Washington State Health Care Authority
Health Technology Assessment

FINAL Key Questions and Background

Lumbar Fusion – Re-Review

Background

Low back pain is an exceedingly common complaint, with a lifetime prevalence ranging from 60-70% (WHO, 2013). Chronic low back pain may be seen in as many as one-quarter of patients six months after an initial episode (Johannes, 2010). The economic impact of low back pain is also substantial. It is the second most common reason for all physician visits in the U.S. (Licciardone, 2008), and is responsible for approximately $30 billion in direct medical costs annually, of which $18.3 billion is related to ambulatory care (Soni, 2010). In addition, low back pain is a major cause of lost productivity; it is estimated that over 3% of the U.S. work force is compensated for back pain or injury each year (Stewart, 2003), with approximately 187 million missed work days and wage losses accounting for an additional $22.4 billion in indirect costs (AAOS, 2009).

Low back pain can be caused by various specific and nonspecific conditions, which differ in prevalence and affect different age groups. Degenerative disc disease (DDD) is a common condition associated with low back pain in many individuals. Use of the term "disease" to describe this condition is something of a misnomer, however, as disc degeneration (dehydration and shrinkage) is a natural consequence of aging, and many individuals never develop overt symptoms of DDD. Diagnosis and subsequent treatment typically involves an initial history and physical examination by a clinician. Depending on the presentation, the clinician might prescribe various self-care therapies or will perform a diagnostic exam to check the patient's pain tolerance, functional capabilities, and reflexes (Pengel, 2003). An MRI and/or CT scan may be used to identify other potential causes of the patient's symptoms, including other co-occurring conditions such as radiculopathy (compression of the root nerve), spondylolisthesis (displacement of the vertebral disc), or spinal stenosis (narrowing of the spinal canal) (Ullrich, 2013).

Multiple treatment options are available for symptoms associated with DDD of the lower back, including so-called "conservative" measures such as physical and exercise therapy, spinal manipulation, alternative therapies (e.g., acupuncture), and medication; minimally-invasive treatments such as spinal injections and radiofrequency ablation; and surgical intervention. Lumbar fusion surgery, which involves the creation of a permanent connection across the vertebral space by means of a graft, is often considered when conservative treatments fail to relieve the patient's pain (Eck, 2014). However, many patients may be at risk of persistent low back pain, as initial surgery is subject to high rates of reoperation with declining success rates after each consecutive surgery. It is estimated that as many as 80,000 cases of so-called "failed back surgery syndrome" are seen in the U.S. each year (Ragab, 2008).

Policy Context

Due to the prevalence of low back pain and the varying nature of the conditions that underlie it, numerous management options are available. These options vary substantially in their intensity, degree of invasiveness, and most importantly, level of evidence regarding their effectiveness. Although there is lack of consensus on when lumbar fusion surgery is indicated, how the surgery should be performed, and long-term prognosis after surgery (Christensen, 2004), the number of lumbar fusion surgeries performed in the U.S. has nevertheless increased more than two-fold between 2000 and 2009 (Yoshihara, 2014). In particular, some studies have shown poor success rates for lumbar fusion when used to treat low back pain caused by disk degeneration alone (Herkowitz, 1995). Not surprisingly, there is significant interest on the part of patients, clinicians, policymakers, and other stakeholders in evaluating the clinical and economic impact of lumbar fusion for patients with chronic low back pain and DDD.

Scope

The Washington State Health Care Authority has commissioned ICER to update a prior assessment on lumbar fusion in patients with chronic low back pain and "uncomplicated" degenerative disk disease (i.e., no confounding spinal injuries or disorders) (ECRI, 2007). Evidence will be culled from RCTs, systematic reviews, and high-quality observational studies. Unlike the original review, we will not assess the role of discography prior to lumbar fusion, as its use in diagnosing and staging DDD has largely been displaced by more recent innovations in imaging (Saboeiro, 2009). In addition, because chronic low back pain is often an occupational concern, the workers'/disability compensation literature will be evaluated along with traditional electronic literature databases.

Population

The target population for this review will be adults (age >17 years) with chronic (≥3 months) lumbar pain and uncomplicated degenerative disk disease. As in the original review, patients with conditions such as radiculopathy, spondylolisthesis (> Grade 1) or severe spinal stenosis, as well as acute trauma or systemic disease affecting the lumbar spine (e.g., malignancy) will be excluded. We recognize that some studies of lumber fusion will involve mixed patient populations; we will abstract data from these studies only if outcomes are reported separately for individuals with chronic low back pain and otherwise uncomplicated DDD. Note that some surgical studies will include patients who have attempted conservative management for varying lengths of time; these will be included regardless of the duration and/or intensity of prior conservative management. Studies that include patients with a history of prior back surgery for any indication will be analyzed separately from patients undergoing lumbar fusion surgery for the first time.

Intervention

The intervention of interest will be the major technical approaches to lumbar fusion surgery, regardless of surgical technique (e.g., anatomic approach, laparoscopic vs. open) or type of hardware utilized.

Comparators

Given the questions that currently exist regarding the benefits of lumbar fusion versus nonsurgical management, the primary comparator of interest will be conservative approaches, alone or in combination, including physical therapy, intensive exercise/rehabilitation, cognitive behavioral therapy, and medication management. We will also include any comparisons of lumbar fusion to minimally-invasive treatments (e.g., radiofrequency ablation, electrothermal therapy) where available. Studies comparing lumbar fusion to artificial disc replacement will be excluded, as artificial discs represent a separate review topic for the HCA.

Outcomes

Outcomes of interest will include: 1) patient- and clinician-reported measures of pain, function, and disability; 2) opioid medication use; 3) requirements for repeat surgery or other retreatment according to type of initial surgery; 4) return to work and/or resumption of normal activities; 5) mortality, stratified according to cause of death where available; 6) other complications and adverse events; 7) measures of "treatment success" or "successful clinical outcome" (e.g., return to work and/or functional goals, cessation of pain medication, available composite measures); and 7) the total costs and cost-effectiveness associated with fusion in comparison to alternative treatment approaches. Functional status will be recorded as measured by standard indices (e.g., Oswestry Disability Index [ODI], Roland-Morris Disability Questionnaire [RDQ]), back pain will be recorded as measured by a visual analog scale (VAS), and quality of life will be abstracted based on validated instruments (e.g., short-form [SF]-36 questionnaire). Of particular interest in this evaluation will be measurement of treatment effects in comparison to varying intensities of conservative management (e.g., interdisciplinary rehabilitation vs. physical and/or behavioral therapy alone).

Recommendations from influential clinical societies and other authoritative sources will be used to inform discussions on the magnitude of improvement as reported on validated measures for pain and/or function. For example, a mean 10-20 point change on a 100-point visual analog pain scale or 5-10 points on the RDQ are generally considered moderate improvements (Chou, 2007). Other published thresholds for clinically-meaningful improvement include at a 30% decrease from baseline on a chronic pain scale or an improvement of at least 20 points on the ODI (Ostelo, 2008). Importantly, while we will seek data on these specific thresholds as reported in clinical studies, we will abstract all measures of clinically-meaningful change as defined in each study, even if they differ from published guidance.

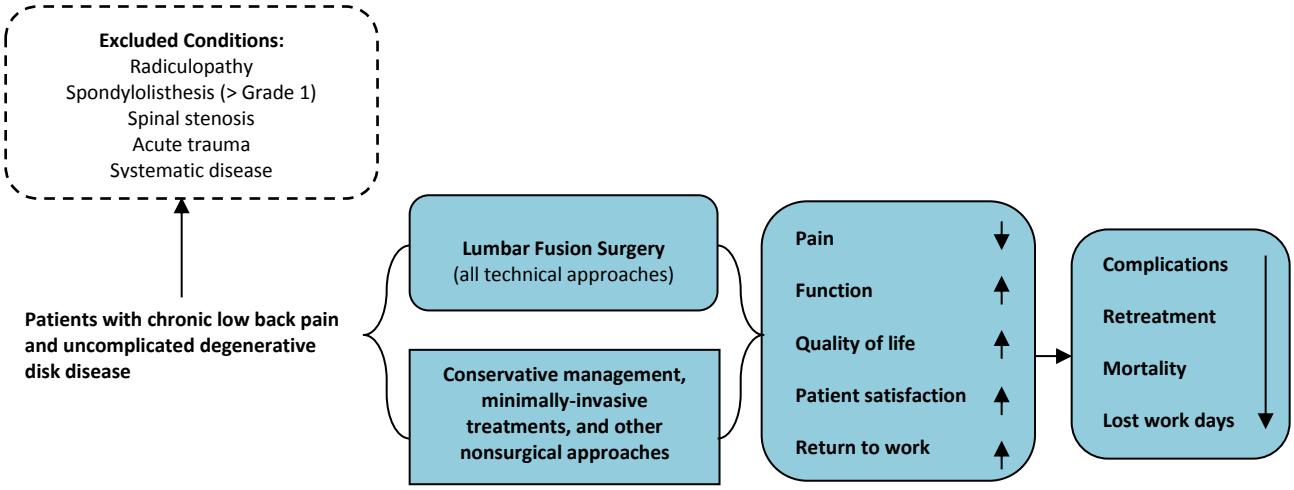
Information on the costs and cost-effectiveness of lumbar fusion procedures compared to alternative treatment will also be assessed from the available economic literature, including treatment-related costs, costs of care over the long-term (e.g., treatment switching, repeat surgery, complications, etc.), and indirect costs (e.g., productivity loss, caregiver burden).

Analytic Framework

The proposed analytic framework for this project is depicted on the following page. It is expected that studies will vary substantially in terms of their entry criteria, as there is no agreed-upon standard of

what constitutes uncomplicated lower back DDD. In addition, the fusion technique and intensity of the nonsurgical intervention may have differential effects on the outcomes of primary interest in low back pain studies, including pain, function, quality of life, patient satisfaction, and work status. Finally, RCTs of fundamentally different interventions (e.g., surgery for pain relief vs. rehabilitation for functional restoration) may have difficulty enrolling and randomizing patients, resulting in many studies with inadequate statistical power or other quality concerns (e.g., high dropout and/or crossover rates). It is therefore important to keep these challenges in mind during the evaluation of different management options for uncomplicated DDD.

Analytical Framework: Lumbar Fusion



Methodology

Evidence Synthesis

We propose a systematic review of all RCTs, higher-quality comparative cohort studies, and prior higher-quality systematic reviews of the effectiveness of lumbar fusion for chronic low back pain with uncomplicated DDD as compared to alternative treatment approaches. Information on safety will also be abstracted from these studies as well as from selected case series focusing on lumbar fusion.

In order to identify high-quality observational studies not incorporated in the original review, the timeframe of the literature search will span from January 2000 to the most recent data available. We will also include any RCTs published since the 2007 ECRI review. We will include randomized controlled trials and comparative cohorts without restrictions on study design parameters. Case series data describing at least 100 patients with a minimum of two years of follow-up (i.e., to adequately capture longer-term outcomes) will also be evaluated. Case series will also be restricted according to certain quality criteria (e.g., sample retention, clearly-described entry criteria, consecutive samples).

The full search strategy will include articles in MEDLINE, EMBASE, the Cochrane Register of Controlled Trials, and the Databases of Abstracts of Reviews of Effects (DARE) maintained by the University of York. We will also conduct a supplementary search with a focus on lumbar fusion in the workers'/disability compensation literature in several databases, including OT Seeker, PEDro, ABI Inform, EconLit, and Health and Psychosocial Instruments. Electronic searches will be supplemented by manual review of retrieved references.

Data on relevant outcomes will be synthesized quantitatively if feasible. Random-effects models will be specified, and will focus on weighted mean differences in "change score" variables such as pain, function, and quality of life as well as rate ratios for binary measures such as treatment success and retreatment. Qualitative evidence tables will also be generated for each key question.

Quality Assessment

Assessment of the quality of clinical trial reports and systematic reviews will follow methods adapted specifically for studies of low back pain from the Cochrane Back Review Group (Chou, 2007). For observational studies, we will follow the approach of the U.S. Preventive Services Task Force (USPSTF) (AHRQ, 2008). Overall strength of evidence for each key question will be described as "high", "moderate", or "low", and will utilize the evidence domains employed in the AHRQ approach (AHRQ, 2012). In keeping with standards set by the Washington HCA, however, assignment of strength of evidence will focus primarily on study quality, quantity of available studies, and consistency of findings.

In addition, summary ratings of the comparative clinical effectiveness and comparative value of the procedures of interest (i.e., *across* multiple key questions) will be assigned using ICER's integrated evidence rating matrix (Ollendorf, 2010). The matrix has been employed in previous Washington HCA assessments of virtual colonoscopy, coronary CT angiography, proton bean therapy, and breast imaging in special populations. The matrix can be found in the Appendix to this document.

Key Questions

We suggest a number of key questions as central to this review. Each question is listed below, along with the source for the evidence necessary to address it.

1. What is the comparative clinical effectiveness of lumbar fusion surgery for patients with chronic low back pain and uncomplicated DDD relative to that of conservative management, minimally-invasive treatments, and other nonsurgical approaches?
    - Sources: RCTs, high-quality comparative cohort studies, and high-quality systematic reviews of lumbar fusion vs. the comparators of primary interest

2. What are the rates of "treatment success" or "successful clinical outcome" of lumbar fusion as defined by measures of clinically-meaningful improvement in pain, function, quality of life, patient satisfaction, and/or work status?

- Sources: RCTs, high-quality comparative cohort studies, and high-quality systematic reviews of lumbar fusion vs. the comparators of primary interest

3. What are the rates of adverse events and other potential harms (perioperative, long-term adverse events, and reoperations) associated with lumbar fusion surgery compared to alternative treatment approaches?
    - Sources: RCTs, high-quality comparative cohort studies, and high-quality systematic reviews of lumbar fusion vs. the comparators of primary interest; selected non-comparative case series

4. What is the differential effectiveness and safety of lumbar fusion according to factors such as age, sex, race or ethnicity, pre-existing conditions (e.g., smoking history), intensity of conservative management (e.g., interdisciplinary rehabilitation vs. physical and/or behavioral therapy alone) technical approach to fusion (e.g., posterolateral vs. interbody, minimally-invasive vs. open procedures), initial vs. repeat surgery, insurance status (e.g., worker's compensation vs. other), and treatment setting (e.g., inpatient vs. ambulatory surgery)?
    - Sources: RCTs, high-quality comparative cohort studies, and high-quality systematic reviews of lumbar fusion vs. the comparators of primary interest; selected non-comparative case series

5. What are the costs and potential cost-effectiveness of lumbar fusion relative to alternative treatment approaches?
    - Sources: Published economic evaluations, agency data

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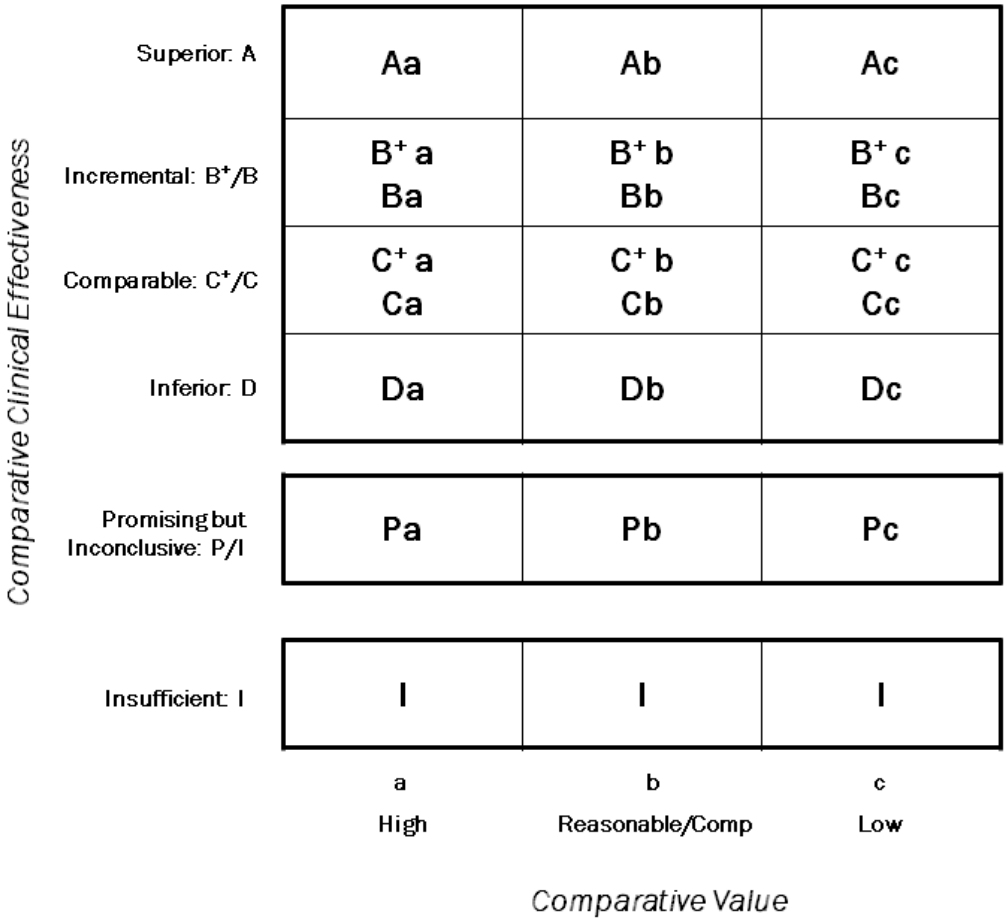
APPENDIX: ICER INTEGRATED EVIDENCE RATING™
(Compares an intervention of interest to a reference comparator)



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