



American  
Association of  
Neurological  
Surgeons



CNS



December 18, 2012

Mark Helfand, M.D., M.P.H.  
Director, Scientific Resource Center, Oregon EPC  
Mail code: BICC  
3181 S.W. Sam Jackson Park Road  
Portland, Oregon 97239-3098

**Re: AHRQ Effective Health Care Program on Spinal Fusion for Treating Painful Lumbar Degenerated Discs or Joints**

Dear Dr. Helfand:

On behalf of the American Association of Neurological Surgeons (AANS), the Congress of Neurological Surgeons (CNS), the AANS/CNS Section on Disorders of the Spine and Peripheral Nerves and the Scoliosis Research Society (SRS) (collectively referred to as the "Societies"), we would like to thank the Agency for Healthcare Research and Quality (AHRQ) for the opportunity to comment on the draft evidence report entitled "Spinal Fusion for Treating Painful Lumbar Degenerated Discs or Joints". We again appreciate the efforts of AHRQ's Effective Health Care Program, and the research summaries regarding the benefits and risks of different treatment options for health conditions based on comparative effectiveness reviews. We also understand that these research summaries are not clinical recommendations or guidelines, but recognize that they are nevertheless frequently utilized as such with respect to healthcare policy development.

We will be providing comments on most of the Key Questions (KQ) presented in the draft. However, as AHRQ noted that no studies were identified that met inclusion criteria to address KQ 2 (Spinal Fusion Compared to Continued Noninvasive Treatment for Painful Degenerative Lumbar Spinal Stenosis) and KQ6 (Spinal Fusion Compared to Other Invasive Procedures for Painful Degenerative Lumbar Spondylolisthesis), *we will not provide any comments on these.*

We also note that many of the key questions include assessment of lumbar stenosis. We wish to clarify that there are different types of lumbar stenosis. Foraminal stenosis with radiculopathy may require resection of the facet joint to address, which may well require a fusion due to iatrogenic instability, but this is a distinct pathology to central lumbar stenosis with neurogenic claudication, which has a distinct CPT code as it typically does not involve resection of the facet joints and so rarely would need a concomitant lumbar fusion in the absence of a spinal deformity. We believe that this highlights the need for the AHRQ document to have meaningful inclusion of subject matter experts on your writing panels, and the Societies would be happy to help in this regards.

**Key Question 1: For adults with pain associated with degenerated disc(s) of the lumbar spine, does spinal fusion performed alone or in conjunction with additional surgery differ from continued noninvasive treatment?**

We noted that the evidence base by AHRQ for this question consisted of four randomized controlled studies (RCTs) without meta-analysis performed due to the differences in non-surgical care such as the conditions of physical therapy varying across the studies (1, 2, 5, 6). Based on this qualitative assessment of the evidence, it was concluded that limited data suggests that fusion leads to greater

improvement in back pain relief and function than physical therapy at 2-year follow-up. AHRQ denoted the strength of evidence as low, and questioned whether the difference is clinically significant. You also noted that no other conclusions are possible, because of insufficient evidence or uninformative statistical findings.

**Response:** While we agree that there is limited literature available to address the key question of whether spinal fusion performed alone or in conjunction with additional surgery differs from continued noninvasive treatment. The papers available highlight the difficulty in a developing a study to address this, such as the Fairbank study with the surgical group being 20 percent non-fusion and intent to treat analysis was performed despite a 25 percent crossover and 20 percent loss to follow-up rate. There are also issues with population differences such as in the Brox study which had failed discectomies and not completely the same as the population in the Fairbank study.

As variations in surgery and non-surgical therapy are inherent in the practice of medicine, despite the difficulties in the literature, to address the key question may need us to perform a meta-analysis of the six strongest studies, which include 547 fusion and 372 non-surgical patients to show a clinically significant weighted average improvement in back pain of 35.3 percent change in the surgical group compared with a 20 percent change in the non-surgical group. Improvement in ODI was also significantly higher in the surgical group with a 29 percent change compared to a 17.5 percent change in the non-surgical group. We agree that only one study reported SF-36 Physical Component Scores (PCS), but note that this does show a clinically significant improvement (48% change) in the surgical group versus the non-surgical group (38% change).

AHRQ also noted that the overall risk-of-bias rating being moderate due largely to the lack of concealment of allocation and/or blinding of patients or outcome assessors to treatment received, or not reporting if concealment or blinding took place in the study.

We do not agree with the application of the overall risk-of-bias rating due to lack of concealment and/or blinding as such methods are not typically considered ethical in surgical treatments. Single blinded studies may be performed with sham procedures leading to ethical issues, but double blinded procedures are not feasible due to inability to blind the performing surgeon on the procedure. Given this, surgical literature should be assessed relative to other surgical studies, as otherwise it would be comparing apples-to-oranges.

### **References for Key Question 1**

1. Brox JI, Sorensen R, Friis A, et al. Randomized clinical trial of lumbar instrumented fusion and cognitive intervention and exercises in patients with chronic low back pain and disc degeneration. *Spine* 2003;28:1913-21.
2. Brox JI, Reikeras O, Nygaard O, et al. Lumbar instrumented fusion compared with cognitive intervention and exercises in patients with chronic back pain after previous fusion for CLBP surgery for disc herniation: a prospective randomized controlled study. *Pain* 2006;122:145-55.
3. Brox JI, Nygaard OP, Holm I, et al. Four-year follow-up of surgical versus non-surgical therapy for chronic low back pain. *Ann Rheum Dis* 2010; 69:1643-8.
4. Fairbank J, Frost H, Wilson-MacDonald J, et al. Randomised controlled trial to compare surgical stabilisation of the lumbar spine with an intensive rehabilitation programme for patients with chronic low back pain: the MRC spine stabilisation trial. *BMJ* 2005;330:1233.
5. Fritzell P, Hagg O, Wessberg P, et al. 2001 Volvo Award Winner in Clinical Studies: Lumbar fusion versus nonsurgical treatment for chronic low back pain: a multicenter randomized controlled trial from the Swedish Lumbar Spine Study Group. *Spine* 2001;26:2521-32.

6. 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;36:347-54.

**Key Question 2:** No comments submitted.

**Key Question 3: For adults with pain associated with degenerative spondylolisthesis of the lumbar spine, does spinal fusion performed alone or in conjunction with additional surgery differ from continued noninvasive treatment in:**

- a. Patient-centered outcomes such as function, quality of life, or pain?
- b. Adverse events?

Because only one study compared fusion versus noninvasive treatment, the evidence is insufficient to support evidence-based conclusions regarding the comparative effectiveness or safety of fusion in adults with low back pain due to degenerative spondylolisthesis.

**Response:** We disagree with the conclusions of the AHRQ draft evidence report and believe that the SPORT study provides important clinical information in treatment of lumbar degenerative spondylolisthesis with stenosis (1). The results of the SPORT trial have been peer reviewed by the editorial boards at the *New England Journal of Medicine*, *Journal of the American Medical Association*, and the *Journal of Bone and Joint Surgery* (1, 2, 3). The “Detailed Synthesis” portion of the AHRQ report summarizes the results of the most recent SPORT publication, detailing the 4 year clinical results for the observational and randomized arms of the study. It is also of note that the SPORT study has generated multiple other publications where its methodology has been validated in the peer-reviewed literature (4, 5, 6, 7).

The analysis of the AHRQ report is correct in noting that while SPORT was designed as a prospective randomized controlled trial, there were study populations compromising both observational patients who did not consent to randomization, and patients undergoing randomization between conservative and operative care. The AHRQ commentary focuses upon the potential source of bias introduced by cross-over of patients between operative and non-operative treatment arms and the as-treated analysis completed in the SPORT reports.

Following an intent-to-treat analysis would generate even greater potential bias by inappropriately grouping operative cases into the non-operative treatment arm. A clinical investigation with presumed equipoise between treatment arms that did not allow for potential cross-over, especially with regard to operative versus non-operative therapy in the face of failure of non-operative therapy, would not be attractive to study participants and likely would be unethical. Obtaining Investigational Review Board approval for such a study methodology would be difficult. A restriction on cross-over likely could encourage increased rates of drop-out by study participants with poor outcomes within their assigned treatment arm, introducing an additional source of bias. The approach taken by the SPORT investigators weighed these issues and answered them appropriately.

With the SPORT results suggesting there may not be equipoise between operative and non-operative treatment of degenerative spondylolisthesis patients, it will be even more difficult to ethically construct a prospective, randomized study that does not allow for treatment cross-over. **Hence, future studies likely will face the same logistical challenges and will harbor the same opportunities for bias.**

The AHRQ report cites as the literature source for the potential sources of bias in the SPORT approach a non-peer reviewed invited online commentary by Stanley Bigos, MD (8). Dr. Bigos

notes that the combined as-treated analysis completed by the SPORT study “may overestimate the benefit of surgery.” He goes on to make suggestions as to other options for future investigations, primarily quantifying degree of instability, standardizing non-operative care, and separately studying different age group patients.

It is of note that none of these suggestions would answer the problem of patient cross-over or of use of an as-treated analysis. While we respect the comments of Dr. Bigos and his suggestions for future studies are logical, we do not feel these non-peer reviewed comments posted online merit dismissal of the entire SPORT effort.

The limitations of the SPORT study are outlined by the authors in their text; there are opportunities for bias in this study, as in any clinical investigation. However, the SPORT study provides the best and highest quality evidence of treatment modalities in a diverse population with lumbar degenerative spondylolisthesis with stenosis available in the literature. While it is a single report, its exemplary patient follow-up, multicenter design, and rigor of analysis make it a paradigm for prospective studies of spine surgery patients.

We believe the comments of the AHRQ report, which notes the SPORT study results are imprecise, inconclusive, and insufficient in assessing fusion versus noninvasive treatments in treatment of lumbar degenerative spondylolisthesis, diminish the significant clinical impact of this ongoing investigation (Table 7). To disavow the contribution of the SPORT investigators’ efforts in investigating the treatment of lumbar spine pathology diminishes the quality of the AHRQ report.

### **References for Key Question 3**

1. Weinstein J, Lurie J, Tosteson T, et al. Surgical compared with nonoperative treatment for lumbar degenerative spondylolisthesis: Four year results in the Spine Patient Outcomes Research Trial (SPORT) randomized and observational cohorts. *JBJS Am.* 2009;91:1295-1304.
2. Weinstein J, Lurie J, Tosteson T, et al. Surgical versus nonoperative treatment for lumbar disc herniation: Four-year results for the Spine Patient Outcomes Research Trial (SPORT). *Spine.* 2008;33:2789-2800.
3. Weinstein J, Tosteson T, Lurie J, et al. Surgical vs. nonoperative treatment for lumbar disk herniation: The Spine Patient Outcomes Research Trial (SPORT): A randomized trial. *JAMA.* 2006;296:2441-2450.
4. JA R, M K, AS H, et al. The Influence of Obesity on the Outcome of Treatment of Lumbar Disc Herniation: Analysis of the Spine Patient Outcomes Research Trial (SPORT). *JBJS Am.* 2012;Epub ahead of print.
5. Y S, DK P, KC B, et al. Single Versus Multilevel Fusion, For Single Level Degenerative Spondylolisthesis and Multilevel Lumbar Stenosis: Four-Year Results of the Spine Patient Outcomes Research Trial. *Spine.* 2012;Epub ahead of print.
6. K R, R H, A H, et al. The Effect of Iliac Crest Autograft on the Outcome of Fusion in the Setting of Degenerative Spondylolisthesis: A Subgroup Analysis of the Spine Patient Outcomes Research Trial (SPORT). *JBJS Am.* 2012;Epub ahead of print.
7. K R, A H, JD L, et al. The impact of epidural steroid injections on the outcomes of patients treated for lumbar disc herniation: a subgroup analysis of the SPORT trial. *JBJS Am.* 2012;94:1353-1358.
8. SJ B. Commentary & perspective on “Surgical compared with nonoperative treatment for lumbar degenerative spondylolisthesis: four-year results in the Spine Patient Outcomes Research Trial (SPORT) randomized and observational cohorts”. *JBJS Am.* 2009:1-4.

**Key Question 4: Spinal Fusion Compared to Other Invasive Procedures for Painful Lumbar Degenerated Disc in:**

- a. Perioperative outcomes such as surgery time, blood loss, or length of hospital stay?
- b. Patient-centered outcomes such as function, quality of life, or pain?
- c. Adverse events?

The AHRQ reviewed two multicenter RCTs investigating lumbar arthroplasty with the ProDisc-L (Synthes Spine, West Chester PA) versus anterior – posterior fusion for the treatment of painful lumbar degenerative discs (1, 2). They concluded that there is limited evidence to suggest that arthroplasty results in shorter surgical time, less blood loss, and shorter inpatient stays with better ODI function at only the 6 week time point. Otherwise, there was insufficient data to support any conclusions with regards to differences between these two procedures.

**Response:** In interpreting the data from these two studies, it is important to note that the lumbar fusion arm of these RCTs was a combined anterior and posterior approach, whereas the arthroplasty arm was an anterior only approach. Combined anterior – posterior lumbar surgery has been demonstrated to increase morbidity compared to single approach surgery (3). Therefore, it stands to reason that perioperative outcomes such as surgical time and blood loss would be greater for the fusion group as they underwent an additional posterior approach to the surgical procedure. Further, the added surgical dissection related to the posterior portion of the fusion surgery may have contributed to a longer inpatient recovery period, although notably this only resulted in an average < 1 additional hospital day for single level procedures, and slightly > 1 additional hospital day for two level procedures.

The FDA IDE trial comparing the Charite (DePuy spine, Raynham, MA) arthroplasty device versus anterior lumbar fusion for similar clinical indications (and inclusion/ exclusion criteria) in fact found no difference between the two groups with respect to surgical time or blood loss, with only a modest increase in hospital stay for the fusion group (average increase of 0.5 hospital day) (4). Both arms of this study (arthroplasty versus fusion) were anterior only surgical approaches representing a more apt comparison for perioperative outcomes. Given the relative equivalence in perioperative outcomes observed in the Charite trial, one can conclude that the differences reported in the ProDisc-L trials were likely due to the additional posterior surgical procedure performed in the fusion group, rather than a true clinical benefit inherent to the arthroplasty device.

Notably both the arthroplasty and fusion groups in the ProDisc-L trials demonstrated long-term improvement for multiple validated clinical outcome measures including VAS pain score, ODI, and SF -36. Narcotic dependence also markedly improved after both procedures. We agree that there is insufficient data to indicate clinical superiority of either lumbar fusion or arthroplasty for painful lumbar degenerative discs, particularly since the investigators and patients were not blinded to the treatment. Any potential bias, however, presumably would have resulted in better reported outcomes with arthroplasty given the affiliation of the researchers with the device manufacturer. Despite this, **the observed clinical improvement in both groups certainly suggests that at least with respect to lumbar fusion, surgical intervention is a reasonable treatment consideration for patients with severe pain and disability due to degenerative disc disease and who have failed nonsurgical measures.**

**References for Key Question 4**

1. Delamarter R, Zigler JE, Balderston RA, Cammisa FP, Goldstein JA, Spivak JM. Prospective, randomized, multicenter Food and Drug Administration investigational device exemption study of the ProDisc-L total disc replacement compared with circumferential arthrodesis for the

- treatment of two-level lumbar degenerative disc disease: results at twenty-four months. *J Bone Joint Surg Am.* 2011;93(8):705-15.
2. Zigler J, Delamarter R, Spivak JM, Linovitz RJ, Danielson GO, 3rd, Haider TT, et al. Results of the prospective, randomized, multicenter Food and Drug Administration investigational device exemption study of the ProDisc-L total disc replacement versus circumferential fusion for the treatment of 1-level degenerative disc disease. *Spine.* 2007;32(11):1155-62; discussion 63.
  3. Resnick DK, Choudhri TF, Dailey AT, Groff MW, Khoo L, Matz PG, et al. Guidelines for the performance of fusion procedures for degenerative disease of the lumbar spine. Part 11: interbody techniques for lumbar fusion. *Journal of neurosurgery Spine.* 2005;2(6):692-9.
  4. Blumenthal S, McAfee PC, Guyer RD, Hochschuler SH, Geisler FH, Holt RT, et al. A prospective, randomized, multicenter Food and Drug Administration investigational device exemptions study of lumbar total disc replacement with the CHARITE artificial disc versus lumbar fusion: part I: evaluation of clinical outcomes. *Spine.* 2005;30(14):1565-75; discussion E387-91.

### **Key Question 5: Spinal Fusion Compared to Other Invasive Procedures for Painful Degenerative Lumbar Stenosis in:**

- a. Perioperative outcomes such as surgery time, blood loss, or length of hospital stay?
- b. Patient-centered outcomes such as function, quality of life, or pain?
- c. Adverse events?

The AHRQ concluded that there is insufficient evidence to support the comparative effectiveness or safety of fusion and decompression in adults with low back pain due to stenosis with degenerative disc.

**Response:** The AANS/ CNS Joint Section on Disorders of the Spine and Peripheral Nerves convened a committee in 2005 to review the evidence for performing fusion procedures for degenerative disease of the lumbar spine (1), and addressed the specific issue of spinal fusion for lumbar stenosis (2, 3) (stenosis with spondylolisthesis is addressed separately in Key Question #6, upon which we are not commenting). With regards to spinal fusion for lumbar stenosis without spondylolisthesis, they concluded that there is insufficient evidence to recommend a treatment standard or guideline (2). There does not appear to be evidence to support the hypothesis that fusion provides any benefit over decompression alone in the treatment of lumbar stenosis in patients in whom there is no evidence of preoperative deformity or instability. There is limited evidence, however, to suggest that the addition of fusion to decompression may be beneficial in patients who have pre-existing instability or who have undergone wide decompression or facetectomy resulting in iatrogenic instability.

We agree that further study is necessary to better define the role of lumbar fusion for stenosis. Future investigation, however, must take note that degenerative stenosis has diverse etiologies and associated conditions. As such, decompressive laminectomy and spinal fusion are not to be viewed as mutually exclusive, competing procedures, as they are often performed in conjunction to treat pain related to either nerve root compression or spinal instability, respectively.

### **References for Key Question 5**

1. Resnick DK, Choudhri TF, Dailey AT, Groff MW, Khoo L, Matz PG, et al. Guidelines for the performance of fusion procedures for degenerative disease of the lumbar spine. Part 1: introduction and methodology. *Journal of neurosurgery Spine.* 2005;2(6):637-8.
2. Resnick DK, Choudhri TF, Dailey AT, Groff MW, Khoo L, Matz PG, et al. Guidelines for the performance of fusion procedures for degenerative disease of the lumbar spine. Part 10:

fusion following decompression in patients with stenosis without spondylolisthesis. Journal of neurosurgery Spine. 2005;2(6):686-91.

3. Resnick DK, Choudhri TF, Dailey AT, Groff MW, Khoo L, Matz PG, et al. Guidelines for the performance of fusion procedures for degenerative disease of the lumbar spine. Part 9: fusion in patients with stenosis and spondylolisthesis. Journal of neurosurgery Spine. 2005;2(6):679-85.

**Key Question 6:** No comments submitted.

**Key Question 7: Spinal Fusion Approaches (e.g., Anterior, Posterior, Combined) and Techniques (e.g., Instrumentation, Graft Material) Compared to One Another for Painful Degenerated Lumbar Disc(s)**

The AHRQ document summarizes the evidence available comparing spinal fusion approaches and techniques for painful degenerated lumbar disc(s) disease. Comparisons made included, fusion with rhBMP-2 versus autogenous bone graft, open mini ALIF versus laparoscopic ALIF, transperitoneal versus retroperitoneal anterior surgical approach, posterolateral fusion with or without variable screw placement versus circumferential fusion.

AHRQ draft concluded that rhBMP-2 was associated with less blood loss than autogenous bone graft, while surgery time and length of hospital stay do not differ substantially in the fusion surgery with the strength of evidence as low. The document notes that for all other outcomes, the data were insufficient to support any conclusions for fusion with rhBMP-2 and fusion with autogenous bone graft, mainly because of inconsistencies in the studies' findings and insufficient reporting of data, or because only one study addressed that outcome or duration of follow-up.

**Response:** The position of our organizations is that BMP is a costly technology, and is not appropriate for the vast majority of spinal fusion procedures; **however, the full potential of BMP as an adjunct to spinal fusion cannot be determined by the current literature.** It is almost certain that there are a number of patients for whom BMP will maximize the potential for a successful clinical outcome and restoration of an acceptable quality of life. Major issues dealing with the use of BMP as an adjunct to spinal fusion, however, remain unaddressed by this assessment and the current literature. Identified risk factors for failed fusion surgery include: cigarette smoking, diabetes, osteoporosis, dialysis dependent renal disease, etc. Individuals with these characteristics are typically excluded from the majority of clinical trials because of their propensity to develop a non-union. Nonetheless, these patients, often because of these risk factors, require spinal fusion surgery due to disabling symptoms. The potential for BMP to enhance fusion rates, as demonstrated in many studies and reported in this assessment, may prove to be a significant clinical benefit to these patients and likely result in a reduced need for revision surgeries. Also not addressed in this assessment are patients who have had bone graft harvested previously and therefore have limited availability of autograft bone. Under these circumstances, allograft bone offers insufficient fusion potential and the compassionate use of BMP is appropriate. Another group not discussed in this review are patients who for religious or cultural reasons or for concerns over the risk of transmission of infectious agents refuse cadaveric allograft yet still have a need for bone graft during surgery. Unfortunately, many of these clinical situations arise with such a low frequency that generating valid medical evidence may prove difficult if not impossible.

The FDA-approved on-label indications of rhBMP2 as an adjunct for anterior interbody lumbar fusion were found to be supported by a valid multicenter randomized controlled trial when used with threaded interbody titanium cages. Advantages identified in the assessment included

equivalent or superior fusion rates, shorter operative times, and decreased bone graft donor site complications. In comparing rhBMP-2 versus autogenous bone graft (from iliac crest), there are several studies not to the level of evidence described have indicated more adverse events short term, with the use of rhBMP-2 (5, 6, 7, 17). Conversely, donor site morbidity from iliac crest harvested bone graft has been reported to be much higher (up to 29% in some studies) (9, 19, 23, 12, 22) than stated, from the paper by Burkus et al (5.9%) (3) used in the analysis. Sengupta et al (18), showed no difference in outcome of local bone versus autogenous iliac crest bone graft in the instrumented posterolateral fusion of the lumbar spine. Currently, rhBMP-2 is used mostly to augment posterolateral and anterior lumbar fusion with harvested local bone or allograft in complex cases (such as, multiple level fusion, spinal deformity) and/or with poor bone morphology (osteoporosis) (4, 8, 11, 13). We agree that the current literature is unclear on the benefit over risk of adverse events with the use of rBMP-2 in routine painful, degenerated lumbar disc (s) disease. However, the full potential of BMP as an adjunct to spinal fusion cannot be determined by the current literature which does not includes those patients who would benefit from the use of this osteobiologic.

In comparing open mini ALIF versus laparoscopic ALIF, transperitoneal versus retroperitoneal anterior surgical approach, posterolateral fusion with or without variable screw placement versus circumferential fusion, evidence currently reviewed and cited in the AHRQ document reveals the need for case by case review by practicing surgeons in finding what is best suited for the individual patient. Numerous prospective and retrospective case series identify several patient populations that benefit from one or more of the outcome metrics used in the document (1, 2, 14, 21, 22)

### **References for Key Question 7**

1. Bjarke Christensen F, Stender Hansen E, Laursen M, Thomsen K, Bunker CE: Long-term functional outcome of pedicle screw instrumentation as a support for posterolateral spinal fusion: Randomized clinical study with a 5-year follow-up. *Spine* 27:1269-1277, 2002
2. Booth KC, Bridwell KH, Lenke LG, Baldus CR, Blanke KM: Complications and predictive factors for the successful treatment of flatback deformity (fixed sagittal imbalance). *Spine (Phila Pa 1976)* 24:1712-1720, 1999
3. Burkus JK, Gornet MF, Dickman CA, Zdeblick TA: Anterior lumbar interbody fusion using rhBMP-2 with tapered interbody cages. *J Spinal Disord Tech* 15:337-349, 2002
4. Carlisle E, Fischgrund JS: Bone morphogenetic proteins for spinal fusion. *Spine J* 5:240S-249S, 2005
5. Chen NF, Smith ZA, Stiner E, Armin S, Sheikh H, Khoo LT: Symptomatic ectopic bone formation after off-label use of recombinant human bone morphogenetic protein-2 in transforaminal lumbar interbody fusion. *J Neurosurg Spine* 12:40-46, 2010
6. Fahim DK, Whitehead WE, Curry DJ, Dauser RC, Luerksen TG, Jea A: Routine use of recombinant human bone morphogenetic protein-2 in posterior fusions of the pediatric spine: Safety profile and efficacy in the early postoperative period. *Neurosurgery* 67:1195-204; discussion 1204, 2010
7. Garrett MP, Kakarla UK, Porter RW, Sonntag VK: Formation of painful seroma and edema after the use of recombinant human bone morphogenetic protein-2 in posterolateral lumbar spine fusions. *Neurosurgery* 66:1044-9; discussion 1049, 2010
8. Glassman SD, Carreon L, Djurasovic M, Campbell MJ, Puno RM, Johnson JR, et al: Posterolateral lumbar spine fusion with INFUSE bone graft. *Spine J* 7:44-49, 2007
9. Graham JJ: Complications of cervical spine surgery. A five-year report on a survey of the membership of the cervical spine research society by the morbidity and mortality committee. *Spine (Phila Pa 1976)* 14:1046-1050, 1989

10. Hallett A, Huntley JS, Gibson JN: Foraminal stenosis and single-level degenerative disc disease: A randomized controlled trial comparing decompression with decompression and instrumented fusion. *Spine (Phila Pa 1976)* 32:1375-1380, 2007
11. Hamilton DK, Jones-Quaidoo SM, Sansur C, Shaffrey CI, Oskouian R, Jane JA S: Outcomes of bone morphogenetic protein-2 in mature adults: Posterolateral non-instrument-assisted lumbar decompression and fusion. *Surg Neurol* 69:457-61; discussion 461-2, 2008
12. Hamilton DK, Smith JS, Reames DL, Williams BJ, Shaffrey CI: Use of recombinant human bone morphogenetic protein-2 as an adjunct for instrumented posterior arthrodesis in the occipital cervical region: An analysis of safety, efficacy, and dosing. *J Craniovertebr Junction Spine* 1:107-112, 2010
13. Luhmann SJ, Bridwell KH, Cheng I, Imamura T, Lenke LG, Schootman M: Use of bone morphogenetic protein-2 for adult spinal deformity. *Spine* 30:S110-7, 2005
14. Okuda S, Miyauchi A, Oda T, Haku T, Yamamoto T, Iwasaki M: Surgical complications of posterior lumbar interbody fusion with total facetectomy in 251 patients. *J Neurosurg Spine* 4:304-309, 2006
15. Pearson A, Lurie J, Tosteson T, Zhao W, Abdu W, Weinstein JN: Who should have surgery for spinal stenosis? treatment effect predictors in SPORT. *Spine (Phila Pa 1976)* 37:1791-1802, 2012
16. Radcliff K, Curry P, Hilibrand A, Kepler C, Zhao W, Lurie J, et al: Risk for adjacent segment and same segment reoperation after surgery for lumbar stenosis: A subgroup analysis of the spine patient outcomes research trial (SPORT). *Spine (Phila Pa 1976)* 2012
17. Robin BN, Chaput CD, Zeitouni S, Rahm MD, Zerris VA, Sampson HW: Cytokine-mediated inflammatory reaction following posterior cervical decompression and fusion associated with recombinant human bone morphogenetic protein-2: A case study. *Spine (Phila Pa 1976)* 35:E1350-4, 2010
18. Sengupta DK, Truumees E, Patel CK, Kazmierczak C, Hughes B, Elders G, et al: Outcome of local bone versus autogenous iliac crest bone graft in the instrumented posterolateral fusion of the lumbar spine. *Spine* 31:985-991, 2006
19. Silber JS, Anderson DG, Daffner SD, Brislin BT, Leland JM, Hilibrand AS, et al: Donor site morbidity after anterior iliac crest bone harvest for single-level anterior cervical discectomy and fusion. *Spine (Phila Pa 1976)* 28:134-139, 2003
20. Smorgick Y, Park DK, Baker KC, Lurie JD, Tosteson TD, Zhao W, et al: Single versus multilevel fusion, for single level degenerative spondylolisthesis and multilevel lumbar stenosis: Four-year results of the spine patient outcomes research trial. *Spine (Phila Pa 1976)* 2012
21. Weinstein JN, Tosteson TD, Lurie JD, Tosteson AN, Blood E, Hanscom B, et al: Surgical versus nonsurgical therapy for lumbar spinal stenosis. *N Engl J Med* 358:794-810, 2008
22. Williams BJ, Smith JS, Fu KM, Hamilton DK, Polly DW, Jr, Ames CP, et al: Does bone morphogenetic protein increase the incidence of perioperative complications in spinal fusion? A comparison of 55,862 cases of spinal fusion with and without bone morphogenetic protein. *Spine (Phila Pa 1976)* 36:1685-1691, 2011
23. Younger EM, Chapman MW: Morbidity at bone graft donor sites. *J Orthop Trauma* 3:192-195, 1989

**Key Question 8: Spinal Fusion Approaches (e.g., Anterior, Posterior, Combined) and Techniques (e.g., Instrumentation, Graft Material) Compared to One Another for Painful Degenerative Lumbar Spinal Stenosis.**

The AHRQ document attempts to summarize the evidence available comparing spinal fusion approaches and techniques for painful degenerative lumbar spinal stenosis. The document notes that because only one study addressed this comparison, the evidence is insufficient to support evidence-

based conclusions regarding the comparative effectiveness or safety of posterolateral fusion versus posterolateral fusion plus transforaminal interbody fusion.

**Response:** We do not believe that the AHRQ document addressed the topic as noted by the key question. The AHRQ cited RCT involved a primary procedure of nerve root decompression for foraminal stenosis (1). However, the two spinal fusion procedures compared in the AHRQ are indicated for augmentation of extensive lumbar central and/or severe foraminal decompression for anticipated, unfavorable, new or progressive instability, from decompression alone. **This has been documented in subgroup analysis of a major RCT not cited (2, 3, 4).** It is not recommended for routine decompression of lumbar foraminal stenosis as which could be interpreted by the AHRQ comparison.

### **References for Key Question 8**

1. Hallett A, Huntley JS, Gibson JN: Foraminal stenosis and single-level degenerative disc disease: A randomized controlled trial comparing decompression with decompression and instrumented fusion. *Spine (Phila Pa 1976)* 32:1375-1380, 2007
2. Pearson A, Lurie J, Tosteson T, Zhao W, Abdu W, Weinstein JN: Who should have surgery for spinal stenosis? treatment effect predictors in SPORT. *Spine (Phila Pa 1976)* 37:1791-1802, 2012
3. Radcliff K, Curry P, Hilibrand A, Kepler C, Zhao W, Lurie J, et al: Risk for adjacent segment and same segment reoperation after surgery for lumbar stenosis: A subgroup analysis of the spine patient outcomes research trial (SPORT). *Spine (Phila Pa 1976)* 2012
4. Smorgick Y, Park DK, Baker KC, Lurie JD, Tosteson TD, Zhao W, et al: Single versus multilevel fusion, for single level degenerative spondylolisthesis and multilevel lumbar stenosis: Four-year results of the spine patient outcomes research trial. *Spine (Phila Pa 1976)* 2012

### **Key Question 9: Spinal Fusion Approaches and Techniques Compared to One Another for Painful Degenerative Lumbar Spondylolisthesis**

The AHRQ document reports that there is insufficient evidence to support conclusions regarding the comparative effectiveness and safety of instrumentation versus no instrumentation mainly due to dissimilarities in the reported outcome of the studies.

**Response:** We do not agree that evidence-based conclusions are unavailable due to dissimilarities in the reported outcomes and instruments used to measure outcomes in the two studies that compared instrumentation to non-instrumentation. The 1997 Fischgrund study reported no differences in clinical patient outcome, however, the metric of successful arthrodesis is still an important independent variable and the promotion of fusion is one of the main reasons for internal stabilization. With this, successful arthrodesis occurred in 82 percent of the instrumented cases versus 45 percent of the noninstrumented cases ( $P = 0.0015$ ). The 1997 paper had only 2 year followup, and in 2004, Kornblum and Fischgrund report better long term follow-up (average 7 years, 8 months) on the noninstrumented degenerative spondylolisthesis patients from the same patient population that was reported in 1997. They compared the noninstrumented patients who have pseudarthrosis to the noninstrumented patients who had successful arthrodesis. Clinical outcome was excellent to good in 86 percent of patients with a solid arthrodesis and in 56 percent of patients with a pseudarthrosis ( $P = 0.01$ ). Significant differences in residual back and lower limb pain was discovered between the two groups. Preoperative back and lower limb pain scores were statistically similar between the two groups. The solid fusion group performed significantly better in the symptom severity and physical function

categories on the self-administered questionnaire. This study clearly shows that pseudarthrosis patients followed long-term are very likely to have worse clinical outcomes than patients with healed fusions.

In the Abdu study it is important to note that the original paper reports a significant difference in the stenosis locations. There was a significantly higher proportion of patients with central stenosis in the noninstrumented group. This likely resulted in the preservation of the facet joints in the noninstrumented group with resultant stability. It is therefore likely that the three groups were not as comparable as one would hope, and hence it makes it more difficult to draw the conclusion that a lack of instrumentation does not provide benefit.

The authors also make note of the fact that the noninstrumented group in Abdu's study benefitted from significantly shorter mean surgical time, smaller blood loss, and fewer transfusions. The numbers quoted are for open procedures. If the study were performed using minimally invasive techniques where pedicle screws were inserted percutaneously, there would be no difference in blood loss or transfusion rates. A recent study (Kotani et al.) compared blood loss in patients undergoing open versus minimally invasive surgery (MIS). The intraoperative blood loss was significantly less in the MIS group (181 ml) when compared to the open group (453 ml). The postoperative bleeding on day 1 was also less in the MIS group (210 ml) when compared to the open group (406 ml). Values reported in the Abdu group were 498.7ml to 666.4ml, which clearly are not representative of minimally invasive techniques. Before one can make the blanket statement that noninstrumented is advantageous regarding blood loss in degenerative spondylolisthesis, one would need to explore MIS techniques first.

In addition, regarding the techniques of fusion, the Abdu study highlights that when patients and surgeons agree on a procedure, there is a good chance of success. As surgeons, we know that not every procedure is appropriate for every patient, and trying to compare techniques across dissimilar populations does not lend to meaningful results. For example, we would not typically offer an anterior-posterior instrumented lumbar fusion on an 80 year old with a collapsed disc and neurogenic claudication due to stenosis, nor would we be likely to offer a non-instrumented fusion in a highly mobile high grade dynamic isthmic spondylolisthesis in a 40 year old patient. Again, we feel that this highlights the need for the AHRQ document to have meaningful inclusion of subject matter experts on your writing panels, and the Societies would be happy to help in this regard.

**If fusion rates are proven to be better with instrumentation and pseudarthrosis will lead to worse clinical outcomes with long term follow up, then it would follow that instrumentation would have a better clinical efficacy than non-instrumented fusions for painful degenerative lumbar spondylolisthesis. Also, advances in surgical techniques such as minimally invasive surgery, need to be considered prior to concluding that noninstrumented is advantageous regarding blood loss in degenerative spondylolisthesis.**

### ***References for Key Question 9***

1. Kornblum MB, Fischgrund JS, Herkowitz HN, Abraham DA, Berkower DL, Ditkoff JS. Spine (Phila Pa 1976). 2004 Apr 1;29(7):726-33; discussion 733-4. Degenerative lumbar spondylolisthesis with spinal stenosis: a prospective long-term study comparing fusion and pseudarthrosis.
2. Kotani Y, Abumi K, Ito M, Sudo H, Abe Y, Minami A. Eur Spine J. 2012 Jun;21(6):1171-7. Epub 2011 Dec 16. Mid-term clinical results of minimally invasive decompression and

posterolateral fusion with percutaneous pedicle screws versus conventional approach for degenerative spondylolisthesis with spinal stenosis.

### **Key Question 10: Patient Characteristics Predictive of Outcomes After Spinal Fusion**

The authors of the AHRQ document conclude that the most important patient characteristic predictive of outcome after spinal fusion is age. They report that older age (65 years or older) is associated with worse patient outcomes following spinal fusion.

**Response:** We do not agree with this statement, and while complication rates are higher in older patients, they still have good outcomes overall with surgery. A recent publication from the spine deformity study group (Smith et al.) comments on this topic. In this paper, the authors reviewed 206 patients undergoing scoliosis surgery, and stratified them by age. While complications were significantly higher in the older patients, improvement in Oswestry disability index and leg pain were significantly greater among elderly patients ( $P=0.001$ ). There were trends for greater improvements in SF-12 ( $P = 0.07$ ), SRS-22 ( $P = 0.048$ ), and back pain ( $P = 0.06$ ) among elderly patients, when compared with younger patients. These data support the surgical treatment of elderly patients with spinal deformity and suggest that the elderly, despite facing the greatest risk of complications, may gain a disproportionately greater improvement in disability and pain with surgery.

In 2007, Glassman et al. reported their clinical outcomes in patients over the age of 65 who underwent lumbar fusion. There was a mean improvement of 6.21 points in SF-36 Physical Composite Score and 5.75 points in SF-36 Mental Composite Score. There was a mean 16.38-point improvement in ODI, 3.08-point improvement in back pain, and 2.65-point improvement in leg pain. There was no difference in outcomes at 2 years postoperatively based on the occurrence of a perioperative complication.

Despite an increase in complication rates in the elderly, outcomes themselves are not necessarily significantly influenced by these complications. The results of this study therefore support the efficacy of lumbar decompression and fusion in patients over 65 years of age, despite the known risk of complications in this patient population.

#### **References for Key Question 10**

1. Smith JS, Shaffrey CI, Glassman SD, Berven SH, Schwab FJ, Hamill CL, Horton WC, Ondra SL, Sansur CA, Bridwell KH; Spinal Deformity Study Group. Spine (Phila Pa 1976). 2011 May 1;36(10):817-24. Risk-benefit assessment of surgery for adult scoliosis: an analysis based on patient age.
2. Glassman SD, Carreon LY, Dimar JR, Campbell MJ, Puno RM, Johnson JR. Spine J. 2007 Sep-Oct;7(5):547-51. Epub 2007 Jan 9. Clinical outcomes in older patients after posterolateral lumbar fusion.

#### **Conclusion**

We appreciate the opportunity to review and comment on the AHRQ draft comparative effectiveness review on "Spinal Fusion for Treating Painful Lumbar Degenerated Discs or Joints." As clinicians specializing in the care of spinal disorders, we understand the concern regarding the over utilization of lumbar fusions in the hands of certain individual practitioners, which becomes the impetus for such assessments. We applaud the goal of improving patient care through the application of scientifically grounded therapies, but have concerns regarding the current AHRQ draft document as noted. We

believe that our suggestions will improve the current proposed draft document, and we look forward to seeing a revision to the document prior to its finalization.

We would be pleased to discuss this further in a meeting or on a telephone conference call before the AHRQ document is finalized. If you have any questions, please feel free to contact Joseph Cheng, MD, Chairperson, AANS/CNS Joint Section on Disorders of the Spine and Peripheral Nerves at [joseph.cheng@vanderbilt.edu](mailto:joseph.cheng@vanderbilt.edu) or Koryn Rubin, AANS/CNS Senior Manager for Quality Improvement [krubin@neurosurgery.org](mailto:krubin@neurosurgery.org).

Thank you for considering our comments.

Sincerely,



Mitchel S. Berger, MD, President  
American Association of Neurological Surgeons



Ali R. Rezai, MD, President  
Congress of Neurological Surgeons



Joseph S. Cheng, MD, MS, Chairman  
AANS/CNS Section on Disorders of the  
Spine and Peripheral Nerves



Kamal N. Ibrahim, MD, FRCS(C), MA, President  
Scoliosis Research Society

**Letter Contributors:**

Joseph S. Cheng, MD, MS  
John K. Ratliff, MD  
Daniel J. Hoh, MD  
Kojo Hamilton, MD  
Charles A. Sansur, MD  
Luis M. Tumialan, MD

**Staff Contact**

Koryn Rubin, Senior Manager for Quality  
Improvement  
AANS/CNS Washington Office  
725 15th Street, NW, Suite 500  
Washington, DC 20005  
Phone: 202-446-2030  
Email: [krubin@neurosurgery.org](mailto:krubin@neurosurgery.org)

**Neurosurgeon Contact**

Joseph S. Cheng, MD, MS, Chair  
AANS/CNS Section on Disorders of the Spine  
and Peripheral Nerves  
T-4224 Medical Center North  
Nashville, TN 37232  
Phone: 615-322-1883  
Email: [joseph.cheng@vanderbilt.edu](mailto:joseph.cheng@vanderbilt.edu)