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RE: Key Questions -- Spinal Fusion for Painful Lumbar Degenerative Disc or Joint Disease

To whom it concerns:

On behalf of the American Association of Neurological Surgeons (AANS) and the Congress of Neurological Surgeons (CNS), we would like to thank the Agency for Healthcare Research and Quality (AHRQ) for the opportunity to comment on the Key Questions regarding proposed research on the topic of ***“Spinal Fusion for Painful Lumbar Degenerative Disc or Joint Disease”***. We 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 are nevertheless frequently utilized as such with respect to healthcare policy development.

For the formulation of each of these Key Questions, AHRQ has requested a description of the included studies including patient indications, methods of diagnosis, inclusion and exclusion criteria, treatments, and surgical techniques and devices used. The AANS and CNS, along with other medical societies, have developed clinical guidelines on this topic and do not feel that another systematic review of these questions will yield useful information where our previous efforts have concluded that there is a paucity of sufficient data and that the quality of the studies is limited. However, as evidenced by the similar limitations in other medical and surgical topics, this does not diminish the benefit of this surgical treatment to our patients. Questions posed for the “Comment on Key Questions” may not be clinically relevant, which may be the genesis for the state of our current medical literature, and why future studies based on these Key Questions may not lead to improvements in patient care.

With these preliminary comments in mind, we will now turn our attention to commenting on the specific questions posed by AHRQ:

1. **For adults with low back pain attributed to degenerative disc disease of the lumbar spine, does spinal fusion differ from nonoperative treatment in the ability to improve:**
  - a. **Patient-centered outcomes such as function, quality of life, or pain?**
  - b. **Adverse events?**

AHRQ has proposed performing a systematic review of the comparative effectiveness and safety of lumbar fusion versus nonsurgical treatment for low back pain attributed to degenerative disc disease.

Currently, the primary treatment for most individuals with low back pain related to lumbar degenerative disease is non-operative therapy. As written, the question reflects a misunderstanding of the issue in that the population of patients treated with surgery is selected from those who have already failed extensive non-operative management. Viewing surgical and nonsurgical therapies as competing is inappropriate in this patient population as they are complementary, and surgery is typically not performed unless non-operative modalities have already failed. In this patient population, non-operative treatments have already been demonstrated to not improve outcomes.

In patients with chronic disabling pain refractory to conservative measures, lumbar fusion surgery is a potential therapeutic option. In this difficult patient population, prospective studies demonstrate a 36.0 - 63.9 percent reduction in back disability as measured by the Oswestry Disability Index (ODI) at 2 years after lumbar fusion (1, 2, 3, 4). Back pain scores also decrease 31.9 - 54.6 percent over the same duration (2, 3, 4). Further, lumbar fusion is associated with a 130.9 – 140.6 percent improvement in overall health as measured by the physical health component of the Medical Outcomes Study 36-item Short Form Health Survey (SF-36) (1).

To date, there are four multicenter randomized controlled trials comparing lumbar fusion surgery versus nonoperative treatment for low back pain attributed to degenerative disc disease. All four studies employed standardized patient-centered outcome measures to assess function and pain. The Swedish Lumbar Spine Study Group randomized patients who failed conservative therapy for  $\geq 2$  years to lumbar fusion surgery versus nonoperative therapy (ranging from physical therapy, education, transcutaneous electrical nerve stimulation, epidural steroid injections, cognitive and functional training, and/ or coping strategies) (5). Patients were evaluated for 2 years post treatment. The surgical group demonstrated a 33 percent reduction in back pain score and a 25 percent decrease in ODI. Sixty-three percent of surgical patients rated themselves as “much better” postoperatively, and 36 percent had returned to work. Comparatively, the nonsurgical group demonstrated only a 7 percent reduction in back pain score and a 6 percent decrease in ODI. Only 29 percent of nonsurgical patients rated themselves as “much better” after treatment, and only 13 percent had returned to work.

Brox et al randomized a much smaller group of patients with low back pain who had failed 1 year of conservative therapy to lumbar fusion versus a nonsurgical treatment protocol consisting of a lengthy inpatient program of physical therapy, cognitive intervention, education and peer counseling which is not available in North America (6). Patients were evaluated for 1 year post treatment. The surgical group demonstrated a 36.6 percent reduction in back pain score and a 37.1 percent decrease in ODI. Conversely, the nonoperative group demonstrated only a 24.0 percent reduction in back pain score and a 30.9 percent decrease in ODI. Overall, 71 percent of surgical patients rated their treatment as successful compared to 63 percent of nonoperative patients. In a similar study, Brox et al randomized patients with low back pain after prior disc herniation surgery to either of the same treatment arms (7). More modest improvements were observed overall with the lumbar fusion group demonstrating a 21.5 percent reduction in back pain score and an 18.9 percent decrease in ODI. The nonsurgical group demonstrated a 23.5 percent reduction in back pain and a 28.4% decrease in ODI.

Fairbank et al randomized patients with degenerative disc disease related low back pain to lumbar fusion surgery versus nonoperative therapy consisting of an intensive inpatient rehabilitation program of cognitive behavioral therapy and exercise (8). Patients were evaluated for 2 years post treatment. The study was plagued by a high rate of crossover and significant patient loss to follow-up which heavily biased the study against surgical intervention given the intent to treat study design. Another significant methodological flaw related to the surgical group. Many patients were treated without fusion, making any statements regarding the efficacy of fusion based on the data from this study highly suspect. Despite the inherent biases against surgical intervention, the surgical group demonstrated a 26.9 percent decrease in ODI compared to only a 19.4 percent decrease observed in the nonoperative group. Overall general

health was assessed via the physical component of the SF-36, with the surgical group demonstrating a 148.5 percent improvement compared to only a 138.0 percent increase seen in the nonoperative group. A recent paper reported the 6-year follow-up of an FDA Phase IV study, combining patients from sites of two previous FDA trials on anterior lumbar interbody fusion for patients with DDD unresponsive to conservative care. This study reported a substantial improvement in patient daily functioning, with improvements in back pain, leg pain, Oswestry disability index (ODI), and Short-form 36 (SF-36) measures (25).

Lumbar fusion surgery for low back pain however carries risk of potential adverse events. Depending on the series, incidences of major and minor complications widely vary. Complications including neurologic events, approach related vascular injuries, wound infection, deep venous thrombosis, pseudoarthrosis, dural tear, and bone graft donor site pain among others ranged from 7.9- 46.4 percent (1, 3, 5, 6, 7, 8). Reoperation rates also widely varied ranging from 7.8 - 37.4 percent (1, 2, 3, 5, 8). Mortality after lumbar fusion surgery in these series was 0 - 0.7 percent (1, 2, 3, 4, 5, 6, 7, 8).

The existing literature demonstrates that both nonsurgical treatment and lumbar fusion surgery may improve function and pain for individuals with low back pain attributed to degenerative disc disease. While limited evidence suggests that lumbar fusion may result in better outcomes compared to nonoperative treatment for certain individuals, several systematic reviews have debated these conclusions (9, 10, 11). In 2005, the American Association of Neurological Surgeons and the Congress of Neurological Surgeons performed a joint systematic review and concluded that there is Class I evidence to support lumbar fusion for carefully selected patients with low back pain intractable to the best medical management (12). They also found that Class III medical evidence suggests that nonsurgical treatment consisting of intensive cognitive and physical therapy may be an efficacious option for patients with chronic disabling low back pain. Given these current systematic reviews, it is unlikely that the AHRQ's proposed re-assessment of the present literature will provide any further clarification of the comparative effectiveness of surgical and nonsurgical treatment of low back pain attributed to lumbar degenerative disc disease.

- 2. For adults with low back pain attributed to degenerative (not congenital) stenosis of the lumbar spine, does spinal fusion differ from nonoperative treatment in the ability to improve:**
  - a. Patient-centered outcomes such as function, quality of life, or pain?**
  - b. Adverse events?**

Fusion is not recommended in patients operated upon for spinal stenosis in the absence of deformity (such as spondylolisthesis, scoliosis, or regional kyphosis) or instability (pre-existing or iatrogenic) (12). There is substantial evidence indicating that surgical intervention improves pain, function, and quality of life (44). There is further evidence that these improvements are durable and cost effective. The use of fusion in this population should be applied selectively to those patients with the above listed risk factors for progressive instability or deformity. There are no non-operative measures demonstrated to improve long term outcomes in patients with neurogenic claudication due to lumbar stenosis (57, 58).

The population of patients with low back covers rather extensive subgroups and diagnoses. As such, these patients are so heterogeneous that comparison of patient-centered outcomes (such as function, quality of life, adverse events, or pain) following spinal fusion versus non-operative management is an impractical task. Several primary and secondary confounding issues, such as return to work, disability requirements, perception bias of type of treatment and also long term and short term goals of the patient, clinical practitioner and medical payer, further cloud the evaluation of effectiveness of both treatment arms considered above (13, 14).

Over the last few decades, an awareness of the above variety of factors and patient demographics have resulted in recent multiple studies trying to elucidate the effect of the two treatment arms discussed with regard to sub populations of adults and also timing of intervention (15, 16, 17).

In designing questions related to patient outcomes, particularly in symptom and function dependent conditions such as lumbar stenosis, specific questions, pertaining to specific subgroup of patients beyond age (e.g. adult versus pediatric), gender, and diagnosis type (e.g. congenital versus degenerative) need to be clarified. It is impossible for current static low back pain classification systems geared toward short term outcomes accurately determine dynamic long term benefits (18, 19, 20).

With regard to guidelines and policies that are government-sponsored, patient-centered outcome studies and recommendations, there is heterogeneity of both medical specialty society recommendations and also that of the medical payer policies due to variations in the literature and also transparency in the development of the policies (21).

In formulating questions on patient-centered outcomes related to function, quality of life, pain or adverse events, due to the complexity of the subject, variation of beneficiaries and lack of effective long term data, it is important to have clearly identified subgroups and also quality studies across specialty/ society groups identifying specific outcomes to avoid erroneous generalizations.

- 3. For adults with low back pain attributed to degenerative spondylolisthesis of the lumbar spine, does spinal fusion differ from nonoperative treatment in the ability to improve:**
  - a. Patient-centered outcomes such as function, quality of life, or pain?**
  - b. Adverse events?**

Several studies have compared fusion surgery to non-operative treatment for the indication of degenerative spondylolisthesis. These studies have shown that for patients who suffer from low back pain due to degenerative spondylolisthesis, surgical intervention in the form of fusion surgery is more effective than non-operative treatment. Weinstein et al showed in the SPORT trial that surgical intervention for the treatment of degenerative spondylolisthesis showed significant improvement in SF-36 for bodily pain and physical function, as well as statistically significant improvement in the Oswestry Disability Index (29). These improvements were maintained for a follow-up of four years.

With regards to surgical complication rate, Sansur et al reviewed over 10,000 patients with degenerative and isthmic spondylolisthesis for complication incidence and factors associated with adverse events (28). The total rate of complications was 9.2 percent, and included dural tears, wound infections, hardware and implant complications, and neurological complications. Factors that correlated with a higher complication rate included higher grade spondylolisthesis, and age > 65 years old. Degenerative spondylolisthesis had a higher complication rate than isthmic spondylolisthesis (8.5 percent vs. 6.6 percent,  $p=0.002$ ). These complication rates do not differ significantly from those in other series published in the literature (40, 41, 42, 43). The complication rate for patients undergoing surgical intervention for degenerative spondylolisthesis, while obviously higher than the complication rate of non-surgical treatment, are consistent with complication rates for spine surgery in general, and should not be a deterrent to pursuing surgical intervention, which provides longer term and more definitive treatment of back pain for degenerative spondylolisthesis.

Lumbar fusion has been shown in multiple studies in the literature to be a more effective treatment for degenerative spondylolisthesis, and provides improvement in pain and disability that is superior to conservative therapy.

- 4. For adults with low back pain attributed to degenerative disc disease of the lumbar spine, does spinal fusion differ from other spinal procedures (e.g., total disc replacement, disc decompression) in the ability to improve:**
- 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?**

It is unclear from well executed randomized prospective trials that there is any difference between lumbar arthroplasty and lumbar fusion in operative treatment of patients with lumbar degenerative disc disease (DDD). Approval of lumbar arthroplasty by the U.S. Food and Drug Administration was predicated upon establishing parity in clinical outcomes with the standard of care, lumbar fusion. The FDA used the criterion of non-inferiority as the foundation for approving lumbar arthroplasty devices for widespread use (25).

A prospective randomized comparative trial of lumbar arthroplasty versus lumbar fusion assigned 72 adult DDD patients to posterolateral fusion (PLF) or posterior lumbar interbody fusion (PLIF) at 1-2 levels. Back pain and ODI scores decreased significantly at 2-years. At 2-years, 76 percent of fusion patients were back to work part or full time and 67 percent were satisfied with their surgery (26). A meta-analysis performed by Bono and Lee reviewed all publications on non-revision fusion for lumbar DDD from during a 20 year period, encompassing over 2000 patients. They report good or excellent clinical outcomes were achieved in over 70 percent of those treated (27).

Disc decompression, dynamic stabilization, facet replacement and many other evolving technologies do not have substantial literature support to allow comment on the relative efficacy of these procedures compared to lumbar fusion.

There are significant complications which may occur in patients undergoing lumbar spine fusions. Previous reports have not found a significant difference between arthroplasty and arthrodesis study cohorts. Disc degeneration may occur in segments adjacent to fusions in the lumbar and cervical spine. It is unclear whether or not these areas of "juxtafusional" disease are caused by the neighboring fusion or if they represent the natural progression of the lumbar and cervical degenerative processes.

These well designed and well executed studies have not demonstrated any differences in patient outcomes. It seems unlikely that further investigations will be superior to these efforts. Observational patient registries may be one means to answer these questions.

- 5. For adults with low back pain attributed to degenerative stenosis of the lumbar spine, does spinal fusion differ from other spinal procedures (e.g., decompressive laminectomy and minimally invasive procedures, including those using devices) in the ability to improve:**
- 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?**

Degenerative stenosis has diverse etiologies, and for Key Question #5 we must assume that the question is restricted to patients without an underlying need for spinal fusion such as in patients with spinal deformity or spondylolisthesis. Low back pain associated with degenerative stenosis without spinal instability or expected iatrogenic instability, such as in patients with spinal deformity or spondylolisthesis, does not alter the recommendations of decompressive laminectomy alone with targeted use of medial facetectomies and foraminotomies, with or without discectomy. Decompressive laminectomy has been supported for superiority over non-operative therapy in degenerative stenosis by

studies such as the SPORT trial. This randomized, prospective trial indicated substantially greater improvement in pain and function through 4 years after decompressive surgery (44).

The 2005 AANS/CNS guidelines on this topic noted that spinal fusion procedures are associated with improved outcomes in patients with pre-operative evidence of spinal instability (45). Hopp and Tsou first introduced the impact of iatrogenic instability occurring during surgery due to extensive facetectomy necessary to achieve decompression in 1988 (46). Subsequent reports have supported the concept (47, 48). Fox et al reported extensive decompression at more than one level without concomitant arthrodesis was associated with worse outcomes following decompressive laminectomy for lumbar degenerative spinal stenosis (48). The AANS/CNS Guidelines for Lumbar Fusion formally endorsed spinal fusion in addition to decompressive laminectomy under those circumstances of iatrogenic instability (45).

Minimally invasive options for the treatment of lumbar degenerative stenosis have gained widespread use but its rapid evolution has made its evaluation a moving target. There is extensive literature on the clinical utility of minimally invasive surgery as a safe and effective for the treatment of degenerative lumbar stenosis. Studies have indicated that minimally invasive spine surgery and traditional open lumbar surgery have similar long-term patient outcomes in terms of pain and quality of life (52, 55, 56). Studies and meta-analyses on peri-operative factors have reported equivalence in complication rates for minimally invasive surgery, with minimally invasive surgery associated with a lower post-operative wound infection, less intra-operative blood loss, longer operative times, with overall no difference in long-term patient outcomes (50, 51, 52). Fourny et al reported a systematic review in 2010 indicating no difference in adverse events (rates of reoperation, dural tear, cerebrospinal fluid leak, nerve injury, and infection) between minimally invasive lumbar decompression and open surgery, with or without fusion (49). Two more recent literature review and cost analysis studies suggested lower infection rates (and lower associated costs) for minimally invasive surgery (53, 54).

Laminectomy and other decompressive procedures are not generally performed for the treatment of axial low back pain. These procedures are performed to treat claudication or radiculopathy, with lumbar fusions indicated if there is pre-operative or expected intra-operative iatrogenic spinal instability.

- 6. For adults with low back pain attributed to spondylolisthesis of the lumbar spine, does spinal fusion differ from other spinal procedures (e.g., repair, vertebrectomy) in the ability to improve:**
- 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 main treatment options for adult spondylolisthesis are decompression with fusion. Treatment of spondylolisthesis with fusion is the most common approach, and is the most clearly documented surgical option in the literature. The largest series reported is from the Scoliosis Research Society, where they reported the results of 10,242 surgically treated cases of adult spondylolisthesis. Out of 10,242 patients, only 532 were treated without fusion (28). Complications rates in patients undergoing fusion versus those undergoing decompression alone were not significantly different (28). In the SPORT trial, the vast majority of patients in the surgical group (who had superior outcomes when compared to the non-operative group) had fusions (29). The reason why this disease is treated mostly through fusion is due to reported risks of deformity progression and chronic pain in patients treated without fusion. Herkowitz demonstrated a high failure rate after decompression without fusion, and better outcomes with fusion (30). Other studies also support fusion in the treatment of this disease over other surgical options (31, 32).

Direct repair of the fractured pars interarticularis (spondylolysis) without fusing adjacent segments is a potential treatment option, but is limited to very minimal degrees of slip in younger patients who would have a better chance for bone formation along the fractured pars. A few studies report direct repair of the fractured pars, but there are no well recognized studies comparing pars repair to fusion, as the circumstances under which one would actually be able to consider pars repair alone are rare (33, 34). As discussed in the question, vertebrectomy is mentioned as a possible surgical alternative. Vertebrectomy would be reserved for very rare and severe circumstances of spondylolisthesis from trauma or oncologic conditions. Again due to the relative rarity of such situations, it cannot even be considered as a comparable treatment option in the routine patient with back pain and or leg symptoms from spondylolisthesis.

Since fusion remains the dominant treatment of choice in this condition, and as it has repeatedly been shown that fusion has more optimal results than decompression alone, it may not be useful to check for differences in perioperative outcomes such as surgery time, blood loss, or length of hospital stay. More long term outcomes, such as re-operation rates and long term quality of life measures have demonstrated that fusion is the superior treatment. Other options such as direct repair of pars, and vertebrectomy are indicated in rare circumstances and hence are not to be considered as comparable entities.

- 7. For adults with low back pain attributed to degenerative disc disease of the lumbar spine, do spinal fusion approaches (e.g., anterior, posterior, combined) and techniques (e.g., instrumentation or graft material) differ in the ability to improve:**
- 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?**

Clinicians understand that more involved procedures, such as combined anterior/posterior fusions, generally entail longer surgery, greater blood loss, and longer hospital stays. They are usually employed, however, in selected patients who are thought, prospectively, to be at risk for a suboptimal outcome from an alternative procedure because of individual patient factors or particular aspects of the patient's pathology. Many of these important differences, such as osteoporosis, significant motion on flexion/extension radiographs, or segmental kyphosis, are not routinely identified and studied in directly comparative investigations. On the contrary, most RCTs and other studies strive to achieve or to demonstrate complete balance between treatment cohorts and therefore treat differences between patients as potential sources of bias rather than as possible key indicators of the likely benefit of one technique over another.

For example, in the treatment of spondylolisthesis, there are several fusion techniques commonly employed including non-instrumented fusion, posterior instrumentation with posterolateral fusion (PLF), posterior instrumentation with interbody fusion, or a combined anterior and posterior approach. Each of these approaches has a role in the treatment of a heterogeneous patient population. An elderly patient with a collapsed disc space and a relatively fixed deformity would likely do well with a non-instrumented fusion whereas a younger patient with a more mobile spine would be at high risk for failure of that fusion construct and would be better treated with a more aggressive approach. The influence of spinal alignment, local anatomical features, osteoporosis, and patient demand (i.e. activity level and age) cannot be overstated. Evidence to this point is provided by Soegaard et al who found that circumferential fusion (the most costly and morbid) was associated with significant benefits and cost savings compared to less aggressive techniques in a working population (Soegaard et al: Circumferential fusion is dominant over posterolateral fusion in a long term perspective. Spine 32: 2405-2411, 2007). It is quite possible, indeed likely, that this benefit would not be apparent in an older patient population.

- 8. For adults with low back pain attributed to degenerative stenosis of the lumbar spine, do spinal fusion approaches (e.g., anterior, posterior, combined) and techniques (e.g., instrumentation or graft material) differ in the ability to improve:**
- 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 response for Key Question #8 mirrors the discussion of Key Question #2. There are diverse indications for fusion in the setting of stenosis, and the approach varies with the diverse pathology and involved patient population. The use of fusion in the setting of stenosis is typically considered when instability is demonstrated pre-operatively or anticipated based on preoperative/intraoperative factors. In these circumstances, lumbar fusion has been shown to be beneficial, with improved function, quality of life, and pain. For symptomatic spinal stenosis with or without degenerative spondylolisthesis, a recent systematic review by Chou et al. found evidence that decompressive surgery is moderately superior to nonsurgical therapy through 1 to 2 years. Surgery for radiculopathy in the setting of 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 is associated with small to moderate benefits compared to standard nonsurgical therapy (10).

As highlighted in other Key Question responses, spinal fusions of any nature can increase surgery time, blood loss, potential for adverse events, and length of hospital stay, in comparison with simple decompression. It is understood by physicians that combined anterior-posterior fusion surgery will typically result in greater intraoperative time, blood loss, and length of hospital stay, and higher risk for adverse events – and that it is typically reserved for patients felt to be at risk for poor outcomes via a more limited approach (so as to improve functional or quality outcomes than would otherwise be expected). The superiority of a particular approach (anterior, posterior, combined) or technique (instrumentation or graft material) has not been proven, as the factors involved in a surgeon's decision are heterogeneous; options for approach are not always equal/competitive. Surgical techniques and approaches are constantly being refined. A study trying to prove superiority of one approach is doomed to limited relevance and will undoubtedly be an immense undertaking with likely equivocal outcomes.

- 9. For adults with low back pain attributed to spondylolisthesis of the lumbar spine, do spinal fusion approaches (e.g., anterior, posterior, combined) and techniques (e.g., instrumentation or graft material) differ in the ability to improve:**
- 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 question put forth by AHRQ regarding the relative efficacy of the various spinal fusion approaches to address low back pain in patients with spondylolisthesis is far too broad a question in the expansive diagnosis of spondylolisthesis to conclusively answer. While examination of the various surgical approaches for a single diagnosis may seem at first glance appear to be a valid question for a homogeneous cohort, in reality spondylolisthesis is far from uniform. This diagnosis has within it various subsets and anatomical considerations that make it a heterogeneous group and therefore difficult to study.

For example, in the treatment of spondylolisthesis, several fusion techniques are commonly employed including non-instrumented fusion, posterior instrumentation with posterolateral fusion (PLF), posterior

instrumentation with interbody fusion, or a combined anterior and posterior approach. Each of these approaches has a role in the treatment of a heterogeneous patient population. An elderly patient with a collapsed disc space and a relatively fixed deformity would likely do well with a non-instrumented fusion whereas a younger patient with a more mobile spine would be at high risk for failure of that fusion construct and would be better treated with a more aggressive approach. The influence of spinal alignment, local anatomical features, osteoporosis, and patient demand (i.e. activity level and age) cannot be overstated. Evidence to this point is provided by Soegaard et al who found that circumferential fusion (the most costly and morbid) was associated with significant benefits and cost savings compared to less aggressive techniques in a working population (Soegaard et al: Circumferential fusion is dominant over posterolateral fusion in a long term perspective. Spine 32: 2405-2411, 2007). It is quite possible, indeed likely, that this benefit would not be apparent in an older patient population.

The largest and most expensive trial to date is the NIH funded Spine Patient Outcomes Research Trial (SPORT). While this trial represents the most comprehensive study to date examining the 3 common fusion methods used in the treatment of degenerative spondylolisthesis, it was not specifically designed to evaluate the three fusion techniques of posterolateral in situ fusion, posterolateral fusion with pedicle screw fixation and 360° fusion (PLIF/TLIF, ALIF augmented with pedicle screw stabilization). Regardless, this trial represents the largest cohort of degenerative spondylolisthesis available for review. The preliminary SPORT data demonstrated that individuals with spinal stenosis and associated degenerative spondylolisthesis treated surgically had substantially greater improvement in pain and function during a period of 4 years than did patients treated nonoperatively (29, 35). A subsequent evaluation of fusion methods within the same study attempted to examine the outcomes of 3 different fusion techniques: PLF, PPS and 360° fusion, but were unable to establish superiority of one approach over another. This is not because the procedures are equivalent, it is because they were each applied in appropriate patient populations and were generally successful.

With regards to the perioperative outcomes of surgery time and blood loss, times ranged from 157 to 274 minutes, with PLF having the shortest operative time and 360° having the longest. Mean blood loss ranged from 499 to 666 ml, again with PLF averaging the lowest and PPS averaging the highest. The most common adverse event was a dural tear, which was highest for PPS (12%) followed by PLF (9%) and lowest in 360° (2%). Incidentally, the rate of an inadvertent durotomy in this report seemed inordinately high. By comparison, Williams and colleagues reported a durotomy rate of 1.9 percent in patients with spondylolisthesis in their review of 108,478 cases (36). The postoperative transfusion rate in the SPORT study followed the same trend, PPS (26%), 360° (17%) and PLF (14%).

With regards to patient centered outcomes, all three groups' demonstrated significant improvement compared to baseline in various validated outcome measures (ODI, SF-36 BP and BF). There was no significant difference between the groups at 4 years (37). It is again important to emphasize that the SPORT study was not specifically designed to evaluate fusion techniques or to validate one form of fusion for the management of degenerative spondylolisthesis. While prospective in design, there was no randomization and therefore the results may have been affected by selection bias. Only a prospective randomized study designed and appropriately powered to evaluate these three fusion techniques in a narrow population with specific anatomical criteria has the capacity to determine which fusion method provides the greatest improvement in outcome measures and is the most cost effective treatment. However, the SPORT data has demonstrated the effectiveness of surgical treatment compared with nonsurgical treatment of degenerative spondylolisthesis.

While there is a constellation of reports in the literature that explore some element of the various subsets of question 9, there is no comprehensive study that unequivocally answers this question and, for the various reasons listed above, we do not foresee such a study ever taking place. What the literature has

unequivocally demonstrated is that surgeons have effectively used all three of these approaches to successfully treat patients with spondylolisthesis.

**10. Are there patient characteristics (e.g., pain severity, prior treatment) that are associated with better or worse outcomes after spinal fusion?**

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

Some patient characteristics may have an effect on outcomes after spinal arthrodesis for lumbar degenerative disease. However, to date, no study has determined definitive preoperative characteristics which may predict optimal or suboptimal outcomes from lumbar arthrodesis. Several smaller studies and meta-analyses have reported preoperative parameters which may be included in the overall evaluation when considering a patient as a candidate for lumbar arthrodesis.

For example, psychiatric comorbidities have been examined as a potential predictor of outcomes. A recent meta-analysis evaluated outcomes from both nonsurgical and fusion treatments to examine the effect of psychiatric comorbidities on outcomes. While there were few studies specifically addressing this question, those studies suggested that patient whose comorbidities include a personality disorder, depression, or neuroticism should preferentially be treated non-operatively (15). Others have corroborated that the presence of depression may be an independent predictor of success for surgery (20). However, as Daubs et al. report, the strength of their recommendation is weak. While there are no definitive studies that would preclude surgery as an option for patients with psychiatric comorbidities, the studies cited suggest that it should be evaluated during decision making.

Other factors have been looked at as well, including preoperative health status, cardiac comorbidity, and work status among others. Preoperative health status self-assessment appears to be the most robust, yet definitive criteria for predicting outcome have not been established (38). Other factors such as radiographic findings have been explored as well. In general, when findings such as spondylolisthesis are present, these have been reported to portend a better outcome (9).

Overall, current literature does not support criteria or strong recommendations for excluding spinal arthrodesis due to specific preoperative patient characteristics (39).

## **Conclusion**

We appreciate the opportunity to comment on the Key Question formulation regarding the AHRQ proposed research on the topic of “***Spinal Fusion for Painful Lumbar Degenerative Disc or Joint Disease***”. The AANS and CNS developed clinical guidelines on this topic in 2005, and we are currently undergoing the process of updating these guidelines. Based on our experience, we do not believe that another systematic review of these questions will yield useful information as there is a paucity of sufficient data and the quality of the studies is limited. **After reviewing the current literature in conjunction with the clinical expertise of our Neurosurgeon members, the AANS and CNS do not believe that this diminishes the benefit of this surgical treatment to our patients.** While we understand that these AHRQ research summaries are not clinical recommendations or guidelines, we remained concerned that this research proposal will involve a large effort with minimal and limited clinical relevance.

Again, thank you for this opportunity to comment and we look forward to seeing your final position pertaining to this proposed research. If you have any questions, please feel free to contact Joseph

Cheng, MD ([joseph.cheng@vanderbilt.edu](mailto:joseph.cheng@vanderbilt.edu)), AANS/CNS Committee for Payor and Policy Responses, or Koryn Rubin, the AANS/CNS Senior Manager for Quality Improvement.

Sincerely,

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