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Chronic Pain Disorder Medical Treatment Guideline 2017
Evidence Summary and Tables

This document contains a summary of the literature critique process and the resulting evidence statements for the Chronic Pain Disorder 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 Chronic Pain Disorder – *Assessment Criteria for Critiques*. Critiques for individual articles are also available on the Division website under Chronic Pain Disorder.

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 Chronic Pain Disorder has a bibliography comprised of 1577 articles, and 161 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.

Evidence Statements Regarding Psychometric Testing			
Good Evidence	Evidence Statement	Citation	Design
	Psychometric testing can have significant ability to predict medical treatment outcome.	(Block, Ohnmeiss, Guyer, Rashbaum, & Hochschuler, 2001)	Prospective cohort study
		(Sinikallio et al., 2009)	Observational cohort study
		(Sinikallio et al., 2010)	Observational cohort 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 Diagnostic Spinal Injections and Steroid Associated Issues			
Strong Evidence	Evidence Statement	Citation	Design
	Epidural steroid injections (ESIs) have a small average short-term benefit for leg pain and disability for those with sciatica.	(Pinto et al., 2012)	Meta-analysis of randomized clinical trials
	ESIs do not, on average, provide clinically meaningful long-term improvements in leg pain, back pain, or disability in patients with sciatica (lumbar radicular pain or radiculopathy).		
	ESIs have no short-term or long-term benefit for low back pain.		
Good Evidence	Evidence Statement	Citation	Design
	The addition of steroids to a transforaminal bupivacaine injection has a small effect on patient reported pain and disability.	(Ng, Chaudhary, & Sell, 2005)	Randomized clinical trial
		(Tafazal, Ng, Chaudhary, & Sell, 2009)	Randomized clinical trial
	There are no significant differences between epidural injections with corticosteroid plus local anesthetic versus local anesthetic alone in patients with symptomatic spinal stenosis. However, there are measureable differences with respect to morning cortisol levels at 3 and 6 weeks after the injection, suggesting that the corticosteroid injection is capable of inducing suppression of the hypothalamic-pituitary-adrenal axis.	(Friedly et al., 2014)	Randomized clinical trial

Evidence Statements Regarding Diagnostic Spinal Injections and Steroid Associated Issues			
Some Evidence	Evidence Statement	Citation	Design
	The addition of steroids to a transforaminal bupivacaine injection may reduce the frequency of surgery in the first year after treatment in patients with neurologic compression and corresponding imaging findings who also are strong candidates for surgery and have completed 6 weeks of therapy without adequate benefit. The benefits for the non-surgical group persisted for at least 5 years in most patients, regardless of the type of block given.	(Riew et al., 2006; Riew et al., 2000)	Randomized clinical trial
	After 6 weeks of conservative therapy for large herniated discs, an epidural injection may be attempted, as it does not compromise the results of a discectomy at a later date. One half of the patients in this study who were randomized to ESIs did not have surgery and this benefit persisted. Because this study did not have a control group that received neither treatment nor a group which received injections without steroids, one cannot make definite conclusions regarding the efficacy of ESI injections in this setting.	(Buttermann, 2004)	Randomized clinical trial
	An intra-articular injection of 80 mg of methylprednisolone acetate into the knee has about a 25% probability of suppressing the adrenal gland response to exogenous adrenocortocotrophic hormone ACTH for four or more weeks after injection, but complete recovery of the adrenal response is seen by week 8	(Habib, Jabbour, Artul, & Hakim, 2014)	Randomized clinical trial

Evidence Statements Regarding Diagnostic Spinal Injections and Steroid Associated Issues			
	after injection.		
Evidence Against			
Good Evidence	Evidence Statement	Citation	Design
	There is good evidence against the use of lumbar facet or epidural injections for relief of non-radicular low back pain.	([Cochrane] Staal, de Bie, de Vet, Hildebrandt, & Nelemans, 2008)	Systematic review of randomized clinical trials

Evidence Statements Regarding Functional Capacity Evaluation			
Some Evidence	Evidence Statement	Citation	Design
	An FCE fails to predict which injured workers with chronic low back pain will have sustained return to work.	(D. P. Gross & Battie, 2004)	Observational prognostic study
	In chronic low back pain patients, (1) FCE task performance is weakly related to time on disability and time for claim closure and (2) even claimants who fail on numerous physical performance FCE tasks may be able to return to work.		
	Time off work and gender are important predictors for return to work, and floor-to-waist lifting may also help predict return to work; however, the strength of that relationship has not been determined.	(Matheson, Isernhagen, & Hart, 2002)	Retrospective Study
	A short form FCE reduced to a few tests produces a similar predictive quality compared to the longer 2-day version of the FCE regarding length of disability and recurrence of a claim after return to work.	(D. P. Gross, Battie, & Asante, 2007)	Randomized clinical trial

Evidence Statements Regarding Acupuncture			
Good Evidence	Evidence Statement	Citation	Design
	The small therapeutic effects of needle acupuncture, active laser acupuncture, and sham acupuncture for reducing pain or improving function among patients older than 50 years with moderate to severe chronic knee pain from symptoms of osteoarthritis are due to non-specific effects similar to placebo.	(Hinman et al., 2014)	Negative randomized clinical trial
	Acupuncture is effective in the treatment of low back pain in patients with positive expectations of acupuncture.	(Haake et al., 2007)	Randomized clinical trial
	Acupuncture, true or sham, is superior to usual care for the reduction of disability and pain in patients with chronic nonspecific low back pain, but true and sham acupuncture are likely to be equally effective.	(Cherkin et al., 2009)	Randomized clinical trial
Some Evidence	Evidence Statement	Citation	Design
	In the setting of chronic joint pain arising from aromatase inhibitor treatment of non-metastatic breast cancer, the symptomatic relief from acupuncture is strongly influenced by the expectations with which patients approach treatment, and a patient who expects significant benefits from acupuncture is more likely to derive benefits from sham acupuncture than a patient with low expectations is to derive benefits from real acupuncture. On average, real and sham acupuncture do not lead to significantly different symptom responses, but different treatment expectations do lead to	(Bauml et al., 2014)	Randomized clinical trial

Evidence Statements Regarding Acupuncture			
	different symptom responses.		
	Acupuncture is better than no acupuncture for axial chronic low back pain.	(Brinkhaus et al., 2006)	Randomized clinical trial
Summary of Evidence Regarding Acupuncture			
Based on the multiple studies with good and some evidence listed above, there is strong evidence that true or sham acupuncture may be useful for chronic low back pain in patients with high expectations, and it should be used accordingly.			

Evidence Statements Regarding Biofeedback			
Good Evidence	Evidence Statement	Citation	Design
	Biofeedback or relaxation therapy is equal in effect to cognitive behavioral therapy for chronic low back pain.	(Hoffman, Papas, Chatkoff, & Kerns, 2007)	Meta-analysis of controlled clinical trials
	Cognitive behavioral therapy, but not behavioral therapy e.g., biofeedback, shows weak to small effects in reducing pain and small effects on improving disability, mood, and catastrophizing in patients with chronic pain.	([Cochrane] A. C. Williams, Eccleston, & Morley, 2012)	Meta-analysis of randomized clinical trials favoring cognitive behavioral therapy over biofeedback

Evidence Statements Regarding Complementary Medicine			
Some Evidence	Evidence Statement	Citation	Design
	A 10-week tai chi program was effective for improving pain symptoms and disability compared with usual care controls for those who have chronic low back pain symptoms.	(Hall, Maher, Lam, Ferreira, & Latimer, 2011)	Assessor single-blind randomized controlled trial

Evidence Statements Regarding Disturbance of Sleep			
Some Evidence	Evidence Statement	Citation	Design
	Group cognitive behavioral therapy reduces the severity and daytime consequences of insomnia for at least six months.	(Morin et al., 2009)	Randomized clinical trial

Evidence Statements Regarding Disturbance of Sleep			
Some Evidence, Continued	Behavioral modification, such as patient education and group or individual counseling with cognitive behavioral therapy, can be effective in reversing the effects of insomnia.	(Currie, Wilson, Pontefract, & deLaplante, 2000)	Randomized clinical trial
	Ramelteon, while producing a small amount of reduction in sleep latency, does not appreciably increase total sleep time or daytime function.	(Mayer et al., 2009)	Randomized clinical trial
	A dietary supplement containing melatonin, magnesium, and zinc, conveyed in pear pulp, taken 1 hour before bedtime, results in significantly better quality of sleep and quality of life than a placebo treatment in long-term care facility residents aged 70 and older with primary insomnia.	(Rondanelli et al., 2011)	Double-blind placebo controlled randomized clinical trial
	The following medications exert different effects with respect to sleep variables. Total sleep time and REM sleep duration are likely to be greater with pregabalin than with duloxetine or amitriptyline. However, pregabalin is likely to lead to dizziness and fatigue more frequently than the other drugs, and oxygen desaturation during sleep also appears to be greater with pregabalin.	(Boyle et al., 2012)	Randomized clinical trial
Summary of Evidence Regarding Disturbance of Sleep			
Based on the multiple studies with some evidence listed above, there is good evidence supporting the use of cognitive behavioral therapy for sleep disturbances.			

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

Evidence Statements Regarding Therapeutic Spinal Injections and Steroid Associated Issues			
Strong Evidence	Evidence Statement	Citation	Design
	Epidural steroid injections (ESIs) have a small average short-term benefit for leg pain and disability for those with sciatica.	(Pinto et al., 2012)	Meta-analysis of randomized clinical trials
	ESIs do not, on average, provide clinically meaningful long-term improvements in leg pain, back pain, or disability in patients with sciatica (lumbar radicular pain or radiculopathy).		
	ESIs have no short-term or long-term benefit for low back pain.		
Good Evidence	Evidence Statement	Citation	Design
	The additional of steroids to a transforaminal bupivacaine injection has a small effect on patient reported pain and disability.	(Ng et al., 2005)	Randomized clinical trial
		(Tafazal, Ng, Chaudhary, & Sell, 2009)	Randomized clinical trial
	There are no significant differences between epidural injections with corticosteroid plus local anesthetic versus local anesthetic alone in patients with symptomatic spinal stenosis. However, there are measureable differences with respect to morning cortisol levels at 3 and 6 weeks after the injection, suggesting that the corticosteroid injection is capable of inducing suppression of the hypothalamic-pituitary-adrenal axis.	(Friedly et al., 2014)	Randomized clinical trial

Evidence Statements Regarding Therapeutic Spinal Injections and Steroid Associated Issues			
Some Evidence	Evidence Statement	Citation	Design
	The addition of steroids to a transforaminal bupivacaine injection may reduce the frequency of surgery in the first year after treatment in patients with neurologic compression and corresponding imaging findings who also are strong candidates for surgery and have completed 6 weeks of therapy without adequate benefit. The benefits for the non-surgical group persisted for at least 5 years in most patients, regardless of the type of block given.	(Riew et al., 2006; Riew et al., 2000)	Randomized clinical trial
	After 6 weeks of conservative therapy for large herniated discs, an epidural injection may be attempted, as it does not compromise the results of a discectomy at a later date. One half of the patients in this study who were randomized to ESIs did not have surgery and this benefit persisted. Because this study did not have a control group that received neither treatment nor a group which received injections without steroids, one cannot make definite conclusions regarding the efficacy of ESI injections in this setting.	(Buttermann, 2004)	Randomized clinical trial
	An intra-articular injection of 80 mg of methylprednisolone acetate into the knee has about a 25% probability of suppressing the adrenal gland response to exogenous adrenocortocotrophic hormone ACTH for 4 or more weeks after injection, but complete recovery of the adrenal response is seen by week 8 after injection.	(Habib et al., 2014)	Randomized clinical trial

Evidence Statements Regarding Therapeutic Spinal Injections and Steroid Associated Issues			
Some Evidence, Continued	Patients who smoke respond less well to non-operative spine care, and quitting smoking results in greater improvement.	(Behrend et al., 2012)	Prospective cohort study
	Translaminar steroid injections do not increase walking tolerance for those with spinal stenosis compared to local anesthetic.	(Fukusaki, Kobayashi, Hara, & Sumikawa, 1998)	Randomized clinical trial
	Intradiscal steroid injection is unlikely to relieve pain or provide functional benefit in patients with non-radicular back pain.	(Khot, Bowditch, Powell, & Sharp, 2004)	Randomized clinical trial
Evidence Against			
Good Evidence	Evidence Statement	Citation	Design
	There is good evidence against the use of lumbar facet or epidural injections for relief of non-radicular low back pain.	([Cochrane] Staal et al., 2008)	Systematic review of randomized clinical trials

Evidence Statements Regarding Botulinum Toxin Injections for Cervical Dystonia			
Strong Evidence	Evidence Statement	Citation	Design
	Botulinum toxin A has objective and asymptomatic benefits over placebo for cervical dystonia.	([Cochrane] Costa et al., 2005)	Meta-analysis of randomized clinical trials
Good Evidence	Evidence Statement	Citation	Design
	A single injection of botulinum toxin type B is more effective than placebo in alleviating the severity and pain of idiopathic cervical dystonia. The duration of effect of botulinum toxin type B is not certain but appears to be approximately 12 to 18 weeks.	([Cochrane] Marques et al., 2016)	Meta-analysis of randomized clinical trials

Evidence Statements Regarding Botulinum Toxin Injections for Cervical Dystonia			
Good Evidence, Continued	Cervical botulinum toxin A injections cause transient dysphagia and neck weakness. Allergic reaction to medications, dry mouth, and vocal hoarseness may also occur. Dry mouth and dysphagia occur 15% of the time after one injection.	(Costa et al., 2005)	Meta-analysis of randomized clinical trials
		(Marques et al., 2016)	Meta-analysis of randomized clinical trials

Evidence Statements Regarding Botulinum Toxin Injections for Piriformis Syndrome			
Some Evidence	Evidence Statement	Citation	Design
	There is some evidence to support injections for electromyographically proven piriformis syndrome.	(Fishman, Anderson, & Rosner, 2002)	Randomized clinical trial

Evidence Statements Regarding Prolotherapy			
Good Evidence	Evidence Statement	Citation	Design
	Prolotherapy alone is not an effective treatment for chronic low back pain.	([Cochrane] Dagenais, Yelland, Del Mar, & Schoene, 2007)	Systematic reviews of controlled clinical trials
Some Evidence	Evidence Statement	Citation	Design
	Prolotherapy of the sacroiliac (SI) joint is longer lasting, up to 15 months, than intra-articular steroid injections. The study was relatively small and long-term blinding was unclear; however, all injections were done under fluoroscopic guidance.	(Kim, Lee, Jeong, Kim, & Yoon, 2010)	Randomized clinical trial

Evidence Statements Regarding Radio Frequency (RF) Denervation - Medial Branch Neurotomy/Facet Rhizotomy			
Good Evidence	Evidence Statement	Citation	Design
	For the lumbar spine, carefully selected patients who had 80% relief with medial branch controlled blinded blocks and then had RF neurotomy will have improved pain relief over 6 months and decreased impairment compared to those who had sham procedures. Pain relief was defined as one hour of 80% relief from the lidocaine injection and two hours of 80% relief with bupivacaine.	(Nath, Nath, & Pettersson, 2008)	Randomized clinical trial
		(van Kleef et al., 1999)	Randomized Clinical Trial

Evidence Statements Regarding Radio Frequency Denervation - Sacro-iliac (SI) Joint Cooled			
Good Evidence	Evidence Statement	Citation	Design
	Cooled RF neurotomy performed in a highly selected population results in better pain relief and functional gains than a sham procedure. The benefits persisted for 9 months. Approximate half of the patients had benefits initially, and approximately half of those reported the pain was completely relieved.	(Patel, Gross, Brown, & Gekht, 2012)	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 et al., 2009)	Cluster randomized trial
		(Lambeek, van Mechelen, Knol, Loisel, & Anema, 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 et al., 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, Kool, Hagen, & Bachmann, 2010)	Meta-analysis of randomized clinical trials

Evidence Statements Regarding Interdisciplinary Rehabilitation Programs			
Some Evidence	Evidence Statement	Citation	Design
	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.	(Kroenke et al., 2014)	Single-blind randomized clinical trial
	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.	(Lambeek et al., 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 et al., 2016)	Randomized clinical trial

Evidence Statements Regarding Anticonvulsants: Gabapentin (Fanatrex, Gabarone, Gralise, Horizant, Neurontin)			
Strong Evidence	Evidence Statement	Citation	Design
	Gabapentin is more effective than placebo in the relief of painful diabetic neuropathy and post-herpetic neuralgia.	([Cochrane] Moore, Wiffen, Derry, Toelle, & Rice, 2014)	Meta-analysis of randomized clinical trials
	Gabapentin is more effective than placebo for neuropathic pain, even though it provides complete pain relief to a minority of patients.	(Irving et al., 2009)	Randomized clinical trial
		(Wiffen, McQuay, Edwards, & Moore, 2005)	Meta-analysis of randomized trials
Good Evidence	Evidence Statement	Citation	Design
	Gabapentin is not superior to amitriptyline.	(Rintala et al., 2007)	Randomized crossover trial
		(Saarto & Wiffen, 2007)	Meta-analysis of randomized trials
Some Evidence	Evidence Statement	Citation	Design
	Gabapentin may benefit some patients with post-traumatic neuropathic pain.	(Gordh et al., 2008)	Randomized clinical trial
	Nortriptyline (Aventyl, Pamelor) and gabapentin are equally effective for pain relief of post-herpetic neuralgia.	(Chandra, Shafiq, Pandhi, Gupta, & Malhotra, 2006)	Randomized clinical trial
	The combination of gabapentin and morphine may allow lower doses with greater analgesic effect than the drugs given separately.	(Gilron et al., 2005)	Randomized crossover trial

Evidence Statements Regarding Anticonvulsants: Gabapentin (Fanatrex, Gabarone, Gralise, Horizant, Neurontin)			
Some Evidence, Continued	A combination of gabapentin and nortriptyline provides more effective pain relief than monotherapy with either drug.	(Gilron et al., 2009)	Randomized crossover trial

Evidence Statements Regarding Anticonvulsants: Pregabalin (Lyrica)			
Strong Evidence	Evidence Statement	Citation	Design
	In the setting of painful diabetic neuropathy, pregabalin as a stand-alone treatment is more effective than placebo in producing a 50% pain reduction, but this goal is realized in only 36% of patients treated with pregabalin compared with 24% of patients treated with placebo.	(Zhang et al., 2015)	Meta-analysis of randomized clinical trials
Good Evidence	Evidence Statement	Citation	Design
	When pregabalin is compared with other first line medications for the treatment of neuropathic pain and diabetic peripheral neuropathy, such as amitriptyline and duloxetine, it is not superior to these medications. Additionally, amitriptyline was found more effective compared to pregabalin for reducing pain scores and disability. Side effects were similar for the two medications.	(Boyle et al., 2012)	Randomized clinical trial
		(Kalita, Kohat, Misra, & Bhoi, 2014)	Open label parallel randomized clinical trial
		(Tesfaye et al., 2013)	Randomized clinical trial
Some Evidence	Evidence Statement	Citation	Design
	Pregabalin may be effective in treating neuropathic pain due to spinal cord injury.	(Cardenas et al., 2013)	Randomized parallel group clinical trial

Evidence Statements Regarding Anticonvulsants: Pregabalin (Lyrica)			
Some Evidence, Continued	Duloxetine, pregabalin, and amitriptyline exert different effects with respect to sleep variables. Total sleep time and REM sleep duration are likely to be greater with pregabalin than with duloxetine or amitriptyline. However, pregabalin is likely to lead to dizziness and fatigue more frequently than the other drugs, and oxygen desaturation during sleep also appears to be greater with pregabalin.	(Boyle et al., 2012)	Randomized clinical trial

Evidence Statements Regarding Anticonvulsants: Topiramate (Topamax, Topiragen)			
Good Evidence	Evidence Statement	Citation	Design
	Topiramate demonstrates minimal effect on chronic lumbar radiculopathy or other neuropathic pain.	(Khoromi et al., 2005)	Randomized crossover trial
		(Raskin et al., 2004)	Randomized clinical trial
		(Thienel, Neto, Schwabe, Vijapurkar, & Topiramate Diabetic Neuropathic Pain Study, 2004)	Randomized clinical trial

Evidence Statements Regarding Anticonvulsants: Carbamazepine			
Good Evidence	Evidence Statement	Citation	Design
	Rapid dose titration produces side-effects greater than the analgesic benefits.	(Beydoun, Shaibani, Hopwood, & Wan, 2006)	Randomized clinical trial
		(Dogra, Beydoun, Mazzola, Hopwood, & Wan, 2005)	Randomized clinical trial

Evidence Statements Regarding Antidepressants: Tricyclics and older agents (e.g., amitriptyline, nortriptyline, doxepin (Adapin, Silenor, Sinequan), desipramine (Norpramin, Pertofrane), imipramine (Tofranil), trazodone (Desyrel, Oleptro))			
Good Evidence	Evidence Statement	Citation	Design
	Gabapentin is not superior to amitriptyline.	(Rintala et al., 2007)	Randomized crossover trial
		(Saarto & Wiffen, 2007)	Meta-analysis of randomized trials
Some Evidence	Evidence Statement	Citation	Design
	In the setting of chronic low back pain with or without radiculopathy, amitriptyline is more effective than pregabalin at reducing pain and disability after 14 weeks of treatment.	(Kalita et al., 2014)	Open label parallel randomized clinical trial
	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 it is possible that it is actually less effective than nortriptyline.	(Gilron, Tu, Holden, Jackson, & DuMerton-Shore, 2015)	Crossover randomized trial
	A combination of some gabapentin and nortriptyline provides more effective pain relief than monotherapy with either drug, without increasing side effects of either drug.	(Gilron et al., 2009)	Randomized crossover trial

Evidence Statements Regarding Antidepressants: Selective Serotonin Nor-epinephrine Reuptake Inhibitor (SSNRI)/Serotonin Nor-epinephrine Reuptake Inhibitors (SNRI).			
Strong Evidence	Evidence Statement	Citation	Design
	Duloxetine monotherapy is more effective than placebo in relieving the pain of diabetic peripheral neuropathy; however, monotherapy leads to a 50% pain reduction in only half of patients who receive a therapeutic dose.	([Cochrane] Lunn, Hughes, & Wiffen, 2014)	Meta-analysis of randomized clinical trials

Evidence Statements Regarding Antidepressants: Selective Serotonin Nor-epinephrine Reuptake Inhibitor (SSNRI)/Serotonin Nor-epinephrine Reuptake Inhibitors (SNRI).			
Good Evidence	Evidence Statement	Citation	Design
	In patients with painful diabetic neuropathy who have not had good responses to monotherapy with 60 mg of duloxetine or 300 mg of pregabalin, a clinically important benefit can be achieved by either of two strategies: doubling the dose of either drug, or combining both drugs at the same dose. It is likely that the strategy of combining the two drugs at doses of 60 and 300 mg respectively is more beneficial overall.	(Tesfaye et al., 2013)	Randomized clinical trial

Evidence Statements Regarding Cannabinoid Products			
Good Evidence	Evidence Statement	Citation	Design
	Cannabinoids containing THC are associated with a small to moderate improvement in chronic pain compared to placebo; however, the dosage needed to produce an analgesic effect is undefined and uncertain.	(Whiting et al., 2015)	Systematic review and meta-analysis of randomized clinical trials
Some Evidence	Evidence Statement	Citation	Design
	Nabiximols can modestly decrease peripheral neuropathic pain with allodynia in some patients who were concomitantly treated with opioids or anticonvulsants; however, the drop-out rate for those who continued the medication longer term was high.	(Nurmikko et al., 2007)	Randomized clinical trial

Evidence Statements Regarding Hypnotics and Sedatives			
Some Evidence	Evidence Statement	Citation	Design
	Zolpidem does not appreciably enhance the effectiveness of Cognitive Behavioral Therapy.	(Morin et al., 2009)	Randomized clinical trial

Evidence Statements Regarding Nonsteroidal Anti-Inflammatory Drugs (NSAIDs)			
Good Evidence	Evidence Statement	Citation	Design
	Celecoxib in a dose of 200 mg per day, administered over a long period, does not have a worse cardiovascular risk profile than naproxen at a dose of up to 1000 mg per day or ibuprofen at a dose of up to 2400 mg per day.	(Nissen et al., 2016)	Randomized noninferiority trial
	Celecoxib has a more favorable safety profile than ibuprofen or naproxen with respect to serious GI adverse events, and it has a more favorable safety profile than ibuprofen with respect to renal adverse events.		
Some Evidence	Evidence Statement	Citation	Design
	Topical NSAIDs are associated with fewer systemic adverse events than oral NSAIDs.	([Cochrane] Massey, Derry, Moore, & McQuay, 2010)	Meta-analysis of randomized clinical trials

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, Maher, Williams, Day, & McLachlan, 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, Midbari, & Eisenberg, 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 et al., 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 et al., 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 180 days from starting opioid treatment.	(Ray, Chung, Murray, Hall, & Stein, 2016)	Retrospective matched cohort study

Evidence Statements Regarding Opioids and Adverse Events			
Good Evidence, Continued	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, Mamdani, Dhalla, Paterson, & Juurlink, 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 et al., 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, Breen, Kimber, & Davoli, 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 et al., 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 with a high opioid dose.	(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	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 et al., 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 et al., 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 et al., 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 et al., 2008)	Prospective cohort study
Some Evidence	Evidence Statement	Citation	Design
	Long-acting oxycodone (Dazidox, Endocodone, ETH-oxydose, 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 it is possible that it is actually less effective than nortriptyline.	(Gilron et al., 2015)	Crossover randomized trial

Evidence Statements Regarding Choice of Opioids, Indications, and Recommendations for Use			
Some Evidence, Continued	Tapentadol can reduce pain to a moderate degree in diabetic neuropathy, average difference 1.4/10 pain scale, with tolerable adverse effects.	(Schwartz et al., 2011)	Randomized clinical trial
	Tapentadol causes less constipation than oxycodone.	([Cochrane] Santos, Alarcao, Fareleira, Vaz-Carneiro, & Costa, 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, Lee, Ma, Nagle, & Schlagheck, 2005)	Three randomized clinical trials
	Tramadol alleviates neuropathic pain following spinal cord injury.	(Norrbrink & Lundeberg, 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, Legallicier, & Kabir-Ahmadi, 2003)	Randomized clinical trial

Evidence Statements Regarding Smoking Cessation Medications and Treatment			
Some Evidence	Evidence Statement	Citation	Design
	Among adults motivated to quit smoking, 12 weeks of open-label treatment including counseling and one of the following: nicotine patch, varenicline, or combination nicotine replacement therapy (nicotine patch and nicotine lozenge) are equally effective in assisting motivated smokers to quit smoking over a period of one year.	(Baker et al., 2016)	Randomized clinical trial

Evidence Statements Regarding Smoking Cessation Medications and Treatment			
Some Evidence, Continued	Among adults motivated to quit smoking, abrupt smoking cessation is the more effective method that leads to lasting abstinence over a period of 4 weeks to 6 months compared to gradual cessation, even for smokers who initially prefer to quit by gradual reduction.	(Lindson-Hawley et al., 2016)	Randomized controlled non-inferiority trial

Evidence Statements Regarding Topical Drug Delivery: Capsaicin			
Strong Evidence	Evidence Statement	Citation	Design
	A single application of 8% capsaicin is more effective than a control preparation of 0.04% capsaicin for up to 12 weeks. However, there may be a need for frequent application, and it is not known whether subsequent applications of capsaicin are likely to be as effective as the first application.	([Cochrane] Derry, Sven-Rice, Cole, Tan, & Moore, 2013)	Meta-analysis of randomized clinical trials
Good Evidence	Evidence Statement	Citation	Design
	Low dose capsaicin (0.075%) applied 4 times per day will decrease pain up to 50%.	(Derry, Lloyd, Moore, & McQuay, 2009).	Meta-analysis of randomized trials
Some Evidence	Evidence Statement	Citation	Design
	In patients who are being treated with capsaicin 8% patches, two methods of pre-treatment are equally effective in controlling application pain and in enabling patients to tolerate the patch: topical 4% lidocaine cream applied to the area for one hour before placement of the capsaicin patch and 50 mg oral tramadol taken 30 minutes before patch placement.	(Jensen et al., 2014)	Randomized clinical trial

Evidence Statements Regarding Topical Drug Delivery: Clonidine			
Good Evidence	Evidence Statement	Citation	Design
	Topical clonidine gel 0.1% is likely to alleviate pain from diabetic peripheral neuropathy in patients who display a nociceptive response to the application of 0.1% capsaicin applied to the pretibial area. It is likely that patients who do not display a pain response to pretibial capsaicin are not likely to have a clinically meaningful analgesic response to clonidine gel. It is unknown if this screening test applies to other types of neuropathic pain.	(Campbell et al., 2012)	Randomized clinical trial

Evidence Statements Regarding Topical Drug Delivery: Ketamine and Tricyclics			
Good Evidence	Evidence Statement	Citation	Design
	Neither 2% topical amitriptyline nor 1% topical ketamine reduces neuropathic pain syndromes.	(Lynch, Clark, Sawynok, & Sullivan, 2005)	Randomized clinical trial

Evidence Statements Regarding Topical Drug Delivery: Lidocaine			
Good Evidence	Evidence Statement	Citation	Design
	Lidocaine 5% plasters, applied for up to 12 hours to the lower extremities of patients with post-herpetic neuralgia and diabetic painful neuropathy, is non-inferior to pregabalin for the same indications. The topical lidocaine is associated with significantly fewer drug-related adverse events over 4 weeks of observation.	(Baron et al., 2009)	Non-inferiority randomized trial

Evidence Statements Regarding Topical Drug Delivery: Lidocaine			
Some Evidence	Evidence Statement	Citation	Design
	A 5% lidocaine patch may be used as a secondary option for patients with focal neuropathic pain. (Meier et al., 2003).	(Meier et al., 2003)	Randomized crossover trial
	The 8% sprays are effective for short-term, 2 week use.	(Kanai et al., 2009)	Randomized crossover trial and open label study

Evidence Statements Regarding Topical Drug Delivery: Topical Salicylates and Nonsalicylates			
Good Evidence	Evidence Statement	Citation	Design
	Diclofenac gel (Voltaren, Solaraze) reduces pain and improves function in mild-to-moderate hand osteoarthritis.	(Altman et al., 2009)	Randomized clinical trial
	Topical diclofenac and ketoprofen are more effective than placebo preparations for purposes of relieving pain attributable to knee osteoarthritis.	(Derry, Conaghan, Da Silva, Wiffen, & Moore, 2016)	Meta-analysis of randomized clinical trials
	Topical NSAIDs probably reduce the risk of GI adverse effects by approximately 1/3 compared to oral NSAIDs.		

Evidence Statements Regarding Other Agents: Glucosamine			
Good Evidence	Evidence Statement	Citation	Design
	Glucosamine does not improve pain related disability in those with chronic low back pain and degenerative changes on radiologic studies; therefore, it is ***not recommended*** for chronic lower spinal or non-joint pain.	(Wilkens, Scheel, Grundnes, Hellum, & Storheim, 2010)	Randomized clinical trial

Evidence Statements Regarding Other Agents: Alpha-Lipoic Acid			
Some Evidence	Evidence Statement	Citation	Design
	Alpha-lipoic acid at a dose of 600 mg per day may reduce the symptoms of painful diabetic neuropathy in the short term of 3 to 5 weeks. The effect of the intravenous route appears to be greater than that of the oral route, but the oral route may have a clinically relevant effect.	(Mijnhout, Kollen, Alkhalaf, Kleefstra, & Bilo, 2012)	Meta-analysis of randomized clinical trials

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 et al., 2014)	Meta-analysis of randomized clinical trials

Evidence Statements Regarding Psychosocial Intervention			
Good Evidence	Evidence Statement	Citation	Design
	Cognitive behavioral therapy, but not behavioral therapy such as biofeedback, shows weak to small effects in reducing pain and small effects on improving disability, mood, and catastrophizing in the treatment of patients with chronic pain.	([Cochrane] A. C. Williams et al., 2012)	Meta-analysis of randomized clinical trials
	CBT may reduce pain and disability in patients with chronic pain, but the magnitude of the benefit is uncertain.	([Cochrane] Eccleston, Williams, & Morley, 2009)	Meta-analysis of randomized clinical trials
	There are no clinically significant differences for pain and disability between physical	(O'Keeffe et al., 2016)	Systematic review and meta-analyses of randomized clinical

Evidence Statements Regarding Psychosocial Intervention			
Good Evidence, Continued	versus behavioral/psychologically informed and combined interventions for nonspecific chronic spinal pain.		trials
	Psychological interventions, especially CBT, are superior to no psychological intervention for chronic low back pain.	(Hoffman et al., 2007)	Meta-analysis of controlled clinical trials
	Self-regulatory interventions, such as biofeedback and relaxation training, may be equally effective.	(Hoffman et al., 2007)	Meta-analysis of controlled clinical trials
	Six group therapy sessions lasting 90 minutes each focused on CBT skills improved function and alleviated pain in uncomplicated sub-acute and chronic low back pain patients.	(Lamb et al., 2010)	Group randomized clinical trial
	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 CBT 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 et al., 2016)	Single-blind randomized clinical trial
	A stepped care program including CBT is more effective than usual care in veterans with chronic musculoskeletal pain. The stepped care program consists of (1) 12 weeks during which nurse case managers take a medication use history and adjust medication dosage and scheduling through telephone contacts with patients every other week, followed by (2) a	(Bair et al., 2015)	Randomized clinical trial

Evidence Statements Regarding Psychosocial Intervention			
Good Evidence, Continued	12 week step in which CBT is administered by 45 minute individual sessions by telephone every other week. Disability and pain interference with daily activity with stepped care were both superior to usual care in which patients were given printed handouts and were followed for all care by their primary treating physicians.		
	In the short-term, operant therapy focused on increasing function shows small effects in reducing pain compared to waiting list controls. Most studies demonstrated a positive effect. However, it was usually below the minimal clinical significant standard. There is good evidence that no specific type of behavioral therapy is more effective than another in the treatment of patients with chronic pain.	([Cochrane] Henschke et al., 2010)	Meta-analyses of randomized clinical trials
Some Evidence	Evidence Statement	Citation	Design
	A 6-week program of cognitive-behavioral group intervention with or without physical therapy can reduce sick leave, health care utilization, and the risk for developing long-term sick leave disability (≥ 15 days) in workers with nonspecific low back or neck pain compared with simple verbal instruction by a physician.	(Linton, Boersma, Jansson, Svard, & Botvalde, 2005)	Randomized clinical trial
	Intensive exercise coupled with CBT is as effective as posterolateral fusion for chronic un-operated low back pain.	(Brox et al., 2010)	Randomized clinical trial
	In the setting of chronic pain, both an 8-week mindfulness	(Wong et al., 2011)	Single-blind randomized clinical trial

Evidence Statements Regarding Psychosocial Intervention			
Some Evidence, Continued	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. However, there were no significant differences in outcomes between the 2 programs.		
	CBT provided in 7 2-hour small group sessions can reduce the severity of insomnia in chronic pain patients.	(Currie et al., 2000)	Randomized clinical trial
	In the setting of chronic low back pain for older adults (mean age 74.5 years), an 8-week mind-body program that taught mindfulness meditation methods resulted in significant, but clinically small improvements in (1) physical function in the short-term (8 weeks) and (2) current and most severe pain in the past week in the long term (6 months) compared to a healthy aging education program.	(Morone et al., 2016)	Single-blind randomized clinical trial
	In the setting of chronic low back pain when disc pathology is present, 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 et al., 2015)	Prospective cohort study

Summary of Evidence Regarding Psychosocial Intervention
Based on the multiple studies with good evidence listed above, there is strong evidence supporting CBT, particularly in conjunction with other active therapy, to decrease pain and disability for chronic pain patients. However, the magnitude of the change is not likely to be large.

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, Zimney, Puentedura, & Diener, 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, Brox, Holm, Koller, & Bo, 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, O'Sullivan, Skouen, Smith, & Kvale, 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, Heywood, & Keating, 2011)	Systematic Review and meta-analysis of randomized clinical trials

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, van Tulder, Esmail, Bombardier, & Koes, 2004)	Systematic review of randomized clinical trials

Evidence Statements Regarding Therapeutic Exercise			
Strong Evidence	Evidence Statement	Citation	Design
	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.	(Bystrom, Rasmussen-Barr, & Grooten, 2013)	Meta-analysis of randomized clinical trials
		(Saragiotto et al., 2016)	Meta-analysis of randomized clinical trials
	Land-based exercise shows a small clinically important benefit for the relief of pain and improvement in function at the completion of a supervised exercise program and these benefits are sustained for at least another 3 to 6 months among people with symptomatic osteoarthritis of the hip.	(Fransen, McConnell, Hernandez-Molina, & Reichenbach, 2014)	Meta-analysis of randomized clinical trials

Evidence Statements Regarding Therapeutic Exercise			
Good Evidence	Evidence Statement	Citation	Design
	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.	(Petersen et al., 2011)	Randomized clinical trial
	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 et al., 2015)	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 et al., 2010)	Meta-analysis of randomized clinical trials
	Supervised exercise therapy with added manual mobilization shows moderate, clinically important reductions in pain compared to non-exercise controls in people with osteoarthritis of the knee.	(Jansen, Viechtbauer, Lenssen, Hendriks, & de Bie, 2011)	Systematic review and meta-analysis of randomized clinical trials

Evidence Statements Regarding Therapeutic Exercise			
Good Evidence, Continued	Land-based exercise shows a moderate clinically important benefit for the relief of pain and improvement in function at the completion of a supervised exercise program and shows that somewhat smaller benefits are sustained for at least another 2 to 6 months among people with symptomatic osteoarthritis of the knee.	(Fransen et al., 2015)	Meta-analysis of randomized clinical trials
Some Evidence	Evidence Statement	Citation	Design
	An unsupervised 12-week, periodized musculoskeletal rehabilitation (PMR) 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, Risi, & Barden, 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 et al., 2011)	Single-blind randomized clinical trial

Evidence Statements Regarding Therapeutic Exercise			
Some Evidence, Continued	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. Cervicolscapular endurance exercises are beneficial for chronic cervicogenic headache. General fitness exercises and upper extremity exercises are unlikely by themselves to be beneficial for mechanical neck pain and are therefore ***not recommended***.	(Kay et al., 2012)	Meta-analysis of randomized clinical trials
	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.	(Michaleff et al., 2014)	Assessor single-blind randomized clinical trial
	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 et al., 2016)	Assessor single-blind randomized controlled superiority multicenter clinical trial

Evidence Statements Regarding Therapeutic Exercise			
Some Evidence, Continued	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 (1 year) in those who have chronic low back pain.	(Bronfort et al., 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 et al., 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 et al., 2013)	Single-blind randomized clinical trial
	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 et al., 2015)	Assessor single-blind randomized clinical trial

Evidence Statements Regarding Therapeutic Exercise			
Some Evidence, Continued	Twelve weeks of behavioral graded activity does not result in better long-term effectiveness in reducing pain or improving function at 5 years than usual exercise therapy in patients with osteoarthritis (OA) of the hip or knee.	(Pisters, Veenhof, Schellevis, De Bakker, & Dekker, 2010)	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, Lauche, Haller, & Dobos, 2013)	Meta-analysis of randomized clinical trials
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 CBT 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 et al., 2016)	Single-blind randomized clinical trial

Evidence Statements Regarding Yoga			
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.	(K. Williams et al., 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 et al., 2011)	Single-blind randomized clinical trial

Evidence Statements Regarding Manual Treatment for Neck			
Good Evidence	Evidence Statement	Citation	Design
	Multiple sessions of thoracic manipulation was more effective in reducing short- and intermediate-term chronic neck pain and improving function and quality of life when compared with multiple sessions of an inactive control for the treatment of patients with chronic neck pain.	(A. Gross et al., 2015)	Meta-analyses of randomized clinical trials and quasi RCTs

Evidence Statements Regarding Manual Treatment for Neck			
Some Evidence	Evidence Statement	Citation	Design
	A three week program of twice weekly home neck exercises with manual physical therapy that includes joint mobilization, muscle energy, and stretching, reduces neck pain and disability compared with a minimal intervention for patients with chronic neck pain at 6 weeks follow-up. It did not persist at one year follow-up.	(Walker et al., 2008)	Randomized clinical trial
	Combination of exercise and spinal manipulation is more effective than manipulation alone in relieving chronic neck pain and that these advantages remain for more than 1 year after the end of treatment.	(Bronfort et al., 2001)	Randomized clinical trial
		(Evans, Bronfort, Nelson, & Goldsmith, 2002)	Randomized clinical trial
	Craniosacral therapy for chronic nonspecific neck pain, performed by a physical therapist trained in the technique, is superior to sham treatment in reducing neck pain intensity at 8 weeks and probably at 20 weeks.	(Haller et al., 2016)	Randomized clinical trial

Evidence Statements Regarding Manual Treatment for Neck			
	12 weeks of supervised high-dose exercise, 20 sessions 1-2 times per week, with or without spinal manipulative therapy, resulted in significantly greater pain reduction in the short-term (12 weeks) compared to low-dose home exercise with advice, in people with chronic neck pain. Disability reduction was also significantly greater. However, the low dose group had only 2 visits with a provider which would generally be expected to diminish the outcome measurements. The effect decreased at one year follow-up.	(Evans et al., 2012)	Assessor single-blinded randomized controlled trial

Evidence Statements Regarding Manual Treatment for Low Back			
Good Evidence	Evidence Statement	Citation	Design
	Spinal manipulative therapy (SMT) is comparable to exercise, standard medical care, and physiotherapy in reducing chronic low back pain, and SMT does not provide a clinically important superior pain relief over these interventions.	(Rubinstein, van Middelkoop, Assendelft, de Boer, & van Tulder, 2011)	Meta-analysis of randomized clinical trials

Evidence Statements Regarding Manual Treatment for Low Back			
	Two sessions of thrust manipulation of the thoracolumbar spine followed by an exercise regimen leads to better low back function at 6 months than oscillatory non-thrust manipulation in patients with subacute low back pain. The study found patients with the following characteristics were likely to benefit from the program: segmental hypomobility, no symptoms distal to the knee, low fear-avoidance scores, and preservation of at least 35 degrees of internal rotation in at least one hip.	(Cleland et al., 2009)	Randomized controlled trial
Some Evidence	Evidence Statement	Citation	Design
	Spinal manipulation/mobilization, followed by active exercises, may be effective for the reduction of disability from nonspecific low back pain lasting more than 12 weeks.	(Balthazard et al., 2012)	Randomized clinical trial

Evidence Statements Regarding Manual Treatment for Low Back			
Some Evidence, Continued	12 sessions of spinal manipulation in 6 weeks from a chiropractor yields the most favorable pain reduction and functional disability improvement compared to a hands-on control in the short-term (12 weeks) for chronic nonspecific LBP. There was little difference in pain and disability scores and no clinically important differences between spinal manipulation dose groups of 6, 12, or 18 manipulations, making it difficult to recommend one treatment dose over another.	(Haas, Vavrek, Peterson, Polissar, & Neradilek, 2014)	Assessor single-blinded randomized controlled 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 (1 year) in those who have chronic low back pain	(Bronfort et al., 2011)	Assessor single-blinded randomized controlled trial
	A combination of spinal manipulation and exercise is more effective than exercise alone in reducing pain and improving function of low back pain for 1 year.	(Aure, Nilsen, & Vasseljen, 2003)	Randomized clinical trial

Evidence Statements Regarding Manual Treatment for Knee			
Good Evidence	Evidence Statement	Citation	Design
	Supervised exercise therapy with added manual mobilization shows moderate, clinically important reductions in pain compared to non-exercise controls in people with osteoarthritis of the knee.	(Jansen et al., 2011)	Systematic review and meta-analysis of randomized clinical trials

Evidence Statements Regarding Massage			
Good Evidence	Evidence Statement	Citation	Design
	Massage therapy in combination with exercise reduces pain and improves function short-term for patients with subacute low back pain.	(Cherkin et al., 2001)	Randomized clinical trial
		(Furlan, Imamura, Dryden, & Irvin, 2008)	Systematic review of controlled clinical trials
		(Preyde, 2000)	Randomized clinical trial
Some Evidence	Evidence Statement	Citation	Design
	10 weeks of either relaxation massage or structural massage are more effective than usual care and equally effective in improving functional disability and reducing symptoms of pain in people with chronic low back pain with benefits lasting at least 6 months.	(Cherkin et al., 2011)	Single-blind parallel group randomized controlled trial.
	In the setting of chronic neck pain, 4 weeks of weekly hour-long massage leads to benefits with both pain and function, and there are incremental benefits from multiple massage sessions per week (up to 3 sessions) over a single massage session.	(Sherman et al., 2014)	Randomized clinical trial with six intervention arms.

Evidence Statements Regarding Percutaneous Electrical Nerve Stimulation (PENS)			
Good Evidence	Evidence Statement	Citation	Design
	PENS produces improvement of pain and function compared to placebo; however, there is no evidence that the effect is prolonged after the initial 3 week treatment episode.	(Ghoname et al., 1999)	Randomized crossover trial
		(Hamza, 2000)	Randomized crossover trial

Evidence Statements Regarding Traction - Mechanical			
Some Evidence	Evidence Statement	Citation	Design
	Mechanical traction, using specific, instrumented axial distraction technique, is not more effective than active graded therapy without mechanical traction.	(Schimmel et al., 2009)	Randomized clinical trial

Evidence Statements Regarding Trigger Point Dry Needling (TDN)			
Some Evidence	Evidence Statement	Citation	Design
	The inclusion of 2 sessions of trigger point dry needling into a twice daily 5-week exercise program was significantly more effective in improving shoulder pain-related disability than an exercise program alone at 3, 6, and 12 month follow-ups in people with chronic subacromial pain syndrome. Both interventions were equally effective in reducing pain over 12 months.	(Arias-Buria, Fernandez-de-Las-Penas, Palacios-Cena, Koppenhaver, & Salom-Moreno, 2017)	Double-blind parallel group randomized clinical trial
	4 sessions of trigger point deep dry needling with passive stretching over 2 weeks was significantly more effective in reducing neck pain and improving neck disability than passive stretching alone in the short-term and at 6-month follow-up in people with chronic nonspecific neck pain.	(Cerezo-Tellez et al., 2016)	Single-blinded parallel group randomized clinical trial

Evidence Statements Regarding Neurostimulation			
Some Evidence	Evidence Statement	Citation	Design
	SCS is superior to reoperation in the setting of persistent radicular pain after lumbosacral spine surgery. Success was defined as achieving 50% or more pain relief.	(North, Kidd, Farrokhi, & Piantadosi, 2005)	Randomized clinical trial

Evidence Statements Regarding Neurostimulation			
Some Evidence, Continued	SCS is superior to conventional medical management in the setting of persistent radicular pain after lumbosacral spine surgery. Success was defined as achieving 50% or more pain relief. However, the study could not demonstrate increased return to work.	(Kumar et al., 2007)	Randomized clinical trial
	A high-frequency, 10 KHz spinal cord stimulator is more effective than a traditional low frequency 50 Hz stimulator in reducing both back pain and leg pain in patients who have had a successful trial of an external stimulator. Two-thirds of the patients had radiculopathy and one-half had predominant back pain. The high frequency device appears to lead to greater patient satisfaction than the low frequency device, which is likely to be related to the fact that the high frequency device does not produce paresthesias in order to produce a pain response. In contrast to the low frequency stimulator, which requires recharging about twice per month, the high frequency stimulator is recommended for daily recharging for 30 to 45 minutes.	(Kapural et al., 2015)	Randomized controlled trial The study was designed as a non-inferiority study for the experimental SCS system, and testing for superiority was done if the non-inferiority margins were met for the outcomes under consideration.
	SCS is superior to re-operation and conventional medical management for severely disabled patients who have failed conventional treatment and have CRPS I or failed back surgery with persistent radicular neuropathic pain.	(Kemler et al., 2000)	Randomized clinical trial
		(Kumar et al., 2007)	Randomized clinical trial
		(North et al., 2005)	Randomized clinical trial

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