



# VA/DoD CLINICAL PRACTICE GUIDELINE FOR THE 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 with a patient-centered approach.

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 <a href="https://www.tricare.mil">www.tricare.mil</a> by contacting your regional TRICARE Managed Care Support Contractor.

Version 3.0 – 2022

# Prepared by:

# The Diagnosis and Treatment of Low Back Pain Work Group

With support from:

Office of Quality and Patient Safety, Veterans Health Administration

&

Clinical Quality Improvement Program, Defense Health Agency

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Based on evidence reviewed through February 1, 2021

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## 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 Committee (HEC) "... on the use of clinical and epidemiological evidence to improve the health of the population ..." across the Veterans Health Administration (VHA) and Military Health System (MHS), by facilitating the development of clinical practice guidelines (CPGs) for the VA and DoD populations. (1) Development and update of VA/DoD CPGs is funded by VA Evidence Based Practice, Office of Quality and Patient Safety. The system-wide goal of evidence-based CPGs is to improve patient health and well-being.

In 2017, the VA and DoD published a CPG for the Diagnosis and Treatment of Low Back Pain (2017 VA/DoD LBP CPG), which was based on evidence reviewed on or after December 2006 to October 2016. Since the release of that CPG, a growing body of research has expanded the evidence base and understanding of low back pain (LBP). Consequently, the VA/DoD EBPWG initiated the update of the 2017 VA/DoD LBP CPG in 2020. This updated CPG's use of GRADE reflects a more rigorous application of the methodology than previous iterations. Consequently, the strength of some recommendations may have been modified due to the confidence in the quality of the supporting evidence (see <a href="Evidence Quality and Recommendation Strength">Evidence Quality and Recommendation Strength</a>).

This CPG provides an evidence-based framework for the diagnosis and treatment of patients with acute, subacute, or chronic LBP with or without neurological symptoms with the aim of improving clinical outcomes. Successful implementation of this CPG will:

- Assist providers in assessing the patient's condition and collaborating with the patient, family, and caregivers to determine optimal management of patient care
- Emphasize the use of patient-centered care and shared decision making
- Minimize preventable complications and morbidity
- Optimize individual health outcomes and quality of life (QoL)

# II. Background

## A. Description of Low Back Pain

LBP has been defined as pain, muscle tension, or stiffness localized below the costal margin and above the inferior gluteal folds with or without leg symptoms. (2) Categorizations defined by duration vary but are often delineated as acute (less than four weeks), subacute (4 – 12 weeks), or chronic (more than 12 weeks) (see the glossary in <a href="Appendix F">Appendix F</a> for additional definitions). Anatomical contributors to LBP may be present; however "non-specific" LBP, in which it is not possible to detect a discrete source, is common and occurs in up to 85% of cases. (3) LBP is influenced by the interplay of physical, psychological, social, lifestyle, comorbid health, and modifiable and non-modifiable health factors. The relative contribution and interaction of these factors is variable, fluctuating, and unique to each individual with LBP and is reflected in the individual's pain, distress, and coping (behavioral) responses which influence levels of disability. (4) Given the potential for multifactorial contributors to the pain experience, patients with LBP can range from low to high levels of complexity.

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Conducting a history and physical examination is considered standard of care and a cornerstone of clinical decision making. History and physical examination should include assessment of signs and symptoms of serious underlying pathology. Signs and symptoms of serious underlying pathology requiring additional diagnostic workup and prompt treatment are generally referred to as "red flags." <u>Table 1</u> lists red flags and serious spinal conditions warranting further investigation.

**Table 1. Red Flags for Possible Serious Conditions** 

Possible Serious Conditions	Red Flags (e.g., signs, symptoms, history)	
Cauda equina syndrome or conus medullaris syndrome	<ul> <li>Urinary retention</li> <li>Urinary or fecal incontinence</li> <li>Saddle anesthesia</li> <li>Changes in rectal tone</li> <li>Severe/progressive lower extremity neurologic deficits</li> </ul>	
Infection	<ul> <li>Fever</li> <li>Immunosuppression</li> <li>IV drug use</li> <li>Recent infection, indwelling catheters (e.g., central line, Foley)</li> </ul>	
Fracture	<ul> <li>History of osteoporosis</li> <li>Chronic use of corticosteroids</li> <li>Older age (≥75 years old)</li> <li>Recent trauma</li> <li>Younger patients at risk for stress fracture (e.g., overuse)</li> </ul>	
Cancer	<ul> <li>History of cancer with new onset of LBP</li> <li>Unexplained weight loss</li> <li>Failure of LBP to improve after 1 month</li> <li>Age &gt;50 years</li> <li>Multiple risk factors present</li> </ul>	

Abbreviations: intravenous: IV; 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. (5) In 2016, of all diseases and injuries contributing to disability-adjusted life years in the U.S., LBP was ranked fifth. (6) LBP is now the leading cause of disability worldwide. (7)

In 2019, approximately 39% of adults 18 years and older in the U.S. reported experiencing LBP in the last three months. (8) Additionally, women are more likely than men to experience LBP (40.6% versus 37.2%, respectively). (8) More than two-thirds of pregnant women experience LBP, and symptoms typically increase with advancing pregnancy; however, pregnancy-related LBP is often self-limited in the post-partum period and may require specialist care only when LBP persists beyond a reasonable period or if red flags are present. (9)

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In a study of U.S. healthcare costs from 1996 through 2016, spending related to LBP and neck pain was the highest out of 154 conditions. In 2016, the estimated spending related to LBP and neck pain was \$134.5 billion.(10)

LBP and neurogenic claudication can be caused by degenerative lumbar spinal stenosis (LSS) which shows increasing prevalence with age (20% in <40 years and 47.2% in >60 years). ( $\underline{11}$ ) Patients with LSS are three times more likely to experience LBP than those without it.( $\underline{11}$ )

LBP can be associated with lumbar radiculopathy, which has an estimated prevalence of 3% - 5% of the population. (12) Degenerative disorders are considered the primary etiology.

### b. Veterans Affairs Population

The 2010 – 2014 National Health Interview Surveys (NHIS) from the National Institutes of Health provided national prevalence estimates of U.S. Veterans with severe pain (including back pain). A sub-analysis of the survey published in 2017 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 lower extremity involvement 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. ( $\underline{13}$ ) An NHIS was completed again in 2015 – 2018 providing national prevalence estimates of U.S. Veterans with chronic pain (27.9%), but data specifically related to LBP was not reported. ( $\underline{14}$ )

## c. Department of Defense Population

In the annual Medical Surveillance Monthly Report burden of disease issue, "other back problems" has been the category responsible for the most medical encounters for active duty U.S. Armed Service Members every year since 2011. In 2020, this category was the primary diagnosis for more than one million medical encounters affecting 213,331 Service Members. (15)

During the years 2010-2014, the overall annual incidence of LBP was 12.0% among active duty Service Members. 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 sex, service, race, and occupation is available in Table 2.(16)

Table 2. Incidence of Low Back Pain in U.S. Armed Forces, 2010-2014(16)

Category	Subgroup	Rate per year (%)
Sex	Male	11.3%
Jex	Female	16.3%
	Army	15.8%
	Navy	7.9%
Service	Air Force	12.6%
	Marine Corps	8.7%
	Coast Guard	10.5%

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Category	Subgroup	Rate per year (%)
	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%

# III. Scope of this Guideline

This CPG is based on published clinical evidence and related information available through February 1, 2021. It is intended to provide general guidance on best evidence-based practices (see <a href="Appendix A">Appendix A</a> for additional information on the evidence review methodology). This CPG is not intended to serve as a standard of care.

### A. Guideline Audience

This CPG is intended for use by VA and DoD primary care providers (PCPs) and others involved in the healthcare team caring for patients with LBP and associated conditions. Additionally, this CPG is intended for community-based clinicians involved in the care of Service Members, beneficiaries, or Veterans with LBP.

# B. Guideline Population

The patient population of interest for this CPG is adults (ages 18 years or older) with acute, subacute, or chronic LBP with or without neurological symptoms, who are eligible for care in the VA or DoD healthcare delivery systems and those who receive care from community-based clinicians. It includes Veterans and Service Members as well as their dependents. Recommended interventions in this CPG are applicable regardless of care setting, unless otherwise indicated, for any patient in the VA and DoD healthcare system.

Management of LBP from visceral disorders, fracture, cancer, infection, inflammatory arthropathy, or other causes is beyond the scope of this CPG. Pregnant women are also excluded from the scope of this CPG.

# IV. Highlighted Features of this Guideline

# A. Highlights in this Guideline Update

The current document is an update to the 2017 VA/DoD LBP CPG. A continued 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 2022 VA/DoD LBP CPG Work Group developed 12 key questions (KQs) which drove the systematic evidence review. Consistent with the 2017 VA/DoD LBP CPG, surgical interventions were excluded from

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the systematic evidence review for this CPG. The KQ topics included the prognostic/clinical impact of different evaluation tools and risk factors on LBP outcomes. In addition to the review of effectiveness of clinician-directed and self-directed physical activity and exercise, a KQ also assessed clinician-directed and self-directed interventions for behavioral health affecting the outcome of LBP. The impact of assessment and treatment of concomitant mental health conditions, pain catastrophizing, and psychosocial stressors on LBP outcomes and the effectiveness of technology-based modalities for self-management were also reviewed.

Other updates include an initial or expanded literature search into complementary and integrative health (CIH) and whole/holistic health approaches, ortho-biologic injections, botulinum toxin injections, neuromodulation treatments, spinal cord stimulation, technology-based modalities, and pharmacologic interventions (including monoclonal antibodies).

Finally, the 2022 VA/DoD LBP CPG includes the 2017 recommendation categorization table (see Appendix D) for easier visualization of similarities and differences between the two versions of the CPG.

The 2022 VA/DoD LBP CPG used a more rigorous application of the methodology than previous iterations. For additional information on GRADE or CPG methodology, see <u>Appendix A</u>. Because of this stricter methodology, the strength of many recommendations was modified from the 2017 VA/DoD LBP CPG due to a change in the confidence in the quality of the evidence.

## B. Components of the Guideline

The 2022 VA/DoD LBP CPG is the second update to this CPG. It provides clinical practice recommendations for the care of patients with LBP (see <u>Recommendations</u>). In addition, the <u>Algorithm</u> incorporates the recommendations in the context of the flow of patient care. This CPG also includes <u>Research Priorities</u>, which list areas the Work Group identified as needing additional research.

To accompany this CPG, the Work Group also developed toolkit materials for providers and patients, including a provider summary, patient summary, and pocket card. These can be found at <a href="https://www.healthquality.va.gov/index.asp">https://www.healthquality.va.gov/index.asp</a>.

# V. Guideline Development Team

The VA Evidence Based Practice, Office of Quality and Patient Safety, in collaboration with the Clinical Quality Improvement Program, Defense Health Agency (DHA), identified the following five clinicians to serve as Champions (i.e., leaders) of this CPG's Work Group: Andrew Buelt, DO and Franz J. Macedo, DO from the VA and LTC Daniel Kang, MD, COLLisa Konitzer, PT, DSc, and Evan N. Steil, MD, MBA, MHA, FAAFP from the DoD.

The Work Group comprised individuals with the following areas of expertise: acupuncture and Chinese medicine, chiropractic care, clinical psychology, neuroradiology, neurology, nursing, orthopedic spine surgery, pain management, pharmacy, physical medicine and rehabilitation, physical therapy (PT), primary care, and sports medicine. See Table 3 for a list of Work Group members.

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This CPG Work Group, led by the Champions, was tasked with:

- Determining the scope of the CPG
- Crafting clinically relevant KQs to guide the systematic evidence review
- Identifying discussion topics for the patient focus group and considering the patient perspective
- Providing direction on inclusion and exclusion criteria for the systematic evidence review and the assessment of the level and quality of evidence
- Developing evidence-based clinical practice recommendations, including determining the strength and category of each recommendation

The Lewin Team, including The Lewin Group, ECRI, Sigma Health Consulting, and Duty First Consulting, was contracted by the VA to help develop this CPG.

Table 3. Guideline Work Group and Guideline Development Team

Organization	Names*	
	Andrew Buelt, DO (Champion)	
	Franz J. Macedo, DO (Champion)	
	Thiru Annaswamy, MD, MA	
	Paul Heideman, PhD, LP	
	Casey Okamoto, DC	
Department of Veterans Affairs	Juli Olson, DC, DACM	
	Sanjog Pangarkar, MD	
	Kellie Rose, PharmD, BCPS, BCACP	
	Friedhelm Sandbrink, MD	
	Lance Spacek, MD	
	Rebecca Vogsland, DPT, OCS	
	LTC Daniel Kang, MD (Champion)	
	COL Lisa Konitzer, PT, DSc (Champion)	
	Evan N. Steil, MD, MBA, MHA, FAAFP (Champion)	
	Maj Danielle Anderson, DPT, DSc, OCS, FAAOMPT	
Department of Defense	LTC Adam J. Bevevino, MD	
Department of Defense	Rachael R. Coller, PharmD, BCPS, BCPP	
	Maj Michael A. Glotfelter, PsyD	
	Maj Mariya Gusman, MD	
	COL Jason Silvernail, DPT, DSc, FAAOMPT	
	Joe C. Wilson, RN, CCM	
VA Evidence Based Practice, Office of Quality and	M. Eric Rodgers, PhD, FNP-BC	
Patient Safety	James Sall, PhD, FNP-BC	
Veterans Health Administration	René Sutton, BS, HCA	
Clinical Overlity Insurance and Dungaran	Elaine P. Stuffel, MHA, BSN, RN	
Clinical Quality Improvement Program Defense Health Agency	Lisa D. Jones, BSN, RN, MHA, CPHQ	
,	Corinne K. B. Devlin, MSN, RN, FNP-BC	

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Organization	Names*
	Cliff Goodman, PhD
	Erika Beam, MS
	Ben Agatston, JD, MPH
The Lewin Group	Charlie Zachariades, MSc
The Lewin Group	Inveer Nijjar, BS
	Savannah Kucera, MPH
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Signey Health Consulting	Frances M. Murphy, MD, MPH
Sigma Health Consulting	James G. Smirniotopoulos, MD
Anjali Jain Research & Consulting	Anjali Jain, MD
	Rachel Piccolino, BA
	Mary Kate Curley, BA
Duty First Consulting	Richa Ruwala, BS
	Anita Ramanathan, BA
	Kate Fennell, MBA

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

# VI. Summary of Guideline Development Methodology

The methodology used in developing this CPG follows the *Guideline for Guidelines*, an internal document of the VA/DoD EBPWG updated in January 2019 that outlines procedures for developing and submitting VA/DoD CPGs.(17) The *Guideline for Guidelines* is available at

http://www.healthquality.va.gov/policy/index.asp. This CPG also aligns with the National Academy of Medicine's (NAM) principles of trustworthy CPGs (e.g., explanation of evidence quality and strength, the management of potential conflicts of interest [COI], interdisciplinary stakeholder involvement, use of systematic review (SR), and external review).(18) Appendix A provides a detailed description of the CPG development methodology.

# A. Evidence Quality and Recommendation Strength

The Work Group used the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach to craft each recommendation and determine its strength. Per GRADE approach, recommendations must be evidence-based and cannot be made based on expert opinion alone. The

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GRADE approach uses the following four domains to inform the strength of each recommendation (see <u>Determining Recommendation Strength and Direction</u>):(19)

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

Using these four domains, the Work Group determined the relative strength of each recommendation (*Strong* or *Weak*). 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 incorporates the four domains. (20) A *Strong* recommendation generally indicates *High* or *Moderate* confidence in the quality of the available evidence, a clear difference in magnitude between the benefits and harms of an intervention, similar patient values and preferences, and understood influence of other implications (e.g., resource use, feasibility).

In some instances, there is insufficient evidence on which to base a recommendation for or against a particular therapy, preventive measure, or other intervention. For example, the systematic evidence review may have found little or no relevant evidence, inconclusive evidence, or conflicting evidence for the intervention. The manner in which this is expressed in the CPG may vary. In such instances, the Work Group may include among its set of recommendations a statement of insufficient evidence for an intervention that may be in common practice even though it is not supported by clinical evidence, and particularly if there may be other risks of continuing its use (e.g., high opportunity cost, misallocation of resources). In other cases, the Work Group may decide to not include this type of statement about an intervention. For example, the Work Group may remain silent where there is an absence of evidence for a rarely used intervention. In other cases, an intervention may have a favorable balance of benefits and harms but may be a standard of care for which no recent evidence has been generated.

Using these elements, the Work Group determines the strength and direction of each recommendation and formulates the recommendation with the general corresponding text (see Table 4).

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Table 4. Strength and Direction of Recommendations and General Corresponding Text

Recommendation Strength and Direction	General Corresponding Text
Strongfor	We recommend
Weak for	We suggest
Neither for nor against	There is insufficient evidence to recommend for or against
Weak against	We suggest against
Strong against	We recommendagainst

It is important to note that a recommendation's strength (i.e., *Strong* versus *Weak*) is distinct from its clinical importance (e.g., a *Weak* recommendation is evidence-based and still important to clinical care). The strength of each recommendation is shown in the Recommendations section.

This CPG's use of GRADE reflects a more rigorous application of the methodology than previous iterations. For instance, the determination of the strength of the recommendation is more directly linked to the confidence in the quality of the evidence on outcomes that are critical to clinical decision making. The confidence in the quality of the evidence is assessed using an objective, systematic approach that is independent of the clinical topic of interest. Therefore, recommendations on topics for which it may be inherently more difficult to design and conduct rigorous studies (e.g., randomized controlled trials [RCTs]) are typically supported by lower quality evidence and, in turn, *Weak* recommendations. Recommendations on topics for which rigorous studies can be designed and conducted may more often be *Strong* recommendations. Per GRADE, if the quality of evidence differs across the relevant critical outcomes, the lowest quality of evidence for any of the critical outcomes determines the overall quality of the evidence for a recommendation. (21, 22) This stricter standard provides a consistent approach to determining recommendation strengths. For additional information on GRADE or CPG methodology, see Appendix A.

## B. Categorization of 2017 Clinical Practice Guideline Recommendations

Evidence-based CPGs should be current. Except for an original version of a new CPG, this typically requires revision of a CPG's previous versions based on new evidence or as scheduled subject to time-based expirations. (23) For example, the U.S. Preventive Services Task Force (USPSTF) has a process for monitoring the emergence of new evidence that could prompt an update of its recommendations, and it aims to review each topic at least every five years for either an update or reaffirmation. (24)

Recommendation categories were used to track how the previous CPG's recommendations could be reconciled. These categories and their corresponding definitions are similar to those used by the National Institute for Health and Care Excellence (NICE, England). (25, 26) Table 5 lists these categories, which are based on whether the evidence supporting a recommendation was systematically reviewed, the degree to which the previous CPG's recommendation was modified and whether a previous CPG's recommendation is relevant in the updated CPG.

Additional information regarding these categories and their definitions can be found in <u>Recommendation Categorization</u>. The 2022 CPG recommendation categories can be found in <u>Recommendations</u>. <u>Appendix D</u> outlines the 2017 VA/DoD LBP CPG's recommendation categories.

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Table 5. Recommendation Categories and Definitions	Table 5. Recomme	ndation Cates	gories and De	efinitionsa
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Evidence Reviewed	Recommendation Category	Definition
	New-added	New recommendation
	New-replaced	Recommendation from previous CPG was carried forward and revised
Reviewed <sup>b</sup>	Notchanged	Recommendation from previous CPG was carried forward but not changed
Reviewed	Amended	Recommendation from previous CPG was carried forward with a nominal change
	Deleted	Recommendation from previous CPG was deleted
	Not changed	Recommendation from previous CPG was carried forward but not changed
Not reviewed <sup>c</sup>	Amended	Recommendation from previous CPG was carried forward with a nominal change
	Deleted	Recommendation from previous CPG was deleted

<sup>&</sup>lt;sup>a</sup> Adapted from the NICE guideline manual (2012) ( $\underline{25}$ ) and Garcia et al. (2014) ( $\underline{26}$ )

Abbreviation: CPG: clinical practice guideline

# C. Management of Potential or Actual Conflicts of Interest

Management of COIs for the CPGs is conducted as described in the *Guideline for Guidelines*. (17) Further, the *Guideline for Guidelines* refers to details in the VHA Handbook 1004.07 Financial Relationships between VHA Health Care Professionals and Industry (November 2014, issued by the VHA National Center for Ethics in Health Care), (27) as well as to disclosure statements (i.e., the standard disclosure form that is completed at least twice by CPG Work Group members and the guideline development team). (17) The disclosure form inquires regarding any relevant financial and intellectual interests or other relationships with, e.g., manufacturers of commercial products, providers of commercial services, or other commercial interests. The disclosure form also inquires regarding any other relationships or activities that could be perceived to have influenced, or that give the appearance of potentially influencing, a respondent's contributions to the CPG. In addition, instances of potential or actual COIs among the CPG Work Group and the guideline development team were also subject to random web-based identification via standard electronic means (e.g., Centers for Medicare & Medicaid Services Open Payments and/or ProPublica).

When an instance of potential or actual COI has been reported, it is referred to the VA and DoD program offices and reviewed with the CPG Work Group Champions. The VA and DoD program offices and the CPG Work Group Champions determine whether, and if so, what, further action is appropriate (e.g., excusing Work Group members from selected relevant deliberations or removal from the Work Group). Early in the Work Group formation, a surgeon (AD) was identified to have a potential conflict related to development of a surgical implant. It was determined that mitigation was not possible and the individual was removed from the Work Group. Disclosure forms are on file with the VA Office of Quality and Patient Safety and are available upon request.

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b The topic of this recommendation was covered in the evidence review carried out as part of the development of the current CPG.

<sup>&</sup>lt;sup>c</sup> The topic of this recommendation was not covered in the evidence review carried out as part of the development of the current CPG.

## D. Patient Perspective

When developing a CPG, consideration should be given to patient perspectives and experiences, which often vary from those of providers. (21, 28) Focus groups can be used to help collect qualitative data on patient perspectives and experiences. VA and DoD Leadership arranged a virtual patient focus group on December 10, 2020. The focus group aimed to gain insights into patients with LBP of potential relevance and incorporate these into the CPG as appropriate. Topics discussed included the patients' priorities, challenges they have experienced, information they have received regarding their care, and the impacts of their care on their lives.

The patient focus group comprised a convenience sample of seven people. There were five males and two females. Four participants were Veterans who received care from the VA health system, and three participants received care from the DoD health system (two of which were active duty Service Members). The Work Group acknowledges this convenience sample is not representative of all patients with LBP within the VA and DoD healthcare systems and, thus, findings are not generalizable and do not comprise evidence. For more information on the patient focus group methods and findings, see <a href="Appendix B">Appendix B</a>. Patient focus group participants were provided the opportunity to review the final draft and provide additional feedback.

### E. External Peer Review

The Work Group drafted, reviewed, and edited this CPG using an iterative process. For more information, see <a href="Drafting and Finalizing the Guideline">Drafting and Finalizing the Guideline</a>. Once the Work Group completed a near-final draft, they identified experts from the VA and DoD healthcare systems and outside organizations generally viewed as experts in the respective field to review that draft. The draft was sent to those experts for a 14-business-day review and comment period. The Work Group considered all feedback from the peer reviewers and modified the CPG where justified, in accordance with the evidence. Detailed information on the external peer review can be provided by the VA Office of Quality and Patient Safety.

# F. Implementation

This CPG and algorithm are designed for adaptation by individual healthcare providers with consideration of unique patient considerations and preferences, local needs, and resources. The algorithm serves as a tool to prompt providers to consider key decision points in the care for a patient with LBP. Robust implementation is identified in VA and DoD internal implementation plans and policies. Additionally, implementation would entail wide dissemination through publication in the medical literature, online access, educational programs, and, ideally, electronic medical record programming in the form of clinical decision support tools at the point of care.

# VII. Approach to Care in Department of Veterans Affairs and Department of Defense

### A. Patient-centered Care

Guideline recommendations are intended to consider patient needs and preferences. Guideline recommendations represent a whole/holistic health approach to care that is patient-centered, culturally appropriate, and available to people with limited literacy skills and physical, sensory, or learning

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disabilities. VA/DoD CPGs encourage providers to use a patient-centered, whole/holistic health approach (i.e., individualized treatment based on patient needs, characteristics, and preferences). This approach aims to treat the particular condition while also optimizing the individual's overall health and well-being.

Regardless of the care setting, all patients should have access to individualized evidence-based care. Patient-centered care can decrease patient anxiety, increase trust in clinicians, and improve treatment adherence. (29, 30) A whole/holistic health approach (<a href="https://www.va.gov/wholehealth/">https://www.va.gov/wholehealth/</a>) empowers and equips individuals to meet their personal health and well-being goals. Good communication is essential and should be supported by evidence-based information tailored to each patient's needs. An empathetic and non-judgmental approach facilitates discussions sensitive to sex, culture, ethnicity, and other differences.

## **B.** Shared Decision Making

This CPG encourages providers to practice shared decision making, which is a process in which providers and patients consider clinical evidence of benefits and risks as well as patient values and preferences to make decisions regarding the patient's treatment. (31) Shared decision making was emphasized in *Crossing the Quality Chasm*, an Institute of Medicine (IOM) (now NAM) report, in 2001, (32) and is inherent within the whole/holistic health approach. Providers must be adept at presenting information to their patients regarding individual treatments, expected risks, expected outcomes, and levels and/or settings of care, especially where there may be patient heterogeneity in risks and benefits. The VHA and MHS have embraced shared decision making. Providers are encouraged to use shared decision making to individualize treatment goals and plans based on patient capabilities, needs, and preferences.

# C. Patients with Co-occurring Conditions

Co-occurring conditions can modify the degree of risk, impact diagnosis, influence patient and provider treatment priorities and clinical decisions, and affect the overall approach to the management of LBP.(33, 34) Many Veterans, Service Members, and their families have one or more co-occurring conditions. Because LBP is sometimes accompanied by co-occurring conditions, it is often best to manage LBP collaboratively with other care providers. Some co-occurring conditions may require early specialist consultation to determine any necessary changes in treatment or to establish a common understanding of how care will be coordinated. This may entail reference to other VA/DoD CPGs (e.g., for use of opioids for chronic pain<sup>a</sup>).

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<sup>&</sup>lt;sup>a</sup> See the VA/DoD Clinical Practice Guideline for the Use of Opioids in the Management of Chronic Pain. Available at: https://www.healthquality.va.gov/.

# VIII. Algorithm

This CPG's algorithm is designed to facilitate understanding of the clinical pathway and decision making process used in managing patients with LBP. This algorithm format represents a simplified flow of the management of patients with LBP and helps foster efficient decision making by providers. It includes:

- An ordered sequence of steps of care
- Decisions to be considered
- Recommended decision criteria
- Actions to be taken

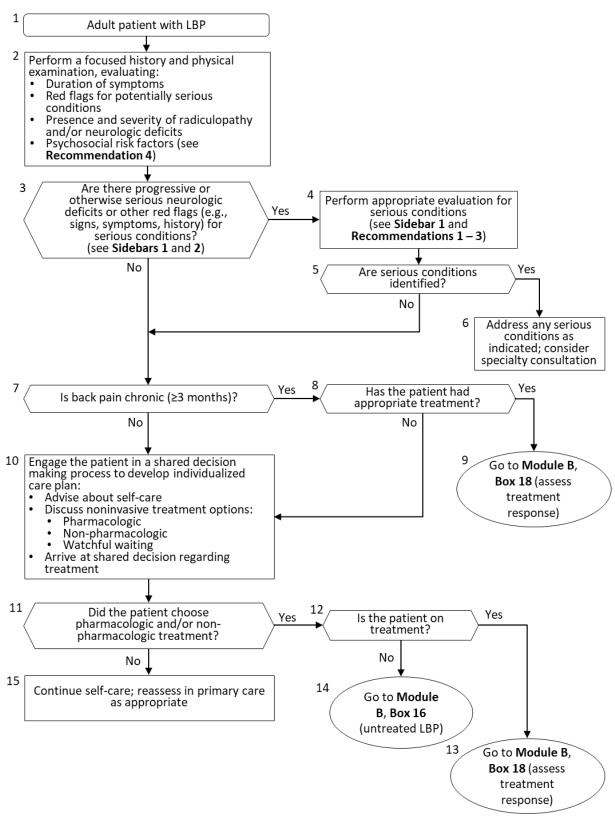
The algorithm is a step-by-step decision tree. Standardized symbols are used to display each step, and arrows connect the numbered boxes indicating the order in which the steps should be followed. (35) Sidebars provide more detailed information to assist in defining and interpreting elements in the boxes.

Shape	Description
	Rounded rectangles represent a clinical state or condition
	Hexagons represent a decision point in the process of care, formulated as a question that can be answered "Yes" or "No"
	Rectangles represent an action in the process of care
	Ovals represent a link to another section within the algorithm

Appendix I contains alternative text descriptions of the algorithm.

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



Abbreviation: LBP: low back pain

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Sidebar 1: Evaluation for Possible Serious Conditions				
Possible Serious Conditions	Suggested Evaluation <sup>a</sup>			
Cauda equina syndrome or conus medullaris syndrome	<ul> <li>Urinary retention</li> <li>Urinary or fecal incontinence</li> <li>Saddle anesthesia</li> <li>Changes in rectal tone</li> <li>Severe/progressive lower extremity neurologic deficits</li> </ul>	• Emergent MRI <sup>b</sup> (preferred)		
Infection	<ul> <li>Fever</li> <li>Immunosuppression</li> <li>IV druguse</li> <li>Recent infection, indwelling catheters (e.g., central line, Foley)</li> </ul>	<ul> <li>MRI<sup>c</sup></li> <li>ESR and/or CRP</li> </ul>		
Fracture	<ul> <li>History of osteoporosis</li> <li>Chronicuse of corticosteroids</li> <li>Older age (≥75 years old)</li> <li>Recent trauma</li> <li>Younger patients at risk for stress fracture (e.g., overuse)</li> </ul>	<ul> <li>Lumbosacral plain radiography</li> <li>For inconclusive results, advanced imaging as indicated</li> </ul>		
Cancer	<ul> <li>History of cancer with new onset of LBP</li> <li>Unexplained weight loss</li> <li>Failure of LBP to improve after 1 month</li> <li>Age &gt;50 years</li> <li>Multiple risk factors present</li> </ul>	MRI <sup>c</sup> Lumbosacral plain radiography		

<sup>&</sup>lt;sup>a</sup> Consider specialty consultation

Abbreviations: CRP: C-reactive protein; CT: computed tomography; ESR: erythrocyte sedimentation rate; IV: intravenous; LBP: low back pain; MRI: magnetic resonance imaging

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

<sup>&</sup>lt;sup>c</sup> MRI without and with contrast, except where contraindicated (e.g., renal insufficiency)

Sidebar 2: Evaluation for Possible Other Conditions <sup>a</sup>					
Possible Other Conditions	Red Flags (e.g., signs, symptoms, history)	Suggested Evaluation <sup>b</sup>			
Hamistad disa	<ul><li>Radicular back pain (e.g., sciatica)</li><li>Lower extremity dysesthesia and/or paresthesia</li></ul>	None			
Herniated disc	<ul><li>Severe/progressive lower extremity neurologic deficits</li><li>Symptoms present &gt;1 month</li></ul>	MRI <sup>c</sup>			
Spinal stenosis	<ul> <li>Radicular back pain (e.g., sciatica)</li> <li>Lower extremity dysesthesia and/or paresthesia</li> <li>Neurogenic claudication</li> <li>Older age</li> </ul>	None			
	<ul><li>Severe/progressive lower extremity neurologic deficits</li><li>Symptoms present &gt;1 month</li></ul>	MRI <sup>c</sup>			
Inflammatory LBP	<ul> <li>Morning stiffness</li> <li>Improvement with exercise</li> <li>Alternating buttock pain</li> <li>Awakening due to LBP duringthe second part of the night (early morning awakening)</li> <li>Younger age</li> </ul>	Radiography of pelvis, SI joint, and spine area of interest			

<sup>&</sup>lt;sup>a</sup> These conditions usually do not require urgent diagnostic evaluation

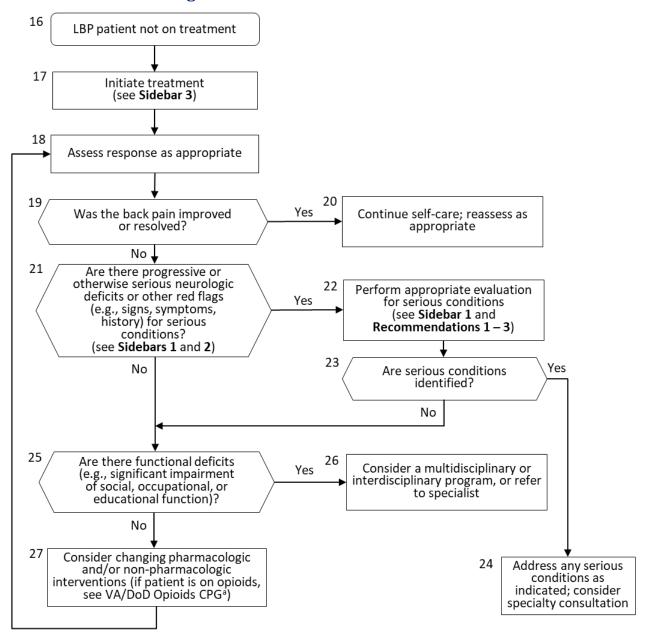
Abbreviations: LBP: low back pain; MRI: magnetic resonance imaging; SI: sacroiliac

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**b** Consider specialty consultation

 $<sup>^{\</sup>rm c}$   $\,$  Some patients may have contraindications to MRI, contrast usually not required

## B. Module B: Management of Low Back Pain



<sup>&</sup>lt;sup>a</sup> See the VA/DoD Clinical Practice Guideline for the Use of Opioids in the Management of Chronic Pain. Available at: https://www.healthquality.va.gov/.

Abbreviation: CPG: clinical practice guideline; DoD: Department of Defense; LBP: low back pain; VA: Department of Veterans Affairs

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Sidebar3: Management of Low Back Pain					
		Low Back Pain Duration			
Category	Intervention (listed alphabetically by category)	Acute <4 Weeks	Subacute or Chronic ≥4 Weeks		
Self-care	Advice to remain active	X	X		
	Acupuncture		X <u>Recommendation 34</u>		
Non-pharmacologic treatment	CBT and/or MBSR		X <u>Recommendation 8</u> and <u>Recommendation 12</u>		
treatment	Clinician-directed exercise program		X <u>Recommendation 9</u>		
	Spinal mobilization/manipulation		X <u>Recommendation 10</u>		
Pharmacologic	Duloxetine		X Recommendation 18		
treatment	NSAIDs	X Recommendation 19	X <u>Recommendation 19</u>		
Other treatment	Multidisciplinary or interdisciplinary program		X Recommendation 39		

Abbreviations: CBT: cognitive behavioral therapy; MBSR: mindfulness-based stress reduction; NSAIDs: nonsteroidal anti-inflammatory drugs

### IX. Recommendations

The following evidence-based clinical practice recommendations were made using a systematic approach considering four domains as per the GRADE approach (see <a href="Summary of Guideline Development">Summary of Guideline Development</a>
<a href="Methodology">Methodology</a>). These domains include: confidence in the quality of the evidence, balance of desirable and undesirable outcomes (i.e., benefits and harms), patient values and preferences, and other implications (e.g., resource use, equity, acceptability).

Recommendations for "patients with low back pain" encompass patient populations with acute, subacute, or chronic LBP with or without neurological symptoms. Recommendations specific to one or more LBP types include additional detail regarding the patient population.

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Topic	#	Recommendation	Strengtha	Categoryb
Evaluation and Diagnostic Approach	1.	For patients with low back pain, we recommend the history and physical examination include evaluation for progressive or otherwise serious neurologic deficits and other red flags (e.g., signs, symptoms, history) associated with serious underlying pathology (e.g., malignancy, fracture, infection).	Strong for	Reviewed, Amended
	2.	For patients with low back pain, we recommend diagnostic imaging and appropriate laboratory testing when neurologic deficits are progressive or otherwise serious or when other red flags (e.g., signs, symptoms, history) are present.	Strong for	Reviewed, Amended
	3.	For patients with acute low back pain, without focal neurologic deficits or other red flags (e.g., signs, symptoms, history), we recommend against routinely obtaining imaging studies or performing invasive diagnostic tests.	Strong against	Reviewed, New-replaced
	4.	For patients with low back pain, we suggest assessing psychosocial factors and using predictive screening instruments (e.g., STarT Back and The Orebro Musculoskeletal Pain Screening Questionnaire) to inform treatment planning.	Weak for	Reviewed, New-replaced
	5.	For patients with low back pain, with or without radicular symptoms, there is insufficient evidence to recommend for or against specific physical exammaneuvers to assist in the diagnosis of facet or sacroiliac joint pain, or a lumbar/lumbo-sacral radiculopathy.	Neither for nor against	Reviewed, New-added
Patient Education and Self-care	6.	For patients with low back pain, there is insufficient evidence to recommend for or against pain neuroscience education, cliniciandirected education with patient-led goalsetting, or backschool.	Neither for nor against	Reviewed, New-replaced
	7.	For the self-management of low back pain, there is insufficient evidence to recommend for or against technology-based modalities.	Neither for nor against	Reviewed, New-added
sive	8.	For patients with chronic lowback pain, we suggest cognitive behavioral therapy.	Weak for	Reviewed, New-replaced
Non-pharmacologic and Non-invasive Therapy	9.	For patients with low back pain, we suggest a structured clinician-directed exercise program (e.g., aerobic, aquatic, mechanical diagnosis and therapy, mobility, motor control, Pilates, strengthening exercises, structured walking program, tai chi).	Weak for	Reviewed, New-replaced
	10.	For patients with chronic lowback pain, we suggest spinal mobilization/manipulation.	Weak for	Reviewed, New-replaced
	11.	For patients with acute low back pain, there is insufficient evidence to recommend for or against spinal mobilization/manipulation.	Neither for nor against	Reviewed, New-replaced
	12.	For patients with chronic lowback pain, there is insufficient evidence to recommend for or against mindfulness-based stress reduction.	Neither for nor against	Reviewed, New-replaced
	13.	For patients with low back pain, there is insufficient evidence to recommend for or against lumbar supports.	Neither for nor against	Reviewed, Amended

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Topic	#	Recommendation	Strengtha	Category <sup>b</sup>
Non-pharmacologic and Non-invasive Therapy (cont.)	14.	For patients with low back pain, with or without radicular symptoms, there is insufficient evidence to recommend for or against mechanical lumbar traction.	Neither for nor against	Reviewed, New-replaced
	15.	For patients with chronic lowback pain, there is insufficient evidence to recommend for or against auricular acupressure.	Neither for nor against	Reviewed, New-added
	16.	For patients with low back pain, there is insufficient evidence to recommend for or against yoga or qi gong.	Neither for nor against	Reviewed, New-replaced
	17.	For patients with low back pain, there is insufficient evidence to recommend for or against cupping, laser therapy, transcutaneous electrical nerve stimulation, and ultrasound.	Neither for nor against	Reviewed, New-replaced
	18.	For patients with chronic lowback pain, we suggest duloxetine.	Weak for	Reviewed, New-replaced
	19.	For patients with low back pain, we suggest nonsteroidal anti-inflammatory drugs.	Weak for	Reviewed, New-replaced
	20.	For patients with low back pain, with or without radicular symptoms, there is insufficient evidence to recommend for or against gabapentin or pregabalin.	Neither for nor against	Reviewed, Amended
	21.	For patients with low back pain, there is insufficient evidence to recommend for oragainst tricyclic antidepressants.	Neither for nor against	Reviewed, New-added
Pharmacotherapy	22.	For patients with low back pain, there is insufficient evidence to recommend for or against topical preparations.	Neither for nor against	Reviewed, Amended
	23.	For patients with acute low back pain, there is insufficient evidence to recommend for or against a non-benzodiazepine muscle relaxant for short-term use.	Neither for nor against	Reviewed, New-replaced
	24.	For patients with chronic lowback pain, we suggest against offering a non-benzodiaze pine muscle relaxant.	Weak against	Reviewed, Not changed
	25.	For patients with low back pain, we suggest against acetaminophen.	Weak against	Reviewed, New-replaced
	26.	For patients with low back pain, we suggest against monoclonal antibodies.	Weak against	Reviewed, New-added
	27.	For patients with chronic low backpain, we suggest against opioids. For patients who are already using long-term opioids, see the VA/DoD CPG for the Use of Opioids in the Management of Chronic Pain.c	Weak against	Reviewed, New-replaced
	28.	For patients with low back pain, with or without radicular symptoms, we suggest against systemic corticosteroids (oral or intramuscular injection).	Weak against	Not reviewed, Amended
	29.	For patients with low back pain, we recommend against benzodiazepines.	Strong against	Reviewed, Not changed
Dietary Supplements	30.	For patients with low back pain, there is insufficient evidence to recommend for or against any specific diet or nutritional, herbal, or homeopathic supplements (e.g., anti-inflammatory diet, turmeric, vitamin D), cannabis, or cannabinoids.	Neither for nor against	Reviewed, New-replaced

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Topic	#	Recommendation	Strengtha	Categoryb
Non-surgical Invasive Therapy	31.	For patients with chronic lowback pain, we suggest lumbar medial branch and/or sacral lateral branch radiofrequency ablation.	Weak for	Reviewed, New-replaced
	32.	For patients with low back pain, there is insufficient evidence to recommend for or against sacroiliac joint injections.	Neither for nor against	Reviewed, New-added
	33.	For patients with low back pain, we suggest against the injection of corticosteroids for intra-articular facet joint injections and the rapeutic medial branch blocks with steroid.	Weak against	Reviewed, New-replaced
	34.	For patients with chronic lowback pain, we suggest acupuncture.	Weak for	Reviewed, Amended
	35.	For patients with acute low back pain, there is insufficient evidence to recommend for or against acupuncture.	Neither for nor against	Reviewed, Amended
	36.	For patients with low back pain, there is insufficient evidence to recommend for or against ortho-biologics (e.g., platelet-rich plasma, stem cells).	Neither for nor against	Reviewed, New-added
	37.	For patients with low back pain, with radicular symptoms, there is insufficient evidence to recommend for or against epidural steroid injections.	Neither for nor against	Reviewed, New-replaced
	38.	For patients with low back pain, we suggest against spinal cord stimulation.	Weak against	Reviewed, New-added
Team Approach	39.	For patients with chronic low back pain, we suggest a multidisciplinary or interdisciplinary program. These programs should include at least one physical component and at least one other component of the biopsychosocial model (psychological, social, and/or occupational) used in an explicitly coordinated manner.	Weak for	Reviewed, Amended

 $<sup>^{</sup>a} \ \ \text{For additional information, see} \underline{\text{Determining Recommendation Strength} \text{ and } \underline{\text{Direction}}.$ 

Abbreviations: CPG: clinical practice guideline; DoD: Department of Defense; VA: Department of Veterans Affairs

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 $<sup>^</sup>b \ \ \text{For additional information, see} \, \underline{\text{Recommendation Categorization}} \, \text{and} \, \underline{\text{Appendix D}}.$ 

<sup>&</sup>lt;sup>c</sup> For additional information, see the VA/DoD Clinical Practice Guideline for the Use of Opioids in the Management of Chronic Pain. Available at: <a href="https://www.healthquality.va.gov/">https://www.healthquality.va.gov/</a>.

## A. Evaluation and Diagnostic Approach

### **Recommendation**

 For patients with low back pain, we recommend the history and physical examination include evaluation for progressive or otherwise serious neurologic deficits and other red flags (e.g., signs, symptoms, history) associated with serious underlying pathology (e.g., malignancy, fracture, infection).<sup>b</sup>

(Strong for | Reviewed, Amended)

### **Discussion**

Evidence suggests that clinicians should specifically identify the presence, duration, progression, and severity of neurologic symptoms about red flag signs, symptoms, and history.

An SR by Galliker et al. (2020) evaluated 10 individual studies with >4,000 patients visiting an emergency department (ED) in which several red flags were associated with moderate to large effect sizes for increased risk of epidural abscess, vertebral fracture, cancers, and serious spinal pathologies. (36) Red flag symptoms included, but were not limited to, new urinary retention and current anticoagulant treatment. Red flag signs included, but were not limited to, saddle sensation disturbance, bladder/suprapubic fullness, abnormal neurologic exam, bowel/bladder sphincter disturbance, fever or other signs of infection, and hemoglobin <100 g/L, and INR  $\geq$ 1. For detection of epidural abscess, there was an increased risk in patients with a history of intravenous (IV) drug use and other infection sites (likelihood ratio [LR]+:13.7), an indwelling vascular catheter (LR+: 15.7), or a history of recent spine fracture (LR+: 9.5). For detection of vertebral fracture, there was a large risk with a history of trauma with neurological findings on physical examination (LR+: 31.1). For detection of cancer-causing LBP, there was a large risk with a combination of a history of cancer and the clinical suspicion of cancer (LR+: 27.9).

Rapidly progressive, 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. (37) A small proportion of LBP may be caused by a specific identifiable underlying condition (e.g., malignancy: 0.7%, infection: 0.01%, vertebral compression fracture: 4%), (37) including the possibility of referred pain from a proximate organ system (e.g., pancreatitis, nephrolithiasis, aortic aneurysm, endocarditis).

There was moderate quality evidence supporting the utility of red flags to determine the likelihood of malignancy and fracture, (37) and low quality evidence that red flags by themselves indicate a high risk for epidural abscess, vertebral fracture, and cancer. (36) Findings from the current systematic evidence review are consistent with the studies included in the 2017 VA/DoD LBP CPG, which were conducted in a greater variety of patient populations. (38-40) History of malignancy is associated with a higher risk of identifying serious underlying causes of LBP. (39) In patients with unexplained weight loss, failure to improve after one month, or age greater than 50 years, the likelihood of cancer as the cause of LBP increased to approximately 1.2%. (40) Another study of nearly 700 patients suggested the following red flags indicated a higher risk for vertebral fracture: older age ( $\geq$ 75 years old), recent trauma, osteoporosis, severe back pain

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b Recommendations for "patients with low back pain" encompass patient populations with acute, subacute, or chronic LBP with or without neurological symptoms.

score  $\geq$ 7 out of 10, and thoracic pain. (38) The study also suggested the presence of multiple red flags increases the probability of fracture to between 42% and 90%. Deyo et al. (1988) reported a history of urinary retention indicating a higher risk of CES, a rare condition with an estimated prevalence of 0.04% among patients presenting with LBP. In patients without urinary retention, the probability of CES was approximately 0.01%. (40)

Patient values and preferences were similar regarding evaluation of their LBP. The patient focus group participants valued the use of shared decision making in which the provider actively listened to their problems, carefully considered the underlying causes of their condition, and developed an individualized plan for their management. Most patients wish to have any serious underlying condition identified early and treated appropriately. While patients value a detailed and probing assessment for red flags to determine the need for further diagnostic evaluation, many patients express frustration and believe that their evaluation is not complete without imaging studies (especially use of magnetic resonance imaging [MRI]) for determining the cause of their LBP.

The Work Group systematically reviewed new evidence related to this recommendation (36) and also considered the evidence put forth in the 2017 VA/DoD LBP CPG. (37-40) Therefore, this is a Reviewed, Amended recommendation. The Work Group's confidence in the quality of the evidence was very low for detection of serious spinal pathologies by history/symptoms or physical examination. The quality of the body of evidence was limited by factors such as retrospective study design, not using the same reference standard in all patients, and no clear blinding of assessors. (36) However, despite the very low quality of evidence for the critical outcome of interest (diagnostic accuracy), the Work Group concluded this recommendation continued to merit a Strong for rating considering the high likelihood of catastrophic harms from a failure to identify a serious underlying condition that is causing LBP. The prevention of disability, morbidity, and mortality and the life-preserving benefits of conducting a history and physical examination to identify red flags for serious underlying medical conditions outweigh very small potential for harms to the patient (e.g., the likelihood of false-positive red flags leading to unnecessary additional diagnostic testing, inherent risks and increased costs with such tests, fear or anxiety that a patient may experience while undergoing such tests). Per GRADE guidelines: 15, which states, "A strong recommendation may be warranted . . . when low quality evidence suggests benefit in a life-threatening situation," the Work Group determined a Strong recommendation is warranted. (19) Patient values and preferences were similar because patients prefer that their clinician carefully evaluate them for underlying causes of their clinical condition. The Work Group believes that all clinicians must be familiar with red flags that warrant further evaluation and emphasize that here. Conducting a history and physical examination including assessment of neurological deficits and red flags is generally feasible and accepted by the providers and patients alike. Thus, the Work Group decided upon a Strong for recommendation.

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### **Recommendation**

2. For patients with low back pain, we recommend diagnostic imaging and appropriate laboratory testing when neurologic deficits are progressive or otherwise serious or when other red flags (e.g., signs, symptoms, history) are present.<sup>c</sup>

(Strong for | Reviewed, Amended)

#### **Discussion**

Evidence suggests most patients with lumbar disc herniation and radiculopathy will improve with noninvasive management within four weeks. (41) Chou et al. (2009) found that imaging (e.g., radiographs, computed tomography [CT], MRI) did not significantly improve outcomes in patients for whom there was no pretest concern for serious underlying conditions. (42) Little additional literature has been published more recently. An SR by Galliker et al. (2020) of 10 diagnostic cohort studies attempted to gather evidence for red flags predictive of serious spinal pathology. (36) Analyzed red flags included suspicion or history of cancer, IV drug use, indwelling vascular catheter, and other infection sites. (36) Unfortunately, this analysis yielded very low quality evidence due to very serious limitations and serious imprecision. The Work Group noted that the laboratory and imaging tests in question posed relatively little harm; however, there is enormous harm caused by failure to diagnose a serious pathology.

Patient values and preferences are likely very similar, as patients uniformly want to know about serious underlying pathology. Most patients wish to have any serious underlying condition identified early and treated appropriately. Identifying and treating serious pathology at an earlier stage is beneficial in terms of resource use and is acceptable and feasible to patients and providers.

Although the quality of evidence related to this recommendation from the current systematic evidence review was very low, the Work Group was strongly persuaded by the potential harm mediated by withholding laboratory and imaging studies from patients with red flags. The recommendation was further bolstered by the moderate quality evidence used to support this recommendation in the 2017 VA/DoD LBP CPG.(41, 42)

The Work Group systematically reviewed evidence related to this recommendation (36) and considered the assessment of the evidence put forth in the 2017 VA/DoD LBP CPG. (41, 42) Therefore, this is a *Reviewed, Amended* recommendation. The Work Group's confidence in the quality of the evidence was very low. The body of evidence had some limitations including patient selection limited to the emergent setting and lack of standard or precise means of diagnosis confirmation. However, despite the very low quality of evidence, the Work Group concluded this recommendation continued to merit a *Strong for* rating considering the high likelihood of catastrophic harms from a failure to identify a serious underlying condition that is causing LBP. The prevention of disability, morbidity, and mortality and the life-preserving benefits of conducting diagnostic imaging and appropriate laboratory testing when neurologic deficits are progressive or otherwise serious or when other red flags are present outweigh the very small potential for harms (e.g., increased time, resource use, and potential incidental findings). Patient values and preferences were similar. Per GRADE guidelines: 15, which states, "A strong recommendation may be warranted... when low quality evidence suggests benefit in a life-threatening

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c Recommendations for "patients with low back pain" encompass patient populations with acute, subacute, or chronic LBP with or without neurological symptoms.

situation," the Work Group determined a *Strong* recommendation is warranted. ( $\underline{19}$ ) Thus, the Work Group decided upon a *Strong for* recommendation.

### **Recommendation**

3. For patients with acute low back pain, without focal neurologic deficits or other red flags (e.g., signs, symptoms, history), we recommend against routinely obtaining imaging studies or performing invasive diagnostic tests.

(Strong against | Reviewed, New-replaced)

### **Discussion**

Since the 2017 VA/DoD LBP CPG, additional evidence has been published supporting the recommendation that early imaging is associated with the potential of worse clinical outcomes. Using a very large retrospective matched cohort (n=405,965) to assess patients presenting with non-specific pain of the lumbar spine, including lumbar sprain, strain, spondylosis, or disk degeneration, Jacobs et al. (2020) evaluated the downstream consequences of lumbar MRI performed within six weeks of symptom onset. (43) The study evaluated uncomplicated LBP in a VA primary care clinic from June 1, 2015, through June 30, 2016, and found MRI of the lumbar spine performed early after onset of LBP symptoms was associated with a higher probability of surgery, greater prescription opioid use, increased costs of care, and higher pain scores.

In this study, the early MRI group was 13 times more likely to undergo lumbar surgery than the group not receiving an early scan (1.48% versus 0.12%).(43) Further, early MRI was associated with greater opioid use and higher pain levels, which may further contribute to the opioid crisis occurring within the U.S. In addition, associated acute care costs were 1.4 times greater in the early lumbosacral-MRI group during the follow-up period (\$8,082 versus \$5,560). It is worth noting that this study was performed at the VA, where providers are typically salaried and may not have the same financial incentives associated with traditional fee-for-service care. Alternatively, because VA providers receive malpractice coverage through the federal government, they may not have the same liability concerns as their non-governmental counterparts when considering ordering diagnostic tests.

Similarly, Lemmers et al. (2019) demonstrated that in patients with LBP who did not have red flags, routine imaging led to increased costs, healthcare utilization, and absence from work. (44) They concluded that imaging did not provide health benefits and suggested medical imaging was often performed because of a clinician's need for a diagnosis, to identify an anatomical defect, to meet the expectations of patients, or for financial incentives. In total, the SR included six RCTs and eight observational studies, which included radiography, CT, and MRI. For both Jacobs et al. (2020) (43) and Lemmers et al. (2019), (44) the quality of evidence was moderate with harms and burdens outweighing benefits.

The Work Group felt there was likely large variation in values and preferences for patients experiencing LBP of less than six weeks. Patients experiencing LBP often wish to understand the source of their symptoms, and imaging has traditionally been used to reduce fears and/or concerns. During the patient focus group, four participants shared difficulties obtaining MRIs early in the diagnostic process, which they felt would have allowed providers to pinpoint the underlying causes of their LBP sooner. Participants

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favored receiving advanced imaging, especially MRIs, early in the assessment process, as they believed imaging would have helped identify the cause of pain earlier.

When patients inquire about imaging modalities for axial LBP of less than six weeks duration, providers are encouraged to provide appropriate education on the limitations of these modalities. These include the findings of potentially higher pain scores, greater prescription opioid use, and increased chance for surgery. In addition, discussion of evidence-based treatments for acute LBP known to provide clinical benefit should be performed. Furthermore, healthcare utilization costs have implications for resource allocation, especially when the harms outweigh the benefits. Finally, some providers may not have access to advanced imaging or testing, and routine use may place an additional burden on the provider and healthcare system.

The Work Group systematically reviewed evidence related to this recommendation (43, 44) and considered the assessment of the evidence put forth in the 2017 VA/DoD LBP CPG. (42, 45-47) Therefore, this is a *Reviewed, New-replaced* recommendation. When determining the strength of this recommendation, the Work Group considered the moderate confidence in the quality of available evidence, the potential for harms/burdens to outweigh the benefits, and the feasibility and resource constraints of routine imaging. Patient and provider preferences may vary, but patient education and discussion of treatment options are generally preferred over diagnostic imaging when red flags are not identified. Other implications include resource use, equity, and acceptability. There is a high cost associated with frequently imaging patients as well as the potential of providing information that may cause anxiety, such as descriptions of degenerative changes. Thus, the Work Group decided upon a *Strong against* recommendation.

### **Recommendation**

4. For patients with low back pain, we suggest assessing psychosocial factors and using predictive screening instruments (e.g., STarTBack and The Orebro Musculoskeletal Pain Screening Questionnaire) to inform treatment planning.<sup>d</sup>

(Weak for | Reviewed, New-replaced)

### **Discussion**

As noted in the 2017 VA/DoD LBP CPG, depression and anxiety are common among patients with chronic pain and are related to developing chronic LBP. (48, 49) Studies identified in the current systematic evidence review suggest assessing for psychosocial factors in patients with LBP can be helpful in treatment planning. (50-56) The STarT Back Screening Tool<sup>e</sup> and the Orebro Musculoskeletal Pain Screening Questionnaire<sup>f</sup> (OMPSQ) are screening instruments aimed at helping to predict the risk of developing chronic pain, disability, and work absenteeism based on the presence of risk factors such as psychosocial factors. (57, 58) The STarT Back consists of nine questions regarding pain and psychosocial factors such as pain catastrophizing, worrying thoughts, and anhedonia while the OMPSQ consists of 25 items. Cut-off

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d Recommendations for "patients with low back pain" encompass patient populations with acute, subacute, or chronic LBP with or without neurological symptoms.

e See the STarT Back Screening Tool. Available at: https://startback.hfac.keele.ac.uk/research/

f See the Orebro Musculoskeletal Pain Screening Questionnaire. Available at: https://academic.oup.com/occmed/article/58/6/447/1375462

scores divide patients into risk groups that help providers recommend a treatment plan. An SR by Karran et al. (2017) suggested these instruments are excellent in predicting work absenteeism outcomes and acceptable for disability outcomes. ( $\underline{53}$ ) However, they are poor/non-informative at predicting pain outcomes at 3-12 months follow-up. ( $\underline{53}$ )

Research suggests QoL and level of functioning for patients with LBP are related to psychosocial factors, but the strength of evidence was very low. One study of poor quality among older adults suggested that despite being in a worse physical condition, those with a more positive outlook on their QoL were more likely to improve after an invasive treatment. (56) Glattacker et al. (2018) suggested baseline levels of pain catastrophizing and depression are associated with a patient's QoL at six month follow-up. (51) Løchting et al. (2017) reported pain catastrophizing, illness perception, and psychological distress were related to QoL, functional status, and general health. (54) Trinderup et al. (2018) suggested fear-avoidance beliefs about work were related to functional status. (55)

There is some variability in patient and provider willingness to assess psychosocial factors related to LBP. Some patients are more biomedically focused and may question the relevance of psychosocial factors when seeking care. There can be a stigma related to assessing psychosocial factors as the patient may worry that the provider believes that the pain is "in their head" or "not real." From the provider's standpoint, assessing for psychosocial factors may seem burdensome (e.g., it requires additional time), and providers may be reluctant to change their practice to include an assessment measure such as the STarT Back tool. Consistent with the 2017 VA/DoD LBP CPG, this Work Group considered the benefits of screening for psychosocial factors to outweigh the burdens/harm.

Providers interested in assessing psychosocial factors related to chronic pain in their clinical practice are encouraged to consider the following instruments utilized in studies from the current systematic evidence review.

- The most commonly used instrument for measuring pain catastrophizing is the Pain
   Catastrophizing Scale (PCS). (59) The PCS is a 13-item self-report questionnaire assessing
   catastrophic thinking related to pain. The PCS has good psychometric properties and provides a
   total score as well as subscales of rumination, magnification, and helplessness.
- The most commonly used instrument for measuring pain self-efficacy is the Pain Self Efficacy
  Questionnaire (PSEQ). (60) The PSEQ is a 10-item self-report questionnaire that assesses the
  confidence people have in performing various activities while in pain. The PSEQ has good
  psychometric properties and yields a total score.
- The Tampa Scale for Kinesiophobia (TSK) is a well-known instrument developed to measure the
  fear of movement related to chronic LBP. (61) The TSK is a 17-item measure that has demonstrated
  good psychometric properties and yields a total score.

The Work Group systematically reviewed evidence related this recommendation (50-56) and considered the evidence put forth in the 2017 VA/DoD LBP CPG. (48, 49) Therefore, this is a *Reviewed, New-replaced* recommendation. Evidence from the current systematic evidence review, which included psychosocial factors such as pain catastrophizing, fear avoidance, and pain self-efficacy, is generally consistent with the 2017 VA/DoD LBP CPG, which highlighted the relationship between mental health conditions, such as depression and anxiety, and the development or maintenance of chronic LBP.

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There is moderate strength of evidence with higher quality studies for predictive screening instruments such as the STarT Back Tool and the OMPSQ compared to very low strength of evidence for individual psychosocial factors. The body of evidence had some limitations including very serious limitations in study quality/risk of bias and serious imprecision of findings. Much of the evidence supporting the use of the STarT Back was found in European studies; data from the U.S. was less compelling. For example, a large study (n=1,701) of moderate quality of evidence conducted in the U.S. did not demonstrate a significant effect of STarT Back screening on patient outcomes of function, pain catastrophizing, pain self-efficacy, or healthcare utilization. (50) This suggests it may be difficult to implement these measures in clinical settings.

The STarT Back Tool and the OMPSQ can help providers stratify risk for developing disability and failing to return to work. However, these instruments appear to be poor/non-informative predictors of pain outcomes, which was a critical outcome. The potential benefits of screening for psychosocial factors outweighed the potential harms of patients questioning the relevance of assessing for psychosocial factors. Patient values and preferences varied somewhat. Despite the very low confidence in the quality of evidence, the Work Group determined it was important to assess for psychosocial factors and depression and anxiety as they are common among patients with chronic pain and contribute to a patient's overall level of suffering. Providers are encouraged to incorporate the findings into treatment planning and consider behavioral health treatment approaches identified in this CPG. Thus, the Work Group decided upon a *Weakfor* recommendation.

### **Recommendation**

5. For patients with low back pain, with or without radicular symptoms, there is insufficient evidence to recommend for or against specific physical exam maneuvers to assist in the diagnosis of facet or sacroiliac joint pain, or a lumbar/lumbo-sacral radiculopathy.

(Neither for nor against | Reviewed, New-added)

### Discussion

Low quality and inconsistent evidence suggests performing relevant provocative tests may assist in the diagnosis of facet or sacroiliac joint pain or of lumbar/lumbosacral radiculopathy in patients with LBP with or without radicular symptoms. ( $\underline{62-66}$ ) However, there is high variability in diagnostic sensitivity and specificity.

Maas et al. (2017) reported findings of an SR in which diagnostic facet joint block was used as a reference standard for detection of LBP originating from lumbar facet joints. (62) Two studies within this SR found non-centralization of LBP had high sensitivity (100%) but very low specificity (11% - 17%) for detection of facet joint-mediated LBP. (67, 68) Additionally, two other studies within the same SR found traumatic onset of pain had low sensitivity (48% - 54%) and specificity (47% - 50%) for detection of facet joint-mediated LBP, (69, 70) and four studies using Revel's criteria individually had highly variable sensitivity (15% - 100%) and specificity (13% - 86%) for detection of facet joint-mediated LBP. (70-73) When Revel's criteria were used as a combined criterion, specificity was less variable (66% - 91%) for detection of facet joint-mediated LBP.

Mekhail et al. (2021) reported findings of their prospective diagnostic cohort study in which they used a diagnostic sacroiliac joint injection as a reference standard. ( $\underline{63}$ ) The Mekhail test, the Patrick test, and the

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Thigh Thrust test had variable sensitivity (53%-82%) and specificity (27%-49%) when used separately and high sensitivity (89%-94%) and low specificity (14%-29%) when used in combination for detection of sacroiliac joint-mediated pain. However, a recent SR by Saueressiget al. (2021), which was not included in the systematic evidence review carried out as part of this CPG and did not influence the strength of the recommendation, reported that negative predictive value of sacroiliac joint provocative test cluster is 92%; however, a positive result from this cluster of tests is only 35% predictive of sacroiliac joint pain. (74)

González Espinosa de Los Monteros et al. (2020) reported findings of their prospective diagnostic cohort study in which they used MRI findings as a reference standard for detection of lumbar and lumbosacral radiculopathy. (64) In their study, several neurological and nerve root tension tests, including the Straight Leg Raise test, the Bragard test, the Fajersztajn test, the Sicard test, the Passive Neck Flexion test, the Kernig test, the Slump test and the Dejerine's triad, had variable rates (low-to-high) of sensitivity and specificity for detection of lumbar and lumbosacral radiculopathy.

Tawa et al. (2019) reported findings of a retrospective diagnostic cohort study in which they used MRI as a reference standard for detection of lumbar/lumbosacral radiculopathy. (65) Another SR by Tawa et al. (2017) reported findings in which the source articles used MRI, CT, surgery, or a combination as the reference standard for detection of lumbar/lumbosacral radiculopathy. (66) These studies reported that findings of neurological examination such as skin sensation, motor strength, tendon reflexes, or a combination of such tests, have acceptable, albeit variable rates of sensitivity and specificity. Further, they reported negative and positive likelihood ratios (Self-Reported Leeds Assessment of Neuropathic Symptoms and Signs [S-LANSS] score LR+: 1.87, -LR: 2.4; sensation LR+: 1.66, LR-: 1.37; strength LR+: 1.8, LR-: 1.76; reflexes LR+: 4, LR-: 1.8; Lowe limb neuro-dynamic tests [LLNDTs] LR+: 1.84, LR-: 2.71) that are likely to have utility in the clinical diagnosis of lumbar/lumbosacral radiculopathy.

Evidence thus indicates some benefits of performing these physical examination tests and maneuvers, which slightly outweigh the burden and harms associated with performing them. (62-66). However, due to high variability in the diagnostic sensitivity and specificity in the body of literature examined as a whole, the Work Group decided upon a *Neither for nor against* recommendation.

There is some variability in patient preferences regarding this diagnostic approach. The patient focus group expressed frustration with lack of early evaluation (especially use of MRIs) for determining the cause of their LBP, but they also valued the use of a shared decision making approach in which the provider listened to their problems, carefully considered the underlying causes of their condition, and developed an individualized plan for their management. Performing several of these diagnostic physical examinations and provocative tests can seem burdensome because it requires additional time during clinical encounters, but it can also be reassuring to the patient. In the referenced studies, these tests, especially the special provocative tests, were performed by trained clinicians. However, the Work Group acknowledges that most of these tests may not be commonly performed in primary care settings and may require additional training for primary care clinicians to perform them reliably. Unfortunately, there is no evidence to support the type and amount of training required, or how such training may improve the reliability of these tests. If a healthcare facility has few providers with adequate training, this may limit patient access to this diagnostic approach. Performing provocative testing to elicit pain in patients who are seeking medical attention for their LBP may not be universally well accepted. Performing

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special provocative testing and certain neurological examination may not be currently feasible in some clinical encounters performed virtually.

The Work Group systematically reviewed evidence related to this recommendation. (62-66) Therefore, this is a Reviewed, New-added recommendation. The Work Group's confidence in the quality of the evidence was very low. The body of evidence had some limitations including not all patients received a diagnostic reference standard, a disputable reference standard (e.g., MRI for diagnosis of radiculopathy), or the same diagnostic reference standard. Further, most studies did not report whether interpretation of the reference test was blinded to imaging findings. (62) The potential benefits of performing relevant physical examination tests (e.g., neurological examination of skin sensation, motor strength, tendon reflex testing; special provocative testing such as the Straight Leg Raise or Bragard tests for detection of lumbar/lumbosacral radiculopathy; Revel's criteria for detection of facet jointmediated LBP) slightly outweighed the potential harm of additional time burden to the clinician or temporary exacerbation of patients' pain. However, the Work Group was concerned about the potential of this recommendation to result in unintended consequences of increased healthcare utilization such as diagnostic testing, and its unclear impact on patient management and outcomes. Patient values and preferences varied somewhat because some patients prefer early diagnostic imaging, but others prefer their clinician carefully evaluate them for underlying causes of their clinical condition. Thus, the Work Group decided upon a *Neither for nor against* recommendation.

### B. Patient Education and Self-care

#### **Recommendation**

6. For patients with low back pain, there is insufficient evidence to recommend for or against pain neuroscience education, clinician-directed education with patient-led goal setting, or back school.g (Neither for nor against | Reviewed, New-replaced)

#### **Discussion**

Proponents of the biopsychosocial model of pain have supported a variety of structured education programs to treat LBP. Pain psychology and pain neuroscience education are pillars of these programs, but considerable differences in strategies and delivery methods warrant individual consideration of the evidence base for each education program captured in this review. Evidence for back school, clinician-directed education with patient-led goal setting, and pain neuroscience education (PNE) was considered.

An SR and meta-analysis by Straube et al. (2016) cited in the 2017 VA/DoD LBP CPG suggested no clinically meaningful benefit for intermediate and long-term pain, disability, and QoL with back school compared to no treatment. (75) More recent evidence aligns with these findings. When compared to no treatment or "standard medical care," a Cochrane review and meta-analysis by Parreira et al. (2017) found back school conferred no statistically significant difference in pain at three months or beyond. Although a statistically significant difference in disability was seen at 3 – 6 months, the magnitude was not considered clinically

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Recommendations for "patients with low back pain" encompass patient populations with acute, subacute, or chronic LBP with or without neurological symptoms.

meaningful (mean difference [MD] -6.34 on a common 100-point scale converted from Roland Morris Disability Questionnaire [RMDQ] and Oswestry Disability Index [ODI]). (76) Other outcomes of interest, such as QoL, kinesiophobia, and catastrophization, were not reported in constituent studies of the review. In summary, evidence for back school has not established benefit on patient-centered outcomes. However, the quality of evidence was very low and further research is likely needed.

Sparse evidence suggests the possibility of a small benefit from clinician-directed education with patient-led goal setting. A single RCT (n=75) was captured in our systematic evidence review and resulted in improved critical outcomes such as QoL (36-Item Short Form Survey<sup>h</sup> [SF-36] MD: 19.5; minimum clinically important difference [MCID]: 10 points), (77) and pain (numeric rating scale [NRS] MD: 2.3; MCID: 2 points), (78) both of which achieved clinical relevance. Clinically significant changes were also seen in important outcomes, such as self-efficacy and kinesiophobia. Further, improvements in intermediate and long-term disability were seen despite falling short of clinical significance (Quebec Back Pain Disability Scale [QBDS] MD: 12.9; MCID: 20 points). (78, 79) Although these results could be viewed as promising, they are based on a single, small clinical trial uncorroborated by subsequent investigation. Additional studies with larger patient populations and similar findings would improve confidence in these results.

An SR and meta-analysis by Wood et al. (2019) was unable to demonstrate important benefits with PNE alone or combined with other interventions such as PT.(80) Based on this review, evidence for intermediate and long-term data is scant and shows no statistically significant benefit in long-term function or pain. Functional benefit was seen in the short-term (RMDQ MD: 3.94 at mean 32 days; MCID: 5 points); (78) however, the benefit did not achieve clinical significance and the follow-up period fell short of the Work Group's pre-specified 12 week threshold for the systematic evidence review. Ancillary evidence published after the Wood et al. (2018) review suggests benefit at three months for important, patient-centered outcomes such as pain catastrophizing and kinesiophobia (PCSi MD: 10.6; MCID: 5.2; TSK MD: 8.5; MCID: 4).(81) However, this is based on a single, small RCT (n=65).(82) Hence, additional studies with large patient populations are needed. Overall, the evidence base for PNE mirrors that of back school, with no demonstrable benefit and very low quality evidence. Consequently, in both cases, further research is likely to have significant impact on management recommendations.

Patient preferences for structured education-based methods are likely to vary considerably. Some patients generally prefer pharmacotherapeutic strategies while others place greater value on education or other non-pharmacologic interventions. Additionally, the time-intensive nature of structured education programs could be repellent or prohibitive for some patients, while others will find the time well-spent if a better understanding of their condition enables them to better self-manage their symptoms. Resource utilization and acceptability could be problematic in some practice settings, stemming from time costs incurred by providers for both training and implementation.

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When articles did not report an MCID or provide a valid reference in support of an MCID for instruments measuring patient reported outcomes, an MCID threshold of 10% was used when comparing the observed between-group difference with the total range of scores for an instrument. Citations for MCID are provided when the article cited a valid reference, or the Work Group used an independent reference to support an MCID threshold.

When articles did not report an MCID or provide a valid reference in support of an MCID for instruments measuring patient reported outcomes, an MCID threshold of 10% was used when comparing the observed between-group difference with the total range of scores for an instrument. Citations for MCID are provided when the article cited a valid reference, or the Work Group used an independent reference to support an MCID threshold.

The Work Group systematically reviewed evidence related to this recommendation (76, 79, 80, 82) and considered the assessment of the evidence put forth in the 2017 VA/DoD LBP CPG. (75, 83) Therefore, this is a *Reviewed, New-replaced* recommendation. The Work Group's confidence in the quality of the evidence was very low. The body of evidence had significant limitations including study bias, publication bias, inconsistency, imprecision, and small sample sizes. (76, 79) The benefits of structured, education-based programs on outcomes such as disability, QoL, pain, kinesiophobia, and pain catastrophization slightly outweighed the potential harms for some programs, but not others. Additionally, the clinical significance of these effects is disputable in some cases, and most of the evidence showed no intermediate or long-term benefits. Patient values and preferences are likely to vary substantially, and resource utilization and acceptability are probable concerns in some practice settings. Consequent to very low quality evidence and the associated likelihood that further research will have a significant impact on management recommendations, the Work Group decided upon a *Neither for nor against* recommendation.

### **Recommendation**

7. For the self-management of low back pain, there is insufficient evidence to recommend for or against technology-based modalities.<sup>j</sup>

(Neither for nor against | Reviewed, New-added)

### **Discussion**

The systematic evidence review identified four studies examining the use of technology-based modalities (mobile health [mHealth], online/web-based applications, Nintendo Wii, phone applications, and telephone-based) compared with usual care in patients with LBP. (84-87) Du et al. (2020) reported that the number of eligible studies was small, and the authors did not compare the effects of e-Health based on self-management program with traditional face-to-face self-management because very few studies were available. (86) E-Health is the delivery of health resources via traditional internet which is called web health, and the other form of e-Health is the dissemination of health information using personal mobile phones which is known as m-Health. Amorim et al. (2019) reported that one potential limitation was that the interventions included several pragmatically delivered components such as health coaching activity trackers and mobile technology (IMPACT App). (84) There also was no follow-up contact with the control group except for weekly surveys sent via mobile text or email. An SR by Dario et al. (2017) was limited to a small number of trials, and there was variability in design, contact, populations investigated, and measurement of outcomes. (85) The study's quantitative synthesis was limited to the outcomes of pain and disability. Suman et al. (2019) suggested that the study must be interpreted with caution because loss-tofollow-up rate was higher for the intervention group than the control group. (87) Most participants in the study did not need or use the intervention and had minimal disability and impaired QoL before the start of the study. The overall quality of the evidence for most of the outcomes assessed was rated low to very low, primarily due to limitations in the methodological quality of the studies reviewed. (84-87)

There is some variability in patient preferences regarding the use of technology-based modalities. For working patients, taking time off for appointments may be difficult. Therefore, some patients may value a technology-based option that would allow them to avoid traveling to receive care. There is a suggestion

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j Recommendations for "patients with low back pain" encompass patient populations with acute, subacute, or chronic LBP with or without neurological symptoms.

that rural patients face the most barriers to care and may therefore be the most interested. However, patients may face travel difficulty (e.g., traffic/lack of transportation) wherever they live, and therapist capacity is less than potential demand in most places. Stigma is another reason patients may prefer technology-based treatment. Further, there may be a lack of internet access in rural areas, and costs associated with internet and technology equipment need to be taken into consideration.

The Work Group systematically reviewed evidence related to this recommendation. (84-87) Therefore, this is a *Reviewed*, *New-added* recommendation. The Work Group's confidence in the quality of the evidence was very low. The body of evidence had some limitations including failure to differentiate between telehealth modalities (hybrid study applications and web-based items grouped under telehealth). Study limitations included lack of intention to treat (ITT) analysis,(85) unclear blinding status,(85) and a high and/or differential attrition rate. (87) In general, the benefits of using technology-based modalities for self-management were balanced with any potential harm, as there were no direct harms associated with the self-management interventions, but costs and infrastructure are burdens worth considering. However, some studies demonstrated marginal improvements in functional status and pain severity in the short-term, for which the Work Group felt the benefits slightly outweighed the potential harms/burden.(85, 86) There was a lack of data demonstrating long-term efficacy. Patient values and preferences were somewhat varied because some patients may not prefer technology-based modalities. Younger patients may be more inclined to adopt such technological tools. Some patients may value not having to travel to medical facilities. Thus, the Work Group decided upon a *Neither for nor against* recommendation.

# C. Non-pharmacologic and Non-invasive Therapy

# **Recommendation**

8. For patients with chronic low back pain, we suggest cognitive behavioral therapy. (Weak for | Reviewed, New-replaced)

#### **Discussion**

As the importance of viewing chronic LBP from a biopsychosocial model has increased, there has been a rise in use of behavioral interventions to assist patients with non-pharmacologic self-management. Evidence suggests that CBT was more effective than usual care in improving the critical outcome of functional status, with moderate confidence in the quality of the evidence. (88, 89) CBT was associated with small improvements in the important outcome of pain. (89) The current body of research on behavioral interventions includes many variations and types of treatment. The intervention can be provided in an individual or group setting with a variable number of sessions and is typically provided by a behavioral health provider. In the studies of CBT for back pain the number of visits usually consisted of 4-12 visits. The content of visits typically followed a manual and includes a structured agenda for the visit as well as between-visit assignments. Some topics include identifying maladaptive cognitions such as catastrophizing and developing ways to reframe these into more adaptive cognitions. Techniques such as relaxation, behavioral activation, and exposure are commonly used to reduce the functional impact of pain as well as improve QoL. (89) One of the areas for future research is the effectiveness of CBT interventions specifically designed to address pain such as cognitive behavioral therapy for chronic pain (CBT-CP).

No studies that addressed other behavioral interventions (e.g., Acceptance and Commitment Therapy [ACT], biofeedback) met criteria for inclusion in the current systematic evidence review. Based on low

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quality evidence, alternative behavioral interventions that include variations of CBT (e.g., fear-avoidance exposure, cognitive patient education, combined neuromuscular exercise, cognitive behavioral back care counseling) demonstrated no difference in QoL compared to no treatment. (90-92) There was no difference in functional status found between MoodGYM, which is a CBT-based intervention with five self-help modules combined with standard physical treatment, and standard physical treatment alone. (93) There was no evidence identified for acute LBP interventions.

An important component of the biopsychosocial model and selection of any intervention is consideration of patient values and preferences. The following factors are important to consider when collaborating with a patient to determine if CBT is an appropriate part of the treatment plan. CBT can be time-intensive, and patients may not want, or have the ability, to dedicate the amount of time necessary to the intervention. Additionally, the specialized training of a behavioral health provider is an important consideration and may decrease availability and feasibility at all facilities and locations. However, the VHA is committed to training providers across the healthcare system in evidenced based treatment to reduce the negative impacts of chronic pain. CBT-CP is readily accessible to most Veterans, decreasing this barrier and demonstrating a strength of the VA. On the other hand, some patients prefer treatments with minimal risk such as CBT (versus potential risks with medications, procedures, etc.) where they can acquire self-managed skills and strategies for pain. Approaches such as CBT may be used in isolation or in conjunction with pharmacotherapy and therefore may also be of interest as an additional component of the treatment plan.

The Work Group systematically reviewed evidence related to this recommendation (89-93) and considered the assessment of the evidence put forth in the 2017 VA/DoD LBP CPG. (88) Therefore, this is a *Reviewed*, *New-replaced* recommendation. The Work Group's confidence in the quality of the evidence was low. The body of evidence had some limitations including unclear randomization, high attrition, deviations from the intended interventions and inability to effectively blind patients and providers. (89) The potential benefits of CBT (e.g., improved functioning and decreased pain severity) continue to outweigh the potential harm (e.g., data on harm was limited but none of the reviewed evidence on CBT suggested serious harm risk.) However, the strength of the recommendation was modified from *Strong for* in the 2017 VA/DoD LBP CPG to *Weakfor* in this updated CPG based on the inability to determine if the critical outcome of QoL is improved with CBT. Patient values and preferences were somewhat varied because time burden was a barrier for decreased acceptance of behavioral interventions. Thus, the Work Group decided upon a *Weak for* recommendation.

# **Recommendation**

 For patients with low back pain, we suggest a structured clinician-directed exercise program (e.g., aerobic, aquatic, mechanical diagnosis and therapy, mobility, motor control, Pilates, strengthening exercises, structured walking program, tai chi). k

(Weak for | Reviewed, New-replaced)

#### Discussion

Evidence suggests clinician-directed exercise improves pain, disability, and physical functioning in patients with LBP. Structured, clinician-directed exercise programs are those involving organized and progressive

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<sup>&</sup>lt;sup>k</sup> Recommendations for "patients with low back pain" encompass patient populations with acute, subacute, or chronic LBP with or without neurological symptoms.

activity prescribed by a clinician to improve pain, disability, and physical function. This includes exercise programs targeted at the lumbar, abdominal, and hip muscles (often referred to as the "core") and generalized exercises not specifically targeting the back (e.g., aerobic training on a bicycle, walking, or arm and leg muscle strengthening exercises using weight machines).

The Work Group found evidence supporting a wide variety of exercise programs including aerobic, (94) aquatic (pool), (95) mechanical diagnosis and therapy (MDT), (96) mobility, (97-99) motor control, (100-106) Pilates, (107-110) strength training, (105) structured walking programs, (111, 112) and tai chi. (113-115) Most of the evidence concerned patients with chronic LBP, but the Work Group did review some evidence on acute LBP. (96, 116) These recommendations were based on a large body of evidence from the 2017 VA/DoD LBP CPG (107, 108, 111, 113, 114) and several SRs (94-96, 100, 101, 112, 115) and RCTs (97-99, 102-106, 109, 110, 117-119) reviewed for this update. Most, but not all, of the studies reviewed for clinician-directed exercise used physical therapists as the treating clinician but the panel reviewed no evidence comparing the efficacy of exercise therapy delivered by different professional groups.

The effect sizes of these interventions on pain, disability, and physical function are generally small to moderate, with individual studies often showing statistically significant and clinically meaningful changes in some outcomes but not others. There was no evidence showing clear superiority of any of these approaches when compared to another in improving pain, disability, or physical functioning. The Work Group found limited and inconsistent evidence favoring supervised versus home-based exercise sessions. (105, 106, 120)

While some studies found no differences between structured exercise programs and a credible placebo intervention, most studies found small to moderate effects in the short to medium term on pain, disability, and physical functioning that were statistically significant and clinically meaningful. Few studies monitored adverse events (AE), and such AEs are typically self-limited temporary exacerbations of pain or symptoms. Representative examples include reporting of mild musculoskeletal complaints such as pain or soreness both in the back and in other body regions, and other AEs (to include systemic disease and emotional/psychosocial events) that were not thought to be related to participation in the exercise program. (98-100) These structured exercise programs are generally safe and well-tolerated by patients. However, there was significant heterogeneity in the studies evaluated, many studies lacked blinding (even of outcome assessors), and many failed to conduct an ITT analysis.

While effects are generally small to moderate and clinically meaningful, there is a burden of ongoing participation in the exercise program, either in a clinical setting (which also involves travel) or independently. The Work Group estimated large variation in the values and preferences of patients toward different modes or types of exercise and their ability or interest to participate. There are also resource considerations, including having an adequate supply of trained clinicians to deliver these programs, having the appropriate equipment needed for some of the options (e.g., gym-based aerobic and strength machines or a pool for aquatic exercise), or having a safe outdoor or indoor space to exercise. Some programs require more vigorous exercise, and some studies were conducted in subpopulations that may not be directly comparable to VA/DoD patients.

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The Work Group systematically reviewed evidence related to this recommendation (94-106, 109, 110, 112, 115, 117-120) and considered the assessment of the evidence put forth in the 2017 VA/DoD LBP CPG. (107, 108, 111, 113, 114) Therefore, this is a *Reviewed, New-replaced* recommendation. The Work Group's confidence in the quality of the evidence was very low. The body of evidence had some limitations including small sample sizes, lack of blinding (even of outcome assessors), and failure to complete ITT analysis. Benefits of structured clinician-directed exercise programs for improved pain, disability, functioning, and QoL slightly outweighed the potential harm (AEs were uncommon and mild) and burdens (requirement to travel or participate in an ongoing exercise therapy regimen). Patient values and preferences vary considerably because many patients have specific values and preferences about the type, mode, and duration of exercise they might desire to participate in. Thus, the Work Group decided upon a *Weak for* recommendation.

# **Recommendation**

- 10. For patients with chronic low back pain, we suggest spinal mobilization/manipulation. (Weak for | Reviewed, New-replaced)
- 11. For patients with acute low back pain, there is insufficient evidence to recommend for or against spinal mobilization/manipulation.

(Neither for nor against | Reviewed, New-replaced)

# **Discussion**

Evidence suggests spinal mobilization/manipulation results in modest but clinically important reductions in pain and disability in patients with chronic LBP. (121-128) Rubinstein et al. (2019) compared spinal manipulative therapy (SMT) to recommended and non-recommended treatments. (128) A treatment was considered recommended or non-recommended if it was designated so in two out of three recent LBP guidelines. Treatment with SMT was as effective as other recommended treatments (e.g., exercise, nonsteroidal anti-inflammatory drugs [NSAIDs]) for reducing pain and disability at one, six, and 12 months. SMT was superior to non-recommended treatments (e.g., short-wave diathermy, ultrasound, light massage, wait list, and electrotherapies) for reduction of disability at one, six, and 12 months but not different for reduction of pain severity.

An SR and meta-analysis by Dal Farra et al. (2021) demonstrated reductions in pain severity (standardized mean difference [SMD]: 0.59) and disability (SMD: 0.42) when comparing osteopathy including manipulative therapy to control. (121) However, only one study (129) included in the meta-analysis tracked outcomes to the predetermined target of 12 weeks. Of patients receiving osteopathic manipulative treatment (OMT), 65% achieved 30% relief and 50% achieved 50% relief compared to 46% and 35%, respectively, in the sham OMT group. (121) Marti-Salvador et al. (2018) compared OMT with manual therapy targeted at the diaphragm to OMT with a sham diaphragm intervention. (122) OMT with diaphragm intervention was superior, but both groups achieved clinically important changes in pain and function. Several studies used to substantiate the recommendation in the 2017 VA/DoD LBP CPG demonstrated similar effects to those reported by Rubinstein et al. (2019). (123-127) Evidence for OMT and SMT were considered together because the treatment modalities are similar, and there was variability in the type of clinician (e.g., Doctor of Osteopathic Medicine [DO], Doctor of Chiropractic [DC], Doctor of Physical Therapy [DPT]) performing manipulation in both groups.

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For acute LBP, the recommendation strength was modified from *Weak for* in the 2017 VA/DoD LBP CPG to *Neither for nor against* in this updated CPG based on limited evidence at or beyond the Work Group's predetermined target of 12 weeks. Of the 20 studies included in an SR and meta-analysis by Rubinstein et al. (2013), only two assessed outcomes at 12 weeks. One study demonstrated clinically important changes in pain and disability when compared to baseline but not when compared to PT. Importantly, this study included patients with neck and LBP, and the Work Group was unable to assess the effect of SMT on LBP alone. Another study reported positive effects for SMT, physiotherapy, and education for pain and disability, but differences between groups were not statistically significant. (130) Similar to exercise, the use of spinal mobilization/manipulation is a relatively low-risk intervention for patients with LBP. Though AEs were not systematically captured in this review, Rubinstein et al. (2013) found AEs, like soreness, to be common but mild and self-limited. (130)

There is some variability in patient preferences regarding this treatment. Courses of SMT vary in length but on average require a significant time commitment for patients and providers. SMT is likely to be available to most patients, as DCs, DOs, and DPTs receive training in the modality.

The Work Group systematically reviewed evidence related to Recommendation 10 (121, 122, 128, 131) and considered the assessment of the evidence put forth in the 2017 VA/DoD LBP CPG. (123-127) Therefore, this is a *Reviewed, New-replaced* recommendation. The Work Group's confidence in the quality of the evidence was low. The body of evidence had some limitations including limited duration of follow-up and difficulty inherent to performing sham manipulations. (121, 122, 128) The benefits of spinal manipulation, including modest improvements in pain and function at or exceeding 12 weeks, slightly outweighed the potential harm of AEs, which was small. Patient values and preferences varied somewhat because some patients may be less tolerant of the hands-on nature of manual therapies or the time required to complete a course of treatment. Thus, the Work Group decided upon a *Weakfor* recommendation.

The Work Group systematically reviewed evidence related to Recommendation 11; however, no studies in the patient population with acute LBP met inclusion criteria. The Work Group also considered the assessment of the evidence put forth in the 2017 VA/DoD LBP CPG. (130, 132) Therefore, this is a *Reviewed, New-replaced* recommendation. The Work Group's confidence in the quality of the evidence was very low. The body of evidence had some limitations including limited duration of follow-up, mixed populations (e.g., LBP and neck pain), and difficulty inherent to performing sham manipulations. (130, 132) The benefits of spinal manipulation/mobilization were balanced with the potential harm of AEs, which was small. Patient values and preferences somewhat varied because some patients may be less tolerant of the hands-on nature of manual therapies or to the time required to complete a course of treatment. Thus, the Work Group decided upon a *Neither for nor against* recommendation.

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# **Recommendation**

12. For patients with chronic low back pain, there is insufficient evidence to recommend for or against mindfulness-based stress reduction.

(Neither for nor against | Reviewed, New-replaced)

# **Discussion**

Mindfulness-based stress reduction (MBSR) is a structured intervention focused on the concept of mindfulness (i.e., being in the present moment, without judgment). Treatment is manualized and includes components such as education, meditative practices, simple yoga poses over eight 2.5 hour group sessions plus a longer retreat, and daily home practice. (88) MBSR requires an instructor with specialized MBSR training and experience.

The current systematic evidence review identified two SRs (89, 133) that examined whether MBSR is helpful for patients with chronic LBP. Skelly et al. (2020) included five trials of MBSR and was low quality. (89) Three of the trials had treatments closely modeled on the program created by Kabat-Zinn while the other two trials had some adaptations. Notably, all trials included a main intervention of 1.5 – 2 hour weekly group sessions for eight weeks. Results suggested no differences in functional status or pain reduction in the short- or long-term when comparing MBSR to usual care/attention control. One of the trials reported a small reduction in pain (-0.75 on a 0 – 10 scale; 95% confidence interval [CI]: -1.29 to -0.34) at intermediate duration follow-up. Skelly et al. (2020) also reported mixed results regarding QoL using the SF-2 and SF-36 with three studies finding no difference between MBSR and usual care/attention control and two studies finding some short-term benefit for MBSR in the physical component and mental component scores of the SF-36. (89) Concerning other potential benefits of MBSR, one trial indicated patients self-reported using less pain medication for LBP at a short-term interval, but not at long-term. Finally, one trial suggested a statistical improvement in a measure of depressive symptoms (0.63 points on the PHQ-8), but this did not reach the threshold of clinical significance.

An SR of nine RCTs (n=959) from Bahnamiri et al. (2020) examined the effectiveness of mindfulness-based interventions (MBIs) on reducing pain for patients with LBP. (133) The authors concluded that MBIs are effective and as effective as CBT at reducing pain intensity. Five of the nine individual trials identified in the SR were consistent with MBSR and showed some evidence of pain reduction; however, these were very low quality evidence and there was no statistical analysis of the pooled data. The remaining four trials included in the SR combined elements of cognitive or CBT-based treatments with MBSR, which made it difficult to evaluate the overall effectiveness of MBSR.

There is some variability in patient preferences regarding MBSR treatment. Some patients may be less open to mindfulness-based approaches. This treatment is considered time-intensive. There is also specialized training needed to facilitate the treatment. This treatment may not be available in all facilities and therefore not available to all patients. However, from a staffing standpoint, training can be completed and treatment can be facilitated by non-mental health staff. This contrasts with CBT, which requires providers with mental health training. Another consideration is that one trial in the Skelly et al. (2020) SR found 29% of patients experienced a brief increase in pain. (89) Overall, the Work Group determined the burdens of MBSR were balanced with potential benefits.

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The Work Group systematically reviewed evidence related to this recommendation (89, 133) and considered the assessment of the evidence put forth in the 2017 VA/DoD LBP CPG. (88) Therefore, this is a *Reviewed, New-replaced* recommendation. MBSR appears to have no benefit for improved functioning and mixed findings for pain and QoL. As noted by Bahnamiri et al. (2020), pain relief is not a primary treatment outcome for MBIs. Thus, the Work Group decided there was insufficient evidence to recommend for or against MBSR as a treatment for patients with chronic LBP. The Work Group's confidence in the quality of the evidence was low. The body of evidence had limitations including serious risk of study bias and very serious imprecision of findings. (89, 133) The harms of MBSR for chronic LBP are balanced with the potential benefits (e.g., one study found a brief increase in pain, resource intensive treatment). Patient values and preferences varied somewhat because some patients may not be open to mindfulness-based treatments, and there is a time and resource burden in implementing this treatment. Thus, the Work Group decided upon a *Neither for nor against* recommendation.

# **Recommendation**

13. For patients with low back pain, there is insufficient evidence to recommend for or against lumbar supports.

(Neither for nor against | Reviewed, Amended)

#### Discussion

The available evidence is insufficient to recommend for or against the use of lumbar supports in patients with LBP. (134) A meta-analysis of three studies by Gignoux et al. (2020) found the use of lumbar supports resulted in a small, statistically insignificant effect on pain severity (SMD: -0.29). (134) The same meta-analysis reported a medium effect on function (SMD: -0.54); however, of the four studies reporting on function, two were disproportionately responsible for the effect and neither reported on outcomes at or beyond the Work Group's predetermined target of 12 weeks. (134) The recommendation in the 2017 VA/DoD LBP CPG was informed by a comparative effectiveness review by Chou et al. (2016), (113) which included three low quality RCTs. (135-137) This evidence suggests that lumbar supports were no more effective than inactive treatments or no treatment and that lumbar supports did not seem to augment the positive effect of an exercise program. (113) An RCT by Sato et al. (2012) found that using lumbar support for chronic LBP improved pain and increased muscle endurance in the short-term. (135) Paravertebral muscle fatigue was not increased by long-term use for chronic LBP, and weakening of the paravertebral muscles was not observed up to six months after the start of corset wear. (113, 135) No harms were associated with the use of lumbar supports, though harms were generally not well-reported. (134)

There is some variability in patient preferences regarding this treatment. Use of a lumbar support may be problematic for Service Members who adhere to dress codes. Although lumbar supports can be relatively inexpensive, LBP is ubiquitous, and even small expenses multiplied by many patients can result in a substantial cost. Further, some patients may seek custom lumbar supports, which can be expensive.

The Work Group systematically reviewed evidence related to this recommendation ( $\underline{134}$ ) and considered the assessment of the evidence put forth in the 2017 VA/DoD LBP CPG. ( $\underline{113}$ ) Therefore, this is a *Reviewed, Amended* recommendation. The Work Group's confidence in the quality of the evidence was very low. The

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Recommendations for "patients with low back pain" encompass patient populations with acute, subacute, or chronic LBP with or without neurological symptoms.

body of evidence had some limitations including limited duration of follow-up and heterogeneity in terms of the type of lumbar support used and frequency and duration of use. (113, 134) The benefits of lumbar supports for reduction of pain severity and improvement in function slightly outweighed the potential harm/burdens. Patient values and preferences varied somewhat because use of a lumbar support may be problematic for Service Members who adhere to dress codes. Further, widespread use may result in substantial costs. Thus, the Work Group decided upon a *Neither for nor against* recommendation.

#### **Recommendation**

14. For patients with low back pain, with or without radicular symptoms, there is insufficient evidence to recommend for or against mechanical lumbar traction.

(Neither for nor against | Reviewed, New-replaced)

#### **Discussion**

The available evidence is insufficient to recommend for or against the use of mechanical traction for patients with LBP with or without radicular symptoms. ( $\underline{138-141}$ ) An SR and meta-analysis of seven studies by Cheng et al. (2020) investigated the effect of traction on adults with LBP and herniated lumbar disc. ( $\underline{138}$ ) Only two of the seven studies collected outcomes at or beyond the Work Group's predetermined target of 12 weeks. The first was a small RCT (n=64) demonstrating clinically meaningful improvement in function (ODI: -19.3) but not pain when compared to baseline. The second was a very small RCT (n=20) comparing physiotherapy versus physiotherapy plus traction, which found no significant difference between the two interventions.

Vanti et al. (2021), in an SR of eight studies and a meta-analysis of five studies, investigated the effect of traction on adults with lumbar radiculopathy. ( $\underline{139}$ ) Of eight studies, three reported on outcomes at or beyond the Work Group's predetermined target of 12 weeks. The studies reported small to moderate improvements in pain and function from baseline but were fraught with limitations including very small sample sizes and high dropout rates.

The Cochrane review by Wegner et al. (2013), which informed the recommendation in the 2017 VA/DoD LBP CPG, found that for adults with LBP with or without sciatica, of any duration, traction had little to no impact on pain intensity, functional status, or global improvement when compared with sham traction, no treatment, other treatments, or when applied as a combination therapy. ( $\underline{140}$ ) An RCT by Diab et al. (2012) found no significant change in pain when comparing stretching plus infrared radiation to traction plus infrared radiation. ( $\underline{141}$ ) AEs were common in the form of aggravations of low back and leg pain and low back stiffness. Less common were headache, dizziness, and fatigue. ( $\underline{139}$ ,  $\underline{140}$ )

There is large variability in patient preferences given the heterogeneity of traction modalities employed and variability of patient tolerance to common AEs. Further, courses of lumbar traction require a significant time commitment by providers and patients and expenditures for the healthcare system.

The Work Group systematically reviewed evidence related to this recommendation ( $\underline{138}$ ,  $\underline{139}$ ) and considered the assessment of the evidence put forth in the 2017 VA/DoD LBP CPG.( $\underline{140}$ ,  $\underline{141}$ ) Therefore, this is a *Reviewed, New-replaced* recommendation. The Work Group's confidence in the quality of the evidence was low. The body of evidence had some limitations including small sample sizes, high drop-out rates, and limited duration of follow-up.( $\underline{138-141}$ ) The benefits of lumbar traction (e.g., modest

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improvements in pain and function from baseline) were balanced with the potential harm of AEs, which were common but mild. Patient values and preferences varied because methods of applying traction were variable, the time commitment associated with lumbar traction is significant, and not all patients will tolerate common AEs. Thus, the Work Group decided upon a *Neither for nor against* recommendation.

# **Recommendation**

15. For patients with chronic low back pain, there is insufficient evidence to recommend for or against auricular acupressure.

(Neither for nor against | Reviewed, New-added)

# **Discussion**

Available evidence is insufficient to recommend for or against the use of auricular acupressure for LBP. One SR by Yang et al. (2017) included seven RCTs (n=369) examining the use of auricular acupressure for treatment of chronic LBP. (142) Outcomes included a small positive impact on short-term pain intensity, but no change in disability as measured by the RMDQ. Controls varied and included exercise (tai chi or walking), usual care, and sham (i.e., auricular acupuncture points not expected to improve chronic LBP).

Yang et al. (2017) found no change in disability at four or 12 weeks. ( $\underline{142}$ ) However, pain intensity was statistically significant at four weeks when compared to sham (five RCTs; MD: -0.89; 95% CI) and at 12 weeks (two RCTs; SMD: -0.56; 95% CI: -0.91 to -0.21; p=0.002). ( $\underline{142}$ ) This SR was rated as fair, and the confidence in the quality of the evidence was low.

No AEs were reported; however, sensitization to adhesive tape used, soreness at the treatment sites, and sleep disturbance were noted. Benefits slightly outweigh burdens due to the low risk associated with auricular acupressure. Burdens of needing to attend treatment and the acceptability of wearing acupressure devices that are visible to others on the ear are additional considerations for the patient. The Work Group considered that many patients value small improvements in pain, but the evidence failed to show a change in disability.

The Work Group expects large variability in patient preferences regarding this treatment. There are efforts to increase the use and acceptability of non-pharmacologic options for pain, and a desire for non-pharmacologic options was noted by the patient focus group; however, auricular acupuncture is unlikely to be a treatment approach with much familiarity for patients and/or providers. Particularly in the DoD setting, a high degree of skepticism toward CIH approaches may be present.

At this time, auricular acupressure is not commonly used within the VA and DoD populations. The Work Group also considered lack of standardization of this type of care in the community if acupressure were not available in a medical facility.

The Work Group systematically reviewed new evidence related to this recommendation. (142) Therefore, this is a *Reviewed, New-added* recommendation. The Work Group's confidence in the quality of the evidence was low. The body of evidence had some limitations including small sample size, heterogeneity of studies, and lack of longer term follow-up (12 weeks and beyond). The benefits of auricular acupressure slightly outweighed the potential harm due to the low risk profile of this treatment. Patient values and

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preferences varied largely because of a lack of familiarity with this type of treatment and accessibility. Thus, the Work Group decided upon a *Neither for nor against* recommendation.

# **Recommendation**

16. For patients with low back pain, there is insufficient evidence to recommend for or against yoga or qi gong.<sup>m</sup>

(Neither for nor against | Reviewed, New-replaced)

# **Discussion**

There is insufficient evidence to recommend the use of yoga to improve disability or QoL when compared to usual care, wait list, or education in patients with LBP.(143) The Zhu et al. (2020) SR reported small SMDs for disability; however, these differences were considered not clinically meaningful. Studies failed to show a clinically significant reduction in pain.(143) A 2016 SR evaluated for the 2017 VA/DoD LBP CPG suggested yoga was beneficial for short- and long-term pain (SMD: -0.48; 95% CI: -0.65 to -0.31; SMD: -0.33; 95% CI: -0.59 to -0.07 respectively) and disability (SMD: -0.35; 95% CI: -0.55 to -0.15), but QoL improvement was uncertain.(144)

When yoga is compared to other exercise interventions (conventional PT or strength training), no significant difference in disability, QoL (physical health or mental health), or pain was shown. ( $\underline{105}$ ,  $\underline{143}$ ) Seven studies from one SR reported AEs (n=1,266). ( $\underline{143}$ ) Mild increased back pain was reported in the yoga intervention group, while a mild to moderate increase in back pain was reported among the exercise intervention group.

Available evidence failed to show that qi gong is effective for improving function or reducing chronic LBP. Nduwinmana et al. (2020) reviewed various mind-body interventions for chronic LBP, including qi gong. ( $\underline{145}$ ) Three RCTs compared qi gong to walking programs, but due to the heterogeneity of the studies, only two trials (n=199) met criteria for the critical outcome of activity limitation. ( $\underline{146-148}$ ) Although one study exhibited favorable outcomes for short-term improvement of activity limitation for qi gong compared to a walking program, the pooled analysis did not show a significant effect. ( $\underline{146}$ ,  $\underline{147}$ ) Similarly for pain, one study favored qi gong, ( $\underline{148}$ ) but the overall analysis of the 242 participants from two trials revealed a non-significant effect. ( $\underline{147}$ ,  $\underline{148}$ )

The quality of evidence was very low, sample sizes were small, and heterogeneity existed among the studies reviewed. Trials did not blind patients, providers, or assessors. A discussion of AEs in the systematic evidence review was lacking.

Large variation exists in patient acceptance of yoga and qi gong as an intervention for LBP. While some may be eager to engage in this practice, others may not consider yoga to meet their values and preferences. There is a time burden for these practices, and studies showed large variation in frequency and duration to achieve benefit. For example, yoga practices studied ranged from seven days (eight hours per day) to 24 weeks (two 90-minute classes per week) of intervention. (143) Patients may need to travel for classes, and resources would be needed for instructor training and class time. Telehealth is an

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m Recommendations for "patients with low back pain" encompass patient populations with acute, subacute, or chronic LBP with or without neurological symptoms.

emerging opportunity for these interventions and it may reduce the need for patients to travel, but additional infrastructure and equipment (e.g., computers, smartphones) would be required.

The Work Group systematically reviewed evidence related to this recommendation (105, 143, 145) and considered the assessment of the evidence put forth in the 2017 VA/DoD LBP CPG. (144) Therefore, this is a *Reviewed, New-replaced* recommendation. The 2017 VA/DoD LBP CPG suggested yoga as a potential part of an exercise program. However, due to the low confidence in the quality of the evidence related to yoga as a stand-alone intervention, the lack of evidence of benefit, and expectation of little harm, the Work Group included yoga as part of this *Neither for nor against* recommendation rather than as part of Recommendation 9 in this CPG update. Qi gong was not assessed in the 2017 VA/DoD LBP CPG, and the Work Group's confidence in the quality of the evidence on qi gong was very low. The body of evidence for this recommendation had limitations including small sample size, heterogeneity of studies especially regarding frequency and duration of intervention, and lack of blinding by assessors. Although resources and patient time would be used for these interventions, harms are expected to be low. However, if yoga or qi gong were used in replacement of another intervention that may be more useful for the LBP patient, delay of appropriate care would be considered a harm. Patient values and preferences vary. Thus, the Work Group decided upon a *Neither for nor against* recommendation.

# **Recommendation**

17. For patients with low back pain, there is insufficient evidence to recommend for or against cupping, laser therapy, transcutaneous electrical nerve stimulation, and ultrasound. 

(Neither for nor against | Reviewed, New-replaced)

#### **Discussion**

There is insufficient evidence to recommend for or against the use of cupping, laser therapy, transcutaneous electrical nerve stimulation (TENS), and ultrasound for reduction of pain and disability in patients with LBP. ( $\underline{113}$ ,  $\underline{149-153}$ ) Wood et al. (2020) systematically reviewed 21 RCTs assessing the effect of cupping on musculoskeletal pain and range of motion. ( $\underline{149}$ ) Of those, only one RCT pertained to LBP and reported on outcomes at or beyond the predetermined target of 12 weeks. That study demonstrated a small difference in pain severity (reduction of 15 points on visual analog scale [VAS]) and no difference in function when comparing cupping plus paracetamol to paracetamol alone.

The Wang et al. (2017) meta-analysis included six RCTs assessing the effect of cupping for LBP. (150) Of those, two reported on outcomes at or beyond the predetermined target of 12 weeks. One reported that cupping had a small effect on function (SMD: -0.31) but no clinically meaningful effect on pain, while the other reported a large effect on function (SMD: -1.56). Mardani-Kivi et al. (2019) conducted an RCT (n=180) and found no difference in pain severity when comparing wet cupping to rest and acetaminophen at three months, and a slight difference in favor of wet cupping at six months. (151) Wet cupping resulted in a borderline clinically significant effect on disability. (149-151) Most AEs were mild and self-limiting, including soreness and ecchymosis. Several instances of blistering were associated with fire-cupping for knee osteoarthritis (OA) but not for LBP. (149)

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Recommendations for "patients with low back pain" encompass patient populations withacute, subacute, or chronic LBP with or without neurological symptoms.

The Glazov et al. (2016) meta-analysis included 15 RCTs comparing low-level laser therapy to sham or other treatments for adults with LBP.(152) Of 15 studies, four reported on outcomes at or beyond the predetermined target of 12 weeks. When comparing laser plus exercise, sham laser plus exercise, and laser alone, all groups achieved clinically meaningful improvements in pain and disability at 12 weeks; however, no difference was found between groups. Comparison of "high dose," "low dose," and sham laser resulted in no clinically meaningful difference in pain or function from baseline or between groups at six months. The two remaining studies favored sham laser over laser for pain reduction at 12 weeks and six months.(152)

The systematic evidence review did not identify new data on the effect of TENS for LBP. The 2017 VA/DoD LBP CPG recommendation was informed by an RCT by Buchmuller et al. (2012), which found no statistical difference between TENS and sham TENS for pain or function at six weeks. (153)

The systematic evidence review did not identify new data on the effect of ultrasound for LBP. The 2017 VA/DoD LBP CPG recommendation was informed by a comparative effectiveness review by Chou et al. (2016) which found low quality evidence that ultrasound was no more effective than sham ultrasound or no difference in outcomes when comparing ultrasound to sham ultrasound. (113)

There is likely to be large variability in patient preferences for cupping. The focus group participants expressed a desire for CIH treatments, specifically non-pharmacologic treatment, and shared decision making. However, cupping techniques vary with some versions including bloodletting or use of an open flame to create suction, which may be unfamiliar to patients and clinicians. Patients may also be averse to the skin markings common after cupping. Completing a course of treatment may require a significant time commitment and travel burden for patients. Clinician time and training should also be considered.

There is likely high variability in patient preferences for laser therapy, TENS, and ultrasound. Laser therapy and ultrasound are usually provided by a clinician, which introduces a time and travel burden. TENS is usually self-administered but application of the electrode pads can be difficult for some patients. Cost to the healthcare system must also be considered as these modalities requires specialized equipment.

The Work Group systematically reviewed evidence related to this recommendation (149-152) and considered the assessment of the evidence put forth in the 2017 VA/DoD LBP CPG. (113, 153) Therefore, this is a *Reviewed, New-replaced* recommendation. The Work Group's confidence in the quality of the evidence was low. The body of evidence had some limitations including small sample sizes, heterogeneity for the applications of modalities, and limited follow-up duration. (149-152) The benefits of cupping, laser therapy, TENS, and ultrasound were balanced with the potential harm of AEs, which were generally mild and self-limiting. Patient values and preferences vary because tolerance to AEs, time and travel burden, and lack of familiarity with the modality likely vary between patients. Thus, the Work Group decided upon a *Neither for nor against* recommendation.

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# D. Pharmacotherapy

# **Recommendation**

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

# **Discussion**

The evidence review identified one SR by Kolber et al. (2021), (154) which included four RCTs comparing duloxetine versus placebo, (155-158) and found that duloxetine (n=832) provided a clinically relevant improvement in pain, defined as a >30% reduction in pain compared to baseline. The analysis revealed 58% of patients receiving duloxetine (n=832) and 47% of patients receiving placebo (n=667) had clinically significant pain relief (risk ratio [RR]: 1. 25; 95% CI: 1.13 to 1.38, p<0.00001). The benefit of duloxetine for chronic LBP for pain and function is demonstrated by moderate quality evidence. (154) However, the amount of pain reduction over placebo was not consistently clinically meaningful as duloxetine resulted in 0.46 to 0.82 points less than placebo on a 10 point scale in two of the studies reviewed in the Kolber et al. (2021). (155, 158)

When function was measured by the RMDQ, the comparative data were inconclusive. ( $\underline{113}$ ) It is also important to keep in mind that the effects of selective serotonin reuptake inhibitors (SSRI) on LBP are inconclusive. ( $\underline{113}$ ) Of the serotonin and norepine phrine reuptake inhibitors (SNRI) class, only studies on duloxetine met criteria for inclusion for the evidence review. Theoretically, the SNRI class may demonstrate some benefit given a similar mechanism of action to duloxetine.

Within the studies reviewed in the Kolber SR, there was a high rate of discontinuation due to AEs for those in the duloxetine arms compared with the placebo arms. Within three of the four studies that documented study dropout rates, the discontinuation rate due to AEs versus placebo was: 15.2% versus 5.4% (p=0.002) for duloxetine 60 mg, (157) 13.9% versus 5.8% (p=0.047) for duloxetine 120 mg, (158) and 24.1% vs. 8.5% for duloxetine 120 mg. (156) While there were no serious AEs found in the evidence review, there are more adverse effects associated with duloxetine when compared to placebo. These include nausea, insomnia, dry mouth, constipation, somnolence, fatigue, and hyperhidrosis. (113) Duloxetine also has sexual side effects that may diminish treatment acceptability and adherence. Additionally, duloxetine has a risk of hepatotoxicity and should not be used in patients with substantial alcohol use or evidence of chronic liver disease. Combining duloxetine with other serotonergic medications increases the risk of serotonin syndrome and should be used with caution. There is a black box warning with antidepressants, including duloxetine, in the treatment of major depressive disorder (MDD) and other psychiatric disorders for increased risk of suicidal thinking and behavior in children, adolescents, and young adults. (159)

There is large variation in patient preferences regarding this treatment. Some patients may prefer to take a medication for their LBP, while others may have difficulty accepting duloxetine for treatment due to the stigma associated with taking an antidepressant and the side effects mentioned above. This medication may be preferred in patients with depression or anxiety as duloxetine is U.S. Food and Drug Administration (FDA) approved for these conditions, in addition to fibromyalgia.

The Work Group systematically reviewed evidence related to this recommendation ( $\frac{154}{}$ ) and considered the assessment of the evidence put forth in the 2017 VA/DoD LBP CPG. ( $\frac{113}{}$ ) The RCTs included in

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Kolber et al. (2021) were also covered in the 2017 VA/DoD LBP CPG's systematic evidence review; thus, there was no new evidence considered in this CPG update. Therefore, this is a *Reviewed, New-replaced* recommendation. The Work Group's confidence in the quality of the evidence was moderate. The body of evidence significant limitations including a high rate of attrition due to non-serious AEs. (154) The Work Group determined the small but statistically significant benefits of improved pain and function slightly outweighed the potential harm of AEs, which were mild and not serious. Patient values and preferences varied because of stigma due to antidepressants and preferences regarding whether to take medication. Thus, the Work Group decided upon a *Weak for* recommendation.

# **Recommendation**

19. For patients with low back pain, we suggest nonsteroidal anti-inflammatory drugs.° (Weak for | Reviewed, New-replaced)

# **Discussion**

Two SRs and one RCT assessed the potential benefits of NSAIDs compared to placebo. ( $\underline{113}$ ,  $\underline{154}$ ,  $\underline{160}$ ) Moderate quality evidence from one SR by Kolber et al. (2021) suggests use of NSAIDs (n=993) in patients with chronic LBP is associated with an improvement in pain and function, defined as a 30% reduction in pain or combination of pain reduction and functional improvement, compared with placebo (n=644), with a number needed to treat (NNT) of 6. ( $\underline{154}$ ) Follow-up ranged from 4 - 16 weeks. Low quality evidence found no difference between NSAIDs (n=383) and placebo (n=271) at 12 weeks or greater. ( $\underline{154}$ )

Low quality evidence from the Kolber et al. (2021) SR demonstrated no significant difference in AEs between placebo and NSAIDs with a follow-up duration of 4-12 weeks. (154) The Chou et al. (2016) SR included five studies that compared cyclooxygenase-2 (COX-2) NSAIDs with traditional NSAIDs. (113) No statistically significant difference for pain relief for acute LBP was seen in four studies. The fifth study found no differences in pain relief between COX-2 and traditional NSAIDs for chronic LBP. (161)

Most comparative trials between NSAIDs showed no significant differences in pain relief. A large noninferiority trial randomized 24,081 patients to receive celecoxib, naproxen, or ibuprofen and found the cardiovascular (CV) risk associated with celecoxib was noninferior to the non-selective NSAIDs. (162) This trial was limited by high rates of drug discontinuation (68.8%), study dropout (27.4%), and the restrictions on the doses of celecoxib. Most patients in the trial (90%) had OA. The dose of celecoxib was limited to 200 mg/day in this group, but dose escalation was allowed for ibuprofen and naproxen.

All NSAIDs have a black box warning for increased risk of CV events and gastrointestinal (GI) events, and these safety issues continue to be high priority when choosing an NSAID.(163) If an NSAID is required in a patient with CV risk, naproxen may be a viable option. (164, 165) Providers should consider other patient risk factors, primarily GI toxicity, when determining whether relatively COX-2 selective NSAIDs should be used over non-selective NSAIDs. The use of relatively selective COX-2 inhibitors reduces the risk for GI events; however, this benefit is negated if the patient is using aspirin. (164) NSAIDs can also exacerbate heart failure and worsen hypertension and renal function. NSAIDs must be used cautiously or avoided in patients with renal impairment or in elderly patients, as these agents may increase serum

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Recommendations for "patients with low back pain" encompass patient populations with acute, subacute, or chronic LBP with or without neurological symptoms.

creatinine, cause sodium and water retention, and cause acute renal failure. ( $\underline{164}$ ) FDA guidance indicates NSAID prescribing should be used at the lowest effective dose for the shortest duration possible to reduce CV, GI, and renal AEs.

The Work Group systematically reviewed evidence related to this recommendation (154) and considered the assessment of the evidence put forth in the 2017 VA/DoD LBP CPG. (113, 160) Therefore, this is a *Reviewed, New-replaced* recommendation. The Work Group's confidence in the quality of the evidence was low. The body of evidence had some limitations including concerns around randomization, allocation procedures, and attrition. (113) The benefits of NSAIDs for pain and function slightly outweighed the potential harm of AEs. Patient values and preferences varied somewhat because some patients prefer medication to treat their pain. In addition, since NSAIDs are over the counter (OTC) and accessible, they may be preferable for patients. In some patient populations including elderly patients, patients with GI or CV risk, NSAIDs may not be preferred due to risk. The strength of the recommendation was modified from *Strong for* in the 2017 VA/DoD LBP CPG to *Weak for* in this updated CPG based on the inclusion of an additional study by Katz et al. (2011), (166) which prompted downgrade to a *Weak for* due to limited benefit for pain and concerns for AEs. Thus, the Work Group decided upon a *Weak for* recommendation.

# **Recommendation**

20. For patients with low back pain, with or without radicular symptoms, there is insufficient evidence to recommend for or against gabapentin or pregabalin.

(Neither for nor against | Reviewed, Amended)

# **Discussion**

The evidence review identified an SR by Shanthanna et al. (2017), which evaluated patients with radicular and non-radicular chronic LBP and included three RCTs. ( $\underline{167}$ ) The SR found no difference between gabapentin (n=91) and placebo (n=94) in reducing pain severity or functional outcomes. The same SR (n=163) found an overall improvement in pain with pregabalin (n=163) versus active analgesic control (n=169), with a pooled SMD of 0.42, (p=0.0002); however, the quality of the evidence was very low. Additionally, the individual studies included in the SR had mixed results, with one of the three studies reporting no benefit for pain with pregabalin versus active analgesic control. ( $\underline{168}$ ) The duration of follow-up with the studies ranged from 4-14 weeks. An RCT studying the treatment of pregabalin in patients with radiculopathy, which was not included in the systematic evidence review carried out as part of this CPG and did not influence the strength of the recommendation, reported no significant reduction in leg pain intensity and a higher incidence of AEs. ( $\underline{169}$ )

There are significant adverse effects associated with the use of gabapentin or pregabalin. Evidence from the Shanthanna et al. (2017) SR and another SR by Atkinson et al. (2016) found higher adverse effects with gabapentin versus placebo, including fatigue, dizziness, loss of balance, and difficulties with mental concentration, memory, and visual accommodation. (167, 170) An increased risk of dizziness was reported with pregabalin when compared to placebo. (167) Additionally, some subpopulations may be at greater risk of sedation and falls with the use of pregabalin or gabapentin. Antiepileptic medications, including pregabalin and gabapentin, increase the risk of suicidal thoughts or behavior in patients taking these medications for any indications. Patients should be monitored for the emergence of worsening depression, suicidal thoughts or behavior, and/or any changes in mood or behavior. (171)

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Pregabalin is a controlled substance with the potential for abuse and dependence. Gabapentin is not a federally scheduled medication; however, some states have scheduled gabapentin as a controlled substance due to concerns of addiction and dependence. Additionally, one study, which was not included in the systematic evidence review carried out as part of this CPG and did not influence the strength of the recommendation, indicates that gabapentin in combination with opioids significantly increases the risk of opioid-related mortality and respiratory depression. (172) Gabapentin or pregabalin may be beneficial in patients with comorbid anxiety or insomnia, as these agents have been used off-label for these indications.

The Work Group systematically reviewed evidence related to this recommendation (167) and considered the assessment of the evidence put forth in the 2017 VA/DoD LBP CPG. (170, 173, 174) The Work Group's confidence in the quality of the evidence was very low. Evidence on antiepileptics was limited to pregabalin and gabapentin, and the recommendation was amended to reflect this. Therefore, this is a *Reviewed, Amended* recommendation. The body of evidence had some limitations including concerns around randomization, allocation, and blinding procedures. Shanthanna et al. (2017) also assessed a high risk of bias for most trials. (167) The potential harms of AEs, including medication abuse and dependence, slightly outweighed the benefits versus placebo. There is large variation in patient values and preferences, as some patients prefer to take a medication for their LBP. Thus, the Work Group decided upon a *Neither for nor against* recommendation.

# **Recommendation**

21. For patients with low back pain, there is insufficient evidence to recommend for or against tricyclic antidepressants.<sup>p</sup>

(Neither for nor against | Reviewed, New-added)

# **Discussion**

The evidence for the use of tricyclic antidepressants (TCAs) demonstrates limited benefit with low to very low quality evidence. In an RCT comparing desipramine (n=37) to benztropine mesylate  $0.125 \, \text{mg}$  (n=33), there was no difference in function (as measured by the RMDQ) or for pain severity at  $12 \, \text{weeks.}(\underline{175})$  Another RCT demonstrated no benefit with low dose amitriptyline (n=72) versus benztropine mesylate (n=74) for function or pain severity at  $3-6 \, \text{month}$  follow-up. ( $\underline{176}$ ) Active placebo in these RCTs was chosen to mimic the side effects of the treatment group. In addition, an SR by Chou et al. (2016) demonstrated no benefit with TCAs for either function or pain. ( $\underline{113}$ ) However, older studies have shown that TCAs as a class provide improvement in pain intensity (moderate effect size of 0.43), but were inconclusive in regards to function, QoL, or healthcare utilization. ( $\underline{177}$ ,  $\underline{178}$ )

Providers should use caution when prescribing TCAs to patients with cardiovascular disease (CVD) or a family history of sudden death. A baseline electrocardiogram (ECG) is indicated in patients who are aged >50 years or with significant cardiacrisk factors. (179) The anticholinergic burden should also be considered when used in patients aged >65 years, and considerations for the use of secondary amines such as nortriptyline or desipramine may be warranted due to decreased anticholinergic burden. When utilizing TCAs, some subpopulations may be at greater risk of sedation and falls. There is also a risk of serotonin syndrome, particularly when combining with other medications (e.g., antidepressants). All antidepressants

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P Recommendations for "patients with low back pain" encompass patient populations with acute, subacute, or chronic LBP with or without neurological symptoms.

carry the black box warning of increased risk of suicidality in children, adolescents, and young adults when taking antidepressants for MDD or other psychiatric disorders. (180)

The Work Group systematically reviewed evidence related to this recommendation. (175, 176) Although there was no recommendation on TCAs in the 2017 VA/DoD LBP CPG, the Work Group considered the evidence put forth in the narrative of Recommendation 22 of that CPG. (113, 177, 178) Therefore, this is a *Reviewed, New-added* recommendation. The Work Group's confidence in the quality of the evidence was very low. The body of evidence had some limitations including small sample size and concerns regarding attrition. (175, 176) The benefits of TCAs on pain and function were balanced with the potential harms including side effects such as dry mouth, dry eyes, sedation, dizziness, blurred vision, and CV risks in certain patients. Patient values and preferences varied somewhat because some patients prefer medications, and TCAs may be used for other comorbidities (e.g., insomnia, headache). Additionally, some patients may be hesitant to take a medication classified as an antidepressant due to stigma surrounding mental health. Thus, the Work Group decided upon a *Neither for nor against* recommendation.

# **Recommendation**

22. For patients with low back pain, there is insufficient evidence to recommend for or against topical preparations.<sup>q</sup>

(Neither for nor against | Reviewed, Amended)

# **Discussion**

Similar to the 2017 VA/DoD LBP CPG, no studies on the effect of topical preparations met inclusion criteria for the 2022 VA/DoD LBP CPG systematic evidence review. However, the Work Group decided the subject still warranted a recommendation because topical preparations (e.g., capsaicin creams, diclofenacgel, lidocaine patches) are widely used. Moreover, the use of these agents generates frequent questions for PCPs.

These medications were addressed in a KQ for the systematic evidence review of this CPG. Therefore, although no new evidence was identified, this is a *Reviewed, Amended* recommendation. As there was no evidence on this topic, the Work Group could not determine the balance of benefits and harms. Patient values and preferences were somewhat varied because many patients see topicals as less risky and less harmful than oral medications and prefer non-invasive treatment options. Providers also value these medications as having less risk for AEs and as being more acceptable by patients. For this reason, the Work Group decided upon a *Neither for nor against* recommendation.

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<sup>&</sup>lt;sup>q</sup> Recommendations for "patients with low back pain" encompass patient populations with acute, subacute, or chronic LBP with or without neurological symptoms.

# **Recommendation**

23. For patients with acute low back pain, there is insufficient evidence to recommend for or against a non-benzodiazepine muscle relaxant for short-term use.

(Neither for nor against | Reviewed, New-replaced)

24. For patients with chronic low back pain, we suggest against offering a non-benzodiazepine muscle relaxant.

(Weak against | Reviewed, Not changed)

# **Discussion**

The systematic evidence review did not identify new studies for use of muscle relaxants to treat LBP; therefore, the Work Group reviewed three studies from the 2017 VA/DoD LBP CPG. One RCT demonstrated moderate level evidence that the addition of cyclobenzaprine to naproxen for patients with acute LBP in an ED setting did not improve functional outcomes or pain at one week follow-up. (181) In one SR, muscle relaxants showed some benefit for short-term pain relief (2 – 7 days). (113) This SR contained 22 studies that included muscle relaxants that are both available within the U.S. (tizanidine, cyclobenzaprine, orphenadrine, chlorzoxazone, carisoprodol, baclofen, dantrolene), but also included muscle relaxers that are not available for use within the U.S. (pridinol and tolperisone). (113) The critical outcomes, most notably pain, were not rated for this SR as our search criteria excluded outcomes with <3 months of follow-up data. (113)

For another SR, there were seven muscle relaxants included in the 15 selected trials, some available in the U.S. (carisoprodol, tizanidine, cyclobenzaprine) and some unavailable in the U.S. (eperisone, thiocolchicoside, pridinol, flupirtine). (182) The agents that demonstrated statistical benefit for pain were unavailable in the U.S. (eperisone and thicolchicoside). Carisoprodol also demonstrated pain relief in the short-term, but the Work Group does not support routine use of this agent. (182) Harms/burdens slightly outweigh benefits of skeletal muscle relaxants as they were associated with an increased risk of central nervous system (CNS) events, primarily sedation. (113, 181, 182) Trials that included carisoprodol were associated with an increased risk of sedation and dizziness versus placebo. (113)

When considering long-term use, there is no evidence to suggest benefit for the use of skeletal muscle relaxants for chronic LBP. One SR included a low quality study demonstrating there was no benefit of skeletal muscle relaxants when compared to placebo in patients with chronic LBP; (182) another SR also showed no benefit. (113)

There is some variability in patient preferences regarding use of muscle relaxants for acute and chronic LBP. Some patients may have concerns regarding the sedative properties of muscle relaxants interfering with their occupation. Many patients dislike the overall sedative properties of muscle relaxants, but some patients may appreciate the sedative properties if their sleep is disrupted due to LBP. The use of muscle relaxants may be of greater concern in the elderly population as sedative effects may be more burdensome, including the increased risk of falls. Furthermore, muscle relaxants can interact with other medications and potentially increase the risk of CNS depression and sedation. The Work Group does not support the use of carisoprodol for acute or chronic LBP due to its adverse effect profile, including risk of dependence. Carisoprodol is metabolized to an agent that binds to the barbiturate receptor and is

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classified as a Schedule IV controlled substance by the U.S. Drug Enforcement Agency. Also, because of its non-formulary status, carisoprodol may require additional effort to obtain and may not be as readily available within the VA.

For Recommendation 23, the Work Group considered the evidence put forth in the 2017 VA/DoD LBP CPG (113, 181, 182) because no studies on the effect of muscle relaxants met inclusion criteria for the 2022 VA/DoD LBP CPG systematic evidence review. Therefore, this is a *Reviewed, New-replaced* recommendation. The Work Group's confidence in the quality of evidence was low. The body of evidence had some limitations, including inadequate reporting of randomization and allocation concealment methods. (113) Low quality trials did not report attrition, had unbalanced groups at baseline, and/or did not conduct ITT analyses. (113) The RCT evaluated did not evaluate the adequacy of patient blinding and results may only be generalized to similar EDs serving a similar patient population. (181) There was also potential publication bias identified. (182) The reviewed studies were of moderate to low quality. In general, the harms/burdens of muscle relaxants were thought to slightly outweigh the benefits as the only benefit with muscle relaxants available in the U.S. was seen with carisoprodol, which has significant potential harms. It was difficult to determine which specific agents, available in the U.S., showed pain relief in the short-term as the evidence available is sparse. Patient values and preferences were somewhat varied as some patients may be less accepting of muscle relaxants or may dislike the sedative effect. Thus, the Work Group decided upon a *Neither for nor against* recommendation.

For Recommendation 24, the Work Group considered the evidence put forth in the 2017 VA/DoD LBP CPG (113, 181, 182) because no studies on the effect of muscle relaxants met inclusion criteria for the 2022 VA/DoD LBP CPG systematic evidence review. Therefore, this is a *Reviewed*, *Not changed* recommendation. The Work Group's confidence in the quality of the evidence was very low. The body of evidence had some limitations including inadequate reporting of randomization and allocation concealment methods. (113) Low quality trials did not report attrition, had unbalanced groups at baseline, and/or did not conduct ITT analyses. (113) The RCT evaluated did not evaluate the adequacy of patient blinding and results may only be generalized to similar EDs serving a similar patient population. (181) There was also potential publication bias identified. (182) The reviewed studies were of moderate to low quality. The harms and side effects associated with the use of muscle relaxants for chronic LBP outweigh the potential benefits, as there was no evidence of benefit in the literature reviewed. Patient values and preferences were somewhat varied as some patients may be less accepting of muscle relaxants or may dislike the sedative effect. Thus, the Work Group decided upon a *Weak against* recommendation.

# **Recommendation**

25. For patients with low back pain, we suggest against acetaminophen. (Weak against | Reviewed, New-replaced)

# **Discussion**

Although the effect of acetaminophen was covered in the 2022 VA/DoD LBP CPG systematic evidence review, no studies on this topic met inclusion criteria. Therefore, the Work Group considered the evidence

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Recommendations for "patients with low back pain" encompass patient populations with acute, subacute, or chronic LBP with or without neurological symptoms.

included in the 2017 VA/DoD LBP CPG and consolidated two recommendations (on acute and chronic LBP) to form this recommendation.

A large SR (n=1,825) found there was no difference between acetaminophen and placebo in treating acute LBP for the outcomes of pain, disability, QoL, or function through 12 weeks. (183) The same SR found no effect of acetaminophen on immediate pain reduction for an acute exacerbation of chronic LBP. In a second SR, the evidence suggested that acetaminophen was no more effective than placebo in treating acute LBP for the outcomes of pain or function through three weeks. (113) In addition, for chronic LBP, this SR found there was insufficient evidence to determine the effects of acetaminophen versus NSAIDs in one trial and versus other interventions in four trials.

Over half of the 2,000 annual cases of acute liver failure in the U.S. are due to intentional and unintentional acetaminophen toxicity. (184) In addition, acetaminophen is the most frequent cause of acute liver injury, with associated healthcare costs and morbidity. (184) Other considerations include ease of accessibility, as acetaminophen is inexpensive and available at a relatively low cost to the patient and the system. It is also readily accessible, both OTC and on formulary. Unfortunately, it is easily overused without proper education, thus risks and adverse effects may not be well understood by the public. This has led to some variation in values and preferences. Some patients may think that acetaminophen is innocuous and be unaware of the adverse effects of taking too much. In addition, elderly individuals and patients with hepatic insufficiency are subgroups that may be at the most risk for harm. As no benefits were shown in the evidence, the Work Group suggested against the use of acetaminophen; the risk of harm in taking acetaminophen predominates other considerations. Other options, such as NSAIDs (see Recommendation 19), can be offered to the patient based on the benefits outweighing the harms.

The Work Group considered the assessment of the evidence put forth in the 2017 VA/DoD LBP CPG. (113, 183) Therefore, this is a *Reviewed, New-replaced* recommendation. The Work Group's confidence in the quality of the evidence was low. The potential harms of taking acetaminophen slightly outweighed the benefits, which were not demonstrated in the evidence base. Patient values and preferences were somewhat varied because some patients may prefer medications, and some are unaware of the side effects of taking too much. Thus, the Work Group decided upon a *Weak against* recommendation.

# **Recommendation**

26. For patients with low back pain, we suggest against monoclonal antibodies.<sup>s</sup> (Weak against | Reviewed, New-added)

# **Discussion**

The utilization and clinical potential of monoclonal antibodies (mAb) for diverse disease processes and illnesses has markedly increased recently. The systematic evidence review found only two RCTs investigating the effectiveness of anti-nerve growth factors fasinumab and tanezumab. At the time of this review, these products were still investigational; neither of them have received final FDA approval in the U.S.

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s Recommendations for "patients with low back pain" encompass patient populations with acute, subacute, or chronic LBP with or without neurological symptoms.

In the RCT by Dakin et al. (2020), fasinumab, with both IV and subcutaneous (SC) delivery methods and two different doses (6 mg and 9 mg) at varying intervals (dosed every 4 or 8 weeks), was compared against placebo. (185) Even though there were some trends toward improvement in functional status and pain severity, many study arms showed no significant difference in effect. More significantly, the interpretation and applicability of this study is confounded by an FDA safety intervention. Due to an adverse joint safety event (JSE) in a patient with co-existing OA, the study was placed on an FDA hold and then terminated early. This led to many patients receiving less than the planned doses (only 35 – 56% of patients received the complete planned dosage). Serious AEs were reviewed at greater than 16 weeks, and in all groups receiving fasinumab some participants developed rapidly progressive osteoarthritis (RPOA). Additionally, a higher number of RPOA cases were reported in the higher dosage group.

In the RCT by Markman et al. (2020),  $(\underline{186})$  tanezumab dosed at 5 mg or 10 mg subcutaneously every eight weeks was compared to placebo or active control (tramadol 100 mg -300 mg). In the critical outcome of pain severity as determined by LBPI, the 5 mg dosage did not statistically differ from the placebo or control. In the 10 mg arm, there was no difference versus control. However, the 10 mg dosage showed a statistically significant difference versus placebo: LBPI: -0.40 (CI: -0.76 to -0.04); on a scale of 1-10; which was considered not clinically meaningful. Although neither dosage of tanezumab met the primary endpoint for statistically and clinically significant improvement, the authors did assess secondary outcomes. Using a LBPI improvement of >30% both dosages demonstrated significant improvement in all comparisons. However, a conclusion of superiority could not be made using only this secondary endpoint. There was an improvement in functional status (as measured by the RMDQ) that reached statistical significance for both 5 mg and 10 mg tanezumab versus placebo and active control at 16 weeks follow-up.

In the evaluation of serious and severe AEs at 16 weeks follow-up, both mAb dosages resulted in fewer AEs than the active control, but an equal or greater number when compared to placebo. (186)

Patients achieving >30% improvement in LBPI, or >15% improvement from baseline in weeks 1-15, continued in a longitudinal follow-up focused on AEs. ( $\frac{186}{1}$ ) In this phase, the patients originally assigned placebo were placed into one of the tanezumab groups (5 mg or 10 mg every eight weeks), and the control was tramadol. At 24 and 56 weeks, the authors reported no treatment-related mortality. Serious and severe AEs were lower in the 5 mg group versus control and slightly higher in the 10 mg treatment group.

More significantly, overall JSEs were reported through 80 weeks follow-up. The authors determined 30 patients had joint AEs that were assessed in depth. The most concerning event was RPOA, which occurred more frequently in tanezumab 5 mg (n=5) than active control (n=1) or placebo (n=0). In addition, the number of RPOA cases (n=16) was higher in the tanezumab 10 mg group, suggesting a dose related effect.

The Work Group systematically reviewed evidence related to this recommendation. (185, 186) Therefore, this is a *Reviewed, New-added* recommendation. The Work Group's confidence in the quality of the evidence was very low. The harms and burdens outweighed the benefit, with serious safety concerns due to adverse JSEs and RPOA in both mAb products. In addition, the interruption of one trial due to AEs and the decision by the FDA to not approve these products would negatively affect provider and patient acceptability. The Work Group also expects the status as a new/experimental drug, and IV or SC administration will lead to decreased acceptability by patients. Patient values and preferences were

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somewhat varied because some patients may not prefer newer medications with unknown side effects; and there is an opportunity cost associated with repeated visits for administration. Thus, the Work Group decided upon a *Weak against* recommendation.

#### **Recommendation**

27. For patients with chronic low back pain, we suggest against opioids. For patients who are already using long-term opioids, see the VA/DoD CPG for the Use of Opioids in the Management of Chronic Paint.<sup>t</sup>

(Weak against | Reviewed, New-replaced)

#### Discussion

While the literature base suggests potential benefit in some patients, the *Weak against* recommendation for opioids is based on the significant risks associated with use of opioids as determined in the VA/DoD CPG for the Use of Opioids in the Management of Chronic Pain. None of the studies from the current LBP CPG systematic evidence review provided data to allow making conclusions on the long-term (more than six months) efficacy and safety of opioids for chronic LBP.

The evidence related to use of opioids in chronic LBP includes one SR and meta-analysis by Petzke et al. (2020) that consisted of 21 RCTs for chronic LBP, with only three RCTs published since the 2017 VA/DoD LBP CPG and the majority rated fair quality. (187) Thus, the majority of evidence for consideration by the Work Group was already included in the 2017 VA/DoD LBP CPG. The current systematic evidence review also included two fair quality individual RCTs. (186, 188)

The RCTs included in Petzke et al. (2020) examined at least four weeks of treatment with opioids for chronic LBP. (187) Opioids in this SR included buprenorphine (transdermal and buccal), hydrocodone, hydromorphone, morphine, oxycodone, oxycodone/naloxone, oxycodone/naltrexone, oxymorphone, tapentadol, and tramadol. Overall, for a 4-15 week follow-up period, most of the evidence comparing opioids with placebo for chronic LBP favored opioids. For the critical outcome of functional status, moderate quality evidence from this SR suggests patients in the opioids group experienced a greater reduction in disability compared with those in the placebo group at 4-15 weeks follow-up for all meta-analyses performed. (187) The authors considered the benefit of opioids in the reduction of disability clinically meaningful in comparison to placebo. For the critical outcome of pain severity, moderate to low quality evidence from this SR suggests that pain improved at follow-up for patients receiving opioids compared with those receiving placebo for all pain measures:  $\geq$ 50% pain relief,  $\geq$ 30% pain relief, mean pain intensity, and patient global impression questionnaire.

The two individual RCTs provide moderate to low quality evidence demonstrating no difference between opioids and placebo for pain or function. Low quality evidence from one RCT comparing tramadol with placebo in a chronic LBP treatment refractory population reported that improvement assessed using the RMDQ did not differ between groups at any time point during weekly assessments up to 16 weeks follow-up, and pain intensity was slightly reduced only at weeks one and eight. (186) Evidence from one RCT suggests that patients receiving extended-release oxycodone and sequestered naltrexone did not differ

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<sup>\*</sup> See the VA/DoD Clinical Practice Guideline for the Use of Opioids in the Management of Chronic Pain. Available at: https://www.healthquality.va.gov/.

from the placebo group at 12 weeks follow-up regarding functional impairment, as assessed by the Work Productivity and Activity Impairment (WPAI) Questionnaire for percentage of work time missed, impairment while working, overall work impairment, and activity impairment. (188) The quality concerns were attrition >20% in one RCT (186) and study design in the other RCT, (188) with an uncontrolled open-label titration period resulting in a study population enriched with treatment responders.

The evidence base also included two SRs already considered in the 2017 VA/DoD LBP CPG that showed small additional analgesic effects with opioids beyond those seen with placebo for acute or chronic LBP (moderate quality evidence). ( $\frac{113}{113}$ ,  $\frac{189}{113}$ ) In the meta-analysis by Abdel et al. (2016), the MD between single-ingredient opioids and placebo in pain intensity was -8.1 on a 0-100 VAS. ( $\frac{189}{113}$ ) In another SR, the standardized MD between strong opioids (e.g., hydromorphone, morphine, oxycodone, oxycodone/naltrexone combination, oxymorphone, and tapentadol) and placebo was -0.43 (seven trials), equivalent to an MD of about one point on a 0-10 NRS. ( $\frac{113}{113}$ ) Neither study reported the percentage of patients who achieved clinically important ( $\geq 30\%$ ) improvements from baseline in pain intensity.

According to a meta-analysis of three RCTs, opioids produced no clinically important improvements in function relative to placebo at 30 to 91 days; however, results were inconclusive with a wide CI. ( $\underline{189}$ ) In an SR, short-term therapy (less than six months) with opioids resulted in small, clinically unimportant additional improvements in function over placebo. ( $\underline{113}$ ) The standardized MD relative to placebo was -0.26 (four trials), representing a difference of about one point on a 24-point RMDQ scale. 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.

Regarding AEs, low quality evidence from one SR indicates that opioid and placebo groups did not differ in serious AEs or mortality. (187) One RCT reported an inconclusive result for serious and severe AEs that were similar in the tramadol and placebo group. (186) The meta-analysis by Abdel et al. (2016) showed that the median incidence of AEs was 68.9% for opioid groups and 49.1% for placebo groups, with a RR of 1.3 (eight trials). In four of the eight trials, 50% of study patients discontinued treatment because of AEs or lack of efficacy. Thus, the small differential benefits of short-term opioid use were counterbalanced by increases in risks of adverse effects seen with short-term opioid use.

In many of the RCTs in the SR by Petzke et al. (2020), there were concerns around randomization and allocation procedures, high attrition, and lack of blinding. (187) The authors themselves identified limitations due to industry sponsoring and publication bias. They note that these were research studies, with most studies excluding patients with clinically relevant somatic or psychiatric diseases, in particular, patients with current or previous substance abuse. None of these studies were in the primary care setting, and there was a lack of diversity, as the majority of the participants were middle-aged white women. They also noted that sleep problems, physical dependence, abuse, and addiction of prescribed opioids were only analyzed in some studies.

Of major concern is that these studies do not allow making conclusions on the long-term (more than six months) efficacy and safety of opioids for chronic LBP. Petzke et al. (2020) noted the limited data for longer than 12 weeks, and the weak finding in the subgroup analysis indicated increased dropout rates for studies with a duration of more than 12 weeks. (187)

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The trials included in the SRs did not assess the risks of long-term opioid use. Opioid risks and risk assessment for chronic non-cancer pain are discussed in more detail in the VA/DoD CPG for the Use of Opioids in the Management of Chronic Pain that documents serious risks with opioid therapy, in particular opioid use disorder (OUD) and overdose, that increase with longer duration and with higher dosage of, opioid therapy but may occur even at low opioid dosage and short-term use.<sup>u</sup>

No clinical trials identified by the systematic evidence review evaluated time-limited (less than seven days) opioid therapy, as such studies were not part of the evidence base. Therefore, the Work Group decided to not make a recommendation regarding the short-termuse of opioids for acute LBP or acute exacerbation of chronic LBP.

Despite moderate to low quality evidence of benefit of opioids compared with placebo for pain and function at 4 – 15 weeks follow-up in the SR by Petzke et al. (2020), and inconclusive evidence for serious AEs and mortality, the Work Group concluded that the potential harms of opioids outweigh the potential benefits in patients with LBP. (187) The available evidence from this SR was only 15 weeks with low quality evidence demonstrating no serious AE. Assessment of abuse and addiction was incomplete. Based on what is known for chronic non-cancer pain in general (not specific to LBP), the small benefit of short-term opioid use 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 risk of addiction during opioid use, which may start with the first dose administered, increases substantially with duration and dosage of opioid therapy, and needs to be taken into consideration and weighed against the actual therapeutic benefits in individual cases. Thus, the Work Group issued a weak recommendation against the use of opioids for chronic LBP.

While not included in the evidence base of this CPG due to the study design (e.g., open-label RCT, no crossover design, allowance for use of tramadol in the non-opioid group) and a mixed treatment population consisting of patients with moderate pain from hip and knee OA in addition to LBP, the study by Krebs et al. (2018) is the only opioids study published that extends to 12 months. (190) Treatment with opioids was not superior to treatment with non-opioid medications for improving pain-related function over 12 months (overall p=0.58). Pain intensity was slightly, but significantly better in the non-opioid group (overall p=.03); and adverse medication-related symptoms were more common in the opioid group over 12 months (overall p=.03).

Patients' values, preferences, and treatment goals regarding opioids 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. Additionally, some subpopulations may be at greater risk of sedation and falls with the use of opioids. The patient focus group participants indicated a desire for education about pain medications, particularly opioids.

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 (SUD), social history, age, frailty, opioid

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See the VA/DoD Clinical Practice Guideline for the Use of Opioids in the Management of Chronic Pain. Available at: https://www.healthquality.va.gov/.

dose, formulation, route of administration, drug interactions, and other factors may influence decisions regarding whether or not to try a time-limited course. For LBP refractory to NSAIDs, or for patients with contraindication to NSAIDs (such as due to anticoagulation), 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 therapy, with no clear evidence of long-term benefit.

The findings from one SR comparing opioids with placebo, identified in the current systematic evidence review, are in line with the evidence from the 2017 VA/DoD LBP CPG. Moderate to low quality evidence shows a benefit of opioids compared with placebo for pain and function at 4-15 weeks follow-up, in patients with chronic LBP, and there is inconclusive evidence for serious AEs and mortality.

The Work Group systematically reviewed evidence related to Recommendation 27 (186-188) and considered the assessment of the evidence put forth in the 2017 VA/DoD LBP CPG. (113, 189) Therefore, this is a *Reviewed, New, Replaced* recommendation. The Work Group's confidence in the quality of the evidence was low. The body of evidence had some limitations particularly in regards to the duration of treatment (no studies >6 months) and long-term follow-up, study population, and lack of assessment for substance abuse and addiction long-term. The concern about potentially catastrophic harm related to OUD and overdose deaths outweighed the benefits that appear small and likely short-term. Patient values and preferences were varied with some patients seeking opioids despite risks, and others avoiding them due to safety concerns. Thus, the Work Group decided upon a *Weak against* recommendation. No studies in the patient population with acute LBP met inclusion criteria, thus the Work Group deleted the specific recommendation for acute LBP from the 2017 VA/DoD LBP CPG (see 2017 Recommendation Categorization Table).

# **Recommendation**

28. For patients with low back pain, with or without radicular symptoms, we suggest against systemic corticosteroids (oral or intramuscular injection).

(Weak against | Not reviewed, Amended)

# **Discussion**

The use of systemic corticosteroids for the treatment of acute or chronic LBP with or without radiculopathy is not recommended. The evidence reviewed for systemic corticosteroids is the same as the previous 2017 CPG update, as there was no new evidence meeting our search criteria for the 2022 VA/DoD LBP CPG systematic evidence review. Moderate quality evidence from one SR and one RCT failed to demonstrate efficacy related to pain. (113, 191). Most of the trials included in the SR were of at least fair quality, all of which showed no significant improvements in pain or function in a variety of settings, with both single intramuscular boluses or oral tapers of varying doses and durations. The RCT did show a statistically significant improvement in disability for patients treated with a 15 day course of oral prednisone (five days each of 60 mg, 40 mg, 20 mg) versus placebo with acute radiculopathy due to a herniated lumbar disk, although the quality of this study was determined to be low. (191) The RCT also favored prednisone vs. placebo for improvement of the mental health component of an SF-36 but no difference was found for the physical component. (191) There is inconclusive evidence that corticosteroids decrease healthcare utilization. (113, 191)

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Moderate quality evidence from the RCT did demonstrate significantly more AEs in the prednisone group compared to placebo at three weeks follow-up, but AEs were minor and included insomnia, nervousness, and increased appetite. (191) The SR was inconclusive regarding AEs, but the included studies were of low to very low quality. (113) While providers and patients may wish to trial systemic corticosteroids for LBP or radiculopathy, the evidence suggests efficacy does not outweigh the potential risks.

There is some variability in patient preferences regarding use of systemic corticosteroids as some patients may seek alternative treatment options when other treatments fail. In addition, repeated use of systemic corticosteroids significantly increases the risk of side effects over time.

The Work Group considered the assessment of the evidence put forth in the 2017 VA/DoD LBP CPG. (113, 191) Therefore, this is a *Not reviewed, Amended* recommendation. The Work Group's confidence in the quality of the evidence was low. Despite moderate quality evidence showing corticosteroids don't benefit pain outcomes, which we acknowledge as critical, the overall quality of the evidence was low based on poor quality evidence for the other critical outcomes of QoL and function. The potential harms of systemic corticosteroids slightly outweighed the benefits. Some well-informed patients might choose treatment with a corticosteroid based on the possibility of improved QoL and function, but most would not, due to proven AEs. Thus, the Work Group decided upon a *Weak against* recommendation.

# **Recommendation**

29. For patients with low back pain, we recommend against benzodiazepines. (Strong against | Reviewed, Not changed)

# **Discussion**

The systematic evidence review included a single RCT for acute LBP, in addition to an SR from the 2017 VA/DoD LBP CPG. The RCT by Friedman et al. (2017) demonstrated, with moderate quality evidence in patients with acute non-radicular back pain, the lack of benefit from adding diazepam to naproxen, with no difference regarding the critical outcomes of pain severity and functional status, after one week and three months. ( $\frac{192}{2}$ ) Specifically, in the active treatment group, diazepam 5 mg tablets with 1-2 tablets every 12 hours as needed were added to naproxen 500 mg twice a day. The RMDQ score of 112 patients after one week was identical between groups. However, more patients reported moderate or severe LBP in the diazepam group (18 of 57 patients, 32%; 95% CI: 21% to 45%) than in the placebo group (12 of 55 patients, 22%; 95% CI: 13% to 35%). At three months follow-up, 6 of 50 patients on diazepam (12%) versus 5 of 53 patients receiving placebo (9%) reported moderate or severe LBP. AEs were reported by 12 of 57 patients in the diazepam group (21%) and 8 of 55 in the placebo group (15%).

The evidence in chronic LBP is less conclusive. A good quality SR by Chou et al. (2016) found inconclusive evidence between diazepam and placebo with respect to LBP improvement. ( $\underline{113}$ ) The SR identified one RCT (n=60) by Brotz et al. (2010) which reported efficacy data for patients randomized to receive placebo or diazepam two times 5 mg daily, followed by a taper. ( $\underline{193}$ ) Follow-up examinations were scheduled at six weeks and one year after discharge. The median duration of the stay in the hospital was shorter in the placebo arm (eight versus ten days, p=0.008), and the probability of pain reduction on the VAS by more

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than 50% was twice as high in placebo patients (12 of 29 patients for diazepam, 23 of 29 for placebo) (p=0.0015). Other outcome measures, though inconclusive, tended to favor placebo over diazepam including workdays lost, disability, and healthcare utilization.

The SR reported low quality evidence for CNS AEs such as somnolence, fatigue, and lightheadedness with benzodiazepines versus placebo. ( $\underline{113}$ ) In addition, the potential for abuse, addiction/dependence, overdose potentially resulting in death, respiratory depression, and sleep apnea do not justify their use. Some subpopulations are at greater risk of sedation and falls with use of benzodiazepines.

There is moderate quality evidence for acute LBP and low quality evidence for chronic LBP indicating that the harms/burden of benzodiazepine use outweigh the benefits. Some patients may prefer benzodiazepines, but the abuse potential should be taken into consideration. The adverse CNS effects (e.g., sedation, cognitive impact) may be even greater in patients also receiving other pain medication with similar side effects (polypharmacy). These associated risks are further compounded when benzodiazepines are combined with opioids, in particular, the risk for respiratory depression and overdose death (see the VA/DoD CPG for the Use of Opioids in the Management Chronic Pain). There are also subgroup considerations such as patients with chronic obstructive pulmonary disease at higher risk for respiratory depression or patients with comorbid SUD.

The Work Group systematically reviewed evidence related to this recommendation (192) and considered the assessment of the evidence put forth in the 2017 VA/DoD LBP CPG. (113) Therefore, this is a *Reviewed, Not changed* recommendation. The Work Group's confidence in the quality of the evidence was moderate for acute LBP and low for chronic LBP. The body of evidence had some limitations including small sample size (192) and inconclusive findings. (113) The harms of benzodiazepines (potentially severe) outweighed the benefits (no benefit on pain severity or functional outcome). Patient values and preferences were somewhat varied because some patients may subjectively prefer benzodiazepines, with the potential for abuse noted by the Work Group. Thus, the Work Group decided upon a *Strong against* recommendation.

# E. Dietary Supplements

# **Recommendation**

30. For patients with low back pain, there is insufficient evidence to recommend for or against any specific diet or nutritional, herbal, or homeopathic supplements (e.g., anti-inflammatory diet, turmeric, vitamin D), cannabis, or cannabinoids.<sup>x</sup>

(Neither for nor against | Reviewed, New-replaced)

# **Discussion**

The body of evidence for using any specific diet or nutritional, herbal, or homeopathic supplement in the treatment or management of LBP is very limited. The systematic evidence review found no study matching the search criteria for any homeopathic preparations, nutraceuticals, or specific diets. Regarding supplements, the systematic evidence review found one SR of vitamin D; no evidence related to other

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w See the VA/DoD Clinical Practice Guideline for the Use of Opioids in the Management of Chronic Pain. Available at: https://www.healthquality.va.gov/.

x Recommendations for "patients with low back pain" encompass patient populations with acute, subacute, or chronic LBP with or without neurological symptoms.

supplements or cannabis was identified. The SR by Zardo et al. (2018) included eight studies of poor methodological quality, with over half of the studies lacking both ITT analysis and blinding of assessors. (194) The included studies failed to demonstrate a difference in pain reduction or harms between vitamin D and any intervention, including placebo.

There is large variability in patient preferences. Some patients prefer to take medication they consider to be more natural or may be interested in specific supplements (e.g., turmeric, cannabinoids), while others do not have a preference. Despite no serum level or dose of vitamin D showing improvement in LBP, the monitoring of vitamin D blood levels is considered a barrier to treatment.

The Work Group systematically reviewed evidence related to this recommendation (194) and considered the assessment of the evidence put forth in the 2017 VA/DoD LBP CPG. (195) Therefore, this is a *Reviewed, New-replaced* recommendation. Given the dearth of data with significant limitations, the Work Group's confidence in the quality of the evidence was very low. Although there was no benefit found over any other treatment, there was also no harm found over any other treatment, including placebo. Patient values and preferences varied, as some patients may prefer specific supplements over others. Thus, the Work Group decided upon a *Neither for nor against* recommendation.

# F. Non-surgical Invasive Therapy

# **Recommendation**

31. For patients with chronic low back pain, we suggest lumbar medial branch and/or sacral lateral branch radiofrequency ablation.

(Weak for | Reviewed, New-replaced)

32. For patients with low back pain, there is insufficient evidence to recommend for or against sacroiliac joint injections.  $^{\text{y}}$ 

(Neither for nor against | Reviewed, New-added)

33. For patients with low back pain, we suggest against the injection of corticosteroids for intraarticular facet joint injections and therapeutic medial branch blocks with steroid.<sup>z</sup> (Weak against | Reviewed, New-replaced)

# **Discussion**

Moderate quality evidence suggests radiofrequency ablation (RFA) of the lumbar medial branches for facet pain or sacral lateral branches for sacroiliac joint pain improves pain at six (MD: -2.12; p<0.001), 12 (MD: -2.82; p=0.024), and 36 (MD: -3.70; p=0.003) months in patients with LBP. (196) The improvements seen in disability and QoL with radiofrequency neurotomy, while statistically significant, were small and determined not to be clinically meaningful. The harms of this intervention were not assessed in the included evidence. In contrast, the highest quality study on RFA in the 2017 VA/DoD LBP CPG found no

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Y Recommendations for "patients with low back pain" encompass patient populations with acute, subacute, or chronic LBP with or without neurological symptoms.

<sup>&</sup>lt;sup>2</sup> Recommendations for "patients with low back pain" encompass patient populations with acute, subacute, or chronic LBP with or without neurological symptoms.

between-group differences for pain versus a placebo comparator and a small but not clinically meaningful difference favoring RFA for function. (197)

Lumbar radiofrequency neurotomy is a procedure offered commonly in VA/DoD pain clinics. There is some variability in patient preferences regarding this treatment as some patients do not prefer invasive procedures. Additionally, some patients may not want to undergo a procedure that is ablating nerves. For patients in more remote or rural areas, access to specialty pain medicine providers is likely limited which would impact the availability of this intervention. For those patients where surgery is not an option for medical or anatomical reasons, this intervention would provide an alternative.

Lumbar medial branch/sacral lateral branch diagnostic injections as well as sacroiliacjoint diagnostic and therapeutic injections are utilized at many VA/DoD facilities for the treatment of LBP and/or in the identification of painful structures in the lumbar spine.

For sacroiliac joint injections, no evidence was retrieved based on the predetermined search criteria and time period for the 2017 or 2022 VA/DoD LBP CPG systematic evidence reviews. The Work Group therefore agreed on a *Neither for nor against* recommendation for sacroiliac joint injections.

The use of intra-articular facet joint injections is less common in pain clinics than in past years due to the lack of evidence for this procedure. However, considerations may be made for subgroups in whom RFA may not be as desirable. In comparison to the 2017 VA/DoD LBP CPG, no studies on these interventions met the search criteria for this CPG update. In the 2017 VA/DoD LBP CPG, evidence assessing the efficacy of facet joint injections (198, 199) and therapeutic medial branch block injections (199) were generally rated as low or very low quality. Facet injections or medial branch blocks using corticosteroids did not generally perform better than saline injections, local anesthetic injections or oral NSAIDs for pain, function, return to work, or QoL. The use of diagnostic medial or lateral branch blocks, which are injections of anesthetic for temporary (hours) blockade of these nerves, is considered standard of care for determining a patient's candidacy for lumbar or sacral radiofrequency neurotomy. This is different than therapeutic blocks which would include addition of corticosteroid to the injectate to provide medium or long-term (weeks to months) benefit; thus, the lack of evidence for therapeutic medial branch blocks in the 2017 VA/DoD LBP CPG does not impact the strength of the recommendation for radiofrequency ablation.

The Work Group systematically reviewed evidence related to Recommendation 31 (196) and considered the assessment of the evidence put forth in the 2017 VA/DoD LBP CPG. (197) Therefore, this is a *Reviewed, New-replaced* recommendation. The Work Group's confidence in the quality of the evidence regarding radiofrequency neurotomy of the lumbar medial branches or sacral lateral branches was moderate. The body of evidence had some limitations including exclusion of patients with uncontrolled depression or psychiatric disorders; evidence in these populations is potentially not generalizable to a chronic pain population. The benefits of improved pain and small impacts on disability and QoL for radiofrequency neurotomy of the lumbar medial or sacral lateral branches were balanced with the potential harms (e.g., post-radiofrequency neuritis, impact of denervation of paraspinal muscles) which were not assessed in the SR by Chen et al. (2019).(196) Patient values and preferences were somewhat varied regarding this treatment. Some patients do not wish to undergo invasive procedures or one that ablates nerves, while other patients may prefer a passive injection-based treatment that provides

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six-plus months of pain reduction over self-management treatments for LBP. Thus, the Work Group decided upon a *Weakfor* recommendation.

The Work Group systematically reviewed evidence related to Recommendation 32 as part of this CPG and as part of the 2017 VA/DoD LBP CPG; however, no studies related to sacroiliac joint injections met inclusion criteria. This is a *Reviewed*, *New-added* recommendation. As there was no evidence identified on the topic of sacroiliac joint injections, the Work Group could not determine the balance of benefits and harms. Patient values and preferences were somewhat varied as some patients may not want to receive injections or undergo an interventional procedure. Thus, the Work Group decided upon a *Neither for nor against* recommendation.

The Work Group systematically reviewed evidence related to Recommendation 33 as part of this CPG update; however, no studies on injection of corticosteroids for intra-articular facet joint injections and therapeutic medial branch blocks with steroid met inclusion criteria. The Work Group also considered the assessment of the evidence put forth in the 2017 VA/DoD LBP CPG. (198, 199) Therefore, this is a Reviewed, New-replaced recommendation. The Work Group's confidence in the quality of the evidence from the 2017 VA/DoD LBP CPG was very low. The body of evidence for intra-articular facet joint injections had some limitations and most findings were inconclusive or were not considered to be clinically meaningful. The benefits of using intra-articular facet joint injections were balanced with any potential harms, such as risks and complications associated with injections. Two small studies assessing therapeutic medial branch blocks were inconclusive for pain and function. (199) While there were no studies demonstrating serious AEs from therapeutic medial branch blocks, the Work Group felt the risks of an invasive procedure involving injection of steroids slightly outweighed the inconclusive effects on pain and function. Patient values and preferences were somewhat varied as some patients may not want to receive injections or undergo an interventional procedure. Thus, the Work Group decided upon a Weak against recommendation.

#### **Recommendation**

- 34. For patients with chronic low back pain, we suggest acupuncture. (Weak for | Reviewed, Amended)
- 35. For patients with acute low back pain, there is insufficient evidence to recommend for or against acupuncture.

(Neither for nor against | Reviewed, Amended)

# **Discussion**

Acupuncture appears to have a small benefit for the reduction of pain for those with chronic LBP in the intermediate-term (3-12 months).  $(\underline{200-202})$  The evidence from two SRs  $(\underline{200}, \underline{201})$  and one small RCT  $(\underline{202})$  favored acupuncture over sham for the critical outcome of pain intensity. The use of sham as a comparator for acupuncture studies complicates the evidence review due to the variety and types of sham comparator used. The effect size reported by Li et al. (2020) was very small (SMD: -0.17), and in Mu et al. (2020), the improvements were statistically significant but did not meet the threshold of clinical relevance as determined by the authors.  $(\underline{201})$  Qin et al. (2020) found results for acupuncture compared to sham for pain intensity were both statistically significant and clinically important at six months in a small RCT (n=80).

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Evidence from Chou et al. (2016) was inconclusive for the comparison of acupuncture to sham related to pain. ( $\underline{113}$ ) The comparison of acupuncture to usual care for pain intensity reported in the meta-analysis (n=1,060) by Li et al. (2020) ( $\underline{200}$ ) favored acupuncture with a moderate effect size (SMD:-0.51) in the intermediate-term (3 – 12 months) but no difference in the long-term (2 years) (n=162). Mu et al. (2020) also analyzed acupuncture compared to usual care for pain intensity and again described the improvements as not clinically relevant (MD: -12.30) despite statistical significance.( $\underline{201}$ )

Evidence surrounding the critical outcomes of disability and back-specific function was mixed for those with chronic LBP based on the data from two SRs and one small RCT. (200-202) Mu et al. (2020) favored acupuncture over sham with a very small effect size (SMD: -0.16) for back-specific function; however, there was no difference noted in pain-related disability. Li et al. (2020) reported no difference for function between acupuncture and the sham comparator. Qin et al. (2020) found that results for acupuncture compared to sham for disability were both statistically significant and clinically important (adjusted mean: -3.8; MCID: 2.25] at 6 months after treatment in a small RCT (n=80). (202) When compared to usual care, Mu et al. (2020) found a statistically significant difference favoring acupuncture with a small effect size (SMD: -0.44) for function. QoL measures were reported by Mu et al. (2020) as statistically significant favoring acupuncture compared to both sham (SMD: 0.21) and usual care (MD: 5.80) in the intermediate-term (4 – 12 months), although the change was not clinically important when compared to sham. (201)

AEs were reported by Mu et al. (2020) in both acupuncture compared to sham and acupuncture compared to usual care. They report that AEs were similar between acupuncture and sham groups (RR: 0.68) based on 4 studies (n=465).(201) In one small study (n=74) included in the review for acupuncture compared to usual care, there were three AEs reported in the acupuncture group and one in the usual care group (RR: 3.34), and all were mild and transient. (201) Qin et al. (2020) report eight participants (three in acupuncture group and five in sham group) experiencing AEs that were mild or moderate and did not require further intervention.

There was insufficient data from which to draw conclusions on the use of acupuncture for the treatment of acute LBP. Patients with acute LBP were included in one SR; (200) however, the data related to acute LBP were not separated in the results. One SR from the 2017 VA/DoD LBP CPG was also evaluated. (113) It included data on acute LBP with low quality evidence and mixed results related to the critical outcomes discussed above.

There is some variability in patient and provider preferences related to acupuncture, as some patients are not comfortable with needle-based treatment while others may prefer such non-pharmacologic provider-delivered treatments. Acupuncture is generally accepted as a safe intervention; however, the clinical relevance of the effects on pain severity may not outweigh the opportunity cost of attending appointments for some patients, given that the data related to function, disability and QoL were mixed. Considerations may be made for subgroups including those who are at risk for adverse outcomes from pharmacologic interventions. Access to qualified acupuncture providers may be a barrier especially in rural areas.

The Work Group systematically reviewed evidence related to Recommendation  $34 (\underline{200-202})$  and considered the assessment of the evidence put forth in the 2017 VA/DoD LBP CPG. ( $\underline{113}$ ) Therefore, this is a *Reviewed, Amended* recommendation. The Work Group's confidence in the quality of the evidence was

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low. The body of evidence had some limitations including risk of bias and imprecision. (113, 200-202) As the data related to the critical outcomes of function, disability, and QoL were mixed, the focus of this recommendation is on the critical outcome of pain severity. The benefits related to pain severity slightly outweighed the potential harm of this relatively safe intervention. Patient values and preferences varied somewhat because some patients may not prefer needle-based interventions such as acupuncture. Thus, the Work Group decided upon a *Weak for* recommendation.

The Work Group systematically reviewed evidence related to Recommendation 35 ( $\underline{200}$ ) and considered the assessment of the evidence put forth in the 2017 VA/DoD LBP CPG.( $\underline{113}$ ) Therefore, this is a *Reviewed*, *Amended* recommendation. The Work Group's confidence in the quality of the evidence was low. The body of evidence had some limitations including imprecision and inconclusive data,( $\underline{113}$ ) and risk of bias.( $\underline{200}$ ) The low risk of harm was balanced with opportunity cost and lack of evidence of efficacy for acute LBP. Patient values and preferences were somewhat varied because some patients may not prefer needle-based interventions or those based on Eastern medical foundations. Thus, the Work Group decided upon a *Neither for nor against* recommendation.

# **Recommendation**

36. For patients with low back pain, there is insufficient evidence to recommend for or against orthobiologics (e.g., platelet-rich plasma, stem cells). aa (Neither for nor against | Reviewed, New-added)

# **Discussion**

Evidence suggests injection of platelet-rich plasma (PRP) results in a statistically significant but not clinically meaningful improvement in pain in patients with LBP. The SR by Xuan et al. (2020) found treatment with PRP was associated with improvements in pain with only low confidence in the quality of evidence. (203) These findings may not be generalizable, as the included studies had varying anatomical targets, the pain score reduction was not a clinically meaningful reduction (MD: -1.47 on a 0-10 scale), and the sample size was small (n<100).

A single RCT by Amirdelfan et al. (2021) assessing a total of 100 patients demonstrated stem cell injections were favored over control with improvements in pain, disability, and QoL, but it is unclear if the differences are statistically significant. (204) This RCT did not report p-values at 12- or 24-month follow-up.

There were no other studies identified in the systematic evidence review for either of these interventions to demonstrate the reproducibility or generalizability of these interventions. Ortho-biologic injections were not assessed in the 2017 VA/DoD LBP CPG; therefore, no prior studies were assessed as part of this evidence review.

There is some variability in patient preferences regarding this treatment. While some patients seek out emerging interventional therapies, ortho-biologic injections for LBP are infrequently requested. As is the case with invasive procedures, some patients who are needle-averse will not pursue or accept this treatment. Additionally, patients may be hesitant to receive donor stem cells which further increases the

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aa Recommendations for "patients with low back pain" encompass patient populations with acute, subacute, or chronic LBP with or without neurological symptoms.

variability of patient preference for stem cell injections. There are equity and feasibility issues with orthobiologic injections, as the few providers with specialized training needed for both PRP and stem cell injections and the infrastructure and cost required to perform them result in limited access.

The Work Group systematically reviewed evidence related to this recommendation. (203, 204) Therefore, this is a *Reviewed, New-added* recommendation. The Work Group's confidence in the quality of the evidence was low. The body of evidence had some limitations including small sample size for both interventions, short-term follow-up and variability in the anatomic targets for the studies assessing platelet-rich plasma injections, and lack of a larger evidence base demonstrating reproducibility of the findings. (203, 204) The Work Group determined the potential harms of injecting PRP or stem cells, such as infection or disruption of the intervertebral disc, slightly outweigh the potential benefits of pain reduction (for both PRP and stem cells) and small benefits seen for pain, disability, and QoL (for stem cells). Patient values and preferences were somewhat varied because these interventions are relatively new and not routinely requested by most patients; however, some patients seek out emerging therapies for pain. Additionally, some patients are needle averse. Thus, the Work Group decided upon a *Neither for nor against* recommendation.

# **Recommendation**

37. For patients with low back pain, with radicular symptoms, there is insufficient evidence to recommend for or against epidural steroid injections.

(Neither for nor against | Reviewed, New-replaced)

# **Discussion**

There is mixed evidence regarding the effect of epidural steroid injections (ESI) on the improvement of pain at three months. This includes one SR (n=490) by Yang et al. (2020) which compared ESI to conservative treatment in patients with lumbosacral radicular pain secondary to lumbar disc herniation or spinal stenosis and found moderate quality evidence for a small, statistically significant improvement in pain at three months. (205) The SR found no difference for functional improvement at three months between ESI and conservative treatment. Yang et al. (2020) represents the only evidence captured for the 2022 VA/DoD LBP CPG assessing ESI in comparison to non-injection treatments.

The findings of short duration reduction in pain but not function noted in the SR from Yang et al. (2020) (205) are consistent with the findings from Chou et al. (2015). (199) The 2015 Chou et al. SR identified moderate quality evidence that ESIs improved pain relief compared to placebo in the immediate term (defined as 5 – 14 days). The size of the pain reduction in the Chou et al. (2015) SR (approximately a 0.75 point reduction on a 10 point scale) was small and not felt to be clinically meaningful. The systematic evidence review did not evaluate outcomes shorterthan three months, so a direct comparison of outcomes less than two weeks is not available.

In contrast to Yang et al. (2020), (205) another SR (n=351) from Manchikanti et al. (2020) (206) assessing the effects of epidural steroids plus bupivacaine in comparison to bupivacaine alone did not find any difference in pain or function between the two groups at three months. This SR assessed the intervention in patients with LBP or radicular pain due to disc herniation or foraminal stenosis.

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The evidence base assessing ESI outcomes at six and 12 months included two SRs, including the SR from Yang et al. (2020), which found a statistically significant and clinically relevant improvement in pain when ESI was compared to conservative treatment. (205) This is in contrast to the SR (n=2,470) from Oliveira et al. (2020) which compared epidural steroids to placebo injection in patients with lumbos acral radicular pain, but excluded central spinal canal stenosis, and found no improvement in back pain or disability at three to 12 months or greater than 12 months. (207)

A single RCT from Abedini et al. (2018) compared epidural steroids to injection with bupivacaine or saline in patients with LBP due to lumbar disc herniation. ( $\frac{208}{208}$ ) This study favored epidural steroids for function but not pain at three months. The small sample size (n=28 in each arm) was not sufficient to impact the findings from the multiple SRs.

The quality of data assessing AEs and harms in the reviewed studies was insufficient to draw any conclusions. In addition, there was a lack of studies assessing the efficacy of ESI in spinal stenosis alone or in LBP alone to draw separate conclusions.

ESIs are an option at many VA/DoD facilities for treating LBP, including lumbar radiculopathy, and are most commonly provided in pain clinics or radiology departments. Unlike other interventional procedures, ESIs are quite common; it is unlikely there would be significant access or equity issues for this particular intervention. As with any invasive procedure, there is some variability in patient preferences. Some patients prefer to avoid needle-based interventions while others would prefer a passive treatment (e.g., injection) over more time-intensive self-care. There are groups of responders who realize short- or intermediate-term benefit for pain and/or function, and request repeat injections as part of their long-term pain management strategy. Additionally, this intervention may provide short-term benefit for patients not eligible for surgery and may choose to undergo repeat injections.

The Work Group systematically reviewed evidence related to this recommendation (205-209) and considered the assessment of the evidence put forth in the 2017 VA/DoD LBP CPG. (199) Therefore, this is a Reviewed, New-replaced recommendation. The Work Group's confidence in the quality of the evidence was low. The body of evidence had some limitations including being limited to only one SR (205) comparing epidural steroids to non-injection-based treatment, whereas the other studies compared injections of steroid to injection of anesthetic or saline into the epidural space, which are not inert substances. Additionally, some studies assessed outcomes at or beyond 6 months, which is inconsistent with the clinical utilization and expected duration of benefit of ESIs for short-term improvements in pain and function, typically on the order of 8 – 12 weeks. Because of this, the Work Group felt that the 2017 recommendation regarding epidurals for the long-term reduction in pain was not relevant and should be deleted. The potential harms of ESIs were not systematically reviewed in the included studies. However, ESIs are an invasive procedure, and therefore, the Work Group determined that the potential harms from an invasive procedure slightly outweigh the inconsistent reduction of pain at three months. Patient values and preferences vary because some patients prefer to avoid needle-based interventions while others would prefer a passive treatment (e.g., injection) over more time-intensive self-care. Thus, the Work Group decided upon a Neither for nor against recommendation.

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# **Recommendation**

38. For patients with low back pain, we suggest against spinal cord stimulation. bb (Weak against | Reviewed, New-added)

# **Discussion**

Evidence from a single RCT (n=218) suggests spinal cord stimulation (SCS) results in statistically significant but not clinically meaningful improvements in the outcomes of pain, leg pain, and health-related QoL in patients with predominant LBP after spinal surgery. (210) No other studies met the search criteria for this evidence review, and the 2017 VA/DoD LBP CPG did not evaluate the effectiveness of SCS.

There is likely significant variability regarding patients choosing to pursue a surgical procedure that involves undergoing a multi-day trial with implanted leads and potentially undergoing surgery to implant a device if the trial lead implantation is deemed successful. This variability is further impacted by the subset of patients who have already undergone spinal surgery with pain that continues to persist. Within this subset of post-surgical patients, some are hesitant for any intervention that involves surgery while other patients are willing to pursue invasive treatments with the hope of pain reduction.

The Work Group systematically reviewed evidence related to this recommendation. (210) Therefore, this is a *Reviewed, New-added* recommendation. The Work Group's confidence in the quality of the evidence was low. The body of evidence had limitations including being limited to a single RCT with a small sample size with intermediate-term follow-up of six months and outcomes for pain, leg pain, and QoL, which were not clinically meaningful. (210) The harms of SCS, such as serious AEs were not assessed in the included study. Despite the lack of specific outcomes for harms, the Work Group determined that the potential harms and burdens of the two-part surgical procedure (trial followed by implant) outweighed the statistically significant, but not clinically meaningful, medium-term (not beyond six months assessed in the included study) improvements in the outcomes of pain, leg pain, and health-related QoL seen in the RCT. (210) Values and preferences were varied because some patients would prefer to avoid further surgical procedures or a multi-step invasive procedure such as SCS, while other patients and providers may consider this treatment in those patients who have failed less invasive evidence-based treatments or are not candidates for spinal surgery. Thus, the Work Group decided upon a *Weak against* recommendation.

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Recommendations for "patients with low back pain" encompass patient populations with acute, subacute, or chronic LBP with or without neurological symptoms.

# G. Team Approach

# **Recommendation**

39. For patients with chronic low back pain, we suggest a multidisciplinary or interdisciplinary program. These programs should include at least one physical component and at least one other component of the biopsychosocial model (psychological, social, and/or occupational) used in an explicitly coordinated manner.

(Weak for | Reviewed, Amended)

# **Discussion**

According to the available evidence, a multidisciplinary biopsychosocial rehabilitation (MBR) approach that targets physical and behavioral/psychological care is beneficial for patients with chronic LBP. 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.(211) Studies examining these programs recognize their varying constitution. The available evidence provided no consensus regarding the definition of a multidisciplinary treatment approach. (211) The term interdisciplinary was used interchangeably in some cases, but multidisciplinary was most consistently used to describe a team approach for treating patients with chronic LBP (see the glossary in Appendix F for the definition of a multidisciplinary or interdisciplinary program). Neither term was consistently defined in the literature reviewed. While there was some variation in the interventions for MBR, the evidence reviewed consistently demonstrated a physical activation component (e.g., PT, exercise, physical activity) in addition to at least one other biopsychosocial-based intervention (e.g., education, psychological and/or behavioral interventions) with involvement of providers from at least 2 different disciplines.

The current systematic evidence review included one SR (212) and four RCTs.(213-216) An SR from Casey et al. (2020) compared MBR to treatments that included physical activation (exercise or physical activity) and/or physical activation in addition to passive interventions (e.g., manual therapies, electrotherapy, acupuncture) for patients with chronic LBP and found results related to the critical outcomes of both pain and disability to be statistically significant in favor of MBR. The outcomes for pain intensity had a small effect size at both three and 12 months (SMD: -0.47 at both intervals) while outcomes for disability had a moderate effect size at three months (SMD: -0.52) and large effect size at 12 months (SMD: -0.82). (212) Two RCTs (n=165) from Schmidt et al. (2020 and 2021) compared two different delivery methods for their MBR for patients with chronic LBP. The authors compared the delivery of the same program content in a four week intensive inpatient program with a blended program involving two weeks at home and two weeks of inpatient care, followed by two, 2-day inpatient booster sessions (eight weeks and 14 weeks). While they did not find any difference between the two methods at any time interval, they found a small but not clinically important improvement in pain for both groups at 26 weeks and one year after treatment, as well as a clinically meaningful improvement in disability at both time intervals. (213, 214) In another RCT (n=197), Tavafian et al. (2017) demonstrated a statistically significant long-term (30 months) improvement in both disability and SF-36 mental health domain measures compared to controls for patients with chronic LBP who participated in MBR. (216) No difference was noted in the SF-36 domains related to physical function, role physical/emotional, bodily pain, general health, vitality or social function at that same time period. Finally, an RCT (n=501) by Mas et al. (2019) examined MBR plus usual care compared to usual care in patients with subacute LBP (2 - 12 weeks) and found a statistically significant

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improvement in pain at three months and in disability at three and 12 month intervals. (215) These findings are consistent with the evidence cited in the 2017 VA/DoD LBP CPG. (211, 217, 218)

There is some variability in patient preferences regarding this treatment. There is often a large time commitment associated with these types of programs; however, the programs included in the current and previous evidence base differed in total time and format. On the whole, these programs tend to be both time and resource intensive. This should be factored into consideration when deciding when and with whom these programs are most appropriately utilized in the course of care. We do not have data to support an optimal dosing for MBR or for where they are best implemented in a course of care. Evidence to date supports positive impacts of MBR on pain and disability, and further research in this area would improve the ability of patients and clinicians to make informed decisions about engaging in MBR. Access to this level of coordinated care may be limited, especially in rural or underserved areas. Additionally, some patients and healthcare providers may have fixed beliefs related to LBP that may be centered around pathoanatomical models and may not be accepting of a biopsychosocial approach to care. A concern for stigmatization for addressing psychosocial elements of pain may further deter patients from pursuing this form of care. However, patients who do prefer a more holistic approach to their care and/or have tried multiple treatment approaches may welcome the comprehensive nature of MBR programs. 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 benefit.

The Work Group systematically reviewed evidence related to this recommendation (212-216) and considered the assessment of the evidence put forth in the 2017 VA/DoD LBP CPG. (211, 217, 218) Therefore, this is a *Reviewed*, *Amended* recommendation. The Work Group's confidence in the quality of the evidence was very low. The body of evidence had some limitations including risk of bias, inconsistency, and imprecision. (212-216) The benefits of MBR on pain and disability slightly outweighed the potential harms related to opportunity cost. Patient values and preferences were somewhat varied because of the time commitment and nature of the treatment. Thus, the Work Group decided upon a *Weakfor* recommendation.

### X. Research Priorities

During the development of the 2022 VA/DoD 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.

# A. Overarching Research Priorities

- Researchers follow best practice consensus documents (such as Consolidated Standards of Reporting Trials [CONSORT] for RCTs) for future studies. Many studies reviewed failed to execute basic quality measures such as blinding of outcome assessors, ITT analysis, and dropout and AE documentation.
- Research on clinical implementation of guideline concordant practice including strategies that may
  help resolve conflicts between drivers of low-value intervention utilization (e.g., patient insistence
  on or specialty care referral requirements for unnecessary diagnostic imaging or ineffective/unsafe
  treatments) and guideline concordant practice.

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- Studies that examine comparative effectiveness, determination of minimum effective dose, and best delivery methods for current care.
- Evidence on cost and risk comparisons for interventions, including cost-effectiveness per quality-adjusted life year (QALY) or similar common measure, documentation of AE rates and types, cost of delivering care, and ways to reduce risk of iatrogenic harm and continued medical care use.
- Research on cost-effectiveness outcome measures that overcome limitations of QALY, which devalues QoL of people with chronic disabilities.
- Research on improving LBP outcome assessment tools that are well-defined, patient-oriented, and responsive to treatment.
- Research on long-term outcomes greater than 12 weeks.
- Research on construct validity of definitions of acute, sub-acute, and chronic LBP.
- Prognostic studies of large cohorts sufficiently powered to better identify valid prognostic factors that influence outcomes.
- Studies to evaluate needs of optimal telehealth evaluation of patients with LBP, and validation and reliability studies on new telehealth technologies and evaluation protocols.

#### B. Low Back Pain Models

- Research on predictive modeling to help identify specific causes of LBP based on patient history and risk factors.
- Research on better validation of biological models of LBP that may better identify discrete "sources" of pain origin.
- Research on outcomes of biological models of LBP (e.g., examining the relative outcomes of different pain models: biological versus behavioral versus biopsychosocial).

## C. Diagnostic Imaging

- Research on routine imaging and invasive diagnostic tests should focus on the economic impact of diagnostic imaging and testing to include the amount of spending attributed to these tests and their subsequent referrals.
- Research to determine the motives for ordering diagnostic testing given the lack of evidence for their utility (e.g., patient satisfaction, referral patterns/networks, health-care provider compensation).
- Research on development and validation of more widely accepted reference standards (gold standard).
- Research to assess education and counseling of patients to enhance understanding of the benefits and harms of performing early diagnostic testing.

#### D. Patient Education and Self-care

• High quality RCTs to assess the effect of pain neuroscience education and clinician-directed education with patient-led goal setting for the treatment of LBP.

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- Research on technology-based modalities for self-management that have long-term follow-up (e.g., three months for acute LBP, and at least six to 12 months for chronic LBP).
- Research to better understand factors (e.g., diagnosis, socioeconomic status) that would influence impact of patient education interventions.

# E. Behavioral Health Screening and Interventions

- Research on the use of the STarT Back in the U.S. and why the STarT Back has demonstrated less utility in U.S. clinics as compared to European clinics.
- Research on behavioral interventions for chronic LBP including an emphasis on the optimal dose, validation of shorter treatment protocols, and incorporation of technology to maximize access to treatment.
- Research on MBSR examining which components of the treatment are most effective for patients with LBP. A recent SR of mindfulness-based programs for adults with psychological conditions suggested that acceptance coupled with awareness and mindfulness meditation training may be key factors in these treatments. (219)
- Research to better evaluate improvement in functional outcomes like QoL, with CBT.
- Research on the comparative effectiveness of different types of CBT-CP such as ACT.
- Research on the comparative effectiveness of delivery settings of behavioral interventions: virtual versus in-person; group versus one-on-one.

# F. Non-pharmacologic Passive Treatments

- Research on passive and provider delivered treatments (e.g., lumbar supports, cupping, laser therapy, TENs, ultrasound, auricular acupressure, and manipulation) pertaining to costeffectiveness and dose-response.
- Research on CIH approaches to LBP with appropriate rigorand comparators.

#### G. Exercise

- Evidence regarding which groups of patients may respond better to a certain exercise intervention. In addition, research on the dosing of exercise, to include duration, intensity, and frequency, as well as the supervision level required to help guide treatment programs.
- Research to better understand and identify patients' values and preferences that make them better candidates for active treatment approaches such as exercise-based treatments.

## H. Dietary Supplements

• High quality research on the use of nutritional, herbal, and homeopathic supplements.

#### I. Pharmacotherapy

- High quality RCTs using SNRIs and TCAs for LBP.
- High quality research on topical pharmacotherapy preparations for the management of LBP.

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- Non-industry, government-funded research with longer follow-up and attention to both treatment effects and AEs (e.g., studies on acute LBP and opioid use).
- High quality RCTs to evaluate efficacy of cannabis and cannabinoid agents in the management of LBP.

# J. Non-surgical Invasive Therapies

- High quality RCTs comparing injection and needle therapies (e.g., traditional acupuncture, battlefield acupuncture, and dry needling) to credible comparators (e.g., sham injection/needling, usual care, or no treatment) to assess for needle effect.
- Research on both short-term and long-term measures of pain and function.
- Research on an atomic targets of ablation and orthobiologics.
- Studies on spinal cord stimulation that are not industry-funded and assess long-term waning effects.
- Research on risk for surgical intervention after use of non-surgical invasive interventions.

# K. Multidisciplinary Biopsychosocial Rehabilitation Programs

- Research to examine the mode of delivery as well as the best intensity, frequency, and components of MBR programs.
- Research regarding which groups of patients may benefit most from this type of intervention and optimal strategies of sequencing this intervention in their treatment plan.

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# Appendix A: Guideline Development Methodology

# A. Developing Key Questions to Guide the Systematic Evidence Review

To guide this CPG's systematic evidence review, the Work Group drafted 12 KQs on clinical topics of the highest priority for the VA and DoD populations. The KQs followed the population, intervention, comparison, outcome, timing, and setting (PICOTS) framework, as established by the Agency for Healthcare Research and Quality (AHRQ) (see <u>Table A-1</u>).

Table A-1. PICOTS (220)

PICOTS Element	Description
Population or Patients	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.
Intervention or Exposure	Treatment (e.g., drug, surgery, lifestyle changes), approach (e.g., doses, frequency, methods of administering treatments), or diagnostic /screening test used with the patient or population.
Comparator	Treatment(s) (e.g., placebo, different drugs) or approach(es) (e.g., different dose, different frequency, standard of care) that are being compared with the intervention or exposure of interest described above.
Outcomes	Results of interest (e.g., mortality, morbidity, quality of life, complications). Outcomes can include short, intermediate, and long-term outcomes.
Timing, if applicable	Duration or follow-up of interest for the particular patient intervention and outcome to occur (or not occur).
Setting, if applicable	Setting or context of interest. Setting can be a location (e.g., primary, specialty, inpatient care) or type of practice.

Abbreviation: PICOTS: population, intervention, comparison, outcome, timing, and setting

Due to resource constraints, all KQs of interest to the Work Group could not be included in the systematic evidence review. Thus, the Work Group selected the 12 highest priority KQs for inclusion in the systematic evidence review (see <u>Table A-2</u>).

Using the GRADE approach, the Work Group rated each outcome on a 1-9 scale (7-9, critical for decision making; 4-6, important, but not critical, for decision making; and 1-3, of limited importance for decision making). Critical and important outcomes were included in the evidence review (see <u>Outcomes</u>); however, only critical outcomes were used to determine the overall quality of evidence (see <u>Determining</u> Recommendation Strength and Direction).

#### a. Population(s)

The population of interest covered in this systematic evidence review includes adults with acute, subacute, or chronic LBP, with or without spinal stenosis and with or without radicular pain.

KQ 8: patients who underwent back surgery are allowed but analyzed separately from other
patients if possible (this may not be feasible in all circumstances, depending on how the data is
reported and analyzed in relevant studies).

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#### b. Interventions

#### KQ 1a and 1b:

#### History

 Age; better with sitting; bilateral versus unilateral symptoms; dermatomal pain location; leg pain greater than or less than back pain; long-term corticosteroid use; occupation; presence of stiffness, length of stiffness, time of stiffness; red flags; shopping cart sign; symptoms related to time or activity; traumatic onset; worse with standing/walking

#### Physical exam

Biering-Sorensen or back extensor endurance testing; centralization; dermatomal sensory deficit; diminished reflex; Flexion, Abduction, External Rotation, and Extension (FABERE); facet loading test (Kemp's); hip clearing tests; hip strength; inspection of spine; Laslett's sacroiliac joint cluster and other clusters as well (e.g., Hancock rule, Cook rule); myotomal weakness; neurologic screen; range of motion; slump; straight leg raise

#### Diagnostic tests

 Blood tests (include spine-specific biomarkers); CT; discograms; electromyography; injections (facet, trigger point, transforaminal); MRI; myelograms; plain films/radiograph (standard and dynamic views with flexion and extension)

#### KQ 1b – Historical factors:

 Smoking; coronary artery disease (CAD); body mass index (BMI); age; red flags; duration of pain; applying for disability/ongoing litigation; surgical history; Optimal Screening for Prediction of Referral and Outcome (OSPRO) - Review of Systems; Oswestry Low Back Pain Disability Questionnaire; fibromyalgianess scale; other assessments

#### • KQ 2:

- Structured education: Back class; pain/therapeutic neuroscience education
- Non-clinician directed physical activity: Aquatic therapy; exercise programs; pilates; Tai chi/Qi gong; yoga
- Weight loss
- Workplace ergonomics: human factors engineering; postural adjustment
- Other CIH self-directed self-care modalities: meditation; mindfulness; self-massage acupressure

#### • KQ 3:

 Cranial electrotherapy stimulation (e.g., Alpha-Stim); cryotherapy; cupping; electrical stimulation; electroacupuncture; hot pack; low-level laser therapy; lumbar support braces; lumbar tractions; massage; microcurrent; osteopathic mobilization/manipulation; spinal manipulation/mobilization; TENS; therapeuticultrasound; trigger points

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- KQ 4 Individualized treatment plans, such as:
  - Back strengthening; core strengthening exercises (guided by physical therapists, prescribed by condition of patient); directional preference exercise; group exercise classes; lumbar stabilization; McKenzie (MDT); motor control exercises; stretching/therapeutic exercises
- KQ 5:
  - ◆ Antidepressants; anticonvulsants; cannabinoids (e.g., dronabinol, Epidiolex™); ergocalciferol; gabapentinoids (e.g., gabapentin, pregabalin, gabapentin enacarbil, extended-release gabapentin); lidocaine patch; monoclonal antibodies (nerve growth factors [e.g., tanezumab, fasinumab, fulranumab]); muscle relaxants; non-opioid analgesics (e.g., acetaminophen, NSAIDs); prescription/OTC medication (topical/oral); prostaglandins (E1); psychotropic medications
- KQ 6:
  - Benzodiazepines; opioids
- KQ 7:
  - Homeopathic preparations
  - Nutraceuticals
  - Supplements: cayenne; cod liver oil; devil's claw; docosahexaenoic acid; eicosapentaenoic acid; flavonoids; ginger; N-3 fatty acids; resveratrol; turmeric/curcumin; Vitamin C; Vitamin D; Vitamin E; willow bark
  - Diets: anti-inflammatory diet, low arachidonic acid diet
  - Cannabis products (e.g., cannabidiol, tetrahydrocannabinol)
- KQ 8:
  - Acupuncture; biologics (e.g., PRP, stem cell injections, viscosupplementation, prolotherapy); botulinum toxin; dry needling; dry needling with percutaneous electrical nerve stimulation; epidural injections; facet blocks; interspinous spacer; neuromodulation (e.g., transcranial magnetic stimulation, deep brain stimulation, peripheral nerve stimulation, dorsal root ganglion stimulation); nerve root blocks; RFA; SCS; trigger point injections
- KQ 9: Initiating treatment with cross-modality combination therapies, including:
  - Active interventions (KQ4)
  - Cognitive Functional Therapy
  - Coordinated rehabilitation program
  - ♦ Functional Restoration Program
  - Intensive Outpatient Program
  - Intensive Pain Rehabilitation Programs

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- Interdisciplinary Pain Rehabilitation Program (even some with Commission on Accreditation of Rehabilitation Facilities accreditation)
- Invasive therapies (KQ8)
- Passive interventions (KQ3)
- Pharmacotherapy (KQs 5 and 6)
- Structured education: Back school; pain/therapeutic neuroscience education
- Whole health (WH) interventions (e.g., WH coaching, personal health inventory)
  - o Whole person care
  - The pathway: Exploration of the Veteran's mission, aspiration, purpose (MAP);
     devising a personal health plan (PHP)
  - Well-being: Well-being programs (self-careskills)
  - WH Clinical Care: All traditional biomedical care especially care which traces back to the MAP and PHP; CIH (e.g., acupuncture, biofeedback/neurofeedback, clinical hypnosis, guided imagery, massage therapy, meditation/MBSR, tai chi/ qigong, yoga)
- KQ 10: Behavioral health interventions alone or as adjunct therapy:
  - ACT; biofeedback; CBT; MBSR; mindfulness/meditation; patient education; psychotherapy; relaxation therapy
- KQ 11: a) Assessment of and b) Treatment of the following mental health conditions, pain catastrophizing, or psychosocial stressors:
  - Mental health condition: Attention deficit hyperactivity disorder; anxiety; depression; posttraumatic stress disorder; traumatic brain injury
  - Psychosocial factors: Death; divorce; duration of pain, disability status, etc.; financial distress; job loss
  - Screening/assessmenttools:
    - o Childhood trauma/Adverse Childhood Events
    - o Chronic pain acceptance questionnaire
    - Columbia-Suicide Severity Rating Scale
    - Exposure to trauma in adulthood
    - Pain catastrophizing: Fear Avoidance Beliefs Questionnaire; Keele STarT Back; Minnesota Multiphasic Personality Inventory-2 (MMPI-2); Minnesota Multiphasic Personality Inventory-2-Restructured Form (MMPI-2RF); Orebro Musculoskeletal Pain Questionnaire; OSPRO; OSPRO – Yellow Flags; Pain Anxiety Symptoms Scale; Pain, Enjoyment of Life and General Activity (PEG) scale; Pain and Impairment Relationship Scale; Pain Catastrophizing Scale; Pain Self-Efficacy Questionnaire; Patient Health Questionnaire-9 (PHQ-9); Tampa Kinesiophobia Scale; Waddell Signs

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- Patient-Reported Outcome Measurement Information System 6b Pain Interference Scale
- Self-efficacy for rehabilitation
- State-Trait Anxiety and Anger Expression Inventory

#### KQ 12:

 mHealth applications; Microsoft Kinect; online or web-based applications (e.g., exercises, stretches, mindfulness); Nintendo Wii; phone applications; telephone-based; virtual reality (e.g., augmented reality, mixed reality, extended reality); Xbox

### c. Comparators

- KQ 1a: Reference standard or, when there is not a reference standard, the usual diagnostic criteria
- KQ 1b: No assessment, or one or a combination of the following:
  - Age, applying for disability/ongoing litigation, BMI, CAD, duration of pain, red flags, smoking, surgical history
- KQ 2: Usual care; wait list; other intervention listed in the previous column
- KQ 3: Usual care; other passive intervention listed in the previous column; active intervention
- KQ 4: Usual care; other active intervention listed in the previous column; passive intervention
- KQ 5: Placebo; non-pharmacologic approach (usual care, waitlist); any other pharmacotherapy
- KQ 6: Placebo; non-pharmacologic approach (usual care, waitlist); any other pharmacotherapy
- KQ 7: Usual care; placebo; non-pharmacologic approach; pharmacotherapy; other diet, nutritional, herbal, or homeopathic supplements
- KQ 8: Usual care; other non-surgical invasive therapies; sham interventions
- KQ 9: Usual care; step-wise approach to treatment with one modality at a time
- KQ 10: Usual care; wait list; self-directed behavioral interventions; other clinician directed behavioral interventions
- KQ 11: a) No assessment of and b) no treatment of mental health conditions, pain catastrophizing, or psychosocial stressors specified in the previous column
- KQ 12: Usual care (i.e., no use of technology-based modalities)

#### d. Outcomes

- KQ 1
  - Critical outcomes: Diagnosticaccuracy (KQ 1a); functional status (KQ 1b); pain severity (KQ 1b); QoL (KQ 1b)
  - Important outcomes: Healthcare costs/utilization (KQ1b); pain medication use (KQ1b); serious AEs (KQ1b)

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- KQ 2
  - Critical outcomes: Functional status; QoL
  - Important outcomes: Fear avoidance/pain acceptance/pain catastrophization/selfefficacy; healthcare costs/utilization; pain medication use; pain severity; pain interference; serious AEs
- KQ 3
  - Critical outcomes: Functional status; pain severity; QoL
  - Important outcomes: Healthcare costs/utilization; pain medication use; pain interference; serious AEs
- KQ 4
  - Critical outcomes: Functional status; QoL
  - Important outcomes: Fear avoidance/pain acceptance/pain catastrophization/self-efficacy; healthcare costs/utilization; pain medication use; pain severity; pain interference
- KQ 5
  - Critical outcomes: Functional status; pain severity; QoL; serious AEs
  - Important outcomes: Healthcare costs/utilization; pain medication use; pain interference
- KQ 6
  - Critical outcomes: Functional status; pain severity; QoL; serious AEs
  - Important outcomes: Healthcare costs/utilization; pain medication use; pain interference
- KQ 7
  - Critical outcomes: Pain severity; QoL; serious AEs
  - Important outcomes: Functional status; healthcare costs/utilization; pain medication use; pain interference
- KQ 8
  - Critical outcomes: Functional status; pain severity; QoL; serious AEs
  - Important outcomes: Healthcare costs/utilization; pain medication use; pain interference
- KQ 9
  - Critical outcomes: Functional status; pain severity; QoL
  - Important outcomes: Healthcare costs/utilization; pain medication use; pain interference; serious AEs
- KQ 10
  - Critical outcomes: Functional status; QoL
  - Important outcomes: Fear avoidance/pain acceptance/pain catastrophization/selfefficacy; pain medication use; pain severity; pain interference; anxiety; depression

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- KQ 11
  - Critical outcomes: Fear avoidance/pain acceptance/pain catastrophization/self-efficacy; functional status; QoL
  - Important outcomes: Pain medication use; pain severity; pain interference
- KQ 12
  - Critical outcomes: Functional status; pain severity; QoL
  - Important outcomes: Fear avoidance/pain acceptance/pain catastrophization/self-efficacy; healthcare costs/utilization; pain medication use; pain interference

### e. Timing

- The minimum follow-up for effectiveness outcomes was 12 weeks
- For diagnostics and harms we set no minimum follow-up

# f. Settings

Any setting

# B. Conducting the Systematic Review

Based on the Work Group's decisions regarding the CPG's scope, KQs, and PICOTS statements, the Lewin Team produced a systematic evidence review protocol before conducting the review. The protocol detailed the KQs, PICOTS criteria, methodology to be used during the systematic evidence review, and the inclusion and exclusion criteria to be applied to each potential study, including study type and sample size. The Work Group reviewed and approved the protocol.

<u>Figure A-1</u> outlines the systematic evidence review's screening process (see also the <u>General Criteria for Inclusion in Systematic Review</u> and <u>Key Question Specific Criteria</u>). In addition, <u>Table A-2</u> indicates the number of studies that addressed each of the questions.

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4,128 Citations Excluded at the Title Level Citations excluded at this level were off-topic, not 7,438 Citations Identified by Searches published in English, or published prior to inclusion date 2,497 Citations Excluded at the Abstract Level Citations excluded at this level were not an SR or CS, 3,310 Abstracts Reviewed clearly did not address a KQ, did not report on an outcome of interest, or were outside cutoff publication dates 431 Citations Excluded at 1st Pass Full Article Level 124 did not address KQ 66 relevant review with no data to abstract 43 not study design of interest 33 not a comparison group of interest 813 Full-length Articles Reviewed 26 less than 50 pts 18 did not report an outcome of interest 17 not a full-length clinical study or SR 17 not population of interest 1 superseded by more recent/comprehensive review 86 other (duplicates, not in date range, not intervention of interest) 239 Citations Excluded at 2nd Pass KQ Level 29 Not a study population of interest 56 Wrong study design or doesn't address a KQ 15 No outcomes of interest 32 Not an intervention or comparator of interest 382 Articles Reviewed 39 Superseded by more comprehensive review or included in an SR 33 Unclear or inadequate follow-up 12 Fewer than 50 patients 23 Other (e.g., duplicate, published outside date range) 143 Included Studies

Figure A-1. Study Flow Diagram

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

### Alternative Text Description of Study Flow Diagram

<u>Figure A-1. Study Flow Diagram</u> is a flow chart with nine labeled boxes linked by arrows that describe the literature review inclusion/exclusion process. Arrows point down to boxes that describe the next literature review step and arrows point right to boxes that describe the excluded citations at each step (including the reasons for exclusion and the numbers of excluded citations).

- 1. Box 1: 7,438 citations identified by searches
  - a. Right to Box 2: 4,128 citations excluded at the title level
    - i. Citations excluded at this level were off-topic, not published in English, or published prior to inclusion date
  - b. Down to Box 3
- Box 3: 3,310 abstracts reviewed
  - a. Right to Box 4: 2,497 excluded at the abstract level
    - i. Citations excluded at this level were not an SR or CS, clearly did not address a KQ, did not report on an outcome of interest, or were outside cutoff publication dates
  - b. Down to Box 5

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- 3. Box 5: 813 full-length articles reviewed
  - a. Right to Box 6: 431 citations excluded at 1st pass full article level
    - i. 124 did not address KQ
    - ii. 66 relevant review with no data to abstract
    - iii. 43 not study design of interest
    - iv. 33 not a comparison group of interest
    - v. 26 less than 50 patients
    - vi. 18 did not report an outcome of interest
    - vii. 17 not a full-length clinical study or SR
    - viii. 17 not population of interest
    - ix. 1 superseded by more recent/comprehensive review
    - x. 86 other (duplicates, not in date range, not intervention of interest)
  - b. Down to Box 7
- 4. Box 7: 382 articles reviewed
  - a. Right to Box 8: 239 citations excluded at 2<sup>nd</sup> pass KQ Level
    - i. 29 not a study population of interest
    - ii. 56 wrong study design or doesn't address a KQ
    - iii. 15 no outcomes of interest
    - iv. 32 not an intervention or comparator of interest
    - v. 39 superseded by a more comprehensive review or included in an SR
    - vi. 33 unclear or inadequate follow-up
    - vii. 12 fewer than 50 patients
    - viii. 23 other (e.g., duplicate, published outside date range)
  - b. Down to Box 9
- 5. Box 9: 143 included studies

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Table A-2. Evidence Base for KQs

KQ Number	KQ	Numberand StudyType
1a	For adults with low back pain, what is the diagnostic utility of history, exam, imaging, and other diagnostic tests?	4 SRs and 10 diagnostic cohort studies
1b	For adults with low back pain, what is the prognostic/clinical impact of different evaluation tools and risk factors on low back pain outcomes?	2 SRs and 21 prognostic studies (1 RCT, 8 secondary analyses of RCTs, 12 cohort studies)
2	For adults with low back pain, what is the effectiveness of structured education, non-clinician directed physical activity, weight loss, workplace ergonomics, and other complementary and integrative health (CIH) self-directed self-care modalities for improving low back pain outcomes?	9 SRs and 7 RCTs
3	For adults with low back pain, what is the effectiveness of passive non-surgical and non-pharmacological interventions?	10 SRs and 2 RCTs
4	For adults with low back pain, what is the effectiveness of active non-surgical and non-pharmacological interventions?	4 SRs and 15 RCTs
5	For adults with low back pain, what is the effect of prescription or over the counter (OTC) pharmacotherapy treatment?	2 SRs and 4 RCTs
6	For adults with low back pain, what is the effect of pharmacotherapy treatment with opioids and benzodiazepines?	1 SR and 2 RCTs
7	For adults with low back pain, what is the effect of dietary, nutritional, herbal, and homeopathic supplements?	1 SR
8	For adults with low back pain, what is the effectiveness of non-surgical invasive therapies?	10 SRs, 5 RCTs, and 1 randomized crossovertrial
9	For adults with low back pain, which cross-modality combination therapy (e.g.,pharmacologicand non-pharmacologic) is most effective?	1 SR and 15 RCTs (in 16 publications)
10	For adults with low back pain, what is the effectiveness of behavioral health interventions? a) What is the effectiveness of clinician directed interventions? b) What is the effectiveness of self-directed interventions?	3 SRs and 5 RCTs
11	For adults with low back pain, what is the impact of a) assessment and b) treatment of mental health conditions, pain catastrophizing, or psychosocial stressors on low back pain outcomes?	2 RCTs
12	For adults with low back pain, what is the effectiveness of technology-based modalities for self-management?	2 SRs and 6 RCTs
	Total Evidence Base	143 studies

Abbreviations: RCT: randomized controlled trial; SR: systematic review

# a. General Criteria for Inclusion in Systematic Evidence Review

- RCTs or SRs published on or after October 1, 2016, to February 1, 2021. If multiple SRs addressed a
  KQ, we selected the most recent and/or comprehensive review. SRs were supplemented with
  RCTs published after the systematic review.
- 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.

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- Systematic reviews must have searched MEDLINE or EMBASE for eligible publications, performed
  a risk of bias assessment of included studies, and assessed the quality of evidence using a
  recognizable rating system, such as GRADE or something compatible (e.g., the Strength of
  Evidence grading used by the Evidence-based Practice Centers of the AHRQ). If an existing review
  did not assess the overall quality of the evidence, evidence from the review must have been
  reported in a manner that allowed us to judge the overall risk of bias, consistency, directness, and
  precision of evidence. We did not use an existing review as evidence if we were unable to assess
  the overall quality of the evidence in the review.
- Study must have enrolled at least 50 patients (25 per study group for treatment studies, 50 total patients for diagnostic or prognostic studies); Small sample size was associated with increased risk of bias and we downgraded small studies in the GRADE domain of precision: one downgrade for imprecision of a single study with <200 patients per study arm.
- Newer Cochrane reviews already took into account small sample size in their estimation of risk of bias. In these cases, where sample size had already contributed to the assessment of the evidence, we did not downgrade those data a second time.
- Study must have enrolled at least 85% of patients who met the study population criteria: adults
  with acute, subacute, or chronic LBP, with or without spinal stenosis and with or without radicular
  pain. For studies examining mixed patient populations, studies must have enrolled at least 85% of
  patients with the relevant condition.
- Study must have reported on at least one outcome of interest.

### b. Key Question Specific Criteria for Inclusion in Systematic Evidence Review

- For all KQs, except KQs 1 and 11, studies must have been prospective, randomized controlled trials with an independent control group. Crossover trials were not included unless they reported data for the first phase of the study separately.
- In addition to RCTs and systematic reviews, KQ1 included observational, diagnostic, and prognostic study designs that compared different assessment methods/tools and their diagnostic accuracy and impact on LBP outcomes.
- For KQ 11, observational studies with a relevant comparator group were acceptable for the assessment part of the question (RCTs and SRs were still required for the treatment part of the question) if SRs and RCTs did not adequately address assessment.

## c. Literature Search Strategy

Information regarding the bibliographic databases, date limits, and platform/provider can be found in <u>Table A-3</u>. See <u>Appendix H</u> for additional information on the search strategies, including topic-specific search terms and search strategies.

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Table A-3. Bibliographic Database Information

	Name	Date Limits	Platform/Provider
	Embase (Excerpta Medica) and MEDLINE	October 1, 2016, to February 1, 2021	Elsevier
Bibliographic Databases	PsycINFO	October 1, 2016, to February 1, 2021	Ovid
	PubMed(In-process and Publisher records)	October 1, 2016, to February 1, 2021	NLM
Crowl iterature	Agency for Healthcare Research and Quality (AHRQ)	October 1, 2016, to February 1, 2021	AHRQ
GreyLiterature	U.S. Department of Veterans Affairs (VA) Evidence Synthesis Program	October 1, 2016, to February 1, 2021	VA

# d. Rating the Quality of Individual Studies and the Body of Evidence

The Lewin Team assessed the methodological risk of bias of individual diagnostic, observational, and interventional studies using the USPSTF method. Each study is assigned a rating of *Good*, *Fair*, or *Poor* based on a set of criteria that vary depending on study design. Detailed lists of criteria and definitions appear in Appendix VI of the USPSTF procedure manual. (221)

Following this, the Lewin Team assessed the overall quality of the body of evidence for each critical and important outcome using the GRADE approach. This approach considers the following factors: overall study quality (or overall risk of bias or study limitations), consistency of evidence, directness of evidence, and precision of evidence. The overall quality of the body of evidence is rated as *High*, *Moderate*, *Low*, and *Very low*.

# C. Developing Evidence-based Recommendations

In consultation with the VA Office of Quality and Patient Safety and the Clinical Quality Improvement Program, DHA, the Lewin Team convened a four-day virtual recommendation development meeting on May 3-6, 2021 to develop this CPG's evidence-based recommendations. Two weeks before the meeting, the Lewin Team finalized the systematic evidence review and distributed the report to the Work Group; findings were also presented during the recommendation development meeting.

Led by the Champions, the Work Group interpreted the systematic evidence review's findings and developed this CPG's recommendations. Where appropriate, the Work Group carried forward and modified recommendations from the 2017 VA/DoD LBP CPG as necessary (see Reconciliation of 2017 Clinical Practice Guideline Recommendations). The Work Group also developed new recommendations not included in the 2017 VA/DoD LBP CPG based on the 2022 VA/DoD LBP CPG systematic evidence review.

The strength and direction of each recommendation were determined by assessing the quality of the overall evidence base, the associated benefits and harms, patient values and preferences, and other implications (see <u>Determining Recommendation Strength and Direction</u>).

#### a. Determining Recommendation Strength and Direction

Per GRADE, each recommendation's strength and direction is determined by the following four domains: (19)

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# 1. Confidence in the Quality of the Evidence

Confidence in the quality of the evidence reflects the quality of the body of evidence supporting a recommendation (see <u>Rating the Quality of Individual Studies and the Body of Evidence</u>). The options for this domain include: *High, Moderate, Low,* or *Very low*. This is a direct reflection of the GRADE ratings for each relevant critical outcome in the evidence review (see <u>Outcomes</u>). Per GRADE, if the quality of evidence differs across the relevant critical outcomes, the lowest quality of evidence for any of the critical outcomes determines the overall quality of the evidence for a recommendation. (<u>21</u>, <u>22</u>)

The recommendation strength generally aligns with the confidence in the quality of evidence. For example, *Strong* recommendations are typically supported by *High* or *Moderate* quality evidence. However, GRADE permits *Low* or *Very low* quality evidence to support a *Strong* recommendation in certain instances (e.g., life-threatening situation). (19)

# 2. Balance of Desirable and Undesirable Outcomes

The balance of desirable and undesirable outcomes (i.e., benefits and harms) refers to the relative magnitudes or tradeoffs of anticipated benefits (e.g., increased longevity, reduced morbidity, improved quality of life, decreased resource use) and harms (e.g., decreased longevity, increased complications, impaired quality of life). The options for this domain include: benefits outweigh harms/burden, benefits slightly outweigh harms/burden, benefits and harms/burdens are balanced, harms/burdens slightly outweigh benefits, and harms/burdens outweigh benefits. This domain assumes most clinicians will offer patients an intervention if its advantages exceed the harms. The Work Group's understanding of the benefits and harms associated with the recommendation influenced the recommendation's strength and direction.

# 3. Patient Values and Preferences

Patient values and preferences is an overarching termthat includes patients' perspectives, beliefs, expectations, and goals for health and life as they may apply to the intervention's potential benefits, harms, costs, limitations, and inconvenience. The options for this domain include: *similar values, some variation*, or *large variation*. For instance, there may be *some variation* in patient values and preferences for a recommendation on the use of acupuncture, as some patients may dislike needles. When patient values seem homogeneous, this domain may increase the recommendation's strength. Alternatively, when patient values seem heterogeneous, this domain may decrease a recommendation's strength. As part of this domain, the Work Group considered the findings from the patient focus group carried out as part of this CPG update (see <u>Appendix B</u>).

#### 4. Other Implications

Other implications encompass the potential consequences or other impacts that might affect the strength or direction of the recommendation. The options for this domain include, e.g.: resource use, equity, acceptability, feasibility, and subgroup considerations. The following are example implications related to equity and subgroup considerations, respectively: some of the indicated population may be geographically remote from an intervention (e.g., complex radiological equipment); a drug may be contraindicated in a subgroup of patients.

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Table A-4. GRADE Evidence to Recommendation Framework

<b>Decision Domain</b>	Questions to Consider	Judgment
Confidence in the quality of the evidence	<ul> <li>Among the designated critical outcomes, what is the lowest quality of relevant evidence?</li> <li>How likely is further research to change the confidence in the estimate of effect?</li> </ul>	<ul><li>High</li><li>Moderate</li><li>Low</li><li>Very low</li></ul>
Balance of desirable and undesirable outcomes	<ul> <li>What is the magnitude of the anticipated desirable outcomes?</li> <li>What is the magnitude of the anticipated undesirable outcomes?</li> <li>Given the best estimate of typical values and preferences, are you confident that benefits outweigh harms/burdens or vice versa?</li> </ul>	<ul> <li>Benefits outweigh harms/burdens</li> <li>Benefits slightly outweigh harm/burden</li> <li>Benefits and harms/burdens are balanced</li> <li>Harms/burdens slightly outweigh benefits</li> <li>Harms/burdens outweigh benefits</li> </ul>
Patient values and preferences	<ul> <li>What are the patients' values and preferences?</li> <li>Are values and preferences similar across the target population?</li> <li>Are you confident about typical values and preferences?</li> </ul>	<ul><li>Similar values</li><li>Some variation</li><li>Large variation</li></ul>
Other implications (e.g., resource use, equity, acceptability, feasibility, subgroup considerations)	<ul> <li>What are the costsper resource unit?</li> <li>Is this intervention generally available?</li> <li>What is the variability in resource requirements across the target population and settings?</li> <li>Are the resources worth the expected net benefit from the recommendation?</li> <li>Is this intervention and its effects worth withdrawing or not allocating resources from other interventions?</li> </ul>	Various considerations

#### b. Recommendation Categorization

A summary of the recommendation categories and definitions is available in Table 5.

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

*Reviewed* refers to recommendations on topics included in this CPG's systematic evidence review. *Reviewed*, *New-added* recommendations are original, new recommendations (i.e., not included in the previous CPG). These recommendations are based entirely on evidence included in the current CPG's systematic evidence review.

Reviewed, New-replaced recommendations were in the previous CPG but revised based on the updated evidence review. These recommendations may have clinically relevant edits. Reviewed, Not changed recommendations were carried forward from the previous CPG unchanged. Reviewed, Amended recommendations were carried forward from the previous CPG with a nominal change. This allowed for the recommendation language to reflect GRADE approach and any other not clinically meaningful edits deemed necessary. These recommendations can be based on a combination of evidence included in the current CPG's systematic evidence review and the evidence base that supported the recommendation in the previous CPG.

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Reviewed, Deleted refers to recommendations from the previous CPG that were deleted after a review of the evidence. This may occur if the evidence supporting the recommendation is outdated (e.g., there is no longer a basis to recommend use of an intervention and/or new evidence suggests a shift in care), rendering the recommendation obsolete.

# 2. 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 CPG without an updated review of the evidence. Given time and resource constraints, the systematic evidence review carried out for this CPG update could not cover all available evidence on LBP; therefore, its KQs focused on new or updated research or areas not covered in the previous CPG.

For areas in which the relevant evidence was not changed and for which recommendations made in the previous CPG were still relevant, recommendations could have been carried forward to the updated CPG without an updated review of the evidence. The evidence supporting these recommendations was thus also carried forward from the previous 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 were carried forward from the previous CPG unchanged. *Not reviewed*, *Amended* recommendations were carried forward from the previous CPG with a nominal change. *Not reviewed*, *Deleted* recommendations were determined by the Work Group to not be relevant. A recommendation may not be relevant if it, for example, pertained to a topic (e.g., population, care setting, treatment) outside of the updated CPG's scope or if it was determined to be common practice.

The recommendation categories for the current CPG are noted in the <u>Recommendations</u>. The recommendation categories from the 2017 VA/DoD LBP CPG are noted in <u>Appendix D</u>.

# D. Drafting and Finalizing the Guideline

The Work Group wrote, reviewed, and edited three drafts of the CPG using an iterative review process to solicit feedback on and make revisions to the CPG. The first and second drafts were posted online for 20 and 14 business days, respectively, for the Work Group to provide feedback. Draft 3 was made available for a 14-day peer review and comment (see <a href="External Peer Review">External Peer Review</a>). The Work Group reviewed all feedback submitted during each review period and made appropriate revisions to the CPG. Following the Draft 3 review and comment period, the Work Group reviewed external feedback and created a final draft of the CPG. The Champions then presented the CPG to the VA/DoD EBPWG for approval. The Work Group considered the VA/DoD EBPWG's feedback and revised the CPG as appropriate to create the final version. To accompany the CPG, the Work Group produced toolkit products, including a provider summary, pocket card, and patient summary. The VA/DoD EBPWG approved the final CPG and toolkit products in February 2022.

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# Appendix B: Patient Focus Group Methods and Findings

#### A. Methods

VA and DoD Leadership recruited seven participants for the focus group, with support from the Champions and other Work Group members as needed. While participant recruitment focused on eliciting a range of perspectives likely to be relevant and informative in the CPG development process, patient focus group participants were not intended to be a representative sample of VA and DoD patients. Participants were not incentivized for their participation or reimbursed for travel expenses.

The Work Group, with support from the Lewin Team, identified topics on which patient input was important to consider in developing the CPG. The Lewin Team developed and the Work Group approved and patient focus group guide covering these topics. The focus group facilitator led the discussion used the guide to elicit the patients' perspectives about their treatment and overall care. Given the limited time and the range of interests of the focus group participants, not all questions were addressed.

# **B.** Patient Focus Group Findings

- a. Participants noted that LBP has had significant impacts on daily life, including being unable to sit or stand for extended periods of time, requiring assistance to perform tasks, and experiencing other issues in addition to LBP, including pain elsewhere and behavioral health changes (e.g., short temper, depression).
- Participants indicated that they experienced daily challenges in their lives and the workplace resulting from LBP and related symptoms.
- Participants noted the impact of LBP on family life and that their goal for treatment is to improve QoL and, following, prevent it from degrading.
- b. Participants expressed frustration with the lack of early evaluation (especially use of MRIs) for determining the cause of LBP and treatment planning.
- Participants expressed concerns with the lack of timely evaluation and diagnosis to understand the cause of their LBP.
- Participants highlighted the importance of early evaluation with advanced imaging.
- c. Participants described treatment approaches they have found to be successful, including complementary and integrative interventions, chiropractic care and other non-pharmacologic approaches, and care received in pain management clinics. Participants shared that they often self-refer to private providers when these interventions are not available at VA and DoD facilities.
- Participants valued being able to choose from a variety of treatment options (e.g., medications, acupuncture, chiropractic care).
- Patients emphasized the effectiveness of non-pharmacologic approaches. Patients also noted the helpfulness of engaging in self-care strategies for relieving LBP.
- Participants expressed frustration with PT and discussed the need to seek care from private providers.

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- d. Participants valued communication with providers and use of a shared decision making approach (in which the provider listened to patient problems, considered the underlying causes of the patient's LBP, and explored a range of treatment options to develop an individualized treatment plan).
- Participants appreciated providers who considered the concerns of patients in using a shared decision making approach and developing individualized treatment plans.
- Participants highlighted the importance of coordination between providers.
- Participants valued education and the benefits of previous education in provoking meaningful conversations.
- e. Participants recognized the importance of continuity of care and communication between providers within and across treatment settings and access to providers, including specialists.
- Participants noted challenges in receiving continuous care when transitioning to new providers and treatment settings.
- Participants expressed concern with accessing providers.
- f. Participants stated that they experienced stigma associated with having LBP and feel that healthcare providers do not take complaints seriously.

  Participants also indicated LBP can affect military careers.
- Participants noted stigma associated with recognizing and treating LBP and provider dismissiveness of patient complaints.
- Participants also recognized how LBP can affect military careers and prevent patients from seeking preventive care.

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# **Appendix C: Evidence Table**

Table C-1. Evidence Table a, b, c, d

Re	commendation	2017 Strength of Recommendation	Evidence	2022 Strength of Recommendation	Recommendation Category
1.	For patients with low back pain, we recommend the history and physical examination include evaluation for progressive or otherwise serious neurologic deficits and other red flags (e.g., signs, symptoms, history) associated with serious underlying pathology (e.g., malignancy, fracture, infection).	Strong for	( <u>36-40</u> ) Additional Reference: ( <u>19</u> )	Strong for	Reviewed, Amended
2.	For patients with low back pain, we recommend diagnostic imaging and appropriate laboratory testing when neurologic deficits are progressive or otherwise serious or when other red flags (e.g., signs, symptoms, history) are present.	Strong for	( <u>36</u> , <u>41</u> , <u>42</u> ) Additional Reference: ( <u>19</u> )	Strong for	Reviewed, Amended
3.	For patients with acute low back pain, without focal neurologic deficits or other red flags (e.g., signs, symptoms, history), we recommend against routinely obtaining imaging studies or performing invasive diagnostic tests.	Strong against, Neither for nor against	(42-47)	Strong against	Reviewed, New- replaced
4.	For patients with low back pain, we suggest assessing psychosocial factors and using predictive screening instruments (e.g., STarT Back and The Orebro Musculoskeletal Pain Screening Questionnaire) to inform treatment planning.	Weak for	( <u>48-56</u> ) Additional References: ( <u>57-61</u> )	Weak for	Reviewed, New- replaced

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<sup>&</sup>lt;sup>a</sup> 2017 Strength of Recommendation column: The 2017 VA/DoD LBP CPG was developed using the GRADE approach to determine the strength of each recommendation. Inclusion of more than one 2017 strength of recommendation indicates that more than one 2017 VA/DoD LBP CPG recommendation is covered by the 2022 recommendation. "Not applicable" indicates that the 2022 VA/DoD LBP CPG recommendation was a new recommendation, and therefore does not have an associated 2017 strength of recommendation. "Neither for nor against" represents updated language for "N/A" used in the 2017 VA/DoD LBP CPG.

b Evidence column: The first set of references listed in each row in the evidence column constitutes the evidence base for the recommendation. To be included in the evidence base for a recommendation, a reference needed to be identified through a systematic evidence review carried out as part of the initial development or update of this CPG. The second set of references in the evidence column (called "Additional References") includes references that provide additional information related to the recommendation, but which were not identified through a systematic evidence review. These references were, therefore, not included in the evidence base for the recommendation and did not influence the strength and direction of the recommendation.

c 2022 Strength of Recommendation column: The 2022 VA/DoD LBP CPG was developed using the GRADE approach to determine the strength of each recommendation. Refer to the Determining Recommendation Strength and Direction section for more information.

d Recommendation Category column: Refer to the Recommendation Categorization section for more information on the description of the categorization process and the definition of each category.

Red	commendation	2017 Strength of Recommendation	Evidence	2022 Strength of Recommendation	Recommendation Category
5.	For patients with low back pain, with or without radicular symptoms, there is insufficient evidence to recommend for or against specific physical exam maneuvers to assist in the diagnosis of facet or sacroiliac joint pain, or a lumbar/lumbosacral radiculopathy.	Not applicable	( <u>62-66</u> ) Additional References: ( <u>67-74</u> )	Neither for nor against	Reviewed, New- added
6.	For patients with low back pain, there is insufficient evidence to recommend for or against pain neuroscience education, clinician-directed education with patient-led goal setting, or back school.	Weak for	( <u>75</u> , <u>76</u> , <u>79</u> , <u>80</u> , <u>82</u> , <u>83</u> ) <b>Additional References:</b> ( <u>77</u> , <u>78</u> , <u>81</u> )	Neither for nor against	Reviewed, New- replaced
7.	For the self-management of low back pain, there is insufficient evidence to recommend for or against technology-based modalities.	Not applicable	( <u>84-87</u> )	Neither for nor against	Reviewed, New- added
8.	For patients with chronic low back pain, we suggest cognitive behavioral therapy.	Strong for	( <u>88-93</u> )	Weak for	Reviewed, New- replaced
9.	For patients with low back pain, we suggest a structured clinician-directed exercise program (e.g., aerobic, aquatic, mechanical diagnosis and therapy, mobility, motor control, Pilates, strengthening exercises, structured walking program, tai chi).	Weak for, Neither for nor against	(94-115, 117-120) Additional Reference: (116)	Weak for	Reviewed, New- replaced
10.	For patients with chronic low back pain, we suggest spinal mobilization/manipulation.	Weak for	( <u>121-128</u> , <u>131</u> ) Additional Reference: ( <u>129</u> )	Weak for	Reviewed, New- replaced
11.	For patients with acute low back pain, there is insufficient evidence to recommend for or against spinal mobilization/manipulation.	Weak for	(130, 132)	Neither for nor against	Reviewed, New- replaced
12.	For patients with chronic low back pain, there is insufficient evidence to recommend for or against mindfulness-based stress reduction.	Weak for	( <u>88</u> , <u>89</u> , <u>133</u> )	Neither for nor against	Reviewed, New- replaced
13.	For patients with low back pain, there is insufficient evidence to recommend for or against lumbar supports.	Neither for nor against	( <u>113</u> , <u>134</u> ) Additional References: ( <u>135-137</u> )	Neither for nor against	Reviewed, Amended
14.	For patients with low back pain, with or without radicular symptoms, there is insufficient evidence to recommend for or against mechanical lumbar traction.	Neither for nor against	( <u>138-141</u> )	Neither for nor against	Reviewed, New- replaced

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Recommendation	2017 Strength of Recommendation	Evidence	2022 Strength of Recommendation	Recommendation Category
15. For patients with chronic low back pain, there is insufficient evidence to recommend for or against auricular acupressure.	Not applicable	( <u>142</u> )	Neither for nor against	Reviewed, New- added
16. For patients with low back pain, there is insufficient evidence to recommend for or against yoga or qi gong.	Weak for	( <u>105</u> , <u>143-145</u> ) Additional References: ( <u>146-148</u> )	Neither for nor against	Reviewed, New- replaced
17. For patients with low back pain, there is insufficient evidence to recommend for or against cupping, laser therapy, transcutaneous electrical nerve stimulation, and ultrasound.	Neither for nor against	( <u>113</u> , <u>149-153</u> )	Neither for nor against	Reviewed, New- replaced
18. For patients with chronic lowback pain, we suggest duloxetine.	Weak for	( <u>113</u> , <u>154</u> ) Additional References: ( <u>155-159</u> )	Weak for	Reviewed, New- replaced
19. For patients with low back pain, we suggest nonsteroidal anti- inflammatory drugs.	Strong for	( <u>113</u> , <u>154</u> , <u>160</u> ) Additional References: ( <u>161-166</u> )	Weak for	Reviewed, New- replaced
20. For patients with low back pain, with or without radicular symptoms, there is insufficient evidence to recommend for or against gabapentin or pregabalin.	Neither for nor against	(167, 170, 173, 174) Additional References: (168, 169, 171, 172)	Neither for nor against	Reviewed, Amended
21. For patients with low back pain, there is insufficient evidence to recommend for or against tricyclic antidepressants.	Not applicable	( <u>113</u> , <u>175-178</u> ) Additional References: ( <u>179</u> , <u>180</u> )	Neither for nor against	Reviewed, New- added
22. For patients with low back pain, there is insufficient evidence to recommend for or against topical preparations.	Neither for nor against	None	Neither for nor against	Reviewed, Amended
23. For patients with acute low back pain, there is insufficient evidence to recommend for or against a non-benzodiazepine muscle relaxant for short-term use.	Weak for	(113, 181, 182)	Neither for nor against	Reviewed, New- replaced
24. For patients with chronic low back pain, we suggest against offering a non-benzodiazepine muscle relaxant.	Weak against	( <u>113</u> , <u>181</u> , <u>182</u> )	Weak against	Reviewed, Not changed
25. For patients with low back pain, we suggest against acetaminophen.	Strong against, Neither for nor against	( <u>113</u> , <u>183</u> ) Additional Reference: ( <u>184</u> )	Weak against	Reviewed, New- replaced
26. For patients with low back pain, we suggest against monoclonal antibodies.	Not applicable	( <u>185</u> , <u>186</u> )	Weak against	Reviewed, New- added

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Rec	commendation	2017 Strength of Recommendation	Evidence	2022 Strength of Recommendation	Recommendation Category
27.	For patients with chronic lowback pain, we suggest against opioids. For patients who are already using long-term opioids, see the VA/DoDCPG for the Use of Opioids in the Management of Chronic Pain. <sup>e</sup>	Strong against	( <u>113</u> , <u>186-189</u> ) Additional Reference: ( <u>190</u> )	Weak against	Reviewed, New- replaced
28.	For patients with low back pain, with or without radicular symptoms, we suggest against systemic corticosteroids (oral or intramuscular injection).	Strong against	( <u>113</u> , <u>191</u> )	Weak against	Not reviewed, Amended
29.	For patients with low back pain, we recommend against benzodiazepines.	Strong against	( <u>113</u> , <u>192</u> ) Additional Reference: ( <u>193</u> )	Strong against	Reviewed, Not changed
30.	For patients with low back pain, there is insufficient evidence to recommend for or against any specific diet or nutritional, herbal, or homeopathic supplements (e.g., anti-inflammatory diet, turmeric, vitamin D), cannabis, or cannabinoids.	Neither for nor against	( <u>194, 195</u> )	Neither for nor against	Reviewed, New- replaced
31.	For patients with chronic low back pain, we suggest lumbar medial branch and/or sacral lateral branch radiofrequency ablation.	Neither for nor against	( <u>196</u> , <u>197</u> )	Weak for	Reviewed, New- replaced
32.	For patients with low back pain, there is insufficient evidence to recommend for or against sacroiliac joint injections.	Not applicable	None	Neither for nor against	Reviewed, New- added
33.	For patients with low back pain, we suggest against the injection of corticosteroids for intra-articular facet joint injections and the rapeutic medial branch blocks with steroid.	Weak against, Neither for nor against	( <u>198, 199</u> )	Weak against	Reviewed, New- replaced
34.	For patients with chronic low back pain, we suggest acupuncture.	Weak for	( <u>113</u> , <u>200-202</u> )	Weak for	Reviewed, Amended
35.	For patients with acute low back pain, there is insufficient evidence to recommend for or against acupuncture.	Neither for nor against	( <u>113</u> , <u>200</u> )	Neither for nor against	Reviewed, Amended
36.	For patients with low back pain, there is insufficient evidence to recommend for or against ortho-biologics (e.g., platelet-rich plasma, stem cells).	Not applicable	( <u>203</u> , <u>204</u> )	Neither for nor against	Reviewed, New- added
37.	For patients with low back pain, with radicular symptoms, there is insufficient evidence to recommend for or against epidural steroid injections.	Weak for	( <u>199</u> , <u>205-209</u> )	Neither for nor against	Reviewed, New- replaced

e For additional information, see the VA/DoD Clinical Practice Guideline for the Use of Opioids in the Management of Chronic Pain. Available at: <a href="https://www.healthquality.va.gov/">https://www.healthquality.va.gov/</a>.

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Recommendation	2017 Strength of Recommendation	Evidence	2022 Strength of Recommendation	Recommendation Category
38. For patients with low back pain, we suggest against spinal cord stimulation.	Not applicable	( <u>210</u> )	Weak against	Reviewed, New- added
39. For patients with chronic low back pain, we suggest a multidisciplinary or interdisciplinary program. These programs should include at least one physical component and at least one other component of the biopsychosocial model (psychological, social, and/or occupational) used in an explicitly coordinated manner.	Weak for	( <u>211-218</u> )	Weak for	Reviewed, Amended

Abbreviations: CPG: clinical practice guideline; DoD: Department of Defense; VA: Department of Veterans Affairs

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# Appendix D: 2017 Recommendation Categorization Table

Table D-1. 2017 LBP CPG Recommendation Categorization Table a,b,c,d,e,f

2017 CPG Recommendation#	2017 CPG Recommendation Text	2017 CPG Strength of Recommen dation	2017 CPG Recommendation Category	2022 CPG Recommendation Category	2022 CPG 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	Reviewed, Amended	1
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	Reviewed, New-replaced	4
3	For patients with acute axial lowback pain (i.e., localized, non-radiating), we recommend against routinely obtaining imaging studies or invasive diagnostic tests.	Strong against	Reviewed, Amended	Reviewed, New-replaced	3
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	Reviewed, Amended	2

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<sup>&</sup>lt;sup>a</sup> 2017 CPG Recommendation # column: This indicates the recommendation number of the recommendation in the 2017 VA/DoD LBP CPG.

b 2017 CPG Recommendation Text column: This contains the wording of each recommendation from the 2017 VA/DoD LBP CPG.

c 2017 CPG Strength of Recommendation column: The 2017 VA/DoD LBP CPG used the GRADE approach to determine the strength of each recommendation. The strength of recommendations in the 2017 VA/DoD LBP CPG were: Strong for, Weak for, N/A, Weak against, or Strong against. "Neither for nor against" represents updated language for "N/A" used in the 2017 VA/DoD LBP CPG.

d 2017 CPG Recommendation Category column: This is the recommendation category assigned during the development of the 2017 VA/DoD LBP CPG. Refer to the Recommendation Categorization section for more information on the description of the categorization process and the definition of each category.

e 2022 CPG Recommendation Category column: This is the recommendation category assigned during the development of the 2022 VA/DoD LBP CPG. Refer to the Recommendation Categorization section for more information on the description of the categorization process and the definition of each category.

f 2022 CPG Recommendation # column: For recommendations that were carried forward to the 2017 VA/DoD LBP CPG, this column indicates the new recommendation(s) to which they correspond.

2017 CPG Recommendation#	2017 CPG Recommendation Text	2017 CPG Strength of Recommendation	2017 CPG Recommendation Category	2022 CPG Recommendation Category	2022 CPG 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.	Neither for nor against	Reviewed, New-added	Reviewed, New-replaced	3
6	For patients with chronic lowback 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	Reviewed, Deleted	-
7	For patients with chronic lowback pain, we suggest adding a structured education component, including pain neurophysiology, as part of a multicomponent selfmanagement intervention.	Weak for	Reviewed, New-added	Reviewed, New-replaced	6
8	For patients with chronic lowback pain, we recommend cognitive behavioral therapy.	Strong for	Reviewed, New-replaced	Reviewed, New-replaced	8
9	For patients with chronic lowback pain, we suggest mindfulness-based stress reduction.	Weakfor	Reviewed, New-replaced	Reviewed, New-replaced	12
10	For patients with acute low back pain, there is insufficient evidence to support the use of specific clinician-directed exercise.	Neither for nor against	Reviewed, New-replaced	Reviewed, New-replaced	9
11	For patients with chronic lowback pain, we suggest offering clinician-directed exercises.	Weakfor	Reviewed, New-replaced	Reviewed, New-replaced	9
12	For patients with acute or chronic low back pain, we suggest offering spinal mobilization/manipulation as part of a multimodal program.	Weakfor	Reviewed, New-replaced	Reviewed, New-replaced	10,11
13	For patients with acute low back pain, there is insufficient evidence to support the use of acupuncture.	Neither for nor against	Reviewed, New-replaced	Reviewed, Amended	35
14	For patients with chronic lowback pain, we suggest offering acupuncture.	Weakfor	Reviewed, New-replaced	Reviewed, Amended	34
15	For acute or chronic low back pain, there is insufficient evidence for or against the use of lumbar supports.	Neither for nor against	Reviewed, Amended	Reviewed, Amended	13
16	For patients with chronic lowback pain, we suggest offering an exercise program, which may include Pilates, yoga, and tai chi.	Weakfor	Reviewed, New-replaced	Reviewed, New-replaced	9,16

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2017 CPG Recommendation#	2017 CPG Recommendation Text	2017 CPG Strength of Recommendation	2017 CPG Recommendation Category	2022 CPG Recommendation Category	2022 CPG Recommendation#
17	For patients with low back pain, there is insufficient evidence to support the use of ultrasound.	Neither for nor against	Reviewed, New-added	Reviewed, New-replaced	17
18	For patients with low back pain, there is inconclusive evidence to support the use of transcutaneous electrical nerve stimulation (TENS).	Neither for nor against	Reviewed, New-added	Reviewed, New-replaced	17
19	For patients with low back pain, there is insufficient evidence to support the use of lumbar traction.	Neither for nor against	Reviewed, New-added	Reviewed, New-replaced	14
20	For patients with low back pain, there is insufficient evidence to support the use of electrical muscle stimulation.	Neither for nor against	Reviewed, New-added	Reviewed, Deleted	-
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	Reviewed, New-replaced	19
22	For patients with chronic lowback pain, we suggest offering treatment with duloxetine, with consideration of patient-specific risks.	Weak for	Reviewed, New-added	Reviewed, New-replaced	18
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	Reviewed, New-replaced	23
24	For patients with chronic lowback pain, we suggest against offering a non-benzodiazepine muscle relaxant.	Weak against	Reviewed, New-added	Reviewed, Not changed	24
25	For patients with low back pain, we recommend against benzodiazepines.	Strong against	Reviewed, New-replaced	Reviewed, Not changed	29
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	Not reviewed, Amended	28
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>g</sup>	Strong against	Reviewed, New-replaced	Reviewed, New-replaced	27

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 $<sup>{\</sup>tt g} \ For \ additional \ information, see the \ VA/DoD \ Clinical \ Practice \ Guideline \ for the \ Use \ of \ Opioids \ in \ the \ Management \ of \ Chronic \ Pain. \ Available \ at: \ \underline{\tt https://www.healthquality.va.gov/}.$ 

2017 CPG Recommendation#	2017 CPG Recommendation Text	2017 CPG Strength of Recommendation	2017 CPG Recommendation Category	2022 CPG Recommendation Category	2022 CPG Recommendation#
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.	Neither for nor against	Reviewed, New-replaced	Reviewed, Deleted	-
29	I recommend for or against the lise of time-limited (less than seven days) acetaminonnen. I		Reviewed, New-replaced	Reviewed, New-replaced	25
30	For patients with chronic lowback pain, we recommend against the chronic use of oral acetaminophen.		Reviewed, New-replaced	Reviewed, New-replaced	25
31	For the treatment of acute or chronic low backpain, 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.	Neither for nor against	Reviewed, New-replaced	Reviewed, Amended	20
32	For the treatment of low backpain, there is insufficient evidence to recommend for or against the use of topical preparations.	Neither for nor against	Reviewed, New-added	Reviewed, Amended	22
33	For the treatment of low back pain, there is insufficient evidence to recommend for or against nutritional, herbal, and homeopathic supplements.	Neither for nor against	Reviewed, New-added	Reviewed, New-replaced	30
34	For the long-term reduction of radicular lowback pain, non-radicular low back pain, or spinal stenosis, we recommend against offering spinal epidural steroid injections.	Strong against	Reviewed, New-added	Reviewed, Deleted	-
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.	Weakfor	Reviewed, New-added	Reviewed, New-replaced	37
36	For the treatment of low back pain, we suggest against offering intra-articular facet joint steroid injections.	Weak against	Reviewed, New-added	Reviewed, New-replaced	33
37	For patients with low back pain, there is inconclusive evidence to recommend for or against medial branch blocks and radiofrequency ablative denervation.	Neither for nor against	Reviewed, New-added	Reviewed, New-replaced	31, 33

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2017 CPG Recommendation#	2017 CPG Recommendation Text	2017 CPG Strength of Recommendation	2017 CPG Recommendation Category	2022 CPG Recommendation Category	2022 CPG 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.	Weakfor	Reviewed, New-replaced	Reviewed, Amended	39

Abbreviations: CPG: clinical practice guideline; DoD: Department of Defense; VA: Department of Veterans Affairs

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# Appendix E: Dosing for Select Pharmacologic Agentsa,b

Category	Generic	Starting Dose	Max/Day	Half-life (t½) (hrs)	
	Baclofen	5 mg TID	80 mg	~ 3.75	
	Cyclobenzaprine <sup>c</sup>	5 mg TID	30 mg	18	
	Metaxalone <sup>c</sup>	800 mg TID	3,200 mg	~ 9	
Muscle Relaxants	Methocarbamol <sup>c</sup>	1.5 gm TID – QID	8 gm (<3 days) 4.5 mg (>3 days)	1-2	
	Orphenadrine <sup>c</sup>	100 mg BID	200 mg	14-16	
	Tizanidine	2 – 4 mg TID	36 mg	2.5	
	Amitriptyline <sup>c</sup>	10 – 25 mg QHS	150 mg	13 – 36	
	Desipramine <sup>c</sup>	10 – 25 mg QHS	150 mg	15 – 24	
Antidepressants	Nortriptyline <sup>c</sup>	10 – 25 mg QHS	150 mg	14-51	
	Duloxetine <sup>c</sup>	20 – 30 mg QD	60 mg	~ 12	
	Venlafaxine ER	37.5 – 75 mg QD	225 mg	~ 11	
	Ibuprofen	400 mg q 4 – 6H	3200 mg	~ 2	
	Indomethacin	25 mg TID	200 mg	2.6 – 11.2	
	Ketoprofen	50 mg QID	300 mg	2-4	
	Ketorolac <sup>e</sup>	10 mg q 4 – 6H	40 mg	~ 5	
	Nabumetone	1,000 mg QD	2,000 mg	~ 24	
	Naproxen	250 mg BID	1,500 mg	12-17	
NSAIDsd	Diclofenac NA	50 – 75 mg BID	150 – 200 mg	~ 2	
	Piroxicam	20 mg QD	20 mg	50	
	Salsalate	1,000 mg TID	3,000 mg	~1	
	Sulindac	150mg BID	400 mg	7.8	
	Celecoxib	100 mg BID	400 mg	~ 11	
	Etodolac	200 mg q 6 – 8H	1,000 mg	6.4	
	Meloxicam	5 – 7.5 mg QD	15 mg	~15-22	

Dosing recommendations obtained from the FDA individual product prescribing information.

Listed in order of increased COX-2 selectivity, more selective at the bottom: (164, 222, 223)

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

- <sup>a</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.
- b For those already on long-term opioid therapy, see the VA/DoD Clinical Practice Guideline for the Use of Opioids in the Management of Chronic Pain. Available at: <a href="https://www.healthquality.va.gov/">https://www.healthquality.va.gov/</a>.
- <sup>c</sup> Use not recommended in patients >65 years of age per American Geriatrics Society 2015 Updated Beers Criteria. (224)
- d Avoid chronic use in the elderly unless other alternatives are not effective and patient can take a gastroprotective agent (proton pump inhibitor or misoprostol).
- e Indicated for short-term use only (up to 5 days in adults).

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

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# Appendix F: Glossary

Category	Term	Definition
	Acute LBP	LBP present for fewer than four weeks. Sometimes grouped with subacute LBP as symptoms present for fewer than 12 weeks.
	Cauda equina syndrome	Compression on nerve roots in the lumbosacral spine, usually due to a massive, centrally herniated disc, or severe lumbar spinal stenosis which can result in urinary retention or incontinence from loss of sphincter function, bilateral motor weakness of the lower extremities, and saddle anesthesia.
	Chronic LBP	LBP present for more than 12 weeks.
	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 numbness, paresthesia, or weakness) while walking or standing, relieved by sitting or spinal flexion. Associated with spinal stenosis.
	Non-radicular LBP	LBP that typically does not radiate past the knee.
	Non-specific LBP	LBP without signs of a serious underlying condition (such as cancer, infection, or CES), spinal stenosisor 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. Often called uncomplicated LBP.
General	Progressive neurologic deficit	Abnormal finding of altered function attributable to pathology of the nerves, spinal cord, or brain which shows evidence of worsening with serial examination. For example, decreased sensation in the skin that progresses to loss of sensation or muscle stretch reflexes that move from diminished to absent, are examples of progressive neurologic deficit.
Ğ	Radicular LBP	Pain in the back and lower limb, 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	Refers to impaired conduction along a spinal nerve or its roots. This can be diagnosed by clinical exam (loss of sensation, myotatic stretch reflexes, or strength) or via electrodiagnostic testing. Radiculopathy may or may not be accompanied by radicular pain.
	Referred pain	Pain that originates from one location but 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	Pain along the path of the sciatic nerve. Sciatica is a symptom rather than a condition. Often used interchangeably with radiculopathy.
	Spinal stenosis	Narrowing of the central spinal canal or neuroforamina, usually produced by degenerative changes – a combination of facet hypertrophy, disc bulge, and buckling or hypertrophy of the ligamentum flavum – but may also be congenital. Spinal stenosis describes a pathoanatomical phenomenon and may or may not present with symptoms like neurogenic claudication.
	Straight leg raise test	A procedure in which the hip is flexed with the knee extended to tension the L4-S1 nerve roots and reproduce a patient's lower extremity symptoms. A test is usually considered positive when the patient's symptoms are reproduced between 30 and 70 degrees of hip flexion. Reproduction of the patient's symptoms on testing of the unaffected legis considered a positive "crossed" straight leg raise test.
	Subacute LBP	LBP present for greater than or equal to four weeks and less than 12 weeks.

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Category	Term	Definition
	Acupuncture	An intervention consisting of the insertion of needles at strategic points on a body.
	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 healthcare professional.
	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, or a combination of the two.
	СВТ	An intervention that involves examining and changing cognitions and behaviors that perpetuate pain and using relaxation and exposure techniques to reduce symptom-related distress.
	MBSR	A structured intervention based on mindfulness (i.e., attending to the present moment, without judgment) with components of relaxation 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 or interdisciplinary program	An intervention that combines and coordinates physical, vocational, and behavioral/psychological components and is provided by multiple healthcare 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.
tions	Pilates	A system of exercise focusing on the relationship between stability and mobility designed to improve physical strength, flexibility, and posture.
Interventions	Progressive relaxation	A technique that involves the deliberate tensing and relaxing of muscles to facilitate the recognition and release of muscle tension.
Int	Qi gong	An ancient Chinese healing art, older than, and similar to tai chi, with a focus on cultivating the body's vital energy, or qi. It involves the coordination of the breath, posture, awareness, visualization, and focused movements. Qi gong may be a stationary or moving meditation.
	Self-care education materials	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.
	Self-care options	Interventions that can be readily implemented by patients without seeing a clinician or that can be implemented based on advice provided at a routine clinic visit.
	Spinal mobilization/ manipulation	Spinal mobilization is a low-velocity technique that does not involve a thrust and is performed within the joint's natural range of motion. Manual therapy in which a high-velocity, low-amplitude thrust is applied to the spine to reduce pain and improve quality and range of motion.
	Tai chi	A form of stylized, meditative exercise, characterized by methodically slow circular stretching movements and positions of bodily balance.
	TENS	Use of a small, battery-operated device to provide continuous electrical impulses via surface electrodes to provide 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 exist, each emphasizing different postures and techniques.

Abbreviations: CBT: cognitive behavioral therapy; CES: cauda equina syndrome; CPG: clinical practice guideline; LBP: low back pain; MBSR: mindfulness-based stress reduction; TENS: transcutaneous electrical nerve stimulation

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# Appendix G: Participant List

# Maj Danielle Anderson, DPT, DSc, OCS, FAAOMPT

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# Evan N. Steil, MD, MBA, MHA, FAAFP (Champion)

Family Physician

Defense Health Agency, Healthcare Risk

Management

Regional Health Command Europe, Primary Care

Service Line

Sembach, Germany

#### Rebecca Vogsland, DPT, OCS

Physical Therapy

Director, Headache Center of Excellence

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#### Joe C. Wilson, RN, CCM

Nurse Case Management

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## Appendix H: Literature Review Search Terms and Strategy

Table H-1. LBP Search Strategy for EMBASE with EMBASE.com syntax

KQ	Set#	Concept	Strategy
acute, with or I with or in	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
tts with a nic LBP, v no sis and cular pai	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 'lumbosacral spine'/exp OR ('low back' OR 'lower back' OR lumbar OR lumbosacral):ti
ılation - Adults with ac cute, or chronic LBP, wi ıt spinal stenosis and w without radicular pain	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
Population - Adults with acute, subacute, or chronic LBP, with or without spinal stenosis and with o without radicular pain	4	Combine population sets	#1 OR (#2 AND #3)
ests,	1	History	'medical history'/mj OR ((patient NEAR/2 history):ab,ti) 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)
m, diagnostic te atification tools ssments)	2	Physical Exam	'physical examination'/mj OR 'range of motion'/mj OR 'slump test'/mj OR 'straight leg raising test'/mj OR 'physical exam*':ab,ti OR 'flexion abduction and external rotation':ab,ti OR 'fabere':ab,ti OR 'facet load*':ab,ti OR kemp* OR ((hip* NEAR/3 clearing):ab,ti) OR laslette*:ab,ti OR ('sacroiliac joint':ab,ti AND 'clust*':ab,ti) OR ((neurolog* NEAR/3 (test* OR screen*)):ab,ti) OR 'range of motion':ab,ti OR 'slump test':ab,ti OR 'straight leg raise':ab,ti
KQ 1 (history, physical exam, diagnostic tests, screening tools, risk stratification tools, and other assessments)	3	Diagnostic Tests	'biological marker'/mj OR 'blood test'/mj OR 'computer assisted tomography'/mj OR 'diffusion weighted imaging'/mj OR 'diskography'/mj OR 'electromyography'/mj OR 'four dimensional computed tomography'/mj OR 'musculoskeletal diagnosis'/mj OR 'myelography'/mj OR 'nuclear magnetic resonance imaging'/mj OR 'single photon emission computer tomography'/mj OR 'spine radiography/mj OR 'thermography'/mj OR 'three dimensional imaging'/mj OR 'trigger point injection'/mj OR 'x ray'/mj OR ((diagnos* NEAR/2 (film* OR imag* OR scan*)):ab,ti) OR biomarker*:ab,ti OR ((comput* NEXT/1 tomogra*):ab,ti) OR 'ct scan*':ab,ti OR discogra*:ab,ti OR diskogra*:ab,ti OR electromyogr*:ab,ti OR 'electrophysiologic test*':ab,ti OR emg:ab,ti OR 'magnetic resonance':ab,ti OR mri*:ab,ti OR myelogr*:ab,ti OR radiograph*:ab,ti OR 'spect ct':ab,ti OR 'x-ray*':ab,ti OR xray*:ab,ti OR ((injection* NEAR/3 (facet OR 'trigger point*' OR triggerpoint* OR transforaminal)):ab,ti)

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KQ	Set#	Concept	Strategy
KQ1 (history, physical exam, diagnostic tests, screening tools, risk stratification tools, and other assessments) (cont.)	4	Screening Tools	'chronic pain acceptance questionnaire'/mj OR 'fear avoidance beliefs questionnaire'/mj OR 'minnesota multiphasic personality inventory 2 restructured form'/mj OR 'oswestry disability index'/mj OR 'pain anxiety symptoms scale'/mj OR 'pain catastrophizing scale'/mj OR 'pain self efficacy questionnaire'/mj OR 'patient health questionnaire 9'/mj OR 'patient reported outcomes measurement information system'/mj OR 'state-trait anger expression inventory'/mj OR 'state trait anxiety inventory'/mj OR 'chronic pain acceptance questionnaire':ab,ti OR 'fear avoidance beliefs questionnaire':ab,ti OR fabq:ab,ti OR fibromyalgianess:ab,ti OR 'fibromyalgia-ness':ab,ti OR 'minnesota multiphasic personality inventory':ab,ti OR mmpi:ab,ti OR 'optimal screening for prediction of referral and outcome':ab,ti OR ospro:ab,ti OR 'oswestry low back pain disability questionnaire':ab,ti OR 'oswestry disability index':ab,ti OR 'pain and impairment relationship scale':ab,ti OR 'pain anxiety symptoms scale':ab,ti OR 'pain catastrophizing scale':ab,ti OR 'pain self efficacy questionnaire':ab,ti OR ((pain NEAR/3 'enjoyment of life' NEAR/3 'general activity'):ab,ti) OR 'peg scale':ab,ti OR 'peg score':ab,ti OR 'patient health questionnaire':ab,ti OR phq:ab,ti OR 'patient reported outcomes measurement information system':ab,ti OR promis:ab,ti OR 'pain interference scale':ab,ti OR 'self-efficacy for rehabilitation':ab,ti OR ((tampa NEAR/3 kinesiophobia):ab,ti) OR ((waddell NEAR/3 sign*):ab,ti)
istory, p	5	Risk Stratification Tools	'orebro musculoskeletal pain questionnaire'/mj OR 'risk stratification'/mj OR 'start back screening tool'/mj OR 'start back tool'/mj OR 'keele start':ab,ti OR orebro:ab,ti OR ompq:ab,ti OR 'ömpq':ab,ti OR ((risk* NEAR/3 stratif*):ab,ti) OR 'start back':ab,ti
KQ1 (h risk	6	KQ 1 Interventions Combined with Population Set	#5 OR #6 OR #7 OR #8 OR #9
ical	1	Structured Education	'pain education'/exp OR 'back class*':ab,ti OR 'pain education':ab,ti OR 'pain neuroscience education':ab,ti OR 'patient education'/exp OR 'structured education':ab,ti OR 'therapeutic neuroscience education':ab,ti
clinician directed physical orkplace ergonomics)	2	Non-Clinician Directed Physical Activity	'aerobic exercise'/exp OR 'anaerobic exercise'/exp OR 'aquatic exercise'/exp OR 'circuit training'/exp OR 'exercise'/exp OR 'exercise intensity'/exp OR 'arm exercise'/exp OR 'exercise tolerance'/exp OR 'isokinetic exercise'/exp OR 'isometric exercise'/exp OR 'isotonic exercise'/exp OR 'kinesiotherapy'/exp OR 'leg exercise'/exp OR 'muscle exercise'/exp OR 'open kinetic chain exercise'/exp OR 'pilates'/exp OR 'plyometrics'/exp OR 'qigong'/exp OR 'resistance training'/exp OR 'static exercise'/exp OR 'stretching exercise'/exp OR 'tai chi'/exp OR 'yoga'/exp OR 'aquatic therap*':ab,ti OR exercis*:ab,ti OR pilates:ab,ti OR 'qi gong':ab,ti OR qigong:ab,ti OR 'tai chi':ab,ti OR yoga:ab,ti
on-clin work	3	Weight Loss	'weight reduction'/exp OR ((weight OR pound*) NEAR/2 (lose OR losing OR loss OR lost OR reduc* OR shed*)):ab,ti
tion, nc ss, and	4	Workplace Ergonomics	'body posture'/exp OR ergonomics/exp OR 'human factors engineering'/exp OR ergonomic*:ab,ti OR 'human factors engineering':ab,ti OR (((posture* OR postural) NEAR/3 (adjust* OR train*)):ab,ti)
KQ 2 (structured education, non- activity, weight loss, and wo	5	Complementary and Integrative Health (CIH) Self-Directed Self-Care Modalities	'acupressure'/exp OR 'acupuncture'/exp OR 'alternative medicine'/exp OR 'electroacupuncture'/exp OR 'integrative medicine'/exp OR 'massage'/exp OR 'meditation'/exp OR 'mindfulness'/exp OR 'mindfulness meditation'/exp OR 'self care'/exp OR acupuncture:ab,ti OR acupressure:ab,ti OR biofeedback:ab,ti OR 'complementary and integrative health':ab,ti OR 'complementary and integrative medicine':ab,ti OR 'guided imagery' OR hypnosis:ab,ti OR meditat*:ab,ti OR mindful*:ab,ti OR neurofeedback:ab,ti OR 'self-care':ab,ti OR 'self-directed':ab,ti OR 'self-massage':ab,ti OR (((alternative OR complementary OR integrat*) NEAR/2 (modalit* OR treat* OR therap*)):ab,ti)
¥	6	KQ 2 Combined Interventions	#11 OR #12 OR #13 OR #14 OR #15

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KQ	Set#	Concept	Strategy
	1	Cranial electrotherapy stimulation	'cranial electrotherapy stimulator'/expOR 'cranial electrotherapy stimulation'/de OR 'cranial electrotherapy stimulat*' OR 'cranial electrotherapy stimulat*' OR 'cranial-electro stimulat*' OR 'cranial electro stimulat*' OR 'cranial electrical stimulat*' OR 'Alpha-Stim' OR 'Alpha Stim' OR 'CES' OR ('ces' OR 'cranial electrotherapy stimulat*' OR 'cranial electrical stimulat*') NEAR/3 (device OR system OR apparatus OR 'headset' OR 'headphone*')
(St	2	Electrical stimulation	'electrostimulation'/de OR 'electrostimulation' OR 'electrical stimulator' OR 'estim' OR 'e stim' OR 'e-stim' OR (electro OR electrical OR electric* OR 'e') NEAR/4 (stim OR stimulation OR stimulator OR stimulat*)
entior	3	Cryotherapy	'cryotherapy'/exp OR 'cryotherapy device'/de OR 'cryotherap*' OR (cyro AND (therapy OR therapeutic OR thereap*))
jicinterv	4	Cupping	'cupping'/de OR 'cupping therapy'/exp OR 'dry cupping' OR 'wet cupping' OR 'cupping*' OR cupping NEAR/4 (therap* OR treatment* OR manipulat* OR wet OR dry OR flash OR fire)
acolog	5	Electroacupuncture	'electroacupuncture'/de OR 'electroacupuncture' OR ((electro OR electrical OR electric* OR 'e') NEAR/3 (acupuncture OR acupoint))
arm T	6	Hot pack	'hot pack'/de OR 'hot pack' OR ((heat* OR hot) NEAR/3 (pad* OR pack*))
on-ph	7	Low-level laser therapy	'low level laser therapy'/de OR 'low level laser therapy' OR (('low level laser' OR 'low-level laser') NEAR/2 (therap* OR treat*))
andne	8	Lumbar support and traction	'lumbar support'/de OR 'lumbar traction*' OR 'traction therapy'/exp
ical	9	Massage	'massage'/exp OR 'massage' OR massage OR massag*
n-surgi	10	Microcurrent	'microcurrent therapy'/de OR 'microcurrent therapy' OR (microcurrent* NEAR/3 (therap* OR treat*))
ssive noi	11	Osteopathic/spinal manipulation/mobilization	'osteopathic manipulation'/de OR 'osteopathic manipulation' OR 'spine manipulation'/de OR 'spine manipulation' OR ((osteopathic OR spine OR spinal OR spin*) NEAR/3 (manipulat* OR mobiliz*))
KQ 3 (passive non-surgical and non-pharmacologic interventions)	12	Transcutaneous electrical nerve stimulation	transcranial electrical stimulation'/exp OR 'transcranial electrical stimulation' OR 'transcranial alternating current stimulation' OR 'transcranial direct current stimulation' OR 'transcranial random noise stimulation' OR 'TENS' OR 'ETNS' OR (transcranial AND (electr* OR electrical OR electric OR 'direct current*') AND (stimulat* OR stimulation OR stimulator*))
	13	Therapeutic ultrasound	'ultrasound therapy'/exp OR 'ultrasound therapy' OR 'therapeutic ultrasound' OR ((ultrasound* OR ultrasonic) NEAR/3 (therap* OR therapy OR therapies or therapeutic OR therapeutic*))
	14	Trigger points	'trigger point'/de OR 'trigger point*' OR 'triggerpoint*'
	15	Combine KQ3 Interventions	#17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30
KQ 4 (active non- surgical and non- pharmacological interventions)	1	KQ 4 Interventions	'core stability exercise'/exp OR 'core stabilization exercise'/exp OR 'physiotherapy'/exp OR 'resistance training'/exp OR 'stretching exercise'/exp OR 'group exercise'/exp OR 'mckenzie therapy'/exp OR 'mckenzie exercise'/exp OR 'mechanical diagnosis and therapy'/exp OR 'motor control exercise'/exp OR (((back OR core OR lumbar OR spine OR spinal) NEAR/3 (exercise* OR stabiliz* OR strength* OR train*)):ab,ti) OR 'physical therap*':ab,ti OR 'directional preference':ab,ti OR 'group exercis*':ab,ti OR ((mckenzie NEAR/3 (exercis* OR method* OR therap*)):ab,ti) OR 'mechanical diagnosis and therapy':ab,ti OR 'motor control exercis*':ab,ti OR stretch*:ab,ti

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KQ	Set#	Concept	Strategy
	1	General Pharmacotherapy Terms	'drug therapy'/mj OR 'non prescription drug'/exp OR ('drug therap*' OR medication* OR medicine* OR 'over the counter' OR OTC OR pharmacotherap*):ti
KQ 5 (prescription/OTC pharmacotherapy treatment)	2	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 'minaserin'/exp OR 'milnacipran'/exp OR 'mirtazapine'/exp OR 'monoamine oxidase inhibitor'/exp OR 'nefazodone'/exp OR 'noradrenalin update inhibitor' 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 'tricyclic antidepressant agent'/exp OR 'triple reuptake inhibitor'/exp OR 'venlafaxine'/exp OR 'vilazodone'/exp OR 'vortioxetine'/exp OR ((amfebutamone:ab,ti OR amitriptyline:ab,ti) AND amoxapine:ab,ti) OR anafranil:ab,ti OR antidepres*:ab,ti OR asendin:ab,ti OR aventyl:ab,ti OR bupropion:ab,ti OR brintellix:ab,ti OR celexa:ab,ti OR cymbalta:ab,ti OR desyrel:ab,ti OR lexomilnacipran:ab,ti OR maoi:ab,ti OR 'mao inhibitor*':ab,ti OR norpramin:ab,ti OR levomilnacipran:ab,ti OR pamelor:ab,ti OR paroxetine:ab,ti OR paxil:ab,ti OR protriptyline:ab,ti OR protriptyline:ab,ti OR protriptyline:ab,ti OR protriptyline:ab,ti OR protriptyline:ab,ti OR serzone:ab,ti OR protriptyline:ab,ti OR soriab,ti OR sinequan:ab,ti OR soriab,ti OR vivactil:ab,ti OR trimipramine:ab,ti OR trimipramine:ab,ti OR trintellix:ab,ti OR vivactil:ab,ti OR wellbutrin:ab,ti OR zoloft:ab,ti OR zonalon:ab,ti OR vivactil:ab,ti OR wellbutrin:ab,ti OR zoloft:ab,ti OR zonalon:ab,ti OR zoloft:ab,ti OR zonalon:ab,ti OR zoloft:ab,ti OR zonalon:ab,ti OR zoloft:ab,ti OR zonalon:ab,ti OR zoloft:ab,ti OR zoloft:ab,ti OR zonalon:ab,ti OR zoloft:ab,ti
(Q.5 (prescription/OTC	3	Anticonvulsants	'anticonvulsive agent'/exp OR carbamazepine/exp OR ethosuximide/exp OR etiracetam/exp OR felbamate/exp OR harkoseride/exp OR lamotrigine/exp OR oxcarbazepine/exp OR rufinamide/exp OR tiagabine/exp OR topiramate/exp OR 'valproic acid'/exp OR zonisamide/exp OR 'anti convuls*':ab,ti OR 'anti seizure*':ab,ti OR anticonvuls*:ab,ti OR antiseizure*:ab,ti OR carbamazepine:ab,ti OR ethosuximide:ab,ti OR etiracetam:ab,ti OR felbamate:ab,ti OR harkoseride:ab,ti OR lacosamide:ab,ti OR lamotrigine:ab,ti OR levetiracetam:ab,ti OR lyrica:ab,ti OR oxcarbazepine:ab,ti OR pregabalin:ab,ti OR rufinamide:ab,ti OR tiagabine:ab,ti OR topiramate:ab,ti OR 'valproic acid':ab,ti OR zonisamide:ab,ti
±	4	Cannabinoids	'cannabidiol'/exp OR 'cannabinoid'/exp OR 'dronabinol'/exp OR cannabidiol*:ab,ti OR cannabinoid*:ab,ti OR cannabinoid*:ab,ti OR cannabigerol:ab,ti OR cannabidivarin:ab,ti OR cannabichromene:ab,ti OR dronabinol:ab,ti OR epidiolex:ab,ti OR tetrahydrocannabin*:ab,ti OR tetrahydrocannabivarin:ab,ti
	5	Ergocalciferol	'ergocalciferol'/exp OR ergocalciferol:ab,ti
	6	Gabapentinoids	gabapentin/exp OR 'gabapentin enacarbil'/exp OR pregabalin/exp OR 'gabapentin enacarbil':ab,ti OR gabapentinoid*:ab,ti OR gabapentin:ab,ti OR gralise:ab,ti OR pregabalin:ab,ti
	7	Lidocaine patch	'lidocaine'/exp OR lidocaine:ab,ti
	8	Monoclonal antibodies	'monoclonal antibody'/exp OR (monoclonal NEAR/2 antibod*):ab,ti

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KQ	Set#	Concept	Strategy
nt) (cont.)	9	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' OR 'neuromuscular depolarizing agent'/exp OR 'orphenadrine'/exp OR 'tizanidine'/exp OR amrix:ab,ti OR baclofen:ab,ti OR benzodiazepine*:ab,ti OR carisoprodol:ab,ti OR chlorzoxazone:ab,ti OR cyclobenzaprine:ab,ti OR dantrium:ab,ti OR dantrolene:ab,ti OR diazepam:ab,ti OR flexeril:ab,ti OR lioresal:ab,ti OR mephenamine:ab,ti OR metaxalone:ab,ti OR methocarbamol:ab,ti OR 'muscle relax*':ab,ti OR orphenadrin:ab,ti OR orphenadrine:ab,ti OR paraflex:ab,ti OR parafon:ab,ti OR robaxin:ab,ti OR skelaxin:ab,ti OR tizanidine:ab,ti OR zanaflex:ab,ti
treatmer	10	Nerve growth factors	'fasinumab'/exp OR 'fulranumab'/exp OR 'nerve growth factor'/exp OR 'tanezumab'/exp OR fasinumab:ab,ti OR fulranumab:ab,ti OR 'nerve growth factor*':ab,ti OR tanezumab:ab,ti
KQ 5 (prescription/OTC pharmacotherapy treatment) (cont.)	11	Non-opioid analgesics	'acetylsalicylic acid'/exp OR celecoxib/exp OR 'choline magnesium '/exp OR 'choline magnesium trisalicylate'/exp OR diclofenac/exp OR diflunisal/exp OR etodolac/exp OR flurbiprofen/exp OR ibuprofen/exp OR ketoprofen/exp OR meclofenamate/exp OR meloxicam/exp OR naproxen/exp OR 'nonsteroid antiinflammatory agent'/exp OR oxaprozin/exp OR paracetamol/exp OR piroxicam/exp OR 'salicylic acid derivative'/exp OR salsalate/exp OR sulindac/exp OR tolmetin/exp OR trilisate/exp OR acetaminophen:ab,ti OR aleve:ab,ti OR aspirin:ab,ti OR clinoril:ab,ti OR daypro:ab,ti OR diclofenac:ab,ti OR disalcid:ab,ti OR feldene:ab,ti OR ibuprofen:ab,ti OR lodine:ab,ti OR mobic:ab,ti OR naproxen:ab,ti OR 'non-opioid*:ab,ti OR nonopioid*:ab,ti OR roudis:ab,ti OR oruvail:ab,ti OR nonsteroid*:ab,ti OR paracetamol:ab,ti OR salicylate*:ab,ti OR 'salicylic acid':ab,ti OR solaraze:ab,ti OR tolectin:ab,ti OR trilisate:ab,ti OR tylenol:ab,ti OR voltaren:ab,ti
KQ 5 (pres	12	Non-prescription/ OTC medication (topical/oral)	'non prescription drug'/expOR 'non prescription':ab,tiOR 'nonprescription':ab,tiOR 'over the counter':ab,ti
	13	Prostaglandins (E1)	'prostaglandin'/exp OR prostaglandin*:ab,ti
	14	Psychotropic medications	'psychotropic agent'/exp OR 'anti-anxiety':ab,ti OR 'anti-psychotic*':ab,ti OR 'mood stabilizer*':ab,ti OR psychoactive:ab,ti OR psychodynamic:ab,ti OR psychopharmaceutic:ab,ti OR psychostimulant*:ab,ti OR psychotropic*:ab,ti OR tranquilizer*:ab,ti
	15	KQ 5 Interventions Combined	#33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41 OR #42 OR #43 OR #44 OR #45 OR #46

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KQ	Set#	Concept	Strategy
	1	Benzodiazepines	'benzodiazepine derivative'/exp OR 'diazepam'/exp OR benzodiazepine*:ab,ti
KQ 6 (opioids and benzodiazepines)	2	Opioids	'acetylmethadol'/exp OR 'alfentanil'/exp OR 'alphaprodine'/exp OR 'betacasomorphin' OR 'buprenorphine'/exp OR 'carfentanil'/exp OR 'codeine'/exp OR 'deltorphin'/exp OR 'dextropropoxyphene'/exp OR 'dezocine'/exp OR 'dihydrocodeine'/exp OR 'dihydrocodeine'/exp OR 'dihydrocodeine'/exp OR 'dihydromorphine'/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 'phenoperidine'/exp OR 'pirinitramide'/exp OR 'remifentanil'/exp OR 'sufentanil'/exp OR 'tapentadol'/exp OR 'tilidine'/exp OR 'tramadol'/exp OR 'trimeperidine'/exp OR alfenta:ab,ti OR buprenex:ab,ti OR buprenorphine:ab,ti OR dalgan:ab,ti OR darvon:ab,ti OR demerol:ab,ti OR dicodid:ab,ti OR dilaudid:ab,ti OR dolophine:ab,ti OR duragesic:ab,ti OR 'hydrostat ir':ab,ti OR 'levo-droman':ab,ti OR meperidine:ab,ti OR methadose:ab,ti OR 'methadyl acetate':ab,ti OR narcotic*:ab,ti OR nubain:ab,ti OR numphan:ab,ti OR oxyfast:ab,ti OR oxyfast:ab,ti OR oxyfast:ab,ti OR percolone:ab,ti OR promedol:ab,ti OR propoxyphene:ab,ti OR oxyfast:ab,ti OR oxyir:ab,ti OR percolone:ab,ti OR ultiva:ab,ti OR ultram:ab,ti OR roxicodone:ab,ti OR talwin:ab,ti OR ultiva:ab,ti OR ultram:ab,ti
	3	KQ 6 Combined Interventions	#48 OR #49
ıts)	1	Homeopathic Preparations	'herbaceous agent'/exp OR 'homeopathic agent'/exp OR herb* OR homeopathic* OR (((diet* OR herb* OR holistic* OR homeopath* OR nutrition* OR omega*) NEAR/2 supplement*):ti,ab)
nen	2	Nutraceuticals	'nutraceutical'/exp OR nutraceutical*:ti,ab
KQ 7 (diet, nutritional, herbal, and homeopathic supplements)	3	Supplements	'alpha tocopherol'/exp OR 'aloe vera'/exp OR 'aloe vera extract'/exp OR 'angelica sinensis'/exp OR 'arnica'/exp OR 'arnica montana'/exp OR 'arnica montana extract'/exp OR 'ascorbic acid'/exp OR 'cannabidiol'/exp OR 'cannabinoid'/exp OR 'capsicum frutescens'/exp OR 'cayenne pepper'/exp OR 'cod liver oil'/exp OR 'comfrey'/exp OR 'commiphora'/exp OR 'curcumin'/exp OR 'curcuma longa extract'/exp OR 'docosahexaenoicacid'/exp OR 'fish oil'/exp OR 'flavonoid'/exp OR 'ginger'/exp OR 'ginger extract'/exp OR 'harpagophytum'/exp OR 'harpagophytum extract'/exp OR 'icosapentaenoic acid'/exp OR 'lavender oil'/exp OR 'lavender'/exp OR 'menthol'/exp OR 'myrrh'/exp OR 'omega 3 fatty acid'/exp OR 'omega 6 fatty acid'/exp OR 'peppermint'/exp OR 'peppermint oil'/exp OR 'resveratrol'/exp OR 'salix alba'/exp OR 'salix extract'/exp OR 'tanacetum parthenium'/exp OR 'tanacetum parthenium extract'/exp OR 'tanacetum parthenium'/exp OR 'tanacetum parthenium extract'/exp OR 'turmeric'/exp OR 'vitamin d'/exp OR aloe:ti,ab OR 'alpha tocopherol':ti,ab OR 'angelica sinensis':ti,ab OR arnica:ti,ab OR 'ascorbic acid':ti,ab OR capsaicin:ti,ab OR capsaicin:ti,ab OR capsaicin:ti,ab OR capsaicin:ti,ab OR commiphora:ti,ab OR cayenne:ti,ab OR ((devil* NEXT/1 claw):ti,ab OR capsaicin:ti,ab OR commiphora:ti,ab OR derocapsentaenoic acid':ti,ab OR flavonoid*:ti,ab OR menthol:ti,ab OR myrrh:ti,ab OR harpagophytum:ti,ab OR 'h. procumbens':ti,ab OR menthol:ti,ab OR myrrh:ti,ab OR lavender:ti,ab OR 'melaleuca alternifolia':ti,ab OR menthol:ti,ab OR myrrh:ti,ab OR 'salix alba':ti,ab OR 'salix extract':ti,ab OR 's. alba':ti,ab OR 'tanacetum parthenium':ti,ab OR 'tea tree':ti,ab OR 'salix extract':ti,ab OR 's. alba':ti,ab OR 'tanacetum parthenium':ti,ab OR 'tea tree':ti,ab OR tetrahydrocannabinol:ti,ab OR 'tanacetum parthenium':ti,ab OR 'tea tree':ti,ab OR tetrahydrocannabinol:ti,ab OR 'tanacetum parthenium':ti,ab OR 'tea tree':ti,ab OR 'tetrahydrocannabinol:ti,ab OR 'vitamin e':ti,ab OR 'willow bark':ti,ab OR 'vitamin c':ti,ab OR 'vitamin d':ti,ab OR 'vitamin d

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KQ	Set#	Concept	Strategy
KQ7 (diet, nutritional, herbal, and homeopathic supplements) (cont.)	4	Diets	'arachidonic acid'/exp OR 'diet therapy'/exp OR ((('anti inflam*' OR antiinflam* OR 'arachidonic acid' OR 'low arachidonic') NEXT/1 diet*):ti,ab) OR (((diet* OR nutrition*) NEAR/3 therap* OR treat*):ti,ab)
KQ7 (diet, nutritional, herbal and homeopathic supplements) (cont.)	5	KQ 7 Interventions Combined	#51 OR #52 OR #53 OR #54
KQ8 (non-surgical invasive therapies)	1	Non-surgical invasive therapies	'acupuncture'/exp OR 'biological product'/exp OR 'botulinum toxin'/exp OR 'brain depth stimulation'/exp OR 'dorsal root ganglion stimulation'/exp OR 'dry needling'/exp OR 'epidural anesthesia'/exp OR 'epidural drug administration'/exp OR 'interspinous spacer'/exp OR 'intraspinal drug administration'/exp OR 'nerve block'/exp OR 'nerve stimulation'/exp OR 'nerve oR 'spinal drug administration'/exp OR 'nerve block'/exp OR 'representation'/exp OR 'readiofrequency ablation'/exp OR 'spinal anesthesia'/exp OR 'spinal cord stimulation'/exp OR 'spinal cord stimulator'/exp OR 'spinal spacer'/exp OR 'spinal cord stimulation'/exp OR 'spinal cord stimulator'/exp OR 'spinal spacer'/exp OR 'spinal cord stimulation'/exp OR 'transcutaneous electrical nerve oR 'transcranial magnetic stimulation'/exp OR 'transcutaneous electrical nerve stimulation'/exp OR 'trigger point injection'/exp OR 'viscosupplementation'/exp OR acupuncture:ab,ti OR biologic:ab,ti OR biologics:ab,ti OR 'biological product*':ab,ti OR 'botulinum toxin':ab,ti OR botox OR 'deep brain':ab,ti OR 'dorsal root ganglion stimulation':ab,ti OR 'dry needling':ab,ti OR (epidural NEAR/3 inject*) OR (facet NEAR/3 block*) OR neuromodulat*:ab,ti OR (nerve* NEAR/3 block*) OR 'platelet-rich plasma':ab,ti OR prp:ab,ti OR ((radiofreq* OR rf) NEAR/2 ablat*):ab,ti OR rfa:ab,ti OR ((interspinous OR lumbar OR spine OR spinal) NEAR/3 spacer*):ab,ti OR ((lumbar OR spine OR spinal) NEAR/3 (inject* OR transplant*)):ab,ti OR 'peripheral nerve stimulat*':ab,ti OR 'prolo therapy':ab,ti OR 'trigger point*' NEAR/3 inject*):ab,ti OR viscosupplementation:ab,ti OR 'percutaneous electrical nerve stimulation':ab,ti OR viscosupplementation:ab,ti OR 'percutaneous electrica
KQ 9 (cross-modality combination therapy)	4	Cross-modality combination therapy	'cognitive functional therapy'/exp OR 'outpatient care'/exp OR 'cognitive functional therapy':ab,ti OR (((combin* OR multimodal) NEAR/3 program*):ab,ti) OR therap*:ab,ti OR treatment*:ab,ti OR cft:ab,ti OR ((coordinat* NEAR/3 rehab*):ab,ti) OR ((function* NEAR/3 restor*):ab,ti) OR frp:ab,ti OR 'intensive outpatient program*':ab,ti OR iop:ab,ti OR 'intensive pain rehabilitation':ab,ti OR iprp:ab,ti OR 'interdisciplinary pain rehabilitation':ab,ti OR ((outpatient* NEAR/3 (care OR program* OR therap*)):ab,ti) OR 'whole health':ab,ti OR ((pain* NEAR/3 (rehab* OR program*)):ab,ti) OR 'whole person care':ab,ti OR 'Exploration of the Veteran's Mission Aspiration Purpose':ab,ti OR 'personal health plan':ab,ti
KQ 10 (behavioral health in terventions)	1	Behavioral health interventions	'acceptance and commitment therapy'/exp OR 'behavioral health'/exp OR 'biofeedback'/exp OR 'biofeedback therapy'/exp OR 'behaviortherapy'/exp OR 'cognitive therapy'/exp OR 'cognitive behavioral therapy'/exp OR 'feedback system'/exp OR 'mindfulness based stress reduction'/exp OR 'mindfulness based stress reduction program'/exp OR 'meditation'/exp OR 'mental health care'/exp OR 'mindfulness'/exp OR 'mindfulness meditation'/exp OR 'patient education/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 'acceptance and commitment therapy':ab,ti OR 'behavioral health*':ab,ti OR biofeedback:ab,ti OR cbt:ab,ti OR meditation:ab,ti OR mindfulness:ab,ti OR 'mindfulness based stress reduction':ab,ti OR mbsr:ab,ti OR 'patient education':ab,ti OR psychotherap*:ab,ti OR relax*:ab,ti OR (((cognitive* OR behavior* OR 'mental health' OR psychotherap*:ab,ti OR relax*:ab,ti OR ((cognitive* OR behavior* OR 'mental health' OR psych*) NEAR/2 (counsel* OR psychother* OR therap* OR treat*)):ab,ti)

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KQ	Set#	Concept	Strategy
KQ 11 (assessmentand treatment of physical and/or mental health conditions, pain catastrophizing, or psychosocial stressors)	1	Physical and/or mental health conditions, pain catastrophizing, or psychosocial stressors	'anxiety'/exp OR 'anxiety disorder'/exp OR 'attention deficit disorder'/exp OR 'catastrophizing'/exp OR 'childhood trauma'/exp OR 'childhood trauma questionnaire'/exp OR 'chronic pain'/exp OR 'columbia suicide severity rating scale'/exp OR 'depression'/exp OR 'divorce'/exp OR 'family stress'/exp OR 'financial stress'/exp OR 'major depression'/exp OR 'mental disease'/exp OR 'mental stress'/exp OR 'minnesota multiphasic personality inventory'/exp OR 'orebro musculoskeletal pain questionnaire'/exp OR 'pain catastrophizing scale'/exp OR 'pain duration'/exp OR 'pain self efficacy questionnaire'/exp OR 'patient health questionnaire 9'/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 'start back screening tool'/exp OR 'start back tool'/exp OR 'trauma exposure'/exp OR 'traumatic brain injury'/exp OR 'unemployment'/exp OR anxiety:ab,ti OR anxious*:ab,ti OR 'attention deficit':ab,ti OR adhd:ab,ti OR 'c-ssrs':ab,ti OR catastrophiz*:ab,ti OR columbia suicide severity rating scale':ab,ti OR death*:ab,ti OR depress*:ab,ti OR 'disability status':ab,ti OR divorce*:ab,ti OR 'fear and avoidance beliefs questionnaire':ab,ti OR fabq:ab,ti OR (((financial* OR money)) NEAR/3 (distress* OR hardship* OR instability OR stress* OR unstable)):ab,ti) OR 'job loss':ab,ti OR 'keele start':ab,ti OR 'minnesota multiphasic personality inventory':ab,ti OR mmpi:ab,ti OR 'optimal screening for prediction of referral and outcome':ab,ti OR 'orebro musculoskeletal pain questionnaire':ab,ti OR ospro:ab,ti OR ((pain* NEAR/3 (chronic OR duration OR length)):ab,ti) OR 'pain and impairment relationship scale':ab,ti OR 'pain catastrophizing scale':ab,ti OR 'pain and impairment relationship scale':ab,ti OR 'pain catastrophizing scale':ab,ti OR 'pain self-efficacy questionnaire':ab,ti OR 'patient health questionnaire':ab,ti OR 'pain self-efficacy questionnaire':ab,ti OR 'patient health questionnaire':ab,ti OR '
KQ 12 (technology-based modalities for self-management)	1	Technology-based modalities for self- management	'augmented reality'/exp OR 'augmented reality system'/exp OR 'health coaching'/exp OR 'internet'/exp OR 'mhealth'/exp OR 'mixed reality'/exp OR 'mobile application'/exp OR 'mobile health application'/exp OR 'mobile health technology'/exp OR 'mobile phone'/exp OR 'online monitoring'/exp OR 'smartphone'/exp OR 'smartphone application'/exp OR 'social media'/exp OR 'technology based intervention'/exp OR 'teleconsultation'/exp OR 'telehealth'/exp OR 'telemedicine'/exp OR 'telemonitoring'/exp OR telerehabilitation/exp OR 'telehealth'/exp OR 'video game'/exp OR 'video game console'/exp OR 'virtual reality'/exp OR 'virtual reality system'/exp OR 'wii balance board'/exp OR 'augmented reality':ab,ti OR cellphone*:ab,ti OR 'ehealth*:ab,ti OR ehealth*:ab,ti OR 'extended reality':ab,ti OR 'm health*:ab,ti OR kinect:ab,ti OR 'mhealth':ab,ti OR microsoft:ab,ti OR 'mixed reality':ab,ti OR 'mobile app*:ab,ti OR 'mobile device*:ab,ti OR 'mobile health*:ab,ti OR 'mobile phone*:ab,ti OR mobile phone:ab,ti OR nintendo:ab,ti OR online:ab,ti OR phone*:ab,ti OR remote*:ab,ti OR 'smart phone*:ab,ti OR smartphone*:ab,ti OR telehealth*:ab,ti OR teletherap*:ab,ti OR telemonitor*:ab,ti OR telerehab*:ab,ti OR telephone:ab,ti OR 'text messag*':ab,ti OR 'virtual reality' OR virtually:ab,ti OR 'web based':ab,ti OR Wii:ab,ti OR xbox:ab,ti
bine Ition &	1	Combine all interventions	#10 OR #16 OR #31 OR #32 OR #47 OR #50 OR #55 OR #56 OR #57 OR #58 OR #59
Combine Population & Interventions	2	Population and Interventions Combined	#4 AND #61

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KQ	Set#	Concept	Strategy
		Limit to results added to the database between October 1, 2016, and February 1, 2021	[1-10-2016]/sd NOT [2-2-2021]/sd
tegy		Limit to English language publications Exclude animal, experimental, and studies focusing on children	AND [english]/lim  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 menopaus*:ti OR mice:ti OR mouse:ti OR neonat*:ti OR newborn*:ti OR paediatric*:ti OR pediatric*:ti OR pregnan*:ti OR premenstrual:ti OR postmenopaus*:ti OR puerperal:ti OR rabbit*:ti OR rat:ti OR rats:ti OR reply:ti OR 'school age*':ti OR school-age*':ti OR scoliosis:ti OR teen*:ti OR toddler*:ti OR
Limits & hedges applied to each search strategy		Remove undesired publication and study types (e.g., case reports, conferences, editorials)	withdrawn:ti OR 'year-old':ti OR young*:ti OR youth*:ti)  NOT (abstract:nc OR annual:nc OR 'book'/exp OR 'case study'/exp OR 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 protocol:ti OR sessions:nc OR 'short survey'/exp OR symposium:nc OR [conference abstract]/lim OR [conference paper]/lim OR [conference review]/lim OR [editorial]/lim OR [letter]/lim OR [note]/lim OR [short survey]/lim OR comment:ti OR book:pt OR 'case report'/de OR 'case report':ti OR 'a case':ti OR 'a patient':ti OR 'year old':ti,ab)
edges applie		Hedge to identify meta-analyses and SRs (applied to all KQs) Hedge to identify	AND ([cochrane review]/lim OR [systematic review]/lim OR [meta analysis]/lim OR cochrane OR 'meta analysis' OR 'meta analyses' OR metaanlysis OR metaanalyses OR search* OR systematic:ti)  AND ('randomized controlled trial'/de OR random*:ab,ti OR nct* OR [randomized
Limits & he		RCTs (applied to all KQs) Hedge to identify observational studies (applied to KQ 1)	controlled trial]/lim)  AND (('cohort analysis' OR 'comparative study'/exp OR 'controlled study'/exp OR 'evaluation study'/de OR 'longitudinal study'/de OR 'major clinical study'/de OR 'observational study'/de OR 'prospective study'/de OR 'retrospective study'/de OR 'treatment outcome'/de) OR ('between groups' OR 'case control*' OR cohort* OR
		·	compar* OR 'control group*' OR 'controlled study' OR 'controlled trial' OR 'cross over' OR crossover OR 'double blind' OR 'double blinded' OR longitudinal OR 'matched controls' OR (observational NEXT/3 study) OR placebo* OR prospective OR retrospective OR random* OR sham):ti,ab OR (versus OR vs):ti)
		Hedge to identify diagnostic accuracy studies (applied to KQ 1)	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))

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 $Table\,H-2.\,General\,LBP\,Search\,Strategy\,for\,PsycINFO\,with\,OVID\,syntax$ 

Set#	Concept	Strategy
1	Lumbar Spine	exp lumbar spinal cord/ or (facet or "low back" or "lower back" or lumbar or lumbosacral or zygapophysial).ti,ab.
2	Low Back Pain and Defined Lumbar Indications	exp back pain/or (degenerative disc* or degenerative disk* or hernia* or pain* or spondylolisthesis or stenotic).ti,ab.
3	Population Combine	1 and 2
4	Study Types	exp meta analysis/ or (meta* or random* or systematic).ti. or (meta analys* or meta-analys* or meta-analys* or meta-analys* or randomized controlled trial* or systematic* or systematic review*).ti,ab.
5	Diagnostic Studies	diagnosis/ or maximum likelihood/ or prediction/ or screening tests/ or test sensitivity/ or test specificity/ or (accuracy or area under the curve or diagnos* or false negative or false positive or likelihood function* or likelihood ratio* or observer variation or predictive value or probability or receiver operating characteristic or reproducibility or sensitivity or specificity or test*).ti,ab.
6	Combined Study Types	4 or 5
7	Combine Population & Study Types	3 and 6
8	Pharmacologic interventions	exp analgesic drugs/ OR exp anticonvulsive drugs/ OR exp antidepressant drugs/ OR antihypertensive drugs/ OR exp benzodiazepines/ OR exp mood stabilizers/ OR narcotic antagonists/ OR exp narcotic drugs/ OR exp sedatives/ OR exp serotonin agonists/ OR exp tranquilizing drugs/ OR "drug therapy"/ OR exp psychopharmacology/ OR ((anti ADJ1 (anxiety OR depress* OR convuls* OR epileptic* OR hypertensive*)) OR antianxiety OR antidepress* OR anticonvuls* OR antiepileptic* OR antihypertensive* OR anxiolytic* OR neuroleptic* OR (serotonin ADJ2 (reuptake OR uptake) ADJ1 inhibitor*) OR SNRI* OR SSRI* OR tricyclic*).ti,ab. OR (drug OR drugs OR medication* OR pharmacologic* OR pharmacotherap*).ti
9	Combine intervention sets	6 OR 7
10	Combine population and intervention sets	5 AND 8
11	Apply general hedges	See General Hedges at the end of this table
	Exclude studies focusing on children	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 menstrua* 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 aged" OR school-age OR school-aged OR scoliosis OR teen* OR toddler* OR withdrawn OR year-old OR young* OR youth*).ti.
	Limit to results added to the database since the prior literature search	limit # to yr="2016 - 2021"

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### Appendix I: Alternative Text Descriptions of Algorithm

The following outline narratively describes the Diagnosis and Treatment of Low Back Pain algorithm. An explanation of the purpose of the algorithm and description of the various shapes used within the algorithm can be found in the <u>Algorithm</u> section. The sidebars referenced within this outline can also be found in the <u>Algorithm</u> section.

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

- 1. Module A begins with Box 1, in the shape of a rounded rectangle: "Adult patient with LBP"
- 2. Box 1 connects to Box 2, in the shape of a rectangle: "Perform a focused history and physical examination, evaluating: Duration of symptoms; Red flags for potentially serious conditions; Presence and severity of radiculopathy and/or neurologic deficits; Psychosocial risk factors (see Recommendation 4)
- 3. Box 2 connects to Box 3, in the shape of a hexagon, which asks the question: "Are there progressive or otherwise serious neurologic deficits or other red flags (e.g., signs, symptoms, history) for serious conditions? (See **Sidebars 1** and **2**)"
  - a. If the answer is "Yes" to Box 3, then continue to Box 4, in the shape of a rectangle: "Perform appropriate evaluation for serious conditions (see Sidebar 1 and Recommendations 1 3)"
    - i. Box 4 connects to Box 5, in the shape of a hexagon, which asks the question: "Are serious conditions identified?"
      - 1. If the answer is "Yes" to Box 5, then continue to Box 6, in the shape of a rectangle: "Address any serious conditions as indicated; consider specialty consultation"
      - 2. If the answer is "No" to Box 5, then continue to Box 7, in the shape of a hexagon, which asks the question: "Is back pain chronic (≥3 months)?"
  - b. If the answer is "No" to Box 3, then continue to Box 7, in the shape of a hexagon, which asks the question: "Is back pain chronic ≥3 months?"
    - i. If the answer is "Yes" to Box 7, then continue to Box 8, in the shape of a hexagon, which asks the question: "Has the patient had appropriate treatment?"
      - 1. If the answer is "Yes" to Box 8, then continue to Box 9, in the shape of an oval: "Go to **Module B**, **Box 18** (assess treatment response)"
      - 2. If the answer is "No" to Box 8, then continue to Box 10, in the shape of a rectangle: "Engage the patient in a shared decision making process to develop individualized care plan: Advise about self care; Discuss non-invasive treatment options: Pharmacologic, Non-pharmacologic, Watchful waiting; Arrive at shared decision regarding treatment"
    - ii. If the answer is "No" to Box 7, then continue to Box 10, in the shape of a rectangle: "Engage the patient in a shared decision making process to develop individualized care plan: Advise about self care; Discuss non-invasive treatment

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options: Pharmacologic, Non-pharmacologic, Watchful waiting; Arrive at shared decision regarding treatment"

- 4. Box 10 connects to Box 11, in the shape of a hexagon, which asks the question: "Did the patient choose pharmacologic and/or non-pharmacologic treatment?"
  - a. If the answer is "Yes" to Box 11, then continue to Box 12, in the shape of a hexagon, which asks the question: "Is the patient on treatment?"
    - i. If the answer is "Yes" to Box 12, then continue to Box 13, in the shape of an oval: "Go to **Module B**, **Box 18** (assess treatment response)"
    - ii. If the answer is "No" to Box 12, then continue to Box 14, in the shape of an oval: "Go to **Module B**, **Box 16** (untreated LBP)"
  - b. If the answer is "No" to Box 11, then continue to Box 15, in the shape of a rectangle: "Continue self-care; reassess in primary care as appropriate"

#### B. Module B: Management of Low Back Pain

- 1. Module B begins with Box 16 in the shape of a rounded rectangle: "LBP patient not on treatment"
- 2. Box 16 connects to Box 17, in the shape of a rectangle: "Initiate treatment (see Sidebar 3)"
- 3. Box 17 connects to Box 18, in the shape of a rectangle: "Assess response as appropriate"
- 4. Box 18 connects to Box 19, in the shape of a hexagon, which asks the question: "Was the back pain improved or resolved?"
  - a. If the answer is "Yes" to Box 19, then continue to Box 20, in the shape of a rectangle: "Continue self-care; reassess as appropriate"
  - b. If the answer is "No" to Box 19, then continue to Box 21, in the shape of a hexagon, which asks the question: "Are there progressive or otherwise serious neurologic deficits or other red flags (e.g., signs, symptoms, history) for serious conditions? (see **Sidebars 1** and **2**)"
    - i. If the answer is "Yes" to Box 21, then continue to Box 22, in the shape of a rectangle: "Performappropriate evaluation for serious conditions (see Sidebar 1 and Recommendations 1-3)"
      - 1. Box 22 connects to Box 23, in the shape of a hexagon, which asks the question: "Are serious conditions identified?"
        - a. If answer is "Yes" to Box 23, then continue to Box 24, in the shape of a rectangle: "Address any serious conditions as indicated; consider specialty consultation"
        - b. If the answer is "No" to Box 23, then continue to Box 25, in the shape of a hexagon, which asks the question: "Are there functional deficits (e.g., significant impairment of social, occupational, or educational function?"

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- ii. If the answer is "No" to Box 21, then continue to Box 25, in the shape of a hexagon, which asks the question: "Are there functional deficits (e.g., significant impairment of social, occupational, or educational function?"
  - 1. If the answer is "Yes" to Box 25, then continue to Box 26, in the shape of a rectangle: "Consider a multidisciplinary or interdisciplinary program, or refer to specialist"
  - 2. If the answer is "No" to Box 25, then continue to Box 27, in the shape of a rectangle: "Consider changing pharmacologic and/or non-pharmacologic interventions (if patient is on opioids, see VA/DoD Opioids CPG<sup>a</sup>)"
    - a. Box 27 connects to Box 18.

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# Appendix J: Abbreviations

Abbreviation	Definition
ACT	acceptance and commitment therapy
AE	adverse event
AHRQ	Agency for Healthcare Research and Quality
ВМІ	body mass index
CAD	coronary artery disease
СВТ	cognitive behavioral therapy
СВТ-СР	cognitive behavioral therapy for chronic pain
CES	cauda equinasyndrome
CI	confidence interval
СІН	complementary and integrative health
CNS	central nervous system
COI	conflicts of interest
COR	contracting officer's representative
COX-2	cyclooxygenase-2
CPG	clinical practice guideline
CRP	C-reactive protein
СТ	computed tomography
CV	cardiovascular
CVD	cardiovascular disease
DHA	Defense Health Agency
DoD	Department of Defense
EBPWG	Evidence-Based Practice Work Group
ED	emergencydepartment
ESI	epidural steroid injection
ESR	erythrocyte sedimentation rate
FABERE	flexion, abduction, external rotation, and extension
FDA	Food and Drug Administration
GI	gastrointestinal
GRADE	Grading of Recommendations Assessment, Development and Evaluation
HEC	Health Executive Committee
ЮМ	Institute of Medicine
ΙП	intention-to-treat
IV	intravenous
JSE	joint safety event
KQ	key question
LBP	low back pain
LBPI	low back pain intensity
LR	likelihoodratio

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Abbreviation	Definition
LSS	lumbar spinal stenosis
mAb	monoclonal antibodies
MAP	mission, aspiration, purpose
MBI	mindfulness-based intervention
MBR	multidisciplinary biopsychosocial rehabilitation
MBSR	mindfulness-based stress reduction
MCID	minimum clinically important difference
MD	mean difference
MDD	major depressive disorder
MDT	mechanical diagnosis and therapy
mHealth	mobile health
MMPI-2	Minnesota Multiphasic Personality Inventory-2
MMPI-2RF	Minnesota Multiphasic Personality Inventory-2-Restructured Form
MRI	magnetic resonance imaging
NAM	National Academy of Medicine
NICE	National Institute for Health and Care Excellence
NRS	numeric rating scale
NSAID	nonsteroidal anti-inflammatory drugs
OA	osteoarthritis
OMPSQ	Orebro Musculoskeletal Pain Screening Questionnaire
OMT	osteopathic manipulative treatment
OSPRO	Optimal Screening for Prediction of Referral and Outcome
ОТС	over the counter
PCP	primary care providers
PCS	Pain Catastrophizing Scale
PEG	Pain, Enjoyment of Life and GeneralActivity
PHP	personal health plan
PHQ	Patient Health Questionnaire
PICOTS	population, intervention, comparison, outcome, timing and setting
PNE	pain neuroscience education
PRP	platelet-rich plasma
PSEQ	Pain Self Efficacy Questionnaire
PT	physical therapy
QALY	quality-adjusted life year
QBDS	Quebec Back Pain Disability Scale
QoL	quality of life
RCT	randomized controlled trial
RFA	radiofrequency ablation denervation
RMDQ	Roland-Morris Disability Questionnaire
RPOA	rapidly progressive osteoarthritis

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Abbreviation	Definition
RR	risk ratio
SC	subcutaneous
SCS	spinal cord stimulation
SF-36	36-Item Short Form Survey
SI	sacroiliac
SMD	standardized mean difference
SMT	spinal manipulative therapy
SNRI	serotonin and norepinephrine reuptake inhibitors
SR	systematic review
SSRI	selective serotonin reuptake inhibitors
SUD	substance use disorder
TCAs	tricyclic antidepressants
TENS	transcutaneous electrical nerve stimulation
TSK	Tampa Scale for Kinesiophobia
U.S.	United States
USPSTF	United States Preventive Services Task Force
VA	Department of Veterans Affairs
VAS	visual analog scale
VHA	Veterans Health Administration
WH	whole health
WPAI	Work Productivity and Activity Impairment Questionnaire

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#### **References**

- U.S. Department of Veterans Affairs/Department of Defense Health Executive Committee (HEC). Evidence based practice work group charter [updated January 9, 2017]. Available from: www.healthquality.va.gov/documents/EvidenceBasedPracticeWGCharter123020161.pdf.
- 2. Koes BW, van Tulder MW, Thomas S. Diagnosis and treatment of low back pain. BMJ. 2006;332(7555):1430-4. Epub 2006/06/17. doi: 10.1136/bmj.332.7555.1430. Pub Med PMID: 16777886; Pub Med Central PMCID: PMC1479671.
- 3. Deyo RA, Weinstein JN. Low back pain. N Engl J Med. 2001;344(5):363-70. Epub 2001/02/15. doi: 10.1056/nejm200102013440508. PubMed PMID: 11172169.
- 4. O'Sullivan P, Caneiro JP, O'Keeffe M, O'Sullivan K. Unraveling the complexity of low back pain. J Orthop Sports Phys Ther. 2016;46(11):932-7. Epub 2016/11/03. doi: 10.2519/jospt.2016.0609. PubMed PMID: 27802794.
- 5. Chou R, Deyo R, Friedly J, Skelly A, Hashimoto R, Weimer M, et al. AHRQ comparative effectiveness reviews. Noninvasive treatments for low back pain. Rockville (MD): Agency for Healthcare Research and Quality (US); 2016.
- 6. Mokdad AH, Ballestros K, Echko M, Glenn S, Olsen HE, Mullany E, et al. The state of US health, 1990-2016: Burden of diseases, injuries, and risk factors among US states. JAMA. 2018;319(14):1444-72. Epub 2018/04/11. doi: 10.1001/jama.2018.0158. PubMed PMID: 29634829; PubMed Central PMCID: PMC5933332.
- 7. Hartvigsen J, Hancock MJ, Kongsted A, Louw Q, Ferreira ML, Genevay S, et al. What low back pain is and why we need to pay attention. Lancet. 2018;391(10137):2356-67. Epub 2018/03/27. doi: 10.1016/s0140-6736(18)30480-x. Pub Med PMID: 29573870.
- 8. Lucas JW, Connor EM, Bose J. Back, lower limb, and upper limb pain among U.S. Adults, 2019. NCHS Data Brief. 2021(415):1-8. Epub 2021/09/03. PubMed PMID: 34473621.
- 9. Liddle SD, Pennick V. Interventions for preventing and treating low-back and pelvic pain during pregnancy. Cochrane Database Syst Rev. 2015;2015(9):Cd001139. Epub 2015/10/01. doi: 10.1002/14651858.CD001139. pub4. PubMed PMID: 26422811; PubMed Central PMCID: PMC7053516.
- 10. Dieleman JL, Cao J, Chapin A, Chen C, Li Z, Liu A, et al. US health care spending by payer and health condition, 1996-2016. JAMA. 2020;323(9):863-84. Epub 2020/03/04. doi: 10.1001/jama.2020.0734. PubMed PMID: 32125402; PubMed Central PMCID:PMC7054840
- 11. Kalichman L, Cole R, Kim DH, Li L, Suri P, Guermazi A, et al. Spinal stenosis prevalence and association with symptoms: The Framingham study. Spine J. 2009;9(7):545-50. Epub 2009/04/29. doi: 10.1016/j.spinee.2009. 03.005. PubMed PMID: 19398386; PubMed Central PMCID:3775665.
- 12. Berry JA, Elia C, Saini HS, Miulli DE. A review of lumbarradiculopathy, diagnosis, and treatment. Cureus. 2019; 11(10):e5934. Epub 2019/12/04. doi: 10.7759/cureus.5934. PubMed PMID: 31788391; PubMed Central PMCID: PMC6858271.
- 13. Nahin RL. Severe pain in Veterans: The effect of age and sex, and comparisons with the general population. J Pain. 2017;18(3):247-54. Epub 2016/11/26. doi: 10.1016/j.jpain.2016.10.021. PubMed PMID: 27884688; PubMed Central PMCID:PMC5337168.
- 14. Zelaya CE BP, Moy E. Crude and age-adjusted percentage and percent distribution of chronic pain among adults aged 20 and over, by Veteran status and other selected characteristics: United States, 2015-2018: National Center for Health Statistics 2020.
- 15. Absolute and relative morbidity burdens attributable to various illnesses and injuries, active component, U.S. Armed Forces, 2020. MSMR. 2021;28(6):2-9. Epub 2021/06/23. PubMed PMID: 34155889.

February 2022 Page 125 of 141

- 16. Clark LL, Hu Z. Diagnoses of low back pain, active component, U.S. Armed Forces, 2010-2014. MSMR. 2015; 22(12):8-11. Epub 2016/01/05. PubMed PMID: 26726722.
- 17. U.S. Department of Veteran Affairs, Department of Defense. Guideline for guidelines: Veterans Health Administration, Office of Quality & Performance, Evidence Review Subgroup [updated January 29, 2019]. Available from: http://www.healthquality.va.gov/policy/index.asp.
- 18. Ransohoff DF, Pignone M, Sox HC. How to decide whether a clinical practice guideline is trustworthy. JAMA. 2013;309(2):139-40. Epub 2013/01/10. doi: 10.1001/jama.2012.156703. PubMed PMID: 23299601.
- 19. Andrews JC, Schünemann HJ, Oxman AD, Pottie K, Meerpohl JJ, Coello PA, et al. GRADE guidelines: 15. Going from evidence to recommendation-determinants of a recommendation's direction and strength. J Clin Epidemiol. 2013;66(7):726-35. Epub 2013/04/11. doi: 10.1016/j.jclinepi.2013.02.003. PubMed PMID: 23570745.
- 20. Andrews J, Guyatt G, Oxman AD, Alderson P, Dahm P, Falck-Ytter Y, et al. GRADE guidelines: 14. Going from evidence to recommendations: The significance and presentation of recommendations. J Clin Epidemiol. 2013; 66(7):719-25. Epub 2013/01/15. doi: 10.1016/j.jclinepi.2012.03.013. PubMed PMID: 23312392.
- 21. 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. Epub 2006/12/07. doi: 10.1186/1478-4505-4-22. PubMed PMID: 17147811; PubMed Central PMCID: Pmc1697808.
- 22. Guyatt GH, Oxman AD, Kunz R, Atkins D, Brozek J, Vist G, et al. GRADE guidelines: 2. Framing the question and deciding on important outcomes. J Clin Epidemiol. 2011;64(4):395-400. Epub 2011/01/05. doi: 10.1016/j.jclinepi.2010.09.012. PubMed PMID: 21194891.
- 23. Newberry SJ, Ahmadzai N, Motala A, Tsertsvadze A, Maglione M, Ansari MT, 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.
- 24. U.S. Preventive Services Task Force. Standards for guideline development. June 2018.
- 25. National Institute for Health and Care Excellence. The guidelines manual. London: National Institute for Health and Care Excellence, 2012.
- 26. 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. Epub 2014/06/13. doi: 10.1186/1748-5908-9-72. PubMed PMID: 24919856; PubMed Central PMCID: Pmc4067507.
- 27. Financial relationships between VHA health care professionals and industry: U.S. Department of Veterans Affairs, Veterans Health Administration [updated November 24, 2014]. Available from: <a href="https://www.ethics.va.gov/docs/policy/VHA">https://www.ethics.va.gov/docs/policy/VHA</a> Handbook 1004 07 Financial Relationships.pdf.
- 28. Clinical practice guidelines we can trust. Washington, DC: National Academies Press, 2011.
- 29. Robinson JH, Callister LC, Berry JA, Dearing KA. Patient-centered care and adherence: Definitions and applications to improve outcomes. J Am Acad Nurse Pract. 2008;20(12):600-7. Epub 2009/01/06. doi: 10.1111/j.1745-7599.2008.00360.x. PubMed PMID: 19120591.
- 30. Stewart M, Brown JB, Donner A, McWhinney IR, Oates J, Weston WW, et al. The impact of patient-centered care on outcomes. J Fam Pract. 2000;49(9):796-804. Epub 2000/10/14. PubMed PMID: 11032203.
- 31. National Learning Consortium. Shared decision making 2013. Available from: <a href="https://www.healthit.gov/sites/default/files/nlc\_shared\_decision\_making\_fact\_sheet.pdf">https://www.healthit.gov/sites/default/files/nlc\_shared\_decision\_making\_fact\_sheet.pdf</a>.
- 32. Institute of Medicine. Crossing the quality chasm: A new health system for the 21st century. Washington DC: National Academies Press, 2001.

February 2022 Page 126 of 141

- 33. Nieminen LK, Pyysalo LM, Kankaanpää MJ. Prognostic factors for pain chronicity in low back pain: A systematic review. Pain Rep. 2021;6(1):e919. Epub 2021/05/14. doi: 10.1097/pr9.000000000000919. PubMed PMID: 33981936; PubMed Central PMCID:PMC8108595.
- 34. Watrous JR, McCabe CT, Jones G, Farrokhi S, Mazzone B, Clouser MC, et al. Low back pain, mental health symptoms, and quality of life among injured service members. Health Psychol. 2020;39(7):549-57. Epub 2020/05/15. doi: 10.1037/hea0000850. PubMed PMID: 32406726.
- 35. Society for Medical Decision Making Committee on Standardization of Clinical Algorithms. Proposal for clinical algorithm standards. Med Decis Making. 1992;12(2):149-54. Epub 1992/04/01. PubMed PMID: 1573982.
- 36. Galliker G, Scherer DE, Trippolini MA, Rasmussen-Barr E, LoMartire R, Wertli MM. Low back pain in the emergency department: Prevalence of serious spinal pathologies and diagnostic accuracy of red flags. Am J Med. 2020;133(1):60-72.e14. Epub 2019/07/07. doi:10.1016/j.amjmed.2019.06.005. PubMed PMID: 31278933.
- 37. Jarvik JG, Deyo RA. Diagnostic evaluation of low back pain with emphasis on imaging. Ann Intern Med. 2002;137(7):586-97. Epub 2002/10/02. doi: 10.7326/0003-4819-137-7-200210010-00010. PubMed PMID: 12353946.
- 38. Enthoven WT, Geuze J, Scheele J, Bierma-Zeinstra SM, Bueving HJ, Bohnen AM, et al. Prevalence and "red flags" regarding specified causes of back pain in older adults presenting in general practice. Phys Ther. 2016; 96(3):305-12. Epub 2015/07/18. doi: 10.2522/ptj.20140525. PubMed PMID: 26183589.
- 39. Downie A, Williams CM, Henschke N, Hancock MJ, Ostelo RW, de Vet HC, et al. Red flagsto screen for malignancy and fracture in patients with low back pain: Systematic review. BMJ. 2013;347:f7095. Epub 2013/12/18. doi: 10.1136/bmj.f7095. PubMed PMID: 24335669; PubMed Central PMCID:PMC3898572
- 40. Deyo RA, Diehl AK. Cancer as a cause of back pain: Frequency, clinical presentation, and diagnostic strategies. J Gen Intern Med. 1988;3(3):230-8. Epub 1988/05/01. doi: 10.1007/bf02596337. PubMed PMID: 2967893.
- 41. Vroomen PC, de Krom MC, Knottnerus JA. Predicting the outcome of sciatica at short-term follow-up. Br J Gen Pract. 2002;52(475):119-23. Epub 2002/03/13. PubMed PMID: 11887877; PubMed Central PMCID:PMC1314232.
- 42. Chou R, Fu R, Carrino JA, Deyo RA. Imaging strategies for low-back pain: Systematic review and meta-analysis. Lancet. 2009;373(9662):463-72. Epub 2009/02/10. doi:10.1016/s0140-6736(09)60172-0. PubMed PMID: 19200918.
- 43. Jacobs JC, Jarvik JG, Chou R, Boothroyd D, Lo J, Nevedal A, et al. Observational study of the downstream consequences of inappropriate MRI of the lumbar spine. J Gen Intern Med. 2020;35(12):3605-12. Epub 2020/09/30. doi: 10.1007/s11606-020-06181-7. PubMed PMID: 32989711; PubMed Central PMCID: PMC7728897.
- 44. Lemmers GPG, van Lankveld W, Westert GP, van der Wees PJ, Staal JB. Imaging versus no imaging for low back pain: A systematic review, measuring costs, healthcare utilization and absence from work. Eur Spine J. 2019;28(5):937-50. Epub 2019/02/24. doi: 10.1007/s00586-019-05918-1. PubMed PMID: 30796513.
- 45. Rihn JA, Lee JY, Khan M, Ulibarri JA, Tannoury C, Donaldson WF, 3rd, 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). 2007;32(14):1555-60. Epub 2007/06/19. doi: 10.1097/BRS.0b013e318067dc55. PubMed PMID: 17572627.
- 46. Jarvik JG, Hollingworth W, Martin B, Emerson SS, Gray DT, Overman S, et al. Rapid magnetic resonance imaging vs radiographs for patients with low back pain: A randomized controlled trial. JAMA. 2003; 289(21): 2810-8. Epub 2003/06/05. doi: 10.1001/jama.289.21.2810. PubMed PMID: 12783911.

February 2022 Page 127 of 141

- 47. Lurie JD, Birkmeyer NJ, Weinstein JN. Rates of advanced spinal imaging and spine surgery. Spine (Phila Pa 1976). 2003;28(6):616-20. Epub 2003/03/19. doi: 10.1097/01.brs.0000049927.37696.dc. PubMed PMID: 12642771.
- 48. Pinheiro MB, Ferreira ML, Refshauge K, Maher CG, Ordoñana JR, Andrade TB, et al. Symptoms of depression as a prognostic factor for low back pain: A systematic review. Spine J. 2016;16(1):105-16. Epub 2015/11/03. doi: 10.1016/j.spinee.2015.10.037. PubMed PMID: 26523965.
- 49. Shaw WS, Means-Christensen AJ, Slater MA, Webster JS, Patterson TL, Grant I, et al. Psychiatric disorders and risk of transition to chronicity in men with first onset low back pain. Pain Med. 2010;11(9): 1391-400. Epub 2010/08/26. doi: 10.1111/j.1526-4637.2010.00934.x. PubMed PMID: 20735749.
- 50. Cherkin D, Balderson B, Wellman R, Hsu C, Sherman KJ, Evers SC, et al. Effect of low back pain risk-stratification strategy on patient outcomes and care processes: The match randomized trial in primary care. J Gen Intern Med. 2018;33(8):1324-36. Epub 2018/05/24. doi: 10.1007/s11606-018-4468-9. Pub Med PMID: 29790073; Pub Med Central PMCID:PMC6082187.
- 51. Glattacker M, Heyduck K, Jakob T. Yellowflags as predictors of rehabilitation outcome in chronic lowback pain. Rehabil Psychol. 2018;63 (3):408-17. Epub 2018/07/20. doi: 10.1037/rep0000200. PubMed PMID: 30024205.
- 52. Hampel P, Köpnick A, Roch S. Psychological and work-related outcomes after inpatient multidisciplinary rehabilitation of chronic low back pain: A prospective randomized controlled trial. BMC Psychol. 2019;7(1):6. Epub 2019/02/17. doi: 10.1186/s40359-019-0282-3. PubMed PMID: 30770763; PubMed Central PMCID: PMC6377771.
- 53. Karran EL, McAuley JH, Traeger AC, Hillier SL, Grabherr L, Russek LN, et al. Can screening instruments accurately determine poor outcome risk in adults with recent onset low back pain? A systematic review and meta-analysis. BMC Med. 2017;15(1):13. Epub 2017/01/20. doi: 10.1186/s12916-016-0774-4. PubMed PMID 28100231; PubMed Central PMCID: PMC5244583.
- 54. Løchting I, Garratt AM, Storheim K, Werner EL, Grotle M. The impact of psychological factors on condition-specific, generic and individualized patient reported outcomes in low back pain. Health Qual Life Outcomes. 2017;15(1):40. Epub 2017/02/23. doi: 10.1186/s12955-017-0593-0. PubMed PMID: 28222741; PubMed Central PMCID:PMC5319018.
- 55. Trinderup JS, Fisker A, Juhl CB, Petersen T. Fear avoidance beliefs as a predictor for long-term sick leave, disability and pain in patients with chronic low back pain. BMC Musculoskelet Disord. 2018;19(1):431. Epub 2018/12/05. doi: 10.1186/s12891-018-2351-9. PubMed PMID: 30509231; PubMed Central PMCID: PMC6278039.
- 56. Zackova M, Aspide R, Braghittoni A, Zenesini C, Palandri G. Yellowflag on prognostic factors for non-specific chronic lowback pain patients subjected to mini-invasive treatment: A cohort study. Eur Spine J. 2020; 29(8):1879-86. Epub 2020/06/05. doi: 10.1007/s00586-020-06475-8. PubMed PMID: 32495278.
- 57. Keele University Impact Accelerator Unit. Start back. Available from: https://startback.hfac.keele.ac.uk/research/.
- 58. Brown G. The örebro musculoskeletal pain questionnaire. Occupational Medicine. 2008;58(6):447-8. doi: 10.1093/occmed/kgn077.
- 59. Sullivan MJL, Bishop SR, Pivik J. The pain catastrophizing scale: Development and validation. Psychological Assessment. 1995;7(4):524-32. doi: 10.1037/1040-3590.7.4.524.
- 60. Nicholas MK. The pain self-efficacy questionnaire: Taking pain into account. Eur J Pain. 2007;11(2):153-63. Epub 2006/02/01. doi: 10.1016/j.ejpain.2005.12.008. PubMed PMID: 16446108.

February 2022 Page 128 of 141

- 61. Miller R, Kori S, Todd D. The Tampa Scale: A measure of kinesiophobia. Clin J Pain. 1991;7(1):51-2
- 62. Maas ET, Juch JN, Ostelo RW, Groeneweg JG, Kallewaard JW, Koes BW, et al. Systematic review of patient history and physical examination to diagnose chronic low back pain originating from the facet joints. Eur J Pain. 2017;21(3):403-14. Epub 2016/10/11. doi: 10.1002/ejp.963. PubMed PMID: 27723170.
- 63. Mekhail N, Saweris Y, Sue Mehanny D, Makarova N, Guirguis M, Costandi S. Diagnosis of sacroiliac joint pain: Predictive value of three diagnostic clinical tests. Pain Pract. 2021;21(2):204-14. Epub 2020/09/24. doi: 10.1111/papr.12950. PubMed PMID: 32965780.
- 64. González Espinosa de Los Monteros FJ, Gonzalez-Medina G, Ardila EMG, Mansilla JR, Expósito JP, Ruiz PO. Use of neurodynamic or orthopedic tension tests for the diagnosis of lumbar and lumbosacral radiculopathies: Study of the diagnostic validity. Int J Environ Res Public Health. 2020;17 (19). Epub 2020/10/01. doi: 10.3390/ijerph17197046. PubMed PMID: 32993094; PubMed Central PMCID: PMC7579046.
- 65. Tawa N, Diener I, Louw Q, Rhoda A. Correlation of the self-reported Leeds assessment of neuropathic symptoms and signs score, clinical neurological examination and MR imaging in patients with lumbo-sacral radiculopathy. BMC Neurol. 2019;19(1):107. Epub 2019/05/31. doi: 10.1186/s12883-019-1333-3. PubMed PMID: 31146710; PubMed Central PMCID:PMC6542141.
- 66. Tawa N, Rhoda A, Diener I. Accuracy of clinical neurological examination in diagnosing lumbo-sacral radiculopathy: A systematic literature review. BMC Musculoskelet Disord. 2017;18(1):93. Epub 2017/02/25. doi: 10.1186/s12891-016-1383-2. PubMed PMID: 28231784; PubMed Central PMCID: PMC5324296.
- 67. Young S, Aprill C, Laslett M. Correlation of clinical examination characteristics with three sources of chronic low back pain. Spine J. 2003;3 (6):460-5. Epub 2003/11/12. doi: 10.1016/s1529-9430(03)00151-7. Pub Med PMID: 14609690.
- 68. Laslett M, McDonald B, Aprill CN, Tropp H, Oberg B. Clinical predictors of screening lumbar zygapophyseal joint blocks: Development of clinical prediction rules. Spine J. 2006;6(4):370-9. Epub 2006/07/11. doi: 10.1016/j.spinee.2006.01.004. PubMed PMID: 16825041.
- 69. Manchikanti L, Pampati V, Fellows B, Bakhit CE. Prevalence of lumbar facet joint pain in chronic low back pain. Pain Physician. 1999;2(3):59-64. Epub 2006/08/15. PubMed PMID: 16906217.
- 70. Manchikanti L, Pampati V, Fellows B, Baha AG. The inability of the clinical picture to characterize pain from facet joints. Pain Physician. 2000;3(2):158-66. Epub 2006/08/15. PubMed PMID: 16906195.
- 71. Revel ME, Listrat VM, Chevalier XJ, Dougados M, N'Guyen MP, Vallee C, et al. Facet joint block for low back pain: Identifying predictors of a good response. Arch Phys Med Rehabil. 1992; 73(9):824-8. Epub 1992/09/01. PubMed PMID: 1387521.
- 72. Revel M, Poiraudeau S, Auleley GR, Payan C, Denke A, Nguyen M, et al. Capacity of the clinical picture to characterize lowback pain relieved by facet joint anesthesia. Proposed criteria to identify patients with painful facet joints. Spine (Phila Pa 1976). 1998;23(18):1972-6; discussion 7. Epub 1998/10/21. doi: 10.1097/00007632-199809150-00011. PubMed PMID: 9779530.
- 73. Laslett M, Oberg B, Aprill CN, McDonald B. Zygapophysial joint blocks in chronic low back pain: A test of Revel's model as a screening test. BMC Musculoskelet Disord. 2004;5:43. Epub 2004/11/18. doi: 10.1186/1471-2474-5-43. PubMed PMID: 15546487; PubMed Central PMCID: PMC534802.
- 74. Saueressig T, Owen PJ, Diemer F, Zebisch J, Belavy DL. Diagnostic accuracy of clusters of pain provocation tests for detecting sacroiliac joint pain: Systematic review with meta-analysis. J Orthop Sports Phys Ther. 2021; 51(9):422-31. Epub 2021/07/03. doi: 10.2519/jospt.2021.10469. Pub Med PMID: 34210160.
- 75. Straube S, Harden M, Schröder H, Arendacka B, Fan X, Moore RA, 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

February 2022 Page 129 of 141

- reviewand meta-analysis. Pain. 2016;157(10):2160-72. Epub 2016/06/04. doi: 10.1097/j.pain. 0000000000000640. PubMed PMID: 27257858; PubMed Central PMCID: PMC5028160 the end of this article.
- 76. Parreira P, Heymans MW, van Tulder MW, Esmail R, Koes BW, Poquet N, et al. Back schools for chronic non-specific low back pain. Cochrane Database Syst Rev. 2017;8(8):Cd011674. Epub 2017/08/05. doi: 10.1002/14651858.CD011674.pub2. PubMed PMID: 28770974; PubMed Central PMCID: PMC6483296.
- 77. Davidson M, Keating JL, Eyres S. A low back-specific version of the sf-36 physical functioning scale. Spine (Phila Pa 1976). 2004;29(5):586-94. Epub 2004/05/07. doi: 10.1097/01.brs.0000103346.38557.73. PubMed PMID: 15129079.
- 78. Ostelo RW, Deyo RA, Stratford P, Waddell G, Croft P, Von Korff M, et al. Interpreting change scores for pain and functional status in low back pain: Towards international consensus regarding minimal important change. Spine (Phila Pa 1976). 2008;33(1):90-4. Epub 2008/01/01. doi: 10.1097/BRS.0b013e31815e3a10. PubMed PMID: 18165753.
- 79. Gardner T, Refshauge K, McAuley J, Hübscher M, Goodall S, Smith L. Combined education and patient-led goal setting intervention reduced chronic low back pain disability and intensity at 12 months: A randomised controlled trial. Br J Sports Med. 2019;53 (22):1424-31. Epub 2019/02/28. doi: 10.1136/bjsports-2018-100080. PubMed PMID: 30808666.
- 80. Wood L, Hendrick PA. A systematic review and meta-analysis of pain neuroscience education for chronic low back pain: Short-and long-termoutcomes of pain and disability. Eur J Pain. 2019;23(2):234-49. Epub 2018/09/05. doi: 10.1002/ejp.1314. PubMed PMID: 30178503.
- 81. Woby SR, Roach NK, Urmston M, Watson PJ. Psychometric properties of the tsk-11: A shortened version of the Tampa Scale for kinesiophobia. Pain. 2005;117(1-2):137-44. Epub 2005/08/02. doi: 10.1016/j.pain.2005. 05.029. PubMed PMID: 16055269.
- 82. Bodes Pardo G, Lluch Girbés E, Roussel NA, Gallego Izquierdo T, Jiménez Penick V, Pecos Martín D. Pain neurophysiology education and the rapeutic exercise for patients with chronic low back pain: A single-blind randomized controlled trial. Arch Phys Med Rehabil. 2018;99(2):338-47. Epub 2017/11/16. doi: 10.1016/j.apmr.2017.10.016. PubMed PMID: 29138049.
- 83. 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. 2015;29(6):538-47. Epub 2014/09/10. doi: 10.1177/0269215514549033. PubMed PMID: 25200879.
- 84. Amorim AB, Pappas E, Simic M, Ferreira ML, Jennings M, Tiedemann A, et al. Integrating mobile-health, health coaching, and physical activity to reduce the burden of chronic low back pain trial (impact): A pilot randomised controlled trial. BMC Musculoskelet Disord. 2019;20(1):71. Epub 2019/02/13. doi: 10.1186/s12891-019-2454-y. PubMed PMID: 30744606; PubMed Central PMCID: PMC6371593.
- 85. Dario AB, Moreti Cabral A, Almeida L, Ferreira ML, Refshauge K, Simic M, et al. Effective ness of telehealth-based interventions in the management of non-specific low back pain: A systematic review with meta-analysis. Spine J. 2017;17(9):1342-51. Epub 2017/04/17. doi: 10.1016/j.spinee.2017.04.008. PubMed PMID: 28412562.
- 86. Du S, Liu W, Cai S, Hu Y, Dong J. The efficacy of e-health in the self-management of chronic low back pain: A meta analysis. Int J Nurs Stud. 2020;106:103507. Epub 2020/04/23. doi: 10.1016/j.ijnurstu.2019.103507. PubMed PMID: 32320936.
- 87. Suman A, Schaafsma FG, van Dongen JM, Elders PJM, Buchbinder R, van Tulder MW, et al. Effectiveness and cost-utility of a multifaceted ehealth strategy to improve back pain beliefs of patients with non-specific low back pain: A cluster randomised trial. BMJ Open. 2019;9(12):e030879. Epub 2019/12/08. doi: 10.1136/bmjopen-2019-030879. PubMed PMID: 31811006; PubMed Central PMCID: PMC6924789.

February 2022 Page 130 of 141

- 88. Cherkin DC, Sherman KJ, Balderson BH, Cook AJ, Anderson ML, Hawkes RJ, 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. 2016;315(12):1240-9. Epub 2016/03/24. doi: 10.1001/jama.2016.2323. PubMed PMID: 27002445; PubMed Central PMCID: PMC4914381.
- 89. Skelly AC, Chou R, Dettori JR, Turner JA, Friedly JL, Rundell SD, et al. Noninvasive nonpharmacological treatment for chronic pain: A systematic review update. Comparative effectiveness review No 227 (Prepared by the Pacific Northwest Evidence-based Practice Center under contract no 290-2015-00009-I) AHRQ publication no 20-EHC009 2020. PubMed PMID: 30179389.
- 90. Løchting I, Storheim K, Werner EL, Småstuen Cvancarova M, Grotle M. Evaluation of individualized quality of life and illness perceptions in low back pain. A patient education cluster randomized controlled trial. Patient Educ Couns. 2016;99(12):1992-8. Epub 2016/08/04. doi: 10.1016/j.pec.2016.05.015. PubMed PMID: 27486051.
- 91. Ryum T, Hartmann H, Borchgrevink P, de Ridder K, Stiles TC. The effect of in-session exposure in fear-avoidance treatment of chronic low back pain: A randomized controlled trial. Eur J Pain. 2021;25(1):171-88. Epub 2020/09/24. doi: 10.1002/ejp.1659. PubMed PMID: 32964624.
- 92. Suni JH, Kolu P, Tokola K, Raitanen J, Rinne M, Taulaniemi A, et al. Effectiveness and cost-effectiveness of neuromuscular exercise and back care counseling in female healthcare workers with recurrent non-specific low back pain: A blinded four-arm randomized controlled trial. BMC Public Health. 2018; 18(1):1376. Epub 2018/12/19. doi: 10.1186/s12889-018-6293-9. PubMed PMID: 30558592; PubMed Central PMCID: PMC6296156.
- 93. Petrozzi MJ, Leaver A, Ferreira PH, Rubinstein SM, Jones MK, Mackey MG. Addition of MoodGYM to physical treatments for chronic low back pain: A randomized controlled trial. Chiropr Man Therap. 2019;27:54. Epub 2019/11/02. doi: 10.1186/s12998-019-0277-4. PubMed PMID: 31673330; PubMed Central PMCID: PMC6814139.
- 94. Wewege MA, Booth J, Parmenter BJ. Aerobic vs. Resistance exercise for chronic non-specific low back pain: A systematic review and meta-analysis. J Back Musculoskelet Rehabil. 2018;31(5):889-99. Epub 2018/06/12. doi: 10.3233/bmr-170920. PubMed PMID: 29889056.
- 95. Shi Z, Zhou H, Lu L, Pan B, Wei Z, Yao X, et al. Aquatic exercises in the treatment of low back pain: A systematic review of the literature and meta-analysis of eight studies. Am J Phys Med Rehabil. 2018;97(2):116-22. Epub 2017/08/02. doi: 10.1097/phm.000000000000001. PubMed PMID: 28759476.
- 96. Lam OT, Strenger DM, Chan-Fee M, Pham PT, Preuss RA, Robbins SM. Effectiveness of the McKenzie method of mechanical diagnosis and therapy for treating low back pain: Literature review with meta-analysis. J Orthop Sports Phys Ther. 2018;48(6):476-90. Epub 2018/04/01. doi: 10.2519/jospt.2018.7562. PubMed PMID: 29602304.
- 97. Schneider MJ, Ammendolia C, Murphy DR, Glick RM, Hile E, Tudorascu DL, et al. Comparative clinical effectiveness of nonsurgical treatment methods in patients with lumbar spinal stenosis: A randomized clinical trial. JAMA Netw Open. 2019;2(1):e186828. Epub 2019/01/16. doi: 10.1001/jamanetworkopen.2018.6828. PubMed PMID: 30646197; PubMed Central PMCID: PMC6324321.
- 98. Schulz C, Evans R, Maiers M, Schulz K, Leininger B, Bronfort G. Spinal manipulative therapy and exercise for older adults with chronic low back pain: A randomized clinical trial. Chiropr Man Therap. 2019;27:21. Epub 2019/05/23. doi: 10.1186/s12998-019-0243-1. PubMed PMID: 31114673; PubMed Central PMCID: PMC6518769

February 2022 Page 131 of 141

- 99. Brodsky M, Hansen A, Bjerke W. Randomized pilot trial for a community-based group stretching exercise program for chronic low back pain. Glob Adv Health Med. 2019;8:2164956119846055. Epub 2019/05/10. doi: 10.1177/2164956119846055. PubMed PMID: 31069163; PubMed Central PMCID: PMC6495440.
- 100. Niederer D, Engel T, Vogt L, Arampatzis A, Banzer W, Beck H, et al. Motor control stabilisation exercise for patients with non-specific low back pain: A prospective meta-analysis with multilevel meta-regressions on intervention effects. J Clin Med. 2020;9(9). Epub 2020/09/26. doi: 10.3390/jcm9093058. PubMed PMID: 32971921; PubMed Central PMCID:PMC7564352.
- 101. Gomes-Neto M, Lopes JM, Conceição CS, Araujo A, Brasileiro A, Sousa C, et al. Stabilization exercise compared to general exercises or manual therapy for the management of low back pain: A systematic review and meta-analysis. Phys Ther Sport. 2017;23:136-42. Epub 2016/10/07. doi: 10.1016/j.ptsp.2016.08.004. PubMed PMID: 27707631.
- 102. Sipaviciene S, Kliziene I. Effect of different exercise programs on non-specific chronic lowbackpain and disability in people who perform sedentary work. Clin Biomech (Bristol, Avon). 2020;73:17-27. Epub 2020/01/11. doi: 10.1016/j.clinbiomech.2019.12.028. PubMed PMID: 31923778.
- 103. Calatayud J, Guzmán-González B, Andersen LL, Cruz-Montecinos C, Morell MT, Roldán R, et al. Effectiveness of a group-based progressive strength training in primary care to improve the recurrence of low back pain exacerbations and function: A randomised trial. Int J Environ Res Public Health. 2020;17(22). Epub 2020/11/15. doi: 10.3390/ijerph17228326. PubMed PMID: 33187076; PubMed Central PMCID: PMC7696327.
- 104. Fritz JM, Sharpe J, Greene T, Lane E, Hadizadeh M, McFadden M, et al. Optimization of spinal manipulative therapy protocols: A factorial randomized trial within a multiphase optimization framework. J Pain. 2020. Epub 2020/12/15. doi: 10.1016/j.jpain.2020.11.008. PubMed PMID: 33309783.
- 105. Brämberg EB, Bergström G, Jensen I, Hagberg J, Kwak L. Effects of yoga, strength training and advice on back pain: A randomized controlled trial. BMC Musculoskelet Disord. 2017;18(1):132. Epub 2017/03/31. doi: 10.1186/s12891-017-1497-1. PubMed PMID: 28356091; PubMed Central PMCID:PMC5372262.
- 106. Matarán-Peñarrocha GA, Lara Palomo IC, Antequera Soler E, Gil-Martínez E, Fernández-Sánchez M, Aguilar-Ferrándiz ME, et al. Comparison of efficacy of a supervised versus non-supervised physical therapy exercise program on the pain, functionality and quality of life of patients with non-specific chronic low-back pain: A randomized controlled trial. Clin Rehabil. 2020;34(7):948-59. Epub 2020/06/11. doi: 10.1177/0269215520927076. PubMed PMID: 32517498.
- 107. Yamato TP, Maher CG, Saragiotto BT, Hancock MJ, Ostelo RW, Cabral CM, et al. Pilates for low back pain. Cochrane Database Syst Rev. 2015;2015(7):Cd010265. Epub 2015/07/03. doi:10.1002/14651858.CD010265. pub2. PubMed PMID: 26133923; PubMed Central PMCID:PMC8078578.
- 108. Kamioka H, Tsutani K, Katsumata Y, Yoshizaki T, Okuizumi H, Okada S, et al. Effectiveness of pilates exercise: A quality evaluation and summary of systematic reviews based on randomized controlled trials. Complement Ther Med. 2016;25:1-19. Epub 2016/04/12. doi: 10.1016/j.ctim.2015.12.018. PubMed PMID: 27062942.
- 109. Miyamoto GC, Franco KFM, van Dongen JM, Franco Y, de Oliveira NTB, Amaral DDV, et al. Different doses of pilates-based exercise therapy for chronic low backpain: A randomised controlled trial with economic evaluation. Br J Sports Med. 2018;52(13):859-68. Epub 2018/03/12. doi: 10.1136/bjsports-2017-098825. PubMed PMID: 29525763.
- 110. Cruz-Díaz D, Romeu M, Velasco-González C, Martínez-Amat A, Hita-Contreras F. The effectiveness of 12 weeks of pilates intervention on disability, pain and kinesiophobia in patients with chronic low back pain: A randomized controlled trial. Clin Rehabil. 2018;32(9):1249-57. Epub 2018/04/14. doi: 10.1177/0269215518768393. PubMed PMID: 29651872.

February 2022 Page 132 of 141

- 111. O'Connor SR, Tully MA, Ryan B, Bleakley CM, Baxter GD, Bradley JM, et al. Walking exercise for chronic musculoskeletal pain: Systematic review and meta-analysis. Arch Phys Med Rehabil. 2015;96(4):724-34.e3. Epub 2014/12/23. doi: 10.1016/j.apmr.2014.12.003. PubMed PMID: 25529265.
- 112. Sitthipornvorakul E, Klinsophon T, Sihawong R, Janwantanakul P. The effects of walking intervention in patients with chronic low back pain: A meta-analysis of randomized controlled trials. Musculoskelet Sci Pract. 2018;34:38-46. Epub 2017/12/20. doi: 10.1016/j.msksp.2017.12.003. PubMed PMID: 29257996.
- 113. Chou R, Deyo R, Friedly J, Skelly A, Hashimoto R, Weimer M, et al. Noninvasive treatments for low back pain. Rockville (MD): Agency for Healthcare Research and Quality (US); 2016.
- 114. Kong LJ, Lauche R, Klose P, Bu JH, Yang XC, Guo CQ, et al. Tai chi for chronic pain conditions: A systematic reviewand meta-analysis of randomized controlled trials. Sci Rep. 2016;6:25325. Epub 2016/04/30. doi: 10.1038/srep25325. PubMed PMID: 27125299; PubMed Central PMCID: PMC4850460.
- 115. Qin J, Zhang Y, Wu L, He Z, Huang J, Tao J, et al. Effect of tai chialone or as additional therapy on low back pain: Systematic review and meta-analysis of randomized controlled trials. Medicine (Baltimore). 2019; 98(37):e17099. Epub 2019/09/14. doi: 10.1097/md.00000000017099. PubMed PMID: 31517838; PubMed Central PMCID:PMC6750325.
- 116. Fritz JM, Sharpe JA, Lane E, Santillo D, Greene T, Kawchuk G. Optimizing treatment protocols for spinal manipulative therapy: Study protocol for a randomized trial. Trials. 2018;19(1):306. Epub 2018/06/06. doi: 10.1186/s13063-018-2692-6. PubMed PMID: 29866131; PubMed Central PMCID: PMC5987587.
- 117. Halliday MH, Pappas E, Hancock MJ, Clare HA, Pinto RZ, Robertson G, et al. A randomized clinical trial comparing the McKenzie method and motor control exercises in people with chronic low back pain and a directional preference: 1-year follow-up. Physiotherapy. 2019; 105(4):442-5. Epub 2019/06/18. doi: 10.1016/j.physio.2018.12.004. PubMed PMID: 31204031.
- 118. Fritz JM, Kim M, Magel JS, Asche CV. Cost-effectiveness of primary care management with or without early physical therapy for acute low back pain: Economic evaluation of a randomized clinical trial. Spine (Phila Pa 1976). 2017;42(5):285-90. Epub 2016/06/09. doi: 10.1097/brs.00000000001729. PubMed PMID: 27270641.
- 119. Minetama M, Kawakami M, Teraguchi M, Kagotani R, Mera Y, Sumiya T, et al. Supervised physical therapy versus unsupervised exercise for patients with lumbar spinal stenosis: 1-year follow-up of a randomized controlled trial. Clin Rehabil. 2021:269215520986688. Epub 2021/01/12. doi: 10.1177/0269215520986688. PubMed PMID: 33423549.
- 120. Cai C, Yang Y, Kong PW. Comparison of lower limb and back exercises for runners with chronic low back pain. Med Sci Sports Exerc. 2017;49(12):2374-84. Epub 2017/08/03. doi: 10.1249/mss.0000000000001396. PubMed PMID: 28767525.
- 121. Dal Farra F, Risio RG, Vismara L, Bergna A. Effectiveness of osteopathic interventions in chronic non-specific low back pain: A systematic review and meta-analysis. Complement Ther Med. 2021;56:102616. Epub 2020/11/17. doi: 10.1016/j.ctim.2020.102616. PubMed PMID: 33197571.
- 122. Martí-Salvador M, Hidalgo-Moreno L, Doménech-Fernández J, Lisón JF, Arguisuelas MD. Osteopathic manipulative treatment including specific diaphragm techniques improves pain and disability in chronic nonspecific low back pain: A randomized trial. Arch Phys Med Rehabil. 2018;99(9):1720-9. Epub 2018/05/23. doi: 10.1016/j.apmr.2018.04.022. PubMed PMID: 29787734.
- 123. 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. 2014; 161(6):381-91. Epub 2014/09/16. doi: 10.7326/m14-0006. PubMed PMID: 25222385.

February 2022 Page 133 of 141

- 124. Bronfort G, Maiers MJ, Evans RL, Schulz CA, Bracha Y, Svendsen KH, et al. Supervised exercise, spinal manipulation, and home exercise for chronic low backpain: A randomized clinical trial. Spine J. 2011; 11(7):585-98. Epub 2011/05/31. doi: 10.1016/j.spinee.2011.01.036. PubMed PMID: 21622028.
- 125. 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). 2011;36(24):1999-2010. Epub 2011/03/02. doi: 10.1097/BRS.0b013e318201ee8e. PubMed PMID: 21358492.
- 126. Cecchi F, Molino-Lova R, Chiti M, Pasquini G, Paperini A, Conti AA, 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. 2010; 24(1): 26-36. Epub 2010/01/08. doi: 10.1177/0269215509342328. PubMed PMID: 20053720.
- 127. 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. 2014;5(4): 154-64. Epub 2015/08/08. doi: 10.1177/2151458514544956. PubMed PMID: 26246937; PubMed Central PMCID: PMC4252156.
- 128. Rubinstein SM, de Zoete A, van Middelkoop M, Assendelft WJJ, de Boer MR, van Tulder MW. Benefits and harms of spinal manipulative therapy for the treatment of chronic low back pain: Systematic review and meta-analysis of randomised controlled trials. BMJ. 2019;364:1689. Epub 2019/03/15. doi: 10.1136/bmj.1689. PubMed PMID: 30867144; PubMed Central PMCID: PMC6396088
- 129. Licciardone JC, Minotti DE, Gatchel RJ, Kearns CM, Singh KP. Osteopathic manual treatment and ultrasound therapy for chronic low back pain: A randomized controlled trial. Ann Fam Med. 2013;11(2):122-9. Epub 2013/03/20. doi: 10.1370/afm.1468. PubMed PMID: 23508598; PubMed Central PMCID: PMC3601389.
- 130. 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). 2013;38(3):E158-77. Epub 2012/11/22. doi: 10.1097/BRS.0b013e31827dd89d. PubMed PMID: 23169072.
- 131. Mo Z, Zhang R, Chen J, Shu X, Shujie T. Comparison between oblique pulling spinal manipulation and other treatments for lumbar disc herniation: A systematic review and meta-analysis. J Manipulative Physiol Ther. 2018;41(9):771-9. Epub 2018/01/01. doi: 10.1016/j.jmpt.2018.04.005. PubMed PMID: 30871713.
- 132. Schneider M, Haas M, Glick R, Stevans J, Landsittel D. Comparison of spinal manipulation methods and usual medical care for acute and subacute low backpain: A randomized clinical trial. Spine (Phila Pa 1976). 2015; 40(4):209-17. Epub 2014/11/26. doi: 10.1097/brs.0000000000000724. PubMed PMID: 25423308; PubMed Central PMCID:PMC4326596.
- 133. Bahnamiri AF, Norouzi A, Reskati HM, Hosseini SH. Effectiveness of mindfulness-based interventions on pain intensity in patients with chronic low back pain: A systematic review. Iran J Psychiatry Behav Sci. 2020;14(4): e102509. Epub 2020-10-02. doi: 10.5812/ijpbs.102509.
- 134. Gignoux P, Lanhers C, Dutheil F, Boutevillain L, Pereira B, Coudeyre E. Non-rigid lumbar supports for the management of non-specific lowback pain: A literature review and meta-analysis. Ann Phys Rehabil Med. 2020:101406. Epub 2020/06/21. doi: 10.1016/j.rehab.2020.05.010. PubMed PMID: 32561503.
- 135. 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):60-5. Epub 2012/07/14. doi: 10.5387/fms.58.60. PubMed PMID: 22790893.

February 2022 Page 134 of 141

- 136. Calmels P, Queneau P, Hamonet C, Le Pen C, Maurel F, Lerouvreur C, et al. Effectiveness of a lumbar belt in subacute low back pain: An open, multicentric, and randomized clinical study. Spine (Phila Pa 1976). 2009; 34(3):215-20. Epub 2009/01/31. doi: 10.1097/BRS.0b013e31819577dc. PubMed PMID: 19179915.
- 137. 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). 2007;32(19):2050-7. Epub 2007/09/01. doi: 10.1097/BRS.0b013e3181453fcc. PubMed PMID: 17762804.
- 138. Cheng YH, Hsu CY, Lin YN. The effect of mechanical traction on low backpain in patients with herniated intervertebral disks: A systemic review and meta-analysis. Clin Rehabil. 2020;34(1):13-22. Epub 2019/08/29. doi: 10.1177/0269215519872528. PubMed PMID: 31456418.
- 139. Vanti C, Panizzolo A, Turone L, Guccione AA, Violante FS, Pillastrini P, et al. Effectiveness of mechanical traction for lumbar radiculopathy: A systematic review and meta-analysis. Phys Ther. 2021;101(3). Epub 2021/01/01. doi: 10.1093/ptj/pzaa231. PubMed PMID: 33382419.
- 140. Wegner I, Widyahening IS, van Tulder MW, Blomberg SE, de Vet HC, Brønfort G, et al. Traction for low-back pain with or without sciatica. Cochrane Database Syst Rev. 2013;2013(8):Cd003010. Epub 2013/08/21. doi: 10.1002/14651858.CD003010.pub5. PubMed PMID: 23959683; PubMed Central PMCID:PMC6823219
- 141. 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. 2012;35(4):246-53. Epub 2012/05/29. doi: 10.1016/j.jmpt.2012.04.021. PubMed PMID: 22632584.
- 142. Yang LH, Duan PB, Hou QM, Du SZ, Sun JF, Mei SJ, et al. Efficacy of auricular acupressure for chronic low back pain: A systematic review and meta-analysis of randomized controlled trials. Evid Based Complement Alternat Med. 2017;2017:6383649. Epub 2017/08/15. doi: 10.1155/2017/6383649. PubMed PMID: 28804504; PubMed Central PMCID: PMC5539928.
- 143. Zhu F, Zhang M, Wang D, Hong Q, Zeng C, Chen W. Yoga compared to non-exercise or physical therapy exercise on pain, disability, and quality of life for patients with chronic low back pain: A systematic review and meta-analysis of randomized controlled trials. PLoS One. 2020;15(9):e0238544. Epub 2020/09/02. doi: 10.1371/journal.pone.0238544. PubMed PMID: 32870936; PubMed Central PMCID: PMC7462307.
- 144. Goode AP, Coeytaux RR, McDuffie J, Duan-Porter W, Sharma P, Mennella H, et al. An evidence map of yoga for low back pain. Complement Ther Med. 2016;25:170-7. Epub 2016/04/12. doi: 10.1016/j.ctim.2016.02.016. PubMed PMID: 27062965.
- 145. Nduwimana I, Nindorera F, Thonnard JL, Kossi O. Effectiveness of walking versus mind-body therapies in chronic lowback pain: A systematic review and meta-analysis of recent randomized controlled trials. Medicine (Baltimore). 2020;99(35):e21969. Epub 2020/09/03. doi: 10.1097/md.0000000000021969. PubMed PMID: 32871946; PubMed Central PMCID:PMC7458239.
- 146. PhattharasupharerkS, Purepong N, Eksakulkla S, Siriphorn A. Effects of qigong practice in office workers with chronic non-specific low back pain: A randomized control trial. J Bodyw Mov Ther. 2018;23 (2):375-81. doi: 10.1016/j.jbmt.2018.02.004. PubMed PMID: 31103123.
- 147. Blödt S, Pach D, Kaster T, Lüdtke R, Icke K, Reisshauer A, et al. Qigong versus exercise therapy for chronic low back pain in adults--a randomized controlled non-inferiority trial. Eur J Pain. 2015;19(1):123-31. Epub 2014/06/07. doi: 10.1002/ejp.529. PubMed PMID: 24902673.
- 148. Teut M, Knilli J, Daus D, Roll S, Witt CM. Qigong or yoga versus no intervention in older adults with chronic low back pain-a randomized controlled trial. J Pain. 2016;17(7):796-805. Epub 2016/04/06. doi: 10.1016/j.jpain. 2016.03.003. PubMed PMID: 27046802.

February 2022 Page 135 of 141

- 149. Wood S, Fryer G, Tan LLF, Cleary C. Dry cupping for musculoskeletal pain and range of motion: A systematic reviewand meta-analysis. J Bodyw Mov Ther. 2020;24(4):503-18. Epub 2020/11/22. doi: 10.1016/j.jbmt. 2020.06.024. PubMed PMID: 33218554.
- 150. Wang YT, Qi Y, Tang FY, Li FM, Li QH, Xu CP, et al. The effect of cupping therapy for low back pain: A meta-analysis based on existing randomized controlled trials. J Back Musculoskelet Rehabil. 2017;30(6):1187-95. Epub 2017/09/28. doi: 10.3233/bmr-169736. PubMed PMID: 28946531.
- 151. Mardani-Kivi M, Montazar R, Azizkhani M, Hashemi-Motlagh K. Wet-cupping is effective on persistent nonspecific low back pain: A randomized clinical trial. Chin J Integr Med. 2019;25(7):502-6. Epub 2018/11/30. doi: 10.1007/s11655-018-2996-0. PubMed PMID: 30484021.
- 152. Glazov G, Yelland M, Emery J. Low-level laser therapy for chronic non-specific lowback pain: A meta-analysis of randomised controlled trials. Acupunct Med. 2016;34(5):328-41. Epub 2016/05/22. doi: 10.1136/acupmed-2015-011036. PubMed PMID: 27207675; PubMed Central PMCID: PMC5099186.
- 153. Buchmuller A, Navez M, Milletre-Bernardin M, Pouplin S, Presles E, Lantéri-Minet M, et al. Value of TENS for relief of chronic low back pain with or without radicular pain. Eur J Pain. 2012;16(5):656-65. Epub 2012/02/18. doi: 10.1002/j.1532-2149.2011.00061.x. PubMed PMID: 22337531.
- 154. Kolber MR, Ton J, Thomas B, Kirkwood J, Moe S, Dugré N, et al. Peer systematic review of randomized controlled trials: Management of chronic low back pain in primary care. Can Fam Physician. 2021;67(1):e20-e30. Epub 2021/01/24. doi: 10.46747/cfp.6701e20. PubMed PMID: 33483410; PubMed Central PMCID:PMC7822613.
- 155. Konno S, Oda N, Ochiai T, Alev L. Randomized, double-blind, placebo-controlled phase III trial of duloxetine monotherapy in Japanese patients with chronic low back pain. Spine (Phila Pa 1976). 2016;41(22):1709-17. Epub 2016/11/11. doi: 10.1097/brs.00000000001707. PubMed PMID: 27831985; PubMed Central PMCID: PMC5113250.
- 156. Skljarevski V, Ossanna M, Liu-Seifert H, Zhang Q, Chappell A, Iyengar S, et al. A double-blind, randomized trial of duloxetine versus placebo in the management of chronic low back pain. Eur J Neurol. 2009;16(9):1041-8. Epub 2009/05/28. doi: 10.1111/j.1468-1331.2009.02648.x. PubMed PMID: 19469829.
- 157. Skljarevski V, Zhang S, Desaiah D, Alaka KJ, Palacios S, Miazgowski T, et al. Duloxetine versus placebo in patients with chronic low back pain: A 12-week, fixed-dose, randomized, double-blind trial. J Pain. 2010;11(12):1282-90. Epub 2010/05/18. doi:10.1016/j.jpain.2010.03.002. PubMed PMID: 20472510.
- 158. Skljarevski V, Desaiah D, Liu-Seifert H, Zhang Q, Chappell AS, Detke MJ, et al. Efficacy and safety of duloxetine in patients with chronic low back pain. Spine (Phila Pa 1976). 2010;35(13):E578-85. Epub 2010/05/13. doi: 10.1097/BRS.0b013e3181d3cef6. PubMed PMID: 20461028.
- 159. U.S. Food and Drug Administration. Cymbalta (duloxetine hydrochloride) delayed-release capsules for oral use. 2010. Available from: <a href="https://www.accessdata.fda.gov/drugsatfda\_docs/label/2010/022516lbl.pdf">https://www.accessdata.fda.gov/drugsatfda\_docs/label/2010/022516lbl.pdf</a>.
- 160. Kivitz AJ, Gimbel JS, Bramson C, Nemeth MA, Keller DS, Brown MT, et al. Efficacy and safety of tanezumab versus naproxen in the treatment of chronic lowback pain. Pain. 2013;154(7):1009-21. Epub 2013/05/01. doi: 10.1016/j.pain.2013.03.006. PubMed PMID: 23628600.
- 161. Zerbini C, Ozturk ZE, Grifka J, Maini M, Nilganuwong S, Morales R, 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. 2005;21(12):2037-49. Epub 2005/12/22. doi: 10.1185/030079905x75069. PubMed PMID: 16368055.

February 2022 Page 136 of 141

- 162. Nissen SE, Yeomans ND, Solomon DH, Lüscher TF, Libby P, Husni ME, et al. Cardiovascular safety of celecoxib, naproxen, or ibuprofen for arthritis. N Engl J Med. 2016;375(26):2519-29. Epub 2016/12/14. doi: 10.1056/NEJMoa1611593. PubMed PMID: 27959716.
- 163. U.S. Food and Drug Administration. Medication guide for non-steroidal anti-inflammatory drugs (NSAIDs). Available from: https://www.accessdata.fda.gov/drugsatfda\_docs/label/1998/074978Orig1s000lbl.pdf.
- 164. Herndon CM, Hutchison RW, Berdine HJ, Stacy ZA, Chen JT, Farnsworth DD, 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. 2008;28(6):788-805. Epub 2008/05/28. doi: 10.1592/phco.28.6.788. PubMed PMID: 18503406.
- 165. Antman EM, Bennett JS, Daugherty A, Furberg C, Roberts H, Taubert KA. Use of nonsteroidal antiinflammatory drugs: An update for clinicians: A scientific state ment from the American Heart Association. Circulation. 2007;115(12):1634-42. Epub 2007/02/28. doi: 10.1161/circulationaha.106.181424. Pub Med PMID: 17325246.
- 166. Katz N, Borenstein DG, Birbara C, Bramson C, Ne meth MA, Smith MD, et al. Efficacy and safety of tanezumab in the treatment of chronic low back pain. Pain. 2011;152(10):2248-58. Epub 2011/06/24. doi: 10.1016/j.pain.2011.05.003. PubMed PMID: 21696889.
- 167. Shanthanna H, Gilron I, Rajarathinam M, AlAmri R, Kamath S, Thabane L, et al. Benefits and safety of gabapentinoids in chronic low back pain: A systematic review and meta-analysis of randomized controlled trials. PLoS Med. 2017;14(8):e1002369. Epub 2017/08/16. doi: 10.1371/journal.pmed.1002369. PubMed PMID: 28809936; PubMed Central PMCID:PMC5557428.
- 168. Romanò CL, Romanò D, Bonora C, Mineo G. Pregabalin, celecoxib, and their combination for treatment of chronic low-back pain. J Orthop Traumatol. 2009;10(4):185-91. Epub 2009/11/19. doi:10.1007/s10195-009-0077-z. PubMed PMID:19921480; PubMed Central PMCID:PMC2784066.
- 169. Mathieson S, Maher CG, McLachlan AJ, Latimer J, Koes BW, Hancock MJ, et al. Trial of pregabalin for acute and chronic sciatica. N Engl J Med. 2017;376(12):1111-20. Epub 2017/03/23. doi: 10.1056/NEJMoa1614292. PubMed PMID: 28328324.
- 170. Atkinson JH, Slater MA, Capparelli EV, Patel SM, Wolfson T, Gamst A, et al. A randomized controlled trial of gabapentin for chronic lowback pain with and without a radiating component. Pain. 2016; 157(7):1499-507. Epub 2016/03/11. doi: 10.1097/j.pain.000000000000554. PubMed PMID: 26963844; PubMed Central PMCID: PMC5001843.
- 171. U.S. Food and Drug Administration. Highlights of prescribing information 2004. Available from: https://www.accessdata.fda.gov/drugsatfda\_docs/label/2018/021446s035,022488s013lbl.pdf.
- 172. Gomes T, Juurlink DN, Antoniou T, Mamdani MM, Paterson JM, van den Brink W. Gabapentin, opioids, and the risk of opioid-related death: A population-based nested case—control study. PLOS Medicine. 2017;14(10): e1002396. doi:10.1371/journal.pmed.1002396.
- 173. 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):103-7. doi: 10.1163/156856901753420945.
- 174. Yildirim K, Şışecıoğlu M, Karatay S, Erdal A, Levent A, Uğur M, et al. The effectiveness of gabapentin in patients with chronic radiculopathy. The Pain Clinic. 2003;15(3):213-8. doi: 10.1163/156856903767650718.
- 175. Gould HM, Atkinson JH, Chircop-Rollick T, D'Andrea J, Garfin S, Patel SM, et al. A randomized placebocontrolled trial of desipramine, cognitive behavioral therapy, and active placebo therapy for low back pain.

February 2022 Page 137 of 141

- Pain. 2020;161(6):1341-9. Epub 2020/02/19. doi: 10.1097/j.pain.000000000001834. PubMed PMID: 32068667.
- 176. Urquhart DM, Wluka AE, van Tulder M, Heritier S, Forbes A, Fong C, et al. Efficacy of low-dose amitriptyline for chronic lowback pain: A randomized clinical trial. JAMA Intern Med. 2018;178(11):1474-81. Epub 2018/10/05. doi: 10.1001/jamainternmed.2018.4222. PubMed PMID: 30285054; PubMed Central PMCID:PMC6248203.
- 177. Staiger TO, Gaster B, Sullivan MD, Deyo RA. Systematic review of antidepressants in the treatment of chronic low back pain. Spine (Phila Pa 1976). 2003;28(22):2540-5. Epub 2003/11/19. doi: 10.1097/01.brs.0000092372. 73527.ba. PubMed PMID: 14624092.
- 178. Salerno SM, Browning R, Jackson JL. The effect of antidepressant treatment on chronic back pain: A meta-analysis. Arch Intern Med. 2002;162(1):19-24. Epub 2002/02/05. doi: 10.1001/archinte.162.1.19. PubMed PMID: 11784215.
- 179. Gelenberg AJ, Freeman MP, Markowitz JC, Rosenbaum JF, Thase ME, Trivedi MH, et al. Practice guideline for the treatment of patients with major depressive disorder, third edition. American Psychiatric Association. 2010.
- 180. U.S. Food and Drug Administration. Revisions to product labeling: Suicidality and antide pressant drugs. Available from: <a href="https://www.fda.gov/media/77404/download">https://www.fda.gov/media/77404/download</a>.
- 181. Friedman BW, Dym AA, Davitt M, Holden L, Solorzano C, Esses D, et al. Naproxen with cyclobenzaprine, oxycodone/acetaminophen, or placebo for treating acute low backpain: A randomized clinical trial. JAMA. 2015;314(15):1572-80. Epub 2015/10/27. doi: 10.1001/jama.2015.13043. PubMed PMID: 26501533.
- 182. Abdel Shaheed C, Maher CG, Williams KA, McLachlan AJ. Efficacy and tolerability of muscle relaxants for low back pain: Systematic review and meta-analysis. Eur J Pain. 2016;21(2):228-37. Epub 2016/06/23. doi: 10.1002/ejp.907. PubMed PMID: 27329976.
- 183. Saragiotto BT, Machado GC, Ferreira ML, Pinheiro MB, Abdel Shaheed C, Maher CG. Paracetamol for low back pain. Cochrane Database Syst Rev. 2016;2016(6):Cd012230. Epub 2016/06/09. doi: 10.1002/14651858. cd012230. PubMed PMID: 27271789; PubMed Central PMCID: PMC6353046
- 184. Rotundo L, Pyrsopoulos N. Liver injury induced by paracetamol and challenges associated with intentional and unintentional use. World J Hepatol. 2020;12(4):125-36. Epub 2020/07/21. doi: 10.4254/wjh.v12.i4.125. PubMed PMID: 32685105; PubMed Central PMCID: PMC7336293.
- 185. Dakin P, Kivitz AJ, Gimbel JS, Skrepnik N, DiMartino SJ, Emeremni CA, et al. Efficacy and safety of fasinumab in patients with chronic low back pain: A phase II/III randomised clinical trial. Ann Rheum Dis. 2020;80(4):509-17. Epub 2020/11/18. doi: 10.1136/annrheumdis-2020-217259. PubMed PMID: 33199274; PubMed Central PMCID: PMC7958114.
- 186. Markman JD, Bolash RB, McAlindon TE, Kivitz AJ, Pombo-Suarez M, Ohtori S, et al. Tanezumab for chronic low back pain: A randomized, double-blind, placebo- and active-controlled, phase 3 study of efficacy and safety. Pain. 2020;161(9):2068-78. Epub 2020/05/27. doi: 10.1097/j.pain.000000000001928. PubMed PMID: 32453139; PubMed Central PMCID:PMC7431140
- 187. Petzke F, Klose P, Welsch P, Sommer C, Häuser W. Opioids for chronic low back pain: An updated systematic reviewand meta-analysis of efficacy, tolerability and safety in randomized placebo-controlled studies of at least 4 weeks of double-blind duration. Eur J Pain. 2020;24(3):497-517. Epub 2019/12/12. doi: 10.1002/eip.1519. Pub Med PMID: 31823442.
- 188. Weil AJ, Masters ET, Barsdorf AI, Bass A, Pixton G, Wilson JG, et al. Patient-reported health-related quality of life, work productivity, and activity impairment during treatment with alo-02 (extended-release oxycodone and sequestered naltrexone) for moderate-to-severe chronic low back pain. Health Qual Life Outcomes.

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- 2017;15(1):202. Epub 2017/10/19. doi: 10.1186/s12955-017-0749-y. PubMed PMID: 29041942; PubMed Central PMCID:PMC5645978.
- 189. 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. 2016;176(7):958-68. Epub 2016/05/24. doi: 10.1001/jamainternmed.2016.1251. PubMed PMID: 27213267.
- 190. Krebs EE, Gravely A, Nugent S, Jensen AC, De Ronne B, Goldsmith ES, et al. Effect of opioid vs nonopioid medications on pain-related function in patients with chronic back pain or hip or knee osteoarthritis pain: The space randomized clinical trial. JAMA. 2018;319(9):872-82. Epub 2018/03/07. doi: 10.1001/jama.2018.0899. PubMed PMID: 29509867; PubMed Central PMCID: PMC5885909
- 191. Goldberg H, Firtch W, Tyburski M, Pressman A, Ackerson L, Hamilton L, et al. Oral steroids for acute radiculopathy due to a herniated lumbar disk: A randomized clinical trial. JAMA. 2015;313(19):1915-23. Epub 2015/05/20. doi: 10.1001/jama.2015.4468. PubMed PMID: 25988461; PubMed Central PMCID: PMC5875432.
- 192. Friedman BW, Irizarry E, Solorzano C, Khankel N, Zapata J, Zias E, et al. Diazepam is no better than placebo when added to naproxen for acute low back pain. Ann Emerg Med. 2017;70(2):169-76.e1. Epub 2017/02/12. doi: 10.1016/j.annemergmed.2016.10.002. PubMed PMID: 28187918; PubMed Central PMCID:PMC5517351.
- 193. Brötz D, Maschke E, Burkard S, Engel C, Mänz C, Ernemann U, et al. Is there a role for benzodiazepines in the management of lumbar disc prolapse with acute sciatica? Pain. 2010;149(3):470-5. Epub 2010/04/07. doi: 10.1016/j.pain.2010.02.015. PubMed PMID: 20362397.
- 194. Zadro JR, Shirley D, Ferreira M, Carvalho Silva AP, Lamb SE, Cooper C, et al. Is vitamin D supplementation effective for low back pain? A systematic review and meta-analysis. Pain Physician. 2018;21(2):121-45. Epub 2018/03/23. PubMed PMID: 29565945.
- 195. Sodha R, Sivanadarajah N, Alam M. The use of glucosamine for chronic low back pain: A systematic review of randomised control trials. BMJ Open. 2013;3(6):e001167. doi: 10.1136/bmjopen-2012-001167.
- 196. Chen CH, Weng PW, Wu LC, Chiang YF, Chiang CJ. Radiofrequency neurotomy in chronic lumbar and sacroiliac joint pain: A meta-analysis. Medicine (Baltimore). 2019;98(26):e16230. Epub 2019/07/03. doi: 10.1097/md.00000000016230. PubMed PMID: 31261580; PubMed Central PMCID: PMC6617467.
- 197. Maas ET, Ostelo RW, Niemisto L, Jousimaa J, Hurri H, Malmivaara A, et al. Radiofrequency denervation for chronic lowback pain. Cochrane Database Syst Rev. 2015 (10): Cd008572. Epub 2015/10/27. doi: 10.1002/14651858.CD008572.pub2. PubMed PMID: 26495910.
- 198. Sae-Jung S, Jirarattanaphochai K. Outcomes of lumbar facet syndrome treated with oral diclofenac or methylprednisolone facet injection: A randomized trial. Int Orthop. 2016;40(6):1091-8. Epub 2016/03/19. doi: 10.1007/s00264-016-3154-y. PubMed PMID: 26987980.
- 199. Chou R, Hashimoto R, Friedly J, Fu R, Dana T, Sullivan S, et al. AHRQ technology assessments. Pain management injection therapies for low back pain. Rockville (MD): Agency for Healthcare Research and Quality (US); 2015.
- 200. Li YX, Yuan SE, Jiang JQ, Li H, Wang YJ. Systematic review and meta-analysis of effects of acupuncture on pain and function in non-specific low back pain. Acupunct Med. 2020;38(4):235-43. Epub 2020/05/28. doi: 10.1136/acupmed-2017-011622. PubMed PMID: 32458717.
- 201. Mu J, Furlan AD, Lam WY, Hsu MY, Ning Z, Lao L. Acupuncture for chronic nonspecific low back pain. Cochrane Database Syst Rev. 2020;12(12):Cd013814. Epub 2020/12/12. doi:10.1002/14651858.cd013814. PubMed PMID: 33306198; PubMed Central PMCID:PMC8095030

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- 202. Qin Z, Ding Y, Xu C, Kwong JSW, Ji Y, Wu A, et al. Acupuncture vs noninsertive shamacupuncture in aging patients with degenerative lumbar spinal stenosis: A randomized controlled trial. Am J Med. 2020;133 (4):500-7.e20. Epub 2019/09/17. doi: 10.1016/j.amjmed.2019.08.038. PubMed PMID: 31525334.
- 203. Xuan Z, Yu W, Dou Y, Wang T. Efficacy of platelet-rich plasma for low back pain: A systematic review and meta-analysis. J Neurol Surg A Cent Eur Neurosurg. 2020;81(6):529-34. Epub 2020/05/22. doi: 10.1055/s-0040-1709170. PubMed PMID: 32438421.
- 204. Amirdelfan K, Bae H, McJunkin T, De Palma M, Kim K, Beckworth WJ, et al. Allogeneic mesenchymal precursor cells treatment for chronic low back pain associated with degenerative disc disease: A prospective randomized, placebo-controlled 36-month study of safety and efficacy. Spine J. 2021;21(2):212-30. Epub 2020/10/13. doi: 10.1016/j.spinee.2020.10.004. PubMed PMID: 33045417.
- 205. Yang S, Kim W, Kong HH, Do KH, Choi KH. Epidural steroid injection versus conservative treatment for patients with lumbosacral radicular pain: A meta-analysis of randomized controlled trials. Medicine (Baltimore). 2020; 99(30):e21283. Epub 2020/08/15. doi: 10.1097/md.00000000001283. PubMed PMID: 32791709; PubMed Central PMCID:PMC7386972.
- 206. Manchikanti L, Knezevic NN, Parr A, Kaye AD, Sanapati M, Hirsch JA. Does epidural bupivacaine with or without steroids provide long-term relief? A systematic review and meta-analysis. Curr Pain Headache Rep. 2020;24(6):26. Epub 2020/04/27. doi: 10.1007/s11916-020-00859-7. PubMed PMID: 32335757.
- 207. Oliveira CB, Maher CG, Ferreira ML, Hancock MJ, Oliveira VC, McLachlan AJ, et al. Epidural corticosteroid injections for lumbosacral radicular pain. Cochrane Database Syst Rev. 2020;4(4):Cd013577. Epub 2020/04/10. doi: 10.1002/14651858.cd013577. PubMed PMID: 32271952; PubMed Central PMCID:PMC7145384
- 208. Abedini N, Pourfathi H, Eskandari M, Parish M. Comparison of epidural methylprednisolone, bupivacaine and normal saline injection in chronic low back pain due to discal hernia. Crescent J Med Biol Sci. 2018;5(1):57-61.
- 209. Lee JH, Kim DH, Kim DH, Shin KH, Park SJ, Lee GJ, et al. Comparison of clinical efficacy of epidural injection with or without steroid in lumbosacral disc herniation: A systematic review and meta-analysis. Pain Physician. 2018; 21(5):449-68. Epub 2018/10/05. PubMed PMID: 30282390.
- 210. Rigoard P, Basu S, Desai M, Taylor R, Annemans L, Tan Y, et al. Multicolumn spinal cord stimulation for predominant back pain in failed back surgery syndrome patients: A multicenter randomized controlled trial. Pain. 2019;160(6):1410-20. Epub 2019/02/06. doi: 10.1097/j.pain.000000000001510. PubMed PMID: 30720582; PubMed Central PMCID:PMC6553955.
- 211. Kamper SJ, Apeldoorn AT, Chiarotto A, Smeets RJ, Ostelo RW, Guzman J, et al. Multidisciplinary biopsychosocial rehabilitation for chronic low back pain. Cochrane Database Syst Rev. 2014(9):Cd000963. Epub 2014/09/03. doi: 10.1002/14651858.CD000963.pub3. PubMed PMID: 25180773.
- 212. Casey MB, Smart KM, Segurado R, Doody C. Multidisciplinary-based rehabilitation (MBR) compared with active physical interventions for pain and disability in adults with chronic pain: A systematic review and meta-analysis. Clin J Pain. 2020;36(11):874-86. Epub 2020/08/11. doi: 10.1097/ajp.0000000000000871. PubMed PMID: 32773436.
- 213. Schmidt AM, Schiøttz-Christensen B, Foster NE, Laurberg TB, Maribo T. The effect of an integrated multidisciplinary rehabilitation programme alternating inpatient interventions with home-based activities for patients with chronic low back pain: A randomized controlled trial. Clin Rehabil. 2020;34(3):382-93. Epub 2020/01/09. doi: 10.1177/0269215519897968. PubMed PMID: 31912752; PubMed Central PMCID: PMC7029437.
- 214. Schmidt AM, Laurberg TB, Moll LT, Schiøttz-Christensen B, Maribo T. The effect of an integrated multidisciplinary rehabilitation programme for patients with chronic low back pain: Long-term follow up of a

February 2022 Page 140 of 141

- randomised controlled trial. Clin Rehabil. 2021;35(2):232-41. Epub 2020/10/13. doi: 10.1177/0269215520963856. PubMed PMID: 33040598; PubMed Central PMCID: PMC7874370.
- 215. Mas RR, López-Jiménez T, Pujol-Ribera E, Martín MIF, Moix-Queraltó J, Montiel-Morillo E, et al. Effectiveness of a multidisciplinary biopsychosocial intervention for non-specific subacute low back pain in a working population: A cluster randomized clinical trial. BMC Health Serv Res. 2019;19(1):962. Epub 2019/12/14. doi: 10.1186/s12913-019-4810-x. PubMed PMID: 31831074; PubMed Central PMCID:PMC6909445.
- 216. Tavafian SS, Jamshidi AR, Mohammad K. Treatment of low back pain: Second extended follow up of an original trial (nct00600197) comparing a multidisciplinary group-based rehabilitation program with oral drug treatment alone up to 30 months. Int J Rheum Dis. 2017;20(12):1910-6. Epub 2014/12/30. doi: 10.1111/1756-185x.12540. PubMed PMID: 25546488.
- 217. 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). 2010;35(5):469-76. Epub 2010/02/12. doi: 10.1097/BRS.0b013e3181b8db2e. PubMed PMID: 20147878.
- 218. O'Keeffe M, Purtill H, Kennedy N, Conneely M, Hurley J, O'Sullivan P, et al. Comparative effective ness of conservative interventions for nonspecific chronic spinal pain: Physical, behavioral/psychologically informed, or combined? A systematic reviewand meta-analysis. J Pain. 2016;17(7):755-74. Epub 2016/02/05. doi: 10.1016/j.jpain.2016.01.473. PubMed PMID: 26844416.
- 219. Stein E, Witkiewitz K. Dismantling mindfulness-based programs: A systematic review to identify active components of treatment. Mindfulness. 2020;11(11): 2470-85. doi: 10.1007/s12671-020-01444-0.
- 220. Agency for Health Research and Quality. The effective health care program stakeholder guide Appendix D: Research questions & PICO(TS) 2011. Available from: <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>.
- 221. U.S. Preventive Services Task Force. Procedure manual Appendix VI. Criteria for assessing internal validity of individual studies 2017. Available from: <a href="https://www.uspreventiveservicestaskforce.org/uspstf/about-uspstf/methods-and-processes/procedure-manual/procedure-manual-appendix-vi-criteria-assessing-internal-validity-individual-studies.">https://www.uspreventiveservicestaskforce.org/uspstf/about-uspstf/methods-and-processes/procedure-manual/procedure-manual-appendix-vi-criteria-assessing-internal-validity-individual-studies.</a>
- 222. 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. 1999;96(13):7563-8. Epub 1999/06/23. Pub Med PMID: 10377455; Pub Med Central PMCID:PMC22126.
- 223. Vane SJ. Aspirin and other anti-inflammatory drugs. Thorax. 2000;55 Suppl 2:S3-9. Epub 2000/09/19. PubMed PMID: 10992545; PubMed Central PMCID:PMC1765977.
- 224. American Geriatrics Society 2015 updated Beers Criteria for potentially inappropriate medication use in older adults. J Am Geriatr Soc. 2015;63(11):2227-46. Epub 2015/10/09. doi: 10.1111/jgs.13702. PubMed PMID: 26446832.

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