Chronic Low Back Pain:
Questions submitted for consideration by workshop participants

Prioritizing Comparative Effectiveness Research Questions:
PCORI Stakeholder Workshops

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1. What is the comparative effectiveness of systemic oral medication therapy vs transdermal medication therapy for individuals with chronic low back pain?

2. Self-care vs Customary Nonoperative Care for Chronic Low Back Pain

    a. PEOPLE: All individuals with chronic low back pain; age 20-65. Exclusions include - severe neural compression, significant radicular symptoms or findings, spondylolisthesis, tumors, infections

    b. RATIONALE: Extensive nonoperative care - physical therapy, chiropractic care, medication management, injection therapies have resulted in little to no improvement in overall pain reduction and quality of life in the patient with chronic low back pain. It is possible that chronic low back pain ought to be addressed less as a medical condition that is "treatable" than an individual situation that requires self-care. The primary pillars of this approach should be:

        i. reassurance of the patient on the absence of medically "dangerous" issues

        ii. understanding by the patient that research shows that various non-operative treatment options used for chronic LBP have shown less than optimal success

        iii. creation of a policy umbrella that legitimizes care of providers who treat this patient group with predominantly "self-care". A system-based legitimacy to this treatment approach is an essential part of the success of the approach and helps with reassurance of the patient that this may be the best medical approach available. It is also necessary to reduce the practice of "defensive medicine" and minimize risk of litigation against providers.

    c. INTERVENTION: Many of these patients have undergone extensive treatment in the past, and repeat treatment is felt unnecessary. Patients may continue the physical therapy exercises at home on a self-supervised basis, and use occasional over-the-counter medications for flare ups of pain, keeping in mind the risks of usage of these medications. Self-care is recommended, perhaps with a booklet outlining basic ergonomic principles, gentle stretching exercises, and other self care measures. Patients who have not done physical therapy in the past may be referred for a brief course (1-6 visits) of therapy, consisting of education in ergonomics, posture training, gentle stretching and flexibility exercises, and gentle core stabilization exercises for those able to tolerate them.

    d. OUTCOMES: Improved outcomes, measured by PROMIS-29, SF-36 or similar general measures of healthcare quality. Decreased medication usage. Visual pain score decrease. Improved back range of motion.

3. Community based Yoga vs Physical Therapy for Chronic Low Back Pain

    a. PEOPLE: All individuals with chronic low back pain; age 20-65. Exclusions include - severe neural compression, significant radicular symptoms or findings, spondylolisthesis, tumors, infections

b. OPTIONS: Yoga therapy through community yoga providers vs. Physical therapy for low back pain.

c. INTERVENTION: Eight to ten sessions of community based yoga vs physical therapy.

d. OUTCOMES: Improved outcomes, measured by PROMIS-29, SF-36 or similar general measures of healthcare quality. Decreased medication usage. Visual pain score decrease.Improved back range of motion.

4. What are the comparative benefits and risks of osteopathic manipulative treatment, pharmacologic treatment (acetaminophen/NSAIDs/muscle relaxants), physical therapy, and orthopedic surgery for adults with chronic low back pain?

    a. PEOPLE: Adults of all ages/ethnicities/gender with chronic low back pain.

    b. OPTIONS: Osteopathic manipulative treatment. Acetaminophen/NSAIDs/muscle relaxants. Physical Therapy. Orthopedic surgery (disc replacement, vertebral fusion)

    c. OUTCOMES: Identify which treatment option has the most benefits and the least harms for the population of interest.

    d. Reason for question: Millions of Americans suffer from low back pain, and these patients lose millions of work days, generate billions of dollars in health care costs each year. Pharmacologic and surgical treatment options have significant risks. Given its low risk of harm, osteopathic manipulative treatment could be a very beneficial treatment option.

5. In patients with acute lower back pain, does early, evidence-based PT (manipulation + exercise) produce superior outcomes compared to delayed evidence-based PT? Early PT would be within 14 days of a primary care visit, delayed PT would be 4-6 weeks after the visit. Outcomes would be function and disability.

6. Is there a subgroup of individuals with low back pain that benefit from early, evidenced-based physical therapy intervention? Subjects would be individuals with first-time lower back pain. Outcomes would be function and disability.

7. What are the benefits in pain, function, and continued participation for participants in 12 session weekly group yoga, 12 session weekly technologically delivered home based yoga, and 12 session weekly physical therapy at post intervention, 3 months, and 1 year period for adults with chronic low back pain?

8. What are the benefits in pain and function for adults with low back pain who participate in Pain Coping Skills Training versus Pain Coping Skills Training +Motivational Intervention versus usual care?

9. Which is more cost efficient, chronic lower back pain surgery earlier on after diagnosis, or as a procedure of last resort? [time frame will need to be defined]

10. If we administer FDA approved & treatment guideline recommended medicines in patients diagnosed with chronic pain including OA, CLBP, and musculoskeletal (MSK) pain, are outcomes (decreased disability, improved productivity) improved compared to subjects who receive treatment that is non-FDA approved and not in the treatment guidelines?

11. Compared with no motivational intervention, can pain and functioning be improved in patients with low back pain and musculoskeletal pain with motivational interventions, (e.g., motivational enhancement treatment (MET) or compliance-enhancing interventions), that improve engagement in multidisciplinary treatment protocol? Outcome: Enhanced motivational factors, less pain intensity, improved physical functions, and increased exercise compliance.

12. Can integrative/CAM treatment protocols (e.g., mindfulness-based stress reduction, acupuncture, structural integration) for patients with spinal disorders improve musculoskeletal chronic pain without surgery? Outcome: Preventing needless surgeries (less invasive treatments).

13. Are there mechanistic subsets of low back pain patients (i.e. nociceptive, neuropathic, centralized) that respond best to certain drug (opioid, centrally acting analgesics e.g. duloxetine, pregabalin) and non-drug (injections, surgery, spinal rehabilitation) treatments? Hence, can treatment options be identified by their efficacy for different mechanistic subsets of low back pain patients (i.e., nociceptive, neuropathic, centralized)? Outcome: Better treatment options would be available for people with low back pain. Based on the subsets of low back patients, health professionals would develop effective treatment protocols based on the subsets.

14. From my perspective, if we are to make real progress in developing an evidence base that can be useful in clinical decision making, most importantly, there are several underlying issues/factors that need to be addressed in study design and execution irrespective of the treatment or clinical approach being studied. Failure to do so, I'm afraid, will result in 'more of the same' evidence that currently exists. I've outlined a few of some of the most important below for your review and consideration. This may be further down the road in the process, but nonetheless, I consider this the most important contribution I can make in this process. Factors that may moderate treatment efficacy in individuals with chronic low back and musculoskeletal pain and crucial to address in CER and pragmatic trial design and execution:

    a. Pain Comorbidities: Many patients with these conditions suffer concurrently with other pain disorders, such as headache disorders, chronic pelvic pain, fibromyalgia and temporomandibular disorders. Growing evidence suggests that those with multi-site pain are more recalcitrant to treatment, have poorer outcomes and increased disability. However, most studies only address the pain condition of primary interest and fail to take into account the impact of other pain disorders on treatment efficacy. Further, a patient-centered holistic treatment approach is to treat pain in the whole person versus fragmented medical care by different specialists for pain in different body sites.

    b. Other Comorbidities and Contributing Factors: Many chronic low back pain patients also experience non-pain comorbidities and contributing factors, such as sleep disturbance, altered mood, fatigue

and decreased physical function, which can serve as moderators of the pain itself. As such, the pain field has advanced to understand that it is insufficient to simply measure pain severity/inference in any clinical study, as multiple domains of health and quality of life, such as those listed above. Further, during the course of treatment, these factors may improve prior to a patient's pain severity or interference improving. Contributing factors are individual to each patient; one patient may experience significant sleep disturbance, while another has altered mood and fatigue. A patient-centered approach to treatment would be a personalized medicine approach that assesses and treats all contributing domains of health and quality of life, in addition to chronic pain. [Recommendations for core domains to be measured in clinical pain research have been put forth by IMMPACT (Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials) and others.

c. Heterogeneity: Countless studies in multiple chronic pain populations have demonstrated that heterogeneity – both phenotypic clustering within a given pain diagnosis (chronic low back pain, chronic musculoskeletal pain) as well as heterogeneity in treatment response – is imperative to address, irrespective of the treatment(s) being studied to identify biological and other predictors of treatment success and failure, as well those more likely to experience adverse effects from a particular treatment(s).

15. Patients with Chronic Low Back Pain with radiologic findings of Degenerative Disc Disease with or without Grade I Spondylolisthesis (defined as antero or retrolisthesis). Options: Physical therapy + CBT vs Lumbar fusion any type. Outcomes: Oswestry; SF12; Continued pain management needs at 1 year. Complications (in %) – E.g. Visceral injury, neural injury, retrograde ejaculation. Reoperations at 1 year (in %).

16. Patients with Chronic Low Back Pain with radiologic findings of Degenerative Disc Disease with or without Grade I Spondylolisthesis (defined as antero or retrolisthesis). Options: Anterior lumbar interbody fusion + Posterolateral fusion vs Posterolateral fusion alone. Outcomes: Oswestry, SF12; Continued pain management needs at 1 year. Complications (in %) – E.g. Visceral injury, neural injury, retrograde ejaculation. Reoperations at 1 year (in %)

17. Patients with Chronic Low Back Pain with/without radiculopathy and radiologic findings of Degenerative Disc Disease. Options: One or two level fusion vs CBT and PT. Outcomes: Oswestry, SF 12; Continued pain management needs at 1 year.

18. Patients with Chronic Low Back Pain with/without radiculopathy and radiologic findings of Degenerative Disc Disease. Options: CBT and PT vs CBT and spinal injections. Outcomes: Oswestry, SF 12; Continued pain management needs at 1 year.

19. Patients with Chronic Low back pain on opioids +/- benzodiazepines. Options: Mindfulness-Based Stress Reduction or Cognitive Behavioral therapy + outpatient medication reduction (opioid/benzo) vs medication management only. Outcomes: VAS, SF36 at 1 year. Medication related ED visits and unscheduled MD visits. Medication related adverse effects (overdose, constipation, falls).

20. As the Topic Briefs attached have so nicely summarized, there are many individual patient characteristics, many different interventions, and many variations of the different interventions. For example, a big issue that came up in the report on Non-invasive treatments for low back pain is which combination of therapies with different pharmacological or nonpharmacological treatments is associated with incremental benefits versus the individual components of the combination therapy, and which combinations and sequences of therapy are the most effective. Similarly, in the Spinal injections report there are different techniques and approaches (caudal vs. transforaminal etc.) for the injections. Complicating this is a question of the role of imaging during the procedure and even more complicated, a question of skill of the provider in outcomes. However, studying each of these variations two at a time in head to head comparisons is probably not going to lead to clarity for the complex multi-step management of these patients. I guess we would suggest that what is needed is to harness "big data" and supplement with Patient related Outcomes information to collect detailed data on patient characteristics, intervention characteristics, outcomes across time, including repeat interventions, multiple interventions (drugs, physical therapy, noninvasive treatments, surgery etc.) given simultaneously or sequentially etc. This data can be analyzed to answer the following questions:

    a. Are there patterns of specific patient characteristics, intervention characteristics etc. that consistently get better outcomes?

    b. Are there patterns of specific patient characteristics, intervention characteristics etc. that consistently get worse outcomes or harms from treatments?

    c. Using this information, very targeted head to head comparisons could be designed to test hypotheses generated from the data.

21. Recent consensus on appropriate outcomes emphasizes the important of functioning rather than pain severity as the primary outcome of importance (i.e., recent National Pain Strategy Draft Report http://iprcc.nih.gov/docs/DraftHHSNationalPainStrategy.pdf). Perhaps leading off the workshop with some clarity about prioritized outcomes could provide a helpful framework for the ensuing discussion as I suspect resulting suggested research questions may be influenced by relative prioritization of outcomes. In the topic briefs, more of the review of the research to date is organized around pain relief for the clinical interventions brief while the broader set of functional measures is emphasized in the systems approach brief. I realized that PCORI by design prioritizes those outcomes of high importance to patients so specifying this a priori may not be possible but the most relevant CER questions may be related to outcomes under consideration.

22. Although not a research question in its own right, might an ensuing RFP in this topic domain be a good place to encourage the use of sequential, multiple assignment, randomized trial (SMART) designs (e.g., Collins, Murphy, & Strecher, Am J Prev Med, 2007) that allow for an efficient examination of a number of modalities alone and in combination that might best inform for whom under what conditions particular components/interventions are most effective?

23. What is the role of active vs. passive treatments in helping patients manage chronic LBP and MSD and maintain optimal functioning/QOL and minimize adverse events? That is, are patients for whom interventions are focused on skills training (coping skills including activity rest cycling, cognitive restructuring, emotional regulation, distraction) and lifestyle based interventions (e.g., increasing physical activity) better or worse off than those who use more passive treatments (pharmacotherapy, injections, surgery)? (an umbrella question that might be too messy in its execution to be useful but is at the core of some of the challenges between what current evidence/recommendations suggest is important (patient activation) and the nature of much of the chronic LBP/MSD care patients current receive within the health care system.)

24. Do provider delivered CAM services (chiropractic care, acupuncture) when combined with supported self-care enhance patients with chronic LBP/MSD long term functioning/QOL when compared with independently provided supported self-management or independent CAM services? This question is pertinent based on the large number of patients that self-report utilizing CAM modalities for management of chronic LBP/MSD (often w/o knowledge of or coordination with conventional medical providers/services) and more recent research suggesting that utilization of CAM modalities with some evidence of reducing pain severity may improve patients' uptake of and adherence to the subsequent use of self-care modalities for pain management.

25. Identify effective strategies to engage patients with chronic low back pain in reconditioning programs.

26. Identify health care provider characteristics associated with the prescription of high dose opioids (> 100 morphine equivalents) for chronic spinal pain.

27. Identify effective tobacco cessation strategies for smokers with chronic spinal pain.

28. What are the comparative benefits and risks of non-opioid medication therapy vs opioid medication therapy for individuals with chronic low back pain?

29. What are the comparative benefits and risks of pain contacts vs no pain contract for individuals with chronic low back pain utilizing chronic opiate therapy?

30. What are the long-term effects of oral or transdermal opioids compared to other available treatment options on pain, function, safety, and addiction (and withdrawal) in people with chronic non-cancer pain conditions, such as osteoarthritis and chronic low back pain?

31. The common theme running though the comments we received on the reports on Non-invasive treatment for Low back pain and The long term benefits and safety of opioids for chronic pain (not just low back pain), we offer another question:

32. What is benefit of chronic opioid treatment (COT) compared to supported self-care management for patients with chronic LBP or MSD for whom primary care providers are considering initiating COT? Using a 2x2factorial design would allow one to examine both theses as individual modalities as well as their combination with a usual care comparison.

33. What is the comparative effectiveness of number-based pain scales (eg 0-10) vs functional-based pain scales in patient-specific rating of pain for individuals with chronic low back and MSK pain?

34. When is the ideal time for referral of a patient with CLBP from a primary care physician to a specialist? [ideal would be defined as the period of time when outcomes are most improved]

35. What are the identifiable risk factors in children that can lead to chronic pain as adults and how can those factors be addressed during childhood to help prevent the development of chronic pain later in life? What types of chronic pain prevention programs instigated in at-risk youth (those with pain, obesity, sports injuries and children of parents with chronic pain) can prevent chronic pain as they age? Outcome: Reduced incidence of chronic pain as adults.

36. In patients with neurological conditions of the spine, would medications, surgery or rehabilitation programs that improve the neurological condition of the spine also improve coexisting musculoskeletal pain? Outcome: improved quality of life for patients, and reduction of the number of people with chronic musculoskeletal pain.

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