



# VA/DoD CLINICAL PRACTICE GUIDELINE FOR DIAGNOSIS AND TREATMENT OF LOW BACK PAIN

## **Department of Veterans Affairs**

## **Department of Defense**

#### **QUALIFYING STATEMENTS**

The Department of Veterans Affairs and the Department of Defense guidelines are based upon the best information available at the time of publication. They are designed to provide information and assist decision making. They are not intended to define a standard of care and should not be construed as one. Neither should they be interpreted as prescribing an exclusive course of management.

This Clinical Practice Guideline is based on a systematic review of both clinical and epidemiological evidence. Developed by a panel of multidisciplinary experts, it provides a clear explanation of the logical relationships between various care options and health outcomes while rating both the quality of the evidence and the strength of the recommendation.

Variations in practice will inevitably and appropriately occur when clinicians take into account the needs of individual patients, available resources, and limitations unique to an institution or type of practice. Every healthcare professional making use of these guidelines is responsible for evaluating the appropriateness of applying them in the setting of any particular clinical situation.

These guidelines are not intended to represent Department of Veterans Affairs or TRICARE policy. Further, inclusion of recommendations for specific testing and/or therapeutic interventions within these guidelines does not guarantee coverage of civilian sector care. Additional information on current TRICARE benefits may be found at www.tricare.mil or by contacting your regional TRICARE Managed Care Support Contractor.

**Version 2.0 – 2017** 

# Prepared by:

# The Diagnosis and Treatment of Low Back Pain Work Group

# With support from:

The Office of Quality, Safety and Value, VA, Washington, DC &

Office of Evidence Based Practice, U.S. Army Medical Command

**Version 2.0 – 2017** 

Based on evidence reviewed through October 21, 2016

September 2017 Page 2 of 110

# **Table of Contents**

I.	Introduction			
II.	Rec	ommendations	6	
III.	Bac	kground	9	
	A.	Description of Low Back Pain	9	
	В.	Epidemiology and Impact	10	
		a. General Population	10	
		b. Veterans Affairs Population		
		c. Department of Defense Population	11	
IV.	Abo	out this Clinical Practice Guideline	12	
	A.	Scope of this Clinical Practice Guideline	12	
	B.	Methods	13	
		a. Grading Recommendations		
		b. Reconciling 2007 Clinical Practice Guideline Recommendations		
		c. Peer Review Process		
	C.	Summary of Patient Focus Group Methods and Findings		
	D.	Conflict of Interest		
	E.	Highlighted Features of this Clinical Practice Guideline	18	
	F.	Patient-centered Care	18	
	G.	Shared Decision Making	18	
	Н.	Implementation	19	
٧.	Gui	deline Work Group	20	
VI.	Alge	orithm	21	
	•	dule A: Initial Evaluation of Low Back Pain		
	Мо	dule B: Management of Low Back Pain	24	
VII.	Disc	cussion of Recommendations	26	
	A.	Diagnostic Approach	26	
	В.	Education and Self-care	31	
	C.	Non-pharmacologic and Non-invasive Therapy	33	
	D.	Pharmacologic Therapy	39	
	E.	Dietary Supplements	46	
	F.	Non-surgical Invasive Therapy	48	
	G.	Team Approach to Treatment of Chronic Low Back Pain	50	

VIII.	Kno	wled	ge Gaps and Recommended Research	51
Арр	endi	x A:	Evidence Review Methodology	53
	A.	Dev	eloping the Scope and Key Questions	53
		a.	Population(s)	53
		b.	Intervention(s)	54
		C.	Comparator(s)	56
		d.	Outcomes	
		e.	Timing	
		f.	Setting	57
	В.	Con	ducting the Systematic Review	57
		a.	Criteria for Study Inclusion/Exclusion	59
		b.	Literature Search Strategy	60
	C.	Con	vening the Face-to-face Meeting	61
	D.	Grad	ding Recommendations	62
	E.	Reco	ommendation Categorization	65
		a.	Categorizing Recommendations with an Updated Review of the Evidence	65
		b.	Categorizing Recommendations without an Updated Review of the Evidence	66
		c.	Recommendation Categories and Definitions	66
	F.	Draf	ting and Submitting the Final Clinical Practice Guideline	67
Арр	endi	x B:	Dosing for Select Pharmacologic Agents <sup>1</sup>	68
Арр	endi	x C:	Evidence Table	69
Арр	endi	x D:	Glossary	74
Арр	endi	x E:	2007 Recommendation Categorization Table	76
Арр	endi	x F:	Participant List	78
Арр	endi	x G:	Patient Focus Group Methods and Findings	80
	A.	Met	hods	80
	В.	Pati	ent Focus Group Findings	81
Арр	endi	x H:	Literature Review Search Terms and Strategy	83
	A.	Topi	c-specific Search Terms	83
	В.	Sear	ch Strategies	94
Арр	endi	x I:	Abbreviation List	101
Refe	rend	res .		103

# I. Introduction

The Department of Veterans Affairs (VA) and Department of Defense (DoD) Evidence-Based Practice Work Group (EBPWG) was established and first chartered in 2004, with a mission to advise the "...Health Executive Council on the use of clinical and epidemiological evidence to improve the health of the population across the Veterans Health Administration and Military Health System," by facilitating the development of clinical practice guidelines (CPGs) for the VA and DoD populations.[1] This CPG is intended to provide healthcare providers with a framework by which to evaluate, treat, and manage the individual needs and preferences of patients with low back pain (LBP).

In 2007, the VA and DoD published the Clinical Practice Guideline for diagnosis and treatment of Low Back Pain (2007 LBP CPG), which was based on evidence reviewed through November 2006. Since the release of that guideline, a growing body of research has expanded the general knowledge and understanding of LBP. Improved recognition of the complex nature of these conditions has led to the adoption of new strategies for diagnosis and treatment of LBP.

Consequently, a recommendation to update the 2007 LBP CPG was initiated in 2016. The updated CPG, titled Clinical Practice Guideline for Diagnosis and Treatment of Low Back Pain (2017 LBP CPG), includes objective, evidence-based information on the diagnosis and management of acute and chronic LBP. It is intended to assist healthcare providers in all aspects of patient care, including, but not limited to, diagnosis, treatment, and management. The system-wide goal of this guideline is to improve the patient's health and wellbeing by providing evidence-based guidance to providers who are diagnosing or treating patients with LBP. The expected outcome of successful implementation of this guideline is to:

- Assess the patient's condition and determine, in collaboration with the patient, the best treatment method
- Optimize each individual's health outcomes and improve quality of life
- Minimize preventable complications and morbidity
- Emphasize the use of patient-centered care

September 2017 Page 5 of 110

# II. Recommendations

#	Recommendation	Strength*	Category†
A. C	Piagnostic Approach		
1.	For patients with low back pain, we recommend that clinicians conduct a history and physical examination, that should include identifying and evaluating neurologic deficits (e.g., radiculopathy, neurogenic claudication), red flag symptoms associated with serious underlying pathology (e.g., malignancy, fracture, infection), and psychosocial factors.	Strong for	Reviewed, Amended
2.	For patients with low back pain, we suggest performing a mental health screening as part of the low back pain evaluation and taking results into consideration during selection of treatment.	Weak for	Reviewed, New-replaced
3.	For patients with acute axial low back pain (i.e., localized, non-radiating), we recommend against routinely obtaining imaging studies or invasive diagnostic tests.	Strong against	Reviewed, Amended
4.	For patients with low back pain, we recommend diagnostic imaging and appropriate laboratory testing when neurologic deficits are serious or progressive or when red flag symptoms are present.	Strong for	Reviewed, Amended
5.	For patients with low back pain greater than one month who have not improved or responded to initial treatments, there is inconclusive evidence to recommend for or against any diagnostic imaging.	Not applicable	Reviewed, New-added
B. E	ducation and Self-care		
6.	For patients with chronic low back pain, we recommend providing evidence-based information with regard to their expected course, advising patients to remain active, and providing information about self-care options.	Strong for	Reviewed, Amended
7.	For patients with chronic low back pain, we suggest adding a structured education component, including pain neurophysiology, as part of a multicomponent self-management intervention.	Weak for	Reviewed, New-added
C. N	Ion-pharmacologic and Non-invasive Therapy		
8.	For patients with chronic low back pain, we recommend cognitive behavioral therapy.	Strong for	Reviewed, New-replaced
9.	For patients with chronic low back pain, we suggest mindfulness-based stress reduction.	Weak for	Reviewed, New-replaced
10.	For patients with acute low back pain, there is insufficient evidence to support the use of specific clinician-directed exercise.	Not applicable	Reviewed, New-replaced
11.	For patients with chronic low back pain, we suggest offering clinician-directed exercises.	Weak for	Reviewed, New-replaced
12.	For patients with acute or chronic low back pain, we suggest offering spinal mobilization/manipulation as part of a multimodal program.	Weak for	Reviewed, New-replaced
13.	For patients with acute low back pain, there is insufficient evidence to support the use of acupuncture.	Not applicable	Reviewed, New-replaced
14.	For patients with chronic low back pain, we suggest offering acupuncture.	Weak for	Reviewed, New-replaced
15.	For acute or chronic low back pain, there is insufficient evidence for or against the use of lumbar supports.	Not applicable	Reviewed, Amended
16.	For patients with chronic low back pain, we suggest offering an exercise program, which may include Pilates, yoga, and tai chi.	Weak for	Reviewed, New-replaced
17.	For patients with low back pain, there is insufficient evidence to support the use of ultrasound.	Not applicable	Reviewed, New-added

September 2017 Page 6 of 110

#	Recommendation	Strength*	Category†	
18.	For patients with low back pain, there is inconclusive evidence to support the use of transcutaneous electrical nerve stimulation (TENS).	Not applicable	Reviewed, New-added	
19.	For patients with low back pain, there is insufficient evidence to support the use of lumbar traction.	Not applicable	Reviewed, New-added	
20.	For patients with low back pain, there is insufficient evidence to support the use of electrical muscle stimulation.	Not applicable	Reviewed, New-added	
D. F	Pharmacologic Therapy			
21.	For patients with acute or chronic low back pain, we recommend treating with nonsteroidal anti-inflammatory drugs, with consideration of patient-specific risks.	Strong for	Reviewed, Amended	
22.	For patients with chronic low back pain, we suggest offering treatment with duloxetine, with consideration of patient-specific risks.	Weak for	Reviewed, New-added	
23.	For patients with acute low back pain or acute exacerbations of chronic low back pain, we suggest offering a non-benzodiazepine muscle relaxant for short-term use.	Weak for	Reviewed, New-added	
24.	For patients with chronic low back pain, we suggest against offering a non-benzodiazepine muscle relaxant.	Weak against	Reviewed, New-added	
25.	For patients with low back pain, we recommend against benzodiazepines.	Strong against	Reviewed, New-replaced	
26.	For patients with acute or chronic low back pain with or without radiculopathy, we recommend against the use of systemic corticosteroids (oral or intramuscular injection).	Strong against	Reviewed, Amended	
27.	For patients with low back pain, we recommend against initiating long-term opioid therapy. For patients who are already prescribed long-term opioid therapy, refer to the VA/DoD CPG for the Management of Opioid Therapy for Chronic Pain. <sup>1</sup>	Strong against	Reviewed, New-replaced	
28.	For patients with acute low back pain or acute exacerbations of chronic low back pain, there is insufficient evidence to recommend for or against the use of time-limited opioid therapy. Given the significant risks and potential benefits of opioid therapy, patients should be evaluated individually, including consideration of psychosocial risks and alternative non-opioid treatments. Any opioid therapy should be kept to the shortest duration and lowest dose possible.	Not applicable	Reviewed, New-replaced	
29.	For patients with acute or chronic low back pain, there is insufficient evidence to recommend for or against the use of time-limited (less than seven days) acetaminophen therapy.	Not applicable	Reviewed, New-replaced	
30.	For patients with chronic low back pain, we recommend against the chronic use of oral acetaminophen.	Strong against	Reviewed, New-replaced	
31.	For the treatment of acute or chronic low back pain, including patients with both radicular and non-radicular low back pain, there is insufficient evidence to recommend for or against the use of antiepileptics including gabapentin and pregabalin.	Not applicable	Reviewed, New-replaced	
32.	For the treatment of low back pain, there is insufficient evidence to recommend for or against the use of topical preparations.	Not applicable	Reviewed, New-added	
E. Dietary Supplements				
33.	For the treatment of low back pain, there is insufficient evidence to recommend for or against nutritional, herbal, and homeopathic supplements.	Not applicable	Reviewed, New-added	

<sup>&</sup>lt;sup>1</sup> See the VA/DoD Clinical Practice Guideline for the Management of Opioid Therapy for Chronic Pain. Available at: <a href="http://www.healthquality.va.gov/guidelines/Pain/cot/">http://www.healthquality.va.gov/guidelines/Pain/cot/</a>

September 2017 Page 7 of 110

#	Recommendation	Strength*	Category†
F. N	Ion-surgical Invasive Therapy		
34.	For the long-term reduction of radicular low back pain, non-radicular low back pain, or spinal stenosis, we recommend against offering spinal epidural steroid injections.	Strong against	Reviewed, New-added
35.	For the very short-term effect (less than or equal to two weeks) of reduction of radicular low back pain, we suggest offering epidural steroid injection.	Weak for	Reviewed, New-added
36.	For the treatment of low back pain, we suggest against offering intra-articular facet joint steroid injections.	Weak against	Reviewed, New-added
37.	For patients with low back pain, there is inconclusive evidence to recommend for or against medial branch blocks and radiofrequency ablative denervation.	Not applicable	Reviewed, New-added
G. 1	Feam Approach to Treatment of Chronic Low Back Pain		
38.	For selected patients with chronic low back pain not satisfactorily responding to more limited approaches, we suggest offering a multidisciplinary or interdisciplinary rehabilitation program which should include at least one physical component and at least one other component of the biopsychosocial model (psychological, social, occupational) used in an explicitly coordinated manner.	Weak for	Reviewed, New-replaced

<sup>\*</sup>For additional information, please refer to <u>Grading Recommendations</u>.

September 2017 Page 8 of 110

<sup>†</sup>For additional information, please refer to <u>Recommendation Categorization</u> and <u>Appendix A.</u>

# III. Background

# A. Description of Low Back Pain

While LBP is a symptom, rather than a disease or a syndrome, the diagnosis and treatment approaches for most patients with axial/non-radiating (previously referred to as non-specific) LBP is similar regardless of the underlying etiology. Therefore, this CPG focuses mainly on the management of patients with axial/non-radiating LBP rather than specific underlying diagnoses.

LBP is often categorized as acute (pain up to four weeks), subacute (4-12 weeks), or chronic (more than 12 weeks), and as such, the management of patients differs with the duration of the pain (see the Glossary in Appendix D for additional definitions). Axial/non-radiating LBP can be caused by mechanical problems, degenerative disc disease, facet joint arthropathy, or bulging or herniated intervertebral discs.[2] LBP may occur in the presence of radiculopathy or neurogenic claudication. The nature of pain in some patients may be myofascial, a symptom of fibromyalgia, and for some have an important underlying psychological component.

Signs and symptoms that indicate serious underlying pathology requiring additional diagnostic workup and prompt treatment are generally referred to as "red flags." <u>Table 1</u> lists some common serious spinal conditions and the red flags that indicate further investigation may be needed.

The various treatments of axial/non-radiating LBP are categorized for this CPG as education and self-care, non-pharmacologic and non-invasive, pharmacologic, dietary supplements, non-surgical invasive procedures, and team approach. Other than surgery, which is out of scope for this CPG, the above-listed therapeutic approaches are discussed in detail in this CPG.

September 2017 Page 9 of 110

Table 1: Serious Underlying Conditions for LBP and Associated Red Flags or Risk Factors

Possible causes or	
conditions	Red flags or risk factors on history or physical examination
	History of cancer with new onset of LBP
Camaan	<ul> <li>Unexplained weight loss</li> </ul>
Cancer	Failure of LBP to improve after one month
	<ul> <li>Age greater than 50 years</li> </ul>
	■ Fever
Infection	<ul> <li>Intravenous drug use</li> </ul>
infection	Recent infection
	<ul><li>Immunosuppression</li></ul>
	History of osteoporosis
	Chronic use of corticosteroids
Fracture	Older age (75 years or older)
	Recent trauma
	Younger patients with overuse at risk for stress fracture
	<ul> <li>Morning stiffness</li> </ul>
	Improvement with exercise
Ankylosing spondylitis	Alternating buttock pain
Ankylosing spondynus	<ul> <li>Awakening due to low back pain during the second part of the night (early morning awakening)</li> </ul>
	Younger age
	Radicular back pain (e.g., sciatica)
	Lower extremity dysesthesia and/or paraesthesia
Herniated disc	<ul> <li>Positive straight-leg-raise test or crossed straight-leg-raise test</li> </ul>
	Severe/progressive lower extremity neurologic deficits
	Symptoms present for more than one month
	Radicular back pain (e.g., sciatica)
	Lower extremity dysesthesia and/or paraesthesia
Spinal stenosis	Neurogenic claudication
Spinal Steriosis	Older age
	Severe/progressive lower extremity neurologic deficits
	Symptoms present for more than one month
	Urinary retention
Coudo oquino or corre	Urinary or fecal incontinence
Cauda equina or conus medullaris syndrome	Saddle anesthesia
meadians syndronic	Changes in rectal tone
	Severe/progressive lower extremity neurologic deficits

Abbreviation: LBP: low back pain

# B. Epidemiology and Impact

# a. General Population

LBP is one of the most frequently experienced medical conditions in the general population, with up to 84% of adults in the United States (U.S.) experiencing LBP at some point in their lives.[3] In 2010, of all diseases and injuries contributing to disability-adjusted life years in the U.S., LBP was ranked third.[4]

September 2017 Page 10 of 110

In 2012, approximately 27.5% of adults 18 years and older in the U.S. reported experiencing LBP in the last three months. This was slightly lower than in 1997 (29.2%) and 2010 (28.4%). Additionally, women are more likely than men to experience LBP (29.6% versus 25.4%, respectively).[5] More than two-thirds of pregnant women experience LBP and symptoms typically increase with advancing pregnancy;[6] however, pregnancy-related LBP often resolves itself in the post-partum period and may require specialist care when LBP persists or red flags are present.

In a study of U.S. healthcare costs from 1996 through 2013, spending related to LBP and neck pain was the third highest out of 155 conditions. In 2013, the estimated spending related to LBP and neck pain was \$87.6 billion, an increase of \$57.2 billion over the past 18 years.[7]

# b. Veterans Affairs Population

The National Institutes of Health 2014 National Health Interview Survey provided national prevalence estimates of U.S. Veterans with severe pain (including back pain). The survey showed that 33% of Veterans reported significant back pain in the prior three months. The back pain was axial in 20% of Veterans and had features of sciatica in 12%. Among Veterans with back pain, 22% reported it as severe, and were more likely to have severe back pain compared to Non-Veterans.[8]

# c. Department of Defense Population

A study of LBP in U.S. Armed Forces found that LBP diagnoses were associated with over six million outpatient visits and over 25,000 hospitalizations among Active Duty Service Members during the years 2010-2014.[9] The overall annual incidence of LBP was 12.0%. Of patients with LBP, 88.3% received a diagnosis of "non-specific LBP," but many received more than one diagnosis for LBP, including degenerative changes (14.1%), herniated disc (9.7%), and spinal stenosis (1.8%). A breakdown of the annual incidence of LBP by gender, service, race, and occupation is available in Table 2.[9]

Table 2: Incidence of Low Back Pain in U.S. Armed Forces, 2010-2014[9]

Category	Subgroup	Rate per year in percent
Gender	Male	11.3%
Gender	Female	16.3%
	Army	15.8%
	Navy	7.9%
Service	Air Force	12.6%
	Marine Corps	8.7%
	Coast Guard	10.5%
	Black, non-Hispanic	13.8%
Race	White, non-Hispanic	11.9%
	Other	11.1%
	Combat	10.8%
Military Occupation	Healthcare	14.8%
Military Occupation	Admin/supply	14.7%
	Other	10.8%

September 2017 Page 11 of 110

# IV. About this Clinical Practice Guideline

This LBP CPG is intended for VA and DoD healthcare practitioners including physicians, nurse practitioners, physician assistants, physical and occupational therapists, psychologists, social workers, nurses, chiropractors, clinical pharmacists, and others involved in the care of Service Members and their beneficiaries, retirees and their beneficiaries, or Veterans with LBP.

As with other CPGs, there are limitations, including significant evidence gaps, and a need to develop effective strategies for guideline implementation and evaluation of the effect of guideline adherence on clinical outcomes. Thus, as stated in the qualifying statements at the beginning of the CPG, this CPG is not intended to serve as a standard of care. Standards of care are determined on the basis of all clinical data available for an individual patient and are subject to change as scientific knowledge and technology advance and patterns evolve. This CPG is based on evidence available through October 2016 and is intended to provide a general guide to best practices. The guideline can assist healthcare providers, but the use of a CPG must always be considered as a recommendation, within the context of a provider's clinical judgment and patient values and preferences, for the care of an individual patient.

# A. Scope of this Clinical Practice Guideline

This LBP CPG is designed to assist healthcare providers in diagnosing or treating patients with LBP. This CPG is not intended for and does not provide recommendations for the diagnosis and treatment of LBP in children or adolescents, or pregnant women. Surgical procedures (including procedures using spinal cord stimulators) are outside the scope of this guideline and excluded from the evidence review. Any patient in the VA or DoD healthcare system should be offered access to the interventions that are recommended in this guideline after taking into consideration the patient's specific circumstances.

Implementation of this guideline is intended to be patient centered. Thus, treatment and care should take into account a patient's needs and preferences. Good communication between healthcare professionals and the patient about the patient's pain experience, treatment goals, and challenges is essential and should be guided by evidence-based information tailored to the patient's needs. An empathetic and non-judgmental approach to communication with a patient is highly recommended in order to build trust and facilitate frank discussions relating to the social, economic, emotional, and cultural factors that influence patients' perceptions, behaviors, and decision making.

The information that patients are given about treatment and care should be culturally appropriate and also appropriate to the patient's level of education or understanding. It should also be accessible to people with additional needs such as physical, sensory, or learning disabilities. Family and/or caregiver involvement should be considered if appropriate.

The systematic review (SR) conducted for the update of this CPG encompassed intervention studies (primarily randomized controlled trials [RCTs]) and observational studies published between December 1, 2006 and October 21, 2016 and targeted nine <a href="key questions">key questions</a> (KQs) focusing on the means by which the delivery of healthcare could be optimized for patients with LBP. Because a comprehensive review of the evidence related to LBP was not feasible, the nine selected KQs were prioritized from many possible KQs. The section on <a href="Recommendations">Recommendations</a> delineates whether or not the current CPG recommendations were based on an updated evidence review. <a href="Appendix E">Appendix E</a> delineates whether the 2007 CPG recommendations

September 2017 Page 12 of 110

were categorized based on an updated evidence review or whether the evidence support is from the previous version of the guideline. The section on <u>Recommendation Categorization</u> further describes the methodology used for the categorization.

#### B. Methods

The current document is an update to the 2007 VA/DoD LBP CPG. The methodology used in developing the 2017 LBP CPG follows the VA/DoD Guideline for Guidelines,[1] an internal document of the VA and DoD EBPWG. The VA/DoD Guideline for Guidelines can be downloaded from <a href="http://www.healthquality.va.gov/policy/index.asp">http://www.healthquality.va.gov/policy/index.asp</a>. This document provides information regarding the process of developing guidelines, including the identification and assembly of the Guideline Champions (Champions) and other subject matter experts from within the VA and DoD, known as the Work Group, and ultimately, the development and submission of an updated LBP CPG. The VA Office of Quality, Safety and Value, in collaboration with the Office of Evidence Based Practice, U.S. Army Medical Command, the proponent for CPGs for the DoD, identified four clinical leaders, Sanjog Pangarkar, MD and Friedhelm Sandbrink, MD from the VA and MAJ Adam Bevevino, MD and MAJ Daniel Kang, MD from the DoD, as Champions for the 2017 LBP CPG.

The Champions and the Work Group for this CPG were charged with developing evidence-based clinical practice recommendations, and writing and publishing a guideline document to be used by providers within the VA and DoD healthcare systems. Specifically, the Champions and the Work Group were responsible for identifying the KQs – those considered most clinically relevant, important, and interesting with respect to the diagnosis and management of patients with LBP. The Champions and the Work Group also provided direction on inclusion and exclusion criteria for the evidence review and assessed the level and quality of the evidence. The amount of new scientific evidence that had accumulated since the previous version of the CPG was taken into consideration in the identification of the KQs. In addition, the Champions assisted in:

- Identifying appropriate disciplines of individuals to be included as part of the Work Group
- Directing and coordinating the Work Group
- Participating throughout the guideline development and review processes

The Lewin Team, including The Lewin Group, Duty First Consulting, ECRI Institute, and Sigma Health Consulting, LLC, was contracted by the VA and DoD to support the development of this CPG and conduct the evidence review. The first conference call was held in June 2016, with participation from the contracting officer's representative (COR), leaders from the VA Office of Quality, Safety and Value and the DoD Office of Evidence Based Practice, and the Champions. During this call, participants discussed the scope of the guideline initiative, the roles and responsibilities of the Champions, the project timeline, and the approach for developing and prioritizing specific research questions on which to base an SR about the diagnosis and treatment of LBP. The group also identified a list of clinical specialties and areas of expertise that were important and relevant to the diagnosis and treatment of LBP, from which Work Group members were recruited. The specialties and clinical areas of interest included: chiropractic care, integrative medicine, neurology, nursing, pain medicine, pharmacy, physical medicine and rehabilitation, physical therapy, primary care, radiology, and surgery.

September 2017 Page 13 of 110

The guideline development process for the 2017 LBP CPG update consisted of the following steps:

- 1. Formulating and prioritizing evidence questions (KQs)
- 2. Conducting the systematic review of the literature
- 3. Convening a face-to-face meeting with the CPG Champions and Work Group members
- Drafting, revising, and submitting a final CPG about the diagnosis and treatment of LBP to the VA/DoD EBPWG

Appendix A provides a detailed description of each of these tasks.

# a. Grading Recommendations

The Champions and Work Group used the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach to assess the quality of the evidence base and assign a grade for the strength for each recommendation. The GRADE system uses the following four domains to assess the strength of each recommendation:[10]

- Balance of desirable and undesirable outcomes
- Confidence in the quality of the evidence
- Patient or provider values and preferences
- Other implications, as appropriate, e.g.,:
  - Resource use
  - Equity
  - Acceptability
  - Feasibility
  - Subgroup considerations

Using this system, the Champions and the Work Group determined the direction (for or against) and relative strength (strong or weak) of each recommendation.[10] The direction indicates that the desirable effects of the recommendation outweigh the undesirable effects of the recommendation (for) or that the opposite is true (against). The strength indicates the Work Group's level of confidence in the balance of desirable and undesirable effects of the recommendation among the intended patient population.[11] A strong recommendation indicates the Work Group is confident in this balance (e.g., that the desirable effects outweigh the undesirable effects). A weak recommendation indicates that the balance is still likely, but the Work Group's confidence in the balance is lower than for a strong recommendation.

Occasionally, instances may occur when the Work Group feels there is insufficient evidence to make a recommendation for or against a particular therapy or preventive measure. This can occur when there is an absence of studies on a particular topic that met evidence review inclusion criteria, studies included in the evidence review report conflicting results, or studies included in the evidence review report inconclusive results regarding the desirable and undesirable outcomes.

Using these elements, the grade of each recommendation is presented as part of a continuum:

September 2017 Page 14 of 110

- Strong For (or "We recommend offering this option ...")
- Weak For (or "We suggest offering this option ...")
- No recommendation for or against (or "There is insufficient evidence ...")
- Weak Against (or "We suggest not offering this option ...")
- Strong Against (or "We recommend against offering this option ...")

The grade of each recommendation made in the 2017 LBP CPG can be found in the section on <u>Recommendations</u>. Additional information regarding the use of the GRADE system can be found in the section on <u>Grading Recommendations</u> in Appendix A.

# b. Reconciling 2007 Clinical Practice Guideline Recommendations

Evidence-based CPGs should be current, which typically requires revisions of previous guidelines based on new evidence or as scheduled, subject to time-based expirations. [12] For example, the United States Preventive Services Task Force (USPSTF) has a process for refining or otherwise updating its recommendations pertaining to preventive services. [13] Further, the inclusion criteria for the National Guideline Clearinghouse specify that a guideline must have been developed, reviewed, or revised within the past five years.

The 2017 LBP CPG is an update of the 2007 LBP CPG. Thus, the content of the 2017 LBP CPG is reflective of the previous version of the CPG, but modified where necessary to reflect new evidence and new clinical priorities.

The Work Group focused largely on developing new and updated recommendations based on the evidence review conducted for the priority areas addressed by the KQs. In addition to those new and updated recommendations, the Work Group considered the current applicability of other recommendations that were included in the previous 2007 LBP CPG without complete review of the relevant evidence, subject to evolving practice in today's environment.

To indicate which recommendations were developed based on the updated review of the evidence versus recommendations that were carried forward from the 2007 version of the CPG, a set of recommendation categories was adapted from those used by the National Institute for Health and Care Excellence (NICE).[14,15] These categories, along with their corresponding definitions, were used to account for the various ways in which older recommendations could have been updated. In brief, the categories took into account whether or not the evidence that related to a recommendation was systematically reviewed, the degree to which the recommendation was modified, and the degree to which a recommendation is relevant in the current patient care environment and within the scope of the CPG. Additional information regarding these categories and their definitions can be found in the section on Recommendation

Categorization. The categories for the recommendations included in the 2017 version of the guideline can be found in the section on Recommendations. The categorizations for each 2007 LBP CPG recommendation can be found in Appendix E.

In cases where a 2007 LBP CPG recommendation was covered by a 2017 KQ, peer-reviewed literature published since the 2007 LBP CPG was considered along with the evidence base used for the 2007 LBP

September 2017 Page 15 of 110

CPG. Where new literature was considered when assessing the strength of the recommendation, it is referenced in the discussion following the corresponding recommendation, as well as in <u>Appendix C</u>.

The CPG Work Group recognizes that, while there are practical reasons for incorporating findings from a previous SR, previous recommendations, or recent peer-reviewed publications into an updated CPG, doing so does not involve an original, comprehensive SR and, therefore, may introduce bias.[16]

#### c. Peer Review Process

The CPG was developed through an iterative process in which the Work Group produced multiple drafts of the CPG. The process for developing the initial draft is described in more detail in <u>Drafting and Submitting the Final Clinical Practice Guideline</u>.

Once a near-final draft of the guideline was agreed upon by the Champions and the Work Group members, the draft was sent out for peer review and comment. The draft was posted on a wiki website for a period of 14 business days. The peer reviewers comprised individuals working within the VA and DoD health systems as well as experts from relevant outside organizations designated by the Work Group members. External organizations that participated in the peer review included the following:

- Oregon Health & Science University
- Parker University
- Stanford Health Care
- University of California San Francisco School of Medicine
- Yale University

VA and DoD Leadership reached out to both the internal and external peer reviewers to solicit their feedback on the CPG. Reviewers were provided a hyperlink to the wiki website where the draft CPG was posted. For transparency, all reviewer feedback was posted in tabular form on the wiki site, along with the name of the reviewer. All feedback from the peer reviewers was discussed and considered by the Work Group. Modifications made throughout the CPG development process were made in accordance with the evidence.

# C. Summary of Patient Focus Group Methods and Findings

When forming guideline recommendations, consideration should be given to the values of those most affected by the recommendations: patients. Patients bring perspectives, values, and preferences into their healthcare experience, and more specifically their pain care experience, that can vary from those of clinicians. These differences can affect decision making in various situations, and should thus be highlighted and made explicit due to their potential to influence a recommendation's implementation. [17,18] Focus groups can be used as an efficient method to explore ideas and perspectives of a group of individuals with an *a priori set* of assumptions or hypotheses and collect qualitative data on a thoughtfully predetermined set of questions.

Therefore, as part of the effort to update this CPG, VA and DoD Leadership, along with the LBP CPG Work Group, held a patient focus group prior to finalizing the KQs for the evidence review. The group met on September 7, 2016, at the William Beaumont Army Medical Center in El Paso, Texas. The aim of the focus

September 2017 Page 16 of 110

group was to further the understanding of the perspectives of patients with LBP within the VA and/or DoD healthcare systems. The focus group explored a set of topics related to diagnosis and treatment of LBP, including knowledge of LBP and other pain treatment options, delivery of care, and the impact of and challenges with LBP.

It is important to note the focus group was a convenience sample and the Work Group recognizes the limitations inherent in the small sample size. Less than 10 people were included in the focus group consistent with the requirements of the federal Paperwork Reduction Act, 1980. The Work Group acknowledges that the sample of patients included in this focus group may not be representative of all VA and DoD patients with LBP. Further, time limitations for the focus group prevented exhaustive exploration of all topics related to pain care in the VA and DoD and the patients' broader experiences with their care. Thus, the Work Group made decisions regarding the priority of topics to discuss at the focus group. These limitations, as well as others, were considered as the information collected from the discussion was used for guideline development. Recruitment for participation in the focus group was managed by the Champions and VA and DoD Leadership, with assistance from coordinators at the facility at which the focus group took place.

The following concepts are ideas and suggestions about aspects of care that are important to patients and family caregivers and that emerged from the discussion. These concepts were needed and important parts of the participants' care and added to the Work Group's understanding of patient values and perspectives. The Work Group considered the focus group feedback while assessing the strength of each recommendation and continued to consider the feedback throughout the LBP CPG development process. Additional details regarding the patient focus group methods and findings can be found in Appendix G.

# **LBP CPG Patient Focus Group Concepts**

- A. Consider patient-specific goals, values, and preferences and use shared decision making to develop a patient-centered plan for timely diagnosis, treatment, and lifestyle adaptation
- B. Address strategies for pain management across all phases of treatment and educate patients about the use of pain medications, particularly opioids
- C. Recognize the importance of communication and collaboration among providers of an interdisciplinary care team
- D. Involve family caregivers to create support and motivation for patients with LBP
- E. Work with providers to ensure continuity of care and ease of access to preferred providers
- F. Reduce the stigma experienced by patients with LBP

## D. Conflict of Interest

At the start of this guideline development process and at other key points throughout, the project team was required to submit disclosure statements to reveal any areas of potential conflict of interest (COI) in the past 24 months. Verbal affirmations of no COI were also used as necessary during meetings throughout the guideline development process. The project team was also subject to random web-based surveillance (e.g., ProPublica, CMS Open Payments).

If a project team member reported a COI (actual or potential), then it was reported to the Office of Evidence Based Practice. It was also discussed with the LBP CPG Work Group in tandem with their review of the evidence and development of recommendations. The Office of Evidence Based Practice and the LBP

September 2017 Page 17 of 110

CPG Work Group determined whether or not action, such as restricting participation and/or voting on sections related to the conflict or removal from the Work Group, was necessary. If it was deemed necessary, action to mitigate the COI was taken by the Champions and Office of Evidence Based Practice, based on the level and extent of involvement. No conflicts of interest were identified for the LBP CPG Work Group members or Champions. Disclosure forms are on file with the Department of Veterans Affairs Evidence Based Practice Program office and available upon request.

# E. Highlighted Features of this Clinical Practice Guideline

The 2017 edition of the VA/DoD LBP CPG is the first update to the original CPG. It provides practice recommendations for the diagnosis and treatment of populations with LBP. A particular strength of this CPG is the multidisciplinary stakeholder involvement from its inception, ensuring representation from the broad spectrum of clinicians engaged in the diagnosis and treatment of LBP.

The framework for recommendations in this CPG considered factors beyond the strength of the evidence, including balancing desired outcomes with potential harms of treatment, equity of resource availability, and the potential for variation in patient values and preferences. Applicability of the evidence to VA/DoD populations was also taken into consideration. A structured algorithm accompanies the guideline to provide an overview of the recommendations in the context of the flow of patient care and clinician decision making and to assist with training providers. The algorithm may be used to help facilitate translation of guideline recommendations into effective practice.

# F. Patient-centered Care

VA/DoD CPGs encourage clinicians to use a patient-centered care approach that is tailored to the patient's capabilities, needs, goals, prior treatment experience, and preferences. Regardless of setting, all patients in the healthcare system should be offered access to evidence-based interventions appropriate to that patient. When properly executed, patient-centered care may decrease patient anxiety, increase trust in clinicians, [19] and improve treatment adherence. [20] Improved patient-clinician communication through patient-centered care can be used to convey openness to discuss any future concerns.

As part of the patient-centered care approach, clinicians should review the outcomes of past treatment experiences and outcomes of possible future treatments with the patient. Additionally, they should involve the patient in prioritizing and setting specific goals regardless of the selected setting or level of care.

# G. Shared Decision Making

Throughout this VA/DoD CPG, the authors encourage clinicians to focus on shared decision making (SDM). The SDM model was introduced in *Crossing the Quality Chasm*, an Institute of Medicine (now the National Academy of Medicine) report, in 2001.[21] It is readily apparent that patients with LBP, together with their clinicians, make decisions regarding the type of treatment they choose to engage in; however, these patients require sufficient information to be able to make informed decisions. Clinicians must be adept at presenting information to their patients regarding individual treatment plans and appropriate locations of care.

September 2017 Page 18 of 110

# H. Implementation

This CPG and algorithm are designed to be adapted by healthcare providers for the treatment of individual patients, bearing in mind patient-level considerations as well as local needs and resources. The algorithm serves as a tool to prompt providers to consider key decision points in the course of care.

Although this CPG represents the recommended practice on the date of its publication, medical practice is evolving and this evolution requires continuous updating based on published information. New technology and more research will improve patient care in the future. Identifying areas where evidence was lacking for the 2017 CPG can help identify priority areas for future research. Future studies examining the results of LBP CPG implementation may lead to the development of new evidence particularly relevant to clinical practice.

September 2017 Page 19 of 110

# V. Guideline Work Group

Guideline Work Group*			
Department of Veterans Affairs	Department of Defense		
Sanjog Pangarkar, MD (Champion)	MAJ Adam Bevevino, MD (Champion)		
Friedhelm Sandbrink, MD (Champion)	MAJ Daniel Kang, MD (Champion)		
David Cory Adamson, MD	Curtis Aberle, RN, MSN, FNP		
Francine Goodman, PharmD, BCPS	MAJ Chris Allen, DPT, DSc, FAAOMPT		
Valerie Johnson, DC, DABCI	Rachael Coller, PharmD, BCPS, BCPP		
Mitchell Nazario, PharmD	LTC Lisa Konitzer, PT, DSc, OCS, FAAOMPT		
Sandra Smeeding, PhD, CNS, FNP	MAJ(P) Lex Mitchell, MD		
Kirsten Tillisch, MD	MAJ Jeremiah Samson, PT, ScD(C), OCS, COMT, FAAOMPT		
Rebecca Vogsland, DPT, OCS	LTC Jason Silvernail, DPT, DSc, FAAOMPT		
	Evan Steil, MD, MBA, MHA		
	Elaine P. Stuffel, BSN, MHA, RN		
Office of Quality, Safety and Value	Office of Evidence Based Practice		
Veterans Health Administration	U.S. Army Medical Command		
Eric Rodgers, PhD, FNP, BC James Sall, PhD, FNP-BC	Corinne K. B. Devlin, MSN, RN, FNP-BC Elaine P. Stuffel, BSN, MHA, RN		
Rene Sutton, BS, HCA	Eldille F. Stullel, BSN, MITA, KN		
Lewin Group	ECRI Institute		
Clifford Goodman, PhD Christine Jones, MS, MPH, PMP Jacqlyn Witmer Riposo, MBA Nicolas Stettler-Davis, MD, MSCE	Jonathan Treadwell, PhD Kristen E. D'Anci, PhD Nancy Sullivan, BA Oluwaseun Akinyede, MPH James Reston, PhD, MPH Joann Fontanarosa, PhD Gina Giradi, MS Amy Tsou, MD Laura Koepfler, MLS		
	Sigma Health Consulting, LLC		
	Frances Murphy, MD, MPH		

<sup>\*</sup>Additional contributor contact information is available in <u>Appendix F</u>.

September 2017 Page 20 of 110

# VI. Algorithm

This CPG follows an algorithm which is designed to facilitate understanding of the clinical pathway and decision-making process used in the diagnosis and treatment of LBP. The use of the algorithm format as a way to represent patient management was chosen based on the understanding that such a format may promote more efficient diagnostic and therapeutic decision making and has the potential to change patterns of resource use. Although the Work Group recognizes that not all clinical practices are linear, the simplified linear approach depicted through the algorithm and its format allows the provider to assess the critical information needed at the major decision points in the clinical process. It includes:

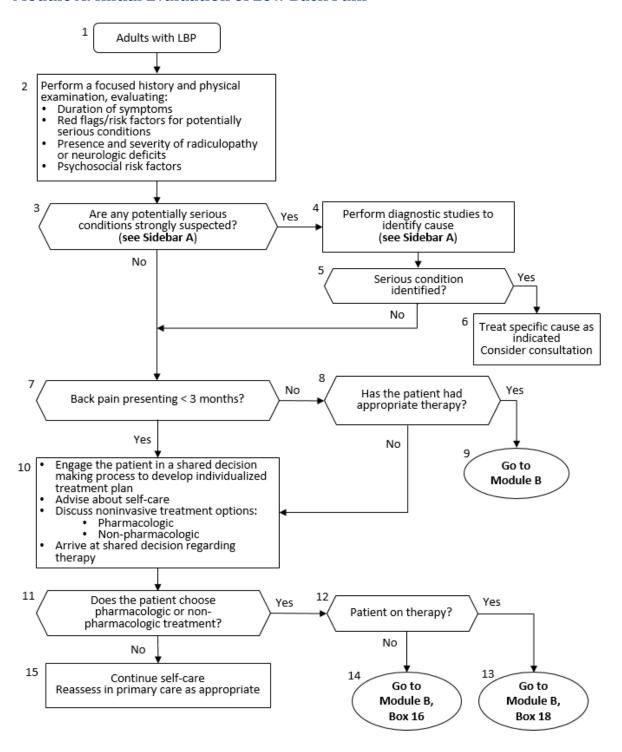
- An ordered sequence of steps of care
- Recommended observations and examinations
- Decisions to be considered
- Actions to be taken

For each guideline, there is corresponding clinical algorithm that is depicted by a step-by-step decision tree. Standardized symbols are used to display each step in the algorithm, and arrows connect the numbered boxes indicating the order in which the steps should be followed.[22]

Rounded rectangles represent a clinical state or condition.
Hexagons represent a decision point in the guideline, formulated as a question that can be answered Yes or No.
Rectangles represent an action in the process of care.

September 2017 Page 21 of 110

# **Module A: Initial Evaluation of Low Back Pain**



September 2017 Page 22 of 110

Sidebar A: Diagnostic Work-up				
Possible causes or conditions	Red flags or risk factors on history or physical examination	Suggested diagnostic imaging		
Cancer	History of cancer with new onset of LBP Unexplained weight loss Failure of LBP to improve after 1 month Age > 50 years Multiple risk factors present	Lumbosacral plain radiography  For inconclusive results, advanced imaging such as MRI with contrast* as appropriate		
Infection	Fever Intravenous drug use Recent infection Immunosuppression	MRI with contrast* ESR		
Fracture	History of osteoporosis Chronic use of corticosteroids Older age (≥75 years old) Recent trauma Younger patients with overuse at risk for stress fracture	Lumbosacral plain radiography  For inconclusive results, advanced imaging such as MRI <sup>†</sup> , CT, or SPECT as appropriate		
Ankylosing spondylitis	Morning stiffness Improvement with exercise Alternating buttock pain Awakening due to low back pain back pain during the second part of the night (early morning awakening) Younger age	Anterior-posterior pelvis plain radiography		
Herniated disc	Radicular back pain (e.g., sciatica) Lower extremity dysesthesia and/or paraesthesia Positive straight-leg-raise test or crossed straight-leg-raise test	None		
	Severe/progressive lower extremity neurologic deficits Symptoms present > 1 month	MRI <sup>†</sup>		
Spinal stenosis	Radicular back pain (e.g., sciatica) Lower extremity dysesthesia and/or paraesthesia Neurogenic claudication Older age	None		
	Severe/progressive lower extremity neurologic deficits Symptoms present > 1 month	MRI <sup>†</sup>		
Cauda equina or conus medullaris syndrome	Urinary retention Urinary or fecal incontinence Saddle anesthesia Changes in rectal tone Severe/progressive lower extremity neurologic deficits	Emergent MRI <sup>†</sup> (preferred)		

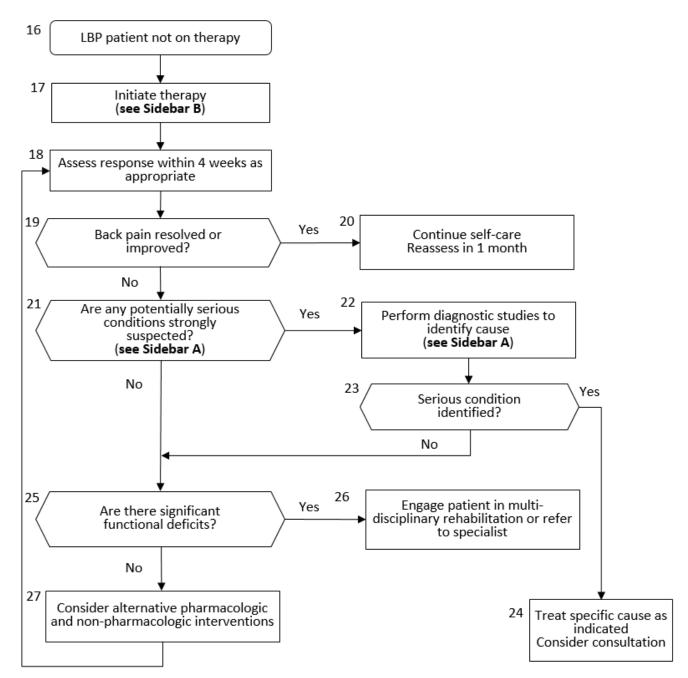
Abbreviations: CT: computed tomography; ESR: electron spin resonance; LBP: low back pain; MRI: magnetic resonance imaging; SPECT: single-photon emission computed tomography

September 2017 Page 23 of 110

<sup>\*</sup>MRI with contrast, except where contraindicated (e.g., renal insufficiency), otherwise MRI without contrast

 $<sup>^{\</sup>dagger}$ MRI, except where contraindicated, (e.g., patients with pacemakers), otherwise CT or CT myelogram

# Module B: Management of Low Back Pain



September 2017 Page 24 of 110

Sidebar B: Interventions				
		Low Back Pain Duration		
Category	Intervention	Acute < 4 Weeks	Subacute or Chronic > 4 Weeks	
	Advice to remain active	Х	X	
Self-care	Books, handout	X	X	
	Application of superficial heat	Х		
	Spinal manipulation		X	
	Clinician-guided exercise		Х	
	Acupuncture		Х	
Non-pharmacologic therapy	CBT and/or mindfulness-based stress reduction		Х	
	Exercise which may include Pilates, tai chi, and/or yoga		Х	
	NSAIDs	Х	Х	
Pharmacologic therapy	Non-benzodiazepine skeletal muscle relaxants	Х		
	Antidepressants (duloxetine)		Х	
Other therapies	Intensive interdisciplinary rehabilitation		Х	

Abbreviations: CBT: cognitive behavioral therapy; NSAIDs: nonsteroidal anti-inflammatory drugs

September 2017 Page 25 of 110

# VII. Discussion of Recommendations

# A. Diagnostic Approach

## Recommendation

1. For patients with low back pain, we recommend that clinicians conduct a history and physical examination, that should include identifying and evaluating neurologic deficits (e.g., radiculopathy, neurogenic claudication), red flag symptoms associated with serious underlying pathology (e.g., malignancy, fracture, infection), and psychosocial factors.

(Strong for | Reviewed, Amended)

#### **Discussion**

Conducting a history and physical examination is considered standard practice and the cornerstone of clinical decision making. The vast majority of patients initially presenting with LBP experience self-limited episodes with substantial improvement of symptoms within the first month. [23-25] However, a small proportion of LBP may be caused by a specific underlying condition (e.g., malignancy 0.7%, infection 0.01%, vertebral compression fracture 4%, spinal stenosis 3%, symptomatic herniated disc 4%), [26] including the possibility of referred pain from a proximate organ system (e.g., pancreatitis, nephrolithiasis, aortic aneurysm, endocarditis). Clinicians should also consider referred pain from the sacroiliac joint, hip joint or trochanteric bursa, which can sometimes manifest as LBP. LBP could also be a manifestation of a systemic condition (e.g., ankylosing spondylitis, rheumatoid arthritis) or multifocal underlying pain disorders (e.g., in patients with myofascial pain or fibromyalgia) that might be missed by addressing individual pain regions in isolation. Therefore, when evaluating LBP, clinicians should use a whole person approach and ask about the location of pain, frequency of symptoms, duration of pain, as well as any history of previous symptoms, treatment, response to treatment, and also evaluate psychosocial factors.

Clinicians should specifically identify the presence, duration, progression, and severity of neurologic symptoms and inquire about red flag symptoms. Rapidly progressive or severe neurologic deficits or LBP associated with a serious underlying condition (e.g., malignancy, fracture, infection, cauda equina syndrome [CES]) may necessitate additional diagnostic workup and prompt treatment.[26] The confidence in available evidence was rated moderate regarding the utility of red flag symptoms to determine the likelihood of two serious underlying conditions (malignancy and fracture). There was insufficient evidence regarding the utility of red flag symptoms for identifying other serious underlying conditions; however, when assessing the strength of the recommendation, the Work Group also considered that the benefits far outweigh potential harms to the patient.

A recent SR, which was rated fair quality and included 14 studies of 14,860 patients with acute LBP, analyzed red flag symptoms for malignancy and fracture.[27] A history of malignancy was the only red flag with significantly increased probability (7% in primary care and 33% in emergency setting) of malignancy as the serious underlying condition for LBP. Other risk factors for malignancy, including unexplained weight loss, failure to improve after one month, and age greater than 50 years, had a post-test probability below 3%.[27] In patients with any one of the other three risk factors, the likelihood of cancer increased to approximately 1.2%.[28]

The evidence review also identified a study that included 669 patients and used a multivariate analysis to

September 2017 Page 26 of 110

investigate red flag symptoms for fracture. [29] Data from the multivariate analysis suggests the following red flags for fracture: (1) older age ( $\geq$ 75 years old), (2) recent trauma, (3) osteoporosis, (4) severe back pain score  $\geq$ 7 out of 10, and (5) thoracic pain. The evidence also suggests that the presence of multiple red flags increases the probability of fracture to between 42% and 90%.[29]

Red flag symptoms of LBP associated with infection have not been well studied, but may include fever, intravenous drug use, or recent infection. [26] CES is a rare condition, typically from an acute massive midline disc herniation, with an estimated prevalence of 0.04% among patients presenting with LBP. The most frequent finding in CES is urinary retention (90% sensitivity), although the constellation of symptoms may include: severe/progressive bilateral radiating leg pain, severe/progressive neurologic deficits at more than one level, saddle anesthesia, and fecal incontinence. In patients without urinary retention, the probability of CES is approximately 1 in 10,000. [28]

The Work Group felt a "Strong for" recommendation was warranted because the benefits of identifying serious underlying pathology outweigh the harms. The main benefit is the identification of a specific condition that requires a different treatment approach targeted at the underlying condition. The harms are the potential false positive red flag symptoms that may cause unnecessary additional diagnostic workup and the inherent risks and increased costs with those modalities, plus the fear or anxiety that may be experienced by the individual when undergoing diagnostic testing. The quality of evidence was moderate regarding the utility of red flag symptoms to determine the likelihood of malignancy and fracture, but was insufficient regarding other serious underlying conditions. Patients and providers have similar values, as both groups highly value and would likely choose to identify a possible serious underlying pathology to optimize outcomes.

Feasibility does not seem to be a major hurdle, given that clinicians perform a history and physical exam as standard practice, and a practical approach may be a screening questionnaire for patients presenting with LBP to reduce the possibility of overlooking neurologic deficits or red flag symptoms. However, the second order consequence on resource burden may be from false positive red flag symptoms, and the over-ordering of additional diagnostic workup for patients with axial LBP. Additional areas of research include utility of red flag symptoms for infection as a serious underlying condition given the potential response to early treatment, as well as predictive modeling to help identify specific causes of LBP based on patient factors.

#### **Recommendation**

 For patients with low back pain, we suggest performing a mental health screening as part of the low back pain evaluation and taking results into consideration during selection of treatment.
 (Weak for | Reviewed, New-replaced)

# **Discussion**

Available evidence indicates that the existence of behavioral health disorders such as depression, anxiety, and posttraumatic stress disorder (PTSD) influence pain and outcomes for those with chronic LBP. For adults with LBP, there is evidence indicating a greater risk of developing chronic LBP when associated with the existence of pre-pain major depressive disorder or generalized anxiety disorder.[30] A VA study

September 2017 Page 27 of 110

reported that 51% of patients with chronic LBP had PTSD symptoms.<sup>2</sup> An SR of fair quality included 17 studies that showed that symptoms of depression at baseline are related to worse LBP outcomes.[31] Patients with depression showed greater pain interference, lower quality of life, more sleep problems, and greater functional disability than the non-depressed patients.[32] It appears that screening is appropriate in patients with acute, subacute, or chronic LBP.

The VA/DoD CPG for The Management of Major Depressive Disorder<sup>3</sup> recommends patients not currently receiving treatment be screened for depression with the Patient Health Questionnaire-2 (PHQ-2). For those with a diagnosis of depression, the Patient Health Questionnaire-9 (PHQ-9) can be used as a quantitative measure of depression severity.

When assessing the strength of the recommendation, the Work Group considered that there are important benefits of mental health screening that outweigh the potential harms of not identifying LBP that is linked to or exacerbated by a coexisting mental health condition. Providers should be sensitive to the large variation of patient preferences, as some patients may worry that there is stigma attached to mental health conditions. Future research is needed on whether or not patients with co-occurring LBP and mental health conditions who are treated for their mental health conditions have improvement in the progression of their LBP over time.

#### **Recommendation**

3. For patients with acute axial low back pain (i.e., localized, non-radiating), we recommend against routinely obtaining imaging studies or invasive diagnostic tests.

(Strong against | Reviewed, Amended)

#### **Discussion**

Patients presenting with less than three months of back pain, that is centered within the lumbar spine (i.e., axial LBP) and does not extend beyond the lower back, do not benefit from routine plain radiographs, computed tomography (CT), magnetic resonance imaging (MRI), or invasive diagnostic testing (discograms and other diagnostic injections).[26,33-37] There is moderate confidence in the quality of evidence to support this recommendation.

This patient population should be distinguished from those with chronic LBP and those with radiating pain. The timeline for distinguishing patients with acute, sub-acute, and chronic LBP is difficult to define based on available evidence. While not absolute, we describe acute and sub-acute symptoms as those that have lasted for less than three months, and it is for this population that the recommendation is intended. Axial/non-radiating LBP is centered within the lower back (mid-spinal or para-spinal) and extends in a lateral direction into the ipsilateral and contralateral para-spinal muscle regions. This is distinctly different from radiating back pain, in which patients endorse symptoms that radiate outside of the lower back region and into the lower extremities.

September 2017 Page 28 of 110

<sup>&</sup>lt;sup>2</sup> See the VA National Center for PTSD Guide for Patients on Chronic Pain and PTSD: https://www.ptsd.va.gov/public/problems/pain-ptsd-guide-patients.asp

<sup>&</sup>lt;sup>3</sup> See the VA/DoD Clinical Practice Guideline for the Management of Major Depressive Disorder. Available at: http://www.healthquality.va.gov/guidelines/MH/mdd/

The Work Group assessed that routine imaging or diagnostic testing in acute axial/non-radiating back pain has harms/burdens that outweigh potential benefits. Advanced imaging, such as MRI, is associated with an extremely high rate of false positive clinically asymptomatic findings. [38] However, once a finding is discovered on imaging, there is pressure on both healthcare provider and patient for further workup and potential specialty referral. This may lead to unnecessary resource utilization and further treatments with associated risks. [39] Although literature regarding "yellow flags" was not included in the evidence review, patients with psychosocial risk factors may be more likely to catastrophize and feel fearful of benign imaging results, leading to worse outcomes. [40] In regard to radiography and CT, the risk of radiation exposure is well established, and the tests should be reserved for circumstances that will affect clinical outcome. The potential for harm is particularly true in the case of discography, which is sometimes used for further evaluation of patients with LBP and MRI findings of disc disease and may lead to unnecessary treatment. There is no high quality evidence to support its use in the management of acute LBP and, in fact, there is evidence to suggest that it may lead to premature disc degeneration. [41]

The Work Group acknowledges that there is some variation in the values and preferences of patients with acute LBP, and understands that many patients present requesting diagnostic testing in hopes of finding an answer for their symptomatology. The Work Group does not advocate discrediting patient complaints, but rather endorses a method of educating patients regarding the lack of clinical benefit that routine diagnostic testing and imaging will provide them. Discussing other treatments for LBP that are associated with clinical benefit is more useful than ordering a diagnostic test.

It is critical to take into account the feasibility and the resource utilization of routine imaging tests and diagnostics. Acute LBP is a common presenting complaint and obtaining diagnostic imaging/testing that is not associated with a clinical benefit can lead to unneeded resource use. Furthermore, many providers do not have easy access to advanced imaging or testing, and routine use of these unindicated studies places an unnecessary burden on providers. The points above are primarily where future research on this topic should focus; specifically, the economic impact of imaging/diagnostics, the amount of spending attributed to these tests and on the subsequent referrals, and determining the main driver for ordering the tests given the lack of medical evidence for their utility (e.g., patient satisfaction, referral patterns/networks, health-care provider compensation).

When determining this recommendation to be a "Strong against," the Work Group considered the moderate confidence in the quality of available evidence, the potential for burdens to outweigh the benefits, and the feasibility and resource constraints of routine imaging. Patient preferences may vary, but patient education and discussion of treatment options are generally preferred over diagnostic imaging without an accompanying SDM approach.

### **Recommendation**

4. For patients with low back pain, we recommend diagnostic imaging and appropriate laboratory testing when neurologic deficits are serious or progressive or when red flag symptoms are present. (Strong for | Reviewed, Amended)

September 2017 Page 29 of 110

#### **Discussion**

Most patients with lumbar disc herniation and radiculopathy will improve in the first four weeks with noninvasive management.[42,43] Additionally, the use of lumbar imaging (e.g., radiographs, CT, MRI) without indications of serious underlying conditions does not significantly improve outcomes.[37]

For patients with LBP and severe/progressive neurologic deficits indicative of a focal neurologic lesion (e.g., acute onset of foot drop) or when underlying serious pathology is suspected, MRI or CT are recommended. Although MRI and CT have similar sensitivity and specificity for the detection of spinal canal stenosis, MRI is preferred due to the increased soft tissue resolution and lack of ionizing radiation. [44,45] Plain radiography cannot visualize discs or accurately evaluate the degree of spinal stenosis to the same extent as MRI or CT, but may be considered as an adjunct imaging modality. [26] See Sidebar A for suggested diagnostic imaging for red flags or risk factors on history or physical examination.

Clinicians should be aware that findings on MRI or CT (e.g., bulging disc without nerve root impingement) are often nonspecific and may not be the cause of LBP. Decisions should be based on the clinical correlation between symptoms and imaging findings, severity of symptoms, patient preferences, costs, surgical risks (including the patient's comorbid conditions), and whether specialist input will be available.[46]

Moderate quality evidence supports the recommendation to perform diagnostic imaging and appropriate laboratory testing when patients have serious or progressive neurologic deficits or when red flag symptoms are present. When assessing the strength of the recommendation, the Work Group also considered the benefits to the patient to greatly outweigh the harms of not detecting a serious underlying condition when neurologic deficits or red flag symptoms are present. In this case, patients will strongly prefer to have imaging or testing to either diagnose or rule out potential serious underlying conditions.

#### **Recommendation**

5. For patients with low back pain greater than one month who have not improved or responded to initial treatments, there is inconclusive evidence to recommend for or against any diagnostic imaging.

(Not applicable | Reviewed, New-added)

#### **Discussion**

Routine diagnostic imaging for the patient with LBP and no red flags is not recommended during the acute period.[37] However, once patients have failed to improve or respond to initial therapies, many patients and/or clinicians consider diagnostic imaging. In these patients beyond the acute period, diagnostic imaging may identify pathologies that warrant further investigation by other specialists as specific treatments may be of benefit. Pathologies of the spinal cord and/or nerve roots such as spinal dysraphism should prompt evaluation by a neurosurgeon. Pathologies of the spinal column beyond age-appropriate degenerative changes, such as severe spondylolisthesis,[47] may necessitate evaluation by a spine surgeon. Adjacent pathology mimicking LBP may warrant subspecialty evaluation, such as nephrolithiasis. Patients with a history of prior lumbar fusion or minor trauma, such as a fall, may benefit from imaging to rule out hardware failure, adjacent segment degeneration, compression fractures, or worsened spondylolisthesis.

September 2017 Page 30 of 110

Diagnostic imaging in the LBP patient who has failed to improve or respond to initial therapies may identify or confirm suspected etiologies of LBP that may help to guide further therapy. Facet or sacroiliac arthropathy may suggest continued judicious use of nonsteroidal anti-inflammatory drugs (NSAIDs) (see Recommendation 21).[48] Even though efficacy studies are lacking for non-surgical invasive procedures, diagnostic imaging may be used by some clinicians in specific scenarios to guide therapies (see Recommendations 34-37).[49] Spinal manipulation clinicians may benefit from assessing the degree of osteoporosis (e.g., in patients with history of steroid use).[50]

The evidence review did not specifically address the question of whether diagnostic imaging could identify all potential specific pathologies of interest in patients with LBP; however, as previously discussed, some data obtained during this review did provide information regarding some pathologies. The benefits of plain radiographs seem to outweigh the potential harms to the patients. The benefits largely encompass the potential to identify specific pathologies that warrant treatments beyond the scope of this CPG (e.g., surgical stabilization of spondylolisthesis). Importantly, routine diagnostic imaging for LBP with no red flags will most likely reveal nonspecific findings unrelated to LBP. For example, lumbar stenosis, degenerative disc changes, or Tarlov cysts are often asymptomatic radiographic findings. There is limited data to suggest that imaging without correlative pathology can help address the psychological impact of coping with LBP beyond the acute period. These harms are important as some suggest that imaging may lead to unnecessary invasive procedures. Excessive imaging may lead to concerns of radiation exposure. [36,51] The values of patients and providers are likely similar in that most would expect imaging if LBP persists beyond the acute period. Feasibility is not a major concern, as most medical treatment facilities have the ability to perform initial diagnostic imaging when indicated. Clinicians should base their decision for imaging studies on an assessment of the individual patient's needs, values, and preferences.

#### B. Education and Self-care

### **Recommendation**

For patients with chronic low back pain, we recommend providing evidence-based information
with regard to their expected course, advising patients to remain active, and providing
information about self-care options.

(Strong for | Reviewed, Amended)

#### **Discussion**

Providing information on LBP, including expected duration of symptoms, evidence-based self-care advice, and appropriate interventions, may reduce patient anxiety and positively affect attitudes regarding future outcomes.[23,25,52,53] Advice based predominantly on anatomic considerations is discouraged in favor of a biopsychosocial model that discusses pain physiology.

Patients with LBP should be advised to remain active and limit bedrest as much as reasonably possible. Use of thermal modalities, such as a heating pad, may increase comfort along with the use of a medium-firm mattress;[54] however, there is not enough evidence about the effect of the application of heat for LBP that lasts longer than three months or the application of cold for any duration. Individualized self-care education and interventions, along with more general information through an appropriate source, such as the Back

September 2017 Page 31 of 110

Book,[55] may improve patient understanding.[56] For patients with overweight or obesity, discuss weight management (see the VA/DoD CPG on Management of Obesity and Overweight).<sup>4</sup> Smoking or tobacco cessation should be discussed with patients who smoke or use other tobacco products (see the VA/DoD CPG for Treating Tobacco Use and Dependence and the VA/DoD SUD CPG).<sup>5,6</sup> Patients should be advised that in most cases the pain will improve in the first month.[23,25]

Additionally, patients should be made aware that routine imaging does not often provide useful information, may have adverse health consequences (e.g., radiation exposure), and can lead to additional, possibly unnecessary, medical interventions and costs. [36,51] Occupation-specific restrictions and/or limitations may be appropriate for certain patients and can be referenced through a number of guidelines.

When assessing the strength of the recommendation, the Work Group considered the moderate confidence in quality of evidence and also that the benefits to patients outweigh any harms. Providing education to patients may require extra time from clinicians, but the intervention does not have major feasibility or resource concerns. Most patients will value the communication from their providers regarding how to care for themselves and alleviate their LBP.

#### **Recommendation**

7. For patients with chronic low back pain, we suggest adding a structured education component, including pain neurophysiology, as part of a multicomponent self-management intervention.

(Weak for | Reviewed, New-added)

#### **Discussion**

One SR and six RCTs evaluated the effectiveness of adding a structured education component to self-care interventions for improving LBP outcomes. Studies evaluating a physically active lifestyle, weight loss, and tobacco cessation did not meet inclusion criteria for the evidence review informing this CPG update and were therefore not considered in the development of this recommendation. The overall confidence in the quality of evidence was low, but the strongest available evidence suggested that education plus active treatment was beneficial compared to active treatment alone.

An RCT evaluated the effectiveness of combining aquatic exercise and pain neurophysiology education with aquatic exercise alone in 62 chronic LBP patients. Education was used to reduce the effects of kinesiophobia and catastrophizing as well as improve outcomes.[57] The education, based on work by Butler and Moseley[58] as well as Nijs et al.,[59] was provided in two 90-minute sessions performed prior to the onset of an aquatic exercise program. The findings demonstrated that adding neurophysiology education to an aquatic exercise program results in less pain and disability.[57]

An SR in adults with chronic LBP compared back school with usual care, active control other than back school, and multimodal treatments. Back school programs were of different duration and content, with

September 2017 Page 32 of 110

<sup>&</sup>lt;sup>4</sup> See the VA/DoD Clinical Practice Guideline for the Management of Obesity and Overweight. Available at: <a href="https://www.healthquality.va.gov/guidelines/CD/obesity/">https://www.healthquality.va.gov/guidelines/CD/obesity/</a>

<sup>&</sup>lt;sup>5</sup> See the VA/DoD Clinical Practice Guideline for Treating Tobacco Use and Dependence. Available at: <a href="https://www.healthquality.va.gov/guidelines/CD/mtu/">https://www.healthquality.va.gov/guidelines/CD/mtu/</a>

<sup>&</sup>lt;sup>6</sup> See the VA/DoD Clinical Practice Guideline for Management of Substance Use Disorder. Available at: https://www.healthquality.va.gov/guidelines/MH/sud/

treatment of patients of variable chronicity of LBP, but all involved education by a therapist with the aim of treating LBP. Evidence suggested that adding back school to an exercise program improved disability scores but was inconclusive regarding effects on pain.[60]

One study evaluated the efficacy of web-based interventions on office workers with subacute and nonspecific LBP. Education was performed through the Preventative Medicine Service website as well as personal e-mail interventions plus standard care. The program was available for nine months, Monday through Friday, compared with the control group which only had access to standard care. The treatment group demonstrated significant improvement in disability, health-related quality of life, and lumbar endurance test compared to controls.[61]

# C. Non-pharmacologic and Non-invasive Therapy

#### **Recommendation**

- 8. For patients with chronic low back pain, we recommend cognitive behavioral therapy. (Strong for | Reviewed, New-replaced)
- 9. For patients with chronic low back pain, we suggest mindfulness-based stress reduction. (Weak for | Reviewed, New-replaced)

#### **Discussion**

As our understanding of pain within the biopsychosocial model has increased, behavioral interventions for chronic LBP have become commonplace. Cognitive behavioral therapy (CBT) has accumulated a sufficient evidence base to justify a "Strong for" recommendation based on moderate quality evidence.[62] Mindfulness-based stress reduction (MBSR) has some evidence to support a "Weak for" recommendation.[62] The overall benefits of MSBR or CBT outweigh any harms or burdens to the patient.

While several types of psychotherapy-based treatment may be helpful for chronic LBP, only CBT garners a "Strong for" recommendation based on moderate confidence in the quality of evidence. CBT is typically delivered by a mental health clinician, usually in an individual setting for eight to 12 visits. CBT for pain involves identifying and changing cognitions and behaviors that perpetuate pain as well as using relaxation and exposure techniques to reduce symptom-related distress.

MBSR is a structured intervention focused on the concept of mindfulness (i.e., being in the present moment, without judgment). The coursework is manualized and the supporting evidence included the following components: education, meditative practices, simple yoga poses over eight 2.5 hour group sessions plus a longer retreat, and daily home practice. [62] MBSR requires a mindfulness instructor with specialized MBSR training and experience, often a licensed independent practitioner. There is evidence for intermediate and long-term benefit of MBSR for pain and function in chronic LBP patients compared to usual care and equivalence of MBSR to CBT for pain, function, and quality of life. [62] Based on the 2014 Quality Enhancement Research Initiative's evidence review of MBSR, there is also a potential benefit of MBSR for several comorbid disorders related to chronic LBP including depression, anxiety, somatization, and pain. [63]

The following factors should be considered when determining whether CBT or MBSR should be recommended to a specific patient: patient preference, appropriateness of the group setting, and

September 2017 Page 33 of 110

practitioner expertise. Based on low to moderate quality evidence, biofeedback, progressive relaxation, telephone-based health coaching, or transtheoretical model-based behavioral change may be used as alternative treatments for chronic LBP based on patient preferences and availability.[3,64,65]

Evaluation of long-term (greater than one year) benefits of MBSR and CBT for LBP has been insufficient. The 2017 American College of Physicians SR led to a strong recommendation for MBSR as an intervention for LBP;[66] however, a more recent meta-analysis showed lack of long-term benefits from MBSR compared to usual care or an active comparator.[67] A follow-up study to a large trial comparing MBSR to CBT for LBP recently reported that CBT maintained a small benefit over usual care at two years while the benefits from MBSR were no longer statistically significant.[68] No studies have evaluated whether follow-up or "booster" sessions of either intervention might improve the long-term outcomes for pain and disability.

While both MBSR and CBT are treatments with low risk of adverse events, the time required to participate can be a burden and may present a barrier to participation. Further, the availability of practitioners with expertise in MBSR and pain-based CBT are not readily available at all health clinics. Future research on behavioral interventions for chronic LBP should include an emphasis on optimal dose, validation of shorter treatment protocols, and incorporation of technology to minimize patient burden and maximize access to treatment. Acceptance and Commitment Therapy (ACT), a contextual behavior therapy, has become increasingly common as an intervention for the management of mood disorder and chronic pain, suggesting that research specifically looking at ACT for chronic LBP is needed. [69-71] No evidence for the use of these interventions for LBP in the acute phase were identified.

#### **Recommendation**

10. For patients with acute low back pain, there is insufficient evidence to support the use of specific clinician-directed exercise.

(Not applicable | Reviewed, New-replaced)

11. For patients with chronic low back pain, we suggest offering clinician-directed exercises. (Weak for | Reviewed, New-replaced)

#### **Discussion**

Clinician-directed exercise is recommended as it is generally favorable for the treatment of chronic LBP. Overall, the demonstrated improvements are small, but may provide meaningful clinical benefit with minimal or no risk as compared to other interventions. The confidence in the quality of evidence was moderate for the effects of exercise to result in modest improvements in pain when compared to placebo, but there were no meaningful changes in function for patients with chronic LBP.[3] When exercise intervention was compared to usual medical care, patients demonstrated moderate short-term improvements in pain, small intermediate and long-term improvements in function, and a lower likelihood of work disability at 12 months.[3]

For specific forms of exercise, one SR reported moderate quality evidence favoring motor control exercise over usual care for intermediate and long-term reduction in both pain and disability.[3] There is moderate to low quality evidence that motor control exercise is only modestly better than general exercise for

September 2017 Page 34 of 110

patient function, and no important difference in terms of pain, disability, or quality of life when compared to general exercise or progressive graded activity.[3] One study with moderate quality evidence suggested that motor control exercise can effectively be delivered in a group setting compared to individualized treatment.[72] Regardless of symptom duration, low quality evidence suggests that patients receiving a symptom-guided exercise program compared to sham exercise were more likely to experience a global improvement.[3] This recommendation is consistent with patient preference to align treatment with patient tolerance and specific goals.

For patients with acute LBP, the effects of clinician-directed exercise are inconclusive and it is unclear if there is any added benefit to the patient. As compared to usual medical care, one SR found low to moderate quality evidence that specific clinician-directed exercise provides no meaningful benefit for pain levels, function, or disability.[3] There is, however, some indication based on moderate evidence that specific motor control exercise may provide a small long-term benefit over general exercise for patient function and need for pain medication,[73] but it is not known how this compares to usual care. Early access to physical therapy, which would include clinician-directed exercise as well as other supported interventions (e.g., education), as compared to usual care results in inconclusive or no important differences for long-term pain, disability, or global perceived effect of intervention.[74,75] However, there is some research, not included in our evidence review, showing that early access to physical therapy in the military healthcare system results in lower healthcare utilization and LBP-related costs over the course of care.[76]

#### **Recommendation**

 For patients with acute or chronic low back pain, we suggest offering spinal mobilization/manipulation as part of a multimodal program.
 (Weak for | Reviewed, New-replaced)

#### **Discussion**

Spinal mobilization/manipulation delivered as an isolated intervention does not provide relevant improvements for patients with chronic LBP as compared to sham interventions.[77] However, when combined with other treatments (e.g., self-care instruction, clinician-directed exercise), there is an indication based on low quality evidence that the addition of spinal mobilization/manipulation may provide long-term benefits in perceived improvement, satisfaction with care, and lower medication use.[77,78] The additive effect of spinal mobilization/manipulation to other treatments provides only small, and not clinically relevant, improvements in pain and disability.

When spinal mobilization/manipulation is compared to other conservative interventions thought to be effective (e.g., supervised exercise, home exercises, McKenzie repeated motion exercise or back school training), there does not appear to be any clear advantage of one form of treatment over another.[77,79-81] Moderate quality data on pain and disability suggest a small, but likely not clinically relevant, advantage of spinal mobilization/manipulation over these other interventions.[82] Regarding other outcomes, there does not appear to be any conclusive findings for spinal mobilization/manipulation as compared with other conservative treatments. Similar to exercise, the use of spinal mobilization/manipulation is a relatively low-risk intervention for patients with LBP, and the benefits likely

September 2017 Page 35 of 110

outweigh potential harms.[83] The feasibility of spinal mobilization/manipulation should be considered on an individual basis, as the availability of providers at nearby medical facilities may vary.

The evidence for spinal mobilization/manipulation for the treatment of acute LBP demonstrates small effect sizes for pain and short-term function. For patients with acute LBP, spinal mobilization/manipulation appears to improve long-term pain intensity, but results in no change in disability when compared to inert interventions (moderate quality evidence).[82] The addition of spinal mobilization/manipulation to other interventions appears to yield short-term improvements in function but no clinically relevant difference for reducing long-term pain levels or disability [82] and results in similar outcomes as usual medical care.[84]

#### **Recommendation**

13. For patients with acute low back pain, there is insufficient evidence to support the use of acupuncture.

(Not applicable | Reviewed, New-replaced)

14. For patients with chronic low back pain, we suggest offering acupuncture. (Weak for | Reviewed, New-replaced)

#### **Discussion**

Acupuncture appears to help patients in the long term (three to six months). There is moderate quality evidence based on two trials to support the use of acupuncture for modest long-term improvements in disability and the perceived impact of pain associated with chronic LBP.[3] Data were inconclusive regarding general quality of life and adverse events. There was variation in comparator groups; standard acupuncture was compared to sham acupuncture with blunt needles, intensive inpatient rehabilitation, or back pain acupuncture.[3] There is also large variation in patient preferences and acceptance of acupuncture. Clinicians should consider personal preferences and focus on SDM when offering acupuncture to patients.

#### Recommendation

15. For acute or chronic low back pain, there is insufficient evidence for or against the use of lumbar supports.

(Not applicable | Reviewed, Amended)

## **Discussion**

There was low confidence in the quality of evidence to support offering lumbar supports for acute or chronic LBP, with no reported associated harms or serious adverse events. Lumbar supports include lumbar braces, commercial lumbar belts and ready-to-use lumbar canvas corsets. One SR included three fair quality RCTs showing favorable results for lumbar supports for long-term disability.[3] In LBP of less than eight weeks duration, low quality evidence slightly favors lumbar supports with a back health educational program compared to a back health educational program alone. There was no statistically significant difference in pain or disability.[85] Low quality evidence favors lumbar support with subacute LBP (one to three months) for less pain, disability, and need for analgesics.[86] In the elderly population, one RCT supports using lumbar support for chronic LBP to improve pain and increase muscle endurance for a short period of time.[87] Paravertebral muscle fatigue was not increased by long-term wearing for

September 2017 Page 36 of 110

chronic LBP and weakening of the paravertebral muscles was not observed up to six months after the start of corset wearing.

Clinicians should explain the proper selection and use of lumbar supports when indicated. Lumbar supports may be used for the temporary relief from LBP or activities that would increase or potentially cause back discomfort (e.g., heavy or repetitive lifting). The harms and benefits are balanced; patients may experience temporary relief while using lumbar supports, but may become less mobile while using supports. There is also large variation in patient preferences, as some individuals may be opposed to using lumbar supports, while others may prefer trying lumbar supports over other interventions. Providing lumbar supports requires appropriate resources, and this medical equipment may not be readily available or accessible to all individuals. The feasibility of using lumbar supports should be assessed on an individual basis with special attention being given to adequate compliance.

### Recommendation

16. For patients with chronic low back pain, we suggest offering an exercise program, which may include Pilates, yoga, and tai chi.

(Weak for | Reviewed, New-replaced)

### **Discussion**

Pilates, tai chi, and yoga have evidence to support better outcomes when compared to minimal interventions, wait list (a control group, randomized to a waiting list, that receives intervention after the active treatment group), no exercise, and controls. Yoga has some evidence to support better outcomes than strengthening exercise. In addition, other exercise options may provide benefit in patients with chronic LBP, including strength/resistance, coordination/stabilization, aquatics, cycling, and walking.

The SRs for Pilates, tai chi and yoga, were graded very low to moderate quality due to variations of study limitations, inconsistency in findings, and imprecision. Studies addressing Pilates and yoga mostly enrolled females which may limit the generalizability of the results to the VA/DoD population.

Given that there is potential for improved outcomes and minimal to no harm with Pilates, tai chi, or yoga, clinicians can suggest one of them as a possible exercise option for patients with chronic LBP. Three SRs, which were not part of the evidence review due to being superseded by the Chou SR,[3] found evidence supporting other types of exercise that may be relevant and useful to consider in addition to Pilates, tai chi, and yoga. These studies found that in patients with chronic LBP, participation in strength/resistance, coordination/stabilization,[88] aquatic,[89] and cycling[90] exercise may also be beneficial. In addition, a study that was not specific to LBP, and therefore not included in our evidence report, found that walking may be beneficial in patients with chronic musculoskeletal pain.[91]

### Yoga

Evidence was inconclusive regarding yoga versus usual care alone, but short-term pain, disability, and quality of life generally improved in studies of yoga compared to education.[92] Data from one RCT showed yoga yields slightly better quality of life than a back book plus advice.[93] Data from one SR favored yoga over all comparators of usual care, education, and exercise for short- and long-term pain and disability.[92] There is low quality evidence favoring yoga over strengthening exercises for pain levels,[3]

September 2017 Page 37 of 110

and quality of life,[93] and moderate quality evidence that was inconclusive for disability comparisons between yoga and exercise.[92]

#### **Pilates**

Pilates was associated with slightly better outcomes of pain, disability, and short-term function compared to minimal interventions and controls in two SRs.[94,95] Evidence is unclear or inconclusive comparing Pilates to other types of exercise,[94,95] massage therapy, and usual care.[96]

### Tai Chi

Evidence favored tai chi over no exercise, wait list, and backward walking and jogging, but not swimming, for improvement in chronic LBP.[3] Evidence also favored tai chi over physical rehabilitation for improvement in pain in two studies; however, the types of rehabilitation are unknown as the SR did not describe the details of the programs and the included studies were not available in English.[97]

### **Recommendation**

17. For patients with low back pain, there is insufficient evidence to support the use of ultrasound. (Not applicable | Reviewed, New-added)

The use of ultrasound for LBP was included in the evidence search; however, there was insufficient evidence to make a recommendation for or against its use for patients with LBP.[3] The existing evidence base, while small and of primarily low quality, suggests that there is there is no difference in outcomes between ultrasound and sham ultrasound.

### **Recommendation**

18. For patients with low back pain, there is inconclusive evidence to support the use of transcutaneous electrical nerve stimulation (TENS).

(Not applicable | Reviewed, New-added)

The use of transcutaneous electrical nerve stimulation (TENS) for LBP was included in the evidence search; however, the evidence was inconclusive and the data did not find a significant difference in patient outcomes. [98] The evidence reviewed suggests an improvement in both radicular and non-radicular pain but is inconclusive regarding other outcomes. TENS is a passive modality that can be applied by the individual as part of a self-management strategy.

### **Recommendation**

19. For patients with low back pain, there is insufficient evidence to support the use of lumbar traction.

(Not applicable | Reviewed, New-added)

Lumbar traction as an intervention to improve LBP was included in the evidence search; however, the evidence was insufficient to support the use of lumbar traction.[99-102]

September 2017 Page 38 of 110

### **Recommendation**

20. For patients with low back pain, there is insufficient evidence to support the use of electrical muscle stimulation.

(Not applicable | Reviewed, New-added)

Electrical muscle stimulation was included in the evidence review; however there was no evidence found to support the use of this intervention for LBP.[3,103]

# D. Pharmacologic Therapy

#### Recommendation

21. For patients with acute or chronic low back pain, we recommend treating with nonsteroidal anti-inflammatory drugs, with consideration of patient-specific risks.

(Strong for | Reviewed, Amended)

### **Discussion**

Evidence favors the use of NSAIDs for both acute and chronic LBP; most comparative trials showed no differences in pain relief among NSAIDs. Statistically significantly fewer adverse effects were observed with the cyclooxygenase-2 (COX-2) NSAIDs versus the traditional NSAIDs. We suggest the use of relatively COX-2 selective NSAIDs over non-selective NSAIDs based on patient risk factors.

For the outcome change in pain intensity, data favors NSAIDs over placebo in patients with both acute and chronic LBP (low to moderate quality evidence). An SR reported that NSAID use improved pain intensity (on visual analog scale [VAS], 0-100 mm) at ≤12 weeks compared to placebo.[3] An RCT reported that naproxen was superior to placebo with regards to improvement in lower back pain intensity (LBPI) from baseline to 16 weeks.[104]

The data for disability and functional outcomes is inconclusive. Pooled results from seven studies that followed patients for three weeks or less found a higher proportion of patients taking NSAIDs reporting global improvements versus placebo. One study reported inconclusive data between naproxen versus placebo with regard to disability and function as measured by the mean change in Roland-Morris Disability Questionnaire (RMDQ) score from baseline to 16 weeks and the mean change in Pain Global Assessment score from baseline to 16 weeks.[104]

An SR found that most trials of comparisons of NSAIDs showed no differences in pain relief in patients with acute or chronic LBP.[3] Five studies compared COX-2 NSAIDs with traditional NSAIDs; no statistically significant difference for pain relief for acute LBP was seen in four of these studies. A fifth, high quality study found moderate evidence that there were no differences in pain relief between COX-2 and traditional NSAIDs for chronic LBP.[3,105]

RCTs reported inconclusive evidence of any differences regarding adverse effects between naproxen and placebo (very low quality evidence, no between-group confidence interval [CI])[104] and dexketoprofen (the dextrorotatory enantiomer of ketoprofen, unavailable in the U.S.) and diclofenac (low quality evidence, no between-group CI).[106] COX-2 NSAIDs had statistically significantly fewer adverse effects than traditional NSAIDs.[3] See Appendix B for a list of select VA and DoD National Formulary NSAIDs.

September 2017 Page 39 of 110

Gastrointestinal (GI) safety continues to be a high priority when choosing an NSAID treatment for pain. We suggest the use of relatively COX-2 selective NSAIDs over non-selective NSAIDs based on patient risk factors, primarily GI toxicity. The use of relatively COX-2 selective inhibitors may reduce the risk for GI events; however, this benefit is negated if the patient is using aspirin. [107]

All NSAIDs, selective and non-selective, have box warnings for increased risk of cardiovascular (CV) events. If an NSAID is required in a patient with CV risk, naproxen with a proton pump inhibitor may be a viable option. [107,108] RCTs of relatively COX-2 selective agents in meta-analyses that did not meet inclusion criteria for the evidence review that informed this guideline reinforce the concern regarding CV events with COX-2 inhibitors. [108] More recently, a large trial that randomized 24,081 patients to receive celecoxib, naproxen, or ibuprofen found that the CV risk associated with the selective COX-2 inhibitor celecoxib is not greater than that associated with non-selective NSAIDs. [109] Any conclusions from this trial are limited by the high rates of drug discontinuation (68.8%), study dropout (27.4%), and the restrictions on the doses of celecoxib. Ninety percent of the patients in the trial had osteoarthritis and the dose of celecoxib was limited to 200mg/day in this group, but dose escalation was allowed for ibuprofen and naproxen.

### **Recommendation**

22. For patients with chronic low back pain, we suggest offering treatment with duloxetine, with consideration of patient-specific risks.

(Weak for | Reviewed, New-added)

### **Discussion**

The benefit of duloxetine for chronic LBP in terms of both pain and function improvement is small as demonstrated by moderate to high quality evidence. [3] In one RCT, duloxetine was associated with improvement in back pain intensity (BPI) from baseline to 14 weeks with a higher proportion of patients at 14 weeks experiencing 50% improvement in the BPI. [110] However, when function was measured with the RMDQ, the comparative data were inconclusive. [3] It is important to keep in mind that the effects of selective serotonin reuptake inhibitors (SSRI) on LBP are inconclusive. [3] Of the serotonin and norepinephrine reuptake inhibitors (SNRI) class, only duloxetine has been studied in LBP; theoretically, the SNRI class may demonstrate some benefit given a similar mechanism of action to duloxetine.

Tricyclic antidepressants (TCAs) may be considered for use in certain patients. In a recent SR, no benefit was found with TCAs for either pain or function[3]; however, older studies have shown that TCAs as a class provide a small improvement in pain intensity, but were inconclusive in regards to function, quality of life, or healthcare utilization.[111,112] Consideration of medical or psychiatric comorbidities are important and may influence the selection of SNRI or TCA. For some patients, addition of a low dose TCA to SSRI may be helpful, depending on medical or psychiatric comorbidities.

There are more adverse effects associated with duloxetine when compared to placebo. These include nausea, insomnia, dry mouth, constipation, somnolence, and fatigue.[3] Additionally, duloxetine has a risk of hepatotoxicity and should not be used in individuals with liver disease. Per the VA/DoD CPG on PTSD, duloxetine may not help to improve PTSD symptoms of patients with concomitant PTSD (see the VA/DoD

September 2017 Page 40 of 110

PTSD CPG).<sup>7</sup> Caution should be used when prescribing TCAs to individuals with cardiac risk factors, and anticholinergic burden should also be taken into account when used in geriatric patients.[113] Additionally, combining TCAs with other serotonergic medications increases the risk of serotonin syndrome and should be used with caution. In patients with LBP with or without radiculopathy, duloxetine and TCAs have been shown to have a small positive effect on both pain and function. Adverse effect burden between agents vary greatly and should be taken into account when choosing an antidepressant. In general, TCAs are not recommended in the elderly population.[114] Using TCAs at bedtime in low dosages may reduce side effects, but limit effectiveness for pain therapy that is dosage related.

#### Recommendation

- 23. For patients with acute low back pain or acute exacerbations of chronic low back pain, we suggest offering a non-benzodiazepine muscle relaxant for short-term use.
  - (Weak for | Reviewed, New-added)
- 24. For patients with chronic low back pain, we suggest against offering a non-benzodiazepine muscle relaxant.

(Weak against | Reviewed, New-added)

#### **Discussion**

Moderate evidence supports offering a non-benzodiazepine muscle relaxant for acute LBP. The benefits of skeletal muscle relaxants were demonstrated in two SRs, although the evidence indicates benefit is limited to short-term use of three to seven days. [3,115] There is limited evidence that suggests benefit of one agent over the other; however, it is important to recognize that the agents differ significantly in adverse effect profiles. Moderate evidence demonstrates no effect on disability in the short term. [115] When comparing an NSAID alone to a combination of an NSAID and the skeletal muscle relaxant cyclobenzaprine, evidence demonstrates no difference in acute LBP. [116]

We suggest against offering a non-benzodiazepine muscle relaxant for chronic LBP. In regard to long-term use, there is no evidence to suggest benefit for the use of skeletal muscle relaxants for chronic LBP. One SR included one low quality study showing that there was no benefit of skeletal muscle relaxants when compared to placebo in patients with chronic LBP;[115] another SR also showed no benefit of skeletal muscle relaxants in outcomes for chronic LBP.[3]

Muscle relaxants were associated with higher rates of adverse events, such as central nervous system (CNS) effects including sedation, nausea, dizziness, and headache.[3,115] While it is important to note that one agent does not confer benefit over another agent, we do not recommend the use of carisoprodol for acute or chronic LBP due to its adverse effect profile, including CNS depression, as well as its risk of dependence. Carisoprodol is metabolized to an agent that binds to the barbiturate receptor and is classified as a Schedule IV controlled substance by the U.S. Drug Enforcement Agency. When considering a skeletal muscle relaxant, clinicians should consider the adverse effect profile that includes risk for CNS depression, particularly in patients taking other CNS depressant medications. Agents such as

September 2017 Page 41 of 110

<sup>&</sup>lt;sup>7</sup> See the VA/DoD Clinical Practice Guideline for Management of Posttraumatic Stress Disorder and Acute Stress Reaction. Available at: <a href="https://www.healthquality.va.gov/guidelines/mh/ptsd">https://www.healthquality.va.gov/guidelines/mh/ptsd</a>

cyclobenzaprine pose higher anticholinergic burden which may be of concern in the geriatric population. This agent in combination with other serotonergic medications may increase risk of serotonin syndrome.

#### Recommendation

25. For patients with low back pain, we recommend against benzodiazepines. (Strong against | Reviewed, New-replaced)

### **Discussion**

There is insufficient evidence to support the use of benzodiazepines for acute LBP; the evidence in chronic LBP is less conclusive. There is low quality data indicating that the harms/burden of benzodiazepine use outweigh the benefits. The potential for abuse, addiction/dependence, overdose potentially resulting in death, respiratory depression, and sleep apnea do not justify their use. Some patients may prefer benzodiazepines, but the potential harms outweigh the benefits. These associated risks are further compounded when combined with opioids (see the VA/DoD CPG on the Management of Opioid Therapy for Chronic Pain).<sup>8</sup>

A good quality SR found inconclusive evidence between diazepam and placebo with respect to LBP improvement.[3] The SR identified one RCT[117] which reported efficacy outcome data for 60 patients randomized to receive placebo or diazepam two times 5 mg daily, followed by a taper. Follow-up examinations were scheduled at six weeks and one year after discharge. The median duration of the stay in hospital was shorter in the placebo arm (8 versus 10 days, p= 0.008), and the probability of pain reduction on the VAS by more than 50% was twice as high in placebo patients (p= 0.0015). Other outcome measures, though inconclusive, tended to favor placebo over diazepam including workdays lost, disability, and healthcare utilization.

There is little evidence regarding adverse events with the use of benzodiazepines for LBP specifically, but an expanded review of pain management and pharmacology literature outside the LBP CPG evidence review suggests potential harms. [118] An SR reporting low quality evidence found CNS adverse events such as somnolence, fatigue, and lightheadedness were reported more frequently with benzodiazepines versus placebo.[3]

### **Recommendation**

26. For patients with acute or chronic low back pain with or without radiculopathy, we recommend against the use of systemic corticosteroids (oral or intramuscular injection).

(Strong against | Reviewed, Amended)

# **Discussion**

The use of systemic corticosteroids for the treatment of acute or chronic LBP with or without radiculopathy is not recommended. There is a lack of evidence for efficacy related to pain or disability.[3,119] There is no compelling evidence that the use of corticosteroids improves quality of life or decreases healthcare utilization in those receiving this treatment.[3,119] The overall quality of the

September 2017 Page 42 of 110

<sup>&</sup>lt;sup>8</sup> See the VA/DoD Clinical Practice Guideline for the Management of Opioid Therapy for Chronic Pain. Available at: http://www.healthquality.va.gov/guidelines/Pain/cot/

evidence addressing disability and quality of life was low. Studies finding no important difference related to pain and mixed results related to healthcare utilization were of moderate quality.

There are risks associated with corticosteroid use in the short term, and repeated use may have more significant implications. [120] A moderate quality study demonstrated significantly more adverse events when comparing prednisone to placebo in the short term. [119] Adverse events included insomnia, nervousness, increased appetite, indigestion, headache, joint pain, and sweating. An SR was inconclusive regarding adverse events, but the included studies were of low to very low quality. [3] While providers and patients may wish to try systemic corticosteroids for LBP or radiculopathy, the evidence suggests that efficacy does not outweigh the potential risks.

### **Recommendation**

- 27. For patients with low back pain, we recommend against initiating long-term opioid therapy. For patients who are already prescribed long-term opioid therapy, refer to the VA/DoD CPG for the Management of Opioid Therapy for Chronic Pain.<sup>9</sup>
  - (Strong against | Reviewed, New-replaced)
- 28. For patients with acute low back pain or acute exacerbations of chronic low back pain, there is insufficient evidence to recommend for or against the use of time-limited opioid therapy. Given the significant risks and potential benefits of opioid therapy, patients should be evaluated individually, including consideration of psychosocial risks and alternative non-opioid treatments. Any opioid therapy should be kept to the shortest duration and lowest dose possible.

  (Not applicable | Reviewed, New-replaced)

### **Discussion**

While the current literature for patients with acute LBP or acute exacerbations of chronic LBP shows insufficient evidence to support time-limited (less than seven days) opioid therapy, on average, the potential harms of short-term opioid therapy (less than six months) outweigh the potential benefits in patients with LBP. Findings of two SRs that showed that opioid therapy for acute or chronic LBP produced small additional analgesic effects beyond those seen with placebo (moderate quality evidence).[3,115] In a meta-analysis, the mean difference between single-ingredient opioids and placebo in pain intensity was − 8.1 on a 0−100 VAS scale.[115] In an SR, the standardized mean difference between strong opioids (i.e., hydromorphone, morphine, oxycodone, oxycodone/naltrexone combination, oxymorphone, and tapentadol) and placebo was −0.43 (seven trials), equivalent to a mean difference of about one point on a 0−10 numeric rating scale.[3] Neither study reported the percentage of patients who achieved clinically important (≥ 30%) improvements from baseline in pain intensity. See the VA/DoD CPG on Opioid Therapy for further discussion pertaining to prescribing opioid therapy.<sup>9</sup>

According to a meta-analysis, opioid therapy produced no clinically important improvements in function relative to placebo at 30 to 91 days; however, results were inconclusive (wide CI; three RCTs).[115] In an SR, short-term therapy (less than six months) with strong opioids resulted in small, clinically unimportant,

September 2017 Page 43 of 110

<sup>&</sup>lt;sup>9</sup> See the VA/DoD Clinical Practice Guideline for the Management of Opioid Therapy for Chronic Pain. Available at: <a href="http://www.healthquality.va.gov/guidelines/Pain/cot/">http://www.healthquality.va.gov/guidelines/Pain/cot/</a>

additional improvements in function over placebo. The standardized mean difference relative to placebo was –0.26 (four trials), representing a difference of about one point on a 24-point RMDQ scale.[3]

Trials that compared opioids and other drug therapies (e.g., acetaminophen, NSAIDs, antidepressants) were limited and the strength of evidence was insufficient to make conclusions for either pain or functional outcomes. No clear differences were seen between long-acting opioids compared to other long-acting opioids or short-acting opioids.[3]

The small differential benefits of short-term opioid therapy were counterbalanced by increases in risks of adverse effects typically seen with short-term opioid therapy. The meta-analysis showed that the median incidence of adverse events was 68.9% for opioid treatment groups and 49.1% for placebo groups, with a risk ratio of 1.3 (eight trials).[115] In four of eight trials, 50% of study patients discontinued treatment because of adverse events or lack of efficacy.[115]

The trials included in the SRs did not assess the risks of long-term opioid therapy. Opioid risks and risk assessment for chronic non-cancer pain are discussed in more detail in the VA/DoD CPG for Management of Opioid Therapy for Chronic Pain. <sup>10</sup> Based on what is known for chronic non-cancer pain in general (not specific to LBP), the small effects of short-term opioid therapy seen in LBP trials may be substantially outweighed by serious risks including potentially fatal respiratory depression, overdose, misuse, abuse, addiction, and diversion — risks that pose considerable harms not only to the patient, but also relatives, friends, and the public. The risks of addiction during opioid therapy, which may start with the first dose administered, need to be taken into consideration and weighed against the actual therapeutic benefits in individual cases.

No clinical trials identified by the evidence review evaluated time-limited (less than seven days) opioid therapy. Some trials may have been omitted from our evidence review if they did not evaluate outcomes after 12 weeks. While the benefits and harms of time-limited opioid therapy for acute LBP are unclear, there is a high likelihood of rapid spontaneous improvement in pain, function, and return to work in the first month.[23] The severity of pain, level of pain-related disability, refractoriness to other therapies, co-occurring medical conditions, current or prior psychiatric or substance use disorders, social history, age, frailty, opioid dose, formulation, route of administration, drug interactions, and other factors may influence decisions regarding whether or not to try a time-limited course. For acute LBP refractory to NSAIDs and non-benzodiazepine skeletal muscle relaxants (see Recommendation 21 and Recommendation 23), opioids are the only remaining drug treatment with evidence of effectiveness, although the analgesic effects were small relative to placebo and pertained to short-term, not necessarily time-limited (greater than seven days), therapy.

Patients' values, preferences, and treatment goals regarding opioid therapy can vary widely, both between individuals and in the same individual over time. Some patients may be reluctant to take opioids because of the risk of addiction or fear of stigma, while others may seek a therapeutic opioid trial despite the marginal benefits over placebo.

September 2017 Page 44 of 110

<sup>&</sup>lt;sup>10</sup> See the VA/DoD Clinical Practice Guideline for the Management of Opioid Therapy for Chronic Pain. Available at: http://www.healthquality.va.gov/guidelines/Pain/cot/

The patient focus group participants indicated a desire for education about pain medications, particularly opioids. When clinicians educate patients about opioid therapy, they can also provide information on some of the questions that remain unanswered. Research gaps specific to LBP include the evaluation of the immediate benefits and harms of a time-limited course of opioid therapy for acute LBP; the risks of hormonal effects, hyperalgesia, overdose, respiratory depression, death, misuse, abuse, addiction, and diversion during long-term opioid therapy; the utility of opioid therapy in patients with risk factors for harm (e.g., substance use disorder); the efficacy of opioid therapy in patients with radicular symptoms; and factors that affect the magnitude of treatment responses in patient subgroups.

### **Recommendation**

- 29. For patients with acute or chronic low back pain, there is insufficient evidence to recommend for or against the use of time-limited (less than seven days) acetaminophen therapy.

  (Not applicable | Reviewed, New-replaced)
- 30. For patients with chronic low back pain, we recommend against the chronic use of oral acetaminophen.

(Strong against | Reviewed, New-replaced)

#### **Discussion**

A large SR found no difference between acetaminophen and placebo on the outcomes of mean pain, disability, quality of life, or function at 12 weeks (moderate quality evidence).[121] A high quality, large RCT (N= 1,652) included in an SR [3] also showed no difference between acetaminophen and placebo at all time points.[122]

As no benefits were shown in the evidence, the consideration of harm/burden predominates because of the risks associated with taking acetaminophen (e.g., long-term liver effects at high dosage). The balance of harms associated with other options that can be provided to patients and the harms of removing acetaminophen as a viable treatment option need to be considered. There is some variation in values and preferences, with some patients thinking that acetaminophen is for pain that is not "serious" and are unaware of the adverse effects of taking too much.

Other implications include easy accessibility, as acetaminophen is inexpensive and therefore available at a relatively low cost to the patient and the system, and also available both over the counter (OTC) and in formulary. It is easily overused without proper education, thus risks and adverse effects may not be well understood by the public. In addition, elderly individuals and patients with hepatic insufficiency are subgroups that may be at the most risk for harm.

### **Recommendation**

31. For the treatment of acute or chronic low back pain, including patients with both radicular and non-radicular low back pain, there is insufficient evidence to recommend for or against the use of antiepileptics including gabapentin and pregabalin.

(Not applicable | Reviewed, New-replaced)

September 2017 Page 45 of 110

### **Discussion**

The evidence for the use of antiepileptics is mixed and we cannot recommend for or against their use in the treatment of LBP. There was no evidence included in our evidence review for the use of antiepileptic agents other than gabapentin or pregabalin. In one moderate quality study, there was no difference in pain intensity between placebo and gabapentin. [123] This study evaluated patients with both radicular and non-radicular chronic LBP. There were two low to very low quality RCTs that indicated a small difference in pain in the short term but the differences were not clinically relevant. [124,125] There were no trials that addressed the use of antiepileptics in acute non-radicular pain. It was shown that pregabalin may have a greater impact on pain and disability when compared to amitriptyline, but the study is not of high enough quality to determine benefit of pregabalin over an antidepressant. [3]

There are significant adverse effects associated with the use of gabapentin or pregabalin. An RCT found significantly higher adverse effects with gabapentin, including fatigue, dry mouth, difficulties with mental concentration, memory, visual accommodation, and loss of balance. [123] The SR reported inconclusive results regarding the difference in adverse events between pregabalin and amitriptyline, although this evidence was rated as very low quality. [3] An RCT studying the treatment of pregabalin in patients with radiculopathy, which was published after the closure of our evidence review, reported no significant reduction in leg pain intensity and a higher incidence of adverse events. [126] It is important to note that pregabalin is a controlled substance, indicating some potential for abuse and dependence. Gabapentin is not a scheduled medication, however there is literature to indicate its misuse and abuse as well. While the use of gabapentin and pregabalin may provide small, short-term benefits, we cannot substantiate that the benefits outweigh the adverse effects due to the lack of efficacy demonstrated in the available literature.

### **Recommendation**

32. For the treatment of low back pain, there is insufficient evidence to recommend for or against the use of topical preparations.

(Not applicable | Reviewed, New-added)

### **Discussion**

Topical pharmacotherapy preparations were included in the evidence search. However, the search yielded no studies that met inclusion criteria for the evidence review. Therefore, no recommendations can be made about these agents due to the lack of evidence at the time this CPG was published.

# **E.** Dietary Supplements

### **Recommendation**

33. For the treatment of low back pain, there is insufficient evidence to recommend for or against nutritional, herbal, and homeopathic supplements.

(Not applicable | Reviewed, New-added)

### Glucosamine

The evidence review identified one SR with very low quality of evidence that included three trials.[127] Two of the studies showed no difference between glucosamine and placebo. However, there was concern that the doses used in the studies were not sufficient to produce clinically significant results (1500 mg used

September 2017 Page 46 of 110

in the studies versus 2000 mg daily). In addition, the studies were sponsored by pharmaceutical companies and the supplement was supplied by the manufacturer, which may increase the risk of bias.

The benefits and harms/burden are balanced. One study considered adverse effects and found they were not significantly different between glucosamine and placebo (both groups had approximately 30% mild and transient GI and dermatological symptoms).[127] For the subgroup consideration of patients with hip and/or knee osteoarthritis, clinicians should not prescribe chondroitin sulfate, glucosamine, and/or any combination of the two, to treat joint pain or improve function (see the VA/DoD CPG for the Non-Surgical Management of Hip & Knee Osteoarthritis).<sup>11</sup>

There is likely to be variation in patient values and preferences regarding the use of glucosamine. Some patients may prefer it as a "natural" supplement, while others may not want to consider using it because they do not see it as a "real" medicine. Moreover, supplements are not regulated by the U.S. Food and Drug Administration (FDA), so the quality may be inconsistent. Finally, although easily accessible OTC, they are not on VA/DoD formularies and therefore may involve costs to the patient.

### Other Nutritional, Herbal, or Homeopathic Supplements

There were no studies nutritional, herbal, or homeopathic supplements identified in the evidence review for this guideline that met inclusion criteria.

The degree of harms/burdens depends on the specific supplement being considered. As a category, due to the wide variety of preparations and their possible bioactivity, it is likely that many supplements used have harms that outweigh benefits (e.g., kava, ephedra). Given the wide range of supplements used, there is concern about the known and unknown adverse effects; drug-to-drug interactions; and the dosage, active ingredient, and purity of the supplements.

As with glucosamine, there is variation in values and preferences regarding the use of nutritional, herbal, and homeopathic supplements; some patients may prefer "natural" supplements, while others may not want to consider using supplements if they are not perceived as "real" medicine. Moreover, supplements are not regulated by the FDA, so the quality may be inconsistent. Finally, although easily accessible OTC, nutritional, herbal, and homeopathic supplements may not be on the VA/DoD formularies and therefore may involve costs to the patient. Realizing that many patients use supplements, it is important for the provider to have a conversation with the patient about their individual use of supplements to identify potential harms that may be associated with specific supplements.

September 2017 Page 47 of 110

<sup>&</sup>lt;sup>11</sup> See the VA/DoD Clinical Practice Guideline for the Non-Surgical Management of Hip & Knee Osteoarthritis. Available at: http://www.healthquality.va.gov/guidelines/CD/OA/

# F. Non-surgical Invasive Therapy

### Recommendation

34. For the long-term reduction of radicular low back pain, non-radicular low back pain, or spinal stenosis, we recommend against offering spinal epidural steroid injections.

(Strong against | Reviewed, New-added)

35. For the very short-term effect (less than or equal to two weeks) of reduction of radicular low back pain, we suggest offering epidural steroid injection.

(Weak for | Reviewed, New-added)

36. For the treatment of low back pain, we suggest against offering intra-articular facet joint steroid injections.

(Weak against | Reviewed, New-added)

37. For patients with low back pain, there is inconclusive evidence to recommend for or against medial branch blocks and radiofrequency ablative denervation.

(Not applicable | Reviewed, New-added)

### **Discussion**

Epidural steroid injections (ESI) are an option at many VA/DoD facilities for treating LBP, including lumbar radiculopathy. Studies assessing the efficacy of epidural steroid joint injections were generally rated as low in quality. ESI did not generally perform better than saline or local anesthetic injections for pain, function, return to work, or quality of life, though wide CIs could not exclude a real difference between groups. [128,129] Individual studies finding between-group differences for comparators versus ESI (including saline injection as placebo, anesthetic injection, usual care, or oral medication) found small effects, but wide CIs for comparisons. [128,129] These results were consistent even in patient groups thought to benefit from injections. For example, a trial of ESI versus usual medical care for lumbar radiculopathy failed to show a benefit of injections. [130] Additionally, an SR did not show a clear reduction in surgical risk for patients undergoing ESI. [129] While the overall evidence was not conclusive for ESI, there is moderate quality evidence that in the immediate term (defined as 5-14 days), ESI provided improved pain relief compared to placebo; however, the size of the pain reduction effect was small, did not meet predefined thresholds for minimum clinically important differences, and most of the patient groups studied had chronic symptoms. [3] Trials examining the transforaminal approach to ESI were of higher quality and more likely to show an improvement versus placebo.

Facet injections are utilized at many VA/DoD facilities in the treatment LBP and in the identification of painful structures in the lumbar spine. Studies assessing the efficacy of facet joint injections and therapeutic medial branch block injections, were generally rated as low or very low quality. Facet injections of steroid did not generally perform better than saline injections for pain, function, return to work, or quality of life.[129] While some individual studies found small effects for pain or function, these differences generally did not meet the threshold for clinical significance (i.e., saline injection, hyaluronic injection, oral NSAID, and oral steroid).[129] One multi-armed comparative trial showed that facet injection and oral NSAID resulted in superior outcomes to oral NSAID alone, though there was no sham control for injection in the study.[131]

September 2017 Page 48 of 110

Selective nerve root block (SNRB) injections and radiofrequency ablation denervation (RFA) are options at many VA/DoD facilities for treating LBP. Studies assessing the efficacy of SNRBs and RFA were rated from very low to moderate in quality. There was inconclusive evidence that SNRB and RFA procedures improve pain, function, return to work, or quality of life.[132-134] One trial comparing SNRB to caudal epidural steroid injection found better results for the caudal epidural injection, but the between-group differences had uncertain clinical significance.[133] The highest quality study reviewed on RFA found no between-group differences for pain versus a placebo comparator (though there was a large variation in response) and a small, but likely not clinically significant, difference favoring RFA for function.[132]

These overall unclear benefits of injection and ablation therapies were assessed against their cost and risk. There were a small number of adverse events reported, although harms were reported inconsistently across trials. There is expected to be some variation in patient values and preferences regarding injection/ablation as the patient focus group revealed preferences for a precise diagnosis and treatment, and these interventions may assist in meeting those expectations. There may be patients who prefer not to undergo an invasive procedure like injection/ablation when there is no clear benefit, and comparable alternatives include oral medication or other noninvasive approaches, including advice on activity and self-management and/or a noninvasive option like physical exercise or behavioral therapy. A SDM approach with discussion of the realistic expectations and risks is suggested. In evaluating patients that require interventional procedures, the clinician should ensure that the history, exam, and imaging studies are supportive and congruent with the procedure being performed. There may be subgroups of patients whose LBP complaint arises primarily from nociception from the lumbar nerve root(s) and who could uniquely benefit from these procedures; however, the evidence to date does not indicate an accurate and reliable way to determine if this subgroup exists, especially considering the reviewed evidence on radiculopathy. Patients with acute and intolerable radicular pain may benefit from referral to a specialist for ESI and may be more likely to benefit from the procedure than patients with more chronic symptoms, though that has yet to be validated in a clinical trial. Based on the evidence reviewed for ESI, and taking into account the recommendations for non-pharmacologic and non-invasive therapies, the primary role for ESI may be to provide a very short-term reduction in pain to support participation in active non-pharmacologic therapies. Given the limited duration of expected benefit and the modest expected effect size, use of ESI for chronic LBP outside of an active rehabilitation treatment plan is not recommended. Feasibility is an important consideration because not all medical treatment facilities will have the appropriate specialists, space, or equipment to perform these non-surgical invasive therapies due to the added costs, maintenance, and space/resource utilization.

Future research in this area should focus on high quality randomized trials comparing injection/ablation to credible comparators such as sham injection and/or noninvasive care, with evaluation of both short-term measures of pain and function, long-term outcomes, and the value of these procedures. Further studies should be performed regarding the targets of ablation and techniques for administration of injection (e.g., interlaminar versus transforaminal), particularly given the trend for improved outcomes with the transforaminal technique. The risk for surgical intervention after these procedures (such as the design of the Spijker-Huiges trial [130]) should be assessed and reported.

September 2017 Page 49 of 110

Our description of the limited evidence for these procedures should not be taken as a recommendation to pursue surgical consultation for patients without a thorough risk/benefit consideration and SDM for such surgical options.

# G. Team Approach to Treatment of Chronic Low Back Pain

### **Recommendation**

38. For selected patients with chronic low back pain not satisfactorily responding to more limited approaches, we suggest offering a multidisciplinary or interdisciplinary rehabilitation program which should include at least one physical component and at least one other component of the biopsychosocial model (psychological, social, occupational) used in an explicitly coordinated manner.

(Weak for | Reviewed, New-replaced)

#### Discussion

According to the available evidence, a multidisciplinary biopsychosocial rehabilitation (MBR) approach that targets physical and behavioral/psychological care may be beneficial for patients with chronic LBP. Studies examining these programs recognize their varying constitution. The available evidence provided no general consensus regarding the definition of a multidisciplinary treatment approach. [135] The term interdisciplinary was used interchangeably in some cases, but multidisciplinary was most consistently used to describe a team approach to chronic LBP treatment. In a study by Nazzal et al., MBR consisted of education, occupational therapy, and massage with a combined exercise program (i.e., aerobic, resistive, stretching, flexibility, and postural exercises with time-limited continuous mode ultrasound and TENS). [136] A total of 36 hours of physical exercise, 12 hours of occupational therapy, and 12 hours of education were provided. Another study comparing an MBR program with active-only treatment described a group-based, 12-week program including 35 hours of hard physical exercise (e.g., aerobic and circuit training), 22 hours of light exercise/occupational therapy, and 16 hours of education. [137]

The effectiveness of MBR programs are evaluated using various outcomes. An SR of 16 trials reported that patients receiving MBR had statistically significantly greater reductions in pain compared to those receiving usual care at both medium-term ( $\geq$  3 months to  $\leq$  12 months) and long-term ( $\geq$  12 months) follow-up.[135] In addition, patients receiving MBR had statistically significantly greater reductions in disability scores versus patients who received usual care at both medium-term ( $\geq$  3 months to  $\leq$  12 months) and long-term ( $\geq$  12 months) follow-up.[135] Empirical evidence found statistically significant improvements in work-related outcomes for patients receiving MBR programs compared to patients receiving physical treatment.[135,136]

In addition to the findings that favored use of MBR, an SR and meta-analysis comparing MBR with physical-only and behavioral/psychological-only interventions found no clinically significant differences between pain and disability for the three approaches. [138]

MBR treatment programs may be most appropriate for patients with severe or complex chronic LBP due to their intensity and significant time and resource commitment from both the patient and healthcare staff. [135] Additional considerations in suggesting MBR for treatment of LBP include a favorable risk to benefit ratio. The evidence indicates that MBR programs pose limited to no risk but yield significant

September 2017 Page 50 of 110

benefit. When weighing the values and preferences of patients, the Work Group determined there may be some variability in patient preferences and that some patients may have limiting factors (e.g., non-flexible work schedules) to allow time for participation in an MBR program. Others may have concerns regarding the stigma associated with missing work or other activities due to the time commitment required to fully partake in MBR. Other implications for MBR programs include a potentially high cost when compared to standard treatment and access limitations for patients who are not within proximity to larger medical centers where a multidisciplinary team may be available to host a program. However, given the national need to emphasize biopsychosocially informed, low-risk, non-pharmacologically based treatment options for chronic pain management, MBR programs provide an option that should be considered, especially for patients with severe or complex LBP or those who have failed a more limited approach.

# **VIII. Knowledge Gaps and Recommended Research**

During the development of the 2017 LBP CPG, the Work Group identified numerous areas for future research, including areas requiring stronger evidence to support current recommendations as well as research exploring new areas to guide future CPGs.

# Serious Underlying Conditions

Additional areas of research include utility of red flag symptoms for infection as a serious underlying condition given the potential response to early treatment, as well as predictive modeling to help identify specific causes of LBP based on patient factors.

## Diagnostic Imaging

Current imaging, namely plain radiographs, nuclear medicine bone scans, CT, or MRI provide some anatomical information; however, emphasis should remain on clinical correlation to radiographic findings that are secondary to the high rate of false positive findings. In the future, more research is needed in the area of imaging-activated pain physiology neural structures. Further advancements in functional or physiological imaging that can map activated central and peripheral pain neural structures may enhance our understanding of this field.

Future research on diagnostic imaging of LBP should focus on the health risks and economic impact of imaging/diagnostics in this patient population, the cost attributed to these tests and on the subsequent referrals, and determining the main driver for ordering the tests given the lack of medical evidence for their utility (e.g., patient satisfaction, referral patterns/networks, healthcare provider compensation).

### **Behavioral Interventions**

Future research on behavioral interventions for chronic LBP should include an emphasis on optimal dose, validation of shorter treatment protocols, and incorporation of technology to minimize patient burden and maximize access to treatment.

### **Exercise**

More evidence regarding which groups of patients might respond better to a certain exercise intervention is needed. In addition, the dosing of exercise to include duration, intensity, and frequency is required to help guide treatment programs.

September 2017 Page 51 of 110

### Comorbid conditions

Future research is needed on whether or not patients with co-occurring LBP and mental health conditions who are treated for their mental health conditions have improvement in the progression of their LBP over time.

## **Dietary Supplements**

Other than for glucosamine, the evidence review for this guideline update did not identify any studies that met inclusion criteria for the use of nutritional, herbal, and homeopathic supplements. High quality research in this area may help future guideline Work Groups develop recommendations for or against supplements for the treatment of LBP.

# **Pharmacotherapy**

No studies on topical pharmacotherapy preparations met inclusion criteria for the evidence review for this guideline update. High quality research in this area could help future Work Groups develop recommendations for or against the use of topical pharmacotherapy preparations.

Additional research on opioid therapy for LBP is needed to evaluate the immediate benefits and harms of a time-limited course of opioid therapy for acute LBP, the efficacy of opioid therapy in patients with radicular symptoms, and factors that affect the magnitude of treatment responses in patient subgroups.

### Injection and Ablation Therapies

Future research in this area should focus on high quality randomized trials comparing injection/ablation to credible comparators such as sham injection and/or noninvasive care and include both short-term measures of pain and function as well as longer-term effects. Different routes of administration of injection (e.g., interlaminar versus transforaminal) or targets of ablation should be studied further to determine whether the technique or approach matters, and whether the trend for improved outcomes with transforaminal approaches continues. The risk for surgical intervention after these should be assessed and reported. This additional evidence would enable a clearer recommendation on the value of these procedures.

### **MBR Programs**

Research on dosing for MBR programs is needed to mitigate the logistic issues of patients participating. It would be useful to know the best intensity, frequency, and components of the program. In addition, research could confirm whether there are yellow flags or other patient factors that make one level of intensity more desirable than others.

September 2017 Page 52 of 110

# Appendix A: Evidence Review Methodology

# A. Developing the Scope and Key Questions

The CPG Champions, along with the Work Group, were tasked with identifying KQs to guide the systematic evidence review of the literature on LBP. These questions, which were developed in consultation with the Lewin Team, addressed clinical topics of the highest priority for the VA and DoD populations. The KQs follow the population, intervention, comparison, outcome, timing and setting (PICOTS) framework for evidence questions, as established by the Agency for Healthcare Research and Quality (AHRQ). Table A-1 provides a brief overview of the PICOTS typology.

### **Table A-1. PICOTS [139]**

P	Patients, Population, or Problem	A description of the patients of interest. It includes the condition(s), populations or sub-populations, disease severity or stage, co-occurring conditions, and other patient characteristics or demographics.
ı	Intervention or Exposure	Refers to the specific treatments or approaches used with the patient or population. It includes doses, frequency, methods of administering treatments, etc.
		Describes the interventions or care that is being compared with the intervention(s) of interest described above. It includes alternatives such as placebo, drugs, surgery, lifestyle changes, standard of care, etc.
· ·		Describes the specific results of interest. Outcomes can include short, intermediate, and long-term outcomes, or specific results such as quality of life, complications, mortality, morbidity, etc.
Timing, if applicable Describes the duration of time that is of interest for the particular patient interve outcome, benefit, or harm to occur (or not occur).		Describes the duration of time that is of interest for the particular patient intervention and outcome, benefit, or harm to occur (or not occur).
(S)	Setting, if applicable	Describes the setting or context of interest. Setting can be a location (such as primary, specialty, or inpatient care).

The Champions, Work Group, and evidence review team carried out several iterations of this process, each time narrowing the scope of the CPG and the literature review by prioritizing the topics of interest. Due to resource constraints, all developed KQs were not able to be included in the SR. Thus, the Champions and Work Group determined which questions were of highest priority, and those were included in the review. Table A-4 contains the final set of KQs used to guide the SR for this CPG.

### a. Population(s)

For KQ 1, the population of interest is adults 18 years or older with undiagnosed LBP. For all other KQs, the population is adults 18 years or older with LBP.

September 2017 Page 53 of 110

# b. Intervention(s)

**Table A-2. Key Question Specific Interventions** 

Question	Interventions			
	Red flags to screen for serious pathology (e.g., fracture, malignancy) Whether smoking history is associated with specific causes of LBP Whether coronary artery disease history is associated with specific causes of LBP			
L (Diagnosis)	Physical exam: Straight leg raise (a.k.a. Lasègue) Physical exam: Facet loading test (a.k.a. Kemp's, Quadrant) Physical exam: FABER test (a.k.a. Patrick's) Other noninvasive test: X-ray Other noninvasive test: CT Other noninvasive test: MRI Other noninvasive test: EMG			
	Other noninvasive test: Blood test Diagnostic injection: facet Diagnostic injection: trigger point Diagnostic injection: transforaminal Discography			
2 (Self-care)	Physically active life style Weight loss Tobacco cessation Work place ergonomics Tai chi Self-guided exercise program Aquatic therapy Education Yoga			
3 (Other noninvasive non-pharmacologic interventions but requiring the participation of a trained professional)	Guided therapeutic exercises (physical therapy, core strengthening, back strengthening, lumbar stabilization, stretching) Spinal manipulation/mobilization Acupuncture TENS Lumbar traction (non-surgical spinal decompression) Hot pack Lumbar supports E-stim Therapeutic ultrasound Cryotherapy Trigger point dry needling			

September 2017 Page 54 of 110

Question	Interventions
,	Capsaicin or lidoderm
	Opioid analgesics (any)
	Antidepressants (TCAs, SNRIs, SSRIs, bupropion, mirtazapine, vilazodone,
	vortioxetine)
	Anticonvulsants (Carbamazepine, Lacosamide, Lamotrigine,
	Levetiracetam, Oxcarbazepine, Pregabalin/gabapentin, Tiagabine,
	Topiramate, Zonisamide, Valproic acid, Felbamate, Ethosuximide,
	Rufinamide)
	NSAIDs (any)
	Cannabinoids
	Skeletal muscle relaxants (any, for example Cyclobenzaprine,
4 (Pharmacologic agents)	
	Metaxalone, Methocarbamol, Orphenadrine citrate, Carisoprodol,
	Tizanidine, Baclofen, Diazepam, Dantrolene)
	NMDA antagonists (Amantadine, Memantine, Ketamine,
	Dextromethorphan)
	Acetaminophen
	Salicylates
	Oral or topical corticosteroids
	Benzodiazepines
	Ketamine
	Ketoprofen
	OTC topicals (Camphor, Menthol, Paractin, Trolamine)
	Willow bark
	Devil's claw
	Cayenne
	Glucosamine
	N-3 fatty acids
	EPA
	DHA
	Cod liver oil
	Vitamin C
5 (Supplements)	Vitamin E
	Resveratrol
	Flavonoids
	Turmeric
	Curcumin
	Ginger
	Anti-inflammatory diet
	Low arachidonic acid diet
	Chondroiten
	Emu oil
	Epidural injections
	Facet blocks
6 (Injections for locally-acting	Medial branch blocks
agents)	Nerve root blocks
	Sacroiliac joint blocks
	Radiofrequency ablation

September 2017 Page 55 of 110

Question	Interventions		
7 (Combination treatment)	Cross-modality treatment (two or more treatments from different modalities, such as physical therapy combined with opioid analgesics)		
8 (Behavioral treatment)	Psychotherapy Cognitive behavioral therapy Biofeedback Mindfulness based stress reduction Relaxation therapy		
9 (Psychosocial factors as prognostic)	Depression Anxiety ADHD PTSD TBI Divorce Death of spouse or family member Job loss		

# c. Comparator(s)

The table below lists the comparators of interest to this SR. The comparators are listed by the KQ they address.

**Table A-3. Key Question Specific Comparators** 

Question	Comparators			
1 (Diagnosis)	Reference standard (diagnostic accuracy), test vs no test (clinical utility)			
2 (Self-care)	Usual care with no self-care and education, other type of self-care / education compared to one-another			
3 (Other noninvasive non-pharmacologic interventions but requiring the participation of a trained professional)	Usual care or standard care or a different non-invasive therapy compared to one another			
4 (Pharmacologic agents)	Placebo therapy, non-pharmacologic approaches, or a different drug			
5 (Supplements)	Placebo therapy, non-pharmacologic approaches, or a different drug			
6 (Injections)	Usual care or standard care			
7 (Cross-modality treatment)	Typical or usual care; Step-wise approach to treatment with one modality at a time			
8 (Behavioral treatment)	Usual care			
9 (Psychosocial factors as prognostic)	Those without the psychosocial factor			

### d. Outcomes

The following outcomes were of interest in the SR:

- Diagnostic accuracy (sensitivity and specificity using a gold standard)
- Influence of a diagnostic test on the choice of treatment or post-treatment outcomes
- Timing of care (wait or recovery time; speed of intervention)

September 2017 Page 56 of 110

- Pain
- Time to reduction of pain
- Resolution of pain with minimal pharmacotherapy approaches
- Functional status and activities of daily living
- Quality of life
- Disability and work status (including work days lost)
- Reduction in analgesics, healthcare utilization and non-pharmacotherapy treatments;
- Reduction in recurrence of LBP
- Patient satisfaction
- Harms

## e. Timing

The minimum follow-up for effectiveness outcome was 12 weeks, and for diagnostics and harms we set no minimum follow-up. We extracted harms data from any studies reporting effectiveness data for 12 or more weeks.

### f. Setting

Any setting.

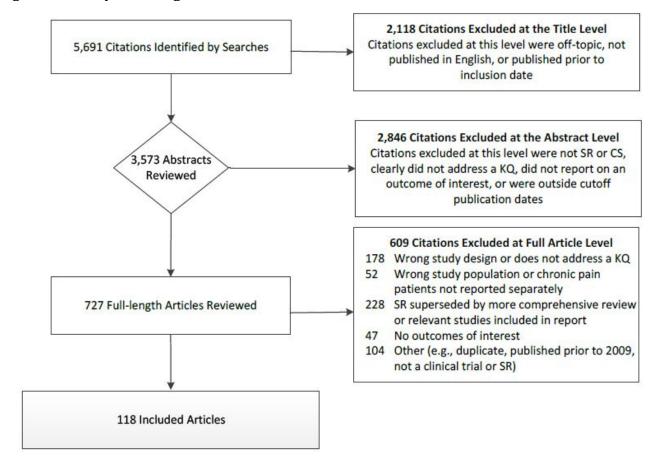
# B. Conducting the Systematic Review

Extensive literature searches using the search terms and strategy included in <u>Appendix H</u> identified 5,691 citations potentially addressing the KQs of interest to this evidence review. Of those, 2,118 were excluded upon title review for clearly not meeting inclusion criteria (e.g., not pertinent to the topic, not published in English, published prior to study inclusion publication date, not a full-length article). Overall, 3,573 abstracts were reviewed with 2,846 of those being excluded for the following reasons: not an SR or clinical study, did not address a KQ of interest to this review, did not enroll a population of interest, or published prior to December 1, 2006. A total of 727 full-length articles were reviewed. Of those, 609 were excluded after a full article review for the following: wrong study design or not addressing a KQ of interest, wrong study population or not reporting chronic pain patients separately, SR superseded by more comprehensive review or relevant studies included in report, no outcomes of interest, or other (e.g., being a duplicate). Reasons for their exclusion are presented in Figure A-1 below.

Overall, 118 articles addressed one or more of the KQs and were considered as evidence in this review. Table A-4 indicates the number of studies that addressed each of the questions.

September 2017 Page 57 of 110

Figure A-1. Study Flow Diagram



Abbreviations: CS: clinical study; KQ: key question; SR: systematic review

September 2017 Page 58 of 110

Table A-4. Evidence Base for Key Questions

Question Number	Question	Number of Studies and Type of Studies	
1a	For adults who present with or have LBP (acute, sub-acute, and chronic LBP),	15 SRs	
	what is the accuracy of history, physical examination, and diagnostic tests, in	7 diagnostic studies	
	identifying the underlying condition?		
1b	For adults who present with or have LBP (acute, sub-acute, and chronic LBP),	1 SR	
	what is the clinical utility of history, physical examination, and diagnostic	2 RCTs	
	tests in improving treatment choices and patient outcomes?		
2	What is the effectiveness of self-care advice, education, or other self-care	7 SRs	
	(weight loss, tobacco cessation, work place ergonomics, yoga, tai chi, and	13 RCTs	
	exercise programs) interventions for improving patient outcomes?		
3	What is the effectiveness of different non-surgical and non-pharmacologic	3 SRs	
	interventions for non-radicular low back pain, radicular low back pain, or	27 RCTs	
	spinal stenosis, and under what circumstances?		
4	For adults with LBP, what is the effect of pharmacotherapy treatment?	5 SR	
		7 RCTs	
5	For adults with LBP, what is the effect of nutritional, herbal, and	1 SR	
	homeopathic supplements?		
6	For adults with LBP, what is the treatment effectiveness of epidural	4 SR	
	injections, facet blocks, nerve root blocks, radiofrequency ablation (RFA)?	9 RCTs	
7	For adults with LBP, which cross-modality combination therapy (e.g.,	4 SR	
	pharmacologic and non-pharmacologic) is most effective?	3 RCTs	
8	For adults with chronic LBP, what is the effectiveness of behavioral	4 SR	
	interventions?	3 RCTs	
9	For adults with low back pain, what is the impact of mental health diagnoses	1 SR	
	(e.g., depression, anxiety, ADHD, PTSD, TBI) or psychosocial stressors (e.g.,	4 prognostic studies	
	divorce, death, job loss) on treatment outcomes?		
	Total Evidence Base	118 articles	

# a. Criteria for Study Inclusion/Exclusion

### i. General Criteria

- Clinical studies or SRs published on or after December 1, 2006 to October 21, 2016. If multiple SRs addressed a key question, the most recent and/or comprehensive review was selected. SRs were supplemented with clinical studies published subsequent to the search dates of the SR.
- Studies must have been published in English.
- Publication must have been a full clinical study or SR; abstracts alone were not included.
   Similarly, letters, editorials, and other publications that were not full-length clinical studies were not accepted as evidence.
- Studies of diagnostic tests must have provided data on at least 50 patients. Studies of treatments must have reported outcome data on at least 50 patients (and at least 25 per study group) unless otherwise noted (see Key Question Specific Criteria below)
- Study must have reported an outcome of interest.

September 2017 Page 59 of 110

Study must have enrolled a patient population in which at least 80% of patients had LBP and
were age 18 years or older. If the percentage was less than 80%, then data must have been
reported separately for this patient subgroup. Study must have reported in its abstract that
patients had LBP. For studies of treatments, patients must not have had spondylolisthesis,
postoperative LBP, or pregnancy-related LBP.

For each treatment or diagnostic test of each KQ, it was first determined whether any SRs addressed the question. If so, only the most comprehensive SR was included. Studies published after the SR's last search date were also considered. If there was not an SR that addressed the KQ, studies from December 2006 onward that met all the inclusion criteria for that KQ were included.

## ii. Key Question Specific Criteria

- For studies of accuracy (KQ1a), studies/reviews must have reported both sensitivity and specificity (or sufficient information to calculate both values), and must have used a reference standard that was independent of the index test.
- For studies of clinical utility (KQ1b), studies/reviews must have compared two groups of
  patients: one that received the diagnostic test of interest, and one that did not, in order to
  measure the influence of the test on treatment choice and/or patient outcomes.
- For KQs 2 through 8, reviews must have been SRs directly addressing a KQ, and studies must have randomly assigned patients to different treatments (the comparator could have been a placebo treatment). The minimum follow-up was 12 weeks for effectiveness outcomes, and there was no minimum follow-up for harms outcomes. Harms data were extracted from any studies reporting effectiveness data beyond 12 weeks follow-up.
- For KQ 9, studies/reviews did not have to be randomized, but did have to compare the post-treatment outcomes of patients who had a psychosocial risk factor to the post-treatment outcomes of patients who did not have that psychosocial risk factor but were otherwise similar.

### b. Literature Search Strategy

Information regarding the bibliographic databases, date limits, and platform/provider can be found in <u>Table A-5</u>, below. Additional information on the search strategies, including topic-specific search terms and search strategies can be found in <u>Appendix H</u>.

September 2017 Page 60 of 110

**Table A-5. Bibliographic Database Information** 

Name	Date Limits	Platform/Provider
Agency for Healthcare Research and Quality (AHRQ)	2006 – September 2016	U.S. Department of Health & Human Services
Canadian Agency for Drugs and Technologies in Health (CADTH)	2006 – September 2016	Canadian Agency for Drugs and Technologies in Health
CINAHL	2006 – September 2016	EBSCO Host
Cochrane Library	2006 – September 2016	John Wiley & Sons, Ltd.
Embase.com (Includes EMBASE and Medline Records)	2006 – September 2016	Elsevier
Healthcare Standards (HCS)	2006 – September 2016	ECRI Institute
National Guideline Clearinghouse (NGC)	2006 – September 2016	AHRQ
National Institute for Health and Care Excellence (NICE)	2006 – September 2016	National Institute for Health and Care Excellence
PsycINFO	2006 – September 2016	OVID Technologies, Inc.
PubMed (In-process and publisher supplied records)	2006 – September 2016	National Library of Medicine

# C. Convening the Face-to-face Meeting

In consultation with the COR, the Champions, and the Work Group, the Lewin Team convened a three and a half day face-to-face meeting of the CPG Champions and Work Group members on December 6-9, 2016. These experts were gathered to develop and draft the clinical recommendations for an update to the 2007 LBP CPG. Lewin presented findings from the evidence review of KQs 1-9 in order to facilitate and inform the process.

Under the direction of the Champions, the Work Group members were charged with interpreting the results of the evidence review, and asked to categorize and carry forward recommendations from the 2007 LBP CPG, modifying the recommendations as necessary. The members also developed new clinical practice recommendations not presented in the 2007 LBP CPG, based on the 2016 evidence review. The subject matter experts were divided into three smaller subgroups at this meeting.

As the Work Group members drafted clinical practice recommendations, they also assigned a grade for each recommendation based on a modified GRADE and USPSTF methodology. Each recommendation was graded by assessing the quality of the overall evidence base, the associated benefits and harms, the variation in values and preferences, and other implications of the recommendation.

In addition to developing recommendations during the face-to-face meeting, the Work Group members also revised the 2007 LBP CPG algorithm to reflect the new and amended recommendations. They discussed the available evidence as well as changes in clinical practice since 2007, as necessary, to update the algorithm.

September 2017 Page 61 of 110

## D. Grading Recommendations

This CPG uses the GRADE methodology to assess the quality of the evidence base and assign a grade for the strength for each recommendation. The GRADE system uses the following four domains to assess the strength of each recommendation: [10]

- Balance of desirable and undesirable outcomes
- Confidence in the quality of the evidence
- Values and preferences
- Other implications, as appropriate, e.g.,:
  - Resource Use
  - Equity
  - Acceptability
  - Feasibility
  - Subgroup considerations

The following sections further describe each domain.

Balance of desirable and undesirable outcomes refers to the size of anticipated benefits (e.g., increased longevity, reduction in morbid event, resolution of symptoms, improved quality of life, decreased resource use) and harms (e.g., decreased longevity, immediate serious complications, adverse event, impaired quality of life, increased resource use, inconvenience/hassle) relative to each other. This domain is based on the understanding that the majority of clinicians will offer patients therapeutic or preventive measures as long as the advantages of the intervention exceed the risks and adverse effects. The certainty or uncertainty of the clinician about the risk-benefit balance will greatly influence the strength of the recommendation.

Some of the discussion questions that fall under this domain include:

- Given the best estimate of typical values and preferences, are you confident that the benefits outweigh the harms and burden or vice versa?
- Are the desirable anticipated effects large?
- Are the undesirable anticipated effects small?
- Are the desirable effects large relative to undesirable effects?

Confidence in the quality of the evidence reflects the quality of the evidence base and the certainty in that evidence. This second domain reflects the methodological quality of the studies for each outcome variable. In general, the strength of recommendation follows the level of evidence, but not always, as other domains may increase or decrease the strength. The evidence review used for the development of recommendations for LBP, conducted by ECRI, assessed the confidence in the quality of the evidence base and assigned a rate of "High," "Moderate," "Low," or "Very Low."

September 2017 Page 62 of 110

The elements that go into the confidence in the quality of the evidence include:

- Is there high or moderate quality evidence that answers this question?
- What is the overall certainty of this evidence?

Values and preferences is an overarching term that includes patients' perspectives, beliefs, expectations, and goals for health and life. More precisely, it refers to the processes that individuals use in considering the potential benefits, harms, costs, limitations, and inconvenience of the therapeutic or preventive measures in relation to one another. For some, the term "values" has the closest connotation to these processes. For others, the connotation of "preferences" best captures the notion of choice. In general, values and preferences increase the strength of the recommendation when there is high concordance and decrease it when there is great variability. In a situation in which the balance of benefits and risks are uncertain, eliciting the values and preferences of patients and empowering them and their surrogates to make decisions consistent with their goals of care becomes even more important. A recommendation can be described as having "similar values," "some variation," or "large variation" in typical values and preferences between patients and the larger populations of interest.

Some of the discussion questions that fall under the purview of values and preferences include:

- Are you confident about the typical values and preferences and are they similar across the target population?
- What are the patient's values and preferences?
- Are the assumed or identified relative values similar across the target population?

Other implications consider the practicality of the recommendation, including resources use, equity, acceptability, feasibility and subgroup considerations. Resource use is related to the uncertainty around the cost-effectiveness of a therapeutic or preventive measure. For example statin use in the frail elderly and others with multiple co-occurring conditions may not be effective and depending on the societal benchmark for willingness to pay, may not be a good use of resources. Equity, acceptability, feasibility, and subgroup considerations require similar judgments around the practically of the recommendation.

The framework below (Table A-6) was used by the Work Group to guide discussions on each domain.

Table A-6. Evidence to Recommendation Framework

Decision Domain	Judgment			
Balance of desirable and undesirable outcomes				
<ul> <li>Given the best estimate of typical values and preferences, are you confident that the benefits outweigh the harms and burden or vice versa?</li> <li>Are the desirable anticipated effects large?</li> <li>Are the undesirable anticipated effects small?</li> <li>Are the desirable effects large relative to undesirable effects?</li> </ul>	Benefits outweigh harms/burden Benefits slightly outweigh harms/burden Benefits and harms/burden are balanced Harms/burden slightly outweigh benefits Harms/burden outweigh benefits			

September 2017 Page 63 of 110

Decision Domain	Judgment			
Confidence in the quality of the evidence				
<ul><li>Is there high or moderate quality evidence that answers this question?</li><li>What is the overall certainty of this evidence?</li></ul>	High Moderate Low Very low			
Values and preferences				
<ul> <li>Are you confident about the typical values and preferences and are they similar across the target population?</li> <li>What are the patient's values and preferences?</li> <li>Are the assumed or identified relative values similar across the target population?</li> </ul>	Similar values Some variation Large variation			
Other implications (e.g., resource use, equity, acceptability, feasi	bility, subgroup considerations)			
<ul> <li>Are the resources worth the expected net benefit from the recommendation?</li> <li>What are the costs per resource unit?</li> <li>Is this intervention generally available?</li> <li>Is this intervention and its effects worth withdrawing or not allocating resources from other interventions?</li> <li>Is there lots of variability in resource requirements across settings?</li> </ul>	Various considerations			

The strength of a recommendation is defined as the extent to which one can be confident that the desirable effects of an intervention outweigh its undesirable effects and is based on the framework above, which combines the four domains. [10] GRADE methodology does not allow for recommendations to be made based on expert opinion alone. While strong recommendations are usually based on high or moderate confidence in the estimates of effect (quality of the evidence) there may be instances where strong recommendations are warranted even when the quality of evidence is low. [140] In these types of instances where the balance of desirable and undesirable outcomes and values and preferences played large roles in determining the strength of a recommendation, this is explained in the discussion section for the recommendation.

The GRADE of a recommendation is based on the following elements:

- Four decision domains used to determine the strength and direction (described above)
- Relative strength (Strong or Weak)
- Direction (For or Against)

The relative strength of the recommendation is based on a binary scale, "Strong" or "Weak." A strong recommendation indicates that the Work Group is highly confident that desirable outcomes outweigh undesirable outcomes. If the Work Group is less confident of the balance between desirable and undesirable outcomes, they present a weak recommendation.

Similarly, a recommendation for a therapy or preventive measure indicates that the desirable consequences outweigh the undesirable consequences. A recommendation against a therapy or preventive measure indicates that the undesirable consequences outweigh the desirable consequences.

September 2017 Page 64 of 110

Occasionally, instances may occur when the Work Group feels there is insufficient evidence to make a recommendation for or against a particular therapy or preventive measure. This can occur when there is an absence of studies on a particular topic that met evidence review inclusion criteria, studies included in the evidence review report conflicting results, or studies included in the evidence review report inconclusive results regarding the desirable and undesirable outcomes.

Using these elements, the grade of each recommendation is presented as part of a continuum:

- Strong For (or "We recommend offering this option ...")
- Weak For (or "We suggest offering this option ...")
- No recommendation for or against (or "There is insufficient evidence ...")
- Weak Against (or "We suggest not offering this option ...")
- Strong Against (or "We recommend against offering this option ...")

Note that weak (For or Against) recommendations may also be termed "Conditional," "Discretionary," or "Qualified." Recommendations may be conditional based upon patient values and preferences, the resources available, or the setting in which the intervention will be implemented. Recommendations may be at the discretion of the patient and clinician, or they may be qualified with an explanation about the issues that would lead decisions to vary.

# E. Recommendation Categorization

# a. Categorizing Recommendations with an Updated Review of the Evidence

Recommendations were first categorized by whether or not they were based on an updated review of the evidence. If evidence had been reviewed, recommendations were categorized as "New-added," "New-replaced," "Not changed," "Amended," or "Deleted."

"Reviewed, New-added" recommendations were original, new recommendations that were not in the 2007 LBP CPG. "Reviewed, New-replaced" recommendations were in the previous version of the guideline, but were modified to align with the updated review of the evidence. These recommendations could have also included clinically significant changes to the previous version. Recommendations categorized as "Reviewed, Not changed" were carried forward from the previous version of the CPG unchanged.

For recommendations carried forward to the updated CPG with review of the evidence and slightly modified wording, the "Reviewed, Amended" recommendation category was used. This allowed for non-substantive (i.e., not clinically meaningful) language changes deemed necessary. The evidence used to support these recommendations was carried forward from the previous version of the CPG and/or was identified in the evidence review for the update.

Recommendations could have also been designated "Reviewed, Deleted." These were recommendations from the previous version of the CPG that were not brought forward to the updated guideline after review of the evidence. This occurred if the evidence supporting the recommendations was out of date, to the extent that there was no longer any basis to recommend a particular course of care and/or new evidence suggests a shift in care, rendering recommendations in the previous version of the guideline obsolete.

September 2017 Page 65 of 110

## b. Categorizing Recommendations without an Updated Review of the Evidence

There were also cases in which it was necessary to carry forward recommendations from the previous version of the CPG without an SR of the evidence. Due to time and budget constraints, the update of the LBP CPG could not review all available evidence on the diagnosis and treatment of LBP, but instead focused its KQs on areas of new or updated scientific research or areas that were not previously covered in the CPG.

For areas of research that have not changed, and for which recommendations made in the previous version of the guideline were still relevant, recommendations could have been carried forward to the updated guideline without an updated SR of the evidence. The support for these recommendations in the updated CPG was thus also carried forward from the previous version of the CPG. These recommendations were categorized as "Not reviewed." If evidence had not been reviewed, recommendations could have been categorized as "Not changed," Amended," or "Deleted."

"Not reviewed, Not changed" recommendations refer to recommendations from the previous version of the LBP CPG that were carried forward unchanged to the updated version. The category of "Not reviewed, Amended" was used to designate recommendations which were modified with non-substantive language changes from the 2007 LBP CPG.

Recommendations could also have been categorized as "Not reviewed, Deleted" if they were determined to be out of scope. A recommendation was out of scope if it pertained to a topic (e.g., population, care setting, treatment, condition) outside of the scope for the updated CPG as defined by the Work Group.

The categories for the recommendations included in the 2017 version of the guideline are noted in the Recommendations. The categories for the recommendations from the 2007 LBP CPG are noted in Appendix E.

### c. Recommendation Categories and Definitions

For use in the 2017 LBP CPG, a set of recommendation categories was adapted from those used by the United Kingdom National Institute for Health and Clinical Excellence (NICE).[14,15] These categories, along with their corresponding definitions, were used to account for the various ways in which recommendations could have been updated from the 2007 LBP CPG. The categories and definitions can be found in Table A-7.

September 2017 Page 66 of 110

**Table A-7. Recommendation Categories and Definitions** 

Evidence Reviewed*	Recommendation Category*	Definition*	
	New-added	New recommendation following review of the evidence	
	New-replaced	Recommendation from previous CPG that has been carried over to the updated CPG that has been changed following review of the evidence	
Reviewed	Not changed	Recommendation from previous CPG that has been carried forward to the updated CPG where the evidence has been reviewed but the recommendation is not changed	
	Amended	Recommendation from the previous CPG that has been carried forward to updated CPG where the evidence has been reviewed and a minor amendm has been made	
	Deleted	Recommendation from the previous CPG that has been removed based on review of the evidence	
	Not changed	Recommendation from previous CPG that has been carried forward to the updated CPG, but for which the evidence has not been reviewed	
Not reviewed	Amended	Recommendation from the previous CPG that has been carried forward to the updated CPG where the evidence has not been reviewed and a minor amendment has been made	
	Deleted	Recommendation from the previous CPG that has been removed because it was deemed out of scope for the updated CPG	

<sup>\*</sup>Adapted from the NICE guideline manual (2012) [14] and Garcia et al. (2014) [15] Abbreviation: CPG: clinical practice guideline

# F. Drafting and Submitting the Final Clinical Practice Guideline

Following the face-to-face meeting, the Champions and Work Group members were given writing assignments to craft discussion sections to support each of the new recommendations and/or to update discussion sections from the 2007 LBP CPG to support the amended "carried forward" recommendations. The Work Group also considered tables, appendices, and other sections from the 2007 LBP CPG for inclusion in the update. During this time, the Champions and Work Group also made additional revisions to the algorithm, as necessary.

After developing the initial draft of the updated CPG, an iterative review process was used to solicit feedback on and make revisions to the CPG. Once they were developed, the first two drafts of the CPG were posted on a wiki website for a period of 14-20 business days for internal review and comment by the Work Group. All feedback submitted during each review period was reviewed and discussed by the Work Group and appropriate revisions were made to the CPG.

Draft 3 of the CPG was made available for peer review and comment. This process is described in <a href="Peer">Peer</a> Review Process. After revisions were made based on the feedback received during the peer review and comment period, the Champions presented the CPG to the EBPWG for their approval. Changes were made based on feedback from the EBPWG and the guideline was finalized.

The Work Group also produced a set of guideline toolkit materials which included a provider summary, pocket card, and a patient summary. The final 2017 LBP CPG was submitted to the EBPWG in September 2017.

September 2017 Page 67 of 110

# Appendix B: Dosing for Select Pharmacologic Agents<sup>1</sup>

Generic	Starting Dose	Max/Day	Half-life (t½) (hrs)			
Muscle Relaxants						
TIZANIDINE	2-4 mg TID	36 mg	2.5			
BACLOFEN	5 mg TID	80 mg	~ 3.75			
CYCLOBENZAPRINE <sup>2</sup>	5 mg TID	30 mg	18			
METAXALONE <sup>2</sup>	800 mg TID	3,200 mg	~ 9			
METHOCARBAMOL <sup>2</sup>	1.5 gm QID	4.5 gm	1-2			
ORPHENADRINE <sup>2</sup>	100 mg BID	200 mg	14-16			
	Antidepressants	3				
AMITRIPTYLINE <sup>2</sup>	10-25 mg QHS	150 mg	~ 13-36			
DESPIRAMINE <sup>2</sup>	10-25 mg QHS	150 mg	15-24			
NORTRIPTYLINE <sup>2</sup>	10-25 mg QHS	150 mg	14-51			
DULOXETINE <sup>2</sup>	30 mg QD	60 mg	~ 12			
VENLAFAXINE ER	37.5 mg QD	225 mg	~ 11			
	NSAIDs <sup>3</sup>					
KETOROLAC	10 mg q 4-6H	40 mg	~ 5			
KETOPROFEN	N 50 mg QID 300 mg		2-4			
INDOMETHACIN	25 mg q 8H	200 mg	2.6-11.2			
NAPROXEN	250 mg BID	1500 mg	12-17			
IBUPROFEN	400 mg q 4-6H	3200 mg	~ 2			
NABUMETONE	1000 mg QD	2000 mg	~ 24			
PIROXICAM	20 mg QD	20 mg	50			
SALSALATE	1000 mg TID	3000 mg	~1			
SULINDAC	150mg BID	400 mg	7.8			
DICLOFENAC NA	50-75 mg BID	150-200 mg	~ 2			
CELECOXIB	100 mg BID	400 mg	~ 11			
MELOXICAM	5-7.5 mg QD	15 mg	~ 15-22			
ETODOLAC	200 mg q 8H	1000 mg	6.4			

Dosing recommendations obtained from the FDA individual product prescribing information. Listed in order of increased COX-2 Selectivity, more selective at the bottom:[107,141,142]

More COX 1 Selective < 5-fold COX-2 Selective 5-50 fold COX-2 Selective

Abbreviations: BID: twice a day; COX-2: cyclooxygenase-2; gm: gram; hrs: hours; max: maximum; mg: milligram; NSAIDs: nonsteroidal anti-inflammatory drug; q 4-6H: every 4-6 hours; q 8H: every 8 hours; QD: one a day; QID: four times a day; QHS: nightly at bedtime; TID: three times a day

September 2017 Page 68 of 110

<sup>&</sup>lt;sup>1</sup> Consult full prescribing information for individual drugs; dosing and half-life may be altered by patient age, renal and hepatic function, and product formulation; consider reduced dosing and/or frequency in the elderly.

<sup>&</sup>lt;sup>2</sup> Use not recommended in patients > 65 years of age per American Geriatrics Society 2015 Updated Beers Criteria.[114]

<sup>&</sup>lt;sup>3</sup> Avoid chronic use in the elderly, unless other alternatives are not effective and patient can take a gastroprotective agent (proton pump inhibitor or misoprostol).

# **Appendix C: Evidence Table**

Re	ecommendation	2007 Grade <sup>12</sup>	Evidence <sup>13</sup>	Strength of Recommendation 14	Recommendation Category <sup>15</sup>
1.	For patients with low back pain, we recommend that clinicians conduct a history and physical examination, that should include identifying and evaluating neurologic deficits (e.g., radiculopathy, neurogenic claudication), red flag symptoms associated with serious underlying pathology (e.g., malignancy, fracture, infection), and psychosocial factors.	Strong recommendation	[23-29]	Strong for	Reviewed, Amended
2.	For patients with low back pain, we suggest performing a mental health screening as part of the low back pain evaluation and taking results into consideration during selection of treatment.	Weak recommendation	[30-32]	Weak for	Reviewed, New- replaced
3.	For patients with acute axial low back pain (i.e., localized, non-radiating), we recommend against routinely obtaining imaging studies or invasive diagnostic tests.	Strong recommendation	[26,33-37,39,41] Additional References: [38,40]	Strong against	Reviewed, Amended
4.	For patients with low back pain, we recommend diagnostic imaging and appropriate laboratory testing when neurologic deficits are serious or progressive or when red flag symptoms are present.	Strong recommendation	[26,37,42-46]	Strong for	Reviewed, Amended
5.	For patients with low back pain greater than one month who have not improved or responded to initial treatments, there is inconclusive evidence to recommend for or against any diagnostic imaging.	Not applicable	[36,37,47,48,51] Additional References: [49,50]	Not applicable	Reviewed, New-added
6.	For patients with chronic low back pain, we recommend providing evidence-based information with regard to their expected course, advising patients to remain active, and providing information about self-care options.	Strong recommendation	[ <u>23,25,36,51-54,56</u> ] Additional Reference: [ <u>55</u> ]	Strong for	Reviewed, Amended

September 2017 Page 69 of 110

<sup>&</sup>lt;sup>12</sup> The 2007 VA/DoD LBP CPG also used the GRADE evidence grading system.

<sup>&</sup>lt;sup>13</sup> The evidence column indicates studies that support each recommendation. For new recommendations, developed by the 2017 guideline Work Group, the literature cited corresponds directly to the 2016 evidence review. For recommendations that have been carried over from the 2007 VA/DoD LBP CPG, slight modifications were made to the language in order to better reflect the current evidence and/or the change in grading system used for assigning the strength of each recommendation (USPSTF to GRADE). For these "modified" recommendations, the evidence column indicates "additional evidence," which can refer to either 1) studies that support the recommendation and which were identified through the 2016 evidence review, or 2) relevant studies that support the recommendation, but which were not systematically identified through a literature review.

<sup>&</sup>lt;sup>14</sup> Refer to the Grading Recommendations section for more information on how the strength of the recommendation was determined using GRADE methodology.

<sup>&</sup>lt;sup>15</sup> Refer to the Recommendation Categorization section for more information on the description of the categorization process and the definition of each category.

Recommendation	2007 Grade <sup>12</sup>	Evidence <sup>13</sup>	Strength of Recommendation 14	Recommendation Category <sup>15</sup>
7. For patients with chronic low back pain, we suggest adding a structured education component, including pain neurophysiology, as part of a multicomponent self-management intervention.	Not applicable	[ <u>57,60,61</u> ] Additional Reference: [ <u>58,59</u> ]	Weak for	Reviewed, New-added
8. For patients with chronic low back pain, we recommend cognitive behavioral therapy.	Weak recommendation	[3,62,64,65] Additional References: [63,66-71]	Strong for	Reviewed, New- replaced
9. For patients with chronic low back pain, we suggest mindfulness-based stress reduction.	Weak recommendation	[3,62,64,65] Additional References: [63,66-71]	Weak for	Reviewed, New- replaced
10. For patients with acute low back pain, there is insufficient evidence to support the use of specific clinician-directed exercise.	Not applicable	[3,72-75] Additional Reference: [76]	Not applicable	Reviewed, New- replaced
11. For patients with chronic low back pain, we suggest offering clinician-directed exercises.	Weak recommendation	[3,72-75] Additional Reference: [76]	Weak for	Reviewed, New- replaced
12. For patients with acute or chronic low back pain, we suggest offering spinal mobilization/manipulation as part of a multimodal program.	Weak recommendation	[77-84]	Weak for	Reviewed, New- replaced
13. For patients with acute low back pain, there is insufficient evidence to support the use of acupuncture.	Not applicable	[ <u>3</u> ]	Not applicable	Reviewed, New- replaced
14. For patients with chronic low back pain, we suggest offering acupuncture.	Weak recommendation	[ <u>3</u> ]	Weak for	Reviewed, New- replaced
15. For acute or chronic low back pain, there is insufficient evidence for or against the use of lumbar supports.	Not applicable	[3,85-87]	Not applicable	Reviewed, Amended
16. For patients with chronic low back pain, we suggest offering an exercise program, which may include Pilates, yoga, and tai chi.	Weak recommendation	[3,92-97] Additional References: [88-91]	Weak for	Reviewed, New- replaced
17. For patients with low back pain, there is insufficient evidence to support the use of ultrasound.	Not applicable	[3]	Not applicable	Reviewed, New-added
18. For patients with low back pain, there is inconclusive evidence to support the use of transcutaneous electrical nerve stimulation (TENS).	Not applicable	[ <u>98]</u>	Not applicable	Reviewed, New-added

September 2017 Page 70 of 110

Recommendation	2007 Grade <sup>12</sup>	Evidence <sup>13</sup>	Strength of Recommendation 14	Recommendation Category <sup>15</sup>
19. For patients with low back pain, there is insufficient evidence to support the use of lumbar traction.	Not applicable	[99-102]	Not applicable	Reviewed, New-added
20. For patients with low back pain, there is insufficient evidence to support the use of electrical muscle stimulation.	Not applicable	[ <u>3,103</u> ]	Not applicable	Reviewed, New-added
21. For patients with acute or chronic low back pain, we recommend treating with nonsteroidal anti-inflammatory drugs, with consideration of patient-specific risks.	Strong recommendation	[3,104-106] Additional References: [107-109]	Strong for	Reviewed, Amended
22. For patients with chronic low back pain, we suggest offering treatment with duloxetine, with consideration of patient-specific risks.	Not applicable	[3,110-112] Additional References: [113,114]	Weak for	Reviewed, New-added
23. For patients with acute low back pain or acute exacerbations of chronic low back pain, we suggest offering a non-benzodiazepine muscle relaxant for short-term use.	Not applicable	[3,115,116]	Weak for	Reviewed, New-added
24. For patients with chronic low back pain, we suggest against offering a non-benzodiazepine muscle relaxant.	Not applicable	[ <u>3,115,116</u> ]	Weak against	Reviewed, New-added
25. For patients with low back pain, we recommend against benzodiazepines.	Strong recommendation	[3,117] Additional Reference: [118]	Weak against	Reviewed, New- replaced
26. For patients with acute or chronic low back pain with or without radiculopathy, we recommend against the use of systemic corticosteroids (oral or intramuscular injection).	Strong recommendation	[3, <u>119]</u> Additional Reference: [ <u>120]</u>	Strong against	Reviewed, Amended
27. For patients with low back pain, we recommend against initiating long-term opioid therapy. For patients who are already prescribed long-term opioid therapy, refer to the VA/DoD CPG for the Management of Opioid Therapy for Chronic Pain. 16	Strong recommendation	[3,23,115]	Strong against	Reviewed, New- replaced

September 2017 Page 71 of 110

<sup>&</sup>lt;sup>16</sup> See the VA/DoD Clinical Practice Guideline for the Management of Opioid Therapy for Chronic Pain. Available at: <a href="http://www.healthquality.va.gov/guidelines/Pain/cot/">http://www.healthquality.va.gov/guidelines/Pain/cot/</a>

Recommendation	2007 Grade <sup>12</sup>	Evidence <sup>13</sup>	Strength of Recommendation 14	Recommendation Category <sup>15</sup>
28. For patients with acute low back pain or acute exacerbations of chronic low back pain, there is insufficient evidence to recommend for or against the use of time-limited opioid therapy. Given the significant risks and potential benefits of opioid therapy, patients should be evaluated individually, including consideration of psychosocial risks and alternative non-opioid treatments. Any opioid therapy should be kept to the shortest duration and lowest dose possible.	Strong recommendation	[ <u>3,23,115]</u>	Not applicable	Reviewed, New- replaced
29. For patients with acute or chronic low back pain, there is insufficient evidence to recommend for or against the use of time-limited (less than seven days) acetaminophen therapy.	Strong recommendation	[ <u>3,121,122</u> ]	Not applicable	Reviewed, New- replaced
30. For patients with chronic low back pain, we recommend against the chronic use of oral acetaminophen.	Strong recommendation	[3,121,122]	Strong against	Reviewed, New- replaced
31. For the treatment of acute or chronic low back pain, including patients with both radicular and non-radicular low back pain, there is insufficient evidence to recommend for or against the use of antiepileptics including gabapentin and pregabalin.	Strong recommendation	[ <u>3,123-125</u> ] Additional Reference: [ <u>126</u> ]	Not applicable	Reviewed, New- replaced
32. For the treatment of low back pain, there is insufficient evidence to recommend for or against the use of topical preparations.	Strong recommendation	None	Not applicable	Reviewed, New-added
33. For the treatment of low back pain, there is insufficient evidence to recommend for or against nutritional, herbal, and homeopathic supplements.	Not applicable	[ <u>127]</u>	Not applicable	Reviewed, New-added
34. For the long-term reduction of radicular low back pain, non-radicular low back pain, or spinal stenosis, we recommend against offering spinal epidural steroid injections.	Not applicable	[3,128-134]	Strong against	Reviewed, New-added
35. For the very short-term effect (less than or equal to two weeks) of reduction of radicular low back pain, we suggest offering epidural steroid injection.	Not applicable	[3,128-134]	Weak for	Reviewed, New-added
36. For the treatment of low back pain, we suggest against offering intra- articular facet joint steroid injections.	Not applicable	[3,128-134]	Weak against	Reviewed, New-added
37. For patients with low back pain, there is inconclusive evidence to recommend for or against medial branch blocks and radiofrequency ablative denervation.	Not applicable	[ <u>3,128-134</u> ]	Not applicable	Reviewed, New-added

September 2017 Page 72 of 110

Recommendation	2007 Grade <sup>12</sup>	Evidence <sup>13</sup>	Strength of Recommendation 14	Recommendation Category <sup>15</sup>
38. For selected patients with chronic low back pain not satisfactorily responding to more limited approaches, we suggest offering a multidisciplinary or interdisciplinary rehabilitation program which should include at least one physical component and at least one other component of the biopsychosocial model (psychological, social, occupational) used in an explicitly coordinated manner.	Not applicable	[135-138]	Weak for	Reviewed, New- replaced

September 2017 Page 73 of 110

# **Appendix D: Glossary**

	Term	Definition
	Acute low back pain	LBP present for fewer than four weeks, sometimes grouped with subacute LBP as symptoms present for fewer than three months.
	Cauda equina syndrome	Compression on nerve roots in the lumbosacral spine, usually due to a massive, centrally herniated disc, which can result in urinary retention or incontinence from loss of sphincter function, bilateral motor weakness of the lower extremities, and saddle anesthesia.
	Chronic low back pain	LBP present for more than three months.
	Herniated disc	Herniation of the nucleus pulposus of an intervertebral disc through its fibrous outer covering, which can result in compression of adjacent nerve roots or other structures.
	Neurogenic claudication	Symptoms of leg pain (and occasionally weakness) while walking or standing, relieved by sitting or spinal flexion, associated with spinal stenosis.
	Non-radicular back pain	Pain perceived as arising from the vertebral column or related tissues, not including clear disorders or diseases of the nerve roots and their ganglions.
	Non-specific low back pain	Axial/non-radiating pain occurring primarily in the back with no signs of a serious underlying condition (such as cancer, infection, or cauda equina syndrome), spinal stenosis or radiculopathy, or another specific spinal cause (such as vertebral compression fracture or ankylosing spondylitis). Degenerative changes on lumbar imaging are usually considered nonspecific, as they correlate poorly with symptoms.
General	Radicular back pain	Pain in the back and lower limb with a component below the knee, associated with a disorder of the spinal nerve root and/or its ganglion. This pain may or may not be accompanied by objective evidence of impaired conduction (radiculopathy).
	Radiculopathy	Radiculopathy is objectively determined, impaired conduction down a spinal nerve or its roots. This can be diagnosed by clinical exam (loss of sensation, muscle stretch reflexes, or strength) or via electrodiagnostic testing.  Radiculopathy may or may not be accompanied by radicular pain.
	Referred pain	Pain which the patient reports spreads away from the primary site such as to the limbs, and is perceived in regions other than the primary site. Referred pain may have a radiating quality but does not involve stimulation of nerve roots, which differentiates it from radicular pain.
	Sciatica	An outdated term for referred pain into the lower limbs associated with lumbar back pain.
	Spinal stenosis	Pain in the back thought to be related to degenerative narrowing of the spinal canal and neural foramina. Spinal stenosis pain is thought to be from compression of neurovascular structures and involves referred pain into the lower limbs and may or may not include radicular pain or radiculopathy.
	Straight-leg-raise test	A procedure in which the hip is flexed with the knee extended in order to passively stretch the sciatic nerve and elicit symptoms suggesting nerve root tension. A positive test is usually considered reproduction of the patient's sciatica when the leg is raised between 30 and 70 degrees. Reproduction of the patient's sciatica when the unaffected leg is lifted is referred to as a positive "crossed" straight-leg-raise test.

September 2017 Page 74 of 110

	Term	Definition
	Acupuncture	An intervention consisting of the insertion of needles at strategic points on a body, most commonly used to treat pain.
	Back school	An intervention consisting of education and a skills program, including exercise therapy, in which all lessons are given to groups of patients and supervised by a paramedical therapist or medical specialist.
	Clinician-directed exercise	A supervised exercise program or formal home exercise regimen, ranging from programs aimed at general physical fitness or aerobic exercise to programs aimed at muscle strengthening, flexibility, stretching, or a combination of these elements.
	Cognitive behavioral therapy	An intervention that involves examining and changing cognitions and behaviors that perpetuate pain as well as using relaxation and exposure techniques to reduce symptom-related distress.
	Mindfulness-based stress reduction	A structured intervention based on the concept of mindfulness (i.e., attending to the present moment, without judgment) with components of relaxation, exercise and meditation.
	Motor control exercise	A form of rehabilitative exercise that aims to restore coordinated and efficient use of the muscles that control and support the spine. Patients are initially guided to practice normal use of the muscles during simple tasks. As the patient's skill increases the exercises are progressed to more complex and functional tasks.
	Multidisciplinary/ interdisciplinary rehabilitation program	An intervention that combines and coordinates physical, vocational, and behavioral/psychological components and is provided by multiple health care professionals with different clinical backgrounds. The intensity and content of the program varies widely. Interdisciplinary emphasizes collaboration among providers from different disciplines in implementing a joint treatment plan.
Interventions	Pilates	A system of exercise using special apparatus, designed to improve physical
	Progressive	strength, flexibility, and posture.  A technique which involves the deliberate tensing and relaxation of muscles, in
	relaxation	order to facilitate the recognition and release of muscle tension.
	Self-care options	Interventions that can be readily implemented by patients without seeing a clinician or that can be implemented on the basis of advice provided at a routine clinic visit.
	Self-care education book	Reading material (e.g., books, leaflets) that provide education and self-care advice for patients with LBP. Although the specific content varies, self-care materials are generally based on principles from published CPGs and encourage a return to normal activity, adoption of a fitness program, appropriate lifestyle modification, and provide advice on coping strategies and managing flares.
	Spinal manipulation	Manual therapy in which loads are applied to the spine by using short- or long-lever methods and high-velocity thrusts are applied to a spinal joint beyond its restricted range of movement. Spinal mobilization, or low-velocity, passive movements within or at the limit of joint range, is often used in conjunction with spinal manipulation.
	Tai chi	A form of stylized, meditative exercise, characterized by methodically slow circular and stretching movements and positions of bodily balance.
	Transcutaneous electrical nerve stimulation	Use of a small, battery-operated device to provide continuous electrical impulses via surface electrodes, with the goal of providing symptomatic relief by modifying pain perception.
	Yoga	An intervention distinguished from traditional exercise therapy by the use of specific body positions, breathing techniques, and an emphasis on mental focus. Many styles of yoga are practiced, each emphasizing different postures and techniques.

September 2017 Page 75 of 110

## **Appendix E: 2007 Recommendation Categorization Table**

2007 Number	2007 Recommendation Text <sup>17</sup>	<b>2007</b> Grade <sup>18</sup>	Category <sup>19</sup>	2017 Recommendation <sup>20</sup>
1	Clinicians should conduct a focused history and physical examination to help place patients with low back pain into 1 of 3 broad categories: nonspecific low back pain, back pain potentially associated with radiculopathy or spinal stenosis, or back pain potentially associated with another specific spinal cause. The history should include assessment of psychosocial risk factors, which predict risk for chronic disabling back pain.	Strong recommendation	Reviewed, Amended	Recommendation 1
2	Clinicians should not routinely obtain imaging or other diagnostic tests in patients with nonspecific low back pain.	Strong recommendation	Reviewed, Amended	Recommendation 3
3	Clinicians should perform diagnostic imaging and testing for patients with low back pain when severe or progressive neurologic deficits are present or when serious underlying conditions are suspected on the basis of history and physical examination.	Strong recommendation	Reviewed, Amended	Recommendation 4
4	Clinicians should evaluate patients with persistent low back pain and signs or symptoms of radiculopathy or spinal stenosis with magnetic resonance imaging (preferred) or computed tomography only if they are potential candidates for surgery or epidural steroid injection (for suspected radiculopathy).	Strong recommendation	Reviewed, Ameded	Recommendation 4
5	Clinicians should provide patients with evidence-based information on low back pain with regard to their expected course, advise patients to remain active, and provide information about effective self-care options.	Strong recommendation	Reviewed, Amended	Recommendation 6
6	For patients with low back pain, clinicians should consider the use of medications with proven benefits in conjunction with back care information and self-care. Clinicians should assess severity of baseline pain and functional deficits, potential benefits, risks, and relative lack of long-term efficacy and safety data before initiating therapy. For most patients, first-line medication options are acetaminophen or nonsteroidal anti-inflammatory drugs.	Strong recommendation	Reviewed, New- replaced	Recommendations 21-32

 $<sup>^{17}</sup>$  The 2007 Recommendation Text column contains the wording of each recommendation from the 2007 LBP CPG.

September 2017 Page 76 of 110

<sup>&</sup>lt;sup>18</sup> The 2007 VA/DoD LBP CPG also used the GRADE evidence grading system.

<sup>&</sup>lt;sup>19</sup> The Category column indicates the way in which each 2007 LBP CPG recommendation was updated.

<sup>&</sup>lt;sup>20</sup> For recommendations that were carried forward to the 2007 LBP CPG, this column indicates the new recommendation(s) to which they correspond.

2007 Number	2007 Recommendation Text <sup>17</sup>	<b>2007</b> Grade <sup>18</sup>	Category <sup>19</sup>	2017 Recommendation <sup>20</sup>
7	For patients who do not improve with self- care options, clinicians should consider the addition of non-pharmacologic therapy with proven benefits—for acute low back pain, spinal manipulation; for chronic or sub-acute low back pain, intensive interdisciplinary rehabilitation, exercise therapy, acupuncture, massage therapy, spinal manipulation, yoga, cognitive-behavioral therapy, or progressive relaxation.	Weak recommendation	Reviewed, New- replaced	Recommendations 8-16, 38

September 2017 Page 77 of 110

# Appendix F: Participant List

Adam Bevevino, MD (Champion)	Daniel Kang, MD (Champion)
Major, U.S. Army	Major, U.S. Army
Chief, Spine Surgery Service	Orthopedic Spine Surgeon
William Beaumont Army Medical Center	Madigan Army Medical Center
El Paso, TX	Tacoma, WA
Sanjog Pangarkar, MD (Champion)	Friedhelm Sandbrink, MD (Champion)
Director, Inpatient and Interventional Pain Service	Chief, Pain Management Program, Department of
West Los Angeles Veterans Hospital	Neurology, Washington DC VA Medical Center
Los Angeles, CA	Deputy National Director Pain Management, Specialty Care
	Services, VHA
	Washington, DC
Curtis Aberle, RN, MSN, FNP	David Cory Adamson, MD, PhD
Chief, McWethy Troop Medical Clinic and Readiness Center	Chair, Neurosurgery Advisory Board
Brooke Army Medical Center	Atlanta VA Medical Center
Fort Sam Houston, TX	Atlanta, GA
Chris Allen, DPT, DSc, FAAOMPT	Rachael Coller, PharmD, BCPS, BCPP
Major, U.S. Army	Clinical Pharmacist
Program Director and Associate Professor, Army-Baylor	Naval Medical Center San Diego
University	San Diego, CA
Brooke Army Medical Center	_
Fort Sam Houston, TX	
Francine Goodman, PharmD, BCPS	Valerie Johnson, DC, DABCI
Clinical Pharmacy Specialist	Chiropractic Residency Director
VA Pharmacy Benefits Management Services	Greater Los Angeles VA Healthcare System
Hines VA Medical Center	Los Angeles, CA
Hines, IL	
Lisa Konitzer, PT, DSc, OCS, FAAOMPT	Lex Mitchell, MD
Lieutenant Colonel, US Army	Major(P), U.S. Army
Chief, Physical Therapy	Diagnostic Neuroradiologist
DiLorenzo TRICARE Health Clinic	Tripler Army Medical Center
Washington, DC	Honolulu, HI
Mitchell Nazario, PharmD	Jeremiah Samson, PT, ScD(C), OCS, COMT, FAAOMPT
VISN 8 PBM Clinical Program Manager, Pain Management	Major, U.S. Air Force
West Palm Beach VA Medical Center	Surgical Services Flight Commander
West Palm Beach, FL	Keesler Air Force Base
	Biloxi, MS
Jason Silvernail, DPT, DSc, FAAOMPT	Sandra Smeeding, PhD, CNS, FNP
Lieutenant Colonel, U.S. Army	Health Promotion Disease Prevention Manager
Chief, Physical Therapy Service	San Francisco VA Health Care System
Walter Reed National Military Medical Center	San Francisco, CA
· ·	San Francisco, CA
Bethesda, MD	

September 2017 Page 78 of 110

Evan Steil, MD, MBA, MHA	Elaine P. Stuffel, BSN, MHA, RN
Administrative Physician	Chronic Disease CPG Coordinator
US Army Medical Command	US Army Medical Command
Clinical Performance Assurance Directorate	Clinical Performance Assurance Directorate
Fort Sam Houston, TX	Office of Evidence Based Practice
	Fort Sam Houston, TX
Kirsten Tillisch, MD	Rebecca Vogsland, DPT, OCS
Chief, Integrative Medicine, GLA VHA	Program Coordinator, Comprehensive Pain Center and
G. Oppenheimer Center for Neurobiology of Stress and	Clinical Specialist
Resilience	Minneapolis Veterans Affairs Medical Center
David Geffen School of Medicine at UCLA	Minneapolis, MN
Los Angeles, CA	

September 2017 Page 79 of 110

### **Appendix G: Patient Focus Group Methods and Findings**

#### A. Methods

On September 7, 2016, as part of the effort to update this CPG, the VA and DoD Leadership, along with the LBP CPG Work Group, held a patient focus group at the William Beaumont Army Medical Center, in El Paso, Texas. Focus group participants comprised seven patients, including one female.

The aim of the focus group was to further the understanding of the perspective of patients undergoing diagnosis and treatment for LBP within the VA and/or DoD healthcare systems, as patients are most affected by the recommendations put forth in the CPG. The focus group explored patient perspectives on a set of topics related to the diagnosis and treatment of LBP in the VA and DoD healthcare systems, including patients' knowledge of LBP treatment options, views on the delivery of care, and the impact of LBP on patients' careers and daily life.

Participants for the focus group were recruited by the LBP CPG Champions and Work Group members. Patient focus group participants were not intended to be a representative sample of VA and DoD patients who have experienced LBP. However, recruitment focused on eliciting a range of perspectives likely to be relevant and informative in the guideline development process. Patients were not incentivized for their participation or reimbursed for travel expenses.

The LBP CPG Champions and Work Group, with support from Lewin, developed a set of questions to help guide the focus group. The focus group facilitator, Frances Murphy, MD, MPH, led the discussion using the previously prepared questions as a general guide to elicit the most important information from the patients regarding their experiences and views about their treatment and overall care. Given the limited time and the range of interests of the focus group participants, not all of the listed questions were addressed. Notes taken during the meeting were synthesized for the following report.

Seven patients participated in the focus group, including one woman. The individuals ranged in age from approximately the 20s age group to the 60s age group. Four participants were active duty in the Army and receiving care in the DoD healthcare system, and three were primarily receiving care through the VA system at the time of the focus group discussion. The patients reported having been told of one or more LBP diagnoses, including bulging discs, torn discs, degenerative discs, lumbar stenosis, vertebral fractures, and arthritis. The length of time the participants' had been experiencing LBP varied from one year to over 25 years. Most of the participants had tried many different treatments, including pharmacologic therapies, surgery, injections, physical therapy, chiropractic care, exercise programs, acupuncture, and many self-care strategies. Participants reported receiving treatment from VA providers, Military Health System providers and from private sector providers.

The following concepts are aspects of care that patients indicated were important during the course of the focus group discussion. Each of these themes was an important and needed aspect of participants' healthcare.

September 2017 Page 80 of 110

#### **B.** Patient Focus Group Findings

Consider patient-specific goals, values, and preferences and use shared decision making to develop a patient-centered plan for timely diagnosis, treatment, and lifestyle adaptation

- Identify patient-specific goals and preferences associated with diagnosis and treatment for LBP.
- Understand the importance that patients place on accurate and timely diagnosis, enabling them to understand the cause of their LBP.
- Discuss the harms, benefits, and likely outcomes of different diagnostic and treatment options, particularly imaging tests, and potential treatments.
- Educate patients about self-care strategies and tools that will help increase their quality of life with LBP.

Address strategies for pain management across all phases of treatment and educate patients about the use of pain medications, particularly opioids

- Discuss pharmacologic options in depth with the patient; seek to understand patient preference regarding reducing or eliminating certain medicines from their treatment plan.
- Be prepared to adjust or otherwise change treatment (e.g., tapering pain medication) subject to patient response, preferences, and changes in priorities and goals.
- When prescribing opioids, educate patients about the potential harms and alternatives to opioid therapy.
- Consider that VA/DoD patients may under-report pain intensity.

Recognize the importance of communication and collaboration among providers of an interdisciplinary care team

- Patients value the expertise and treatment options available from multiple specialists on their care team (e.g., primary care provider, physical therapist, surgeon).
- Patients benefit when the care team is in close communication and agreement regarding the individualized treatment plan.
- Providers should work together to ensure each patient receives timely referrals and smooth transitions between different members of their care team.

Involve family caregivers to create support and motivation for patients with low back pain

- Include family members early in discussions about what to expect during each stage of diagnosis and treatment, especially with regards to lifestyle adaptation and self-care.
- Build and maintain trust, respect, and support with the patient and their family.

Work with providers to ensure continuity of care and ease of access to preferred providers

- When planning treatment, consider proximity of care sites and try to minimize travel and time requirements as appropriate.
- Work with providers to ensure continuity of care and ease of access to preferred specialists.

September 2017 Page 81 of 110

• Recognize that the active duty populations that may face unique challenges in continuity of and access to care, especially with physically demanding jobs and frequent regional relocation.

#### Reduce the stigma experienced by patients with LBP

- Clinicians should acknowledge the potential difficulty the military and Veteran populations face when describing pain.
- Patients feel they are not taken seriously when providers assume they are using pain to get out of work, which impacts the diagnosis and treatment for their LBP.
- Patients may experience workplace stigma, particularly military populations who may struggle with feeling they are no longer valued.
- Active duty populations may be particularly concerned about medical boards and loss of benefits once they are being treated for LBP.

September 2017 Page 82 of 110

## **Appendix H: Literature Review Search Terms and Strategy**

### A. Topic-specific Search Terms

The search strategies employed combinations of free-text keywords as well as controlled vocabulary terms including (but not limited to) the following concepts. Strategies for each bibliographic database follow this table.

Table G-1. EMTREE, Medical Subject Headings (MeSH), PsycInfo, and Keywords

Concept	Controlled Vocabulary	Keywords			
Patient population	Patient population				
Low Back Pain and	low back pain	low back			
Associated Indications	lumbar disk hernia	lower back			
	lumbar spinal stenosis	lumbar			
		lumbosacral			
		pain*			
Lumbar Spine	fifth lumbar vertebrae	low back			
	first lumbar vertebrae	lower back			
	fourth lumbar vertebrae	lumbar			
	lumbar disk	lumbosacral			
	lumbar spinal cord				
	lumbar spine				
	lumbosacral spine				
Associated Indications	intervertebral disk	degenerat*			
	degeneration intervertebral disk disease	hernia*			
	intervertebral disk hernia	radicular			
	nerve root compression	radiculo*			
	radiculopathy	stenos*			
		stenotic			

September 2017 Page 83 of 110

Concept	Controlled Vocabulary	Keywords
KQ1a	bone scintiscanning	assess*
For adults who present	computer assisted tomography	comput*
with or have LBP (acute,	diagnostic imaging	CT scan*
sub-acute, and chronic	diagnostic test	diagnos*
LBP), what is the accuracy	diffusion weighted imaging	discogra*
of history, physical	diskography	diskogra*
examination, and	echography	electromyogr*
diagnostic tests, in	electromyography	electrophysiologic test*
identifying the underlying	four dimensional computed tomography	emg
condition?	medical history	episode*
	musculoskeletal diagnosis	exam*
KQ1b	myelography	faber*
For adults who present	nuclear magnetic resonance imaging	facet load*
with or have LBP (acute,	physical examination	film*
sub-acute, and chronic	radiodiagnosis	flexion abduction and external rotation
LBP), what is the clinical	radiography	health
utility of history, physical	single photon emission computer	history
examination, and	tomography	image*
diagnostic tests in	spine radiography	imaging
improving treatment	thermography	inciden*
choices and patient	three dimensional imaging x ray	kemp*
outcomes?		lasegue
		magnetic resonance
		medical*
		mri*
		myelogr*
		occur*
		patrick*
		physical*
		previous*
		prior
		quadrant*
		radiograph*
		scan*
		spect-ct
		straight leg raise*
		symptom*
		test*
		tomogra*
		ultraso*
		x-ray*
		xray*

September 2017 Page 84 of 110

Concept	Controlled Vocabulary	Keywords
<u>KQ2</u>	behavior modification coping behavior	adjust*
What is the effectiveness	ergonomics	back school*
of self-care advice,	lifestyle modification	behav*
education, or other self-	patient education	care*
care (weight loss, tobacco	self care	change*
cessation, work place	self monitoring	cope*
ergonomics, exercise	smoking cessation	coping
programs) interventions	smoking cessation program	ergonomic*
for improving patient	support group	help*
outcomes?	weight reduction	lifestyle
		lose
		losing
		loss
		lost
		manag*
		modif*
		pound*
		reduc*
		self*
		shed*
		smok*
		support group*
		tobacco
		weight*

September 2017 Page 85 of 110

Concept	Controlled Vocabulary	Keywords
KQ3	acupuncture	acupressure
What is the effectiveness	aerobic exercise	acupuncture
of different non-surgical	anaerobic exercise	brace*
and non-pharmacologic	aguatic exercise	chiropract*
interventions for non-	arm exercise	conservative*
radicular low back pain,	athletic tape	core
radicular low back pain,	body posture	cryother*
or spinal stenosis, and	brace	decompression
under what	chiropractic	dry needl*
circumstances?	circuit training	e-stim*
0.100.11000.1	conservative treatment	electroacupuncture
	cryotherapy	electrostim*
	electroacupuncture	exercise*
	electrostimulation	heating pad*
	exercise	hot pack*
	exercise intensity	laser*
	exercise tolerance	lumbar
	hyperthermic therapy	manip*
	isokinetic exercise	mechanical*
	isometric exercise	neuroreflexotherapy
	isotonic exercise	non-invasiv*
	kinesiotherapy	noninvasiv*
	leg exercise	non-operativ*
	low level laser therapy	nonoperativ*
	manipulative medicine massage	non-surgical*
	muscle exercise	nonsurgical*
	open kinetic chain exercise	out
	physiotherapy	pens
	pilates	physical therap*
	plyometrics	physiotherap
	rehabilitation medicine	pilates
	reiki	rehab*
	resistance training	spinal
	spinal cord decompression	strength*
	static exercise	stretch*
	stretching exercise	superficial heat
	tai chi	tai chi
	traction therapy	tape*
	transcutaneous nerve stimulation	taping
	ultrasound therapy	tens
	yoga	therap*
	yogu	thermother*
		traction*
		train*
		trigger point*
		ultrasound*
		work*
		work workout*
		yoga
	<u>l</u>	y∨ga

September 2017 Page 86 of 110

Concept	Controlled Vocabulary	Keywords
KQ4	General Terminology	General Terminology
For adults with LBP, what	drug therapy	drug therap*
is the effect of	arag merapy	medication*
pharmacotherapy	Analgesics/Anesthetics/	medicin*
treatment?	Anti-inflammatories (Oral/Topical)	pharmacotherap*
treatment:	analgesic agent	pharmacotherap
	anti-inflammatory agent	Analgesics/Anesthetics/
	bipuvacaine	Anti-inflammatories (Oral/Topical)
	capsaicin	agent*
	dronabinol	amitriptyline
	etanercept	anaesth*
	infliximab	analges*
	lidocaine	anesth*
		anti inflam*
	local anesthetic agents	antiinflam*
	Anticonyulcanto	baclofen
	Anticonvulsive agent	
	anticonvulsive agent carbamazepine	bipuvacaine
	ethosuximide	camphor
	etiracetam	capsaicin chondroitin
	felbamate	compound* corticosteroid*
	gabapentin	
	harkoseride	cream*
	lamotrigine	diclofenac
	oxcarbazepine	dronabinol
	pregabalin	embrel
	rufinamide	emu oil
	tiagabine	etanercept
	topiramate	gabapentin
	valproic acid	gel*
	zonisamide	glucosamine
	Carticastaraids	hydromorphone hydrophilic
	Corticosteroids betamethasone	infliximab
	corticosteroid	ketamine
	cortisone	ketoprofen
	dexamethasone	lidocaine
	fludrocortisone	lidoderm
	hydrocortisone	lotion*
	methylprednisolone	medication*
	prednisolone	medicin*
	prednisone	menthol*
	triamcinolone	opioid*
	Muselo Delevents	paractin
	Muscle Relaxants baclofen	patch*
		qutenza
	benzodiazepine derivative	remicade
	carisoprodol	rofenac
	central muscle relaxant	salicylate*
	chlorzoxazone	spray*
	cyclobenzaprine	topical*

September 2017 Page 87 of 110

Concept	Controlled Vocabulary	Keywords
	dantrolene	transdermal*
	diazepam	trolamine
	directly acting muscle relaxant	Columnic
	flexeril	Anticonvulsants
	metaxalone	anti convuls*
	methocarbamol	anti seizure*
	muscle relaxant agent	anticonvuls*
		antiseizure*
	neuromuscular blocking agent	
	neuromuscular depolarizing agent	carbamazepine ethosuximide
	orphenadrin	
	tizanidine	etiracetam
	NINADA Antaganista	felbamate
	NMDA Antagonists	gabapentin
	amantadine	harkoseride
	dextromethorphan	lacosamide
	ketamine	lamotrigine
	memantine	levetiracetam
	n methyl dextro aspartic acid receptor	lyrica
	blocking agent	oxcarbazepine
		pregabalin
	Non-prescription	rufinamide
	acetylsalicylic acid	tiagabine
	ibuprofen	topiramate
	naproxen	valproic acid
	non prescription drug	zonisamide
	paracetamol	
		<u>Corticosteroids</u>
	<u>NSAIDs</u>	aristospan
	celecoxib	betamethasone
	choline magnesium	celestone
	choline magnesium trisalicylate	cortef
	diclofenac	corticosteroid*
	diflunisal	cortisone
	etodolac	dexamethasone
	flurbiprofen	ethamethasoneb
	ketoprofen meclofenamate meloxicam	florinef
	nonsteroid antiinflammatory agent	fludrocortisone
	oxaprzin	hydrocortisone
	piroxicam	kenalog
	salicylic acid derivative	medrol
	salsalate	methylprednisolone
	sulindac	orapred
	tolmetin	prednisolone
	trilisate	prednisone
		prelone
	<u>Opioids</u>	triamcinolone
	acetylmethadol	
	alfentanil	Muscle Relaxants
	alphaprodine	amrix
	beta-casomorphin	baclofen
	carfentanil	benzodiazepine*

September 2017 Page 88 of 110

Concept	Controlled Vocabulary	Keywords
Concept	codeine	carisoprodol
	deltorphin	chlorzoxazone
	dextropropoxyphene	cyclobenzaprine
	dezocine	dantrolene
	dihydrocodeine	diazepam
	dihydromorphine	flexeril
	etorphine	lioresal
	ethylketocyclazocine	mephenamine
	ethylmorphine	metaxalone
	hydrocodone	methocarbamol
	hydromorphone	'muscle relax*'
	ketobemidone	orphenadrin
	levorphanol	orphenadrine
	lofentanil	paraflex
	meptazinol	parafon
	methadone	robaxin
	morphine	skelaxin
	nalbuphine	tizanidine
	narcotic analgesic agent	zanaflex
	opiate	NMDA Antagonists
	oxycodone	amantadine
	oxymorphone	dextromethorphan
	pentazocine	ketamine
	pethidine	memantine
	phenazocine	'nmda antagonist*
	phenoperidine	
	pirinitramide	Non-prescription
	remifentanil	acetaminophen
	sufentanil	aleve
	tapentadol	aspirin
	tilidine	dantrium
	tramadol	duragesic
	trimeperidine	ibuprofen
		naproxen
		non prescription
		non-prescription
		nonprescription
		over the counter
		over-the-counter
		paracetamol
		tylenol
		tylerioi
		NSAIDe
		NSAIDs clinoril
		daypro
		diclofenac
		disalcid
		feldene
		lodine
		mobic
		non-steroid*

September 2017 Page 89 of 110

Concept	Controlled Vocabulary	Keywords
·		nonsteroid*
		nsaid*
		ocufen
		orudis
		oruvail
		salicylate*
		salicylic acid
		solaraze
		tolectin
		trilisate
		voltaren
		<u>Opioids</u>
		alfenta
		buprenex
		dalgan
		darvon
		demerol
		dicodid
		dilaudid
		dolophine
		hydrostat ir
		levo-droman
		meperidine
		methadose
		methadyl acetate narcotic*
		nubain
		numphan
		opana
		opiate*
		opioid*
		oxycodone
		oxycontin
		oxyfast
		oxyir
		percolone
		promedol
		propoxyphene
		roxicodone
		talwin
		ultiva
		ultram

September 2017 Page 90 of 110

Concept	Controlled Vocabulary	Keywords
KQ5	arachidonic acid	anti-inflam*
For adults with LBP, what	arnica	antiinflam*
is the effect of nutritional,	ascorbic acid	arachidonic acid
herbal, and homeopathic	cannabinoid	arnica
supplements?	cayenne pepper	cannabi*
	chinese medicine	cayenne
	cod liver oil	claw
	curcuma longa	curcumin*
	diet supplementation	devil*
	diet therapy	dha
	docosahexaenoic acid	diet*
	fish oil	eicosapentaenoic acid
	flavonoid	epa
	ginger	fish oil
	harpagophytum	flavonoid
	harpagophytum extract	ginger
	herbaceous agent	harpagophytum
	icosapentaenoic acid	herb*
	omega 3 fatty acid	holistic
	omega 6 fatty acid	
	resveratrol	homeopath
	vitamin d	n 3 fatty acid* nutrition*
	vitamin d	
		omega*
		resveratrol
		supplement*
		tumeric
		vitamin c
		vitamin d
		willow bark
<u>KQ6</u>	epidural anesthesia	anaesthes*
For adults with LBP, what	epidural drug administration	anesthes*
is the treatment	intraspinal drug administration	block*
effectiveness of epidural	nerve block	corticosteroid*
injections, facet blocks,	radiofrequency ablation spinal anesthesia	epidural
nerve root blocks, radio		facet
frequency ablation (RFA)?		foraminal
		inject*
		interspin*
		intraspin*
		lumbar
		nerve
		paraspin*
		radiofrequency*
		rf
		rfa
		spinal
		trigger point*
		zygapophyseal

September 2017 Page 91 of 110

Concept	Controlled Vocabulary	Keywords
<u>KQ7</u>	drug combination	care
For adults with LBP, what		combin*
combination therapy		drug*
(pharmacologic and non-		integrat*
pharmacologic) is most		modalit*
effective?		multi*
		pharm*
		therap*
		treat*
<u>KQ8</u>	behavior therapy	behavior*
For adults with chronic	cognitive therapy	biofeedback
LBP, what is the	feedback system	cognitive*
effectiveness of	meditation	counsel*
behavioral interventions?	mental health care	mbsr
	mindfulness	meditat*
	psychiatric treatment	mental health
	psychologic assessment	mindful*
	psychological distress assessment	psych*
	psychological well being	psychother*
	psychological well being assessment	relax*
	psychosocial rehabilitation	stress*
	psychotherapy	therap*
	relaxation training	treat*

September 2017 Page 92 of 110

Concept	Controlled Vocabulary	Keywords
KQ8	amfebutamone	amfebutamone
Antidepressants	amitriptyline	amitriptyline
	amoxapine	amoxapine
	antidepressant activity	anafranil
	antidepressant agent	antidepres*
	citalopram	asendin
	clomipramine	aventyl
	desipramine	bupropion
	desvenlafaxine	brintellix
	doxepin	celexa
	duloxetine	cymbalta
	escitalopram	desyrel
	fluvoxamine	effexor
	imipramine	emsam
	maprotiline	fetzima
	mianserin	fluoxetine
	milnacipran	lexapro
	mirtazapine	levomilnacipran
	monoamine oxidase inhibitor	maoi
	nefazodone	mao inhibitor*
	noradrenalin update inhibitor	norpramin
	nortriptyline	oleptro
	paroxetine	pamelor
	protriptyline	paroxetine
	selegiline	paxil
	serotonin noradrenalin reuptake	pristiq
	inhibitor	protriptyline
	serotonin uptake inhibitor	prozac
	tetracyclic antidepressant agent	prudoxin
	trazodone	remeron
	tricyclic antidepressant agent	savella
	trimipramine	sertraline
	triple reuptake inhibitor venlafaxine	serzone
	vilazodone	sinequan
	vortioxetine	sndri
		ssri
		tofranil
		tricyclic
		trimipramine
		trintellix
		viibryd
		vivactil
		wellbutrin
		zoloft
		zonalon
		zyban

September 2017 Page 93 of 110

Concept	Controlled Vocabulary	Keywords
<u>KQ9</u>	anxiety	adhd
For adults with low back	anxiety disorder	anxiety
pain, what is the impact	attention deficit disorder	anxious*
of mental health	catastrophizing	attention deficit
diagnoses (e.g.,	depression	catastrophiz*
depression, anxiety,	family stress	death*
ADHD, PTSD, TBI) or	mental disease	depress*
psychosocial stressors	mental stress posttraumatic stress	divorce*
(e.g., divorce, death, job	disorder	post-traumatic
loss) on treatment	psychosocial care psychosocial disorder	post traumatic
outcomes?	psychosocial	psychosocial
	environment psychosocial withdrawal	ptsd
	social psychology	stress*
	traumatic brain injury	tbi
	unemployment	traumatic brain
		unemploy*

## **B.** Search Strategies

Table G-2. EMBASE/Medline Search Strategies Conducted using EMBASE Syntax

Set #	Concept	Search Statement
1	Low Back Pain and Defined Lumbar Indications	(('low back' OR 'lower back' OR lumbar OR lumbosacral) AND pain*):ti OR 'low back pain'/exp OR 'lumbar disk hernia'/exp OR 'lumbar spinal stenosis'/exp
2	Lumbar Spine	'fifth lumbar vertebrae' OR 'first lumbar vertebrae' OR 'fourth lumbar vertebrae' OR 'lumbar disk'/exp OR 'lumbar spinal cord'/exp OR 'lumbar spine'/exp OR ('low back' OR 'lower back' OR lumbar OR lumbosacral):ti
3	Associated Spinal Indications	'intervertebral disk degeneration'/exp OR 'intervertebral disk disease'/exp OR 'intervertebral disk hernia'/exp OR 'nerve root compression'/exp OR 'radiculopathy'/exp OR (degenerat* OR hernia* OR radicular OR radiculo* OR stenos* OR stenotic):ti
4	For adults who present with or have LBP (acute, sub-acute, and chronic LBP), what is the accuracy of history, physical examination, and diagnostic tests, in identifying the underlying condition?  KQ1b  For adults who present with or have LBP (acute, sub-acute, and chronic LBP), what is the clinical utility of history, physical examination, and diagnostic tests in improving treatment choices and patient outcomes?	'bone scintiscanning'/exp OR 'computer assisted tomography'/exp OR 'diagnostic imaging'/exp OR 'diagnostic test'/exp OR 'diffusion weighted imaging'/exp OR diskography/exp OR echography/exp OR electromyography/exp OR 'four dimensional computed tomography'/exp OR 'medical history'/exp OR 'musculoskeletal diagnosis'/exp OR myelography/exp OR 'nuclear magnetic resonance imaging'/exp OR 'physical examination'/exp OR radiodiagnosis/exp OR radiography/exp OR 'single photon emission computer tomography'/exp OR 'spine radiography'/exp OR thermography/exp OR 'three dimensional imaging'/exp OR 'x ray'/exp OR ((health OR medical* OR physical* OR previous* OR prior) NEAR/2 (assess* OR episode* OR exam* OR history OR inciden* OR occur* OR symptom*)):ab,ti OR (comput* NEXT/1 tomogra*):ab,ti OR (diagnos* NEAR/2 (film* OR imag* OR scan* OR test*)):ab,ti OR ('CT scan*' OR discogra* OR diskogra* OR electromyogr* OR faber* OR 'facet load*' OR 'electrophysiologic test*' OR emg OR 'flexion abduction and external rotation' OR image* OR imaging OR kemp* OR lasegue OR 'magnetic resonance' OR MRI* OR myelogr* OR patrick* OR quadrant OR 'straight leg raise' OR radiograph* OR scan* OR spect-ct OR ultraso* OR 'x-ray*' OR xray*):ab,ti

September 2017 Page 94 of 110

Set#	Concept	Search Statement
5	KQ2 What is the effectiveness of self-care advice, education, or other self-care (weight loss, tobacco cessation, work place ergonomics, exercise programs) interventions for improving patient outcomes?	'behavior modification'/exp OR 'coping behavior'/exp OR ergonomics/exp OR 'lifestyle modification'/exp OR 'patient education'/exp OR 'self care'/exp OR 'self monitoring'/exp OR 'smoking cessation'/exp OR 'smoking cessation program'/exp OR 'support group'/exp OR 'weight reduction'/exp OR ('back school*' OR cope* OR coping OR ergonomic* OR smok* OR tobacco OR 'support group*'):ab,ti OR ((behav* OR lifestyle) NEAR/2 (adjust* OR change* OR modif*)):ab,ti OR ((weight OR pound*) NEAR/2 (lose OR losing OR loss OR lost OR reduc* OR shed*)):ab,ti OR (self* NEXT/1 (care* OR help* OR manag*)):ab,ti
6	KQ3 What is the effectiveness of different non-surgical and non-pharmacologic interventions for non-radicular low back pain, radicular low back pain, or spinal stenosis, and under what circumstances?	acupuncture/exp OR 'aerobic exercise'/exp OR 'anaerobic exercise'/exp OR 'aquatic exercise'/exp OR 'arm exercise'/exp OR 'athletic tape'/exp OR 'body posture'/exp OR brace/exp OR chiropractic/exp OR 'circuit training'/exp OR 'conservative treatment'/exp OR cryotherapy/exp OR electroacupuncture/exp OR electrostimulation/exp OR exercise/exp OR 'exercise intensity'/exp OR 'exercise tolerance'/exp OR 'hyperthermic therapy'/exp OR 'isokinetic exercise'/exp OR 'isometric exercise'/exp OR 'isotonic exercise'/exp OR kinesiotherapy/exp OR 'leg exercise'/exp OR 'low level laser therapy'/exp OR 'manipulative medicine'/exp OR massage/exp OR 'muscle exercise'/exp OR 'open kinetic chain exercise'/exp OR physiotherapy/exp OR pilates/exp OR plyometrics/exp OR 'rehabilitation medicine'/exp OR reiki/exp OR 'resistance training'/exp OR 'spinal cord decompression'/exp OR 'static exercise'/exp OR 'stretching exercise'/exp OR 'tai chi'/exp OR 'traction therapy'/exp OR 'transcutaneous nerve stimulation'/exp OR 'ultrasound therapy'/exp OR yoga/exp OR (core NEAR/2 (strength* OR train*)):ab,ti OR ((spinal OR lumbar) NEXT/2 manipulat*) OR (acupressure OR acupuncture OR brace* OR chiropractic* OR conservative* OR cryother* OR 'dry needl*' OR 'e-stim' OR electrostim* OR electroacupuncture OR electrostim* OR exercise* OR 'heating pad*' OR 'hot pack*' OR laser* OR lumbar OR manip* OR neuroreflexotherapy OR non-invasiv* OR noninvasiv* OR non-operativ* OR nonoperativ* OR nonsurgical* OR ponsurgical* OR pens OR 'physical therap*' OR physiotherap* OR pilates OR rehab* OR spinal OR stretch* OR 'superficial heat' OR 'tai chi' OR tape* OR taping OR tens OR therap* OR thermother* OR traction* OR train* OR 'trigger point*' OR ultrasound* OR workout* OR yoga):ab,ti OR (decompression NEAR/1 (mechanical* OR non-operativ* OR nonoperativ* OR non-surg* OR nonsurg*)):ab,ti OR (work* NEXT/1 out*):ab,ti
7	KQ4 For adults with LBP, what is the effect of pharmacotherapy treatment? (General Terminology)	'drug therapy'/mj OR ('drug therap*' OR medication* OR medicine* OR pharmacotherap*):ti

September 2017 Page 95 of 110

Set #	Concept	Search Statement
8	KQ4 Analgesics/Anesthetics/ Antiinflammatories (Misc. Drug Classes - Oral/Topical)	'analgesic agent'/exp OR 'antiinflammatory agent'/exp OR bipuvacaine/exp OR capsaicin/exp OR dronabinol/exp OR etanercept/exp OR infliximab/exp OR lidocaine/exp OR 'local anesthetic agents'/exp OR (analges* OR 'anti inflam*' OR antiinflam* OR bipuvacaine OR capsaicin OR dronabinol OR embrel OR etanercept OR infliximab OR lidocaine OR lidoderm OR remicade):ab,ti OR ((compound*) NEAR/2 (cream* OR gel* OR lotion* OR patch* OR spray* OR topical*)):ab,ti OR ((compound* OR cream* OR gel* OR lotion* OR patch* OR spray*) NEAR/2 (amitriptyline OR baclofen OR camphor OR capcaicin OR chondroitin OR corticosteroid* OR diclofenac OR 'emu oil ' OR gabapentin OR glucosamine OR hydromorphone OR hydrophilic OR ketamine OR ketoprofen OR lidocaine OR lidoderm OR menthol* OR opioid* OR paractin OR qutenza OR rofenac OR salicylate* OR trolamine)):ab,ti OR ((topical* OR transdermal*) NEAR/2 (agent* OR amitriptyline OR anaesth* OR analges* OR anesth* OR 'anti inflam*' OR antiinflam* OR baclofen OR camphor OR capcaicin OR chondroitin OR corticosteroid* OR cream* OR diclofenac OR 'emu oil ' OR gabapentin OR gel* OR glucosamine OR hydromorphone OR hydrophilic OR ketamine OR ketoprofen OR lidocaine OR lidoderm OR lotion* OR medication* OR medicin* OR menthol* OR opioid* OR paractin OR patch* OR qutenza OR rofenac OR salicylate* OR spray* OR trolamine)):ab,ti
9	KQ4 Anticonvulsants	'anticonvulsive agent'/exp OR carbamazepine/exp OR ethosuximide/exp OR etiracetam/exp OR felbamate/exp OR gabapentin/exp OR harkoseride/exp OR lamotrigine/exp OR oxcarbazepine/exp OR pregabalin/exp OR rufinamide/exp OR tiagabine/exp OR topiramate/exp OR 'valproic acid'/exp OR zonisamide/exp OR ('anti convuls*' OR 'anti seizure*' OR anticonvuls* OR antiseizure* OR carbamazepine OR ethosuximide OR etiracetam OR felbamate OR gabapentin OR harkoseride OR lacosamide OR lamotrigine OR levetiracetam OR lyrica OR oxcarbazepine OR pregabalin OR rufinamide OR tiagabine OR topiramate OR 'valproic acid' OR zonisamide):ab,ti
10	K4 Corticosteroids	betamethasone/exp OR corticosteroid/exp OR cortisone/exp OR dexamethasone/exp OR fludrocortisone/exp OR hydrocortisone/exp OR methylprednisolone/exp OR prednisolone/exp OR prednisone/exp OR triamcinolone/exp OR (aristospan OR betamethasone OR celestone OR cortef OR corticosteroid* OR cortisone OR dexamethasone OR ethamethasoneb OR florinef OR fludrocortisone OR hydrocortisone OR kenalog OR medrol OR methylprednisolone OR orapred OR prednisolone OR prednisone OR prednisolone OR prednisolone OR prednisolone OR prednisolone OR prednisolone
11	KQ4 Muscle Relaxants	baclofen/exp OR 'benzodiazepine derivative'/exp OR carisoprodol/exp OR 'central muscle relaxant'/exp OR chlorzoxazone/exp OR cyclobenzaprine/exp OR dantrolene/exp OR diazepam/exp OR 'directly acting muscle relaxant'/exp OR flexeril/exp OR metaxalone/exp OR methocarbamol/exp OR 'muscle relaxant agent'/exp OR 'neuromusclular blocking agent'/exp OR 'neuromuscular depolarizing agent'/exp OR orphenadrine/exp OR tizanidine/exp OR (amrix OR baclofen OR benzodiazepine* OR carisoprodol OR chlorzoxazone OR cyclobenzaprine OR dantrolene OR diazepam OR flexeril OR lioresal OR mephenamine OR metaxalone OR methocarbamol OR 'muscle relax*' OR orphenadrin OR orphenadrine OR paraflex OR parafon OR robaxin OR skelaxin OR tizanidine OR zanaflex):ab,ti
12	KQ4 NMDA Antagonists	amantadine/exp OR dextromethorphan/exp OR ketamine/exp OR memantine/exp OR 'n methyl dextro aspartic acid receptor blocking agent'/exp OR (amantadine OR dextromethorphan OR ketamine OR memantine OR 'nmda antagonist*'):ab,ti

September 2017 Page 96 of 110

Set #	Concept	Search Statement
13	KQ4 Non-prescription Drugs	'acetylsalicylic acid'/exp OR ibuprofen/exp OR naproxen/exp OR 'non prescription drug'/exp OR paracetamol/exp OR (acetaminophen OR aleve OR aspirin OR dantrium OR duragesic OR ibuprofen OR naproxen OR 'non prescription' OR non-prescription OR 'nonprescription' OR 'over the counter' OR over-the-counter OR paracetamol OR tylenol):ab,ti
14	KQ4 NSAIDs	celecoxib/exp OR 'choline magnesium '/exp OR 'choline magnesium trisalicylate'/exp OR diclofenac/exp OR diflunisal/exp OR etodolac/exp OR flurbiprofen/exp OR ketoprofen/exp OR meclofenamate/exp OR meloxicam/exp OR 'nonsteroid antiinflammatory agent'/exp OR oxaprzin/exp OR piroxicam/exp OR 'salicylic acid derivative'/exp OR salsalate/exp OR sulindac/exp OR tolmetin/exp OR trilisate/exp OR (clinoril OR daypro OR diclofenac OR disalcid OR feldene OR lodine OR mobic OR non-steroid* OR nonsteroid* OR nsaid* OR ocufen OR orudis OR oruvail OR salicylate* OR 'salicylic acid' OR solaraze OR tolectin OR trilisate OR voltaren):ab,ti
15	KQ4 Opioids	acetylmethadol/exp OR alfentanil/exp OR alphaprodine/exp OR 'beta-casomorphin'/exp OR carfentanil/exp OR codeine/exp OR deltorphin/exp OR dextropropoxyphene/exp OR dezocine/exp OR dihydrocodeine/exp OR dihydrocodeine/exp OR dihydromorphine/exp OR etorphine/exp OR ethylketocyclazocine/exp OR ethylmorphine/exp OR hydrocodone/exp OR hydromorphone/exp OR ketobemidone/exp OR levorphanol/exp OR lofentanil/exp OR meptazinol/exp OR methadone/exp OR morphine/exp OR nalbuphine/exp OR 'narcotic analgesic agent'/exp OR opiate/exp OR oxycodone/exp OR oxymorphone/exp OR pentazocine/exp OR pethidine/exp OR phenazocine/exp OR phenazocine/exp OR phenazocine/exp OR prinitramide/exp OR remifentanil/exp OR sufentanil/exp OR tapentadol/exp OR tilidine/exp OR tramadol/exp OR trimeperidine/exp OR (alfenta OR buprenex OR dalgan OR darvon OR demerol OR dicodid OR dilaudid OR dolophine OR 'hydrostat ir' OR 'levo-droman' OR meperidine OR methadose OR 'methadyl acetate' OR narcotic* OR nubain OR numphan OR opana OR opiate* OR opioid* OR oxycodone OR oxycontin OR oxyfast OR oxyir OR percolone OR promedol OR propoxyphene OR roxicodone OR talwin OR ultiva OR
16	KQ5 For adults with LBP, what is the effect of nutritional, herbal, and homeopathic supplements?	ultram):ab,ti  'arachidonic acid'/exp OR arnica/exp OR 'ascorbic acid'/exp OR cannabinoid/exp OR 'cayenne pepper'/exp OR 'chinese medicine'/exp OR 'cod liver oil'/exp OR 'curcuma longa'/exp OR 'diet supplementation' OR 'diet therapy'/exp OR 'docosahexaenoic acid'/exp OR 'fish oil'/exp OR 'flavonoid'/exp OR ginger/exp OR harpagophytum/exp OR 'harpagophytum extract'/exp OR 'herbaceous agent'/exp OR 'icosapentaenoic acid'/exp OR 'omega 3 fatty acid'/exp OR 'omega 6 fatty acid'/exp OR 'resveratrol'/exp OR 'vitamin d'/exp OR ((diet* OR herb* OR holistic* OR homeopath* OR nutrition* OR omega*) NEAR/2 (supplement*)):ab,ti OR (('anti inflam*' OR antiinflam* OR 'arachidonic acid') NEXT/1 diet*):ab,ti OR (devil* NEXT/1 claw):ab,ti OR (arnica OR cannabi* OR cayenne OR curcumin* OR dha OR 'eicosapentaenoic acid' OR epa OR 'fish oil' OR flavonoid OR ginger OR harpagophytum OR 'n 3 fatty acid*' OR resveratrol OR tumeric OR 'vitamin c' OR 'vitamin d' OR 'willow bark'):ab,ti
17	KQ6 For adults with LBP, what is the treatment effectiveness of epidural injections, facet blocks, nerve root blocks, radio frequency ablation (RFA)?	'epidural anesthesia'/exp OR 'epidural drug administration'/exp OR 'intraspinal drug administration'/exp OR 'nerve block'/exp OR 'radiofrequency ablation'/exp OR 'spinal anesthesia'/exp OR ((corticosteroid* OR epidural OR facet OR foraminal OR interspin* OR intraspin* OR lumbar OR nerve OR paraspin* OR spinal OR 'trigger point' OR zygapophyseal) NEAR/2 (anaesthes* OR anesthes* OR block* OR inject*)):ab,ti OR (radiofreq* OR rf OR rfa):ab,ti

September 2017 Page 97 of 110

Set #	Concept	Search Statement
18	KQ7 For adults with LBP, what combination therapy (pharmacologic and nonpharmacologic) is most effective?	'drug combination'/exp OR ((combin* OR integrat* OR multi*) NEAR/1 (care OR drug* OR modalit* OR pharm* OR therap* OR treat*)):ab,ti
19	For adults with chronic LBP, what is the effectiveness of behavioral interventions?	'behavior therapy'/exp OR 'cognitive therapy'/exp OR 'feedback system'/exp OR 'meditation'/exp OR 'mindfulness'/exp OR 'mental health care'/exp OR 'psychiatric treatment'/exp OR 'psychologic assessment'/exp OR 'psychological distress assessment'/exp OR 'psychological well being'/exp OR 'psychological well being assessment'/exp OR 'psychosocial rehabilitation'/exp OR psychotherapy/exp OR 'relaxation training'/exp OR ((cognitive* OR behavior* OR 'mental health' OR psych*) NEAR/2 (counsel* OR psychother* OR therap* OR treat*)):ab,ti OR (biofeedback* OR mbsr OR meditat* OR mindful* OR relax*):ab,ti
20	KQ8 Antidepressants	amfebutamone/exp OR amitriptyline/exp OR amoxapine/exp OR 'antidepressant activity'/exp OR 'antidepressant agent'/exp OR citalopram/exp OR clomipramine/exp OR desipramine/exp OR desvenlafaxine/exp OR doxepin/exp OR duloxetine/exp OR escitalopram/exp OR fluvoxamine/exp OR imipramine/exp OR maprotiline/exp OR mianserin/exp OR milnacipran/exp OR mirtazapine/exp OR 'monoamine oxidase inhibitor'/exp OR nefazodone/exp OR 'noradrenalin update inhibitor'/exp OR nortriptyline/exp OR paroxetine/exp OR protriptyline/exp OR selegiline/exp OR 'serotonin noradrenalin reuptake inhibitor'/exp OR 'serotonin uptake inhibitor'/exp OR 'tetracyclic antidepressant agent'/exp OR trazodone/exp OR 'triple reuptake inhibitor'/exp OR venlafaxine/exp OR vilazodone/exp OR vortioxetine/exp OR (amfebutamone OR amitriptyline amoxapine OR anafranil OR antidepres* OR asendin OR aventyl OR bupropion OR brintellix OR celexa OR cymbalta OR desyrel OR effexor OR emsam OR fetzima OR fluoxetine OR lexapro OR levomilnacipran OR maoi OR 'mao inhibitor*' OR norpramin OR oleptro OR pamelor OR paroxetine OR paxil OR pristiq OR protriptyline OR prozac OR prudoxin OR remeron OR savella OR sertraline OR serzone OR sinequan OR sndri OR ssri OR tofranil OR tricyclic OR trimipramine OR trintellix OR viibryd OR vivactil OR wellbutrin OR zoloft OR zonalon OR zyban):ab,ti
21	For adults with low back pain, what is the impact of mental health diagnoses (e.g., depression, anxiety, ADHD, PTSD, TBI) or psychosocial stressors (e.g., divorce, death, job loss) on treatment outcomes?	anxiety/exp OR 'anxiety disorder'/exp OR 'attention deficit disorder'/exp OR catastrophizing/exp OR depression/exp OR 'family stress'/exp OR 'mental disease'/exp OR 'mental stress'/exp OR 'posttraumatic stress disorder'/exp OR 'psychosocial care'/exp OR 'psychosocial disorder'/exp OR 'psychosocial environment'/exp OR 'psychosocial withdrawal'/exp OR 'social psychology'/exp OR 'traumatic brain injury'/exp OR unemployment/exp OR (adhd OR anxiety OR anxious* OR 'attention deficit' OR catastrophiz* OR death* OR depress* OR divorce* OR post-traumatic OR 'post traumatic' OR psychosocial OR ptsd OR stress* OR tbi OR 'traumatic brain' OR unemploy*):ab,ti
22	Lumbar Set	S1 OR (S2 AND S3)
23	Lumbar Set Combined with Key Questions	S22 AND (S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16 OR S17 OR S18 OR S19 OR S20 OR S21)
24	Apply Limits	S23 AND [english]/lim AND [2006-2016]/py AND ([article in press]/lim OR [humans]/lim OR [in process]/lim)

September 2017 Page 98 of 110

Set #	Concept	Search Statement
25	Remove Youth and Selected Subgroup Populations	S24 NOT (adolescen* OR bifida OR birth* OR boy OR boys OR case* OR child* OR comment* OR cyst* OR dysmenor* OR editorial OR errata OR erratum OR girl OR girls OR infan*OR letter OR menopaus* OR neonat* OR newborn* OR paediatric* OR pediatric* OR pregnan* OR premenstrual OR postmenopaus* OR puerperal OR rat OR rats OR reply OR 'school age*' OR 'school-age*' OR scoliosis OR teen* OR toddler* OR withdrawn OR 'year-old' OR young* OR youth*):ti
26	Remove Specific Study Designs	S25 NOT (abstract:nc OR annual:nc OR book/exp OR case*:ti OR 'case report'/exp OR 'case study'/exp conference:nc OR 'conference abstract':it OR 'conference paper'/exp OR 'conference paper':it OR 'conference proceeding':pt OR 'conference review':it OR congress:nc OR editorial/exp OR editorial:it OR erratum/exp OR letter:it OR note/exp OR note:it OR meeting:nc OR sessions:nc OR 'short survey'/exp OR symposium:nc)
27	Apply Therapy Study Design Filter	S26 AND (metaanaly*:ti OR 'meta anal*':ti OR 'meta-anal*':ti OR 'meta analysis'/exp OR random*:ti OR 'randomized controlled trial'/exp OR systematic*:ti OR 'systematic review'/exp)
28	Lumbar Set Combined with Diagnostic Tests Set	S22 AND S4
29	Apply Limits	S28 AND [english]/lim AND [2006-2016]/py AND ([article in press]/lim OR [humans]/lim OR [in process]/lim)
30	Remove Youth and Selected Subgroup Populations	S29 NOT (adolescen* OR bifida OR birth* OR boy OR boys OR case* OR child* OR comment* OR cyst* OR dysmenor* OR editorial OR errata OR erratum OR girl OR girls OR infan*OR letter OR menopaus* OR neonat* OR newborn* OR paediatric* OR pediatric* OR pregnan* OR premenstrual OR postmenopaus* OR puerperal OR rat OR rats OR reply OR 'school age*' OR 'school-age*' OR scoliosis OR teen* OR toddler* OR withdrawn OR 'year-old ' OR young* OR youth*):ti
31	Remove Unwanted Study Designs	S30 NOT (abstract:nc OR annual:nc OR book/exp OR case*:ti OR 'case report'/exp OR 'case study'/exp conference:nc OR 'conference abstract':it OR 'conference paper'/exp OR 'conference paper':it OR 'conference proceeding':pt OR 'conference review':it OR congress:nc OR editorial/exp OR editorial:it OR erratum/exp OR letter:it OR note/exp OR note:it OR meeting:nc OR sessions:nc OR 'short survey'/exp OR symposium:nc)
32	Apply Diagnostic Filter	S31 AND (accuracy:ti OR 'area under the curve'/exp OR diagnos*:ti OR 'diagnostic accuracy'/exp OR 'diagnostic error'/exp OR 'diagnostic test accuracy study'/exp OR 'false negative result'/exp OR 'observer variation'/exp OR 'predictive value':ab,ti OR 'predictive value'/exp OR probability/exp OR 'receiver operating characteristic'/exp OR reproducibility/exp OR sensitivity:ti OR 'sensitivity analysis'/exp OR 'sensitivity and specificity'/exp OR specificity:ti OR test*:ti OR (false NEXT/1 (negativ* OR positiv*)):ab,ti OR (likelihood NEXT/1 (function OR ratio*)):ab,ti)
33	Remove Selected Populations and Study types	S32 NOT (adolescen*:ti OR bifida:ti OR birth*:ti OR boy:ti OR boys:ti OR case*:ti OR child*:ti OR comment:ti OR cyst*:ti OR dysmenor*:ti OR editorial:ti OR errata:ti OR erratum:ti OR girl:ti OR girls:ti OR infan*:ti OR letter:ti OR menstrua*:ti OR menopaus*:ti OR neonat*:ti OR newborn*:ti OR paediatric*:ti OR pediatric*:ti OR postmenopaus*:ti OR pregnan*:ti OR premenstrual:ti OR puerperal:ti OR rat:ti OR rats:ti OR reply:ti OR 'school age*':ti OR scoliosis:ti OR teen*:ti OR toddler*:ti OR withdrawn:ti OR 'year-old':ti OR young*:ti OR youth*:ti)
34	Combine Therapy and Diagnostic Sets	S27 OR S33
		ı

September 2017 Page 99 of 110

#### **EMBASE.com Syntax:**

\* (within or following a term) = truncation character (wildcard)

:ab = limit to abstract

:ab,ti = limit to abstract and title

NEAR/n = search terms within a specified number (n) of words from each other in any order

/exp = "explodes" controlled vocabulary term (e.g., expands search to all more specific related terms

in the vocabulary's hierarchy)

:it. = limit to publication type

:ti. = limit to title

September 2017 Page 100 of 110

# Appendix I: Abbreviation List

Abbreviation	Definition
ACT	acceptance and commitment therapy
AHRQ	Agency for Healthcare Research and Quality
BPI	back pain intensity
CBT	cognitive behavioral therapy
CES	cauda equina syndrome
CI	confidence interval
CNS	central nervous system
COI	conflict of interest
COR	contracting officer's representative
COX-2	cyclooxygenase-2
CPG	clinical practice guideline
СТ	computerized tomography
CV	cardiovascular
DoD	Department of Defense
EBPWG	Evidence-Based Practice Work Group
ESI	epidural steroid injection
ESR	electronic spin resonance
FDA	Food and Drug Administration
GI	gastrointestinal
GRADE	Grading of Recommendations Assessment, Development and Evaluation
KQ	key question
LBP	low back pain
LBPI	lower back pain intensity
MBR	multidisciplinary biopsychosocial rehabilitation
MBSR	mindfulness-based stress reduction
MeSH	Medical Subject Headings
MRI	magnetic resonance imaging
NICE	National Institute for Health and Care Excellence
NSAID	nonsteroidal anti-inflammatory drugs
ОТС	over the counter
PHQ	Patient Health Questionnaire
PICOTS	population, intervention, comparison, outcome, timing and setting
RCT	randomized controlled trial
RFA	radiofrequency ablation denervation
RMDQ	Roland-Morris Disability Questionnaire
SNRB	selective nerve root blocks
SNRI	serotonin and norepinephrine reuptake inhibitors
SR	systematic review
SSRI	selective serotonin reuptake inhibitors

September 2017 Page 101 of 110

Abbreviation	Definition
TCA	tricyclic antidepressants
TENS	transcutaneous electrical nerve stimulation
U.S.	United States
USPSTF	United States Preventive Services Task Force
VA	Department of Veterans Affairs
VAS	visual analog scale
VHA	Veterans Health Administration

September 2017 Page 102 of 110

#### References

- 1. U.S. Department of Veteran Affairs, Department of Defense. Guideline for Guidelines. Veterans Health Administration, Office of Quality & Performance, Evidence Review Subgroup; Revised April 10, 2013.
- 2. National Institute of Arthritis and Musculoskeletal and Skin Diseases. Handout on health: Back pain *NIH Publication No. 16-5282.* 2016.
- 3. Chou R, Deyo R, Friedly J, et al. AHRQ comparative effectiveness reviews. *Noninvasive treatments for low back pain*. Rockville (MD): Agency for Healthcare Research and Quality (US); 2016.
- 4. Murray CJ, Atkinson C, Bhalla K, et al. The state of US health, 1990-2010: Burden of diseases, injuries, and risk factors. *JAMA*. Aug 14 2013;310(6):591-608.
- 5. Centers for Disease Control and Prevention. Severe headache or migraine, low back pain, and neck pain among adults aged 18 and over, by selected characteristics: United States, selected years 1997–2012. *National Health Survey* 2012.
- 6. Liddle SD, Pennick V. Interventions for preventing and treating low-back and pelvic pain during pregnancy. *Cochrane Database Syst Rev.* Sep 30 2015(9):Cd001139.
- 7. Dieleman JL, Baral R, Birger M, et al. US spending on personal health care and public health, 1996-2013. *JAMA*. Dec 27 2016;316(24):2627-2646.
- 8. Nahin RL. Severe pain in Veterans: The effect of age and sex, and comparisons with the general population. *J Pain*. Mar 2017;18(3):247-254.
- 9. Clark LL, Hu Z. Diagnoses of low back pain, active component, U.S. Armed forces, 2010-2014. *Msmr.* Dec 2015;22(12):8-11.
- 10. Andrews J, Guyatt G, Oxman AD, et al. GRADE guidelines: 14. Going from evidence to recommendations: The significance and presentation of recommendations. *J Clin Epidemiol.* Jul 2013;66(7):719-725.
- 11. Guyatt GH, Oxman AD, Kunz R, et al. Going from evidence to recommendations. *BMJ.* May 10 2008;336(7652):1049-1051.
- 12. Newberry SJ, Ahmadzai N, Motala A, et al. AHRQ methods for effective health care. *Surveillance and identification of signals for updating systematic reviews: Implementation and early experience*. Rockville (MD): Agency for Healthcare Research and Quality (US); 2013.
- 13. Guirguis-Blake J, Calonge N, Miller T, Siu A, Teutsch S, Whitlock E. Current processes of the U.S. Preventive Services Task Force: Refining evidence-based recommendation development. *Ann Intern Med.* Jul 17 2007;147(2):117-122.
- 14. *The guidelines manual.* London: National Institute for Health and Care Excellence;2012. <a href="https://www.nice.org.uk/process/pmg6/chapter/introduction">https://www.nice.org.uk/process/pmg6/chapter/introduction</a>.
- 15. Martinez Garcia L, McFarlane E, Barnes S, Sanabria AJ, Alonso-Coello P, Alderson P. Updated recommendations: An assessment of NICE clinical guidelines. *Implement Sci.* 2014;9:72.
- 16. White CM, Ip S, McPheeters M, et al. AHRQ methods for effective health care using existing systematic reviews to replace de novo processes in conducting comparative effectiveness reviews. *Methods guide for effectiveness and comparative effectiveness reviews*. Rockville (MD): Agency for Healthcare Research and Quality (US); 2008.
- 17. Institute of Medicine (US) Committe on Standards for Developing Trustworthy Clinical Practice Guidelines, R Graham, M Mancher, D Miller Wolman, et al., editors. *Clinical practice guidelines we can trust*. Washington, DC: National Academies Press;2011.
- 18. Schunemann HJ, Fretheim A, Oxman AD. Improving the use of research evidence in guideline development: 10. Integrating values and consumer involvement. *Health Res Policy Syst.* 2006;4:22.
- 19. Bertakis KD, Azari R. Patient-centered care is associated with decreased health care utilization. *J Am Board Fam Med.* May-Jun 2011;24(3):229-239.

September 2017 Page 103 of 110

- 20. Robinson JH, Callister LC, Berry JA, Dearing KA. Patient-centered care and adherence: Definitions and applications to improve outcomes. *J Am Acad Nurse Pract*. Dec 2008;20(12):600-607.
- 21. *Crossing the quality chasm: A new health system for the 21st century.* Washington DC: National Academies Press;2001.
- 22. Society for Medical Decision Making Committee on Standardization of Clinical Algorithms. Proposal for clinical algorithm standards. *Med Decis Making*. Apr-Jun 1992;12(2):149-154.
- 23. Pengel LH, Herbert RD, Maher CG, Refshauge KM. Acute low back pain: Systematic review of its prognosis. *BMJ*. Aug 09 2003;327(7410):323.
- 24. van Tulder MW, Assendelft WJ, Koes BW, Bouter LM. Spinal radiographic findings and nonspecific low back pain. A systematic review of observational studies. *Spine (Phila Pa 1976)*. Feb 15 1997;22(4):427-434.
- 25. Hestbaek L, Leboeuf-Yde C, Manniche C. Low back pain: What is the long-term course? A review of studies of general patient populations. *Eur Spine J.* Apr 2003;12(2):149-165.
- 26. Jarvik JG, Deyo RA. Diagnostic evaluation of low back pain with emphasis on imaging. *Ann Intern Med.* Oct 01 2002;137(7):586-597.
- 27. Downie A, Williams CM, Henschke N, et al. Red flags to screen for malignancy and fracture in patients with low back pain: Systematic review. *BMJ*. Dec 11 2013;347:f7095.
- 28. Deyo RA, Diehl AK. Cancer as a cause of back pain: Frequency, clinical presentation, and diagnostic strategies. *J Gen Intern Med.* May-Jun 1988;3(3):230-238.
- 29. Enthoven WT, Geuze J, Scheele J, et al. Prevalence and "red flags" regarding specified causes of back pain in older adults presenting in general practice. *Phys Ther.* Mar 2016;96(3):305-312.
- 30. Shaw WS, Means-Christensen AJ, Slater MA, et al. Psychiatric disorders and risk of transition to chronicity in men with first onset low back pain. *Pain Med.* Sep 2010;11(9):1391-1400.
- 31. Pinheiro MB, Ferreira ML, Refshauge K, et al. Symptoms of depression as a prognostic factor for low back pain: A systematic review. *Spine J.* Jan 01 2016;16(1):105-116.
- 32. Yarlas A, Miller K, Wen W, et al. A subgroup analysis found no diminished response to buprenorphine transdermal system treatment for chronic low back pain patients classified with depression. *Pain Pract.* Apr 2016;16(4):473-485.
- 33. Kendrick D, Fielding K, Bentley E, Kerslake R, Miller P, Pringle M. Radiography of the lumbar spine in primary care patients with low back pain: Randomised controlled trial. *BMJ*. Feb 17 2001;322(7283):400-405.
- 34. Kerry S, Hilton S, Dundas D, Rink E, Oakeshott P. Radiography for low back pain: A randomised controlled trial and observational study in primary care. *Br J Gen Pract*. Jun 2002;52(479):469-474.
- 35. Gilbert FJ, Grant AM, Gillan MG, et al. Low back pain: Influence of early MR imaging or CT on treatment and outcome--multicenter randomized trial. *Radiology*. May 2004;231(2):343-351.
- 36. Jarvik JG, Hollingworth W, Martin B, et al. Rapid magnetic resonance imaging vs radiographs for patients with low back pain: A randomized controlled trial. *JAMA*. Jun 04 2003;289(21):2810-2818.
- 37. Chou R, Fu R, Carrino JA, Deyo RA. Imaging strategies for low-back pain: Systematic review and meta-analysis. *Lancet*. Feb 07 2009;373(9662):463-472.
- 38. Brinjikji W, Luetmer PH, Comstock B, et al. Systematic literature review of imaging features of spinal degeneration in asymptomatic populations. *AJNR Am J Neuroradiol*. Apr 2015;36(4):811-816.
- 39. Cohen SP, Gupta A, Strassels SA, et al. Effect of MRI on treatment results or decision making in patients with lumbosacral radiculopathy referred for epidural steroid injections: A multicenter, randomized controlled trial. *Arch Intern Med.* Jan 23 2012;172(2):134-142.
- 40. Nicholas MK, Linton SJ, Watson PJ, Main CJ. Early identification and management of psychological risk factors ("yellow flags") in patients with low back pain: A reappraisal. *Phys Ther.* May 2011;91(5):737-753.

September 2017 Page 104 of 110

- 41. Margetic P, Pavic R, Stancic MF. Provocative discography screening improves surgical outcome. *Wien Klin Wochenschr*. Oct 2013;125(19-20):600-610.
- 42. Vroomen PC, de Krom MC, Knottnerus JA. Predicting the outcome of sciatica at short-term follow-up. *Br J Gen Pract*. Feb 2002;52(475):119-123.
- 43. Weber H. Lumbar disc herniation. A controlled, prospective study with ten years of observation. *Spine (Phila Pa 1976).* Mar 1983;8(2):131-140.
- 44. Wassenaar M, van Rijn RM, van Tulder MW, et al. Magnetic resonance imaging for diagnosing lumbar spinal pathology in adult patients with low back pain or sciatica: A diagnostic systematic review. *Eur Spine J.* Feb 2012;21(2):220-227.
- 45. van Rijn RM, Wassenaar M, Verhagen AP, et al. Computed tomography for the diagnosis of lumbar spinal pathology in adult patients with low back pain or sciatica: A diagnostic systematic review. *Eur Spine J.* Feb 2012;21(2):228-239.
- 46. Chou R, Qaseem A, Snow V, et al. Diagnosis and treatment of low back pain: A joint clinical practice guideline from the American College of Physicians and the American Pain Society. *Ann Intern Med.* Oct 02 2007;147(7):478-491.
- 47. Rihn JA, Lee JY, Khan M, et al. Does lumbar facet fluid detected on magnetic resonance imaging correlate with radiographic instability in patients with degenerative lumbar disease? *Spine (Phila Pa 1976)*. Jun 15 2007;32(14):1555-1560.
- 48. Manchikanti L, Abdi S, Atluri S, et al. An update of comprehensive evidence-based guidelines for interventional techniques in chronic spinal pain. Part II: Guidance and recommendations. *Pain Physician*. Apr 2013;16(2 Suppl):S49-283.
- 49. Beresford ZM, Kendall RW, Willick SE. Lumbar facet syndromes. *Curr Sports Med Rep.* Jan-Feb 2010;9(1):50-56.
- 50. Whedon JM, Mackenzie TA, Phillips RB, Lurie JD. Risk of traumatic injury associated with chiropractic spinal manipulation in Medicare part b beneficiaries aged 66 to 99 years. *Spine (Phila Pa 1976)*. Feb 15 2015;40(4):264-270.
- 51. Lurie JD, Birkmeyer NJ, Weinstein JN. Rates of advanced spinal imaging and spine surgery. *Spine* (*Phila Pa 1976*). Mar 15 2003;28(6):616-620.
- 52. Hagen KB, Hilde G, Jamtvedt G, Winnem M. Bed rest for acute low-back pain and sciatica. *Cochrane Database Syst Rev.* Oct 18 2004(4):Cd001254.
- 53. Hilde G, Hagen KB, Jamtvedt G, Winnem M. Advice to stay active as a single treatment for low back pain and sciatica. *Cochrane Database Syst Rev.* 2002(2):Cd003632.
- 54. Kovacs FM, Abraira V, Pena A, et al. Effect of firmness of mattress on chronic non-specific low-back pain: Randomised, double-blind, controlled, multicentre trial. *Lancet*. Nov 15 2003;362(9396):1599-1604.
- S5. Royal College of General Practitioners, NHS Executive. *The Back Book; the best way to deal with back pain; get back active.* Second ed. Norwich, UK: The Stationary Office; 2002.
- 56. Burton AK, Waddell G, Tillotson KM, Summerton N. Information and advice to patients with back pain can have a positive effect. A randomized controlled trial of a novel educational booklet in primary care. *Spine (Phila Pa 1976)*. Dec 01 1999;24(23):2484-2491.
- 57. Pires D, Cruz EB, Caeiro C. Aquatic exercise and pain neurophysiology education versus aquatic exercise alone for patients with chronic low back pain: A randomized controlled trial. *Clin Rehabil.* Jun 2015;29(6):538-547.
- 58. Butler D, Moseley L. Explain pain. *Noigroup* 2003.
- 59. Nijs J, Paul van Wilgen C, Van Oosterwijck J, van Ittersum M, Meeus M. How to explain central sensitization to patients with 'unexplained' chronic musculoskeletal pain: Practice guidelines. *Man Ther.* Oct 2011;16(5):413-418.

September 2017 Page 105 of 110

- 60. Straube S, Harden M, Schroder H, et al. Back schools for the treatment of chronic low back pain: Possibility of benefit but no convincing evidence after 47 years of research-systematic review and meta-analysis. *Pain*. Oct 2016;157(10):2160-2172.
- 61. del Pozo-Cruz B, del Pozo-Cruz J, Adsuar JC, Parraca J, Gusi N. Reanalysis of a tailored web-based exercise programme for office workers with sub-acute low back pain: Assessing the stage of change in behaviour. *Psychol Health Med.* 2013;18(6):687-697.
- 62. Cherkin DC, Sherman KJ, Balderson BH, et al. 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*. Mar 22-29 2016;315(12):1240-1249.
- 63. Hempel S, Taylor SL, Marshall NJ, et al. VA evidence-based synthesis program reports. *Evidence map of mindfulness*. Washington (DC): Department of Veterans Affairs (US); 2014.
- 64. Kent P, Laird R, Haines T. The effect of changing movement and posture using motion-sensor biofeedback, versus guidelines-based care, on the clinical outcomes of people with sub-acute or chronic low back pain-a multicentre, cluster-randomised, placebo-controlled, pilot trial. *BMC Musculoskelet Disord*. May 29 2015;16:131.
- 65. Holden J, Davidson M, O'Halloran PD. Health coaching for low back pain: A systematic review of the literature. *Int J Clin Pract*. Aug 2014;68(8):950-962.
- 66. Chou R, Deyo R, Friedly J, et al. Nonpharmacologic therapies for low back pain: A systematic review for an American College of Physicians clinical practice guideline. *Ann Intern Med.* Apr 04 2017;166(7):493-505.
- 67. Anheyer D, Haller H, Barth J, Lauche R, Dobos G, Cramer H. Mindfulness-based stress reduction for treating low back pain: A systematic review and meta-analysis. *Ann Intern Med.* Jun 06 2017;166(11):799-807.
- 68. Cherkin DC, Anderson ML, Sherman KJ, et al. Two-year follow-up of a randomized clinical trial of mindfulness-based stress reduction vs cognitive behavioral therapy or usual care for chronic low back pain. *JAMA*. Feb 14 2017;317(6):642-644.
- 69. Veehof MM, Trompetter HR, Bohlmeijer ET, Schreurs KM. Acceptance- and mindfulness-based interventions for the treatment of chronic pain: A meta-analytic review. *Cogn Behav Ther*. 2016;45(1):5-31.
- 70. Ost LG. The efficacy of acceptance and commitment therapy: An updated systematic review and meta-analysis. *Behav Res Ther.* Oct 2014;61:105-121.
- 71. Veehof MM, Oskam MJ, Schreurs KM, Bohlmeijer ET. Acceptance-based interventions for the treatment of chronic pain: A systematic review and meta-analysis. *Pain.* Mar 2011;152(3):533-542.
- 72. Diaz-Arribas MJ, Kovacs FM, Royuela A, et al. Effectiveness of the Godelieve Denys-Struyf (GDS) method in people with low back pain: Cluster randomized controlled trial. *Phys Ther.* Mar 2015;95(3):319-336.
- 73. Lehtola V, Luomajoki H, Leinonen V, Gibbons S, Airaksinen O. Sub-classification based specific movement control exercises are superior to general exercise in sub-acute low back pain when both are combined with manual therapy: A randomized controlled trial. *BMC Musculoskelet Disord*. Mar 22 2016;17:135.
- 74. Lau PM, Chow DH, Pope MH. Early physiotherapy intervention in an accident and emergency department reduces pain and improves satisfaction for patients with acute low back pain: A randomised trial. *Aust J Physiother.* 2008;54(4):243-249.
- 75. Fritz JM, Magel JS, McFadden M, et al. Early physical therapy vs usual care in patients with recent-onset low back pain: A randomized clinical trial. *JAMA*. Oct 13 2015;314(14):1459-1467.
- 76. Childs JD, Fritz JM, Wu SS, et al. Implications of early and guideline adherent physical therapy for low back pain on utilization and costs. *BMC Health Serv Res.* Apr 09 2015;15:150.

September 2017 Page 106 of 110

- 77. Rubinstein SM, van Middelkoop M, Assendelft WJ, de Boer MR, van Tulder MW. Spinal manipulative therapy for chronic low-back pain: An update of a Cochrane review. *Spine (Phila Pa 1976)*. Jun 2011;36(13):E825-846.
- 78. Bronfort G, Hondras MA, Schulz CA, Evans RL, Long CR, Grimm R. Spinal manipulation and home exercise with advice for subacute and chronic back-related leg pain: A trial with adaptive allocation. *Ann Intern Med.* Sep 16 2014;161(6):381-391.
- 79. Bronfort G, Maiers MJ, Evans RL, et al. Supervised exercise, spinal manipulation, and home exercise for chronic low back pain: A randomized clinical trial. *Spine J.* Jul 2011;11(7):585-598.
- 80. Petersen T, Larsen K, Nordsteen J, Olsen S, Fournier G, Jacobsen S. 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*). Nov 15 2011;36(24):1999-2010.
- 81. Cecchi F, Molino-Lova R, Chiti M, et al. Spinal manipulation compared with back school and with individually delivered physiotherapy for the treatment of chronic low back pain: A randomized trial with one-year follow-up. *Clin Rehabil*. Jan 2010;24(1):26-36.
- 82. Rubinstein SM, Terwee CB, Assendelft WJ, de Boer MR, van Tulder MW. Spinal manipulative therapy for acute low back pain: An update of the Cochrane review. *Spine (Phila Pa 1976)*. Feb 01 2013;38(3):E158-177.
- 83. Dougherty PE, Karuza J, Dunn AS, Savino D, Katz P. Spinal manipulative therapy for chronic lower back pain in older Veterans: A prospective, randomized, placebo-controlled trial. *Geriatr Orthop Surg Rehabil*. Dec 2014;5(4):154-164.
- 84. Schneider M, Haas M, Glick R, Stevans J, Landsittel D. Comparison of spinal manipulation methods and usual medical care for acute and subacute low back pain: A randomized clinical trial. *Spine* (*Phila Pa 1976*). Feb 15 2015;40(4):209-217.
- 85. Oleske DM, Lavender SA, Andersson GB, Kwasny MM. Are back supports plus education more effective than education alone in promoting recovery from low back pain?: Results from a randomized clinical trial. *Spine (Phila Pa 1976)*. Sep 01 2007;32(19):2050-2057.
- 86. Calmels P, Queneau P, Hamonet C, et al. Effectiveness of a lumbar belt in subacute low back pain: An open, multicentric, and randomized clinical study. *Spine (Phila Pa 1976)*. Feb 01 2009;34(3):215-220.
- 87. Sato N, Sekiguchi M, Kikuchi S, Shishido H, Sato K, Konno S. Effects of long-term corset wearing on chronic low back pain. *Fukushima J Med Sci.* 2012;58(1):60-65.
- 88. Searle A, Spink M, Ho A, Chuter V. Exercise interventions for the treatment of chronic low back pain: A systematic review and meta-analysis of randomised controlled trials. *Clin Rehabil*. Dec 2015;29(12):1155-1167.
- 89. Waller B, Lambeck J, Daly D. Therapeutic aquatic exercise in the treatment of low back pain: A systematic review. *Clin Rehabil.* Jan 2009;23(1):3-14.
- 90. Marshall PW, Kennedy S, Brooks C, Lonsdale C. Pilates exercise or stationary cycling for chronic nonspecific low back pain: Does it matter? A randomized controlled trial with 6-month follow-up. *Spine (Phila Pa 1976)*. Jul 01 2013;38(15):E952-959.
- 91. O'Connor SR, Tully MA, Ryan B, et al. Walking exercise for chronic musculoskeletal pain: Systematic review and meta-analysis. *Arch Phys Med Rehabil*. Apr 2015;96(4):724-734.e723.
- 92. Goode AP, Coeytaux RR, McDuffie J, et al. An evidence map of yoga for low back pain. *Complement Ther Med.* Apr 2016;25:170-177.
- 93. Aboagye E, Karlsson ML, Hagberg J, Jensen I. Cost-effectiveness of early interventions for non-specific low back pain: A randomized controlled study investigating medical yoga, exercise therapy and self-care advice. *J Rehabil Med.* Feb 2015;47(2):167-173.

September 2017 Page 107 of 110

- 94. Kofotolis N, Kellis E, Vlachopoulos SP, Gouitas I, Theodorakis Y. Effects of Pilates and trunk strengthening exercises on health-related quality of life in women with chronic low back pain. *J Back Musculoskelet Rehabil.* Nov 21 2016;29(4):649-659.
- 95. Yamato TP, Maher CG, Saragiotto BT, et al. Pilates for low back pain: Complete republication of a Cochrane review. *Spine (Phila Pa 1976)*. Jun 2016;41(12):1013-1021.
- 96. Kamioka H, Tsutani K, Katsumata Y, et al. Effectiveness of Pilates exercise: A quality evaluation and summary of systematic reviews based on randomized controlled trials. *Complement Ther Med.* Apr 2016;25:1-19.
- 97. Kong LJ, Lauche R, Klose P, et al. Tai chi for chronic pain conditions: A systematic review and metaanalysis of randomized controlled trials. *Sci Rep.* Apr 29 2016;6:25325.
- 98. Buchmuller A, Navez M, Milletre-Bernardin M, et al. Value of tens for relief of chronic low back pain with or without radicular pain. *Eur J Pain*. May 2012;16(5):656-665.
- 99. Wegner I, Widyahening IS, van Tulder MW, et al. Traction for low-back pain with or without sciatica. *Cochrane Database Syst Rev.* Aug 19 2013(8):Cd003010.
- 100. Moustafa IM, Diab AA. Extension traction treatment for patients with discogenic lumbosacral radiculopathy: A randomized controlled trial. *Clin Rehabil.* Jan 2013;27(1):51-62.
- 101. Diab AA, Moustafa IM. Lumbar lordosis rehabilitation for pain and lumbar segmental motion in chronic mechanical low back pain: A randomized trial. *J Manipulative Physiol Ther.* May 2012;35(4):246-253.
- 102. Diab AA, Moustafa IM. The efficacy of lumbar extension traction for sagittal alignment in mechanical low back pain: A randomized trial. *J Back Musculoskelet Rehabil*. 2013;26(2):213-220.
- 103. Luedtke K, Rushton A, Wright C, et al. Effectiveness of transcranial direct current stimulation preceding cognitive behavioural management for chronic low back pain: Sham controlled double blinded randomised controlled trial. *BMJ*. Apr 16 2015;350:h1640.
- 104. Kivitz AJ, Gimbel JS, Bramson C, et al. Efficacy and safety of tanezumab versus naproxen in the treatment of chronic low back pain. *Pain.* Jul 2013;154(7):1009-1021.
- 105. Zerbini C, Ozturk ZE, Grifka J, et al. Efficacy of etoricoxib 60 mg/day and diclofenac 150 mg/day in reduction of pain and disability in patients with chronic low back pain: Results of a 4-week, multinational, randomized, double-blind study. *Curr Med Res Opin.* Dec 2005;21(12):2037-2049.
- 106. Zippel H, Wagenitz A. A multicentre, randomised, double-blind study comparing the efficacy and tolerability of intramuscular dexketoprofen versus diclofenac in the symptomatic treatment of acute low back pain. *Clin Drug Investig.* 2007;27(8):533-543.
- 107. Herndon CM, Hutchison RW, Berdine HJ, et al. Management of chronic nonmalignant pain with nonsteroidal antiinflammatory drugs. Joint opinion statement of the Ambulatory Care, Cardiology, and Pain and Palliative Care Practice and Research Networks of the American College of Clinical Pharmacy. *Pharmacotherapy*. Jun 2008;28(6):788-805.
- 108. Antman EM, Bennett JS, Daugherty A, Furberg C, Roberts H, Taubert KA. Use of nonsteroidal antiinflammatory drugs: An update for clinicians: A scientific statement from the American Heart Association. *Circulation*. Mar 27 2007;115(12):1634-1642.
- 109. Nissen SE, Yeomans ND, Solomon DH, et al. Cardiovascular safety of celecoxib, naproxen, or ibuprofen for arthritis. *N Engl J Med*. Dec 29 2016;375(26):2519-2529.
- Konno S, Oda N, Ochiai T, Alev L. A randomized, double-blind, placebo-controlled phase III trial of duloxetine monotherapy in Japanese patients with chronic low back pain. *Spine (Phila Pa 1976)*. May 23 2016.
- 111. Staiger TO, Gaster B, Sullivan MD, Deyo RA. Systematic review of antidepressants in the treatment of chronic low back pain. *Spine (Phila Pa 1976)*. Nov 15 2003;28(22):2540-2545.
- Salerno SM, Browning R, Jackson JL. The effect of antidepressant treatment on chronic back pain: A meta-analysis. *Arch Intern Med.* Jan 14 2002;162(1):19-24.

September 2017 Page 108 of 110

- 113. Pamelor [package insert]. Hazelwood, MO: Mallinckrodt LLC. October 2012.
- 114. American Geriatrics Society 2015 updated Beers criteria for potentially inappropriate medication use in older adults. *J Am Geriatr Soc.* Nov 2015;63(11):2227-2246.
- 115. Abdel Shaheed C, Maher CG, Williams KA, Day R, McLachlan AJ. Efficacy, tolerability, and dose-dependent effects of opioid analgesics for low back pain: A systematic review and meta-analysis. *JAMA Intern Med.* Jul 01 2016;176(7):958-968.
- 116. Friedman BW, Dym AA, Davitt M, et al. Naproxen with cyclobenzaprine, oxycodone/acetaminophen, or placebo for treating acute low back pain: A randomized clinical trial. *JAMA*. Oct 20 2015;314(15):1572-1580.
- 117. Brotz D, Maschke E, Burkard S, et al. Is there a role for benzodiazepines in the management of lumbar disc prolapse with acute sciatica? *Pain*. Jun 2010;149(3):470-475.
- 118. French DD, Spehar AM, Campbell RR, et al. Advances in patient safety outpatient benzodiazepine prescribing, adverse events, and costs. In: K. Henriksen, J. B. Battles, E. S. Marks, D. I. Lewin, eds. *Advances in patient safety: From research to implementation (volume 1: Research findings)*. Rockville (MD): Agency for Healthcare Research and Quality (US); 2005.
- 119. Goldberg H, Firtch W, Tyburski M, et al. Oral steroids for acute radiculopathy due to a herniated lumbar disk: A randomized clinical trial. *JAMA*. May 19 2015;313(19):1915-1923.
- 120. Stanbury RM, Graham EM. Systemic corticosteroid therapy--side effects and their management. *Br J Ophthalmol.* Jun 1998;82(6):704-708.
- 121. Saragiotto BT, Machado GC, Ferreira ML, Pinheiro MB, Abdel Shaheed C, Maher CG. Paracetamol for low back pain. *Cochrane Database Syst Rev.* Jun 07 2016(6):Cd012230.
- 122. Williams CM, Maher CG, Latimer J, et al. Efficacy of paracetamol for acute low-back pain: A double-blind, randomised controlled trial. *Lancet*. Nov 01 2014;384(9954):1586-1596.
- 123. Atkinson JH, Slater MA, Capparelli EV, et al. A randomized controlled trial of gabapentin for chronic low back pain with and without a radiating component. *Pain.* Jul 2016;157(7):1499-1507.
- 124. McCleane GJ. Does gabapentin have an analgesic effect on background, movement and referred pain? A randomised, double-blind, placebo controlled study *The Pain Clinic*. 2001;13(2):103-107.
- 125. Yildirim K, Şışecıoğlu M, Karatay S. The effectiveness of gabapentin in patients with chronic radiculopathy. *The Pain Clinic*. 2003;15(3):213-218.
- 126. Mathieson S, Maher CG, McLachlan AJ, et al. Trial of pregabalin for acute and chronic sciatica. *N Engl J Med.* Mar 23 2017;376(12):1111-1120.
- 127. Sodha R, Sivanadarajah N, Alam M. The use of glucosamine for chronic low back pain: A systematic review of randomised control trials. *BMJ Open*. Jun 20 2013;3(6).
- 128. Manchikanti L, Knezevic NN, Boswell MV, Kaye AD, Hirsch JA. Epidural injections for lumbar radiculopathy and spinal stenosis: A comparative systematic review and meta-analysis. *Pain Physician*. Mar 2016;19(3):E365-410.
- 129. Chou R, Hashimoto R, Friedly J, et al. AHRQ technology assessments. *Pain management injection therapies for low back pain*. Rockville (MD): Agency for Healthcare Research and Quality (US); 2015.
- 130. Spijker-Huiges A, Winters JC, van Wijhe M, Groenier K. Steroid injections added to the usual treatment of lumbar radicular syndrome: A pragmatic randomized controlled trial in general practice. *BMC Musculoskelet Disord*. Oct 11 2014;15:341.
- 131. Sae-Jung S, Jirarattanaphochai K. Outcomes of lumbar facet syndrome treated with oral diclofenac or methylprednisolone facet injection: A randomized trial. *Int Orthop.* Jun 2016;40(6):1091-1098.
- 132. Maas ET, Ostelo RW, Niemisto L, et al. Radiofrequency denervation for chronic low back pain. *Cochrane Database Syst Rev.* Oct 23 2015(10):Cd008572.

September 2017 Page 109 of 110

- 133. Singh S, Kumar S, Chahal G, Verma R. Selective nerve root blocks vs. Caudal epidural injection for single level prolapsed lumbar intervertebral disc; a prospective randomized study. *Journal of Clinical Orthopaedics & Trauma*.
- 134. Koh W, Choi SS, Karm MH, et al. Treatment of chronic lumbosacral radicular pain using adjuvant pulsed radiofrequency: A randomized controlled study. *Pain Med.* Mar 2015;16(3):432-441.
- 135. Kamper SJ, Apeldoorn AT, Chiarotto A, et al. Multidisciplinary biopsychosocial rehabilitation for chronic low back pain. *Cochrane Database Syst Rev.* Sep 02 2014(9):Cd000963.
- 136. Nazzal ME, Saadah MA, Saadah LM, et al. Management options of chronic low back pain. A randomized blinded clinical trial. *Neurosciences (Riyadh)*. Apr 2013;18(2):152-159.
- 137. Dufour N, Thamsborg G, Oefeldt A, Lundsgaard C, Stender S. Treatment of chronic low back pain: A randomized, clinical trial comparing group-based multidisciplinary biopsychosocial rehabilitation and intensive individual therapist-assisted back muscle strengthening exercises. *Spine (Phila Pa 1976)*. Mar 01 2010;35(5):469-476.
- 138. O'Keeffe M, Purtill H, Kennedy N, et al. Comparative effectiveness of conservative interventions for nonspecific chronic spinal pain: Physical, behavioral/psychologically informed, or combined? A systematic review and meta-analysis. *J Pain*. Jul 2016;17(7):755-774.
- 139. Agency for Health Research and Quality. The Effective Health Care Program stakeholder guide Appendix D: Research questions & PICO(TS) 2011.

  <a href="https://www.ahrq.gov/research/findings/evidence-based-reports/stakeholderguide/appendixc.html">https://www.ahrq.gov/research/findings/evidence-based-reports/stakeholderguide/appendixc.html</a>.
- 140. Andrews JC, Schunemann HJ, Oxman AD, et al. GRADE guidelines: 15. Going from evidence to recommendation-determinants of a recommendation's direction and strength. *J Clin Epidemiol.* Jul 2013;66(7):726-735.
- 141. Warner TD, Giuliano F, Vojnovic I, Bukasa A, Mitchell JA, Vane JR. Nonsteroid drug selectivities for cyclo-oxygenase-1 rather than cyclo-oxygenase-2 are associated with human gastrointestinal toxicity: A full in vitro analysis. *Proc Natl Acad Sci U S A.* Jun 22 1999;96(13):7563-7568.
- 142. Vane SJ. Aspirin and other anti-inflammatory drugs. *Thorax*. Oct 2000;55 Suppl 2:S3-9.

September 2017 Page 110 of 110