



Complex Regional Pain Syndrome Medical Treatment Guideline 2017 Evidence Summary and Table

This document contains a summary of the literature critique process and the resulting evidence statements for the Complex Regional Pain Syndrome (CRPS) Medical Treatment Guideline.

See the *Search Strategy and Study Selection* documents (“General Medical Literature Search Strategy” and “Search Terms and Topics”) on the Division of Workers’ Compensation website for more information on how studies were selected to be critiqued:

<https://www.colorado.gov/pacific/cdle/medical-treatment-guidelines>.

Articles were critiqued using the Division’s literature critique criteria. The literature critique criteria are located on the Division website under *CRPS – Assessment Criteria for Critiques*. Critiques for individual articles are also available on the Division website under *CRPS*.

Some articles were excluded after a critique was started, and reasons for exclusion were provided in the critique. A shortened version of the critique was completed if reasons for exclusion were identified early in the critique process.

Articles that were given a complete critique were given an assessment of “inadequate,” “adequate,” or “high quality.” It should be noted that one article may be graded at different levels for different interventions. Also, in multiple cases, literature from the Cochrane Collaboration was reviewed. When Division of Workers’ Compensation staff completed additional statistical pooling using RevMan (Cochrane Collaboration of Systematic Reviews), this is noted in the “Assessment by DOWC Staff” column of the critique.

For those studies deemed inadequate, a brief rationale was provided. The articles that were graded as either adequate or high quality were used for evidence statements. Three levels (“**some evidence**,” “**good evidence**,” and “**strong evidence**”) were then used to describe strength of evidence for recommendations based on the amount and quality of the supporting literature. These levels of evidence are defined in the General Guidelines Principles, which are located in each of the Division Medical Treatment Guidelines.

- “Some” means the recommendation considered at least one adequate scientific study, which reported that a treatment was effective. The Division recognizes that further research is likely to have an impact on the intervention’s effect.
- “Good” means the recommendation considered the availability of multiple adequate scientific studies or at least one relevant high-quality scientific study, which reported that a treatment was effective. The Division recognizes that further research may have an impact on the intervention’s effect.



- “Strong” means the recommendation considered the availability of multiple relevant and high-quality scientific studies, which arrived at similar conclusions about the effectiveness of a treatment. The Division recognizes that further research is unlikely to have an important impact on the intervention’s effect.

Because the Division synthesizes the medical evidence as much as possible, one assessment (or group of assessments) may potentially create more than one evidence statement. It is also possible that multiple assessments may be combined for a higher level of evidence (e.g., two “adequate” studies might strengthen the evidence supporting a recommendation from “some” to “good”).

Note that other recommendations in the Medical Treatment Guideline are consensus statements. Consensus statements are used only when adequate evidence was not available in the published literature reviewed by the Division or when published evidence was conflicting. The multidisciplinary Task Force makes consensus recommendations based on general medical principles and apply the following values: functional benefit to the patient, acceptable risk and morbidity, length of disability and timeframe to recovery, and lastly, acceptable cost. Consensus statements are often designated in Medical Treatment Guideline as “generally well accepted,” “generally accepted,” “acceptable/accepted,” or “well-established.”

The Medical Treatment Guideline for CRPS has a bibliography comprised of 443 references, and 67 of those were used in evidence statements. The following evidence table is a *summary* of evidence based on critique of scholarly articles. See full critiques, available on the Division’s Website, for more details on specific studies and assessment of them.

Note that several sections of the CRPS medical treatment guideline refer to the Division’s Chronic Pain Disorder Medical Treatment Guideline for background information, recommendations, and evidence. Please see that guideline and its evidence tables for evidence in those sections.

Evidence Statements Regarding Diagnosis of CRPS			
Good Evidence	Evidence Statement	Citation	Design
	CRPS is characterized by inhibition of sympathetic cutaneous responses on the affected side and by blunted sympathetic response to physiologic stimuli.	(Krumova, 2008)	Physiology experiment
		(Wasner, 2001)	Basic science (physiologic) study



Evidence Statements Regarding Diabetic Patients			
Some Evidence	Evidence Statement	Citation	Design
	Diabetic patients with upper extremity disorders have sub-optimal control of their diabetes.	(Ramchurn et al., 2009)	Cross-sectional study

Evidence Statements Regarding Education / Informed Decision Making			
Some Evidence	Evidence Statement	Citation	Design
	Information provided only by video is not sufficient education.	(Newcomer, 2008)	Prospective randomized controlled trial

Evidence Statements Regarding Other Intravenous Medications and Regional Blocks			
Some Evidence	Evidence Statement	Citation	Design
	There is little advantage of IV regional block with guanethidine over saline blocks with respect to the resolution of tenderness in the affected hand, but the resolution of vasomotor instability may be delayed by guanethidine.	(Livingstone, 2002)	Randomized clinical trial

Evidence Statements Regarding Epidural Infusions			
Some Evidence	Evidence Statement	Citation	Design
	There is high rate of infection (33%), which can include meningitis.	(Rauck, Eisenach, Jackson, Young, & Southern, 1993)	Crossover randomized clinical trial



Evidence Statements Regarding Interdisciplinary Rehabilitation Programs			
Good Evidence	Evidence Statement	Citation	Design
	Interdisciplinary programs that include screening for psychological issues, identification of fear-avoidance beliefs and treatment barriers, and establishment of individual functional and work goals will improve function and decrease disability.	(Dobscha, 2009)	Cluster randomized trial
		(Lambeek, 2010)	Randomized clinical trial
	Multidisciplinary rehabilitation (physical therapy and either psychological, social, or occupational therapy) shows small effects in reducing pain and improving disability compared to usual care, and multidisciplinary biopsychosocial rehabilitation is more effective than physical treatment for disability improvement after 12 months of treatment in patients with chronic low back pain. Patients with a significant psychosocial impact are most likely to benefit.	([Cochrane] Kamper, 2014)	Meta-analyses of randomized clinical trials
	Exercise alone or as part of a multi-disciplinary program results in decreased disability for workers with non-acute low back pain.	(Oesch, 2010)	Meta-analysis of randomized clinical trials



Evidence Statements Regarding Interdisciplinary Rehabilitation Programs			
Some Evidence	Evidence Statement	Citation	Design
	<p>Telephone-delivered collaborative care management intervention for primary care veteran patients produced clinically meaningful improvements in pain at 12-month follow-up compared with usual care by increasing non-opioid analgesic medications and without changing opioid usage for the management of chronic musculoskeletal pain. The management was directed by nurse case managers. Because the control group was usual care rather than an attention control, the non-specific effects of attention received in the intervention group could have contributed to the effectiveness of the intervention. If an attention control had been used as the control group, the effect size observed for improvement in pain in the intervention group may have been smaller. It is unknown how successful this would be with injured workers.</p>	(Kroenke, 2014)	Single-blind randomized clinical trial
	<p>An integrated care program, consisting of workplace interventions and graded activity teaching that pain need not limit activity, is effective in returning patients with chronic low back pain to work, even with minimal reported reduction of pain.</p>	(Lambeek, 2010)	Randomized clinical trial



Evidence Statements Regarding Medication Management			
Some Evidence	Evidence Statement	Citation	Design
	In the setting of uncomplicated low back pain lasting longer than 3 months, patients who were willing to participate in a trial of capsules clearly labelled as placebo experienced short-term reductions in pain and disability after the principles of the placebo effect had been explained to them.	(Carvalho, 2016)	Randomized clinical trial

Evidence Statements Regarding CRPS Specific Medication Management			
Good Evidence	Evidence Statement	Citation	Design
	There is little clinical outcome difference between amitriptyline (Elavil, Endep, Vanatrip) and gabapentin or carbamazepine (Carbatrol, Eptol, Equetro, Tegretol), although gabapentin may be better tolerated.	(Rintala, 2007)	Randomized crossover trial
		(Rowbotham, 2004)	Randomized clinical trial
		(Saarto, 2007)	Meta-analysis of randomized trials

Evidence Statements Regarding CRPS-Specific Medications: Oral Steroids			
Good Evidence	Evidence Statement	Citation	Design
	There is good evidence to support oral steroid use early in the course of CRPS.	(Christensen, 1982)	Randomized clinical trial
		(Kalita, 2006)	Randomized clinical trial

Evidence Statements Regarding CRPS-Specific Medications: Bisphosphonates			
Good Evidence	Evidence Statement	Citation	Design
	Use of bisphosphonates effectively decreases pain.	(Varena, 2000)	Randomized clinical trial



Evidence Statements Regarding CRPS-Specific Medications: Bisphosphonates			
Some Evidence	Evidence Statement	Citation	Design
	Use of bisphosphonates increases joint motion in patients with CRPS.	(Manicourt, 2004)	Randomized clinical trial

Evidence Statements Regarding CRPS-Specific Medications: Vitamin C			
Some Evidence	Evidence Statement	Citation	Design
	Vitamin C 500mg to 2 grams taken for 50 days after a wrist fracture may help to prevent CRPS.	(Perez, 2010)	Randomized clinical trial

Evidence Statements Regarding CRPS-Specific Medications: Ketamine Hydrochloride			
Some Evidence	Evidence Statement	Citation	Design
	In CRPS I patients, low dose daily infusions of ketamine can provide pain relief compared to placebo. The relief, however, faded within a few weeks.	(Sigtermans, 2009)	Randomized clinical trial

Evidence Statements Regarding Effectiveness and Side Effects of Opioids			
Strong Evidence	Evidence Statement	Citation	Design
	In the setting of chronic nonspecific low back pain, the short and intermediate term reduction in pain intensity of opioids, compared with placebo, falls short of a clinically important level of effectiveness.	(Abdel Shaheed, 2016)	Systematic review and meta-analysis
	Adverse events such as constipation, dizziness, and drowsiness are more frequent with opioids than with placebo.		



Evidence Statements Regarding Effectiveness and Side Effects of Opioids			
Good Evidence	Evidence Statement	Citation	Design
	Opioids are more efficient than placebo in reducing neuropathic pain by clinically significant amounts.	([Cochrane] McNicol, 2013)	Systematic review and meta-analysis of randomized clinical trials
	Opioids produce significantly more adverse effects than placebo such as constipation, drowsiness, dizziness, nausea, and vomiting.		
	Naloxegol can alleviate opioid induced constipation and 12.5 mg starting dose has an acceptable side effect profile.	(Chey, 2014)	Two identical and simultaneous multicenter randomized double-blind studies
Some Evidence	Evidence Statement	Citation	Design
	In the setting of chronic low back pain with disc pathology, a high degree of anxiety or depressive symptomatology is associated with relatively less pain relief in spite of higher opioid dosage than when these symptoms are absent.	(Wasan, 2015)	Prospective cohort study

Evidence Statements Regarding Opioids and Adverse Events			
Good Evidence	Evidence Statement	Citation	Design
	In generally healthy patients with chronic musculoskeletal pain, treatment with long-acting opioids, compared to treatments with anticonvulsants or antidepressants, is associated with an increased risk of death of approximately 69%, most of which arises from non-overdose causes, principally cardiovascular in nature. The excess cardiovascular mortality principally occurs in the first	(Ray, 2016)	Retrospective matched cohort study



Evidence Statements Regarding Opioids and Adverse Events			
Good Evidence, Continued	180 days from starting opioid treatment.		
	Prescription opioids in excess of 200 MME average daily doses are associated with a near tripling of the risk of opioid-related death, compared to average daily doses of 20 MME. Average daily doses of 100-200 mg and doses of 50-99 mg per day may be associated with a doubling of mortality risk, but these risk estimates need to be replicated with larger studies.	(Gomes, 2011)	Nested case-control study with incidence density sampling
Some Evidence	Evidence Statement	Citation	Design
	Compared to an opioid dose under 20 MME per day, a dose of 20-50 mg nearly doubles the risk of death, a dose of 50 to 100 mg may increase the risk more than fourfold, and a dose greater than 100 mg per day may increase the risk as much as sevenfold. However, the absolute risk of fatal overdose of in chronic pain patients is fairly low, and may be as low as 0.04%.	(Bohnert, 2011)	Case-cohort study
Summary of Evidence Regarding Opioids and Adverse Events			
Based on the studies with good evidence and some evidence listed above, there is strong evidence that any dose above 50 MME per day is associated with a higher risk of death and 100 mg or greater appears to significantly increase the risk.			



Evidence Statements Regarding Choice of Opioids, Indications, and Recommendations for Use			
Strong Evidence	Evidence Statement	Citation	Design
	In patients being treated with opioid agonists for heroin addiction, methadone is more successful than buprenorphine at retaining patients in treatment. The rates of opiate use, as evidenced by positive urines, are equivalent between methadone and buprenorphine.	(Mattick, 2014)	Meta-analysis of randomized clinical trials
	Buprenorphine is superior to placebo with respect to retention in treatment.		
Good Evidence	Evidence Statement	Citation	Design
	Buprenorphine is superior to placebo with respect to positive urine testing for opiates.	(Mattick, 2014)	Meta-analysis of randomized clinical trials
	In the setting of new onset chronic noncancer pain, there is a clinically important relationship between opioid prescription and subsequent opioid use disorder. Compared to no opioid use, short-term opioid use approximately triples the risk of opioid use disorder in the next 18 months. Use of opioids for over 90 days is associated with very pronounced increased risks of the subsequent development of an opioid use disorder, which may be as much as one hundredfold when doses greater than 120 MME are taken for more than 90 days. The absolute risk of these disorders is very uncertain but is likely to be greater than 6.1% for long duration treatment	(Edlund et al., 2014)	Retrospective cohort study using claims data from a large health care database



Evidence Statements Regarding Choice of Opioids, Indications, and Recommendations for Use			
Good Evidence, Continued	with a high opioid dose.		
	Extended release tapentadol is more effective than placebo and comparable to oxycodone. The percent of patients who achieved 50% or greater pain relief was: placebo, 18.9%, tapentadol, 27.0%, and oxycodone, 23.3%.	(Buynak, 2010)	Randomized clinical trial
	Transdermal buprenorphine is noninferior to oral tramadol in the treatment of moderate to severe musculoskeletal pain arising from conditions like osteoarthritis and low back pain. The population of patients for whom it is more appropriate than tramadol is not established but would need to be determined on an individual patient basis if there are clear reasons not to use oral tramadol.	(Leng, 2015)	Phase III noninferiority trial
	Transdermal fentanyl and transdermal buprenorphine are similar with respect to analgesia and sleep quality, and they are similar with respect to some common adverse effects such as constipation and discontinuation due to lack of effect. However, buprenorphine probably causes significantly less nausea than fentanyl, and it probably carries a lower risk of treatment discontinuation due to adverse events. It is also likely that both transdermal medications cause less constipation than oral morphine.	(Wolff, 2012)	Network meta-analysis of randomized clinical trials



Evidence Statements Regarding Choice of Opioids, Indications, and Recommendations for Use			
Good Evidence, Continued	In the setting of common low back injuries, when baseline pain and injury severity are taken into account, a prescription for more than seven days of opioids in the first 6 weeks is associated with an approximate doubling of disability one year after the injury.	(Franklin, 2008)	Prospective cohort study
Some Evidence	Evidence Statement	Citation	Design
	Long-acting oxycodone (Dazidox, Endocodone, ETH-oxycodone, Oxycontin, Oxyfast, OxyIR, Percolone, Roxicodone) and oxymorphone have equal analgesic effects and side effects, although the milligram dose of oxymorphone (Opana) is ½ that of oxycodone.	(Hale, Dvergsten, & Gimbel, 2005)	Randomized clinical trial
	Extended release hydrocodone has a small and clinically unimportant advantage over placebo for relief of chronic low back pain among patients who are able to tolerate the drug and that 40% of patients who begin taking the drug do not attain a dose which provides pain relief without unacceptable adverse effects. Hydrocodone ER does not appear to improve function in comparison with placebo.	(Hale, Zimmerman, Eyal, & Malamut, 2015)	Randomized trial with a screening period of 7-14 days followed by an open-label titration period of up to 6 weeks followed by a double blind treatment period of up to 12 weeks
	In the setting of neuropathic pain, a combination of morphine plus nortriptyline produces better pain relief than either monotherapy alone, but morphine monotherapy is not superior to nortriptyline monotherapy, and	(Gilron, 2015)	Crossover randomized trial



Evidence Statements Regarding Choice of Opioids, Indications, and Recommendations for Use			
Some Evidence, Continued	it is possible that it is actually less effective than nortriptyline.		
	Tapentadol can reduce pain to a moderate degree in diabetic neuropathy, average difference 1.4/10 pain scale, with tolerable adverse effects.	(Schwartz, 2011)	Randomized clinical trial
	Tapentadol causes less constipation than oxycodone.	([Cochrane] Santos, 2015)	Meta-analysis of randomized clinical trials
	Dextromethorphan does not potentiate the effect of morphine opioids and therefore is not recommended to be used with opioids.	(Galer, 2005)	Three randomized clinical trials
	Tramadol alleviates neuropathic pain following spinal cord injury.	(Norrbrink, 2009)	Randomized clinical trial
	Tramadol yields a short-term analgesic response of little clinical importance relative to placebo in postherpetic neuralgia which has been symptomatic for approximately 6 months.	(Boureau, 2003)	Randomized clinical trial

Evidence Statements Regarding Opioid Addiction Treatment			
Strong Evidence	Evidence Statement	Citation	Design
	In patients being treated with opioid agonists for heroin addiction, methadone is more successful than buprenorphine at retaining patients in treatment. The rates of opiate use, as evidenced by positive urines, are equivalent between methadone and buprenorphine.	([Cochrane] Mattick, 2014)	Meta-analysis of randomized clinical trials



Evidence Statements Regarding Patient Education			
Good Evidence	Evidence Statement	Citation	Design
	Pain neuroscience education combined with a physical intervention is more effective in reducing pain, improving disability, and reducing healthcare utilization compared with either usual care, exercise, other education or another control group for the treatment of patients with chronic musculoskeletal pain.	(Louw, 2016)	Narrative systematic review of randomized clinical trials
Some Evidence	Evidence Statement	Citation	Design
	A cognitive intervention consisting of 2 consultations lasting 1 hour each with a physical medicine specialist and a physical therapist covering coping strategies and patient education on motion produces short-term reductions in sub-acute back disability.	(Storheim, 2003)	Randomized clinical trial
	In the setting of non-specific chronic low back pain, patient-centered cognitive functional therapy from physical therapists produced superior outcomes for pain reduction and functional improvement compared with traditional manual therapy and exercise at post-intervention and at 12-month follow-up.	(Vibe Fersum, 2013)	Single-blind randomized clinical trial



Evidence Statements Regarding Aquatic Therapy			
Good Evidence	Evidence Statement	Citation	Design
	Aquatic exercise and land-based exercise show comparable outcomes for function and mobility among people with symptomatic osteoarthritis of the knee or hip.	(Batterham, 2011)	Systematic Review and meta-analysis of randomized clinical trials

Evidence Statements Regarding Mirror Therapy - Graded Motor Imagery			
Some Evidence	Evidence Statement	Citation	Design
	Mirror box therapy 30 minutes per day for 4 weeks is likely to reduce pain in CRPS.	(Cacchio, 2009)	Randomized clinical trial
		(Smart, 2016)	Systematic Review and Meta-Analysis

Evidence Statements Regarding Neuromuscular Re-education			
Some Evidence	Evidence Statement	Citation	Design
	There is a modest benefit from adding a back school to other treatments such as NSAIDs, massage, transcutaneous electrical nerve stimulation (TENS), and other physical therapy modalities.	([Cochrane] Heymans, 2004)	Systematic review of randomized clinical trials



Evidence Statements Regarding Therapeutic Exercise			
Strong Evidence	Evidence Statement	Citation	Design
	<p>In the short, intermediate, and long-term, motor control exercises that emphasize the transversus abdominis and multifidi are at least as effective as other forms of exercise and manual therapy. They are possibly more effective than other minimal interventions in reducing pain and improving disability in patients for the treatment of chronic non-specific low back pain.</p>	(Bystrom, 2013)	Meta-analysis of randomized clinical trials
		(Saragiotto, 2016)	Meta-analysis of randomized clinical trials
Good Evidence	Evidence Statement	Citation	Design
	<p>A 12 week course of treatment in the McKenzie method is at most modestly more effective than spinal manipulation of similar duration in reducing disability in patients with persistent (more than 6 weeks duration, mean = 95 weeks) nonspecific low back pain, although a clinically relevant difference was not apparent. The McKenzie method should not be utilized if there is severe nerve root involvement with motor, sensory, or reflex abnormality.</p>	(Petersen, 2011)	Randomized clinical trial



Evidence Statements Regarding Therapeutic Exercise			
Good Evidence, Continued	Pilates is more effective in reducing pain and improving disability compared with a minimal intervention at intermediate term follow-up, but Pilates is equally as effective as other forms of exercise in improving disability at short- or intermediate-term follow-up for the treatment of patients with chronic non-specific low back pain.	([Cochrane] Yamato, 2015)	Meta-analyses of randomized clinical trials
	Exercise alone or part of a multi-disciplinary program results in decreased disability for workers with non-acute low back pain.	(Oesch, 2010)	Meta-analysis of randomized clinical trials
Some Evidence	Evidence Statement	Citation	Design
	An unsupervised 12-week, periodized musculoskeletal rehabilitation program of weight training conducted 2, 3, or 4 days a week is effective at improving musculoskeletal strength and quality of life and at reducing pain and disability in untrained persons with chronic low back pain. The 4 days a week training volume is most effective. The volume (total number of reps) of PMR exercise prescribed is important.	(Kell, 2011)	Randomized clinical trial
	Trunk balance exercises combined with flexibility exercises are more effective than a combination of strength and flexibility exercises in reducing disability and improving physical function in patients with chronic low back pain.	(Gatti, 2011)	Single-blind randomized clinical trial



Evidence Statements Regarding Therapeutic Exercise			
Some Evidence, Continued	<p>An exercise program which includes resistance training of the cervical and scapulothoracic muscles, combined with stretching of the same muscles, is likely to be beneficial for mechanical neck pain.</p> <p>Cervicolscapular endurance exercises are beneficial for chronic cervicogenic headache.</p> <p>General fitness exercises and upper extremity exercises are unlikely by themselves to be beneficial for mechanical neck pain and are therefore <i>not recommended.</i></p>	(Kay, 2012)	Meta-analysis of randomized clinical trials
	<p>There is no significant difference in the effectiveness of an 12-week, 20 session comprehensive supervised exercise program and an unsupervised simple exercise program with advice for improvement in average pain intensity in the preceding week in people with a mild chronic whiplash-associated disorder even though both interventions resulted in small reductions of pain over 12 months.</p>	(Michaleff, 2014)	Assessor single-blind randomized clinical trial



Evidence Statements Regarding Therapeutic Exercise			
Some Evidence, Continued	A 4-month intervention for chronic neck pain patients containing pain education, specific exercises and graded activity training shows a significant effect, although clinically small, on improved physical and mental health related quality of life compared with controls receiving pain education alone. Good adherence increased the effect in favor of the exercise group.	(Ris, 2016)	Assessor single-blind randomized controlled superiority multicenter clinical trial
	12 weeks of supervised high-dose exercise, spinal manipulative therapy, or low-dose home exercise with advice are all equally effective for reducing pain in the short- and long-term (one year) in those who have chronic low back pain.	(Bronfort, 2011)	Assessor single-blinded randomized controlled trial
	Intensive exercise coupled with cognitive behavioral therapy is as effective for chronic un-operated low back pain as posterolateral fusion.	(Brox, 2010)	Randomized clinical trial
	In the setting of non-specific chronic low back pain, patient-centered cognitive functional therapy from physical therapists produced superior outcomes for pain reduction and functional improvement compared with traditional manual therapy and exercise at post-intervention and at 12-month follow-up.	(Vibe Fersum, 2013)	Single-blind randomized clinical trial



Evidence Statements Regarding Therapeutic Exercise			
Some Evidence, Continued	There is no significant difference in the effectiveness of an 8-week supervised walking program, an evidence-based group exercise class, and usual physiotherapy for improvement in functional disability after 6 months for people with chronic low back pain even though all 3 interventions resulted in small, significant improvements in physical function, reduction of pain, quality of life, and fear avoidance over time.	(Hurley, 2015)	Assessor single-blind randomized clinical trial

Evidence Statements Regarding Yoga			
Strong Evidence	Evidence Statement	Citation	Design
	Yoga has small to moderate advantages over providing only a booklet in reducing low back pain and back-specific disability, but there is no evidence that yoga is superior to stretching and strengthening classes led by a licensed physical therapist.	(Cramer, 2013)	Meta-analysis of randomized clinical trials



Evidence Statements Regarding Yoga			
Good Evidence	Evidence Statement	Citation	Design
	In the setting of chronic low back pain, 8 weeks of 2 hour weekly group sessions of either mindfulness based stress reduction meditation program with yoga or Cognitive Behavioral Therapy results in small, significant improvements in physical function and reduction in pain compared to usual care at 26 weeks with no significant differences in outcomes between the 2 treatments.	(Cherkin, 2016)	Single-blind randomized clinical trial
Some Evidence	Evidence Statement	Citation	Design
	Iyengar yoga, which avoids back bending, results in improved function and decreased chronic mechanical low back pain for up to 6 months. Instruction occurred 2 times per week for 24 weeks and was coupled with home exercise. One quarter of the participants dropped out.	(Williams, 2009)	Randomized clinical trial
	In the setting of chronic pain, both an 8-week mindfulness based stress reduction meditation program with yoga and an 8-week multidisciplinary pain intervention program with exercise resulted in small, significant reductions in pain intensity and pain-related distress post intervention but with no significant differences in outcomes between the 2 programs.	(Wong, 2011)	Single-blind randomized clinical trial



Evidence Statements Regarding Dorsal Root Ganglion Stimulator			
Good Evidence	Evidence Statement	Citation	Design
	Dorsal root ganglion stimulation is non-inferior to conventional spinal cord stimulation with respect to pain relief for CRPS patients with lower extremity pain.	(Deer et al., 2016)	Randomized non-inferiority clinical trial
Some Evidence	Evidence Statement	Citation	Design
	Dorsal root ganglion stimulation is superior to spinal cord stimulation with respect to pain relief for up to 12 months after implantation. Neurological deficits related to stimulation with either device appear to be rare. 46% of the DRG patients had more serious complications compared to 26% for SCS.	(Deer et al., 2016)	Randomized non-inferiority clinical trial

Evidence Statements Regarding Vitamin C			
Some Evidence	Evidence Statement	Citation	Design
	Vitamin C 500mg taken for 50 days after a wrist fracture may help to prevent CRPS.	(Zollinger, 2007)	Randomized clinical trial



REFERENCES

- Abdel Shaheed, C. M., C. G.; Williams, K. A.; Day, R.; McLachlan, A. J. (2016). Efficacy, Tolerability, and Dose-Dependent Effects of Opioid Analgesics for Low Back Pain: A Systematic Review and Meta-analysis. *JAMA Intern Med*, 176(7), 958-968. doi:10.1001/jamainternmed.2016.1251
- Batterham, S. I. H., S.; Keating, J. L. (2011). Systematic review and meta-analysis comparing land and aquatic exercise for people with hip or knee arthritis on function, mobility and other health outcomes. *BMC Musculoskelet Disord*, 12, 123. doi:10.1186/1471-2474-12-123
- Bohnert, A. S. V., M.; Bair, M. J.; Ganoczy, D.; McCarthy, J. F.; Ilgen, M. A.; Blow, F. C. (2011). Association between opioid prescribing patterns and opioid overdose-related deaths. *Jama*, 305(13), 1315-1321. doi:10.1001/jama.2011.370
- Boureau, F. L., P.; Kabir-Ahmadi, M. (2003). Tramadol in post-herpetic neuralgia: a randomized, double-blind, placebo-controlled trial. *Pain*, 104(1-2), 323-331.
- Bronfort, G. M., M. J.; Evans, R. L.; Schulz, C. A.; Bracha, Y.; Svendsen, K. H.; Grimm, R. H., Jr.; Owens, E. F., Jr.; Garvey, T. A.; Transfeldt, E. E. (2011). Supervised exercise, spinal manipulation, and home exercise for chronic low back pain: a randomized clinical trial. *Spine J*, 11(7), 585-598. doi:10.1016/j.spinee.2011.01.036
- Brox, J. I. N., O. P.; Holm, I.; Keller, A.; Ingebrigtsen, T.; Reikeras, O. (2010). Four-year follow-up of surgical versus non-surgical therapy for chronic low back pain. *Ann Rheum Dis*, 69(9), 1643-1648. doi:10.1136/ard.2009.108902
- Buynak, R. S., D. Y.; Okamoto, A.; Van Hove, I.; Rauschkolb, C.; Steup, A.; Lange, B.; Lange, C.; Etropolski, M. (2010). Efficacy and safety of tapentadol extended release for the management of chronic low back pain: results of a prospective, randomized, double-blind, placebo- and active-controlled Phase III study. *Expert Opin Pharmacother*, 11(11), 1787-1804. doi:10.1517/14656566.2010.497720
- Bystrom, M. G. R.-B., E.; Grooten, W. J. (2013). Motor control exercises reduces pain and disability in chronic and recurrent low back pain: a meta-analysis. *Spine (Phila Pa 1976)*, 38(6), E350-358. doi:10.1097/BRS.0b013e31828435fb
- Cacchio, A. D. B., E.; De Blasis, V.; Santilli, V.; Spacca, G. (2009). Mirror therapy in complex regional pain syndrome type 1 of the upper limb in stroke patients. *Neurorehabil Neural Repair*, 23(8), 792-799. doi:10.1177/1545968309335977
- Carvalho, C. C., J. M.; Cunha, L.; Rebouta, P.; Kaptchuk, T. J.; Kirsch, I. (2016). Open-label placebo treatment in chronic low back pain: a randomized controlled trial. *Pain*, 157(12), 2766-2772. doi:10.1097/j.pain.0000000000000700
- Cherkin, D. C. S., K. J.; Balderson, B. H.; Cook, A. J.; Anderson, M. L.; Hawkes, R. J.; Hansen, K. E.; Turner, J. A. (2016). Effect of Mindfulness-Based Stress Reduction vs Cognitive Behavioral Therapy or Usual Care on Back Pain and Functional Limitations in Adults With Chronic Low Back Pain: A Randomized Clinical Trial. *Jama*, 315(12), 1240-1249. doi:10.1001/jama.2016.2323
- Chey, W. D. W., L.; Sostek, M.; Lappalainen, J.; Barker, P. N.; Tack, J. (2014). Naloxegol for opioid-induced constipation in patients with noncancer pain. *N Engl J Med*, 370(25), 2387-2396. doi:10.1056/NEJMoa1310246
- Christensen, K. J., E. M.; Noer, I. (1982). The reflex dystrophy syndrome response to treatment with systemic corticosteroids. *Acta Chir Scand*, 148(8), 653-655.
- Cramer, H. L., R.; Haller, H.; Dobos, G. (2013). A systematic review and meta-analysis of yoga for low back pain. *Clin J Pain*, 29(5), 450-460. doi:10.1097/AJP.0b013e31825e1492
- Deer, T. R., Levy, R. M., Kramer, J., Poree, L., Amirdelfan, K., Grigsby, E., . . . Mekhail, N. (2016). Dorsal root ganglion stimulation yielded higher treatment success rate for complex regional pain



- syndrome and causalgia at 3 and 12 months: a randomized comparative trial. *Pain*. doi:10.1097/j.pain.0000000000000814
- Dobscha, S. K. C., K.; Perrin, N. A.; Hanson, G. C.; Leibowitz, R. Q.; Doak, M. N.; Dickinson, K. C.; Sullivan, M. D.; Gerrity, M. S. (2009). Collaborative care for chronic pain in primary care: a cluster randomized trial. *Jama*, 301(12), 1242-1252. doi:10.1001/jama.2009.377
- Edlund, M. J., Martin, B. C., Russo, J. E., DeVries, A., Braden, J. B., & Sullivan, M. D. (2014). The role of opioid prescription in incident opioid abuse and dependence among individuals with chronic noncancer pain: the role of opioid prescription. *Clin J Pain*, 30(7), 557-564. doi:10.1097/AJP.0000000000000021
- Franklin, G. M. S., B. D.; Turner, J. A.; Fulton-Kehoe, D.; Wickizer, T. M.; Disability Risk Identification Study, Cohort. (2008). Early opioid prescription and subsequent disability among workers with back injuries: the Disability Risk Identification Study Cohort. *Spine (Phila Pa 1976)*, 33(2), 199-204. doi:10.1097/BRS.0b013e318160455c
- Galer, B. S. L., D.; Ma, T.; Nagle, B.; Schlagheck, T. G. (2005). Morphidex (morphine sulfate/dextromethorphan hydrobromide combination) in the treatment of chronic pain: three multicenter, randomized, double-blind, controlled clinical trials fail to demonstrate enhanced opioid analgesia or reduction in tolerance. *Pain*, 115(3), 284-295. doi:10.1016/j.pain.2005.03.004
- Gatti, R. F., S.; Tettamanti, A.; Barbero, M.; Balestri, A.; Calori, G. (2011). Efficacy of trunk balance exercises for individuals with chronic low back pain: a randomized clinical trial. *J Orthop Sports Phys Ther*, 41(8), 542-552. doi:10.2519/jospt.2011.3413
- Gilron, I. T., D.; Holden, R. R.; Jackson, A. C.; DuMerton-Shore, D. (2015). Combination of morphine with nortriptyline for neuropathic pain. *Pain*, 156(8), 1440-1448. doi:10.1097/j.pain.0000000000000149
- Gomes, T. M., M. M.; Dhalla, I. A.; Paterson, J. M.; Juurlink, D. N. (2011). Opioid dose and drug-related mortality in patients with nonmalignant pain. *Arch Intern Med*, 171(7), 686-691. doi:10.1001/archinternmed.2011.117
- Hale, M. E., Dvergsten, C., & Gimbel, J. (2005). Efficacy and safety of oxycodone extended release in chronic low back pain: results of a randomized, double-blind, placebo- and active-controlled phase III study. *J Pain*, 6(1), 21-28. doi:10.1016/j.jpain.2004.09.005
- Hale, M. E., Zimmerman, T. R., Eyal, E., & Malamut, R. (2015). Efficacy and safety of a hydrocodone extended-release tablet formulated with abuse-deterrence technology in patients with moderate-to-severe chronic low back pain. *J Opioid Manag*, 11(6), 507-518. doi:10.5055/jom.2015.0304
- Heymans, M. W. v. T., M. W.; Esmail, R.; Bombardier, C.; Koes, B. W. (2004). Back schools for non-specific low-back pain. *Cochrane Database Syst Rev*(4), CD000261. doi:10.1002/14651858.CD000261.pub2
- Hurley, D. A. T., M. A.; Lonsdale, C.; Boreham, C. A.; van Mechelen, W.; Daly, L.; Tynan, A.; McDonough, S. M. (2015). Supervised walking in comparison with fitness training for chronic back pain in physiotherapy: results of the SWIFT single-blinded randomized controlled trial (ISRCTN17592092). *Pain*, 156(1), 131-147. doi:10.1016/j.pain.0000000000000013
- Kalita, J. V., A.; Misra, U. K. (2006). Comparison of prednisolone with piroxicam in complex regional pain syndrome following stroke: a randomized controlled trial. *QJM*, 99(2), 89-95. doi:10.1093/qjmed/hcl004
- Kamper, S. J. A., A. T.; Chiarotto, A.; Smeets, R. J.; Ostelo, R. W.; Guzman, J.; van Tulder, M. W. (2014). Multidisciplinary biopsychosocial rehabilitation for chronic low back pain. *Cochrane Database Syst Rev*(9), Cd000963. doi:10.1002/14651858.CD000963.pub3



- Kay, T. M. G., A.; Goldsmith, C. H.; Rutherford, S.; Voth, S.; Hoving, J. L.; Bronfort, G.; Santaguida, P. L. (2012). Exercises for mechanical neck disorders. *Cochrane Database Syst Rev*(8), Cd004250. doi:10.1002/14651858.CD004250.pub4
- Kell, R. T. R., A. D.; Barden, J. M. (2011). The response of persons with chronic nonspecific low back pain to three different volumes of periodized musculoskeletal rehabilitation. *J Strength Cond Res*, 25(4), 1052-1064. doi:10.1519/JSC.0b013e3181d09df7
- Kroenke, K. K., E. E.; Wu, J.; Yu, Z.; Chumbler, N. R.; Bair, M. J. (2014). Telecare collaborative management of chronic pain in primary care: a randomized clinical trial. *Jama*, 312(3), 240-248. doi:10.1001/jama.2014.7689
- Krumova, E. K. F., J.; Klauenberg, S.; Richter, H.; Wasner, G.; Maier, C. (2008). Long-term skin temperature measurements - a practical diagnostic tool in complex regional pain syndrome. *Pain*, 140(1), 8-22. doi:10.1016/j.pain.2008.07.003
- Lambeek, L. C. v. M., W.; Knol, D. L.; Loisel, P.; Anema, J. R. (2010). Randomised controlled trial of integrated care to reduce disability from chronic low back pain in working and private life. *Bmj*, 340, c1035. doi:10.1136/bmj.c1035
- Leng, X. L., Z.; Lv, H.; Zheng, Y.; Liu, Y.; Dai, K.; Yao, C.; Yan, X.; Zeng, X. (2015). Effectiveness and Safety of Transdermal Buprenorphine Versus Sustained-release Tramadol in Patients With Moderate to Severe Musculoskeletal Pain: An 8-Week, Randomized, Double-Blind, Double-Dummy, Multicenter, Active-controlled, Noninferiority Study. *Clin J Pain*, 31(7), 612-620. doi:10.1097/ajp.0000000000000144
- Livingstone, J. A. A., R. M. (2002). Intravenous regional guanethidine blockade in the treatment of post-traumatic complex regional pain syndrome type 1 (algodystrophy) of the hand. *J Bone Joint Surg Br*, 84(3), 380-386.
- Louw, A. Z., K.; Puenteadura, E. J.; Diener, I. (2016). The efficacy of pain neuroscience education on musculoskeletal pain: A systematic review of the literature. *Physiother Theory Pract*, 32(5), 332-355. doi:10.1080/09593985.2016.1194646
- Manicourt, D. H. B., J. P.; Boutsen, Y.; Depreux, G.; Devogelaer, J. P. (2004). Role of alendronate in therapy for posttraumatic complex regional pain syndrome type I of the lower extremity. *Arthritis Rheum*, 50(11), 3690-3697. doi:10.1002/art.20591
- Mattick, R. P. B., C.; Kimber, J.; Davoli, M. (2014). Buprenorphine maintenance versus placebo or methadone maintenance for opioid dependence. *Cochrane Database Syst Rev*(2), CD002207. doi:10.1002/14651858.CD002207.pub4
- McNicol, E. D. M., A.; Eisenberg, E. (2013). Opioids for neuropathic pain. *Cochrane Database Syst Rev*(8), Cd006146. doi:10.1002/14651858.CD006146.pub2
- Michaleff, Z. A. M., C. G.; Lin, C. W.; Rebbeck, T.; Jull, G.; Latimer, J.; Connelly, L.; Sterling, M. (2014). Comprehensive physiotherapy exercise programme or advice for chronic whiplash (PROMISE): a pragmatic randomised controlled trial. *Lancet*, 384(9938), 133-141. doi:10.1016/s0140-6736(14)60457-8
- Newcomer, K. L. V. D., K. S.; Shelerud, R. A.; Long, K. H.; Crawford, B. (2008). Is a videotape to change beliefs and behaviors superior to a standard videotape in acute low back pain? A randomized controlled trial. *Spine J*, 8(6), 940-947. doi:10.1016/j.spinee.2007.08.007
- Norrbrink, C. L., T. (2009). Tramadol in neuropathic pain after spinal cord injury: a randomized, double-blind, placebo-controlled trial. *Clin J Pain*, 25(3), 177-184. doi:10.1097/AJP.0b013e31818a744d
- Oesch, P. K., J.; Hagen, K. B.; Bachmann, S. (2010). Effectiveness of exercise on work disability in patients with non-acute non-specific low back pain: Systematic review and meta-analysis of randomised controlled trials. *J Rehabil Med*, 42(3), 193-205. doi:10.2340/16501977-0524



- Perez, R. S. Z., P. E.; Dijkstra, P. U.; Thomassen-Hilgersom, I. L.; Zuurmond, W. W.; Rosenbrand, K. C.; Geertzen, J. H.; Crps I. task force. (2010). Evidence based guidelines for complex regional pain syndrome type 1. *BMC Neurol*, 10, 20. doi:10.1186/1471-2377-10-20
- Petersen, T. L., K.; Nordsteen, J.; Olsen, S.; Fournier, G.; Jacobsen, S. (2011). The McKenzie method compared with manipulation when used adjunctive to information and advice in low back pain patients presenting with centralization or peripheralization: a randomized controlled trial. *Spine (Phila Pa 1976)*, 36(24), 1999-2010. doi:10.1097/BRS.0b013e318201ee8e
- Ramchurn, N., Mashamba, C., Leitch, E., Arutchelvam, V., Narayanan, K., Weaver, J., . . . Kelly, C. (2009). Upper limb musculoskeletal abnormalities and poor metabolic control in diabetes. *Eur J Intern Med*, 20(7), 718-721. doi:10.1016/j.ejim.2009.08.001
- Rauck, R. L., Eisenach, J. C., Jackson, K., Young, L. D., & Southern, J. (1993). Epidural clonidine treatment for refractory reflex sympathetic dystrophy. *Anesthesiology*, 79(6), 1163-1169; discussion 1127A.
- Ray, W. A. C., C. P.; Murray, K. T.; Hall, K.; Stein, C. M. (2016). Prescription of Long-Acting Opioids and Mortality in Patients With Chronic Noncancer Pain. *Jama*, 315(22), 2415-2423. doi:10.1001/jama.2016.7789
- Rintala, D. H. H., S. A.; Courtade, D.; Fiess, R. N.; Tastard, L. V.; Loubser, P. G. (2007). Comparison of the effectiveness of amitriptyline and gabapentin on chronic neuropathic pain in persons with spinal cord injury. *Arch Phys Med Rehabil*, 88(12), 1547-1560. doi:10.1016/j.apmr.2007.07.038
- Ris, I. S., K.; Gram, B.; Agerbo, K.; Boyle, E.; Juul-Kristensen, B. (2016). Does a combination of physical training, specific exercises and pain education improve health-related quality of life in patients with chronic neck pain? A randomised control trial with a 4-month follow up. *Man Ther*, 26, 132-140. doi:10.1016/j.math.2016.08.004
- Rowbotham, M. C. G., V.; Kunz, N. R.; Lei, D. (2004). Venlafaxine extended release in the treatment of painful diabetic neuropathy: a double-blind, placebo-controlled study. *Pain*, 110(3), 697-706. doi:10.1016/j.pain.2004.05.010
- Saarto, T. W., P. J. (2007). Antidepressants for neuropathic pain. *Cochrane Database Syst Rev*(4), CD005454. doi:10.1002/14651858.CD005454.pub2
- Santos, J. A., J.; Fareleira, F.; Vaz-Carneiro, A.; Costa, J. (2015). Tapentadol for chronic musculoskeletal pain in adults. *Cochrane Database Syst Rev*(5), Cd009923. doi:10.1002/14651858.CD009923.pub2
- Saragiotto, B. T. M., C. G.; Yamato, T. P.; Costa, L. O.; Menezes Costa, L. C.; Ostelo, R. W.; Macedo, L. G. (2016). Motor control exercise for chronic non-specific low-back pain. *Cochrane Database Syst Rev*(1), Cd012004. doi:10.1002/14651858.cd012004
- Schwartz, S. E., M.; Shapiro, D. Y.; Okamoto, A.; Lange, R.; Haeussler, J.; Rauschkolb, C. (2011). Safety and efficacy of tapentadol ER in patients with painful diabetic peripheral neuropathy: results of a randomized-withdrawal, placebo-controlled trial. *Curr Med Res Opin*, 27(1), 151-162. doi:10.1185/03007995.2010.537589
- Sigtermans, M. J. v. H., J. J.; Bauer, M. C.; Arbous, M. S.; Marinus, J.; Sarton, E. Y.; Dahan, A. (2009). Ketamine produces effective and long-term pain relief in patients with Complex Regional Pain Syndrome Type 1. *Pain*, 145(3), 304-311. doi:10.1016/j.pain.2009.06.023
- Smart, K. M. W., B. M.; O'Connell, N. E. (2016). Physiotherapy for pain and disability in adults with complex regional pain syndrome (CRPS) types I and II. *Cochrane Database Syst Rev*, 2, Cd010853. doi:10.1002/14651858.CD010853.pub2
- Storheim, K. B., J. I.; Holm, I.; Koller, A. K.; Bo, K. (2003). Intensive group training versus cognitive intervention in sub-acute low back pain: short-term results of a single-blind randomized controlled trial. *J Rehabil Med*, 35(3), 132-140.



- Varenna, M. Z., F.; Ghiringhelli, D.; Binelli, L.; Bevilacqua, M.; Bettica, P.; Sinigaglia, L. (2000). Intravenous clodronate in the treatment of reflex sympathetic dystrophy syndrome. A randomized, double blind, placebo controlled study. *J Rheumatol*, 27(6), 1477-1483.
- Vibe Fersum, K. O. S., P.; Skouen, J. S.; Smith, A.; Kvale, A. (2013). Efficacy of classification-based cognitive functional therapy in patients with non-specific chronic low back pain: a randomized controlled trial. *Eur J Pain*, 17(6), 916-928. doi:10.1002/j.1532-2149.2012.00252.x
- Wasan, A. D. M., E.; Edwards, R. R.; Katz, J. N.; Nedeljkovic, S. S.; Dolman, A. J.; Janfaza, D.; Isaac, Z.; Jamison, R. N. (2015). Psychiatric Comorbidity Is Associated Prospectively with Diminished Opioid Analgesia and Increased Opioid Misuse in Patients with Chronic Low Back Pain. *Anesthesiology*, 123(4), 861-872. doi:10.1097/aln.0000000000000768
- Wasner, G. S., J.; Heckmann, K.; Maier, C.; Baron, R. (2001). Vascular abnormalities in reflex sympathetic dystrophy (CRPS I): mechanisms and diagnostic value. *Brain*, 124(Pt 3), 587-599.
- Williams, K. A., C.; Steinberg, L.; Doyle, E.; Epstein, B.; Smith, D.; Hobbs, G.; Gross, R.; Kelley, G.; Cooper, L. (2009). Evaluation of the effectiveness and efficacy of Iyengar yoga therapy on chronic low back pain. *Spine (Phila Pa 1976)*, 34(19), 2066-2076. doi:10.1097/BRS.0b013e3181b315cc
- Wolff, R. F. A., D.; Truysers, C.; Hernandez, A. V.; Misso, K.; Riemsma, R.; Kleijnen, J. (2012). Systematic review of efficacy and safety of buprenorphine versus fentanyl or morphine in patients with chronic moderate to severe pain. *Curr Med Res Opin*, 28(5), 833-845. doi:10.1185/03007995.2012.678938
- Wong, S. Y. C., F. W.; Wong, R. L.; Chu, M. C.; Kitty Lam, Y. Y.; Mercer, S. W.; Ma, S. H. (2011). Comparing the effectiveness of mindfulness-based stress reduction and multidisciplinary intervention programs for chronic pain: a randomized comparative trial. *Clin J Pain*, 27(8), 724-734. doi:10.1097/AJP.0b013e3182183c6e
- Yamato, T. P. M., C. G.; Saragiotto, B. T.; Hancock, M. J.; Ostelo, R. W.; Cabral, C. M.; Menezes Costa, L. C.; Costa, L. O. (2015). Pilates for low back pain. *Cochrane Database Syst Rev*(7), CD010265. doi:10.1002/14651858.CD010265.pub2
- Zollinger, P. E. T., W. E.; Breederveld, R. S.; Kreis, R. W. (2007). Can vitamin C prevent complex regional pain syndrome in patients with wrist fractures? A randomized, controlled, multicenter dose-response study. *J Bone Joint Surg Am*, 89(7), 1424-1431. doi:10.2106/JBJS.F.01147