



Transforming Healthcare with Evidence

Update Literature Search, 2007 WA HTA on Lumbar Fusion
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OVERVIEW

This update literature search provides a basis for deciding whether to update the fusion portion (Key Questions 1 through 3) of the report on *Spinal Fusion and Discography for Chronic Low Back Pain and Uncomplicated Lumbar Degenerative Disc Disease* prepared for the Washington HTA Program by ECRI in 2007.

The following objectives reflect methods guidance for systematic review updates published by the Agency for Healthcare Research and Quality (AHRQ) (Tsertsvadze et al., 2011). They are accompanied by key findings.

Objectives

- **Estimate the volume of new literature published since 2007, relative to each component of Key Questions 1 through 3, and using the same general inclusion criteria that were specified for the 2007 report.**

Findings:

- 4 new systematic reviews, including a draft report by AHRQ (posted November 2012) and 3 RCTs addressing effectiveness. Whereas the 2007 ECRI report was focused on uncomplicated degenerative disc disease (DDD), at least two of the four newer systematic reviews, including the one by AHRQ, were not restricted to uncomplicated DDD.
- Large body of observational studies, including at least 2 very large database analyses of adverse event rates.
- At least 3 systematic reviews evaluating differential effectiveness/safety by baseline patient characteristic.
- Numerous systematic reviews and trials on differential effectiveness according to surgical approach, graft material, or other procedure-related factors. [This evidence does *not* correspond to a key question in the 2007 report.]

- **Identify any new harms that have been reported since 2007.**

Findings: No indication of new types of harms in the material reviewed, including Background of the Executive Summary of the AHRQ report, but no in-depth search was made.

- **Assess whether new evidence fills gaps in the evidence available as of 2007.**

Findings:

- Accumulating evidence regarding adverse event rates and differential effectiveness/safety.
- 1 RCT with long follow-up (11-13 years) is available.

- **Assess whether lumbar fusion has been studied in subpopulations or in comparison with specific nonoperative treatments that were not addressed as of 2007.**

Findings:

- Newer reviews include subpopulations with complicated lumbar DDD [outside scope of 2007 report]. Nevertheless, the AHRQ report includes only 1 RCT not included in the 2007 report, and it is unclear whether this RCT includes complicated DDD.
 - cursory review suggests newer evidence covers nonoperative treatments similar to those addressed in 2007 report.
- **Assess whether new evidence allows stronger conclusions or is likely to modify conclusions, including estimates of the magnitude of benefit.**

Findings:

- Newer systematic reviews have somewhat more positive conclusions regarding effectiveness, compared with the conclusions in the 2007 report.
- Newer evidence might allow more reliable estimates of adverse event rates than were possible previously, but the AHRQ report concludes that variation in surgical technique precludes conclusive estimates.
- It appears that the evidence might remain insufficient for determining differential effectiveness/safety according to patient characteristics.

Other Comments

- Although moderate- to high-quality evidence pertaining to the effectiveness of lumbar fusion, versus nonoperative treatment, appears to be lacking in the literature published since 2007, studies comparing current techniques with older techniques might provide some evidence of whether effectiveness is improving.
- No in-depth search for new harms data, e.g. review of FDA Maude reports or recently published narrative reviews, was made.
- No search for new cost or cost-effectiveness data was made.
- No search for new FDA clearances was made.

Changes in CMS Policy

Although the 2007 report listed CPT codes for which there was CMS coverage, no National Coverage Determination (NCD) appears on the CMS website currently. AHRQ has posted a draft report on spinal fusion, which may signal upcoming CMS review.

See [Table 1](#) on next page or more detail and commentary by Key Question.

Table 1. Summary of New Literature

Key Question and Conclusions, 2007 Report* (uncomplicated DDD)	New Systematic Reviews/Technology Assessments	RCTs published July 2007 or later	Observational Studies	Potential Impact of New Evidence
<p>1. Does lumbar fusion surgery reduce pain and improve functional status/quality of life more effectively than nonsurgical treatments?</p> <p>Negative: Vs intensive exercise/rehab plus CBT, w/ or w/out prior back surgery Vs nonintensive PT, w/out prior back surgery (4 RCTs, 1-2 yrs f/u)</p>	<p>AHRQ 2011 (draft) (RCTs or studies that control for confounders; 18 studies, 20 publications selected; search date Feb. 7, 2012; <i>not</i> restricted to uncomplicated DDD) Fusion vs physical and exercise therapies: Positive (favors fusion) for back pain and Oswestry Disability Index; inconclusive for other outcomes.</p> <p>Chou 2009 (qualitative, # studies and inclusion criteria unclear but uncomplicated appears to have been included) Negative: Fair evidence that fusion is not better than intensive rehabilitation with a cognitive/behavioral emphasis for improvement in pain or function Positive: Slight to moderately superior to standard (nonintensive) nonsurgical therapy.</p> <p>Coe 2009 (4 RCTs; scope similar to 2007 report, i.e., restricted to uncomplicated DDD) Negative: Similar to structured nonoperative treatment Positive: Appears superior to unstructured nonoperative treatment Methodological difficulties limit conclusions.</p> <p>Carreon 2008 (M-A, 25 RCTs, inclusion of unpublished studies [mentioned in abstract] and/or use of less restrictive inclusion criteria [unknown] may account for larger # RCTs than in 2007 WA report]). Positive findings.</p>	<p><i>PubMed Search:</i> Slatis 2011 (n=94; 6- yr f/u); positive findings Andersen 2008 (n=?; 11-13 yrs f/u); positive findings Ohtori 2011 The only RCT added by AHRQ; positive findings. (AHRQ excluded Fairbank 2011 because <85% patients had DDD.)</p>	<p>An 11-6 search of PubMed for Clinical Trials not picked up by the RCT search yielded 1070 hits.</p>	<p>Compared with the 2007 report, newer systematic reviews are more positive. New RCT evidence of long-term benefits might lead to more positive conclusions, especially if corroborating evidence from observational studies is available, but combined evidence might be of low quality.</p> <p><i>Helpful inclusions in AHRQ report:</i> Observational, but well-controlled data Table of Minimal Clinically Important Differences (MCIDs) for different lumbar fusion outcome measures.</p>

	Ibrahim 2008 (M-A, 3 RCTs; only evaluated ODI change): Negative conclusion (results favored fusion but were nonsignificant and suggested only marginal benefit)			
<p>2. What are the rates of adverse events (perioperative, long-term events, and reoperations) for lumbar fusion surgery and nonsurgical treatments?</p> <p>Overall intraoperative or early AEs: 12.7%-18%</p> <p>Overall late AEs: 0-7.4%</p> <p>(23 studies)</p>	<p>Lawrence 2012, risk of (meta-analysis; 5 studies): mean annual incidence of clinical adjacent segment pathology, 0.6%-3.9%</p> <p>Lee 2012 (M-A, # studies unknown): radiological adjacent segment pathology, 25.3%, mean 2.3 yrs f/u</p> <p>Ibrahim 2008 (M-A, 3 RCTs)</p>	<p>Ekman 2009: Restricted to patients with isthmic spondylolisthesis (isthmic spondylolysis excluded from 2007 report; any isthmic etiology excluded from AHRQ report). Greater adjacent segment disease with fusion, compared with exercise, but no demonstrated association between adjacent segment disease and clinical outcomes.</p>	<p><u>Large studies identified fortuitously in systematic review search:</u></p> <p>Deyo 2010 (n=32,152, including decompression alone procedures): Life-threatening complications, 5.6% in pts undergoing complex fusions.</p> <p>Fu 2010 (n=3720 pts undergoing fusion+decompression): complications, 7.0%; deaths, 0.1%; new neurological deficits, 0.6%</p> <p>Patil 2008 (n=?): visual loss</p> <p><u>Potentially</u></p>	<p>New evidence is available; extent to which it will change conclusions is unclear but confidence in conclusions might improve.</p> <p><i>NOTE:</i> No inclusion of large uncontrolled studies for absolute adverse event rates in the AHRQ report.</p>

			<u>relevant non-RCTs Identified with AE search defined in 2007 report</u> : 84 studies	
3. What patient characteristics (i.e., workers' compensation population, patients with chronic pain, psychological distress, and age-groups) are associated with differences in the benefits and adverse events of lumbar fusion surgery? Insufficient evidence (1 RCT, n=294)	Lawrence 2012 (only looked at prediction of adjacent segment pathology; meta-analysis; 5 studies, no apparent limitation on study design) Jensen 2011 (association between modic changes and outcome; only 1 study identified for fusion) AHRQ : Insufficient evidence (based on RCTs and well-controlled observational studies)		<u>Identified in SR and RCT searches</u> Abbot 2011 Patil 2008	General conclusions are unlikely to change, depending on the specifics of studies included in and excluded from AHRQ report.
Differential effectiveness/safety by type of bone graft	Chen 2012 (M-A; 10 RCTs) AHRQ 2011, rhBMP02 vs autogenous bone graft : Inconclusive for most outcomes Hayes 2011 : C for (rhBMP)-2 and lumbar fusion; otherwise, D Agarwal 2009	Several	Not searched	Outside scope of 2007 report
Differential effectiveness/safety by type of fusion (posterolateral, posterior interbody, transforaminal interbody, anterior interbody, circumferential)	Jiang 2012 Lee 2011 Umeta 2011 Zhou 2011 Han 2009	Several	Not searched	Outside scope of 2007 report
Differential	Parker 2011	Several	Not searched	Outside scope of 2007 report

effectiveness/safety by minimally invasive vs open technique	Wu 2010 Hayes 2007 (HTB)			
Differential effectiveness/safety by other technical factors	Chou 2009 (instrumentation vs noninstrumentation) Martin 2007 (instrumentation vs noninstrumentation)	Several		Outside scope of 2007 report

*Excluded studies with n<10; > 20% loss to follow-up or withdrawal; < 3 months lumbar pain; > 20% patients had radiculopathy, functional neurologic deficits, spondylolisthesis > Grade 1, isthmic spondylolysis, primary neurogenic claudication associated with stenosis, fracture, tumor, infection, inflammatory disease, or degenerative disease due to significant deformity; outdated lumbar fusion procedure.

METHODS

Systematic Search #1 (Key Systematic Reviews and Technology Assessments)

Databases Searched

The following databases were searched on November 2 and again on November 30, using the term *lumbar fusion* and limiting searches to publication in July 2007 or later:

- a. PubMed, using filters for systematic review, meta-analysis, practice guideline, or NIH Consensus Conference
- b. Hayes Knowledge Center
- c. Centre for Reviews and Dissemination (CRD)
- d. Cochrane Library
- e. AHRQ

Exclusions

- Assessments of lumbar fusion compared with surgical alternatives, such as disc replacement

18 potentially relevant systematic reviews (some outside scope of previous report), several with meta-analyses, were identified. See [Table 1](#), for details. See Appendix I for a list of identified publications with abstracts.

Systematic Search #2 (RCTs)

1. Searched Embase and MEDLINE (OVID), July 2007 to November 6, 2012 to identify new trials (limited to RCTs, as in 2007 report) to answer Key Questions 1, 2, and 3.
 - a. Search terms (modification of search terms used in 2007 report, with additional guidance from reports in Hayes Knowledge Library)
 1. *(spinal fusion) or (bone morphogenetic protein) or (recombinant protein) or rhBMP or "INFUSE" or "OP-1" or "Ne-Osteo" or polyetheretherketone or "PEEK" or AxiaLIF or "axial lumbar interbody fusion" or "XLIF" or "eXtreme Lateral Interbody Fusion" or "bone void filler"*
 2. *Lumbar*
 3. 1 and 2
 - b. Limited to English language (as in 2007 report)
 - i. Used Randomized Controlled Trial filter (article type). Exclude irrelevant studies. No studies with < 10 individuals per treatment arm were identified.

(3 RCTs relevant to previous Key Questions 1-3 added to Summary Table). (Another check on November 30 was made for recently added RCTs; none identified.)

- ii. Use Clinical Query filter for *therapy, sensitive/broad* (combined with previous search using 'NOT') to identify large observational studies that might have safety or differential effectiveness/safety data.

(11-6-12: 1070 hits; not reviewed; many are likely not actually clinical studies)

NOTES: (1) Inclusion criteria 6 through 9, e.g., dropout rates $\leq 20\%$, of the 2007 report were not be observed since the information required to apply these criteria is often not available in abstracts and since strict exclusion criteria may not be desirable for evidence pertaining to new subpopulations or comparisons. (2) Other databases searched for the 2007 report were CINAHL (Cumulative Index to Nursing and Allied Health Literature), databases within the Cochrane Library, CARE (Database of Abstracts of Reviews of Effects), ECRJ library, Embase, and PsychInfo. A search of PubMed only was considered sufficient to establish the need for an update report.

2. Identify uncontrolled, noncomparative studies of lumbar fusions reporting adverse events.

Same search terms as in step 1 with the following filter (borrowed from 2007 report):

*((adverse effects or complications or side effect or contraindication).fs. or (harm\$ or iatrogen\$ or nosocom\$ or hazard\$ or safety or nnh) ti.ab. or (morbidity\$ or mortality\$.).fs.mp. or (treatment outcome or patient satisfaction or reoperation).de. or exp *pain/ or exp postoperative complications/)*

(11-7-12: 123 hits; 23 RCTs eliminated [already covered in previous search]; 84 remaining studies [not yet reviewed for relevance or sample size])

NOTE: The 2007 report excluded studies with < 100 for purposes of collecting adverse event rates. Search results were not checked for sample size. The 2007 report also included systematic reviews of nonoperative treatments for data on absolute event rates in comparator treatments. If an update report is undertaken, the same approach might be advisable. However, for purposes of determining the need for an update report, no search for systematic reviews of nonoperative treatments was performed.

APPENDIX I. Bibliography

SYSTEMATIC REVIEWS (listed in reverse chronological and then alphabetical order)

Chen Z, Ba G, Shen T, Fu Q.

Recombinant human bone morphogenetic protein-2 versus autogenous iliac crest bone graft for lumbar fusion: a meta-analysis of ten randomized controlled trials.

***Arch Orthop Trauma Surg.* 2012;**

BACKGROUND: Recombinant human bone morphogenetic protein-2 (rhBMP-2) as a substitute for iliac crest bone graft (ICBG) has been increasingly widely used in lumbar fusion. It has been proven non-inferior in fusion success and clinical outcomes when compared with ICBG. However, increasingly, some potentially uncommon and serious complications associated with the use of rhBMP-2 have been of great concern to surgeons. The purpose of this study was to determine whether rhBMP-2 could be considered an effective and, more importantly, a relatively safe substitute for ICBG in lumbar fusion. METHODS: **Randomized controlled trials that compared rhBMP-2 with ICBG** for lumbar fusion were identified by computer and manual searching. The risk of bias and clinical relevance of the included studies were assessed. Publication bias was explored using funnel plot and statistical tests (Egger's test and Begg's test). Meta-analyses were performed using the Cochrane systematic review methods. RESULTS: Ten randomized controlled trials (1,342 patients) met the inclusion criteria. Compared with ICBG, the use of rhBMP-2 significantly decreased the risk of fusion failure at all time intervals (6 months: $p < 0.0001$, RR = 0.55, 95 % CI = 0.42-0.72; 12 months: $p = 0.0003$, RR = 0.53, 95 % CI = 0.37-0.75; 24 months: $p < 0.00001$, RR = 0.31, 95 % CI = 0.21-0.46) and the rate of reoperation ($p = 0.0001$, RR = 0.52, 95 % CI = 0.37-0.72). There was no statistical difference in clinical improvement on the Oswestry Disability Index, although a favorable trend in the rhBMP-2 group was found ($p = 0.12$, RR = 0.73, 95 % CI = 0.49-1.08). Subgroup analyses stratified by the type of surgical procedure yielded similar results. Owing to the different data formats, meta-analysis on adverse events was not performed. CONCLUSION: RhBMP-2 was superior to the ICBG for achieving fusion success and avoiding reoperation. However, evidence from the Food and Drug Administration document and subsequent independent studies has demonstrated that original, industry-sponsored trials underestimated rhBMP-2-related adverse events. There are still security risks in the use of rhBMP-2.

Chou D, Dekutoski M, Hermsmeyer J, Norvell DC.

The treatment of lumbar adjacent segment pathology after a previous lumbar surgery: a systematic review.

***Spine.* 2012;37(22 Suppl):S180-188.**

STUDY DESIGN.: Systematic review. OBJECTIVE.: To perform a systematic review, evaluating the best available evidence regarding the treatment of lumbar adjacent segment pathology (ASP) to facilitate clinical recommendations for treatment. SUMMARY OF BACKGROUND DATA.: It is unclear how nonoperative treatment of lumbar clinical ASP (CASP) compares with operative treatment, and it is also unclear if 1 type of operative treatment is superior to another in the treatment of lumbar CASP. Given that ASP occurs with a known frequency after fusion, it is important to understand outcomes for treatment based on the best available evidence. METHODS.: We conducted a systematic search in PubMed and the Cochrane Library for

literature published through February 2012 for lumbar ASP. Our first goal was to **identify studies comparing operative with nonoperative management of lumbar ASP**. Our second goal was to identify studies comparing operative with operative management of lumbar CASP. Our third goal was to identify case series evaluating outcomes after the treatment of lumbar CASP. The overall body of evidence with respect to each clinical question was determined on the basis of precepts outlined by the Grades of Recommendation Assessment, Development, and Evaluation (GRADE) working group and recommendations made by the Agency for Healthcare Research and Quality. RESULTS.: No studies comparing operative with nonoperative management or comparing operative with operative management of CASP were identified in the literature. Eight case series were identified for the treatment of CASP with decompression alone, decompression and fusion, or decompression and disc arthroplasty. CONCLUSION.: The strength of evidence supporting these clinical questions was insufficient based on GRADE criteria; therefore, conclusions are based on the best available evidence and clinical experience. Operative management for lumbar CASP should be considered after failure of nonoperative management. When considering the type of operative treatment for lumbar CASP, clinical judgment, radiographical appearance, and patient preference should guide operative intervention. If a patient's disability secondary to lumbar CASP is high enough, consideration should be given to operative treatment. All these recommendations are weak based on GRADE. CONSENSUS STATEMENT:

Jiang S-D, Chen J-W, Jiang L-S.

Which procedure is better for lumbar interbody fusion: anterior lumbar interbody fusion or transforaminal lumbar interbody fusion?

Archives of Orthopaedic and Trauma Surgery. 2012;132(9):1259-1266.

Lawrence BD, Wang J, Arnold PM, et al.

Predicting the risk of adjacent segment pathology after lumbar fusion: a systematic review. *Spine*. 2012;37(22 Suppl):S123-132.

STUDY DESIGN.: Systematic review. OBJECTIVE.: To perform a systematic review to define the **incidence of clinical adjacent segment pathology (CASP) after lumbar fusion surgery and define potential risk factors** for the development of CASP. SUMMARY OF BACKGROUND DATA.: Concerns for the longevity of current arthrodesis constructs and the effects of arthrodesis on adjacent segments have received increasing attention during the past decade. There is a lack of precision regarding the terminology used to describe the pathologies of adjacent segment disease. The term ASP is proposed as an umbrella term to refer to the breadth of clinical and/or radiographical changes at adjacent motion segments that developed subsequent to a previous spinal intervention. METHODS.: A systematic search was performed in Medline and the Cochrane Collaboration Library for literature published through January 2012. Level of evidence ratings were assigned to each article independently by 2 reviewers. Extracted were the percentage risks of CASP during 5- and 10-year time periods, risk factors, the effect estimates (relative risks and odds ratios), and corresponding confidence intervals reported from each study's multivariate analyses. Forest plots of odds ratios or relative risks with their 95% confidence intervals evaluating patient, disease, and surgical risk factors were constructed using the data provided by the individual studies. RESULTS.: We identified 162 total citations from our literature search. Of these, 31 full-text articles were evaluated for meeting inclusion criteria. From these 31 studies, 5 studies met inclusion criteria. The mean patient ages ranged from 50 to 64 years. The mean annual incidence of CASP ranged from 0.6% to 3.9%. With respect to patient

factors, age more than 60 years was associated with an increased risk of developing CASP. Other factors that may increase the risk of developing CASP are pre-existing facet degeneration, degenerative disc disease, performing a multilevel fusion, stopping a construct at L5, performing a laminectomy adjacent to a fusion, and excessive disc height distraction during posterior interbody fusion. CONCLUSION.: This systematic review was limited to higher-quality studies that evaluated risk factors using multivariate analyses. Identified were key patient, disease, surgical, and radiographical factors that may be considered when counseling and treating patients with degenerative conditions. Further high-quality studies are required before any concrete conclusions can be made about this controversial topic. CONSENSUS STATEMENTS:

Lee MJ, Dettori JR, Standaert CJ, Ely CG, Chapman JR.

Indication for spinal fusion and the risk of adjacent segment pathology: does reason for fusion affect risk? A systematic review.

***Spine.* 2012;37(22 Suppl):S40-51.**

STUDY DESIGN.: A systematic review. OBJECTIVE.: To determine **whether different indications or reasons for spinal fusion are associated with different risks of subsequent adjacent segment pathology (ASP)** in the lumbar and cervical spine. SUMMARY OF BACKGROUND DATA.: Pre-existing degeneration at levels adjacent to an arthrodesis may play a role in the development of symptomatic adjacent segment pathology. Although most spinal arthrodeses occur in patients with degenerative spinal disease, spinal fusion occurs in the pediatric and trauma population, and also congenitally. Evaluating the risk of ASP in these populations may shed light on its etiology. METHODS.: A systematic search was conducted in PubMed and the Cochrane Library for articles published between January 1, 1990, and December 31, 2011. We included all articles that described the risk of radiographical adjacent segment pathology (RASP) following surgical fusion for degenerative disease, for trauma, or for conditions requiring fusion in pediatrics in the lumbar or cervical spine. In addition, we included studies recording ASP in patients with congenital fusion. RESULTS.: Nineteen studies met our inclusion criteria. In patients who underwent fusion in the lumbar spine for degenerative reasons, the RASP rate averaged 12.4% during an average of 5.6-year follow-up. For patients who underwent fusion in the cervical spine for degenerative reasons, the average RASP rate was 25.3% during a 2.3-year follow-up. For patients with Klippel-Feil syndrome and congenital fusion, the RASP rate averaged 49.7% during an average of 23.5-years of follow-up. In patients who were fused for scoliosis, the average RASP rate was 20.3% of 3.9-year follow-up. However there is significant variation between studies in patient population, follow-up, and definition of RASP. CONCLUSION.: In the cervical spine, the rate of RASP in patients with fusion for degenerative reasons indications is greater than the rate of RASP in patients with congenital fusion suggesting that the pre-existing health and status of the adjacent level at the time of fusion may play a contributory role in the development of ASP. There is insufficient evidence in the literature to determine whether the indication/reason for fusion affects the risk of RASP in the lumbar spine CONSENSUS STATEMENT: In the cervical spine, the rate of RASP in patients with fusion for degenerative reasons indications is greater than the rate of RASP in patients with congenital fusion suggesting that the pre-existing health and status of the adjacent level at the time of fusion may play a contributory role in the development of ASP. Strength of Statement: Weak.

Wang H, Lu F, Jiang J, et al.

Minimally invasive lumbar interbody fusion via MAST Quadrant retractor versus open surgery: a prospective randomized clinical trial.

Chinese Medical Journal. 2011;124(23):3868-74.

BACKGROUND: In recent years, a variety of minimally invasive lumbar surgery techniques have achieved desirable efficacy, but some dispute remains regarding the advantages over open surgery. This study aimed to compare minimally invasive lumbar interbody fusion via MAST Quadrant retractor with open surgery in terms of perioperative factors, postoperative back muscle function, and 24-month postoperative follow-up results.

Jensen RK, Leboeuf-Yde C.

Is the presence of modic changes associated with the outcomes of different treatments? A systematic critical review.

BMC Musculoskelet Disord. 2011;12:183.

BACKGROUND: **Modic changes (MCs) have been identified as a diagnostic subgroup associated with low back pain (LBP).** The aetiology of MCs is still unknown and there is no effective treatment available. If MCs constitute a specific subgroup of LBP, it seems reasonable to expect different effects from different treatments. The objective of this systematic critical literature review was therefore **to investigate if there is evidence in the literature that the presence of MCs at baseline is associated with a favourable outcome depending on the treatment provided for LBP.**METHODSThe databases MEDLINE and EMBASE were searched for relevant articles from 1984 to December 2010. A checklist including items related to the research questions and quality of the articles was used for data extraction and quality assessment. Of the 1650 articles found, five (six studies) were included in this review but because the studies were so heterogeneous, the **results have been reported separately** for each study.RESULTSThe treatments studied were: lumbar epidural steroid injections (n = 1), lumbar intradiscal steroid injections (n = 2), lumbar disc replacement (n = 1), **fusion surgery (n = 1)** and exercise therapy (n = 1). One of the two studies investigating treatment with intradiscal steroid injections and the study investigating fusion surgery reported that MCs were positively associated with the outcomes of pain and disability. The other study on lumbar intradiscal steroid injections and the study on lumbar epidural steroid injections reported mixed results, whereas the study on lumbar disc replacement and the study on exercise therapy reported that MCs were not associated with the outcomes of pain and disability.CONCLUSIONSThe available studies on the topic were too few and too heterogeneous to reach a definitive conclusion and it is therefore still unclear if MCs may be of clinical importance when guiding or prescribing the “right” treatment for a patient with LBP.

Lee CS, Hwang CJ, Lee D-H, Kim Y-T, Lee HS.

Fusion rates of instrumented lumbar spinal arthrodesis according to surgical approach: a systematic review of randomized trials.

Clin Orthop Surg. 2011;3(1):39-47.

BACKGROUND:Lumbar spine fusion rates can vary according to the surgical technique. Although many studies on spinal fusion have been conducted and reported, the heterogeneity of the study designs and data handling make it difficult to identify which approach yields the highest fusion rate. This paper reviews studies that compared the **lumbosacral fusion rates achieved with different surgical techniques.**METHODSRelevant randomized trials comparing the fusion rates of different surgical approaches for instrumented lumbosacral spinal fusion surgery were identified through highly sensitive and targeted keyword search strategies. A methodological quality assessment was performed according to the checklist suggested by the Cochrane

Collaboration Back Review Group. Qualitative analysis was performed. RESULTS A literature search identified six randomized controlled trials (RCTs) comparing the fusion rates of different surgical approaches. One trial compared anterior lumbar interbody fusion (ALIF) plus adjunctive posterior transpedicular instrumentation with circumferential fusion and posterolateral fusion (PLF) with posterior lumbar interbody fusion (PLIF). Three studies compared PLF with circumferential fusion. One study compared three fusion approaches: PLF, PLIF and circumferential fusion. CONCLUSIONS One low quality RCT reported no difference in fusion rate between ALIF with posterior transpedicular instrumentation and circumferential fusion, and PLIF and circumferential fusion. There is moderate evidence suggesting no difference in fusion rate between PLF and PLIF. The evidence on the fusion rate of circumferential fusion compared to PLF from qualitative analysis was conflicting. However, no general conclusion could be made due to the scarcity of data, heterogeneity of the trials included, and some methodological defects of the six studies reviewed.

Parker SL, Adogwa O, Witham TF, et al.

Post-operative infection after minimally invasive versus open transforaminal lumbar interbody fusion (TLIF): literature review and cost analysis.

***Minim Invasive Neurosurg.* 2011;54(1):33-37.**

INTRODUCTION: **Surgical site infection (SSI)** in the setting of lumbar fusion is associated with significant morbidity and medical resource utilization. To date, there have been no studies conducted with sufficient power to directly compare the incidence of **SSI following minimally invasive (MIS) vs. open TLIF procedures**. Furthermore, studies are lacking that quantify the direct medical cost of SSI following fusion procedures. We set out to determine the incidence of SSI in patients undergoing MIS vs. open TLIF reported in the literature and to determine the direct hospital cost associated with the treatment of SSI following TLIF at our institution. METHODS A systematic Medline search was performed to identify all published studies assessing SSI after MIS or open TLIF. The cumulative incidence of SSI was calculated from all reported cohorts and compared between MIS vs. open TLIF. In order to determine the direct hospital costs associated with the treatment of SSI following TLIF, we retrospectively reviewed 120 consecutive TLIFs performed at our institution, assessed the incidence of SSI, and calculated the SSI-related hospital costs from accounting and billing records. RESULTS To date, there have been 10 MIS-TLIF cohorts (362 patients) and 20 open-TLIF cohorts (1 133 patients) reporting incidences of SSI. The cumulative incidence of reported SSI was significantly lower for MIS vs. open-TLIF (0.6% vs. 4.0%, $p=0.0005$). In our experience with 120 open TLIF procedures, SSI occurred in 6 (5.0%) patients. The mean hospital cost associated with the treatment of SSI following TLIF was \$ 29,110 in these 6 cases. The 3.4% decrease in reported incidence of SSI for MIS vs. open-TLIF corresponds to a direct cost savings of \$ 98,974 per 100 MIS-TLIF procedures performed. CONCLUSIONS Post-operative wound infections following TLIF are costly complications. MIS vs. open TLIF is associated with a decreased reported incidence of SSI in the literature and may be a valuable tool in reducing hospital costs associated with spine care.

Umeta RSG, Avanzi O.

Techniques of lumbar-sacral spine fusion in spondylosis: systematic literature review and meta-analysis of randomized clinical trials.

***Spine J.* 2011;11(7):668-676.**

BACKGROUND CONTEXT Spine fusions can be performed through different techniques and are used to treat a number of vertebral pathologies. However, there seems to be no consensus

regarding which technique of fusion is best suited to treat each distinct spinal disease or group of diseases. **PURPOSE**To study the effectiveness and complications of the different techniques used for spinal fusion in patients with lumbar spondylosis. **STUDY DESIGN**Systematic literature review and meta-analysis. **SAMPLERandomized clinical studies comparing the most commonly performed surgical techniques for spine fusion in lumbar-sacral spondylosis, as well as those reporting patient outcome** were selected. **OUTCOME MEASURES**Identify which technique, if any, presents the best clinical, functional, and radiographic outcome. **METHODS**Systematic literature review and meta-analysis based on scientific articles published and indexed to the following databases: PubMed (1966-2009), Cochrane Collaboration-CENTRAL, EMBASE (1980-2009), and LILACS (1982-2009). The general search strategy focused on the surgical treatment of patients with lumbar-sacral spondylosis. **RESULT**Eight studies met the inclusion criteria and were selected with a total of 1,136 patients. Meta-analysis showed that patients who underwent interbody fusion presented a significantly smaller blood loss ($p=.001$) and a greater rate of bone fusion ($p=.02$). Patients submitted to fusion using the posterolateral approach had a significantly shorter operative time ($p=.007$) and less perioperative complications ($p=.03$). No statistically significant difference was found for the other studied variables (pain, functional impairment, and return to work). **CONCLUSION**The most commonly used techniques for lumbar spine fusion in patients with spondylosis were interbody fusion and posterolateral approach. Both techniques were comparable in final outcome, but the former presented better rates of fusion and the latter the less complications.

Zhou Z-J, Zhao F-D, Fang X-Q, Zhao X, Fan S-W.

Meta-analysis of instrumented posterior interbody fusion versus instrumented posterolateral fusion in the lumbar spine.

J Neurosurg Spine. 2011;15(3):295-310.

OBJECTThe authors **compared the effectiveness of instrumented posterior lumbar interbody fusion (iPLIF) and instrumented posterolateral fusion (iPLF)** for the treatment of low-back pain (LBP) due to degenerative lumbar disease. **METHODS: Relevant randomized controlled trials (RCTs) and comparative observational studies** through December 2009 were identified using a retrieval strategy of sensitive and specific searches. The study design, participant characteristics, interventions, follow-up rate and period, and outcomes were abstracted after the assessment of methodological quality of the trials. Analyses were performed following the method guidelines of the Cochrane Back Review Group. **RESULTS**Nine studies were identified-3 RCTs and 6 comparative observational studies. No significant difference was found between the 2 fusion procedures in the global assessment of clinical outcome (OR 1.51, 95% CI 0.71-3.22, $p = 0.29$) and complication rate (OR 0.55, 95% CI 0.16-1.86, $p = 0.34$). Both techniques were effective in reducing pain and improving functional disability, as well as restoring intervertebral disc height. Instrumented PLIF was more effective in achieving solid fusion (OR 2.60, 95% CI 1.35-5.00, $p = 0.004$), a lower reoperation rate (OR 0.20, 95% CI 0.03-1.29, $p = 0.09$), and better restoration of segmental angle and lumbar lordotic angle than iPLF. There were no significant differences between the fusion methods regarding blood loss (weighted mean difference -179.63, 95% CI -516.42 to 157.15, $p = 0.30$), and operating time (weighted mean difference 8.03, 95% CI -45.46 to 61.53, $p = 0.77$). **CONCLUSION**The authors' analysis provided moderate-quality evidence that iPLIF has the advantages of higher fusion rate and better restoration of spinal alignment over iPLF. No significant differences were identified between iPLIF and iPLF concerning clinical outcome, complication rate, operating time, and blood loss.

AHRQ 2010. *Bone Morphogenetic Protein: The State of the Evidence on On-Label and Off-label Use.*

Wu RH, Fraser JF, Härtl R.

Minimal access versus open transforaminal lumbar interbody fusion: meta-analysis of fusion rates.

Spine. 2010;35(26):2273-2281.

STUDY DESIGN A quantitative **meta-analysis** was conducted on published studies reporting **fusion rates after open or minimally invasive/mini-open transforaminal lumbar interbody fusion (TLIF) procedures** for single or multilevel degenerative disease including **stenosis with spondylolisthesis and degenerative disc disease**. OBJECTIVE The primary aim of this study was to establish **benchmark fusion rates for open TLIF and minimally invasive TLIF (mTLIF)** based on published studies. A secondary goal was to review complication rates for both approaches. SUMMARY OF BACKGROUND DATA Lumbar fusion for the treatment of degenerative disease has evolved from a purely posterior noninstrumented approach to a combination of anterior and/or posterior surgery with instrumentation. The increasingly popular transforaminal approach has advanced to incorporate minimally invasive spinal techniques. There currently exist no controlled comparisons between open TLIF and mTLIF. METHODS A Medline search was performed to identify studies reporting fusion rate on open TLIF or mTLIF with instrumentation. A database including patient demographic information, fusion rate, and complication rate was created. Fusion and complication rates were pooled according to whether TLIF was performed with open or minimally invasive technique. Publication bias was assessed with Egger's test, and adjustments were performed using Duval and Tweedie's Trim and Fill algorithm. RESULTS Twenty-three articles were identified that fit inclusion criteria. In each of the 23 studies, TLIF was performed with pedicle fixation and fusion was evaluated using radiograph or computed tomography scan at minimum 6-month follow-up. Overall, the studies included 1028 patients, 46.8% of which were female. The mean age of all patients was 49.7 (range, 38-64.9), and mean follow-up interval for assessment of fusion was 26.6 months (range, 6-46 months). The usage of recombinant bone morphologic protein was higher in the mTLIF group (50% vs. 12%). Mean fusion rate from 16 studies (716 patients) of open TLIF was 90.9%, whereas mean fusion rate from 8 studies (312 patients) of mTLIF was 94.8%. Complication rate was 12.6% and 7.5% for open and mTLIF, respectively. CONCLUSION Fusion rates for both open and mTLIF are relatively high and in similar ranges. Complication rates are also similar, with a trend toward mTLIF having a lower rate. This analysis provides clear benchmarks for fusion rates in open and mTLIF procedures for spine surgeons.

Agarwal R, Williams K, Umscheid CA, Welch WC.

Osteoinductive bone graft substitutes for lumbar fusion: a systematic review.

J Neurosurg Spine. 2009;11(6):729-740.

OBJECTIVE: **Autograft and allograft, the standard approaches** for lumbar fusion procedures, have important disadvantages. **Bone graft substitutes** such as recombinant human bone morphogenetic proteins (rhBMP-2 and rhBMP-7) have emerged **as viable alternatives**. The authors conducted a systematic review to compare the efficacy and safety of osteoinductive bone graft substitutes using autografts and allografts in lumbar fusion. METHODS A search for prospective controlled trials was conducted on MEDLINE, EMBASE, and the Cochrane Central Register of Controlled Trials databases. Data were extracted for key outcomes including radiographically demonstrated nonunion, **Oswestry Disability Index**, operating time, blood loss,

and length of hospital stay. The quality of randomized controlled trials was assessed using the Jadad scale. Meta-analyses were performed when feasible, and heterogeneity was assessed using the Q statistic and the I(2) statistic. RESULTS Seventeen of 732 potential studies met the inclusion criteria, with 9 examining rhBMP-2, 3 examining rhBMP-7, 3 examining demineralized bone matrix, and 2 examining autologous growth factor. Recombinant human BMP-2 significantly decreased radiographic nonunion when compared with autologous iliac crest bone graft (AIBG) in a meta-analysis (relative risk 0.27, 95% CI 0.16-0.46). Stratification of meta-analyses by the type of surgical procedure performed yielded similar results. Funnel plots suggested publication bias. Trials of rhBMP-2 suggested reductions in the operating time and surgical blood loss, with less effect on the length of hospital stay. There was no difference in radiographic nonunion with the use of rhBMP-7 when compared with AIBG (relative risk 1.02, 95% CI 0.52-1.98). Neither rhBMP-2 nor rhBMP-7 demonstrated a significant improvement on the Oswestry Disability Index when compared with AIBG. The limited data on demineralized bone matrix and autologous growth factor showed no significant improvement in radiographic outcomes. **CONCLUSIONS: Recombinant human BMP-2 may be an effective alternative to AIBG in lumbar fusion. Data are limited for other bone graft substitutes.**

Chou R., Baisden J., Carragee E.J., et al.

Surgery for low back pain: A review of the evidence for an American pain society clinical practice guideline.

***Spine.* 2009;1094-1109.**

STUDY DESIGN.: Systematic review. OBJECTIVE.: To systematically assess benefits and harms of surgery for nonradicular back pain with **common degenerative changes, radiculopathy with herniated lumbar disc, and symptomatic spinal stenosis.** SUMMARY OF BACKGROUND DATA.: Although back surgery rates continue to increase, there is uncertainty or controversy about utility of back surgery for various conditions. METHODS.: Electronic database searches on Ovid MEDLINE and the Cochrane databases were conducted through July 2008 to identify randomized controlled trials and systematic reviews of the above therapies. All relevant studies were methodologically assessed by 2 independent reviewers using criteria developed by the Cochrane Back Review Group (for trials) and Oxman (for systematic reviews). A qualitative synthesis of results was performed using methods adapted from the US Preventive Services Task Force. RESULTS.: For nonradicular low back pain with common degenerative changes, we found fair evidence that fusion is no better than intensive rehabilitation with a cognitive-behavioral emphasis for improvement in pain or function, but slightly to moderately superior to standard (nonintensive) nonsurgical therapy. Less than half of patients experience optimal outcomes (defined as no more than sporadic pain, slight restriction of function, and occasional analgesics) following fusion. Clinical benefits of instrumented versus noninstrumented fusion are unclear. For radiculopathy with herniated lumbar disc, we found good evidence that standard open discectomy and microdiscectomy are moderately superior to nonsurgical therapy for improvement in pain and function through 2 to 3 months. For symptomatic spinal stenosis with or without degenerative spondylolisthesis, we found good evidence that decompressive surgery is moderately superior to nonsurgical therapy through 1 to 2 years. For both conditions, patients on average experience improvement either with or without surgery, and benefits associated with surgery decrease with long-term follow-up in some trials. Although there is fair evidence

that artificial disc replacement is similarly effective compared to fusion for single level degenerative disc disease and that an interspinous spacer device is superior to nonsurgical therapy for 1- or 2-level spinal stenosis with symptoms relieved with forward flexion, insufficient evidence exists to judge long-term benefits or harms. CONCLUSION.: Surgery for radiculopathy with herniated lumbar disc and symptomatic spinal stenosis is associated with short-term benefits compared to nonsurgical therapy, though benefits diminish with long-term follow-up in some trials. For nonradicular back pain with common degenerative changes, fusion is no more effective than intensive rehabilitation, but associated with small to moderate benefits compared to standard nonsurgical therapy. 2009, Lippincott Williams & Wilkins.

Coe M., Mirza S., Sengupta D.

The Role of Fusion for Discogenic Axial Back Pain Without Associated Leg Pain, Spondylolisthesis or Stenosis: An Evidence-Based Review.
Seminars in Spine Surgery. 2009;246-256.

The objective of this review was to examine the randomized controlled trials evaluating fusion surgery for **discogenic axial back pain without associated leg pain, spondylolisthesis, or stenosis**. Six studies were reviewed: 4 that considered spinal fusion in comparison with nonoperative treatment, and 2 that considered fusion in comparison with artificial disc replacement. We found that methodological difficulties limit the ability to draw definitive conclusions, but that fusion appears superior to unstructured nonoperative treatment, similar to structured nonoperative treatment, and similar to short-term results of artificial disc replacement. Further long term, well-constructed randomized controlled trials are warranted. 2009 Elsevier Inc. All rights reserved.

Han X, Zhu Y, Cui C, Wu Y.

A meta-analysis of circumferential fusion versus instrumented posterolateral fusion in the lumbar spine.

Spine. 2009;34(17):E618-625.

STUDY DESIGN meta-analysis of **circumferential fusion versus instrumented posterolateral fusion (PLF)** in the lumbar spine. OBJECTIVE To **compare the clinical efficacy** of circumferential fusion and instrumented PLF and to collate the scientific evidence to find a useful fusion method. SUMMARY OF BACKGROUND DATA Clinical results, advantages, and postoperative complications of circumferential fusion and instrumented PLF were shown in many studies. However, there are different opinions among surgeons concerning the preferred method for the 2 fusion methods. METHODSA highly sensitive search strategy was used to identify all published randomized controlled trials up to December 2007. A criteria list taken from Koes et al was used to evaluate the risk of bias of the included studies. The 5 questions that were recommended by the Cochrane Back Review Group were used to evaluate the clinical relevance. Cochrane methodology was used for the results of this meta-analysis. RESULTS Four randomized controlled trials of surgery for lumbar degenerative disease were identified. No significant difference was found in the primary beneficial clinical outcome (odds ratios[OR]: 0.96, 95% confidence limits[95% CI]: [0.59, 1.55], [P = 0.87]). Significant difference was found in the complication rate (OR: 1.89, 95% CI: [1.14, 3.14], [P = 0.01]), which reflects the primary harm outcome. In the secondary outcomes, significant differences were found between circumferential fusion and instrumented PLF in the fusion rate (OR: 2.11, 95% CI: [1.06, 4.19], [P = 0.03]), the reoperation rate (OR: 0.44, 95% CI: [0.25, 0.77], [P = 0.004]), and the amount of blood loss (WMD = 349.95,

95% CI: [138.26, 561.64], [P = 0.001]). No significant difference was found the operating time (WMD = 90.24, 95% CI: [-9.71, 190.20], [P = 0.08]). CONCLUSION Compared with instrumented PLF, circumferential fusion can increase the fusion rate and reduce the reoperation rate, but it can also increase the complication rate and the amount of blood loss. No significant difference was found in the global assessment of clinical outcome about the 2 fusion procedures.

Hayes 2009 (Medical Technology Directory Report)

Recombinant Human Bone Morphogenetic Protein for Use in Spinal Fusion

Searches conducted through July 2011.

C – For rhBMP-2 for lumbar fusion in skeletally mature patients with degenerative disc disease and who have specific risk factors for nonunion. For patients with a metabolic bone disease (e.g., osteomalacia or osteoporosis), adverse exposure (e.g., tobacco, radiation), or specific anatomic risks for nonunion, the risk/benefit ratio of rhBMP-2 may be acceptable. However, discussion of the specific risks of rhBMP-2 with patients is warranted.

D1 – For rhBMP-2 for lumbar fusion in patients without specific risk factors for nonunion. This Rating reflects serious safety concerns.

D1 – For use of rhBMP-2 in cervical fusion. This Rating reflects the safety concerns for this application.

The following **Hayes Ratings** are assigned for rhBMP-7:

D1 – For use of rhBMP-7 for lumbar fusion. This Rating reflects the finding that in 3 of 4 randomized clinical trials, rhBMP-7 was not better than AICBG.

D2 – For use of rhBMP-7 in cervical fusion. This Rating reflects the lack of data and safety concerns for this application.

Carreon LY, Glassman SD, Howard J.

Fusion and nonsurgical treatment for symptomatic lumbar degenerative disease: a systematic review of Oswestry Disability Index and MOS Short Form-36 outcomes.

***Spine J.* 2008;8(5):747-755.**

BACKGROUND CONTEXT Although numerous studies have been published, controversy still exists regarding fusion and nonsurgical treatment for symptomatic degenerative lumbar spine conditions. Definite conclusions are difficult to draw because of differences in patient inclusion criteria, fusion technique, nonoperative treatment regimen, and clinical outcome measures used to determine success. **PURPOSE** The objective of this study was to evaluate lumbar fusion and nonsurgical interventions for various degenerative spine disorders using the Oswestry Disability Index (ODI) as a primary outcome measure in a systematic review. A secondary objective was to determine whether there is a difference in clinical outcomes based on the specific diagnosis. **STUDY DESIGN/SETTINGS** Systematic review. **PATIENT SAMPLE** Patients with low back pain of at least 12 weeks duration and older than 18 years, with prospectively collected ODI scores and at least a 12-month follow-up. **OUTCOME MEASURES** ODI and Short Form-36 (SF-36). **METHODS** A MEDLINE, HealthSTAR, CINAHL, and Cochrane database search was done using the search strategy recommended by the Cochrane Back Review Group. Proceedings from annual meetings of various spine societies and reference lists from review articles and retrieved articles were evaluated for possible inclusion. Criteria for inclusion were prospective randomized clinical trials in patients with low back pain of at least 12 weeks duration and older than 18 years; with prospectively collected ODI scores and at least a 12-month follow-up. The methodological quality of the studies was assessed using the van Tulder criteria. Data extracted

from each study included demographics, study design, diagnosis, baseline and change in ODI, and baseline and change in SF-36 Physical Composite Score (PCS). The data were pooled and analyzed based on the primary reported inclusion diagnosis: degenerative disc disease (DDD), chronic low back pain (CLBP), and spondylolisthesis; and treatment: fusion (unspecified, posterior, anterior, combined) and nonsurgical. **RESULT** Twenty-five studies met the inclusion criteria. The distribution of sex and smokers was similar across diagnoses and treatments. Patients with spondylolisthesis were older than patients with DDD and CLBP. Patients with spondylolisthesis had the greatest ODI improvement followed by patients with DDD and CLBP. **The three fusion types produced similar amounts of improvement in ODI. Nonsurgical patients did not improve as much but had a lower baseline ODI. Improvements in the SF-36 PCS were fairly consistent across diagnostic groups and treatment types.** **CONCLUSION** Substantial improvement can be expected in patients treated with fusion, regardless of technique, when an established indication such as spondylolisthesis or DDD exists. CLBP patients are less disabled and experience less improvement.

Ibrahim T, Tleyjeh IM, Gabbar O.

Surgical versus non-surgical treatment of chronic low back pain: a meta-analysis of randomised trials.

***Int Orthop.* 2008;32(1):107-113.**

We performed a **meta-analysis** of randomised controlled trials to investigate the effectiveness of **surgical fusion** for the treatment of chronic low back pain **compared to non-surgical intervention**. Several electronic databases (MEDLINE, EMBASE, CINAHL and Science Citation Index) were searched from 1966 to 2005. The meta-analysis comparison was based on the mean difference in Oswestry Disability Index (ODI) change from baseline to the specified follow-up of patients undergoing surgical versus non-surgical treatment. Of the 58 articles identified, three studies were eligible for primary analysis and one study for sensitivity analysis, with a total of 634 patients. The pooled mean difference in ODI between the surgical and non-surgical groups was in favour of surgery (mean difference of ODI: 4.13, 95%CI: -0.82 to 9.08, $p = 0.10$, $I(2) = 44.4\%$). Surgical treatment was associated with a 16% pooled rate of early complication (95%CI: 12-20, $I(2) = 0\%$). Surgical fusion for chronic low back pain favoured a marginal improvement in the ODI compared to non-surgical intervention. This difference in ODI was not statistically significant and is of minimal clinical importance. Surgery was found to be associated with a significant risk of complications. Therefore, the cumulative evidence at the present time does not support routine surgical fusion for the treatment of chronic low back pain.

Papakostidis C, Kontakis G, Bhandari M, Giannoudis PV.

Efficacy of autologous iliac crest bone graft and bone morphogenetic proteins for posterolateral fusion of lumbar spine: a meta-analysis of the results.

***Spine.* 2008;33(19):E680-692.**

STUDY DESIGN Meta analysis of randomized control trials. **OBJECTIVE** To evaluate the radiographic and clinical effectiveness of bone morphogenetic proteins (BMPs) within the context of posterolateral fusion of the lumbar spine (LS). **SUMMARY OF BACKGROUND DATA** Various bone graft substitutes have been used in the setting of posterolateral lumbar fusions. Recently, great interest has been shown in BMPs. Clinical trials have tested the efficacy of BMPs to iliac crest bone graft (ICBG) in posterolateral fusion procedures of the LS. A cumulative result of these studies would give more credit to the final conclusions. **METHODS** A systematic search of electronic databases, and references from eligible articles was conducted.

Comparative studies reporting on the results of posterolateral fusion for treatment of degenerative disease of LS and including 2 treatment groups either **ICBG (control group)** or **BMP (experimental group)** for achievement of fusion were regarded eligible. A pooled estimate of effect size was produced using both random and fixed effect model. RESULTS Seven randomized control trials (n = 331 patients) and 1 prospective comparative study (n = 52 patients) were included in the present study. BMPs appeared more efficacious to ICBG in achieving solid fusion [relative risk (RR) = 0.42, 95% confidence interval (CI) = 0.28-0.61, P < 0.00001], but with significant heterogeneity (I = 42.5%). rBMP-2 was more efficacious to ICBG in promoting fusion (RR = 0.29, 95% CI = 0.18-0.47, P < 0.00001), whereas rhBMP-7 (osteogenic protein-1) appeared equivalent to ICBG in that respect (RR = 1.17, 95% CI = 0.54-2.54, P = 0.70). Patients treated with BMPs had a shorter hospitalization (by 1.03 days, 95% CI = 0.61-1.45 days) compared with those that were treated with ICBG. BMPs appeared more efficient in instrumented than noninstrumented posterolateral fusions. CONCLUSION Although the radiographic results appeared better in the group of BMPs, the exact role of type, dose and carrier of BMPs and the cost-effectiveness of their use need further clinical delineation.

Tsutsumimoto T, Shimogata M, Yoshimura Y, Misawa H.

Union versus nonunion after posterolateral lumbar fusion: a comparison of long-term surgical outcomes in patients with degenerative lumbar spondylolisthesis.

***Eur Spine J.* 2008;17(8):1107-1112.**

It has been reported that in patients undergoing posterolateral lumbar fusion (PLF), the fusion status is not related to the short-term operative results. To determine whether the fusion status influences the long-term operative results of PLF, we retrospectively examined the surgical outcomes of uninstrumented PLF for a minimum of 8 years (average, 9.5 years), by comparing cases exhibiting union with those exhibiting nonunion. Uninstrumented PLF was performed for the treatment of lumbar canal stenosis (LCS) with degenerative spondylolisthesis. Since nine patients were lost to final follow-up, the study included 42 patients, and the follow-up rate was 82.4%. The mean age of the patients was 64.1 years (range 46-77 years). Eight patients exhibited fusion at the L3-4 level and 34 patients, at the L4-5 level. The fusion status was assessed using plain radiographs. The clinical outcomes were evaluated using the Japanese Orthopaedic Association (JOA) scores. Nonunion was noted in 26% (11/42) of the patients. There were no statistically significant differences between the groups exhibiting union and nonunion with respect to age, sex, preoperative JOA score, or preoperative lumbar instability. The union group achieved better operative results than the nonunion group at the 5-year and final follow-up (P = 0.006 and 0.008, respectively) although there was no significant difference in the percent recovery at 1 and 3-year follow-up (P = 0.515 and 0.506, respectively). A stepwise regression analysis revealed that the best combination of predictors for percent recovery at the time of final follow-up included the fusion status and the presence of comorbid disease. The results indicate that the fusion status following PLF is a critical factor influencing the long-term but not short-term operative results in the treatment of LCS with degenerative spondylolisthesis.

Martin CR, Gruszczynski AT, Braunsfurth HA, et al.

The surgical management of degenerative lumbar spondylolisthesis: a systematic review.

***Spine.* 2007;32(16):1791-1798. (includes pooled estimates)**

STUDY DESIGN Systematic review. OBJECTIVE To identify whether there is an advantage to instrumented or noninstrumented spinal fusion over decompression alone for patients with degenerative lumbar spondylolisthesis. SUMMARY OF BACKGROUND DATA The operative

management of degenerative spondylolisthesis includes spinal decompression with or without instrumented or noninstrumented spinal fusion. Evidence on the operative management of degenerative spondylolisthesis is still divisive. **METHODS** Relevant **RCT and comparative observational studies** between **1966 and June 2005** were identified. Abstracted outcomes included clinical outcome, reoperation rate, and solid fusion status. Analyses were separated into: 1) **fusion versus decompression alone** and 2) **instrumented fusion versus noninstrumented fusion**. **RESULTS** Thirteen studies were included. The studies were generally of low methodologic quality. A satisfactory clinical outcome was significantly more likely with fusion than with decompression alone (relative risk, 1.40; 95% confidence interval, 1.04-1.89; $P < 0.05$). The use of adjunctive instrumentation significantly increased the probability of attaining solid fusion (relative risk, 1.37; 95% confidence interval, 1.07-1.75; $P < 0.05$), but no significant improvement in clinical outcome was recorded (relative risk, 1.19; 95% confidence interval, 0.92-1.54). There was a nonsignificant trend toward lower repeat operations with fusion compared with both decompression alone and instrumented fusion. **CONCLUSIONS** Spinal fusion may lead to a better clinical outcome than decompression alone. No conclusion about the clinical benefit of instrumenting a spinal fusion could be made. However, there is moderate evidence that the use of instrumentation improves the chance of achieving solid fusion.

Hayes 2007 (Health Technology Brief)

Minimally Invasive Transforaminal Lumbar Interbody Fusion (MITLIF) for Treatment of Lumbar Disc Disease Effectiveness According to Graft Material

Hayes Rating: D

Update Search, Sept. 2009: No anticipated impact on Hayes Rating.

Archived Oct. 2010

LARGE OBSERVATIONAL STUDIES WITH SAFETY DATA

Deyo RA, Mirza SK, Martin BI, et al.

Trends, major medical complications, and charges associated with surgery for lumbar spinal stenosis in older adults.

JAMA. 2010;303(13):1259-1265.

CONTEXT In recent decades, the fastest growth in lumbar surgery occurred in older patients with spinal stenosis. Trials indicate that for selected patients, decompressive surgery offers an advantage over nonoperative treatment, but surgeons often recommend more invasive fusion procedures. Comorbidity is common in older patients, so benefits and risks must be carefully weighed in the choice of surgical procedure. **OBJECTIVE:** To examine trends in use of different types of **stenosis operations** and the **association of complications and resource use with surgical complexity**. **DESIGN, SETTING, AND PATIENTS:** **Retrospective cohort analysis of Medicare claims** for 2002-2007, focusing on 2007 to assess complications and resource use in US hospitals. Operations for Medicare recipients undergoing surgery for lumbar stenosis (**n = 32,152** in the first 11 months of 2007) were grouped into **3 gradations of invasiveness: decompression alone, simple fusion (1 or 2 disk levels, single surgical approach), or complex fusion** (more than 2 disk levels or combined anterior and posterior approach). **MAIN OUTCOME MEASURES** Rates of the 3 types of surgery, major complications, postoperative mortality, and resource use. **RESULTS** Overall, surgical rates declined slightly from 2002-2007, but the rate of complex fusion procedures increased 15-fold, from 1.3 to 19.9 per 100,000 beneficiaries. **Life-threatening complications** increased with increasing surgical invasiveness, from 2.3% among patients having decompression alone to 5.6% among those having complex fusions. After

adjustment for age, comorbidity, previous spine surgery, and other features, the odds ratio (OR) of life-threatening complications for complex fusion compared with decompression alone was 2.95 (95% confidence interval [CI], 2.50-3.49). A similar pattern was observed for rehospitalization within 30 days, which occurred for 7.8% of patients undergoing decompression and 13.0% having a complex fusion (adjusted OR, 1.94; 95% CI, 1.74-2.17). Adjusted mean hospital charges for complex fusion procedures were US \$80,888 compared with US \$23,724 for decompression alone. CONCLUSIONS Among Medicare recipients, between 2002 and 2007, the frequency of complex fusion procedures for spinal stenosis increased while the frequency of decompression surgery and simple fusions decreased. In 2007, compared with decompression, simple fusion and complex fusion were associated with increased risk of major complications, 30-day mortality, and resource use.

Fu K-MG, Smith JS, Polly DW Jr, et al.

Morbidity and mortality in the surgical treatment of 10,329 adults with degenerative lumbar stenosis.

J Neurosurg Spine. 2010;12(5):443-446.

OBJECTIVE The purpose of this study was to evaluate the prospectively collected Scoliosis Research Society (SRS) database to assess the incidences of morbidity and mortality (M&M) in the operative treatment of degenerative lumbar stenosis, one of the most common procedures performed by spine surgeons. **METHODS** All patients who underwent surgical treatment for degenerative lumbar stenosis between 2004 and 2007 were identified from the SRS M&M database. Inclusion criteria for analysis included an age ≥ 21 years and no history of lumbar surgery. Patients were treated with **either decompression alone or decompression with concomitant fusion**. Statistical comparisons were performed using a 2-sided Fisher exact test. **RESULTS** Of the **10,329 patients** who met the inclusion criteria, 6609 (64%) were treated with decompression alone, and 3720 (36%) were treated with decompression and fusion. Among those who underwent fusion, instrumentation was placed in 3377 (91%). The overall mean patient age was 63 \pm 13 years (range 21-96 years). Seven hundred nineteen complications (7.0%), including 13 **deaths** (0.1%), were identified. **New neurological deficits** were reported in 0.6% of patients. Deaths were related to cardiac (4 cases), respiratory (5 cases), pulmonary embolus (2 cases), and sepsis (1 case) etiologies, and a perforated gastric ulcer (1 case). Complication rates did not differ based on patient age or whether fusion was performed. Minimally invasive procedures were associated with fewer complications and fewer new neurological deficits ($p = 0.01$ and 0.03 , respectively). **CONCLUSION** The results from this analysis of the SRS M&M database provide surgeons with useful information for preoperative counseling of patients contemplating surgical intervention for symptomatic degenerative lumbar stenosis.

Patil CG, Lad EM, Lad SP, Ho C, Boakye M.

Visual loss after spine surgery: a population-based study.

Spine. 2008;33(13):1491-1496.

STUDY DESIGN Retrospective cohort study using **National inpatient sample** administrative data. **OBJECTIVE** To determine **national estimates of visual impairment and ischemic optic neuropathy after spine surgery**. **SUMMARY OF BACKGROUND DATA** Loss of vision after spine surgery is rare but has devastating complications that has gained increasing recognition in the recent literature. National population-based studies of visual complications after spine surgery are lacking. **METHODS** All patients from 1993 to 2002 who underwent spine surgery (Clinical Classifications software procedure code: 3, 158) and who had ischemic optic neuropathy (ION)

(ICD9-CM code 377.41), central retinal artery occlusion (CRAO) (ICD9-CM code 362.31) or non-ION, non-CRAO perioperative visual impairment (ICD9-CM codes: 369, 368.4, 368.8-9368.11-13) were included. Univariate and multivariate analysis were performed to identify potential risk factors. RESULT The overall incidence of visual disturbance after spine surgery was 0.094%. Spine surgery for scoliosis correction and **posterior lumbar fusion** had the highest rates of **postoperative visual loss** of 0.28% and **0.14%** respectively. Pediatric patients (<18 years) were 5.8 times and elderly patients (>84 years) were 3.2 times more likely than, patients 18 to 44 years of age to develop non-ION, non-CRAO visual loss after spine surgery. Patients with peripheral vascular disease (OR = 2.0), hypertension (OR = 1.3), and those who received blood transfusion (OR = 2.2) were more likely to develop non-ION, non-CRAO vision loss after spine surgery. Ischemic optic neuropathy was present in 0.006% of patients. Hypotension (OR = 10.1), peripheral vascular disease (OR = 6.3) and anemia (OR = 5.9) were the strongest risk factors identified for the development of ION. CONCLUSION We used multivariate analysis to identify significant risk factors for visual loss after spine surgery. National population-based estimate of visual impairment after spine surgery confirms that ophthalmic complications after spine surgery are rare. Since visual loss may be reversible in the early stages, awareness, evaluation and prompt management of this rare but potentially devastating complication is critical.

NEW RCTs (reverse chronological and then alphabetical order)

Slätis P, Malmivaara A, Heliövaara M, et al.

Long-term results of surgery for lumbar spinal stenosis: a randomised controlled trial.

***Eur Spine J.* 2011;20(7):1174-1181.**

We randomised a total of 94 patients with **long-standing moderate lumbar spinal stenosis (LSS)** into a surgical group and a non-operative group, with 50 and 44 patients, respectively. The operative treatment comprised undercutting laminectomy of stenotic segments, augmented with transpedicular-instrumented fusion in suspected lumbar instability. The primary outcome was the Oswestry disability index (ODI), and the other main outcomes included assessments of leg and back pain and self-reported walking ability, all based on questionnaire data from 85 patients at the 6-year follow-up. At the 6-year follow-up, the mean difference in ODI in favour of surgery was 9.5 (95% confidence interval 0.9-18.1, P-value for global difference 0.006), whereas the intensity of leg or back pain did not differ between the two treatment groups any longer. Walking ability did not differ between the treatment groups at any time. Decompressive surgery of LSS provided modest but consistent improvement in functional ability, surpassing that obtained after non-operative measures.

Ohtori S, Koshi T, Yamashita M, et al.

Surgical versus nonsurgical treatment of selected patients with discogenic low back pain: a small-sized randomized trial.

***Spine.* 2011;36(5):347-54.**

No abstract.

Ekman P, Moller H, Shalabi A, Yu Y, Hedlund R.

A prospective randomised study on the long-term effect of lumbar fusion on adjacent disc degeneration.

***European Spine Journal.* 2009;18(8):1175-86.**

The existence and importance of an accelerated adjacent segment disc degeneration (ASD) after lumbar fusion have previously not been demonstrated by RCTs. The objectives of this study were, to determine whether lumbar fusion in the long term accelerates degenerative changes in the adjacent disc and whether this affects the outcome, by using a prospective randomised design. A total of 111 patients, aged 18-55, with isthmic spondylolisthesis were randomised to exercise (EX, n = 34) or posterolateral fusion (PLF, n = 77), with (n = 37) or without pedicle screw instrumentation (n = 40). The minimum 10 years FU rate was 72%, with a mean FU time of 12.6 years (range 10-17 years). Three radiographic methods of ASD quantification were used, i.e. two digital radiographic measurement methods and the semi quantitative UCLA grading scale. One digital measurement method showed a mean disc height reduction by 2% in the EX group and by 15% in the PLF group (p = 0.0016), and the other showed 0.5 mm more disc height reduction in the PLF compared to the Ex group (ns). The UCLA grading scale showed normal discs in 100% of patients in the EX group, compared to 62% in the PLF group (p = 0.026). There were no significant differences between instrumented and non-instrumented patients. In patients with laminectomy we found a significantly higher incidence of ASD compared to non laminectomised patients (22/47 vs. 2/16 respectively, p = 0.015). In the longitudinal analysis, the posterior and anterior disc heights were significantly reduced in the PLF group, whereas in the EX group only the posterior disc height was significantly reduced. Except for global outcome, which was significantly better for patients without ASD, the clinical outcome was not statistically different in patients with and without ASD. In conclusion, the long-term RCT shows that fusion accelerates degenerative changes at the adjacent level compared with natural history. The study suggests that not only fusion, but also laminectomy may be of pathogenetic importance. The clinical importance of ASD seems limited, with only the more severe forms affecting the outcome.

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The positive effect of posterolateral lumbar spinal fusion is preserved at long-term follow-up: a RCT with 11-13 year follow-up.

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INTRODUCTIONFew studies have investigated the long-term effect of posterolateral lumbar spinal fusion on functional outcome.**AIM**To investigate the long-term result after posterolateral lumbar spinal fusion with and without pedicle screw instrumentation.**METHODS**Questionnaire survey of 129 patients originally randomised to posterolateral lumbar spinal fusion with or without pedicle screw instrumentation. Follow-up included Dallas Pain Questionnaire (DPQ), Oswestry Disability Index (ODI), SF-36 and a question regarding willingness to undergo the procedure again knowing the result as global outcome parameter.**RESULTS**Follow-up was 83% of the original study population (107 patients). Average follow-up time was 12 years (range 11-13 years). DPQ-scores were significantly lower than preoperatively in both groups (P < 0.005) and no drift towards the preoperative level was seen. No difference between the two groups were observed (instrumented vs. non-instrumented): DPQ Daily Activity mean 37.0 versus 32.0, ODI mean 33.4 versus 30.6, SF-36 PCS mean 38.8 versus 39.8, SF-36 MCS mean 49.0 versus 53.3. About 71% in both groups were answered positively to the global outcome question. Patients who had retired due to low back pain had poorer outcome than patients retired for other reasons, best outcome was seen in patients still at work (P = 0.01 or less in all questionnaires, except SF-36 MCS P = 0.08).**DISCUSSION**Improvement in functional outcome is preserved for 10 or more years after posterolateral lumbar spinal fusion. No difference between instrumented

fusion and non-instrumented fusion was observed. Patients who have to retired due to low back pain have the smallest improvement.