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Pacific Northwest Evidence-based Practice Center

DRAFT Systematic Review Protocol
Project Title: Guidelines for the management of acute low back pain

I. Background

Among musculoskeletal conditions, low back pain (LBP) accounts for the highest prevalence. Among all health conditions LBP is the leading cause of disability globally and within the United States.[14,15,40] Treatment for LBP and spine disorders accounts for the highest costs among medical problems in the United States. Although LBP can be encountered in a variety of clinical settings, acute LBP is most often managed in outpatient primary and ambulatory care settings.[9,20]

Acute pain is usually characterized as lasting 7 days but often extends up to 30 days.[19] Acute LBP will be defined as lasting less than 6 weeks for purposes of this review. Although prognosis for acute LBP is favorable for most patients,[23,28] there is some evidence to challenge the assumption that ALBP typically completely resolves within 3 months.[18,25] A systematic review reported that a median of 26% of patients (range 2% to 48%) with acute LBP transition to chronic LBP.[8] Chronic LBP tends to be persistent, can be challenging to manage, and accounts for a majority of costs associated with treatment of LBP.[7,33] Therefore, reducing the likelihood of transitioning from acute to chronic LBP is an important goal.

Pain is complex. It substantially impacts quality of life as well as physical and mental function. Pain is greatly influenced by a variety of factors including psychosocial factors, general health status and environmental factors, which may predict who will develop chronic disabling pain as well as treatment response. Thus, a biopsychosocial framework to understanding LBP that considers biological as well as psychological and social factors is important.[8] Guideline concordant management of acute LBP involves assessment of biological as well as psychological and social factors to rule out serious or specific causes of acute LBP (e.g., cancer, infection, vertebral fracture) and to consider next steps for assessment (e.g., imaging) and treatment.[7] The majority of patients who present to primary care have LBP that cannot be attributed to a specific disease or spinal abnormality. Imaging of patients without factors suggesting a serious or specific cause of low back pain has been discouraged in clinical guidelines and has not been associated with improved outcomes[5] but may still be common.

The overarching goal of pain management is to relieve pain and improve function. A number of approaches and treatments are available for acute LBP management. A guideline-supported initial approach for acute LBP management is provision of information to reassure patients of the likelihood of resolution and encouragement to maintain physical activity.[21,22,27] Systematic review evidence supports a variety of pharmacological and noninvasive, nonpharmacological approaches for further

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treatment options for low back pain.[4,7,31,32] Pharmacological treatments include simple analgesics such as acetaminophen or nonsteroidal anti-inflammatory drugs (NSAIDs), as well as skeletal muscle relaxants, topical medications, systemic corticosteroids, opioids, herbal medications, and others. Nonpharmacologic treatments often include heat/cold therapies, exercise therapy, psychological therapies, massage, acupuncture, spinal manipulation, mind-body treatments (e.g., mindfulness-based relaxation, others). Interventional procedures are rarely used in patients with acute nonspecific LBP but may be considered on a case-by-case basis. Recent guidelines have prioritized use of nonpharmacological therapies for acute LBP due to a more favorable balance of benefits to harms compared to pharmacological therapies.[10,29] The 2017 American College of Physicians (ACP) LBP guideline did not recommend opioids for acute LBP and the 2022 Centers for Disease Control and Prevention (CDC) guideline recommends judicious, short-term use of opioids for acute pain based on an individualized assessment of potential benefits and harms.[10,29] In general, current evidence-based guidelines do not describe additional important clinical considerations regarding opioid use including optimal dosing, duration of treatment and use of risk mitigation strategies while optimizing and individualizing patient care based on the range of available options. Additional evidence has been published subsequent to many of these guidelines. A 2020 National Academies of Science, Engineering and Medicine (NASEM) Consensus Report[1] highlights some of these concerns and identifies gaps in current evidence and clinical guidelines related to acute low back pain management, identifying acute LPB as a priority for developing updated guidelines. The Food and Drug Administration (FDA) is interested in an updated evidence-based clinical practice guideline (CPG) that advances safe prescribing of opioid analgesics and considers evidence for the range of treatment options.

Purpose of the Review

The key decisional management dilemma for acute low back pain is selection of appropriate interventions to provide adequate pain relief, improve quality of life, improve function, and facilitate recovery, while minimizing adverse effects and judiciously using opioid and non-opioid pharmacologic treatments. To address this dilemma, the purpose of this systematic review is to provide an updated evidence base on the assessment of patients presenting with acute low back pain and on usual treatment options for acute low back pain. This systematic review will form the basis of new clinical practice guidelines on the assessment and management of acute low back pain. The review process will be conducted according to rigorous and accepted standards developed by the Agency for Healthcare Research and Quality (AHRQ).[2] The Key Questions and scope of the review (Populations, Interventions, Comparators, Outcomes, Timing, and Settings – PICOTS) serve as the basis for the review and are described below.

II. Key Questions

An initial set of Key Questions (KQs) were updated with input from the project sponsor (FDA), Advisory Board (AB) members, Guideline Development Group (GDG) members, Technical Expert Panel (TEP) members, and American Academy of Pain Medicine (AAPM) partners; and application of

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Evidence-based Practice Center (EPC) team expertise. The following KQs and inclusion criteria and logic conceptual framework reflect these discussions.

History/physical, imaging (KQs 1 and 2)

KQ 1. In adults presenting with acute (<6 weeks duration) LBP in any setting

a. How accurate is a focused patient history and physical exam (including risk factor and symptom assessment, presence and severity neurologic deficit and psychological risk factors) for identifying serious underlying conditions, specifically cancer, infection, inflammatory arthropathy, blunt force trauma, fracture (including vertebral compression fracture), or low back pain associated with severe or progressive neurological deficits including cauda equina?

b. What is the association between a focused patient history and physical exam (or components of these) and the likelihood of chronic low back pain and long-term disability?

c. Does the use of screening tools (e.g., Keele STarT Back Screening Tool) improve short or long-term patient outcomes (versus not using such a tool) based on prognosis?

d. Does accuracy or predictive utility differ based on (1) patient demographics or characteristics including those related to social risk factors for health; (2) patient medical or psychiatric comorbidities; (3) type or characteristic of back pain (e.g., duration, severity, recurrent, radicular, non-radicular); (4) clinical setting, provider type?

KQ 2. In adults with acute (<6 weeks duration) LBP, with or without radiculopathy who *do not* present with historical or clinical features suggestive of serious low back problems (e.g., absence of "red flag" symptoms"),

a. Does immediate/early lumbar spine imaging improve patient health outcomes versus usual care without imaging in the short term or long term?

b. What harms are associated with immediate lumbar spine imaging versus usual care without imaging?

c. Does outcome differ based on (1) patient demographics or characteristics including those related to social risk factors for health, access to imaging; (2) patient medical or psychiatric comorbidities; (3) type or characteristic of back pain (e.g., onset, duration, severity, recurrent, radicular, non-radicular); (4) imaging modality used (e.g., radiography, magnetic resonance imaging [MRI], computed tomography [CT]); (5) clinical setting, provider type?

d. What is the cost-effectiveness of immediate/early lumbar spine imaging versus usual care without imaging? (include only full economic studies)

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Treatment (KQs 3-8)

Opioid therapy

KQ 3. In adults presenting with acute (<6 weeks duration) LBP, including back pain with radiculopathy

a. What is the comparative effectiveness of systemic opioid therapy versus (1) placebo; (2) nonopioid pharmacologic therapy; or (3) noninvasive nonpharmacologic therapy on health outcomes at short term and long term?

b. What is the comparative effectiveness of systemic opioid therapy combined with a *nonopioid pharmacologic* intervention (e.g., hydrocodone with acetaminophen, codeine with acetaminophen) versus (1) placebo; (2) the same opioid alone; (3) the same nonopioid intervention alone; (4) a different nonopioid pharmacologic therapy; or (5) a noninvasive nonpharmacologic therapy on health outcomes at short term and long term?

c. What is the comparative effectiveness of systemic opioid therapy combined with a *nonpharmacologic* intervention versus (1) placebo or sham; (2) the same opioid alone; (3) the same nonpharmacologic intervention alone; or (4) a different nonpharmacologic therapy on health outcomes at short term and long term?

d. What are the effects of prescribing opioid therapy versus not prescribing opioid therapy for acute LBP on continued need for prescription pain relief, such as need for opioid refills, short-term and long-term opioid use?

e. What are the comparative harms of opioid therapy (alone or in combination with a nonopioid or in combination with a nonpharmacologic treatment) versus placebo, no opioid, nonopioid pharmacologic therapy, or nonpharmacologic therapy including (1) overdose; (2) misuse, withdrawal, opioid use disorder or other substance use disorder, and related outcomes; (3) diversion; (4) serious adverse events (AEs); (5) other harms (e.g., gastrointestinal-related harm, sedation/fatigue, pruritus, dizziness, falls, fractures, motor vehicle accidents, endocrinological harms, cardiovascular events, cognitive harms); (6) withdrawals due to AEs; (7) psychological harms (e.g., depression, anxiety, suicidal ideation or suicidal behavior)?

f. Does effectiveness of a systemic opioid (alone or in combination with a nonopioid) vary based on prescribing strategy (dose, frequency, dosing interval, duration of therapy, quantity dispensed, type of opioid dispensed [e.g., long-acting, sustained release]), and what is the impact of different prescribing strategies on refill requests and quantity of pills?

g. Do the harms of a systemic opioid (alone or in combination with a nonopioid) vary based on prescribing strategy (dose, frequency, dosing interval, duration of therapy, quantity dispensed, type of opioid dispensed [e.g., long-acting, sustained release]), and what is the impact of

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different prescribing strategies on (1) long-term opioid use; (2) overdose; (3) misuse, withdrawal, opioid or other substance use disorder, and related outcomes; (4) diversion; (5) serious AEs; (6) other harms (e.g., gastrointestinal-related harm, sedation/fatigue, pruritus, dizziness, nausea, falls, fractures, motor vehicle accidents, endocrinological harms, cardiovascular events, cognitive harms); (7) withdrawals due to AEs; (8) psychological harms (e.g., depression, anxiety, suicidal ideation or behavior)?

h. Do effectiveness or harms (questions a-g) differ based on (1) patient demographics or characteristics including those related to social risk factors related to health; (2) patient medical or psychiatric comorbidities; (3) type or characteristic of back pain (e.g., onset, duration, severity, recurrent, radicular, non-radicular, history of prior LBP), coexistent lower extremity pain without progressive/severe neurologic deficit; (4) dose of opioids, frequency, interval between doses; (5) timing and duration of therapy; (6) type of opioid; (7) current treatment for opioid use disorder; (8) opioid use history; (9) substance use history; (10) use of concomitant therapies; (11) clinical setting, provider type?

KQ 4. In adults with acute (<6 weeks duration) LBP, including back pain with radiculopathy, being considered for opioid therapy or who have been prescribed opioids for acute LBP

a. What is the effect of the following factors on the decision to prescribe opioids:
   Policy related factors including (1) existing opioid management plans; (2) patient education; (3) urine drug screening; (4) use of prescription drug monitoring program data; (5) availability of close follow-up; (6) prescribing/provision of naloxone (or other opioid antagonists);
   Patient related factors including (1) patient presentation (e.g., pain severity, etiology); (2) prior opioid prescription and experience; (3) patient expectations for pain control; (4) contraindications to other treatment options (e.g., to NSAIDs), 5) history of substance use disorder?

   [Notes: Comparison of mitigation strategies specific to acute pain that include one or more of these factors vs. not using one or more of these factors]

b. What is the effect of the following factors on patient health outcomes (1) existing opioid management plans; (2) patient education; (3) urine drug screening; (4) use of prescription drug monitoring program data; (5) availability of close follow-up; (6) prescribing/provision of naloxone (or other opioid antagonists)?

c. What is the impact of shared decision making on opioid prescription strategy, health outcomes, continued opioid use or harms?

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[Notes: Interventions: specified shared decision-making strategy vs. not using the strategy; comparison of strategies]

d. What is the accuracy of instruments for predicting risk of opioid misuse, withdrawal, opioid use disorder, or overdose in patients with acute LBP?

   [Notes: Interventions: Instruments, genetic/metabolic tests for predicting risk of misuse, opioid use disorder, and overdose; Comparison to reference standard for misuse, opioid use disorder, or overdose; or other benchmarks]

e. What is the effectiveness of instruments for predicting risk of long-term use of opioids, opioid misuse, withdrawal, opioid use disorder, or overdose in patients with acute LBP versus usual care (i.e., not using a formal instrument)?

Nonopioid Pharmacologic Therapy

KQ 5. In adults presenting with acute (<6 weeks duration) LBP, including back pain with radiculopathy

a. What is the comparative effectiveness of a single nonopioid pharmacologic therapy (e.g., acetaminophen, NSAIDs, antidepressants, anticonvulsants, systemic corticosteroids, benzodiazepines, muscle relaxants, lidocaine, ketamine, cannabis, common herbal remedies [e.g., willow-bark]) versus: (1) placebo; (2) other nonopioid pharmacologic treatments (e.g., those in a different medication class); or (3) nonpharmacologic therapy on health outcomes at short term and long term?

b. What is the comparative effectiveness of a combination of a maximum of two nonopioid pharmacologic therapies, one of which must be an NSAID or acetaminophen, versus: (1) placebo; (2) an NSAID or acetaminophen alone; or (3) nonpharmacologic therapy on health outcomes at short term and long term?

c. What is the comparative effectiveness of nonopioid pharmacologic therapy combined with a *nonpharmacologic* intervention versus (1) placebo or sham; (2) the same nonopioid pharmacologic therapy alone; (3) the same *nonpharmacologic* intervention alone; (4) a different *nonpharmacologic* therapy on health outcomes at short term and long term?

d. What are the comparative harms of nonopioid therapy (alone or in combination with a nonpharmacologic treatment or other nonopioid) versus placebo, a different class of nonopioid medication or nonpharmacologic therapy including (1) overdose; (2) misuse, withdrawal, opioid use disorder or other substance use disorder, and related outcomes; (3) serious AEs; (4) other harms (e.g., gastrointestinal-related harm, sedation/fatigue, pruritus, dizziness, nausea, falls, fractures, motor vehicle accidents, endocrinological harms, cardiovascular events,

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cognitive harms); (5) withdrawal due to AEs; (6) psychological harms (e.g., depression, anxiety, suicidal ideation or behavior)?

e. Do effectiveness or harms (questions a-d) differ based on (1) patient demographics or characteristics including those related to social risk factors related to health; (2) patient medical or psychiatric comorbidities; (3) type or characteristic of back pain (e.g., onset, duration, severity, recurrent, radicular, non-radicular); (4) timing of treatment; (5) dose, frequency/dosing interval, and route of administration of nonopioid; (6) duration of therapy; (7) type of nonopioid or type of drug combination; (8) current treatment for opioid use disorder; (9) opioid use history; (10) substance use history; (11) use of concomitant therapies; (12) clinical setting, provider type?

Noninvasive, Nonpharmacologic Therapy

KQ 6. In adults presenting with acute (<6 weeks duration) LBP, including back pain with radiculopathy

a. What is the comparative effectiveness of noninvasive nonpharmacologic therapies (e.g., exercise, cognitive behavioral therapy, acupuncture) versus: (1) sham; (2) waitlist, usual care, attention control, no treatment; or (3) other included noninvasive, nonpharmacologic treatments on health outcomes at short term and long term?

b. What are the comparative harms of noninvasive, nonpharmacologic therapy versus sham, waitlist, usual care, attention control, no treatment or other included noninvasive, nonpharmacologic treatments including (1) harms specific to the treatment used; (2) withdrawal due to AEs; (3) psychological harms (e.g., depression, suicidal ideation, suicidal behavior); (4) misuse, withdrawal, opioid use disorder, substance use disorder and related outcomes; (6) serious AEs?

c. Do effectiveness or harms (questions a, b) differ based on (1) patient demographics or characteristics including those related to social risk factors related to health; (2) patient medical or psychiatric comorbidities; (3) type or characteristic of back pain (e.g., onset, duration, severity, recurrent, radicular, non-radicular); (4) timing of treatment; (5) dose, frequency of treatment; (6) duration of treatment; (7) type of nonpharmacologic, noninvasive treatment; (8) current treatment for opioid use disorder; (9) opioid use history; (10) substance use history; (11) use of concomitant therapies; (12) clinical setting, provider type?

d. What is the effectiveness of policy approaches for reducing barriers and improving access to noninvasive, nonpharmacologic treatments?

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Selected Interventional Procedures

KQ 7. In adults presenting with acute (<6 weeks duration) LBP, including back pain with radiculopathy

a. What is the comparative effectiveness of selected interventional procedures (e.g., botulinum toxin, trigger point injection, epidural steroids/peri-radicular injections, SI joint/extra-articular injections, dry needling) compared with: (1) placebo or sham; (2) with each other; (3) systemic opioid therapy; (4) nonopioid pharmacologic treatments; or (5) nonpharmacologic therapy on health outcomes at short term and long term?

b. What are the comparative harms of selected interventional procedures (e.g., botulinum toxin, trigger point injection, epidural steroids, SI joint/extra-articular injections, peri-radicular injections, dry needling) compared with placebo or sham, another included procedure, systemic opioid therapy, nonopioid pharmacologic treatments or noninvasive, nonpharmacologic therapy including (1) harms specific to the treatment used; (2) withdrawal due to AEs; (3) psychological harms (e.g., depression, suicidal ideation, suicidal behavior); (4) misuse, withdrawal, opioid use disorder, substance use disorder and related outcomes; (5) serious AEs?

c. Do effectiveness or harms (questions a, b) differ based on 1) patient demographics or characteristics including those related to social risk factors related to health; (2) patient medical or psychiatric comorbidities; (3) type or characteristic of back pain (e.g., onset, duration, severity, recurrent, radicular, non-radicular); (4) timing of treatment; (5) dose, frequency of treatment; (6) duration of treatment; (7) type of procedure; (8) current treatment for opioid use disorder; (9) opioid use history; (10) substance use history; (11) use of concomitant therapies; (12) clinical setting, provider type?

Management strategies or pathways

KQ 8. In adults presenting with acute (<6 weeks duration) LBP, including back pain with radiculopathy

a. What is the comparative effectiveness of specific management strategies (e.g., stratification by risk for poor prognosis, early referral to therapy [e.g., manipulation therapies, exercise, physical therapy modalities)], matching therapies through treatment-based classification of patients, stepped care models, interdisciplinary models) versus (1) waitlist, usual care, or no treatment; or (2) other strategies on health outcomes short term and long term?

b. What are the comparative harms of management strategies versus waitlist, usual care, no treatment or other strategies including (1) harms specific to the strategy/pathway; (2) withdrawal due to AEs; (3) psychological harms (e.g., depression, suicidal ideation, suicidal

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behavior); (4) overdose; (5) misuse, withdrawal, opioid use disorder/substance use disorder and related outcomes; (6) serious AEs?

c. Do effectiveness or harms (questions a, b) differ based on (1) patient demographics or characteristics including those related to risk factors related to of health; (2) patient medical or psychiatric comorbidities; (3) type or characteristic of back pain (e.g., onset, duration, severity, recurrent, radicular, non-radicular); (4) timing of strategy; (5) dose, frequency of strategy; (6) duration of strategy; (7) type or components of the strategy; (8) current treatment for opioid use disorder; (9) opioid use history; (10) substance use history; (11) use of concomitant therapies; (12) clinical setting, provider type?

Special populations and factors to evaluate for modification for all treatments:

(1) patient demographics or characteristics including those related to social risk factors related to health; (2) patient medical or psychiatric comorbidities; (3) type or characteristic of back pain (e.g., onset/acuity, duration, severity, recurrent LBP, prior history of LBP, radicular, non-radicular, coexistent lower extremity pain without progressive/severe neurologic deficit); (4) timing of treatment (e.g., relative peak pain); (5) dose, frequency, interval between doses of medication (or frequency/intensity of nonpharmacologic treatment); (6) duration of therapy; (7) type of treatment (e.g., type of opioid, nonopioid, nonpharmacologic, etc.); (8) current treatment for opioid use disorder; (9) opioid use history; (10) substance use history; (11) use of concomitant therapies; (12) clinical setting, provider type

Cost-effectiveness of treatment (KQ 9)

Key Question 9. What is the cost-effectiveness of pharmacologic, nonpharmacologic, interventional procedures and management strategies for treatment of acute (<6 weeks duration) LBP, including back pain with radiculopathy? (Include only full economic studies.)

III. Population, Intervention, Comparator, Outcome, Timing, Setting, Study Design (PICOTS)

The criteria for inclusion and exclusion of studies for the systematic review will be based on the KQs and on the specific criteria for population, interventions, comparators, outcomes, timing, and settings (PICOTS), listed in Tables 1-7.

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Table 1. KQs 1 and 2: History/physical, imaging

PICOTS Element	Include	Exclude
Population	**Assessment KQ 1** Adults presenting with acute LBP (<6 weeks duration), including back pain with radiculopathy Note: Including pregnant/breastfeeding adults **Assessment KQ 2** Adults with acute LBP (< 6 weeks duration) with or without radiculopathy who do not present with historical or clinical features suggestive of serious low back problems (e.g., absence of "red flag" symptoms") Note: including pregnant/breastfeeding adults **Special populations/factors** (1) patient demographics or characteristics including those related to social risk factors for health, access to imaging; (2) patient medical or psychiatric comorbidities; (3) type or characteristic of back pain (e.g., onset, duration, severity, recurrent, radicular, non-radicular); (4) clinical setting (2) In addition, for Assessment KQ 2: type of imaging	**Assessment KQ 1** • Adults with subacute (6 to 12 weeks) or chronic LBP (>12 weeks) • Mixed chronic, subacute, and/or acute low back pain populations if study does not report results separately for acute LBP or if <80% of the population does not have acute LBP • Children and adolescents (age <18 years) **Assessment KQ 2** • Adults with subacute (6 to 12 weeks) or chronic LBP (>12 weeks) • Mixed chronic, subacute, and/or acute low back pain populations if study does not report results separately for acute LBP or if <80% of the population does not have acute LBP • Children and adolescents (age <18 years) • Patients with acute LBP due to tumor, cancer, infection, inflammatory arthropathy, blunt force trauma, fracture (including vertebral compression fracture); or LBP associated with severe or progressive neurological deficits including cauda equina
Intervention	**Assessment KQ 1** • Focused patient history and physical exam to identify serious underlying conditions • Use of screening tools for patient stratification **Assessment KQ 2** • Early/immediate lumbar imaging in patients	
Comparators	**Assessment KQ 1** • Appropriate reference standard for condition (e.g., imaging findings) • Usual care (not using screening tool) **Assessment KQ 2** • Usual care (no use of early/immediate imaging)	

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PICOTS Element	Include	Exclude
Outcomes	**Assessment KQ 1** • Diagnostic accuracy metrics • Prognostic factors, factors predicting chronic LBP, long term disability • Patient health outcomes (e.g., pain, function, quality of life) **Assessment KQ 2** • Patient health outcomes (e.g., pain, function, quality of life) • KQ 2d: ICER or similar outcome comparing treatment options and describing change in costs per change in benefits or harms, cost per specific beneficial outcome or harm, etc. **Harms** • Assessment related • Imaging related • KQ 2: Harms related to subsequent additional testing or treatment	
Timing	At presentation, follow-up appropriate to determine outcomes	
Settings	Any outpatient, urgent care, or emergency care setting, pre-hospital settings (e.g., during ambulance transport for KQ1)	• Inpatient setting
Study design	**Assessment KQ 1** • Studies of diagnostic accuracy • Prognostic, predictive studies that control for confounding • RCTs of stratification tools **Assessment KQ 2** • RCTs • Full economic studies (KQ2d) that include modeling of downstream utilization	• Editorials, letters, white papers, conference proceedings, citations that have not been peer-reviewed or are not part of a government technology assessment, duplicate publications of the same study that do not report on different outcomes or preliminary reports when results are published in later versions • Costing studies

ICER = incremental cost-effectiveness ratio; KQ = Key Question; LBP = low back pain; RCT = randomized controlled trial.

Special populations and factors to evaluate for modification

The following variables are relevant to all KQs related to treatment (KQs 3-8; Tables 2-6):
(1) patient demographics or characteristics including those related to social risk factors related to health; (2) patient medical or psychiatric comorbidities; (3) type or characteristic of back pain (e.g., onset/acuity, duration, severity, recurrent LBP, prior history of LBP, radicular, non-radicular, coexistent lower extremity pain without progressive/severe neurologic deficit); (4) timing of treatment (e.g., relative peak pain); (5) dose, frequency, interval between doses of medication (or frequency/intensity of nonpharmacologic treatment); (6) duration of therapy; (7) type of treatment (e.g., type of opioid, nonopioid, nonpharmacologic, etc.); (8) current treatment for opioid use disorder; (9) opioid use history; (10) substance use history; (11) use of concomitant therapies; (12) clinical setting, provider type

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Table 2. KQs 3 and 4: Opioid therapy

PICOTS Element	Include	Exclude
Population	Adults with acute (<6 weeks) LBP, including back pain with radiculopathy Note: including pregnant/breast-feeding adults	• Adults with subacute (6 to 12 weeks) or chronic LBP (>12 weeks) • Mixed chronic, subacute, and/or acute low back pain populations if study does not report results separately for acute LBP or if <80% of the population does not have acute LBP • Children and adolescents (age <18 years) • Patients with LBP due to tumor, cancer, infection, inflammatory arthropathy, blunt force trauma, fracture (including vertebral compression fracture); or LBP associated with severe or progressive neurological deficits including cauda equina

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PICOTS Element	Include	Exclude
Intervention	**KQ 3 a-c, e, g** • Systemic opioid therapy including agonists, partial agonists, and mixed mechanism opioids (tapentadol or tramadol); transdermal patches, topical opioids • Systemic opioid combined with a nonopioid pharmacologic therapy • Systemic opioid combined with nonpharmacologic therapy **KQ 3d** • Opioid prescription **KQ 3f** • Opioid prescribing strategy **KQ 4a** • Factors: (1) existing opioid management plans; (2) patient education; (e) urine drug screening; (4) use of prescription drug monitoring program data; (5) availability of close follow-up; (6) prescribing, provision of naloxone (or other opioid antagonists); 7) patient presentation (e.g., pain severity, etiology); 8) prior opioid prescription and experience; 9) patient expectations for pain control; 10) contraindications to other treatment options (e.g., to NSAIDs) **KQ 4b** • Factors: (1) existing opioid management plans; (2) patient education; (e) urine drug screening; (4) use of prescription drug monitoring program data; (5) availability of close follow-up; (6) prescribing, provision of naloxone (or other opioid antagonists) **KQ 4c** • Shared decision-making strategy, tool **KQ 4 d** • Instruments, genetic/metabolic tests for predicting risk of misuse, opioid use disorder, and overdose **KQ 4 e** • Instruments for predicting risk of long-term use of opioids, opioid misuse, opioid use disorder, or overdose	• Interventions to treat opioid use disorder, misuse, or overdose • Opioids not available in the U.S. • Non-FDA-approved opioids

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PICOTS Element	Include	Exclude
Comparators	**KQ 3 a-c, e, g** • Placebo • Nonopioid pharmacologic therapy • Noninvasive, nonpharmacologic therapy • For opioids combined with a nonopioid compare with the nonopioid alone or another nonopioid and with opioid alone • For opioids combined with a nonpharmacologic compare with the nonpharmacologic therapy alone or another nonpharmacologic treatment and with opioid alone **KQ 3d** • No opioid prescription **KQ 3f** • Different opioid prescribing strategy vs. intervention strategy; stronger vs. weaker opioids; different administration routes **KQ 4a, b** • Not utilizing decision factors in 4a, b above (in interventions) **KQ 4c** • No shared decision-making strategy • Different tool **KQ 4d** • Reference standard for misuse, opioid use disorder, or overdose; or other benchmarks **KQ 4e** • Usual care (no tool) • Different tool	• Included therapies vs. excluded therapies • Opioids not available in the U.S. • Non-FDA-approved opioids

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PICOTS Element	Include	Exclude
Outcomes	**KQ 3, KQ 4b, 4c** **Primary health outcomes (validated measures)** • Function • Pain • Pain relief satisfaction, completeness of pain relief • Quality of life • Sleep quality, sleep disturbance • Psychological distress (including depression, anxiety, etc.) • Return to work • Recurrence of LBP • Patient perception of improvement • Use of rescue medication • Continued opioid use (KQ 3a, b, c) **KQ 4a** • Opioid prescribing rates **KQ 4d** • Measures of diagnostic accuracy **KQ 4e** • Persistent opioid use **KQ 3, KQ 4b, 4c** **Harms** • Shorter term harms (e.g., sedation, fatigue, pruritus, dizziness, nausea, etc.) • Gastrointestinal-related harms (e.g., including opioid induced constipation) • Other harms (e.g., falls, fractures, motor vehicle accidents) • Endocrinological harms • Cardiovascular events • Cognitive harms, etc. • Serious AEs • Withdrawal due to AEs • Psychological harms (e.g., depression, suicidal ideation, suicidal behavior, etc.) • Overdose • Misuse, withdrawal, opioid use disorder, substance use disorder and related outcomes • Diversion	• Nonclinical outcomes (e.g., non-harm lab measures) • Non-validated measures or non-validated instruments for health outcomes (e.g., pain, function, quality of life) or psychological measures (e.g., depression, anxiety)
Timing	<1 day; 1 day to <1 week (also divide into 2-3 days and 4 days to 1 week); 1 week to <2 weeks; 2 weeks to <4 weeks; ≥4 weeks	
Settings	Any outpatient, urgent care, or emergency care setting, pre-hospital settings (e.g., during ambulance transport)	• Inpatient setting

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PICOTS Element	Include	Exclude
Study design	• RCTs to be the focus for effectiveness, benefits (including cross-over, cluster and pragmatic trials) • Comparative NRSI that control for confounding; Preference for what is best evidence (e.g., RCTs, prospective studies with least potential for bias) • NRSI for harms/AEs • Pre-post studies will be considered for KQ 4a	• Case series, pre-post, single arm studies for effectiveness outcomes; case reports • Case-control studies for effectiveness outcomes • Cross-sectional studies • Uncontrolled NRSI • Studies with historic controls • Editorials, letters, white papers, conference proceedings, citations that have not been peer-reviewed, duplicate publications of the same study that do not report on different outcomes or follow-up times, preliminary reports when results are published in later versions • Studies with fewer than 20 patients per treatment arm or 40 patients total

AE = adverse event; FDA = Food and Drug Administration; KQ = Key Question; LBP = low back pain; NRSI = nonrandomized studies of interventions; RCT = randomized controlled trial; U.S. = United States.

Table 3. KQ 5: Nonopioid pharmacologic therapy

PICOTS Element	Include	Exclude
Population	Adults with acute (<6 weeks) LBP, including back pain with radiculopathy Note: including pregnant/breast-feeding adults	• Adults with subacute (6 to 12 weeks) or chronic LBP (>12 weeks) • Mixed chronic, subacute, and/or acute low back pain populations if study does not report results separately for acute LBP or if <80% of the population does not have acute LBP • Children and adolescents (age <18 years old) • Patients with LBP due to tumor, cancer, infection, inflammatory arthropathy, blunt force trauma, fracture (including vertebral compression fracture); or LBP associated with severe or progressive neurological deficits including cauda equina
Intervention	Oral, parenteral (IV, IM), transmucosal, or topical nonopioid pharmacological therapy used for acute pain (e.g., acetaminophen, nonsteroidal anti-inflammatory drugs, systemic corticosteroids, skeletal muscle relaxants, benzodiazepines, antidepressants, anticonvulsants); lidocaine, sub-dissociative does of ketamine, cannabis, common herbal remedies (e.g., willow bark) Combination of two non-opioid drugs, one of which must be an NSAID or acetaminophen	• Combination of more than 2 non-opioid drugs • Combinations that do not include either an NSAID or acetaminophen

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PICOTS Element	Include	Exclude
Comparators	• Placebo or sham • Other nonopioid pharmacological therapy or noninvasive nonpharmacological therapy • For nonopioids combined with another therapy (e.g., nonpharmacologic therapy) compare the combination with the same individual therapy alone • Compare combination of 2 non-opioid drugs vs. NSAID or acetaminophen ***NOTE:*** *Include oral vs. topical NSAID studies as well as aspirin vs. NSAID studies; include comparisons between different classes of nonopioids*	• Included therapies vs. excluded therapies. • For comparison of combination of nonopioid drugs, comparators other than and NSAID or acetaminophen
Outcomes	**Primary health outcomes (validated measures)** • Function • Pain • Pain relief satisfaction, completeness of pain relief • Quality of life • Sleep quality, sleep disturbance • Psychological distress (including depression, anxiety, etc.) • Return to work • Recurrence of LBP • Patient perception of improvement • Use of rescue medication • Opioid use, continued opioid use **Harms** • Short term harms (e.g., sedation, fatigue, pruritus, dizziness, nausea, etc.) • Gastrointestinal-related harms • Other harms (e.g., falls, fractures, motor vehicle accidents, endocrinological harms, cardiovascular events, cognitive harms, etc.) • Serious AEs • Withdrawal due to AEs • Psychological harms (e.g., depression, suicidal ideation, suicidal behavior, etc.) • Overdose • Misuse, withdrawal, opioid use disorder, substance use disorder and related outcomes • Diversion	• Nonclinical outcomes (e.g., non-harm lab measures) • Non-validated measures or instruments for health outcomes (e.g., pain, function, quality of life, depression)
Timing	<1 day; 1 day to <1 week (also divide into 2-3 days and 4 days to 1 week); 1 week to <2 weeks; 2 weeks to <4 weeks; ≥4 weeks	

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PICOTS Element	Include	Exclude
Settings	Any outpatient, urgent care, or emergency care setting, pre-hospital settings (e.g., during ambulance transport)	• Inpatient setting
Study design	• RCTs to be the focus for effectiveness, benefits (including cross-over, cluster and pragmatic trials) • Comparative NRSI that control for confounding; Preference for what is best evidence (e.g., RCTs, prospective studies with least potential for bias) • NRSI for harms/AEs	• Case series, pre-post, single arm studies for effectiveness outcomes; case reports • Case-control studies for effectiveness outcomes • Cross-sectional studies • Uncontrolled NRSI • Studies with historic controls • Editorials, letters, white papers, conference proceedings, citations that have not been peer-reviewed, duplicate publications of the same study that do not report on different outcomes or follow-up times, preliminary reports when results are published in later versions • Studies with fewer than 20 patients per treatment arm or 40 patients total

AE = adverse event; KQ = Key Question; IM = intramuscular; IV = intravenous; LBP = low back pain; NRSI = nonrandomized studies of interventions; NSAID = nonsteroidal anti-inflammatory drug; RCT = randomized controlled trial.

Table 4. KQ 6: Noninvasive, nonpharmacologic treatments

PICOTS Element	Include	Exclude
Population	Adults with acute (<6 weeks) LBP, including back pain with radiculopathy Note: including pregnant/breast-feeding adults	• Adults with subacute (6 to 12 weeks) or chronic LBP (>12 weeks) • Mixed chronic, subacute, and/or acute low back pain populations if study does not report results separately for acute LBP or if <80% of the population does not have acute LBP • Children and adolescents (age <18 years) • Patients with LBP due to tumor, cancer, infection, inflammatory arthropathy, blunt force trauma, fracture (including vertebral compression fracture); or LBP associated with severe or progressive neurological deficits including cauda equina

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PICOTS Element	Include	Exclude
Intervention	• Exercise (and related therapies, including self-guided exercise e.g., from a physical therapist, stretching) • Psychological therapies (e.g., CBT, operant therapy, others) • Hypnosis • Eye movement desensitization and reprocessing (EMDR) therapy • Mindfulness practices (e.g., Mindfulness Base Stress Reduction [MBSR]) • Manual therapies (e.g., musculoskeletal manipulation/mobilization) • physical modalities [transcutaneous electrical nerve stimulation, ultrasound, braces, traction, heat, cold] • Transcranial magnetic stimulation • Meditation • Relaxation • Music therapy • Virtual reality • Acupuncture • Massage • Cupping • Mind-body practices (e.g., Yoga, Tai Chi) • Energy therapy (e.g., Reiki) • Advice to stay active, patient education • Standardized/structured self-management (e.g., Back School) • Support groups • Self-management methods (e.g., use of back support, postural changes, bedding support, etc.)	• Studies evaluating incremental value of adding a noninvasive nonpharmacological intervention to another noninvasive nonpharmacological intervention • Invasive nonsurgical treatments (e.g., injections, nerve block, parenterally administered medications) • Others not listed for inclusion
Comparators	• Sham • Waitlist, usual care, attention control, no treatment • Other included noninvasive, nonpharmacologic treatments listed	• Comparisons to interventions not listed • Comparisons within nonpharmacological intervention types (e.g., comparisons of different types of exercise with each other, different types of massage with each other)

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PICOTS Element	Include	Exclude
Outcomes	**Primary health outcomes (validated measures)** • Function • Pain • Pain relief satisfaction, completeness of pain relief • Quality of life • Sleep quality, sleep disturbance • Psychological distress (including depression, anxiety, etc.) • Return to work • Recurrence of LBP • Patient perception of improvement • Use of rescue medication • Opioid use, continued opioid use **Harms** • Harms specific to the treatment used • Serious AEs • Withdrawal due to AEs • Psychological harms (e.g., depression, suicidal ideation, suicidal behavior, etc.) • Misuse, withdrawal, opioid use disorder/substance use disorder and related outcomes	• Nonclinical outcomes (e.g., non-harm lab measures) • Non-validated measures or instruments for health outcomes (e.g., pain, function, quality of life, depression)
Timing	<1 day; 1 day to <1 week (also divide into 2-3 days and 4 days to 1 week); 1 week to <2 weeks; 2 weeks to <4 weeks; ≥4 weeks	
Settings	Any outpatient, urgent care, or emergency care setting, pre-hospital settings (e.g., during ambulance transport)	• Inpatient setting
Study design	• RCTs to be the focus for effectiveness, benefits (including cross-over, cluster and pragmatic trials) • Comparative NRSI that control for confounding; Preference for what is best evidence (e.g., RCTs, prospective studies with least potential for bias) • NRSI for harms/AEs	• Case series, pre-post, single arm studies for effectiveness outcomes; case reports • Case-control studies for effectiveness outcomes • Cross-sectional studies • Uncontrolled NRSI • Studies with historic controls • Editorials, letters, white papers, conference proceedings, citations that have not been peer-reviewed, duplicate publications of the same study that do not report on different outcomes or follow-up times, preliminary reports when results are published in later versions • Studies with fewer than 20 patients per treatment arm or 40 patients total

AE = adverse event; CBT = cognitive behavioral therapy; KQ = Key Question; LBP = low back pain; NRSI = nonrandomized studies of interventions; RCT = randomized controlled trial.

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Table 5. KQ 7: Selected interventions and procedures

PICOTS Element	Include	Exclude
Population	Adults with acute (<6 weeks) LBP, including back pain with radiculopathy Note: including pregnant/breast-feeding adults	• Adults with subacute (6 to 12 weeks) or chronic LBP (>12 weeks) • Mixed chronic, subacute, and/or acute low back pain populations if study does not report results separately for acute LBP or if <80% of the population does not have acute LBP • Children and adolescents (age <18 years) Patients with LBP due to tumor, cancer, infection, inflammatory arthropathy, blunt force trauma, fracture (including vertebral compression fracture); or LBP associated with severe or progressive neurological deficits including cauda equina
Interventions	• Trigger point injection, fascial plane block • Botulinum toxin • Epidural steroid injection, peri-radicular injection • SI joint injection • Dry needling	• Surgical procedures • Others not listed for inclusion
Comparators	• Sham • Waitlist, attention control, no treatment • Usual care • Included interventions	• Non-included procedures
Outcomes	**Primary health outcomes (validated measures)** • Function • Pain • Pain relief satisfaction, completeness of pain relief • Quality of life • Sleep quality, sleep disturbance • Psychological distress (including depression, anxiety, etc.) • Return to work • Recurrence of LBP • Patient perception of improvement • Use of rescue medication • Opioid use, continued opioid use **Harms** • Harms specific to the treatments used • Serious AEs • Withdrawal due to AEs • Psychological harms (e.g., depression, suicidal ideation, suicidal behavior, etc.) • Misuse, withdrawal, opioid use disorder/substance use disorder and related outcomes	• Nonclinical outcomes (e.g., non-harm lab measures) • Non-validated measures or instruments for health outcomes (e.g., pain, function, quality of life, depression)

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PICOTS Element	Include	Exclude
Timing	<1 day; 1 day to <1 week (also divide into 2-3 days and 4 days to 1 week); 1 week to <2 weeks; 2 weeks to <4 weeks; ≥4 weeks	
Settings	Any outpatient, urgent care, or emergency care setting, pre-hospital settings (e.g., during ambulance transport)	• Inpatient setting
Study design	• RCTs to be the focus for effectiveness, benefits (including cross-over, cluster and pragmatic trials) • Comparative NRSI that control for confounding; Preference for what is best evidence (e.g., RCTs, prospective studies with least potential for bias) • NRSI for harms/AEs	• Case series, pre-post, single arm studies for effectiveness outcomes; case reports • Case-control studies for effectiveness outcomes • Cross-sectional studies • Uncontrolled NRSI • Studies with historic controls • Editorials, letters, white papers, conference proceedings, citations that have not been peer-reviewed, duplicate publications of the same study that do not report on different outcomes or follow-up times, preliminary reports when results are published in later versions • Studies with fewer than 20 patients per treatment arm or 40 patients total

AE = adverse event; KQ = Key Question; LBP = low back pain; NRSI = nonrandomized studies of interventions; RCT = randomized controlled trial; SI = sacroiliac.

Table 6. KQ 8: Management strategies or pathways

PICOTS Element	Include	Exclude
Population	Adults with acute (<6 weeks) LBP, including back pain with radiculopathy Note: including pregnant/breastfeeding adults	• Adults with subacute (6 to 12 weeks) or chronic LBP (>12 weeks) • Mixed chronic, subacute, and/or acute low back pain populations if study does not report results separately for acute LBP or if <80% of the population does not have acute LBP • Children and adolescents (age <18 years) • Patients with LBP due to tumor, cancer, infection, inflammatory arthropathy, blunt force trauma, fracture (including vertebral compression fracture); or LBP associated with severe or progressive neurological deficits including cauda equina
Intervention	• Stratification by risk for poor prognosis • Early referral to therapy (e.g., manipulation therapies, exercise, physical therapy modalities) • Matching therapies through treatment-based classification of patients, • Stepped care strategies, interdisciplinary models	

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PICOTS Element	Include	Exclude
Comparators	• Waitlist or no treatment • Usual care • Another included strategy	
Outcomes	**Primary health outcomes (validated measures)** • Function • Pain • Pain relief satisfaction, completeness of pain relief • Quality of life • Sleep quality, sleep disturbance • Psychological distress (including depression, anxiety, etc.) • Return to work • Recurrence of LBP • Patient perception of improvement • Use of rescue medication • Opioid use continued, opioid use **Harms** • Harms specific to the strategy/pathway • Serious AEs • Withdrawal due to AEs • Psychological harms (e.g., depression, suicidal ideation, suicidal behavior, etc.) • Overdose • Misuse, withdrawal, opioid use disorder/substance use disorder and related outcomes	• Nonclinical outcomes (e.g., non-harm lab measures) • Non-validated measures or instruments for health outcomes (e.g., pain, function, quality of life, depression)
Timing	<1 day; 1 day to <1 week (also divide into 2-3 days and 4 days to 1 week); 1 week to <2 weeks; 2 weeks to <4 weeks; ≥4 weeks	
Settings	Any outpatient, urgent care, or emergency care setting, pre-hospital settings (e.g., during ambulance transport)	• Inpatient setting

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PICOTS Element	Include	Exclude
Study design	• RCTs to be the focus for effectiveness, benefits (including cross-over, cluster and pragmatic trials) • Comparative NRSI that control for confounding; Preference for what is best evidence (e.g., RCTs, prospective studies with least potential for bias) • NRSI for harms/AEs	• Case series, pre-post, single arm studies for effectiveness outcomes; case reports • Case-control studies for effectiveness outcomes • Cross-sectional studies • Uncontrolled NRSI • Studies with historic controls • Editorials, letters, white papers, conference proceedings, citations that have not been peer-reviewed, duplicate publications of the same study that do not report on different outcomes or follow-up times, preliminary reports when results are published in later versions • Studies with fewer • Studies with fewer than 20 patients per treatment arm or 40 patients total

AE = adverse event; KQ = Key Question; LBP = low back pain; NRSI = nonrandomized studies of interventions; RCT = randomized controlled trial.

Table 7. KQ 9: Cost-effectiveness of treatment

PICOTS Element	Include	Exclude
Population	Adults with acute (<6 weeks) LBP, including back pain with radiculopathy Note: including pregnant/breastfeeding adults	• Adults with subacute (6 to 12 weeks) or chronic LBP (>12 weeks) • Mixed chronic, subacute, and/or acute low back pain populations if study does not report results separately for acute LBP or if <80% of the population does not have acute LBP • Children and adolescents (age <18 years) • Patients with LBP due to tumor, cancer, infection, inflammatory arthropathy, blunt force trauma, fracture (including vertebral compression fracture); or LBP associated with severe or progressive neurological deficits including cauda equina
Intervention	• Systemic opioid therapy • Nonopioid therapy • Nonpharmacologic, noninvasive therapy • Selected interventional procedures • Management strategies, pathways	• Treatments on included for the review
Comparators	• Placebo/sham • Usual care • Included treatment(s) vs. other included treatment(s)	• Included therapies vs. excluded therapies

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PICOTS Element	Include	Exclude
Outcomes	• ICER or similar outcome comparing treatment options and describing change in costs per change in benefits or harms, cost per specific beneficial outcome or harm, etc.	• Cost of treatment only
Timing	Any	
Settings	Any outpatient, urgent care, or emergency care setting, pre-hospital settings (e.g., during ambulance transport)	• Inpatient setting
Study design	• Full economic studies (e.g., cost-utility, cost-benefit) • Preference given to U.S. studies, populations	• Costing studies • Editorials, letters, white papers, conference proceedings, citations that have not been peer-reviewed or are not part of a government technology assessment, duplicate publications of the same study that do not report on different outcomes or preliminary reports when results are published in later versions

ICER = incremental cost-effectiveness ratio; KQ = Key Question; LBP = low back pain; RCT = randomized controlled trial; U.S. = United States.

IV. Methods

Criteria for Inclusion/Exclusion of Studies in the Review

The criteria for inclusion and exclusion of studies will be based on the Key Questions and are described in the previous PICOTS section (section III). Below are additional details on the scope of this project:

Study Designs: We will use a best evidence approach[35] and randomized controlled trials (RCTs) will be sought initially. Given that their will likely be a paucity of RCTs available to answer some key questions, high quality prospective comparative nonrandomized studies (i.e., comparative observational studies) of interventions (NRSI) that control for confounding will be considered; if none are identified, high quality retrospective NRSI that control for confounding will be considered. We will exclude uncontrolled observational studies, case series, and case reports. For KQ 1, we will include studies of diagnostic accuracy that use an appropriate reference standard (questions a and d) and prognostic or predictive studies that control for confounding (questions b and d). For KQ 4a, we will include pre-post studies. For KQ 4c we will include studies that evaluate the performance of a risk prediction instrument against a reference standard for opioid misuse, opioid use disorder, or overdose. For evaluation of harms, we will include NRSI with a focus on those specifically designed to evaluate harms. Systematic reviews may be considered as primary sources of evidence if they are a strong match to our key questions and PICOTS criteria and are assessed as being low risk of bias using the AMSTAR-2 quality tool, on factors such as the methods used to conduct searches, select studies,

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abstract data, assess risk of bias, and synthesize data.[2,30] We will update the findings of any included systematic reviews with any new primary studies identified in our searches.

Non-English Language Studies: We will restrict to English-language articles but will review English language abstracts of non-English language articles to identify studies that would otherwise meet inclusion criteria, to assess the likelihood of language bias.

Literature Search Strategies for Identification of Relevant Studies to Answer the Key Questions

Publication Date Range: Electronic searches for evidence will be conducted from database inception through January 2024. Electronic searches will be updated while the draft report is out for public review to identify new publications. Literature identified during the updated search will be assessed by following the same process of dual review as all other studies considered for inclusion in the report. If any pertinent new literature is identified for inclusion in the report, it will be incorporated before the final submission of the report.

Literature Databases: PubMed® MEDLINE PsycINFO®, Embase®, Cochrane Central Register of Controlled Trials, and Cochrane Database of Systematic Reviews will be searched to capture published literature. Search strategies for MEDLINE are available in Appendix A.

Hand Searching: Reference lists of included articles and relevant systematic reviews will also be reviewed for includable literature.

Contacting Authors: In the event that information regarding methods or results appears to be omitted from the published results of a study, or if we are aware of unpublished data, we will contact authors to obtain this information.

Process for Selecting Studies

In accordance with the Methods Guide for Effectiveness and Comparative Effectiveness Reviews,[2] we will use the pre-established criteria above to screen citations (titles and abstracts) identified through our searches to determine eligibility for full-text review. We will use DistillerSR® to improve efficiency in screening articles and risk of bias assessment. Given the likely paucity of RCTs for portions of this review, we will include NRSIs. We will follow a "best-evidence" approach[35] and to the extent possible, focus on comparative NRSIs with concurrent controls and which control for confounding as appropriate to the key question. We will focus on primary studies and review systematic review (SR) references for relevant studies as it is unlikely that SRs will fully answer the key questions. If all studies in a systematic review meet inclusion criteria and report on outcomes of interest to this review, consideration will be given to updating the SR analyses with new evidence and the totality of the evidence will be evaluated. All excluded abstracts will be dual reviewed to assure accuracy for inclusion. All citations deemed appropriate for inclusion by at least one reviewer will be retrieved. Each full-text article will be independently reviewed for eligibility by a minimum of two team members, including any articles suggested by the GDG, AB, TEP members, peer reviewers or

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that arise from the public posting process. Any disagreements regarding inclusion will be resolved by consensus. A record of studies excluded at the full-text level with reasons for exclusion will be maintained.

Data Abstraction and Data Management

After studies are selected for inclusion, data will be abstracted using standardized templates into categories that include but are not limited to: study design, year, setting, country, sample size, eligibility criteria, participant enrollment methods, population and clinical characteristics, intervention characteristics, results relevant to each Key Question as outlined in the previous PICOTS section and information related to special populations and factors which may impact treatment effectiveness or harms. Information on confounders (in addition to those already identified for abstraction related to patient and intervention characteristics and methods of adjustment for them will also be abstracted. Information relevant for assessing applicability will be abstracted and include the number of patients randomized relative to the number of patients enrolled, use of run-in or wash-out periods, and characteristics of the population, intervention, and care settings. All study data will be verified for accuracy and completeness by a second team member.

Assessment of Methodological Risk of Bias of Individual Studies

Predefined criteria will be used to determine the risk of bias for all included studies. Methods from the *Methods Guide for Effectiveness and Comparative Effectiveness Review*[2] will be used in concordance with the approach recommended in the chapter, Assessing the Risk of Bias of Individual Studies When Comparing Medical Interventions.[2,37] Randomized trials will be evaluated using criteria outlined in the *Cochrane Handbook for Systematic Reviews of Interventions (Chapter 8.5 Risk of Bias Tool)*[17] and methods developed by the Cochrane Back and Neck Review Group.[12,13] NRSI will be evaluated based on instruments tailored to observational studies[34,38] and criteria developed by the U.S. Preventive Services Task Force[36] which include methods of patient selection (e.g., consecutive patients, use of an inception cohort) and appropriate control for confounding. Studies of diagnostic accuracy will be assessed using QUADAS-2[39] and the Quality in Prognosis Studies (QUIPS) tool for studies evaluating risk factors will be used for prognostic studies.[16] Systematic reviews will be assessed using the AMSTAR-2 quality rating instrument on factors such as the methods used to conduct searches, select studies, abstract data, assess risk of bias, and synthesize data.[30]

Studies will be rated as being "low," "moderate," or "high" risk of bias.

Studies rated at low risk of bias and their results are generally considered valid. Good-quality intervention studies include clear descriptions of the population, setting, interventions, and comparison groups; a valid method for allocating patients to treatment; low dropout rates and clear reporting of dropouts; appropriate means for preventing bias; and appropriate measurement of outcomes. Good-quality diagnostic accuracy studies use unbiased methods to select patients; report interpretation of the index test without knowledge of the reference standard; report a predefined threshold for a positive index test; report use of an appropriate reference standard; apply the reference standard to all patients;

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report interpretation of the reference standard blinded to the results of the index test; and report low attrition.

Studies rated at moderate risk of bias are susceptible to some bias, though not enough to invalidate the results. These studies may not meet all the criteria for a rating of good quality, but no flaw or combination of flaws is likely to cause major bias. The study may be missing information, making it difficult to assess limitations and potential problems. The fair-quality category is broad, and studies with this rating vary in their strengths and weaknesses. The results of some studies at moderate risk of bias are likely to be valid, while others may be only possibly valid.

Studies rated at high risk of bias have significant flaws that imply biases of various types that may invalidate the results. They have a serious or "fatal" flaw (or combination of flaws) in design, analysis, or reporting; large amounts of missing information; discrepancies in reporting; or serious problems in the delivery of the intervention. The results of these studies are at least as likely to reflect flaws in the study design as to show true difference between the compared interventions. We will not exclude studies rated at high risk of bias a priori, but high risk of bias studies will be considered less reliable than higher-quality studies when synthesizing the evidence, particularly if discrepancies between studies are present.

Two team members will independently assess quality. Any disagreements will be resolved by consensus.

Data Synthesis

We will construct evidence tables identifying the study and patient characteristics (as discussed above), results of interest, and quality ratings for all included studies, as well as summary tables and/or figures to highlight the main findings. We will review and highlight studies by using the best evidence focus for our synthesis for each Key Question. We will analyze randomized trials and NRSI separately and report them separately unless findings are very consistent across study designs and the studies are clinically homogeneous. Studies with the least risk of bias will be summarized separately and compared with summarized results from studies at high risk of bias.

Findings will be synthesized qualitatively (e.g., ranges and descriptive analysis, with interpretation of results) and quantitatively (meta-analysis) when appropriate. To address anticipated heterogeneity in reported outcomes, variation in their definitions and criteria for what constitutes response, we will focus on validated outcomes for pain, function, and quality of life for example. We will seek input from the GDG, AB and TEP regarding outcomes and their prioritization. We will consider classifying the magnitude of effects for continuous measures of pain and function using a similar system as in prior AHRQ reviews on pain[4,6,24,31,32,37] and will evaluate the proportion of patients meeting thresholds for clinically important differences (e.g., ≥30% pain relief) when reported. For analysis of continuous measures across the same outcome measures (e.g., visual analog scale [VAS] for pain) we will report

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mean differences and use standardized mean differences for outcomes measures with similar constructs together with 95% confidence intervals.

We will consider pooling studies if there are two to five clinically and methodologically comparable studies.[11,26] For NRSI, pooled estimates will be based on author-reported effect estimates that adjust for key confounders; these will be evaluated separately from RCT estimates. Sensitivity and subgroup analyses will be performed to explore statistical heterogeneity and differences by study quality, study design, intervention differences, patient characteristics, and outcome measurement as data permit. We will summarize within-study analyses of subgroup differences focusing on studies that test for modification and will perform study-level analyses on key demographic, intervention, and clinical factors as data permit in attempt to evaluate differential effectiveness and harms. Evidence gaps and applicability to U.S. practice settings will be assessed based on the EPC Methods Guide, using the PICOTS framework.[3]

Grading the Strength of Evidence (SOE) for Major Comparisons and Outcomes

Outcomes to be assessed for strength of evidence will be prioritized based on input from the GDG, AB and TEP. Based on this prioritized list, the strength of evidence for comparison-outcome pairs within each KQ will be initially assessed by one researcher for each clinical outcome (see PICOTS) by using the approach described in the *Methods Guide for Effectiveness and Comparative Effectiveness Review*.[2] To ensure consistency and validity of the evaluation, the initial assessment will be independently reviewed by at least one other experienced investigator using the following criteria:

- Study limitations (low, medium, or high level of study limitations)
    - This is the degree to which studies for a given outcome are likely to have reduced bias based on study design, analysis, and conduct. The aggregate risk of bias across individual studies reporting an outcome is considered.
- Consistency (consistent, inconsistent, or unknown/not applicable)
    - This is the degree to which studies report similar magnitudes of effect (i.e., range sizes are similar) or same direction of effect (i.e., effect sizes have the same sign).
- Directness (direct or indirect)
    - This is degree to which the outcome is directly or indirectly related to health outcomes of interest. Patient centered outcomes are considered direct.
- Precision (precise or imprecise)
    - Describes the level of certainty of the effect estimate for a particular outcome with a precise estimate being one that allows a clinically useful conclusion. This may be based on sample size sufficiency and number of events. If these are adequate, the interpretation of the confidence interval is also considered. When quantitative synthesis is not possible, sample size and assessment of variance within individual studies will be considered.
- Reporting bias (suspected or undetected)
    - Publication bias, selective outcome reporting, and selective analysis reporting are types of reporting bias. Reporting bias is difficult to assess as systematic identification of

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unpublished evidence is challenging. If sufficient numbers of RCTs (>10) are available, quantitative funnel plot analysis may be done.

The strength of evidence will be assigned an overall grade of high, moderate, low, or very low according to a four-level scale (Table 8) by evaluating and weighing the combined results of the above domains.

Table 8. Description of the strength of evidence grades

Strength of Evidence	Description
High	We are very confident that the estimate of effect lies close to the true effect for this outcome. The body of evidence has few or no deficiencies. We believe that the findings are stable, i.e., another study would not change the conclusions.
Moderate	We are moderately confident that the estimate of effect lies close to the true effect for this outcome. The body of evidence has some deficiencies. We believe that the findings are likely to be stable, but some doubt remains.
Low	We have limited confidence that the estimate of effect lies close to the true effect for this outcome. The body of evidence has major or numerous deficiencies (or both). We believe that additional evidence is needed before concluding either that the findings are stable or that the estimate of effect is close to the true effect.
Very Low	We are unable to estimate an effect, or we have no confidence in the estimate of effect for this outcome. The body of evidence has unacceptable deficiencies which precludes reaching a firm conclusion. If no evidence is available, it will be noted as "no evidence"

Bodies of evidence consisting of RCTs are initially considered as high strength while bodies of comparative observational studies begin as low-strength evidence. The strength of the evidence may be downgraded based on the limitations described above. There are also situations where the observational evidence may be upgraded (e.g., large magnitude of effect, presence of dose-response relationship or existence of plausible unmeasured confounders), if there are no downgrades on the primary domains, as described in the AHRQ Methods Guide.[2,37] Where both RCTs and observational studies are included for a given intervention-outcome pair, we follow the additional guidance on weighting RCTs over observational studies, assessing consistency across the two bodies of evidence, and determining a final rating.[2]

Summary tables will include ratings for individual strength of evidence domains (risk of bias, consistency, precision, directness) based on the totality of underlying evidence identified.

Assessing Applicability

Applicability will be assessed in accordance with the AHRQ's Methods Guide,[2] using the PICOTS framework. Applicability refers to the degree to which outcomes associated with the intervention are likely to be similar across patients and settings relevant to the care of patients undergoing treatment for acute LBP on the populations, interventions, comparisons, and outcomes synthesized across included studies. Multiple factors identified a priori that are likely to impact applicability may include (but are not limited to) type or characteristic of back pain (e.g., onset/acuity, duration, severity, recurrent LBP,

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prior history of LBP, radicular, non-radicular, coexistent lower extremity pain without progressive/severe neurologic deficit), clinical setting (e.g., ED vs. primary care), provider type, treatment characteristics (type, dose, frequency, duration, etc.), or characteristics of enrolled patient populations (e.g., sex, age, social risk factors related to health, health and functional status, comorbidities). Review of abstracted information on these factors will be used to assess situations for which the evidence is most relevant and to evaluate applicability to real-world clinical practice in typical U.S. settings. We will provide a qualitative summary of our assessment.

V. References

1. Framing Opioid Prescribing Guidelines for Acute Pain: Developing the Evidence National Academies of Sciences, Engineering, and Medicine; Health and Medicine Division; Board on Health Care Services; Committee on Evidence-Based Clinical Practice Guidelines for Prescribing Opioids for Acute Pain. Framing Opioid Prescribing Guidelines for Acute Pain: Developing the Evidence. Washington (DC): National Academies Press (US); 2019 Dec 19. PMID: 32182005.

2. Methods Guide for Effectiveness and Comparative Effectiveness Reviews. Content last reviewed October 2022. Effective Health Care Program, Agency for Healthcare Research and Quality, Rockville, MD. Chapters available at: https://effectivehealthcare.ahrq.gov/topics/cer-methods-guide/overview. .

3. Atkins D, Chang S, Gartlehner G, et al. Assessing the Applicability of Studies When Comparing Medical Interventions. Methods Guide for Effectiveness and Comparative Effectiveness Reviews AHRQ Publication No 11-EHC019-EF Rockville, MD: Agency for Healthcare Research and Quality (US); 2010.

4. Chou R, Deyo R, Friedly J, et al. Noninvasive Treatments for Low Back Pain. Comparative Effectiveness Review No. 169. (Prepared by the Pacific Northwest Evidence-based Practice Center under Contract No. 290-2012-00014-I.) AHRQ Publication No. 16-EHC004-EF. Rockville, MD2016 February.

5. Chou R, Fu R, Carrino JA, Deyo RA. Imaging strategies for low-back pain: systematic review and meta-analysis. Lancet 2009;373:463-72.

6. Chou R, Hartung D, Turner J, et al. Opioid Treatments for Chronic Pain. Comparative Effectiveness Review No. 229. (Prepared by the Pacific Northwest Evidence-based Practice Center under Contract No. 290-2015-00009-I.) AHRQ Publication No. 20-EHC011. Rockville, MD: Agency for Healthcare Research and Quality. April 2020. DOI: https://doi.org/10.23970/AHRQEPCCER229.2020.

7. Chou R, Qaseem A, Snow V, et al. Diagnosis and treatment of low back pain: a joint clinical practice guideline from the American College of Physicians and the American Pain Society. Ann Intern Med 2007;147:478-91.

8. Chou R, Shekelle P. Will this patient develop persistent disabling low back pain? JAMA 2010;303:1295-302.

9. Dieleman JL, Cao J, Chapin A, et al. US Health Care Spending by Payer and Health Condition, 1996-2016. JAMA 2020;323:863-84.

10. Dowell D, Ragan KR, Jones CM, Baldwin GT, Chou R. CDC Clinical Practice Guideline for Prescribing Opioids for Pain - United States, 2022. MMWR Recomm Rep 2022;71:1-95.

11. Fu R, Gartlehner G, Grant M, et al. Conducting quantitative synthesis when comparing medical interventions: AHRQ and the Effective Health Care Program. J Clin Epidemiol 2011;64:1187-97.

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12. Furlan AD, Malmivaara A, Chou R, et al. 2015 Updated Method Guideline for Systematic Reviews in the Cochrane Back and Neck Group. Spine (Phila Pa 1976) 2015;40:1660-73.

13. Furlan AD, Pennick V, Bombardier C, van Tulder M, Editorial Board CBRG. 2009 updated method guidelines for systematic reviews in the Cochrane Back Review Group. Spine (Phila Pa 1976) 2009;34:1929-41.

14. G. B. D. Low Back Pain Collaborators. Global, regional, and national burden of low back pain, 1990-2020, its attributable risk factors, and projections to 2050: a systematic analysis of the Global Burden of Disease Study 2021. Lancet Rheumatol 2023;5:e316-e29.

15. Global Burden of Disease Collaborative Network. Global Burden of Disease Study 2019 (GBD 2019) results. https://www.healthdata.org/research-analysis/gbd. Accessed August 9 2023.

16. Hayden JA, van der Windt DA, Cartwright JL, Cote P, Bombardier C. Assessing bias in studies of prognostic factors. Ann Intern Med 2013;158:280-6.

17. Higgins JP, Green S, eds. Cochrane Handbook for Systematic Reviews of Interventions. Version 5.1.0 [updated March 2011]. The Cochrane Collaboration, 2011. Available from: www.handbook.cochrane.org.

18. Itz CJ, Geurts JW, van Kleef M, Nelemans P. Clinical course of non-specific low back pain: a systematic review of prospective cohort studies set in primary care. Eur J Pain 2013;17:5-15.

19. Kent ML, Tighe PJ, Belfer I, et al. The ACTTION-APS-AAPM Pain Taxonomy (AAAPT) Multidimensional Approach to Classifying Acute Pain Conditions. Pain Med 2017;18:947-58.

20. Kim LH, Vail D, Azad TD, et al. Expenditures and Health Care Utilization Among Adults With Newly Diagnosed Low Back and Lower Extremity Pain. JAMA Netw Open 2019;2:e193676.

21. Koes BW, van Tulder M, Lin CW, Macedo LG, McAuley J, Maher C. An updated overview of clinical guidelines for the management of non-specific low back pain in primary care. Eur Spine J 2010;19:2075-94.

22. Koes BW, van Tulder MW, Ostelo R, Kim Burton A, Waddell G. Clinical guidelines for the management of low back pain in primary care: an international comparison. Spine (Phila Pa 1976) 2001;26:2504-13; discussion 13-4.

23. Koes BW, van Tulder MW, Thomas S. Diagnosis and treatment of low back pain. BMJ 2006;332:1430-4.

24. McDonagh MS, Selph SS, Buckley DI, et al. Nonopioid Pharmacologic Treatments for Chronic Pain. AHRQ Comparative Effectiveness Reviews No. 228. (Prepared by the Pacific Northwest Evidence-based Practice Center under Contract No. 290-2015-00009-I.) AHRQ Publication No. 20-EHC010. Rockville, MD: Agency for Healthcare Research and Quality; April 2020. DOI:

https://doi.org/10.23970/AHRQEPCCER228.

25. Mehling WE, Gopisetty V, Bartmess E, et al. The prognosis of acute low back pain in primary care in the United States: a 2-year prospective cohort study. Spine (Phila Pa 1976) 2012;37:678-84.

26. Morton SC, Murad MH, O'Connor E, et al. AHRQ Methods for Effective Health Care Quantitative Synthesis—An Update. (Prepared by the Scientific Resource Center under Contract No. Oregon Health & Science University–Pacific Northwest EPC Appendix 2, Page 4 290-2012-0004-C). AHRQ Publication No. 18-EHC007-EF. Methods Guide for Effectiveness and Comparative Effectiveness Reviews. Rockville, MD: Agency for Healthcare Research and Quality (US); 2018.

27. Oliveira CB, Maher CG, Pinto RZ, et al. Clinical practice guidelines for the management of non-specific low back pain in primary care: an updated overview. Eur Spine J 2018;27:2791-803.

28. Pengel LH, Herbert RD, Maher CG, Refshauge KM. Acute low back pain: systematic review of its prognosis. BMJ 2003;327:323.

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29. Qaseem A, Wilt TJ, McLean RM, et al. Noninvasive Treatments for Acute, Subacute, and Chronic Low Back Pain: A Clinical Practice Guideline From the American College of Physicians. Ann Intern Med 2017;166:514-30.

30. Shea BJ, Reeves BC, Wells G, et al. AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. BMJ 2017;358:j4008.

31. Skelly AC, Chou R, Dettori JR, 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. Rockville, MD2020 April.

32. Skelly AC, Chou R, Dettori JR, et al. Noninvasive Nonpharmacological Treatment for Chronic Pain: A Systematic Review. Comparative Effectiveness Review No. 209. (Prepared by the Pacific Northwest Evidence-based Practice Center under Contract No. 290-2015-00009-I.) AHRQ Publication No 18-EHC013-EF. Rockville, MD2018 June.

33. Spears CA, Hodges SE, Kiyani M, et al. Health Care Resource Utilization and Management of Chronic, Refractory Low Back Pain in the United States. Spine (Phila Pa 1976) 2020;45:E1333-E41.

34. Sterne J, Hernán M, McAleenan A, Reeves B, Higgins J. Chapter 25: Assessing risk of bias in a non-randomized study. In: Cochrane Handbook for Systematic Reviews of Interventions version 2019;60.

35. Treadwell JR, Singh S, Talati R, McPheeters ML, Reston JT. A Framework for "Best Evidence" Approaches in Systematic Reviews. AHRQ Methods for Effective Health Care (Prepared by the ECRI Institute Evidence-based Practice Center under Contract No HHSA 290-2007-10063-I) AHRQ Publication No 11-EHC046-EF. Rockville, MD: Agency for Healthcare Research and Quality (US); 2011.

36. U.S. Preventive Services Task Force Procedure Manual. 2015. (Accessed August 25, 2020, at https://www.uspreventiveservicestaskforce.org/uspstf/procedure-manual.)

37. Viswanathan M, Ansari MT, Berkman ND, et al. Chapter 9: Assessing the Risk of Bias of Individual Studies in Systematic Reviews of Health Care Interventions. In: Methods Guide for Effectiveness and Comparative Effectiveness Reviews. AHRQ Publication No. 10(14)-EHC063-EF. Rockville, MD: Agency for Healthcare Research and Quality. January 2014. Chapters available at: www.effectivehealthcare.ahrq.gov.

38. Viswanathan M, Berkman ND. Development of the RTI item bank on risk of bias and precision of observational studies. J Clin Epidemiol 2012;65:163-78.

39. Whiting PF, Rutjes AW, Westwood ME, et al. QUADAS-2: a revised tool for the quality assessment of diagnostic accuracy studies. Ann Intern Med 2011;155:529-36.

40. World Health Organization. Low back pain. 2023. https://www.who.int/news-room/fact-sheets/detail/low-back-pain. Accessed August 10 2023. 2023.

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VI. Definition of Terms

Table 2. Abbreviations

AAPM	American Academy of Pain Medicine
AB	Advisory Board
CPG	Clinical Practice Guideline
GDG	Guideline Development Group
EPC	Evidence-based Practice Center
FDA	Food and Drug Administration
LBP	Low back pain
KQ	Key Questions
PICOTS	Population, Intervention, Comparator, Timing, Study Design
OHSU	Oregon Health and Science University
RCT	Randomized Control Trial
TEP	Technical Expert Panel

VII. Summary of Protocol Amendments

If needed, protocol amendments will be added in the future.

VIII. Review of Key Questions

Initial KQs were revised based on EPC discussions with the project sponsor (FDA), AB members, GDG members, and AAPM partners; and application of EPC team expertise. The EPC will refine and finalize the KQs after input from the TEP. This input is intended to ensure that the KQs are specific and relevant.

IX. AAPM Partners/Consultants

The Pacific Northwest EPC at OHSU has partnered with the American Academy of Pain Medicine (AAPM) a professional society with a vast, multidisciplinary network of providers and constituents, and with established outreach capabilities for this project. Three AAPM members serve as consultants for this project and will provide input at specific time points throughout the project. To date, the consultants have provided input into the drafting of the key questions and scope for this review and the related guideline. AAPM has nominated individuals for the advisory board, guideline group and technical expert panel. AAPM will play a major role in dissemination and evaluation of guideline uptake. They will assist with public posting of the systematic review and guideline. The Pacific Northwest EPC at OHSU will lead and oversee all phases of the project and is responsible for the conduct of the systematic review.

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X. Advisory Board

The independent AB will provide diverse multidisciplinary clinician input as well as input from patients, patient advocates and other constituents to all phases of this project. Input will complement and enhance input from the systematic review team, the guideline development group, clinical experts from professional organization partners and patient groups.

Members of the AB must disclose any financial conflicts of interest (COI) greater than $5,000 and any other relevant business or professional conflicts of interest. Because of their unique perspective, clinical or content expertise, individuals are invited to serve as SB members and those who present with potential conflicts may be retained. The EPC works to balance, manage, or mitigate any potential conflicts of interest identified.

XI. Guideline Development Group

The GDG will transparently develop a clinical practice guideline on the evaluation and management of acute low back pain based on general IOM/NASEM guidance for "Trustworthy Guidelines" and similar standards. The GDG will provide input into the related systematic review during topic refinement, will formulate a guideline protocol and will follow that protocol to develop the guideline. The GDG will constitute a multidisciplinary panel.

Members will need to be eligible under COI policies for transparent guideline development and will be requested to submit COI disclosures and confidentiality forms. Members of the GDG must disclose any financial COI greater than $5,000 and any other relevant business or professional conflicts of interest. Because of their unique clinical or content expertise, individuals are invited to serve as GDG members and those who present with potential conflicts may be retained. The EPC works to balance, manage, or mitigate any potential conflicts of interest identified.

XII. Technical Experts

Technical Experts constitute a multi-disciplinary group of clinical, content, and methodological experts who provide input in defining populations, interventions, comparisons, or outcomes and identify particular studies or databases to search. The Technical Expert Panel is selected to provide broad expertise and perspectives specific to the topic under development. Divergent and conflicting opinions are common and perceived as healthy scientific discourse that results in a thoughtful, relevant systematic review. Therefore, study questions, design, and methodological approaches do not necessarily represent the views of individual technical and content experts. Technical Experts provide information to the EPC to identify literature search strategies and suggest approaches to specific issues as requested by the EPC. Technical Experts do not do analysis of any kind; nor do they contribute to the writing of the report. They do not review the report, except as given the opportunity to do so through the peer or public review mechanism.

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Members of the TEP must disclose any financial conflicts of interest greater than $10,000 and any other relevant business or professional conflicts of interest. Because of their unique clinical or content expertise, individuals are invited to serve as Technical Experts and those who present with potential conflicts may be retained. The EPC works to balance, manage, or mitigate any potential conflicts of interest identified.

XIII. Peer Reviewers

Peer reviewers are invited to provide written comments on the draft report based on their clinical, content, or methodological expertise. The EPC considers all peer review comments on the draft report in preparing final report. Peer reviewers do not participate in writing or editing of the final report or other products. The final report does not necessarily represent the views of individual reviewers.

Potential Peer Reviewers must disclose any financial conflicts of interest greater than $5,000 and any other relevant business or professional conflicts of interest and should have <$10,000 in financial COI. Peer reviewers who disclose potential business or professional conflicts of interest can submit comments on draft reports through the public comment mechanism.

XIV. EPC Team Disclosures

EPC core team members must disclose any financial conflicts of interest greater than $1,000 and any other relevant business or professional conflicts of interest. Direct financial conflicts of interest that cumulatively total more than $1,000 will usually disqualify EPC core team investigators. EPC members have no financial conflicts of interest.

XV. Role of the Funder

This project is supported by the Food and Drug Administration (FDA) of the U.S. Department of Health and Human Services (HHS) as part of a financial assistance award [FAIN] totaling $1,999,980.00 with 100 percent funded by FDA/HHS. The contents are those of the author(s) and do not necessarily represent the official views of, nor an endorsement, by FDA/HHS, or the U.S. Government.

XVI. Registration

This protocol will be registered in the international prospective register of systematic reviews (PROSPERO).

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Appendix A: Acute Low Back Pain – Search Strategies

Database: PubMed® MEDLINE

KQ 1: ((((("Acute Pain"[Mesh]) OR (acute[Title/Abstract] AND pain[Title/Abstract])) AND (back[Title/Abstract] OR spine[Title/Abstract] OR spinal[Title/Abstract] OR lumbar[Title/Abstract] OR radicular[Title/Abstract] OR radiculopath*[Title/Abstract])) OR (("Low Back Pain"[Mesh]) AND (acute[Title/Abstract]))) AND (((((("Medical History Taking"[Mesh:NoExp]) OR ("Physical Examination"[Mesh:NoExp])) OR ("Decision Support Techniques"[Mesh])) OR ("Prognosis"[Mesh])) OR (patient[Title/Abstract] AND (history[Title/Abstract] OR exam*[Title/Abstract] OR screen*[Title/Abstract])))

KQ 2: ((((("Acute Pain"[Mesh]) OR (acute[Title/Abstract] AND pain[Title/Abstract])) AND (back[Title/Abstract] OR spine[Title/Abstract] OR spinal[Title/Abstract] OR lumbar[Title/Abstract] OR radicular[Title/Abstract] OR radiculopath*[Title/Abstract])) OR (("Low Back Pain"[Mesh]) AND (acute[Title/Abstract]))) AND (("Lumbar Vertebrae/diagnostic imaging"[Mesh]) OR (lumbar[Title/Abstract] AND imag*[Title/Abstract]))

KQ 3-4: ((((("Acute Pain"[Mesh]) OR (acute[Title/Abstract] AND pain[Title/Abstract])) AND (back[Title/Abstract] OR spine[Title/Abstract] OR spinal[Title/Abstract] OR lumbar[Title/Abstract] OR radicular[Title/Abstract] OR radiculopath*[Title/Abstract])) OR (("Low Back Pain"[Mesh]) AND (acute[Title/Abstract]))) AND ((("Analgesics, Opioid"[Mesh]) OR (opioid*[Title/Abstract])) OR (buprenorphine[Title/Abstract] OR butorphanol[Title/Abstract] OR codeine[Title/Abstract] OR dihydrocodeine[Title/Abstract] OR fentanyl[Title/Abstract] OR hydrocodone[Title/Abstract] OR hydromorphone[Title/Abstract] OR levorphanol[Title/Abstract] OR meperidine[Title/Abstract] OR methadone[Title/Abstract] OR morphine[Title/Abstract] OR nalbuphine[Title/Abstract] OR oxycodone[Title/Abstract] OR oxymorphone[Title/Abstract] OR pentazocine[Title/Abstract] OR tapentadol[Title/Abstract] OR tramadol[Title/Abstract]))

KQ 5: ((((("Acute Pain"[Mesh]) OR (acute[Title/Abstract] AND pain[Title/Abstract])) AND (back[Title/Abstract] OR spine[Title/Abstract] OR spinal[Title/Abstract] OR lumbar[Title/Abstract] OR radicular[Title/Abstract] OR radiculopath*[Title/Abstract])) OR (("Low Back Pain"[Mesh]) AND (acute[Title/Abstract]))) AND ((((((((("Acetaminophen"[Mesh]) OR (acetaminophen[Title/Abstract] OR paracetamol[Title/Abstract])) OR (("Analgesics, Non-Narcotic"[Mesh]) OR ("nonsteroidal anti-inflammatory"[Title/Abstract] OR "non-steroidal anti-inflammatory"[Title/Abstract] OR NSAID*[Title/Abstract] OR celecoxib[Title/Abstract] OR diclofenac[Title/Abstract] OR diflunisal[Title/Abstract] OR etodolac[Title/Abstract] OR fenoprofen[Title/Abstract] OR flurbiprofen[Title/Abstract] OR ibuprofen[Title/Abstract] OR indomethacin[Title/Abstract] OR ketoprofen[Title/Abstract] OR ketorolac[Title/Abstract] OR mefenamic acid[Title/Abstract] OR meloxicam[Title/Abstract] OR nabumetone[Title/Abstract] OR naproxen[Title/Abstract] OR oxaprozin[Title/Abstract] OR piroxicam[Title/Abstract] OR sulindac[Title/Abstract] OR

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tolmetin[Title/Abstract])))) OR ((("Steroids"[Mesh]) OR ("Adrenal Cortex Hormones"[Mesh])) OR (corticosteroid*[Title/Abstract] OR glucocorticosteroid* [Title/Abstract] OR steroid*[Title/Abstract] OR corticoid*[Title/Abstract] OR prednisone[Title/Abstract] OR methylprednisone[Title/Abstract] OR dexamethasone[Title/Abstract] OR betamethasone[Title/Abstract] OR hydrocortisone[Title/Abstract] OR cortisone[Title/Abstract] OR triamcinolone[Title/Abstract]))) OR (("Neuromuscular Agents"[Mesh]) OR ("skeletal muscle relaxant*"[Title/Abstract] OR baclofen[Title/Abstract] OR carisoprodol[Title/Abstract] OR chlorzoxazone[Title/Abstract] OR cyclobenzaprine[Title/Abstract] OR dantrolene[Title/Abstract] OR eperisone[Title/Abstract] OR idrocilamide[Title/Abstract] OR metaxalone[Title/Abstract] OR methocarbamol[Title/Abstract] OR orphenadrine[Title/Abstract] OR pridinol[Title/Abstract] OR thiocolchicoside[Title/Abstract] OR tizanidine[Title/Abstract]))) OR (("Benzodiazepines"[Mesh]) OR (benzodiazepine*[Title/Abstract] OR alprazolam[Title/Abstract] OR bromazepam[Title/Abstract] OR brotizolam[Title/Abstract] OR chlordiazepoxide[Title/Abstract] OR clobazam[Title/Abstract] OR clonazepam[Title/Abstract] OR clorazepate[Title/Abstract] OR clotiazepam[Title/Abstract] OR diazepam[Title/Abstract] OR estazolam[Title/Abstract] OR etizolam[Title/Abstract] OR flurazepam[Title/Abstract] OR ketazolam[Title/Abstract] OR lorazepam[Title/Abstract] OR lormetazepam[Title/Abstract] OR medazepam[Title/Abstract] OR midazolam[Title/Abstract] OR nitrazepam[Title/Abstract] OR oxazepam[Title/Abstract] OR pinazepam[Title/Abstract] OR prazepam[Title/Abstract] OR quazepam[Title/Abstract] OR temazepam[Title/Abstract] OR tetrazepam[Title/Abstract] OR tofisopam[Title/Abstract] OR triazolam[Title/Abstract]))) OR (("Antidepressive Agents"[Mesh]) OR (antidepressant*[Title/Abstract] OR citalopram[Title/Abstract] OR escitalopram[Title/Abstract] OR fluoxetine[Title/Abstract] OR fluvoxamine[Title/Abstract] OR paroxetine[Title/Abstract] OR sertraline[Title/Abstract] OR desvenlafaxine[Title/Abstract] OR duloxetine[Title/Abstract] OR levomilnacipran[Title/Abstract] OR milnacipran[Title/Abstract] OR venlafaxine[Title/Abstract] OR bupropion[Title/Abstract] OR mirtazapine[Title/Abstract]))) OR (("Anticonvulsants"[Mesh]) OR (anticonvulsant*[Title/Abstract] OR antiseizure[Title/Abstract] OR carbamazepine[Title/Abstract] OR ethosuximide[Title/Abstract] OR gabapentin[Title/Abstract] OR lacosamide[Title/Abstract] OR lamotrigine[Title/Abstract] OR oxcarbazepine[Title/Abstract] OR phenytoin[Title/Abstract] OR pregabalin[Title/Abstract] OR topiramate[Title/Abstract] OR valproic acid[Title/Abstract] OR zonisamide[Title/Abstract]))) OR ((("Cannabinoids"[Mesh]) OR ("Cannabis"[Mesh])) OR (cannabis[Title/Abstract] OR cannabinoid[Title/Abstract] OR cannabidiol[Title/Abstract] OR CBD[Title/Abstract]))) OR (herbal[Title/Abstract] OR plant[Title/Abstract] OR "willow bark"[Title/Abstract]) OR (("Lidocaine"[Mesh]) OR (lidocaine[Title/Abstract])) AND (topical[Text Word]))

KQ 6: (((("Acute Pain"[Mesh]) OR (acute[Title/Abstract] AND pain[Title/Abstract])) AND (back[Title/Abstract] OR spine[Title/Abstract] OR spinal[Title/Abstract] OR lumbar[Title/Abstract] OR radicular[Title/Abstract] OR radiculopath*[Title/Abstract])) OR (("Low Back Pain"[Mesh]) AND (acute[Title/Abstract]))) AND ((((((((((("Exercise Therapy"[Mesh]) OR ("Psychotherapy"[Mesh])) OR ("Complementary Therapies"[Mesh])) OR ("Musculoskeletal Manipulations"[Mesh])) OR ("Transcutaneous Electric Nerve Stimulation"[Mesh])) OR ("Ultrasonic Therapy"[Mesh])) OR ("Braces"[Mesh])) OR ("Traction"[Mesh])) OR ("Hyperthermia, Induced"[Mesh])) OR

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("Cryotherapy"[Mesh])) OR ("Transcranial Magnetic Stimulation"[Mesh])) OR ("Patient Education as Topic"[Mesh:NoExp])) OR ((exercise[Title/Abstract] OR psychological[Title/Abstract] OR "cognitive behavioral therapy"[Title/Abstract] OR "cognitive behavioural therapy"[Title/Abstract] OR "CBT"[Title/Abstract] OR "cognitive therapy"[Title/Abstract] OR "operant therapy"[Title/Abstract] OR nonpharm*[Title/Abstract] OR complementary[Title/Abstract] OR integrative OR hypnosis[Title/Abstract] OR "eye movement desensitization"[Title/Abstract] OR EMDR[Title/Abstract] OR mindfulness[Title/Abstract] OR manual[Title/Abstract] OR "musculoskeletal manipulation"[Title/Abstract] OR "musculoskeletal mobilization"[Title/Abstract] OR "musculoskeletal mobilisation"[Title/Abstract] OR "transcutaneous electrical nerve stimulation"[Title/Abstract] OR TENS[Title/Abstract] OR ultrasound[Title/Abstract] OR brace*[Title/Abstract] OR bracing[Title/Abstract] OR heat[Title/Abstract] OR cold[Title/Abstract] OR cryo*[Title/Abstract] OR "transcranial magnetic stimulation"[Title/Abstract] OR meditation[Title/Abstract] OR relaxation[Title/Abstract] OR music[Title/Abstract] OR "virtual reality"[Title/Abstract] OR acupuncture[Title/Abstract] OR massage[Title/Abstract] OR cupping[Title/Abstract] OR "mind-body"[Title/Abstract] OR yoga[Title/Abstract] OR "tai chi"[Title/Abstract] OR "tai ji"[Title/Abstract] OR reiki[Title/Abstract] OR advice[Title/Abstract] OR education[Title/Abstract]) AND (therap*[Title/Abstract] OR treatment[Title/Abstract] OR intervention*[Title/Abstract])))

KQ 7: ((((("Acute Pain"[Mesh]) OR (acute[Title/Abstract] AND pain[Title/Abstract])) AND (back[Title/Abstract] OR spine[Title/Abstract] OR spinal[Title/Abstract] OR lumbar[Title/Abstract] OR radicular[Title/Abstract] OR radiculopath*[Title/Abstract])) OR (("Low Back Pain"[Mesh]) AND (acute[Title/Abstract]))) AND ((((((("Trigger Points"[Mesh]) OR ("Botulinum Toxins"[Mesh])) OR ("Sacroiliac Joint"[Mesh])) AND ("Injections"[Mesh])) OR ("Injections, Epidural"[Mesh])) OR (("trigger point"[Title/Abstract] OR botulinum[Title/Abstract] OR (epidural[Title/Abstract] AND steroid[Title/Abstract]) OR sacroiliac[Title/Abstract]) AND injection*[Title/Abstract]))

KQ 8: ((((("Acute Pain"[Mesh]) OR (acute[Title/Abstract] AND pain[Title/Abstract])) AND (back[Title/Abstract] OR spine[Title/Abstract] OR spinal[Title/Abstract] OR lumbar[Title/Abstract] OR radicular[Title/Abstract] OR radiculopath*[Title/Abstract])) OR (("Low Back Pain"[Mesh]) AND (acute[Title/Abstract]))) AND ((((((("Patient Care Management"[Mesh]) OR ("Critical Pathways"[Mesh])) OR ("Patients/classification"[Mesh])) OR ("Referral and Consultation"[Mesh])) OR ("Risk Assessment"[Mesh])) OR ((patient*[Title/Abstract] AND (management[Title/Abstract] OR referral[Title/Abstract] OR classification[Title/Abstract])) OR (pathway*[Title/Abstract]))))

Note: There is no separate search strategy for **KQ 9**; relevant studies should be captured by the KQ 1-8 searches.