



PATIENT-CENTERED OUTCOMES RESEARCH INSTITUTE

Chronic Low Back Pain: Topic Brief

June 9, 2015

High-Level Research Question

What is the comparative effectiveness of combination interventions versus single interventions in the treatment of chronic low back pain?

Assignment for Workgroup Participants

- Based on your perspective (patient, clinician, payer, etc.), what are two to three of the most relevant comparative effectiveness research (CER) questions related to the care of chronic low back pain?
- Submitted questions will be used to generate the agenda for the workgroup meeting.

This document was prepared for informational purposes only and should not be construed as medical advice or used for clinical decision making.



Opportunity Snapshot

As part of PCORI's efforts to fund high-impact and useful research on critical patient-centered health and healthcare issues, PCORI is hosting a multistakeholder workgroup to discuss high-priority topics that focus on the comparative effectiveness of treatments for chronic low back pain. PCORI intends to use feedback from the workgroup to conduct further gap analyses and to develop a funding announcement in this area. The objective of the workgroup is to create a set of comparative research questions whose findings could improve patient-centered outcomes.

1. Introduction

One of the most prevalent chronic conditions, chronic low back pain is defined as low back pain occurring on at least half of the days in a 6-month period. Interventions range from exercise and psychosocial interventions to spine surgery. Hundreds of randomized trials have had uniform results, showing either no effect or small effect sizes. The quality of these studies varies, but there is a core of high-quality studies. Physicians and patients face the challenge of choosing from a relatively small selection of modestly effective treatments, with little or no information to help decide which option is best for an individual patient. Fortunately, if one treatment fails, there are many more to choose from.

2. Patient Centeredness

The outcomes (pain relief) matter to patients, caregivers, and clinicians, as well as to other key stakeholders, such as employers.

3. Impact (Burden) of the Condition on the Health of Individuals and Populations

More than 26 million Americans between the ages of 20 and 64 suffer from frequent back pain.¹ Up to 36 percent of adults—including those who have had a history of back pain—experience a new pain episode every year. One large survey in the United States indicated that 26 percent of adults had back pain lasting a full day during the 3 months before the survey.² Another survey indicated that, among American adults under treatment for back pain, 72 percent had given up exercise or sports, 60 percent were unable to perform their usual daily activities, and 46 percent had given up sex. In the United States, low back pain is the largest contributor to years lived with disability for at least the past 25 years.³ In 2010, low back pain was the third-largest contributor to disability-adjusted life years in the United States.³ Common causes for back pain are unlikely to result in mortality. Back pain is most prevalent in the elderly, women, and white non-Hispanics. African Americans have the worst measures of suffering.

In the United States, an estimated 149 million work days are lost every year due to low back pain.⁴ The total costs of back pain exceed \$100 billion per year in the United States, and 5 percent of back pain patients generate 75 percent of these costs. A 2008 review found that the largest proportion of direct

medical costs for low back pain are physical therapy (17 percent) and inpatient services (17 percent), followed by pharmacy (13 percent) and primary care (13 percent).⁵

4. Ongoing Evidence Gaps

Practice Guidelines: Treatment of Low Back Pain (ACP-American Pain Society, October 2007).⁶⁻⁸ The recommended first-line treatment of low back pain is acetaminophen (preferred because it is safer) or nonsteroidal anti-inflammatory drugs (NSAIDs). A time-limited, judicious trial of opioids is an option for pain not controlled by first-line therapy. Skeletal muscle relaxants are another second-line treatment, but all have sedating effects, adverse liver effects, and addiction risk (benzodiazepines). Antidepressants are recommended only if the patient has depression. Herbal therapies, principally capsicum, are safe but have small effects. Systemic corticosteroids are not recommended.

Recommended second-line nonpharmacologic therapies for chronic low back pain include acupuncture, exercise, massage, yoga, cognitive-behavioral therapy, spinal manipulation, and intensive interdisciplinary rehabilitation. The evidence for these treatments varies from fair to good; the evidence is insufficient to make a recommendation for laser therapy, diathermy, ultrasonography, and back schools. Referral to a back specialist may be appropriate; however, guidelines about when to refer a patient vary from 3 months to 2 years of failure to respond to treatment.

Systematic Reviews: This section is a summary of the findings of Cochrane systematic reviews of the many interventions for chronic low back pain; the recurring theme is the variable quality and small effect sizes of the research.

Interventions with Good Evidence on Pain Relief:

- Muscle relaxants:⁹ High-quality evidence suggests that these treatments are more effective than placebo (most studies are in acute back pain); however, adverse events, especially nervous system effects and addiction, are increased.
- Spinal manipulative therapy (SMT):¹⁰ High-quality evidence supports that SMT has a small, statistically significant but clinically insignificant effect on pain.
- Total disc replacement versus fusion of adjacent vertebrae:¹¹ There is a clinically insignificant but statistically significant difference.
- Multidisciplinary biopsychosocial rehabilitation:¹² This intervention results in less pain than usual care or a physical treatment. Differences are small but statistically significant.
- Exercise:¹³ Evidence shows small, statistically significant effects on pain.
- Back schools:¹⁴ There is moderate evidence for effectiveness versus other nonsurgical treatments; the body of evidence is heterogeneous.
- NSAIDS¹⁵ versus placebo: Evidence shows that NSAIDs are effective in the short-term (28 high-quality trials) but with small effects. Side effects are more common.

Interventions with Weak or Conflicting Evidence on Pain Relief:

- Therapeutic ultrasound:¹⁶ Evidence shows no statistically significant effects on pain.
- Prolotherapy¹⁷ (injections of irritants to strengthen lumbosacral ligaments): Evidence shows no effect versus sham injections. It is a heterogeneous evidence base.
- Physical condition for return to work versus usual care:¹⁸ There is a small reduction of days lost from work; pain outcomes were not discussed.
- Herbal medicines:¹⁹ *Capsicum frutescens* (cayenne) was found to be more effective than placebo (3 trials of moderate quality). Studies of other herbal preparations were of lower quality and “probably” showed differences.
- Spinal traction:²⁰ No effect on pain was found. Authors recommend against future research.
- Transcutaneous electrical nerve stimulation²¹ (TENS) versus placebo needling: Four high-quality studies showed heterogeneous results. Authors feel more research is needed.
- Behavioral therapy²² (operant, cognitive, or respondent): The effects, if any, were short term; there were no long-term effects versus exercise. No type of intervention was superior. Authors thought that large high-quality studies could change the estimates.
- Opioids:²³ Opioids were effective versus placebo but were not more effective than NSAIDS. In short-term studies, opioids did not have serious side effects. Short-term studies had high drop-out rates. There is no evidence supporting long-term use.
- Injection therapy²⁴ (injecting steroids, local anesthetics, and other substances into facet joints, trigger points, and the epidural space): The evidence base is heterogeneous, and there is no strong evidence that injections are effective.
- Antidepressants:²⁵ In studies of antidepressants versus placebo, there was no effect.
- Acupuncture and dry needling for myofascial pain:²⁶ Acupuncture was found to give immediate relief that decreases over time. The studies were of low methodological quality, and more studies are needed.

Synthesis of Findings: The high frequency of back pain symptoms in clinical practice would make these data a high priority for practitioners and healthcare organizations to systematize. CER on back pain has been limited by several factors, including: 1) a lack of consensus on the clinically meaningful difference in the main outcome measures used in trials (for example, the Oswestry Disability Index); 2) a lack of difference shown among most therapies when compared with each other; and 3) an inadequate classification system for back pain symptoms, anatomy, and behavioral/psychosocial factors that may influence treatment and response to therapy. Because treatment options for low back pain are aligned with different professional disciplines (e.g., acupuncture, physical therapy, spinal manipulation), existing referral patterns and availability of providers may limit implementation of new CER or multimodality approaches across specialties. Existing data on current treatment and lack of notable innovations in therapy suggest that new CER is unlikely to provide better guidance on clinical decision making; however, the large number of affected patients and high burden of symptoms could make even small improvements clinically important.

The main opportunities for a study to change practice for chronic low back pain are interventions for which the evidence base has few studies and/or low-quality studies, combinations of treatments for which high-quality studies show effects, and studies of non-opioid interventions as an adjunct to opioid therapy to reduce opioid dose or enhance withdrawal. Based on the systematic review authors' assessments, potential targets would be acupuncture, behavioral therapy, and TENS. Meta-analyses of high-quality studies show small effects, and there are many recent studies underway or completed but not yet incorporated into systematic reviews. The outlook for new studies to sharply reduce the burden of chronic low back pain is poor, a conclusion reached by a PCORI expert group on low back pain 2 years ago. However, most ongoing chronic low back pain randomized controlled trials (RCTs) are very small, which creates a potential niche for a large CER trial. Moreover, small effects in the huge population of chronic low back pain sufferers would have large population-level effects.

5. Ongoing Research

A March 23, 2015, search of clinicaltrials.gov under “chronic low back pain” yielded 164 active studies, of which 129 were randomized trials and 35 were observational or other designs. The size distribution of the randomized studies was informative: the target enrollment (all studies) was less than 100 in 102, 100 to 500 in 57, 500 to 1,000 in 5 (all RCTs) and >1000 in 2 observational studies. Among the 5 RCTs with more than 400 target enrollees, the subjects were cognitive-behavioral therapy, osteopathic manipulation, TENS, physiotherapy, and a referral model. This survey shows that most studies are quite small and that there are opportunities for large, well designed CER trials, especially for topics whose existing body of evidence is small or of poor quality.

6. Likelihood of Implementation in Practice

- [Availability of Effective Countermeasures](#): As summarized above, interventions have small effects, and clinicians are desperate for effective measures.
- [Guidelines](#): There are many, many guidelines for management of low back pain.
- [Back Pain Advocacy Groups](#): there are many chronic pain advocacy groups
- [Variation in Practice](#): There is substantial uncertainty about the best treatment, as indicated by large regional variation—varying by a factor of almost six—in overall spine surgery rates among Medicare enrollees.
- [Potential for Systems of Care to Take Up Advances in Treatment](#): Many large healthcare organizations have organized their approaches to low back pain; these systems are a point of leverage for implementing advances in care.

7. Durability of Information

The back pain field moves very slowly. Practice-changing research results would be durable.

8. Potential Research Questions

PCORI consulted with experts in the field of chronic back pain treatment and its literature to identify key research questions. A number of experts noted that CER studies addressing the following key research opportunities* would help in clinical decision making:

- Studies comparing combination therapy using two proven interventions versus one of the interventions.
- Studies comparing integrated combination therapy using two proven interventions in a system of back pain care versus one of the interventions (or the two interventions but not in an integrated care environment; “integrated care” means use in a system of back pain care in which the two interventions are managed in concert, allowing titration of the two elements against each other).
- Studies of TENS, behavioral therapy (cognitive, operant, or respondent) versus control.
- Studies powered to examine heterogeneity of treatment effect, allowing tailoring the choice of treatment to the patient’s specific clinical features and preferences. Studies have not been powered for this purpose.
- Using a study population of people on long-term opioids, compare low back pain interventions as adjunctive therapy to enhance withdrawal (or dose reduction) from opioids. This research question reflects a theme across chronic pain management: methods to reduce the use of opioids.
- A comparative effectiveness study on surgical options for chronic low back pain patients who do not have a specific diagnosis (disc herniation, spondylolisthesis, and spinal stenosis) and have failed nonoperative treatment. The Spine Patient Outcomes Research Trial (funded by the National Institute of Arthritis and Musculoskeletal and Skin Diseases) showed that patients who had surgery for disc herniation, spondylolisthesis, and spinal stenosis did well in the long term and did well sooner than patients with nonoperative care. Many of these patients have “degenerative disc disease” or “black disc disease” (named for the appearance of the disc space on MRI), and they often fare poorly after major back surgery. CER topics include:
 - Operative versus optimized nonoperative management
 - Simple versus more complex operative procedures
 - Total disc replacement versus other interventions
 - Identification of patients who would benefit from this surgery

**It has been noted that the study of acupuncture would be of less importance, given the 630-patient National Institutes of Health acupuncture trial.*

9. Conclusion

There are many good opportunities for a pragmatic clinical study to inform decision making in patients with chronic low back pain. The research question that best fits with the chronic pain management topic area is comparison of back pain interventions that might reduce the use of opioids. The study population



would be patients on long-term opioids for chronic low back pain. The intervention would be nonopioid interventions for low back pain. The comparison would be between interventions that have been shown to have an effect in high-quality randomized trials. The primary outcome would be opioid dosage. Several other research questions are also attractive, particularly those related to surgery versus nonoperative treatment for degenerative disc disease.

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