have used the Ohio Automated RX Reporting System (OARRS) to assess whether a KNR client had previously been prescribed controlled substances.

RESPONSE:

Objection. This Request is not reasonably calculated to lead to the discovery of admissible evidence, it contains vague and undefined terms, and it is not related to class certification, nor does the information sought "overlap" with any issues related to class certification. In addition, this Request is not reasonably limited to any specific time period and is therefore overly broad and unduly burdensome.

Further answering, and without waiving said objection, Defendant is not in possession of any responsive documents.

AS TO OBJECTIONS.

/s/ Bradley J. Barmen

Respectfully submitted,

/s/ Bradley J. Barmen
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CERTIFICATE OF SERVICE

I hereby certify that a copy of the foregoing Supplemental Responses to Plaintiff's First Set of Requests for Production of Documents, has been served this 1st day of April, 2018 upon the following:

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