Technology Assessment

DRAFT

Spinal Fusion for Treatment of Degenerative Disease Affecting the Lumbar Spine

DRAFT

Technology Assessment Program

November 1, 2006

Agency for Healthcare Research and Quality
540 Gaither Road
Rockville, Maryland 20850

Spinal Fusion for Treatment of Degenerative Disease

Affecting the Lumbar Spine

Duke Evidence-based Practice Center

DRAFT

November 1, 2006

Douglas C. McCrory, MD, MHS

Dennis A. Turner, MA, MD

Meenal B. Patwardhan, MD, MHSA

William J. Richardson, MD

Declarations of finacial, business and professional interests for each author are as follows:
Dr. McCrory - Medical staff of Duke University Medical Center
Dr. Turner - Consultant to Depuy Spine; consultant to Integra Life Sciences.
Dr. Patwardhan - None
Dr. Richardson - None

Acknowledgement:

The authors wish to thank Udita Patel and R. Julian Irvine, Project Coordinators, for their assistance in managing the database, retrieving and distributing the articles, as well as copy editing this Technology Assessment.

TABLE OF CONTENTS

EXECUTIVE SUMMARY

Primary Question

In patients 65 years of age or older with degenerative disc disease (DDD) and/or degenerative joint disease (DJD) of the lumbar spine, what is the evidence regarding indications and outcomes including adverse events (overall net health benefit) of lumbar spinal fusion as compared to non-surgical conservative treatment/management or other surgical strategies?

Methods

A systematic literature search (including primary studies and guidelines/reviews) and a qualitative synthesis was performed to assess the data underlying lumbar fusion.

Results

There is no randomized control trial (RCT) evidence that directly compares lumbar spinal fusion with non-surgical conservative treatments in populations older than 65 years of age for any indication. For axial back pain due to isolated degenerative disc disease (without spondylolisthesis) in middle-aged populations with mean age between 40-45 years, four randomized controlled trials failed to demonstrate clinically meaningful improvement in Oswestry Disability Index (ODI) for lumbar spinal fusion compared with rehabilitation; the two studies reporting statistically significant benefit on the ODI found a difference of less than 15 points, which is generally accepted as the minimum clinically meaningful difference. In patients with spondylolisthesis, one RCT in middle aged persons demonstrated statistically significant improvements in pain and disability up to two years; but at long term follow-up to as long as nine years after surgery, these differences were no longer significant. Various fusion procedures including anterior lumbar interbody fusion (ALIF), posterolateral fusion (PLF), posterior lumbar interbody fusion (PLIF) and transforaminal lumbar interbody fusion (TLIF®), and anterior-posterior combined fusion (A/P fusion) do not differ in significantly in pain or disability outcomes, although there are qualitative differences in complications related to the surgical approach.

Lumbar fusion has significant short term risks, particularly in the elderly in whom mortality rates of 1-1.6% have been reported. Long-term reoperation rates following lumbar fusion is up to 3.7% annually, but this rate is only slightly higher than the reoperation rate for non-fusion lumbar spine operations suggesting that progression of degenerative disease in the spine is the major factor leading to reoperation. Except for recombinant human bone morphogenic protein (rhBMP-2) for anterior lumbar interbody fusion, there is little evidence that bone graft substitutes contribute to fusion efficacy. There is good evidence that instrumentation augments fusion rate, though the risks in the short-term are increased with instrumentation, and the effect on better symptomatic improvement has not been demonstrated.

Conclusions

The evidence for lumbar spinal fusion does not conclusively demonstrate short-term or long-term benefits compared with non-surgical treatment, especially when considering patients over 65 years of age, for degenerative disc disease; for spondylolisthesis, considerable uncertainty exists due to lack of data, particularly for older patients.

INTRODUCTION

Spinal fusion is a surgical procedure that aims to provide internal stability by facilitating bony interconnection between two or more of the vertebrae in the spine, leading to absence of motion between these segments. There are several operative indications for lumbar spinal fusion, including instability (such as spondylolisthesis or scoliosis) causing axial spine discomfort or secondary neural compression, threatened instability as an adjunct to nerve decompression procedures (e.g., instability which may occur as a consequence of laminectomy in the presence of facet joint disease), and axial back pain (e.g., for the alleviation of pain due to motion in arthritic joints, including facet arthritis or intervertebral disc degeneration).

These operative indications have developed informally over many years within the disciplines of neurosurgery and orthopedics, based upon evolving concepts of pain generation within spinal joints (i.e., disc and facet joints), instability, and the treatment of secondary neural compression. The surgical techniques to achieve lumbar spinal fusion are numerous, and include different surgical approaches (anterior or posterior) to the spine, different areas of fusion (intervertebral body, transverse process), different fusion materials (bone graft or metal instrumentation), and a variety of ancillary techniques to augment fusion. Internal spine implants include various kinds of screws (i.e., pedicle screws, facet screws, anterior screws and plates), cages (boxes to provide both immediate stability and to serve as a bony conduit) and various biological agents to augment fusion.

This diversity of indications and techniques complicates the assessment of lumbar spinal fusion’s efficacy, safety and effectiveness compared to non-surgical management. Several reviews have summarized the literature, most recently, an updated systematic review of randomized control trials from the Cochrane Collaboration[1] and a broader review[2] that included not only RCTs but also prospective and retrospective uncontrolled studies. The reviews note deficiencies in the body of studies including generally low methodological quality, substantial heterogeneity in results, lack of assessment of long-term outcomes, limited evidence for differences between the treatments, and an inadequate assessment of adverse effects.

Recent years have seen a large increase in the use of many spine surgical procedures[3-6], particularly lumbar spine fusion. This increase in lumbar fusion has been remarkable particularly in the population over 60 years of age, from 42/100,000 population in 1993 to 108/100,000 in 2003.[3]

The effectiveness of spinal fusion in the elderly has not been systematically evaluated. Due to age-related changes in the spine, including disc and facet arthritic disease, as well as an increase in the prevalence of comorbid conditions with age, the risk and benefits of lumbar spinal fusion in patients over 65 years of age may be different from that in younger adults.

The following report is a systematic review of the indications and outcomes of lumbar spinal fusion used for either degenerative disc disease (DDD) and/or facet degenerative disease (DJD), leading to axial or mechanical low back pain, instability of the spine (including spondylolisthesis), spinal stenosis (leading to radicular leg pain or neurogenic claudication), and combinations of these symptoms with special attention to data from older adult populations, particularly those over 65 years of age.

BACKGROUND

What Are Degenerative Changes in the Spine?

Each spine motion segment includes several vertebral bony elements, such as the vertebral body, transverse processes, pedicles, facets and lamina, and three primary joints. The main joint bearing axial load (~80%) is the disc joint, which consists of a very firm outer, ligamentous structure, the annulus, and an inner, hydrated viscous nucleus pulposus. In childhood, the nucleus is a hydrogel, consisting of approximately 80% water, which is signified by a bright disc on T2-weighted magnetic resonance imaging (MRI) images, usually with a thin cleft in the middle on sagittal images.[7] The hydrogel in the nucleus is considered by some researchers to be generated by remnant notochord cells which dissipate by programmed cell death in the first few years of life.[8, 9] According to this hypothesis, desiccation of the hydrogel is a delayed, programmed process (similar to puberty) which progresses from childhood. As the disc hydrogel desiccates, the disc nucleus loses height and on the T2-weighted MRI images becomes darker (termed the “dark disc syndrome”). Because of the decreased height, the annulus becomes less tense and “bulges” anteriorly and posteriorly. Corresponding changes occur in the vertebral endplate, which becomes sclerotic and less permeable for nutrition to the disc. These changes of disc desiccation and disc narrowing are collectively termed “degenerative”, or degenerative disc disease (DDD). However, all these changes may, in fact simply be a form of development or maturation since they are ubiquitous in the population by the age of 40 according to multiple MRI investigations.[10] As the disc narrows, typical degenerative processes intervene, particularly the formation of osteophytes on the margins, which is common in patients over 60 years of age. The disc joint has additional peculiarities, since there is no direct blood supply into the hydrogel, the nucleus is shielded from the general circulation and hence from the immune system. Therefore disc nutritive sources are dependent on diffusion across the endplate. As degenerative processes evolve, the vertebral endplate adjacent to the disc joint becomes less permeable and sclerotic, further hastening disc desiccation. As the degenerative process continues, the annulus also becomes more densely innervated by pain fibers. Hence, one of the sources of axial back pain may be the degenerated joint.

Another result of the narrowing disc is that additional load is applied to the facet joints. The facet joints bear less than 20% of the axial loading of the spine when the disc is of normal height, and are ordinary synovial joints. These joints are positioned to hinder excessive rotation and front/back movement. As usual degenerative processes evolve, loss of synovial fluid occurs, the joint space narrows, and the joint enlarges with formation of osteophytes and sclerosis at the margins. If the facet joints hypertrophy into the spinal canal (they form the posterior borders of the canal) spinal stenosis may occur, leading to nerve pressure and either radiculopathy or neurogenic claudication. With severe degeneration, facet joints become incompetent as well, leading to degenerative spondylolisthesis of the vertebral bodies, a condition that is particularly prevalent in older patients. Due to the inter-relationship between the disc and facet joints at every level of the spine, it is usually assumed that isolated degeneration of one or the other likely does not occur, and that degeneration of either joint can lead to axial back pain as well as secondary neurological complications.

Conservative Treatments

In the US, conservative treatments are generally performed routinely before any surgery is considered in axial back pain. This includes medical management (such as NSAIDs, etc.), pain management, injections, physical therapy, exercise and various forms of cognitive rehabilitation. Such conservative treatments are seldom applied in a comprehensive, well-organized rehabilitation program, although some such programs do exist.[11] Conservative treatments are usually tried for at least 6 to 12 months before considering a patient for surgery for any form of lumbar fusion. Several reviews of these therapies[12, 13] note that there is no evidence about the effectiveness of any of these therapies for low back or radicular pain beyond about six weeks.

Recently, several randomized trials of lumbar spinal fusion surgery conducted outside the US have tested systematic, organized rehabilitation therapy approaches in non-surgical control arms, and measured outcomes at longer duration (i.e., six months to two years).[14-17]

What are Common Surgical Indications?

Many clinical practice guidelines are currently available regarding appropriate indications for lumbar spine surgery.[12, 13, 18-39] We will briefly summarize these protocols, which vary considerably across the US and across disciplines, depending upon the background and training of the surgeons, and how individual surgeons interpret their own outcomes

The most common pathological occurrences of the lumbar spine are herniated lumbar discs, lumbar stenosis and lumbar spondylolisthesis. These conditions are commonly treated surgically if conservative treatments do not give sufficient pain relief to the patient, particularly for refractory leg pain from radicular compression, which can be very severe. Even with spondylolisthesis, the most common symptom is leg pain, from secondary radicular compression arising from foramina, lateral recess or central spinal stenosis; most lumbar fusions are an adjunct to the nerve decompression procedure. An early study of lumbar fusion in spondylolisthesis[18], for example, showed that recurrence of leg pain was predictable if a prophylactic fusion was not performed at the time of the nerve decompression procedure. The performance of lumbar fusion in the case of spondylolisthesis is now considered routine, with minimal disagreement among the guidelines (although this is being tested as one arm of the randomized SPORT study[19]).

The other indications for lumbar fusion focus on improvement in axial lumbar pain (i.e., near the midline and not involving nerve roots or leg pain). These indications include lumbar instability, such as degenerative lumbar scoliosis, spondylolisthesis for axial pain alone, and for less common problems, such as discitis, lumbar flat back syndrome[20], neoplastic bone invasion and collapse, and chronic fractures, such as osteoporotic fractures which develop into burst fractures over time.

In general, anterior lumbar fusion procedures have been recommended for the treatment of axial low back in young individuals (i.e., aged 20 to 40 years), who on MRI scan have “dark disc syndrome”, and who have severe, concordant axial back pain upon discography. The usual criteria to consider an anterior lumbar fusion (or anterior lumbar arthroplasty) include a young person (average age of 40 years or younger) with either one or two dark discs on MRI scan, a concordant discogram indicating the axial pain is likely arising from the degenerated joints, and failure of previous conservative measures to improve the back pain over a period of time, with a minimum of six months' conservative treatment. As patients age into their 40's and 50's the disc and facet degenerative processes slowly worsen, and it is much less likely to find patients with isolated arthritis. Therefore anterior fusion is less often indicated for older patients. Posterior fusion may be preferable in such cases in order to stabilize facet joint disease. Of note, the posterior approach itself involves significant muscle dissection, resulting in severe back pain in the post-operative period, and is avoided by some surgeons.

The discogram procedure itself remains highly controversial, and recent reports suggest that relying on the MRI findings of dark disc and limiting the discogram to just those levels may improve definition of a "positive discogram".[21-24] However, the high rate of false positives with normal disc spaces is problematic, as well as the high rate of prevalence of dark disc syndrome.[25]

An alternative to lumbar spinal fusion for patients with axial back pain and isolated disc disease is to replace the disc with an artificial mechanical device. This procedure, called an arthroplasty, has the potential benefit of enhanced motion and perhaps decreased adjacent segment stenosis, although this has not been proven. Two such disc replacements, Charité and ProDisc, have been approved by the FDA.

In the elderly population, the most common indications for lumbar fusion are spinal instability, particularly spondylolisthesis and severe lumbar degenerative scoliosis, or threatened instability, such as severe facet degeneration leading to lumbar stenosis (laminectomy for treating lumbar stenosis may have led to instability).

Almost all lumbar spine surgery, including lumbar fusion, is considered “elective” or “optional” in the context of medical care overall, and performed almost solely to reduce the subjective patient symptoms of axial lumbar spine or radicular leg pain. Thus, patient education, to inform patients of their choices is considered critical. For example, a study assessing the usefulness of a video outlining treatment options for lumbar stenosis found that the rate of patients electing lumbar laminectomy decreased from over 40% to 20% of those enrolled, after viewing the video.[26] The video highlighted the large differences between patients' views on surgery for the same symptoms and the same degree of stenosis on MRI scans, based on the perceived worth of the outcome in terms of their own, individual lifestyles. Rarely in the lumbar spine are there any significant consequences to not having surgery performed, except for the continued pain syndrome, hence it is hard to categorize lumbar spine surgery as “necessary”. Critical patient information that should be provided includes data on outcome (i.e., likelihood of relief of back or leg pain), risks of the procedure (i.e., anesthesia, infection, hemorrhage, neurological worsening and non-fusion/hardware issues), and the recovery time needed to regain normal activities.

Common Surgical Approaches for Lumbar Fusion

Almost all spine hardware was developed as primitive prototypes in the 1960's and 1970's, particularly the use of rods (such as Harrington rods) and bone screws. These reached the clinical spine market in the 1980's, including pedicle screws and plate constructs, as well as the more recently introduced metal and graphite cages, which act as spacers in the interspace.

Prior to the 1980's both anterior and posterior non-instrumented lumbar fusions were commonly performed, using primarily bone graft in the disc space anteriorly and/or posterolaterally over the transverse processes, or over the facets and intact lamina. As pedicle screws became more widely used, it was noted that the rate of fusion increased from ~65% with bone graft alone to nearly 95%, with the instrumentation to provide immediate internal support for the bone graft. However, bone graft is more flexible than the metal (titanium and stainless steel) used in pedicle screws. Thus, the insertion of screws and rods (as with a typical pedicle screw fusion construct) may lead to the spine being much "stiffer", as compared to a non-instrumented anterior or posterolateral fusion with bone graft alone. Such increased stiffness is hypothesized to lead to increased degeneration at spine segments adjacent to the fusion, so-called adjacent segment stenosis.

In an interbody fusion, a structural bone graft (such as a femoral allograft ring) provides both structural support for the spine as well as a conductive material providing a framework for later fusion. A recent alternative is the use of inert metallic or graphite cages to provide support, the internal hollow structure of these cages providing room for internal bone graft. An interbody fusion can be performed either from an anterior approach (i.e., through the abdomen, transperitoneal or retroperitoneal approach) or from a posterior approach (through the back muscles and working around the nerve roots). The use of small autografts or allografts inserted into the disc space is an old procedure, pioneered in the 1950's by Cloward, and termed posterior lumbar interbody fusion (PLIF). The disadvantage of this procedure is that the approach, with partial facet removal, tends to weaken spine support structures, and there is a high incidence of the bone graft dislocating, often into an adjacent nerve root. Additionally, a considerable degree of nerve root retraction is needed to place the grafts, often incurring additional leg pain and/or paresthesias from nerve root stretch.

Thus, PLIF has been used less often, and more recently supplanted by a transforaminal approach to the placement of cages into the disc space, termed transforaminal lumbar interbody fusion (TLIF®, a term patented by DePuy). This interbody cage placement, along with bone graft, is usually supplemented by pedicle screws and a posterolateral fusion (except in the case of percutaneous fusion approaches). The procedure thus includes both an anterior and a posterior fusion (termed a 360 degree or circumferential fusion) in one exposure.

New alternatives include resorbable implants, which have the advantage of providing some internal support before dissolving, but in the long run not altering the bone properties as with metal.[27] These resorbable cages can also be applied with recombinant human bone morphogenic protein (rhBMP-2) to increase fusion rates.[28]

Bone fusion in ectopic sites (such as the disc joint and posterolaterally along the transverse processes) requires appropriate bone-generating cells to be present (osteoblasts or their equivalent converted from fibroblasts), a matrix along which bone can form, and an extracellular media with appropriate growth factors to promote cellular migration into the matrix and subsequent remodeling with bone formation. The autogenous iliac crest is ideal, since the patient's own bone marrow cells are present and alive in great numbers, a matrix is present, and extracellular factors (such as growth factors) are also present. However, the harvesting of iliac crest graft is often painful, usually requires a second incision, and can lead to sacral insufficiency fractures, hence newer approaches are often used instead. Bone morphogenic proteins (BMPs) can provide the appropriate growth factors, both to convert fibroblasts into osteoblasts for bone formation, as well as provide part of the extracellular media for cell migration. Collagen sponges and demineralized bone matrix can provide a scaffold for migration of bone cells, but in and of themselves provide neither the cells nor the extracellular media required for bone growth. Other growth factors have also been marketed to enhance fusion, including platelet-derived factors among others, as well as factors derived directly from the iliac crest to provide cells and factors.

Study Outcome Measures for Lumbar Fusion

A variety of measures of patient outcomes has been used in clinical studies of low back pain. A standardized set of clinical outcomes measures would make it easier to compare the results of clinical studies of similar treatment. Historically, one of the most common outcomes is for patients or treating physicians to rate outcomes on a categorical scale such as *excellent-good-fair-poor*. Results are sometimes presented by reporting the proportion of patients reporting a successful result by aggregating those reporting *excellent* and *good* outcomes. However, such scales have not been precisely defined and may vary from study to study; these factors make it difficult to pool results in the form of a meta-analysis.

The two types of outcome measures included in most contemporary studies include patient-reported general and spine specific measures, and radiographic outcomes. Attempts are currently being made to standardize these and other outcome measurements in clinical trials and other types of outcome research.[29]

In most recent studies both a general patient-centered outcome measure (Short Form – 36 [SF-36]) and a spine specific measure (typically Oswestry Disability Index [ODI])[30] have been included. The FDA has chosen a minimum 15-point change in ODI for spinal surgery patients as a clinically meaningful difference. The general pain scale and the combined pain and function scale from the SF-36 are as responsive as ODI to changes in low back and leg outcomes associated with spine surgery.[31] Both the SF-36 and ODI are equally affected by non-spine-related morbidity, such as depression.

Since lumbar fusion is almost solely for relief of a completely subjective symptom, pain, these patient-centered approaches are the best clinical outcome measures, and neurological outcomes are important. Prospectively collected measures are more reliable than measures based on patients' recall, since most patients do not accurately recall their health status at a remote time point, particularly with a surgical procedure involved.[32] Measures such as patient satisfaction are based on a patient's ability to accurately recall presurgical pain and other symptoms. Despite potential bias, these measures are commonly used and reported in the literature, including recent reviews of the spinal fusion literature.[1, 2]

Radiographic outcomes have commonly been used as a surrogate outcome measure in studies of spinal fusion.[33] Radiographic outcomes assess the primary goal of a fusion: is there bony bridging across the spine motion segment and reduced motion? Certain technical issues lead to some uncertainty in the radiographic ascertainment of fusion; for example, in the face of metallic hardware, bony interconnection can be difficult to assess due to artifact. Its use as a surrogate outcome is also limited by the fact that radiographic outcomes do not necessarily correlate with patient-oriented clinical outcomes such as pain scales, ODI, or satisfaction with surgery.[34]

Studies Assessing Lumbar Fusion: Design Limitations

Several trials from Europe (Norwegian, Swedish and Medical Research Council) have compared lumbar fusion for treatment of axial lumbar spine pain to a rehabilitation program, even though the rehabilitation programs offered in the trial are not clinically available outside of the trial. In US studies, such non-surgical controls have seldom been used, under the assumption that 1) surgical candidates have already failed all such conservative measures, including pain medications, orthotics (corsets), spine injections, and rehabilitation treatments, and 2) that the natural history of the disease, at least among patients who have not responded to a trial of conservative management, does not involve improvement over time. In this context, the patient is his/her own internal control. Patients are, therefore, randomized to various surgical interventions, for example, anterior lumbar fusion compared to anterior lumbar arthroplasty.

METHODS

Key Question to be Addressed

In patients 65 years of age or older with degenerative disc disease (DDD) and/or degenerative joint disease (DJD) of the lumbar spine, what is the evidence regarding indications and outcomes including adverse events (overall net health benefit) of lumbar spinal fusion as compared to non-surgical conservative treatment/management or other surgical strategies?

Literature Review

We identified candidate studies from a variety of sources. First, known recent systematic reviews and other recent publications brought to our attention by the sponsor of this report[35, 36] were used to identify previous studies. Second, recently available data was sought from leads in the news, from experts in the field and on the FDA web site (for example, recent approval of the second arthroplasty device, the Pro-Disc[37]). Third, a computerized bibliographic search of MEDLINE was undertaken both to update the search described in the Cochrane review[38] and also to identify non-RCTs (since the Cochrane review was limited to RCTs). Note that non-RCT studies were primarily identified from citations in recent systematic and non-systematic review articles on the topic.

The MEDLINE search is shown in Appendix A, and was limited to studies published with abstracts in the English language since 2003. We separately reviewed 806 citations likely to be primary studies and 273 studies likely to be review articles.

Citations, including the title, abstract, and other citation information, were reviewed by a physician reviewer and selected for further evaluation. Full texts of those citations selected were retrieved, and then the full text article was reviewed. If it fulfilled the selection criteria (see below), data was abstracted into an evidence table by a physician investigator. All evidence tables were reviewed and categorized for relevance by the neurosurgeon author.

Inclusion and Exclusion Criteria

1. Patients – Patients with axial (or mechanical) low back pain due to degenerative joint disease of the lumbar spine (DJD, including disc degeneration or DDD, and facet joint disease; both together termed collectively as spondylosis); patients with latent or manifest lumbar spine instability (spondylolisthesis, scoliosis, or severe facet joint degenerative disease). Patients may have low back pain symptoms or not; or symptoms of neurogenic claudication with leg pain. [Note studies with patients age < 65 were not excluded; although, the intended population is those older than 65 years of age.] Prior studies suggest that these distinct subdiagnoses among indications for lumbar spinal fusion may have prognostic implications[39], therefore, we attempted to categorize the study populations according to the diagnostic subgroups used by Bono and Lee.[39] The categories are:

   DDDsp = degenerative spondylolisthesis (primarily due to facet incompetence)

   DH = herniated disc (DH)

   DDDsc = degenerative scoliosis (DSc)

DDDu = unstable degenerative disease with dynamic instability

DDDs = stable degenerative disc disease (no evidence of instability)

DDDn = degenerative disc disease not specified as either DDDs or DDDu, excluding DDDsp, DH, or DDDsc

Because these subgroups were limited to a classification for degenerative disc disease, it did not include categories for the entire range of study populations included in this review. Therefore, we added three additional categories:

IS = isthmic spondylolisthesis

SSa = spinal stenosis alone

Src = revision surgery

2. Intervention – Any of several different surgical techniques of fusion (including instrumented [e.g., using screws, metal and bone cages] or non-instrumented fusion) –
    a. Posterior approach
        i. Posterolateral fusion surgery with or without pedicle screws
        ii. Posterior lumbar interbody fusion (PLIF) or transforaminal lumbar interbody fusion (TLIF®) surgery
        iii. Other
    b. Anterior approach
        i. Anterior/posterior combined lumbar fusion
        ii. Anterior lumbar interbody fusion
    c. Components used for lumbar spinal fusion

i. Bone graft from the iliac crest (autogenous graft or autograft)
ii. Bone graft from donor (allograft)
iii. Bone morphogenetic proteins (BMP)
iv. Collagen sponges
v. Demineralized bone matrix
vi. Platelet-derived growth factors
vii. Other

3. Comparisons/controls –
   a. no surgery
   b. conservative treatment [Note that chiropractic interventions will not be included] – including
      i. injection
      ii. medication (particularly narcotic pain medication)
      iii. rehabilitation
   c. other (non-fusion) surgical such as
      i. lumbar arthroplasty (ie, Charité Lumbar Disc arthroplasty or Pro-Disc)
      ii. dynamic stabilization devices, etc.

4. Outcomes –
   a. Short term outcomes
      i. quality of life (QOL, e.g., SF-36)

    ii. Oswestry Disability Index (ODI)
    iii. pain
    iv. narcotic use
    v. other reported outcomes (mortality, infections, other morbidity)

b. Persistence of benefits/harms over time—long term results –
    i. incidence of adjacent segment disease
    ii. reoperation
    iii. pain
    iv. narcotic use
    v. QOL
    vi. ODI
    vii. other reported outcomes

[Note that radiographic evidence of fusion was recorded, but, if it was the only outcome measure, the study was not included.]

5. Design/Other –
    a. For randomized control trials comparing fusion to a control intervention, we did not impose any restriction on study size.
    b. For uncontrolled studies (including case series (retrospective) or uncontrolled clinical trials (prospective) or cohort studies) we required a minimum sample size of 50 patients.
    c. We included only study reports available in the English language.

Quality Evaluation and Assessment

Studies were evaluated primarily according to study design as the main feature affecting the internal validity. In addition, for controlled trials important issues including randomization, adequacy of concealment of allocation, blinding and the completeness of accounting of drop-outs and withdrawals were evaluated. Furthermore, additional features relating to the internal validity of individual studies were commented upon, when recognized, by methodologist reviewers.

External validity, or applicability, was evaluated in relation to the population of interest. In particular, careful attention was given to characterizing the study population in terms of the underlying back disorder, previous surgery (laminectomy or fusion), and age of the population.

RESULTS

The results of the literature search and selection process are described in Figure 1 below.

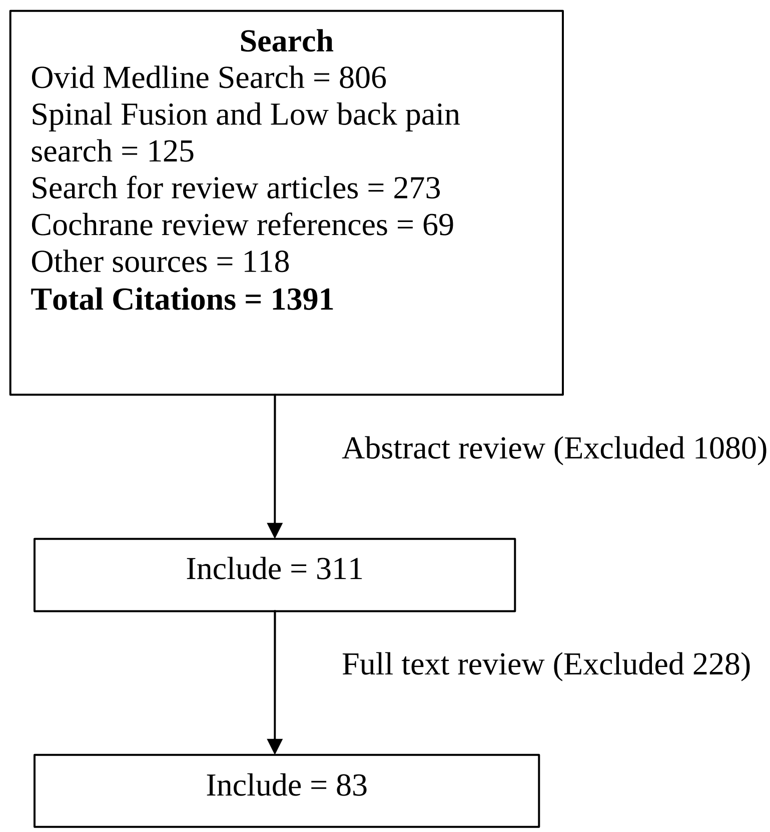

Figure 1: Number of citations identified and selected in the literature review process.

The discussion of evidence begins with studies most relevant to the comparison in the key question; then describes other types of evidence that are indirectly related to the comparison articulated in the key question. The discussion will follow this outline:

A. Lumbar spinal fusion for axial back pain due to DDD, comparisons with non-surgical treatments
B. Anterior lumbar interbody fusion for axial back pain due to DDD, controlled and uncontrolled studies
C. Posterior approach fusion procedures for axial back pain due to DDD, controlled and uncontrolled studies
D. Total disc arthroplasty for axial back pain due to DDD, comparisons with lumbar spinal fusion.
E. Lumbar spinal fusion for spondylolisthesis
F. Incidence of adjacent segment disease after lumbar spinal fusion
G. Instrumented versus non instrumented fusion
H. Studies of lumbar spinal fusion in older patients, with particular emphasis on perioperative complications
I. Complications associated with lumbar spinal fusion
J. Techniques to augment fusion, interbody and transverse process

Lumbar Spinal Fusion for Axial Back Pain Due to DDD, Comparisons with Non-Surgical Treatments (Table 1)

There is no randomized control trial (RCT) evidence that directly compares lumbar spinal fusion with non-surgical conservative treatments in populations older than 65 years of age.

A recent systematic review and meta-analysis from the Cochrane Collaboration[1, 38] reported on two RCTs that compared, for the treatment of axial low back pain, posterior transpedicular fusion and postoperative physical therapy (PT), cognitive therapy or exercises.[15, 17] While the Norwegian study by Brox et al.[15] found no differences between fusion and exercise and rehabilitation, the Swedish study by Fritzell et al.[17] reported better results from fusion for both ODI and pain when compared to conventional physiotherapy. The magnitude of improvement in ODI was an average of 11 points at two years for fusion, but only two points for conventional PT; a difference of nine ($p<0.05$). Despite this one positive trial, in aggregate, the review concluded that no conclusions were possible about the relative effectiveness of fusion.

Since the Cochrane review was last updated in 2005, two additional RCTs have been published.[14, 16] One of these, conducted in patients with axial back pain after previous discectomy, did not show any significant improvement in axial back pain or ODI compared to cognitive intervention and exercises.[14] The MRC trial,[16] designed to test superiority of lumbar fusion, was powered to detect a difference of only four points in ODI. Although the study did find a statistically significant improvement in ODI among lumbar fusion versus a cognitive-behavioral therapy (CBT) based rehabilitation program, the authors point out that the difference, at approximately 4.1 points in ODI, is smaller than that generally felt to be clinically important. Other outcomes such as shuttle walk and quality of life (SF-36) did not show any statistically significant differences between treatments.

The four trials differed in the intensity of the rehabilitation or exercise intervention. While the Cochrane review commented that the Swedish study[17] used an ineffective control, Brox et al.[14] used a more intensive, “modern,” rehabilitation approach including education and three weeks of supervised intensive exercise sessions. The

MRC trial[16] used a control intervention similar to the Norwegian study by Brox et al.[15] in the type of intervention, yet still more intensive and longer in duration.

It is important to note that the mean age for these study populations ranges between 40 and 43.5. Overall, two of the trials showed statistically significant differences between surgical therapy and rehabilitation in ODI[16, 17], but in both cases the relative difference in ODI was, on average, less than the minimal clinically important difference.

Anterior Lumbar Interbody Fusion for Axial Back Pain Due to DDD, Controlled and Uncontrolled Studies (Table 2)

A recent review that used uncontrolled studies to compare different fusion procedures in terms of fusion rate and clinical outcome estimated that ALIF accounted for the lowest proportion of total fusions performed in the 1980's and 1990's.[2] In that review, fusion rates for ALIF were 86%, based on a total of 583 patients. This compared to fusion rates of 85%-91% for PLF, PLIF and A/P fusions. *Good* or *excellent* subjective clinical outcomes (as rated by patients on a categorical scale) were reported in 70% of ALIF compared to 73-88% for other fusion procedures.

We summarize ten recent studies that describe outcomes associated with ALIF for patients with DDD in Table 2. Most of these studies were designed to compare different techniques to promote interbody fusion. None of these studies included a nonsurgical or conservative management control group.

Data from studies of patients undergoing ALIF show that the change in ODI from before surgery to one or two years after surgery exceeded 15 points in every study, with changes ranging from 16 to 31.3 points. Similar improvements were shown in other back-specific outcomes and pain outcomes, though these were less consistently reported. The lack of concurrent non-surgical control groups makes it difficult to estimate what the difference between ALIF and non-surgical treatment would be were these strategies compared directly. The 2-12 point average improvement observed in non-surgical groups in the RCTs of fusion for axial back pain (Table 1) suggests that ALIF would be expected to exceed non-surgical treatment at 2 years by as few as 4 to as many as 30 points on the ODI. This greater change in ODI from before to after surgery for ALIF compared with posterior or A/P fusion (as observed in the controlled trials) might be explained by the fact that anterior spine procedures, through either the peritoneum or retroperitoneum, require no posterior muscle and ligamentous dissection, hence result in less post-operative axial back pain associated with the procedure itself.

There are notable risks to either anterior approach, particularly the rate of retrograde ejaculation in men and sexual dysfunction in women (from dissection around the sympathetic lumbar chain) as well as risks of bowel perforation and vessel disruption. The incidence of retrograde ejaculation ranged from 1.7 to 17.5%.[40-44] One study[42] reported that the incidence of retrograde ejaculation was ten times higher for a transperitoneal approach than a retroperitoneal approach. Minimally invasive (i.e., laparoscopic) ALIF is technically more complicated but did not demonstrate any significant clinical or radiographic differences in a study of 54 patients.[45]

Posterior Approach Fusion Procedures for Axial Back Pain Due to DDD, Controlled and Uncontrolled Studies (Table 3)

Posterior fusions have been recommended for axial back pain in spite of the posterior muscular tissue dissection needed. One recent review reported fusion rates by fusion location from a meta-analysis of mostly uncontrolled studies from the 1980s and 1990s.[2] Fusion rates were 85%, 89% and 91% for PLF, PLIF and A/P fusions, respectively. The same review estimated the rate of *good* or *excellent* clinical outcome among studies from the 1990s as 73%, 88% and 76% for PLF, PLIF and A/P fusions, respectively. The Cochrane review[1] reported on two RCTs comparing A/P fusion with PLF[46, 47] and concluded that there was no difference in fusion failure, complications, or patient-judged improvement in symptoms. However, one trial reported a lower reoperation rate for A/P fusion compared with posterolateral fusion.[46] The Cochrane review reported no other comparisons between different types of posterior approach fusion procedures.

We describe 23 reports in Table 3 which include studies of PLF, PLIF, TLIF® and A/P fusion. Many of these studies are comparative studies, some randomized comparisons of different instrumentation or fusion techniques. Two comparative studies including one RCT[47] and one retrospective study[48] present comparisons between specific types of posterior procedures in terms of ODI. Fritzell et al.[47] reported similar reductions in pain and ODI (ranging from 9 to 15 points from before surgery to two years after surgery) among three groups: non instrumented PLF, PLF+pedicle screw fixation (PSF), and PLIF (or A/P fusion according to surgeons' preference). In contrast, Glassman[48] reported significant differences in ODI improvement among PLF, PLIF/TLIF®, ALIF and A/P fusion such that PLF and ALIF groups improved more than A/P fusion and PLIF/TLIF® groups, respectively. However, baseline imbalances in ODI, SF-36, age, gender, and number of levels fused may confound the interpretation of those comparisons.

Other studies do not provide direct comparisons between the different fusion procedures, but provide additional estimates of changes in clinical outcomes observed following surgery.

Total Disc Arthroplasty for Axial Back Pain Due to DDD, Comparisons with Lumbar Spinal Fusion (Table 4)

We identified seven recently concluded trials of arthroplasty for axial back pain due to DDD. These trials include data on the Charité artificial disc[43, 49], Prodisc, Prodisc II and Prodisc-L[37, 50-53] and Maverick[54] (Table 4). All of the controlled trials of arthroplasty devices used a comparison with anterior lumbar interbody fusion (ALIF)[43] or anterior-posterior combined fusion.[37, 53, 55] Inclusion criteria for all of these studies required degenerative disc disease at a single level, or no more than two adjacent levels, with no other spine disease (such as degenerative facet joint disease, spondylolisthesis, scoliosis or spinal stenosis). Mean age, when reported, ranged from 39.5 to 47.5 among these study populations.

In each study, the change in ODI from preoperative baseline to postoperative follow-up (ranging from six months to 31 months) exceeded 15 points on the ODI scale for arthroplasty arms, as well as for ALIF or A/P fusion control arms. None of the studies detected any statistically significant differences in ODI or pain between arthroplasty and fusion arms (except at an early time point in one study[53]). However, each of these trials appeared to be designed as non-inferiority studies. They support the conclusion that arthroplasty is non-inferior to ALIF or A/P fusion. Two trials clearly specified a non-inferiority hypothesis for “clinical success rate” with predefined threshold for differences of 12.5%[56] and 15%[43] between groups. Clinical success rates were defined differently between these studies, in both studies using a change in ODI among other criteria, but requiring a 15 point change from preoperative value in one study[56], or at least a 25% change from preoperative value in the other.[43] Given the baseline ODI of 50-52 points, a 25% change could be achieved with less than a 15 point change from baseline scores in most cases, but the change in mean ODI observed, indicates that most patients did exceed this value. In summary, the comparative studies of Charité artificial disc demonstrate non-inferiority to ALIF and the randomized study of ProDisc-L demonstrates non-inferiority to A/P combined fusion.

The most complete reporting of adverse events comes from an FDA summary from a clinical trial of the PRODISC-L.[37]

Lumbar Spinal Fusion for Spondylolisthesis (Table 5)

We identified several existing reviews focusing on lumbar spinal fusion for spondylolisthesis.[57-59] Each of these reviews catalogs similar evidence. Wenger et al.[59] describes fusion rates and success rates in 14 studies from1991-2003; Kwon[57] describes 34 reports from 1966-2003 and reports that anterior-posterior combined fusions were more likely to have successful fusion, and a successful clinical outcome, similarly, instrumented versus non instrumented fusions were also more likely to have successful fusion and clinical outcome. The neurosurgery guidelines[12, 13, 23, 33, 34, 58, 60-70] describe 32 studies between 1985-2002 of patients with both spinal stenosis and degenerative spondylolisthesis.

We have summarized (Table 5) ten studies from 1997 to 2005. The only trial directly comparing spinal fusion surgery to conservative treatment is the trial reported by Moller and Hedlund[71] which also reports long-term follow-up in a separate report.[72] This study found improvements in the Disability Rating Index with surgery compared to exercise at two years and improvements in pain index as well; however, in subsequent long-term follow-up, pain index worsened in the surgery group, but improved in the exercise group, so that there was no significant difference in pain index at long-term follow-up. Similarly, there was no significant difference in ODI at long-term follow-up.

One non-randomized prospective study did include a conservative treatment comparison group.[73] This study found that the control group (n=18), with less impaired pain and walking ability at baseline, did not improve over the two-year observation period. The patients undergoing surgery (laminectomy with or without fusion) demonstrated improvement in the Japanese Orthopedic Association (JOA) score, the outcome measure utilized in this study. Other studies included controlled studies comparing different fusion techniques (instrumentation or other components to augment fusion rates).[74-76]

Incidence of Adjacent Segment Disease after Lumbar Spinal Fusion (Tables 6, 7, and 8)

Since lumbar fusions stabilize DJD at the levels fused, it is unlikely for progression of DJD at these levels (unless there is a pseudoarthrosis or hardware failure leading to lack of fusion). It is hypothesized that fusion at one level increases stress on joints at adjacent levels during ordinary spine motion, hence leading to accelerated DJD at these adjacent levels, as compared to the natural history of DJD progression. Table 6 describes studies that permit calculation of the risk of adjacent segment disease (ASD) following spinal fusion.

We have defined symptomatic adjacent level stenosis as that leading to reoperation, usually for instability or DJD progression and lumbar stenosis at that adjacent level. However, most studies (with the exception of Ghiselli et al.[77]) do not give the time to reoperation from the initial surgery on a patient by patient basis. Hence, the rate of ASD is annualized for comparison between studies, by using the overall rate and the average follow-up time. The annualized rate of adjacent segment disease for reoperations ranges from 0% to 3.7% per year.

As a comparison to the reoperation rate for fusion related ASD, we identified several relatively recent large studies that describe the rate of reoperation following laminectomy for spinal stenosis or other indications (Table 7). Laminectomy usually is performed without fusion when there is no evidence of instability at the time of surgery. Over time, following laminectomy, there is progression of disease. Recurrent lumbar stenosis may occur at the same level (due to persistent or even enhanced motion at that level) or at adjacent levels. This may represent the natural history of DJD progression as a comparison for the rate of ASD following a fusion. The annualized rate of reoperation among these studies ranged from 1.7% to 3.4% per year. Such reoperations were usually performed for recurrent stenosis or for instability which can develop over time after a laminectomy. This is a similar rate to the ASD rate after fusion, suggesting that DJD progression is the major factor leading to reoperation, rather than an intrinsic acceleration of DJD. The SPORT study,[19, 78] when results are available, may provide directly comparable data after its long-term follow-up, since there are both laminectomy and fusion (for spondylolisthesis) arms.

Many studies in the literature report the incidence of adjacent segment disease based on radiographic findings. These rates are described in Table 8. The rate of MRI disease progression is somewhat higher. Various definitions for which radiographic findings are considered disease are described in the table. Furthermore, various lengths of follow-up may explain some of the wide variation in the incidence of ASD. For example, in one study[79] patients were followed years later after a lumbar fusion with lumbar MRI scans (average 21 years), which had been performed for isthmic (pars defect) spondylolisthesis. There was more advanced lumbar DJD in the fusion group, compared to a healthy control group, but there was no correlation with Oswestry or other clinical outcome measures. A shorter term study[80], two years average, demonstrated on follow-up MRI that there were no more advanced adjacent level changes at levels with significant DJD at the time of the fusion, than normal appearing levels. A study of L4/5 fusion assessed the L5/S1 interspace and DJD at an average of 7.3 years later, suggesting that the L5/S1 level did not appear to show advanced DJD over this time period.[81]

Whether an instrumented fusion may increase adjacent segment disease is another controversial point, but without much evidence.

Instrumented Versus Non-Instrumented Fusion (Table 9)

Studies have shown that instrumentation may increase the radiographic fusion rate[2]; few have evaluated symptomatic outcomes. Among studies that have attempted to correlate radiographic fusion with clinical symptoms, an association has not consistently been found.[34]

There have been several direct comparisons between instrumented and non-instrumented fusion. The Cochrane review[1] reported eight RCTs comparing posterolateral fusion versus bone graft only, that use of instrumentation was associated with a higher rate of radiographic evidence of fusion (OR=2.2 ; 95% CI 1.1, 4.8) and a higher rate of "good clinical outcome" (OR 2.05; 95% CI 1.19, 3.54). Another recent review included not only RCTs, but also case series and uncontrolled trials[2] and reported significantly higher fusion rates with instrumented (rigid, 88%; semirigid, 91%; any instrumented, 89%) or noninstrumented fusion (84%). Unlike the Cochrane review, this analysis found no significant difference between *good or excellent result* rates between instrumented (75%) and non-instrumented (79%) fusions (p=0.089).

Not covered in the Cochrane review was one recent RCT of patients with axial back pain randomized to various fusion approaches which found significant improvement in several outcome measures including ODI and pain (Swedish study group).[17] In a subsequent report comparing the different treatment arms[47], the least demanding surgical technique (posterolateral fusion without instrumentation), led to ODI results not significantly worse than the instrumented groups (posterolateral fusion and anterior/posterior combined fusion, but with a decreased fusion rate (72% vs 91%). This result was similar to that of an earlier study[74], in which the addition of instrumentation to posterolateral fusion did not improve pain or functional status.

Long term data regarding the association between successful fusion and symptoms are inconsistent. In one long-term study[82] of 47 patients, pain was improved in patients with a solid fusion (86%) versus those with pseudoarthrosis (56%), suggesting that the benefits of fusion may require years to fully ascertain. On the other hand, Lamberg et al.[83] indicated that on long-term follow-up (nearly 21 years average) after lumbar fusions for isthmic spondylolisthesis, there was minimal correlation between clinical and radiographic outcomes. Madan et al.[84] compared ALIF between anterior cage fixation and bone graft, and found that fusion rate increased with the anterior cage, but did not correlate with ODI. Lidar et al.[85] indicated that enhancing disc space height posteriorly (with PLIF) did not improve pain or radiographic fusion rates significantly, compared to posterolateral fusion alone.

Studies of Lumbar Spinal Fusion in Older Patients, with Particular Emphasis on Perioperative Complications (Table 10)

We separately tabulated studies that report on older populations (mean age ≥ 55) as potentially more applicable to the over-65 years of age Medicare population. Table 10 describes these studies and the reported rates of perioperative and later complications.

Four studies include data exclusively on populations over 65 years of age[86-89], two of which use higher age cut-off of 75 years[89] and 80 years[88].

Kilincer et al.[87] studied the effects of advanced age on posterior lumbar fusion, assessing 129 patients retrospectively, and comparing the complications in older (age ≥ 65 years) and younger (age < 65 years) patients. The younger patients more often underwent procedures involving instrumentation. The total complication rate was 8.75%, with 12.5% (5/40) in older patients and 5% (2/40) in younger patients (p>0.05); however, hospital stay was longer in the younger patient group. Carreon et al.[90] indicated that perioperative complications increased with older age, and overall their results suggest a high complication rate (10% wound infection rate, for example). Among the other studies, none of which provided age group comparison data, there was a high degree of variability in the rates reported for specific adverse events, total major, and total minor complications. At least some of the studies reported high rates of complications; however, comparisons with complication rates in studies of younger patients is difficult.

Few studies in older patients provided data on efficacy outcomes such as pain, functional ability or quality of life.

Complications Associated with Lumbar Spinal Fusion (Table 11)

Complications associated with fusion surgery are different for anterior versus posterior procedures, and generally fall into six main categories: 1) risks of general anesthesia; 2) infection; 3) hemorrhage and unexpected bleeding intra-operatively or post-operatively; 4) risk of the approach, particularly for the anterior approach; 5) neurological complications; and 6) non-fusion and hardware failure complications. Finally, comorbid conditions can modify risks; for example, one study showed that patients with diabetes mellitus had a statistically significant greater risk of complications (>50% versus 21% in controls) following lumbar fusion, particularly infection and nonunion.[91] Other risk factors for complications include age over 60 years, smoking, increased body mass index and alcohol abuse.[92]

Mortality was rarely observed and reported in individual series or trials (Table 11).[40-42, 89, 91, 93-100] A recent large national inpatient study sample (NIS) indicated that fusions resulted in less than 1% mortality for patients older than 60 years.[3] This is similar to mortality observed among medicare beneficiaries undergoing spinal fusion from 1985, in whom lumbar fusion resulted in a mortality between 1% and 1.3%.[86]

The range of rates reported for specific types of complications of lumbar fusion surgery are reported in Table 11. Certain specific complications were associated with certain types of fusion procedures. Anterior fusion, by either retroperitoneal or transperitoneal approaches, results in a risk of retrograde ejaculation in men from dissection around the sympathetic lumbar chain. This risk ranged from 5.5% -17.5%; one study[42] reported that a transperitoneal approach was associated with a ten times greater risk of retrograde ejaculation compared to a retroperitoneal approach. In the anterior approach, vessel disruption was observed in 1.9%-2.2% in the studies reviewed.

The posterior approach involves a risk for neurologic injury that is theoretically greater than that for anterior approaches. Scaduto et al.[99] suggested that PLIF procedures involved more neurological complications (31%) than ALIF (8%) for the treatment of axial low back pain, particularly following previous lumbar surgery. However, data from other series and trials results in wide, overlapping estimates for neurologic complication rates: 8%-17% for ALIF and 2%-31% for PLIF. Dural tear or CSF leaks are also a theoretical risk associated with the posterior approach; these were reported in 5%-20% of operations involving a posterior approach, compared to none in anterior approach only surgery (ALIF). Donor site pain, independent of approach to the lumbar spine, is reported at rates ranging from 5%-18%.

Techniques to Augment Fusion, Interbody and Transverse Process (Table 12)

We found a guideline summarizing six studies of bone graft extenders and substitutes from 1999-2003.[62] This review concluded that there are "very few data regarding the use of…" synthetic bone graft substitutes or extenders for fusion in lumbar degenerative disease; however it singles out rhBMP-2 as having sufficient data to support its use as an alternative to autograft bone for interbody fusion (it is FDA approved for ALIF) or PLF.

We found several additional studies from 2003-2006 (Table 12). Studies of rhBMP-2 in ALIF and PLIF lead to no worse fusion rates than autologous iliac crest bone graft.[101, 102] Two studies of coralline hydroxyapatite in PLF suggested coralline hydroxyapatite alone led to lower fusion success than autologous iliac crest bone graft or the combination of autologous iliac crest bone graft and coralline hydroxyapatite.[103, 104] One study of autologous growth factor (AGF) gel in TLIF® procedures suggested AGF actually decreases the fusion rate.[105]

Several smaller studies did not meet our selection criteria. These studies report findings consistent with those that we have included in this analysis. Cammisa et al.[106] indicated that Grafton® DBM can extend the amount of autograft or local bone used in the graft, with nearly equivalent results. However, AGF (derived from arterial blood at the time of the procedure) did not facilitate fusion in one study of 32 patients.[107] In another study of 23 patients, AGF also did not enhance spinal fusion rates[108], whereas Jenis et al.[109] indicated that AGF plus allograft resulted in a similar interbody fusion rate compared to iliac crest graft, though the cases were supplemented with posterior fusion.

Few studies reported extensive data on symptom or functional outcomes; and those that did report these data did not identify any statistically significant or clinically important differences.

DISCUSSION/LIMITATIONS OF THE LITERATURE

Many of the limitations found in the literature supporting lumbar spinal fusion have been described previously.[2] Documentation deficiencies noted among 84 reports from 1979-2000 included: study design (45%); brace use (45%); fusion criteria (20%); graft source (12%); fusion rate (5%) and fusion location (2%). Our findings include similar deficiencies, which we will not discuss further.

We will discuss several limitations that are particularly relevant to the goals of this review, which, in contrast to previous reviews, focuses on patient-centered outcomes, comparisons with non-surgical treatment, and data applicable to patients over 65 years of age.

The outcomes reported in the literature are heterogeneous. Patient centered outcomes are desirable, and include pain, disability, and quality of life. However, adverse effects are also important but are not easily balanced against standard efficacy outcomes. Traditionally, surrogate outcomes such as radiographic evidence of fusion success have been reported. Clinical success rate, in older literature is often judged by treating physician, or judged by patients based on recall. Indeed, even the Cochrane review[38] used clinical success as the outcome measure for its meta-analyses. The present review concentrates upon not only more recent literature, but also on more reliable outcome measures.

More recently, it has become commonplace to use formal instruments to measure health status, pain or functional ability both preoperatively, and at follow-up, and estimating efficacy from the change in these measures. While the literature displays several measures that have been used, the ODI is becoming the de facto standard for functional outcome. The SF-36 is the most commonly reported health related quality of life (HRQoL) measure, and pain measures, while usually measured using a Visual Analogue Scale (VAS) approach, remain non-standardized.

In controlled studies comparing lumbar spinal fusion to non-surgical treatment, differences in not only the patient populations but also in the non-surgical treatments used hamper the ability to compare the results of studies. Non-surgical conservative studies varied in intensity, duration, and feasibility in a clinical practice setting.

In uncontrolled studies of lumbar spinal fusion, patient populations are often poorly described, especially if series selected are based on the procedure performed, rather than the presenting complaint or specific diagnosis of the patient. Given that the same procedure may be done for several different conditions (in particular, fusion may be performed when there is spinal instability [spondylolisthesis], for threatened instability [laminectomy, spinal stenosis], or when there is no instability [discogenic back pain]), such lack of specific data about patients' back disorders limits the applicability of the data.

Furthermore, the applicability of controlled trials comparing lumbar spinal fusion to non-surgical treatment to the over-65 years of age Medicare population is severely limited by the fact that all of these studies were performed in populations with mean ages in the late 30's and early 40's, with few subjects in the population of interest (over 65 years of age).

Other studies of spinal fusion performed in older populations (mean ages in late 50's and older) show that older patients receive fusion surgery for different spine disorders and have higher rates of perioperative complications.

One of the few large, multicenter NIH-funded trials proposed on spine surgery, the SPORT trial, includes a randomization for disc herniation, lumbar stenosis and spondylolisthesis patients (to surgery or no surgery), and a secondary cohort analysis on patients who do not agree to randomization.[19, 78] Some preliminary information is available on the characteristics of the patients in the cohort aspect of the trial, but the relative numbers of the randomized and non-randomized aspects of the trial have not been published. However, further preliminary information from this trial may be available beginning in late 2006. The trial is designed to assess the role of lumbar fusion for the basic, common indication of spondylolisthesis; there are, to our knowledge, no planned or ongoing RCTs comparing lumbar fusion with conservative treatment for axial back pain alone in patients without instability.

CONCLUSIONS

There is no randomized control trial (RCT) evidence that directly compares lumbar spinal fusion with non-surgical conservative treatments in populations older than 65 years of age for any indication. Direct comparative trial evidence suggests that lumbar spinal fusion may result in some benefit compared to usual care or a variety of conservative management options in middle-aged patients with axial back pain, who have severe disability (baseline ODI 41-48) or pain from disc disease. These benefits include improvements in back pain or functional disability. In some studies, statistically significant benefits in ODI accrue, but in others, the improvements in ODI are similar for surgery and conservative management groups. The magnitude of benefit is, on average, less than a 15 point improvement in ODI; however, the relative benefit (compared to conservative management) is much lower. Recent trials are from one to two year duration. Conservative management strategies tested in controlled trials have differed substantially from each other, and also from clinically available rehabilitation services.

Total disc replacement has no worse outcomes than fusion for a narrower spectrum of patients including middle-aged patients with single level DDD (or post discectomy) and back pain. Theoretical advantages to preserving intervertebral motion (such as reducing adjacent segment disease) have not been demonstrated in clinical trials, which may have not yet followed patients long enough to demonstrate this potential benefit.

None of the above data concerns use of fusion in older patients (Medicare population) who more often have facet disease, spondylolisthesis, stenosis and other comorbid spine and non-spine conditions with neurological symptoms far worse than axial back pain.

Lumbar spinal fusion has been shown to improve pain and disability in middle-age patients with spondylolisthesis in a randomized control trial. Older populations have shown similar improvements in uncontrolled studies.

We sought additional data on uncontrolled series to address questions about the use of fusion in populations with a wider variety of spine disorders, older patients, the rates of events including adverse events, and the rate of long-term complications such as adjacent segment disease.

Instrumentation in posterolateral fusion is associated with somewhat higher rates of fusion success than the use of bone graft. There is conflicting evidence regarding whether the increase in fusion rates result in better patient-centered outcomes such as pain or disability measures.

Perioperative complication rates associated with spinal fusion in patients over 65 years of age are higher than for nonfusion lumbar surgery, and may be higher than for patients under 65 years of age. Few data are available to evaluate whether the benefit of surgery is similar for patients over 65 years of age compared with patients less than 65 years of age. The rates and types of complications vary by surgical approach and location of fusion; variability in ascertaining, defining and reporting adverse events and complications makes systematic evaluation difficult.

Longer term complications of lumbar spinal fusion surgery include late hardware failure and adjacent segment disease requiring reoperation, which is observed to occur at up to 3.7% per year. Whether fusion accelerates the progression of spine disease is uncertain, however, since similar reoperation rates are observed following laminectomy and non-fusion surgery.

Of ancillary components used to augment fusion, rhBMP-2 with demineralized bone matrix has been shown to provide fusion success rates equivalent to autologous iliac crest bone graft; this has the advantage of eliminating pain (sometimes long lasting) from iliac crest bone harvesting.

TABLES

Table 1. Axial back pain: lumbar spinal fusion versus conservative management

Study	Design	N	Age	Procedure	Follow-up time	Baseline ODI	Follow-up ODI	Other outcome	Comment
Brox 2006[14]	RCT	60	43 yrs (35-50)	PLF+ pedicle screw	1 yr	47	38*	Pain#	
				Cognitive intervention/ exercises		45	32*		
Brox 2003[15]	RCT	64	43.3 yrs. (25-60)	PLF + pedicle screws + physiotherapy	1 yr.	41	26		
				Cognitive intervention and exercise		42	30		
Fritzell 2001[17]	RCT	294	43.5 yrs (25-65)	Fusion (PLF or ALIF) No surgery	2 yrs	47 48	36*,# 46	Pain*,#	
Swedish									
Fairbank 2005[16]	RCT	349	~40	Fusion Intensive CBT-based rehab	2 yrs	46.5 48	34.0*, # 36.1		
MRC									

* indicates significant (*p<0.05 or **p<0.01) improvement from baseline to followup
# indicates significant (#p<0.05 or ##p<0.01) difference between treatment groups

ALIF – anterior lumbar interbody fusion; CBT – cognitive-behavioral therapy; MRC – Medical Research Council(UK); ODI – Oswestry Disability Index; PLF – posterolateral fusion; RCT – randomized controlled trial

Table 2. Axial back pain: ALIF

Study	Design	N	Age	Procedure	Follow-up time	Baseline ODI	Follow-up ODI	Other outcome	Comment
Burkus 2002[110]	Prospective randomized non-blinded	279	42.8	ALIF+ cage (LT-CAGE®) + rhBMP-2 versus ALIF + autogenous iliac crest bone graft	24 mo	53.7 55.1	23.9* 23.8*	Back pain* Leg pain *	
Burkus 2002[101]	Prospective randomized non-blind	46	43	ALIF with threaded cortical allograft dowels + rhBMP-2 versus ALIF + autogenous iliac crest bone graft	24 mo	52.4 55.3	18.9*,# 32.8*	Back pain** Pain – leg**	
Chung 2003[45]	Prospective study	47	50 (27-67)	ALIF Open mini-ALIF Versus laparoscopic ALIF of L5-S1	Open – 30 mo (24-40) Laparoscopic – 43 mo (36-49)	43 41	23* 25*	Pain-VAS* preop postop Laparoscopic 9.1 4.0 Open 9.4 3.7	
Glassman 2006[48]	Retrospective study	497	47 (17–86)	PLF (n=119) PLIF/TLIF (n=152) A/P fusion (n=95) ALIF (n=125)	1-2 yr	55.9 46.1 51.4 47.8	32.8*,# 30.1* 33.5* 26.2*,#		
Greenough 1994[111]	Case series	151	41 median (17–62)	ALIF	23 mos (men) 24mos (women)	NR	NR		Low back outcome score used
Kuslich 1998[112]	Prospective non-randomized clinical trial	947	41.5 (19-73)	PLIF + cage (BAK) (n=356) Or ALIF + cage (BAK) (n=591)	2 yr	NR	NR	Pain pre 1yr 2yr P=0.001 5.0 3.2 2.9 Other Dysfunction (7-32 pt) 15.2	Functional impact scale "similar to Prolo"
Madan 2003[84]	Retrospective series, concurrent controls	51	42 yrs. (25-67)	ALIF + cage ALIF + bone graft	3 yr 4.7 yr	NR	33.3 32.2	Pain drawing: 5.2/5.1 20.9 14.4	ODI categorical outcome similar between groups (p=0.73)
Penta 1997[113]	Retrospective consecutive series, prospective f/u	108	48 yrs (28-73)	ALIF + autologous bone blocks (n=60) or Crock dowels (n=65)	10 - 12.6 years	NR	NR	Pain Median 4 (range, 0-10) Other LBOS Fused 44 (11-75) Nonunion 39 (4-60)	Low back outcome score used
Tiusanen	Prospective	134	30.1	ALIF	5.2 yrs (2-10)	47.8	20*		

Study	Design	N	Age	Procedure	Follow-up time	Baseline ODI	Follow-up ODI	Other outcome	Comment
1996[41] **And** **Tiusanen 1995**[40]	study		(9-60)						
Trief 2006[114]	Prospective study	160	44.2 ± 8.6 (26-67)	ALIF	2 yrs	60.6	39.8*	Pain – back Baseline 1 yr 2 yrs 74.8±21.5 45.3±31.5 44.5±32.0** Pain – leg 61.3±27.8 37.1±32.3 38.4±32.0** SF-36 PCS 28.5±6.1 36.8±11.4 36.3±12.1**	

* indicates significant (*p<0.05 or **p<0.01) improvement from baseline to followup
# indicates significant (#p<0.05 or ##p<0.01) difference between treatment groups

A/P – anterior-posterior; ALIF – anterior lumbar interbody fusion; BAK – Bagby and Kuslich cage a.k.a. "Bagby basket"; L5 – lumbar 5; LBOS – low back outcome score; LT-CAGE® – lumbar tapered fusion device; ODI – Oswestry Disability Index; PLF – posterolateral fusion; PLIF – posterior lumbar interbody fusion; rhBMP-2 – recombinant human bone morphogenic protein; S1 – sacral 1; TLIF – transforaminal lumbar interbody fusion; VAS – visual analog scale

Table 3: Axial back pain: lumbar spinal fusion from posterior approach (posterolateral, PLIF, A/P fusion)

Study	Design	N	Age	Procedure	Follow-up time	Baseline ODI	Follow-up ODI	Other outcome	Comment
Agazzi, 2001[115]	Retrospective study	71	NR	PLF	28 mos	NR	NR	Radicular pain (6)	
Brantigan 2000[116]	Prospective study	221	44.3	PLIF + cage (Brantigan I/F) + PSF using Variable Screw Placement System (VSP)	NR	NR	NR	Pain (5 point Likert scale – higher is better) Pre 6mo 12mo 24mo 48mo 2.0-> 3.7-> 3.7-> 3.8-> 4.1	Prolo score showed improvement over time
Christensen 2002[117]	RCT	129	45	PLF + Cotrel- Dubousset fixation (n=64) versus PLF+ AICBG (n=66)	5 yrs	NR	NR	DPQ*	
Christensen 2002[46]	RCT	148	NR	PLF + titanium cage (n=73) versus A/P fusion + cage (Brantigan)(n=75)	2 yrs	NR	NR	DPQ at 2 yr* Leg pain, at 1yr*,#; 2yr*	
DeBerard 2002[118]	Retrospective cohort study	370	40	PLF (n=130) versus ALIF + cage (BAK) (n=77)	5 yrs	NR	NR	Roland and Morris questionnaire: 11.4 for PL and 8.79 for BAK gp. Stauffer-Coventry data: No difference in 2 gps. SF-20 data: BAK procedure pts. Perceived better health on 3 subscales.	
Folman 2003[119]	Prospective study	87	45.2	PLIF with B-Twin spacer	15 mos	31	12.7*		
Freeman 2000[120]	Retrospective comparative study	60	44 yrs	PLIF + PSF Interbody fusion included any of autograft, allograft or interbody cages	5.3 yrs	NR	NR	Pain - reduction >90% 40 (83%) 50-90% 8 (17%) <50% 0 (0%)	79% (38/48) pts had post op ODI < 30
Fritzell 2002[47]	RCT	201	(25–65)	PLF (non-instrumented) versus PLF+VSP versus PLF+VSP + ALIF (n=56) or PLIF (n=72) (according to preference of surgeon)	2 yrs	47.3 48.4 47.3	36.5* 33.6* 38.5*	Pain – reduced significantly in all 3 groups, but increased in all groups between 12 and 24 mo	
Gepstein 2005[121]	Prospective study	62	50.6 yrs	PLIF with B-Twin expandable spinal spacer (B-Twin ESS) performed percutaneously Compared to Open PLIF with B-Twin expandable spinal spacer (B-Twin ESS) – historical controls	29 mo	42.8	16.6	Pain VAS preop 8.5 ± 1.3 (5.8-9.2) Followup 2.9 ± 1.8 (1.2-6.2) 66% decrease*	
Gertzbein	Prospective	82	44 yrs	A/P fusion + FRA + PSF	2 yrs	NR	NR	Pain (VAS)	

Study	Design	N	Age	Procedure	Follow-up time	Baseline ODI	Follow-up ODI	Other outcome	Comment
1996[122]	study		(11 - 80)					Back 7.2->2.1 (p<0.006) Leg 5.8->1.5 (p<0.0001)	
Glassman 2006[48]	Retrospective study	497	47 yrs (17–86)	PLF (n=119) PLIF/TLIF (n=152) A/P fusion (n=95) ALIF (n=125)	NR	55.9 46.1 51.4 47.8	32.8*,# 30.1* 33.5* 26.2*,#	QOL – ALIF pts had better general health status (p=0.002) postoperatively; ALIF and PLF showed greater improvement than PLIF/TLIF and combined.	
Haid 2004[102]	Randomized non-blind study	67	NR	PLIF + cage (cylindrical) + rhBMP-2 RCT comparing rhBMP-2 of autologous bone graft	NR	NR	NR	Pain Back pain - improved in both groups; greater improvement in rhBMP-2 than control at 24 mo p=0.009). Leg pain - improved in both groups; no difference between groups.	ODI Δ ≥15pt imp -29.6 69% -24.9 55.6%
Hinkley 1997[123]	Prospective study	81	37.9 yrs (22 - 57)	Anterior/posterior combined lumbar fusion + allograft + PSF	2 yrs	NR	NR	Pain (VAS) preop 6 mo 1yr 2yr 73.3 58.2 55.8 60.4 15.7 20.6 21.7 25.6 sd Other Reoperation 7 (8.6%) Pain Disability Index; Activity Level; Interference to life; Self-efficacy; Depression symptoms	
Jang 2005[124]	Retrospective comparative study	84	58.9	Percutaneous facet screw fixation (PFSF) after ALIF compared to Post-ALIF screw fixation	27.4 mo	68.4 64.8	28.6* 32.2*		
Lee 1995[125]	Prospective study	62	37.9 yrs	PLIF+ autogenous IC bone graft	34 mo (range, 18-84) in 54/62 (87.1%) of patients	NR	NR	Pain None 14 (25.9%); mild 33 (61.1%); mod-severe 7 (13%) Narcotic use None 32 (59.2%); non-narcotic 16 (29.6%); narcotic 6 (11.1%) Other Reoperation for non-fusion - 2 Physical restriction; Return to work; Patient satisfaction	
Lettice 2005[126]	Retrospective study	298	44.3 yr	Anterior/posterior combined lumbar fusion Short segment group: Fusion at 1-2 levels	2 yr	NR	NR	SF-36 variances did not show significant differences	

Study	Design	N	Age	Procedure	Follow-up time	Baseline ODI	Follow-up ODI	Other outcome	Comment
				Long segment group: Fusion at 3-5 levels					
Madan 2003[127]	Prospective comparative study	74	42	PLIF Anterior lumbar interbody fusion	2 years	NR	NR	Pain drawing 5.2/5.1	
McKenna 2005[128]	RCT	83	40	A/P fusion + FRA (n=37) versus A/P fusion + titanium cage (TC)(n=41)	2 yrs	57 54	42*,# 48*	Back pain - VAS 6mo 1y 2y FRA 7.2->5.0->4.8->5.2 (Δ1.9) Pre TC 7.1->5.8->6.4->6.0 (Δ1.1) Leg pain – VAS 6mo 1y 2y FRA 3.8->2.3->2.8->2.5 (Δ1.3) TC Pre 4.3->3.0->4.6->4.7 (Δ0.4)	
Pavlov 2004[129]	Prospective study	52	37 yrs	A/P fusion + cage (SynCage)	4 yrs	45.8	24	Pain – VAS Decreased over time (p+0.000). higher at 4 than 2 yrs, but at 4 yr, still better than preop**(data not reported, except in fig)	
Potter 2005[130]	Retrospective case series	100	38 yrs	TLIF®	34 mo	NR	NR	Pain >50% relief 66 (81%) Pain free (29%)	Roland & Morris disability scores
Pradhan 2002[131]	Retrospective study	122	46yrs	PLF (n=64) ALIF + cage (n=58)	24 mos	NR	NR		
Schofferman 2001[132]	Prospective randomized comparison	48	42 yrs	A/P fusion + FRA + PLF with autogenous posterior iliac crest bone versus ALIF + FRA + transpedicular instrumentation without PLF	25 mo (range, 24-45)	57.5 61.2	38.2* 40.1*	Pain 360 7.8->4.3 270 7.2->4.7 (p=NR)	

* indicates significant (*p<0.05 or **p<0.01) improvement from baseline to followup
# indicates significant (#p<0.05 or ##p<0.01) difference between treatment groups

A/P – anterior-posterior; ALIF – anterior lumbar interbody fusion; AICBG – autogenous iliac crest bone graft; BAK – Bagby and Kuslich cage a.k.a. "Bagby basket"; DPQ – Dallas Pain Questionaire; ESS – expandable spinal spacer; FRA – femoral ring allograft; IC – iliac crest; ODI – Oswestry Disability Index; PFSF – percutaneous facet screw fixation; PL – posterolateral; PLF – posterolateral fusion; PLIF – posterior lumbar interbody fusion; PSF – posterior spinal fusion; QOL – Quality of Life; RCT – randomized control trial; rhBMP-2 – recombinant human bone morphogenic protein; SF-36 – short form 36; TC – titanium cage; VAS – visual analog scale; VSP – variable screw placement system

Table 4. Axial back pain: arthroplasty (total disc replacement) versus conservative management

Study	Design	N	Age	Procedure	Follow-up time	Baseline ODI	Follow-up ODI	Other outcome	Comment
Bertagnoli 2005[51]	Prospective uncontrolled clinical trial	118	47.5 yrs	ProDisc total disc arthroplasty	31 mos	53	29	Pain-back Preop 12mo 24mo Reg 84.6%->11.9%->9% Occ 15.3%->59.4%->59.2% Pain-radicular Reg 42.6%->13.2%->8.8% Occ 45.5%->41.6%->29.5%	
Blumenthal 2005[43]	RCT	304	39.6 yrs (19-60)	ALIF+ cage (BAK) Total disc arthroplasty (Charité)	24 mos	52.1 50.6	30.5 26.3	Pain VAS pre 6 mo 12 mo 24 mo TDR 72->33.1->32.9->31.2 ALIF 72->43.9->40.4->37.5 P 0.004 0.042 0.107 Narcotic usedur f/u 24 mo TDR 72% 64% ALIF 86% 80% (p=0.0083)	
Blumenthal 2003[49]	Prospective uncontrolled clinical trial	57	(18-60)	Link SB Charité disc replacement device	12 mos	53	22	Pain -VAS pre-op 6-wk 3-mo 6-mo 12-mo 70 33 35 28 31	
Food and Drug Administration 2006[37]	RCT	212	~40 yrs	A/P fusion +FRA + PLF+autogenous iliac crest bone graft+pedicle screw (n=80) ProDisc-L Total Disc Replacement (n=162)	24 mos	NR NR	34.5 39.8	Pain VAS – all 3 groups improved compared to baseline; no sig diff betw Prodisc and fusion except at 3 mo time point fusion 73.2±14.5 Prodisc 75.1±16.4 ProdiscNR 72±18	ODI ≥15 point improvement 55% fusion 68% ProDisc-L
Le Heuc 2005[54]	Series	64	44 yr	Maverick lumbar total disc replacement	2 yrs	43.8	23.1		
Zigler 2003[55]	Series	39	18-60 yrs	A/P fusion (n=11) ProDisc II (n=25)	6 mo	60 62	42 34*	Pain (NS)	
Zigler 2004[53]	Prospective study	78	~40 yrs	Total disc arthroplasty using ProDisc II Versus A/P fusion	6-12 mo			Pain VAS NSD between groups, but trend toward increasing improvement over time in ProDisc group	ODI-prog decr in ProDisc group during 6-mo; smaller decr in fusion group; stat sig only at 3-mo (p=0.02)

A/P – anterior-posterior; ALIF-anterior lumbar interbody fusion; BAK-Bagby and Kuslich cage a.k.a "Bagby basket"; FRA – femoral ring allograft; NSD – no significant difference; ODI – Oswestry Disability Index; PLF – posterolateral fusion; TDR – total disc replacement; VAS – visual analog scale

Table 5: Spondylolisthesis: lumbar spinal fusion surgery

Study	Design	N	Age	Procedure	Follow-up time	Baseline ODI	Follow-up ODI	Other outcome	Comment
Dehoux 2004[133]	Prospective non-random study	52	39.5 yrs (14 - 63)	PLF + PSF (Cotrel Dubousset) OR PLIF + PSF (Steffee) + cage (Brantigan)	75 – 100 mos	NR	NR	77% pts had good or very good result with PLIF and 68% with PLF; Fusion rates had not significant influence on functional outcome.	
Ekman 2005[72]	RCT	111	18-55 yrs	PLF + PSF or PLF with no instrumentation Compared to Conservative treatment – exercise program (1 yr duration)	9 yrs	NR NR	28 31	Pain- Between 2 yr and long-terms f/u pain index worsened in surgery group** but improved in exercise group*. NSD between groups at long-term f/u Fusion 37->40 Exercise 56->49	This study reports long-term f/u of patients in Moller & Hedlund (2000) trial
Hackenberg 2005[134]	Prospective study	52	48.6 yrs (19 - 69)	TLIF® (n=52) Isthmic spondylolisthesis gp Degen. Spondylolisthesis	46 mos	 41.6 58.4	 31.6 39	Pain: Pain relief on VAS was significant	
Matsudaira 2005[73]	Prospective controlled trial, non-randomized	53	67 yrs	PLF+ PSF (n=19) Decompression of spinal canal with laminectomy (n=18) Compared to Conservative treatment (n=16)	2 yrs.	NR	NR		
Moller 2000[71]	RCT	111	39 yrs (18 - 55)	PLF (n=77) + no instrumentation (n=40) + PSF (n=37) Compared to Exercise (n=34)	2 yrs	NR	NR	Pain index 63/35/37** Pain index 65/54/56*	Disability Rating Index improved in surgery group*,# but not in exercise group at 2 yr
Suk 2001[76]	Prospective controlled non-randomized	56	~50 yrs	PLF + PSF A/P fusion + PSF	~36mo	NR	NR	Pain –back PLF 7.3 (1-10) 360 8 (2-10)* Leg PLF 7.8 (1-9.5) 360 8.5 (0-9.5)	
Suk 1997[135]	Retrospective study	76	NR	PLF (n=40) PLIF (n=36)	NR	NR	NR		
Thomsen	RCT	130	~45 yrs	PLF	NR	NR	NR	Pain – Dallas Pain	

Study	Design	N	Age	Procedure	Follow-up time	Baseline ODI	Follow-up ODI	Other outcome	Comment
1997[74]			(20 – 67)	+ no instrumentation (n=66) or PLF + PSF (Cotrel-Dubousset)(n=64)				Questionnaire No significant difference between groups (4 domains x 10 outcome categories x 2 groups = unwieldy table)	
Vaccaro 2004[75]	RCT	36	64 yrs (43 - 80)	PLF + autogenous iliac crest bone graft (n=12) versus PLF + OP-1 (BMP-7) putty (n=24)	12 mos	47 46	NR NR		73% had >20%imp in ODI 86% had >20%imp in ODI
Wenger 2005[59]	Retrospective study	132	40.6 yrs (15 - 70)	PLF + PSF	9.9 yrs	NR	NR	Pain – back 2.13 Pain – leg 1.59	

* indicates significant (*p<0.05 or **p<0.01) improvement from baseline to followup
# indicates significant (#p<0.05 or ##p<0.01) difference between treatment groups

A/P – anterior-posterior; NSD – no significant difference; ODI – Oswestry Disability Index; PLF – posterolateral fusion; PLIF – posterior lumbar interbody fusion; PSF – posterior spinal fusion; TLIF – transforaminal lumbar interbody fusion; VAS – visual analog score

Table 6: Summary of studies reporting incidence of adjacent segment disease^ requiring reoperation following lumbar or lumbosacral fusion.

Study	No. of patients	Incidence of ASD	Reoperation (annualized)	Criteria for ASD	Follow-up (mo)	Fusion type
Aiki et al., 2005[136]	117	8% reoperation for ASD	1.1%	Symptomatic	84	PL
Ghiselli et al., 2004[77]	215	27.4%	3.7%	Symptomatic	80	PL
Chou et al., 2002[137]	32		0%	Symptomatic	48	PL
Kanayama et al., 2001[138]	27	18.5% stenosis/HNP	3.5%	Symptomatic	60	PL + screw-rod fixation
Kuslich et al., 2000[139]	196	5.6% disc degeneration or HNP	1.3%	Symptomatic	48	Interbody cage
Booth et al., 1999[140]	41	12.2%	1.8%	Symptomatic	~80	PL + screw-rod/plate fixation
Etebar et al., 1999[141]	125	14.4% listhesis/HNP/stenosis/ compression fracture/scoliosis	3.7%	Symptomatic	44.8	PL + screw-rod/plate fixation
Butterman et al., 1998[142]	165	9% reoperation	1.7%	Symptomatic	60	PL
Rahm et al., 1996[143]	49	16%	3.0%	Symptomatic	~60	PL + screw-rod + PLIF in 25 pts
Frymoyer et al., 1979[144]	96	5.2% HNP	0.4%	Symptomatic	164	PM

^Adjacent segment disease may include disc degeneration (loss of disc height, disc space narrowing); listhesis (anterolisthesis, retrolisthesis), instability, herniated nucleus pulposus, stenosis, hypertrophic facet arthritis, osteophyte formation, scoliosis, vertebral compression fracture. When described in individual studies, the definitions are given.
*23 patients total, 10 of whom had a mobile segment below the fusion. 11 of the 23 patients also underwent MRI evaluation, 5 of whim had a mobile segment below the fusion

ASD – adjacent segment disease; HNP – herniated nucleus pulposus; MRI – magnetic resonance imaging; PL – posterolateral; PLIF posterior lumbar interbody fusion; PM – posterior midline

Table 7: Summary of reoperation rates following non-fusion lumbar surgery

Study	No. of patients	Incidence of ASD	Reoperation (annualized)	Criteria for ASD	Follow-up (mo)	Type of surgery
Jansson et al., 2005[145]	9664	6.5% re operated	1.7%	Symptomatic	45	Laminectomy
Atlas et al., 2005[146]	148	23% re operated	2.1%	Symptomatic	120	Laminectomy for spinal stenosis (fusion was uncommon; internal fixation devices were not used)
Malter et al., 1998[147]	5325	14.6% re operated	2.8%	Symptomatic	60	Non-fusion lumbar surgery
Johnsson et al., 1997[148]	105	18% re operated	3.4%	Symptomatic	60	Laminectomy

ASD – adjacent segment disease

Table 8: Summary of studies reporting incidence of adjacent segment disease^ based on radiographic criteria following lumbar or lumbosacral fusion.

Study	No. of patients	Incidence of ASD	Reoperation (annualized)	Criteria for ASD	Follow-up (mo)	Fusion type
Remes et al., 2005 [79]	102	27% speckled discs 27% black discs 21% narrowed intervertebral disc spaces		Radiographic	252	PLF
Greiner-Perth et al., 2004 [149]	1680	5.1% multisegmental PLIF 2.3% mono- or bi-segmental PLIF		Radiographic	60	PLIF
Lai et al., 2004[150]	101	24.3% w/o preserved posterior complex integrity 6.5% with preserved posterior complex integrity		Radiographic	72	PL
Okuda et al., 2004[151]	87	33% listhesis/stenosis/loss of disc height		Radiographic	24	PLIF
Ghiselli et al, 2003[81]	32	0% at L5-S1 only		Radiographic	88	Single segment L4-L5 PL
Gillet, 2003[152]	NR	41%	2.4%	Radiographic	60	NR
Chou et al., 2002[137]	32	18.8% 16.7% mon- or bi-segmental PLIF 21.4% multisegmental PLIF	0%	Radiographic	48	PL + screw-rod fixation
Ishihara et al., 2001[153]	23 [10]*	52% [70%] disc space narrowing/listhesis/osteophyte 73% [100%] disc degeneration/HNP/ligamentum hypertrophy		Radiographic-MRI	~160	Anterior interbody
Kumar et al., 2001[154]	83	36.1% listhesis/stenosis/loss of disc height	3.2%	Radiographic	60	PL + screw-rod + PLIF in 30 pts
Kumar et al., 2001[155]	28	35.7% loss of disc height 14.2% instability		Radiographic	~360	PM + interspinous wiring
Miyakoshi et al., 2000[156]	45	100% loss of disc height		Radiographic	72	PLIF + screw-rod fixation
Nakai et al., 1999[157]	48	31% loss of disc height		Radiographic	~103	PLIF + screw-rod fixation
Booth et al., 1999[140]	41	24.4% stenosis	1.8%	Radiographic	~80	PL + screw-rod/plate fixation
Wiltse et al., 1999[158]	83	48% 6% adjacent segment stenosis		Radiographic	84	PL
Hambly et al., 1998[159]	42	17% anterolisthesis 7.1% retrolisthesis 7.1% instability 19% loss of disc height		Radiographic	~271	PL
Chen et al., 1997[160]	185	9.7% instability		Radiographic	42	PL + screw-rod fixation
Seitsalo et al., 1997[161]	145	17-34% loss of disc height		Radiographic	~185	PM (87 pts), PL (55 pts), ALIF (3 pts)
Wimmer et al., 1997[162]	120	10.8% listhesis (anteroposterior translation)		Radiographic	36	C + screws/laminar hooks

Study	No. of patients	Incidence of ASD	Reoperation (annualized)	Criteria for ASD	Follow-up (mo)	Fusion type
Rahm et al., 1996[143]	49	35% SI pain/olisthesis/stenosis/ HNP/kyphosis/diskogram	3.0%	Radiographic	~60	PL + screw-rod + PLIF in 25 pts
Pihlajamaki et al., 1996[163]	63	8% disc degeneration		Radiographic	48	PL + screw-rod fixation
Aota et al., 1995[164]	65	24.6% instability		Radiographic	39	PL + screw-rod fixation
Penta et al., 1995[165]	81	32% disc degeneration		Radiographic-MRI	~120	Anterior interbody
Axelsson et al., 1994[166]	54	20% disc degeneration		Radiographic	42	PL
Roy-Camille et al., 1993[167]	43	43%	0%	Radiographic	138	PL
Lehmann et al., 1987[168]	62	45% instability 30% stenosis	0.2%	Radiographic	396	PM
Leong et al., 1983[169]	40	52.5% disc degeneration		Radiographic	~152	Anterior interbody

ALIF – anterior lumbar interbody fusion; ASD – adjacent segment disease; C – circumferential fusion; HNP – herniated nucleus pulposus; L5 – lumbar 5; MRI – magnetic resonance imaging; PL – posterolateral; PLF – posterolateral fusion; PLIF – posterior lumbar interbody fusion; PM – posterior midline; S1 – sacral 1; SI - sacroiliac

Table 9: Instrumented versus non-instrumented fusion

Study	Design	N	Age	Procedure	Follow-up time	Baseline ODI	Follow-up ODI	Other outcome	Comment
Christensen 2002[117]	RCT	129	45 yrs (20-67)	PLF + PSF (Cotrel-Dubousset)(n=64) versus PLF+ autogenous IC bone graft (n=66)	5 yrs	NR	NR	DPQ*	
Ekman 2005[72]	RCT	111	(18-55) yrs	PLF + PSF OR PLF + no instrumentation Compared to Conservative treatment – exercise program (1 yr duration)	9 yrs	26 28	28 31	Pain- Between 2 yr and long-terms f/u pain index worsened in surgery group (p<0.0001) but improved in exercise group (p=0.013). NSD between groups at long-term f/u Fusion 37->40 Exercise 56->49	
Fritzell 2002[47]	RCT	201	25-65	PLF (noninstrumented) PLF+VSP PLF+VSP + ALIF (n=56) or PLIF (n=72) (according to preference of surgeon)	2 yrs	47.3 48.4 47.3	36.5* 33.6* 38.5*	Pain – reduced significantly in all 3 groups, but increased in all groups between 12 and 24 mo	No significant differences between groups.
Glaser 2003[170]	Retrospective cohort study	94	45 yrs (19 - 73)	PLF + PSF	12.6 ± 1.6 yrs.			Pain Narcotic use: 26% used less, 56% used same, 18% greater** Pain thermometer (n=71): mean 2.91 (sd 1.39) Pain interference (n=74): mean 53.44 (sd 22.15) Long term results: (10 yrs) Pain thermometer (n=71): mean 2.87 (sd 1.09) Pain interference (n=74): mean 58.33 (sd 24.96) SF-36: reports of bodily pain and physical functioning below age and gender-adjusted means but disability and function scores showed distinct improvement.	
Kim 2006[171]	RCT	167	55 yrs (38 - 79)	PLF (n=62) (Group1) PLIF (n=57) (Group 2) PLF+ PLIF (n=48) (Group 3)	57 in younger, 22 in older			Pain: Reduced pain significantly** Group 2 showed better results than groups 1 and 3 for back pain, (NS) Groups 2 and 3 had better results than group 1 at 6 mo, 1 yr (NS)	
Kornblum 2004[82]	RCT	47	73 solid fusion,	Posterolateral gutter fusion surgery	7yrs 8 mo (5-14			Pain (0-5 scale) At 3 years: relief of pain and	

Study	Design	N	Age	Procedure	Follow-up time	Baseline ODI	Follow-up ODI	Other outcome	Comment
			72 pseudo-arthrosis	PLIF with autogenous bone graft Compared to Pseudoarthrosis	yrs)			increase in activity in 86% (solid fusion), 56% (pseudoarthrosis)** (All results: solid fusion/pseudoarthrosis) Pre-op back pain 3.7/3.5 Pre-op leg pain 4.5/4.2 Post-op. back pain 1.4/2.6* Post-op leg pain 0.5/2.1**	
Korovessis 2004[172]	RCT	135 (45 in each of 3 groups: rigid (A), semi-rigid (B) and dynamic (C))	65 ± 9 / 59 ± 16 / 62 ± 10 yrs	PLF + rigid instrumentation +semi-rigid inst +dynamic	47 ± 14 mo.			SF-36 preop: 13, 14, 11. A, B, C 1-yr post-op: 61,61,65 2 -yrs post-op and onwards: 74, 75, 77	
McGuire 1993[173]	RCT	28	35 yrs (24 - 42)	Posterolateral fusion surgery with autogenous iliac crest graft (n=14) Versus Posterolateral fusion surgery with VSP and screws (n=13)	2 yrs				
McKenna 2005[128]	RCT	83	40 yrs (24 - 65)	A/P fusion + FRA (n=37) Versus A/P fusion + cage (titanium) (n=41)	2 yrs	57 54	42 48	Pain VAS-back 6mo 1y 2y Pre FRA 7.2->5.0->4.8->5.2 (Δ1.9) TC 7.1->5.8->6.4->6.0 (Δ1.1) VAS-leg 6mo 1y 2y Pre FRA 3.8->2.3->2.8->2.5(Δ1.3) TC 4.3->3.0->4.6->4.7(Δ0.4)	
Moller 2000[71]	RCT	77	39 yrs (18 - 55)	PLF + PSF(Cotrel-Dubousset [CDI])(n=39) Versus PLF + no instrumentation (autogenous IC bone graft) (n=41)	2 yrs	NR	NR	Pain (VAS) pre 1yr 2yr CDI 63 36 40 Noninst 63 35 34	

* indicates significant (*p<0.05 or **p<0.01) improvement from baseline to followup
\# indicates significant (#p<0.05 or ##p<0.01) difference between treatment groups

A/P – anterior-posterior; ALIF – anterior lumbar interbody fusion; CDI – Cotrel-Dubousset Instrumentation; DPQ – Dallas Pain Questionaire; FRA – femoral ring allograft; IC – iliac crest; NS – not significant; NSD – no significant difference; ODI – Oswestry Disability Index; PLF – posterolateral fusion; PLIF – posterior lumbar interbody fusion; PSF – posterior spinal fusion; RCT – randomized control trial; SF-36 – short form 36; TC – titanium cage; VAS – visual analog score; VSP – variable spine plating

Table 10: Complications of spinal fusion surgery in older populations

Study	Design	N	Age	Procedure	Major complications	Minor complications	Wound infection	Neurologic	Comment
Carreon 2003[90]	Retrospective study	98	72 yrs (65 - 84)	NR	Mortality 2 (2%) Infections Pneumonia 5 (5%) Other morbidity Renal failure 5(%) MI 3 (3%) Resp distress 2 (2%) CHF 2 (2%) CVA 1 (1%)		10 (10%)	Neurologic deficit 2 (2%)	No data on efficacy outcomes
Deyo 1993[86]	Retrospective study	1524	70.2 yrs (59-97)	NR	Mortality No fusion Any 1.2% 0.7% Disc 1.1% 0.6% Lam Fusion 1.1% 0.9% Fusion 1.6% SS 1.0%* 0.8% Spond- 0.4% ylolisthesis 1.8%*				Study limited to Medicare claims in 1985
Hsu 2005[103]	Prospective study	58	63.9 yrs	PLF + autogenous iliac crest bone graft (n=20), coralline hydroxyapatite (n=19) or both (n=19)		For group 3 the fusion rate (7.9%) was markedly lower than that in groups 1and 2 (90% and 78.9%)			No efficacy and only limited complication data presented (radiographic fusion)
Jang 2005[124]	Retrospective study	84	58.9 yrs (46 - 70)	Percutaneous facet screw fixation (PFSF) after ALIF (n=44) compared to Post-ALIF screw fixation (n=40)	No reoperations. Group1: Fusion rate 95.8% Subsidence of cage was noted at four fusion sites, one showed a collapsed non-union. 46 of 48 showed osseous union. Group 2: Fusion rate 97.5% (p>0.05) Subsidence of cage was noted at two fusion sites, all showed a collapsed non-union. 46 of 48 showed osseous union.	Total complications 10.7% liac vein injury: 4 cases Incisional hernia: 1 cases Dural injury: 2 cases DVT: 2 cases No blood transfusions reqd.	None		ODI scores were 68.4 preop to 28.6 postop (p<0.05) Group 2: 64.8 preop to 32.2 postop (p<0.05) No inter-group difference
Kilincer 2005[87]	Retrospective study	129	58.6 yrs (25 - 91) Grp I: 85 pts younger than 65	PLIF + PSF 57 in younger, 22 in older PSF 26 in younger, 16 in older	Mortality: none Removal of instrumentation: 1 case	Total complications 11% (2 in younger and 5 in older gp, difference stat. significant) CSF leak 6 cases	Infections: 3 cases with deep wound infections		Older patients did not demonstrate an increased incidence of complications.

Study	Design	N	Age	Procedure	Major complications	Minor complications	Wound infection	Neurologic	Comment
			yrs. Grp II: 44 pts 65 yrs or older	Other: Non-instrumented fusion: 2 in younger, 6 in older		Medical complications: 4 cases ICU admissions: 2 (for cardiac and pulmonary monitoring)			
Kornblum 2004[82]	Prospective randomized study	47	73 solid fusion, 72 pseudo-arthrosis	PLF with autogenous bone graft	2 patients in arthrodesis group and 5 in solid fusion group required reoperation	NR	None	None	
Korovessis 2005[104]	Prospective randomized study	57	61 yrs	PLF + CH (Gp A) 45 + AICBG (Gp B) + both (Gp C)	NR	hematoma 1 1 screw breakage in Gp A at 18 mo, 2 breakages in Gp C at 3 yr	1 superficial	NR	
Korovessis 2004[172]	Prospective randomized study	135 (45 in each of 3 groups)(RCT)	65 $\pm$ 9 59 $\pm$ 16 62 $\pm$ 10	PLF + rigid (A), + semi-rigid (B) + dynamic (C)) instrumentation	NR	All fusions healed without pseudoarthrosis or malunion 2 patients in gp C showed delayed hardware failure 1 year and 180d post-op. without radiological pseudoarthrosis	NR	NR	
Lai 2004[150]	Retrospective study	101	61 yrs (36 - 78)	PLF + PSF		I case: postop. epidural hematoma, 2 cases had broken implants, 1 case had osteoporotic compression fracture ASD: 23 cases (19 cranial; 3 caudal; 1 skipping)			
Lai 2004[174]	Retrospective comparative study	70	59.6 yrs (36 - 77)	PLF		5 cases with complications: 3 implant failures, 1 pseudoarthrosis, 1 screw malposition ASD: 13 patients (10 cranial; 3 caudal)			

Study	Design	N	Age	Procedure	Major complications	Minor complications	Wound infection	Neurologic	Comment
Matsudaira 2005[73]	RCT	53	67 yrs	Group 1: Decompression laminectomy +PLF+PSF (19) Group 2: Decompression of spinal canal + laminectomy (18) Compared to Conservative treatment (16)			Deep infection, migration of screw and stenosis at adjacent level in one case		
Raffo 2006[88]	Retrospective case series	20	≥ 80 yrs	PLF + PSF (75%) and iliac crest autograft	Major complication 7 (35%) 4 (20%) As inpatient 4 (20%) As outpatient	Minor complication Inpatient 6 (30%) Outpt 4 (23%)			
Sengupta 2006[175]	Retrospective comparative study	76	60 yrs (27 - 83)	PLF + PSF + local (n=40) or + iliac crest (n=36) bone graft	NR	NR			
Vaccaro 2004[75]	RCT	36	64 yrs (43-80)	Posterolateral fusion surgery Autogenous iliac crest bone graft (n=12) versus OP-1 (BMP-7) putty (n=24)	No removals, revisions or supplemental fixations in 1 year	AEs 29/36 pts No ectopic bone formation or recurrent spinal stenosis			
Wang 2003[89]	Retrospective case series	88 (52 underwent fusion)	>75 yrs	NR	Mortality- No perioperative deaths	12 dural tears 16 systemic complications	12 wound compli-cations		

* indicates significant (*p<0.05 or **p<0.01) improvement from baseline to followup
\# indicates significant (#p<0.05 or ##p<0.01) difference between treatment groups

AE – adverse events; AICBG – autoiliac crest bone graft; ALIF – anterior lumbar interbody fusion; ASD – adjacent segment disease; BMP-7 – bone morphogenic protein; CH – coralline hydroxyapatite; CHF – chronic heart failure; CSF – cerebro-spinal fluid; CVA – cerebrovascular accident; DVT – deep vein thrombosis; ICU – intensive care unit; MI – myocardial infarction; ODI – Oswestry Disability Index; OP-1 – osteogenic protein 1; PLIF – posterior lumbar interbody fusion; PSF – posterior spine fusion; PSFS – percutaneous facet screw fixation; PLF – posterolateral fusion; SS – spinal stenosis;

Table 11. Reported complication rates of lumbar spinal fusion surgery

Complication	**PLF + instrumentation**	**PLF - instrumentation**	**ALIF**	**PLIF/ TLIF**	**A/P combined fusion**
Mortality	NR	NR	0%	NR	NR
All device related	NR	NR	NR	NR	20%
Intraoperative complications	NR	NR	4.8% (threaded) 0.4% (non-threaded)	93.6%	NR
Postoperative complications	NR	NR	12.5% 3.5% (threaded) 1.6% (non-threaded)	9.7%	NR
Major complications	24% (NIDDM) 33% (IDDM) 7% (control)	NR	4% (neuro)	NR	NR
Major postoperative complications	NR	NR	3.41%	61.29%	NR
Minor complications	13.6 29% (NIDDM) 23% (IDDM) 14% (control)	NR	8.1% (neuro)	NR	NR
Neurologic	NR	NR	8%-17.2%	31% 2% (open) 6.8% (min. invasive)	4.6%
Vascular	NR	NR	1.9%-2.2%	NR	NR
Hematoma	NR	NR	NR	3.9% (open) 4.1% (min. invasive)	NR
Anemia	NR	NR	NR	NR	4.6%
CSF leak			0%	19.6% (open)	4.6%
Retrograde ejaculation	NR	NR	5.5%-17.5%	NR	NR
Infection	2.4%	NR	3%	10%	NR
Donor site pain >1 year	5.1%	NR	12.5% - 18.2%	NR	NR
Residual numbness over donor site	1.7%	NR	NR	NR	NR
Post op sensation of nerve route pain	3.1%	NR	5.56%	11.11%	NR
Pedicle screw malposition without reoperation	NR	NR	NR	9.8% (open) 10.9% (min. invasive)	NR
Thrombosis or DVT	NR	NR	0%	NR	1.3%
Nonunion/pseudoarthrosis	NR	NR	9.1%	NR	NR
Revision rate	20% (NIDDM) 34% (IDDM) 19% (control)	NR	NR	NR	NR
Reoperation	NR	NR	1%	NR	NR

A/P – anterior-posterior; ALIF – anterior lumbar interbody fusion; IDDM – insulin dependent diabetes mellitus; NIDDM – non-insulin dependent diabetes mellitus; PLF – posterolateral fusion; PLIF – posterior lumbar interbody fusion; TLIF – transforaminal lumbar interbody fusion

Table 12. Techniques to augment fusion

Study	Design	N	Age	Procedure	Follow-up time	Baseline ODI	Follow-up ODI	Fusion rate	Comment
Burkus 2002[101]	Prospective non-blind study	46	43 yrs (19 – 68)	ALIF+ threaded cortical allograft dowels with InFUSE Bone Graft (rhBMP-2) versus ALIF + autogenous iliac crest bone graft	2 yr	52.4 55.3	18.9 32.8	6 mos: 90.5% versus 65% (p=0.067) 12 mos: 100% versus 89.5% (p=NR)	
Castro 2004[105]	Prospective comparative study	84	49 ± 2 yrs (SD)	TLIF + Activated Growth Factor (AGF) gel Versus TLIF and no AGF gel	NR	NR	NR	Fusion rate appears to be decreased with AGF gel.	
Haid 2004[102]	RCT	67	NR	PLIF + cage + rhBMP-2 PLIF + AICBG + rhBMP-2	NR	NR NR	[-29.6] [-24.9]	92.3% (rhBMP-2) vs 77.8% (ABG) (NS)	Follow-up ODI scores indicate change from baseline
Hsu 2005[103]	Prospective case control study	58	63.9 yrs	PLF + PSF + AICBG PLF+PSF+CH&AICBG PLF+PSF+CH	12 mos	NR	NR	90% 78.9% 7.9%	
Korovessis 2005[104]	RCT	57	61 yrs	PLF + CH PLF + AICBG PLF + both	48 mos	NR NR NR	41 47 43	NR	
Sengupta 2006[175]	Retrospective comparative study	76	60 yrs (27 - 83)	PLF+ PSF + autogenous local (n=40) or + iliac crest (n=36) bone graft	28 mos			65% ~80% 20% 75% ~80% 66% (p=0.391) NS (p=0.029)	
Vaccaro 2004[75]	RCT	36	64 yrs (43 - 80)	Posterolateral fusion surgery Autogenous iliac crest bone graft (n=12) versus OP-1 (BMP-7) putty (n=24)	NR	46 47	86% had >20%imp 73% had >20%imp	74% BMP-7; 60% ICBG	Follow-up ODI indicates percent change from patients baseline score

ABG – autogenous bone graft; AGF – activated growth factor; AICBG – autogenous iliac crest bone graft ; ALIF – anterior lumbar interbody fusion; BMP-7 – bone morphogenic protein 7; CH – coralline hydroxyapatite; NS – not significant; ODI – Oswestry Disability Index; OP-1 – osteogenic protein 1; PLIF – posterior lumbar interbody fusion; PLF – posterolateral fusion; PSF – posterior spinal fusion; rhBMP-2 – recombinant human bone morphogenic protein; TLIF – transforaminal lumber interbody fusion

Table 13. Relationship between presurgical psychological morbidity and outcome of surgery.

Study	Design	N	Age	Procedure	Follow-up time	Baseline ODI	Follow-up ODI	Other outcome	Comment
Block 2001[176]	Case series	86 (fusion) 118 (laminectomy/ disc)	41.8 yrs (21 – 72)	NR (presumably posterior)	8.6 mo	67.9	53.5	Pain VAS 6.8 pre->5.2 post (p<0.001)	
Trief 2006[114]	Prospective study	160	44.2 yrs (26 - 67)	Anterior lumbar interbody fusion	2 yrs	60.6	39.8	Pain – back Baseline 1 yr 2 yrs 74.8±21.545.3±31.5 44.5±32.0 (p<0.001) Pain – leg 61.3±27.837.1±32.3 38.4±32.0 (p<0.001)	

ODI – Oswestry Disability Index; VAS – visual analog score

REFERENCES

1. Gibson JNA, Waddell G. Surgery for degenerative lumbar spondylosis.[update of Cochrane Database Syst Rev. 2005;(2):CD001352; PMID: 15846617]. Cochrane Database of Systematic Reviews. 2005;CD001352(4):1-90.
2. Bono CM, Lee CK. Critical analysis of trends in fusion for degenerative disc disease over the past 20 years: influence of technique on fusion rate and clinical outcome. Spine. 2004;29(4):455-63; discussion Z5.
3. Cowan JA, Jr., Dimick JB, Wainess R, Upchurch GR, Jr., Chandler WF, La Marca F. Changes in the utilization of spinal fusion in the United States. Neurosurgery. 2006;59(1):15-20; discussion 15-20.
4. Deyo RA, Gray DT, Kreuter W, Mirza S, Martin BI. United States trends in lumbar fusion surgery for degenerative conditions. Spine. 2005;30(12):1441-5; discussion 1446-7.
5. Deyo RA, Mirza SK. Trends and variations in the use of spine surgery. Clinical Orthopaedics & Related Research. 2006;443:139-46.
6. Patil PG, Turner DA, Pietrobon R. National trends in surgical procedures for degenerative cervical spine disease: 1990-2000. Neurosurgery. 2005;57(4):753-8; discussion 753-8.
7. Gruber HE, Hanley EN, Jr. Recent advances in disc cell biology. Spine. 2003;28(2):186-93.
8. Gruber HE, Hanley EN, Jr. Biologic strategies for the therapy of intervertebral disc degeneration. Expert Opinion on Biological Therapy. 2003;3(8):1209-14.

9. Martin MD, Boxell CM, Malone DG. Pathophysiology of lumbar disc degeneration: a review of the literature. Neurosurgical Focus. 2002;13(2):E1.

10. Boden SD, Davis DO, Dina TS, Patronas NJ, Wiesel SW. Abnormal magnetic-resonance scans of the lumbar spine in asymptomatic subjects. A prospective investigation. Journal of Bone & Joint Surgery - American Volume. 1990;72(3):403-8.

11. Mayer TG, Polatin P, Smith B, et al. Spine rehabilitation. Secondary and tertiary nonoperative care. Spine. 1995;20(18):2060-6.

12. Resnick DK, Choudhri TF, Dailey AT, et al. Guidelines for the performance of fusion procedures for degenerative disease of the lumbar spine. Part 13: injection therapies, low-back pain, and lumbar fusion. Journal of Neurosurgery Spine. 2005;2(6):707-15.

13. Resnick DK, Choudhri TF, Dailey AT, et al. Guidelines for the performance of fusion procedures for degenerative disease of the lumbar spine. Part 14: brace therapy as an adjunct to or substitute for lumbar fusion. Journal of Neurosurgery Spine. 2005;2(6):716-24.

14. 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 surgery for disc herniation: a prospective randomized controlled study.[see comment]. Pain. 2006;122(1-2):145-55.

15. 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(17):1913-21.

16. 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(7502):1233.
17. Fritzell P, Hagg O, Wessberg P, Nordwall A, Swedish Lumbar Spine Study G. 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(23):2521-32; discussion 2532-4.
18. Herkowitz HN, Kurz LT. Degenerative lumbar spondylolisthesis with spinal stenosis. A prospective study comparing decompression with decompression and intertransverse process arthrodesis. Journal of Bone and Joint Surgery - American. 1991;73-A(6):802-8.
19. Birkmeyer NJO, Weinstein JN, Tosteson ANA, et al. Design of the Spine Patient outcomes Research Trial (SPORT). Spine. 2002;27(12):1361-72.
20. Danisa OA, Turner D, Richardson WJ. Surgical correction of lumbar kyphotic deformity: posterior reduction "eggshell" osteotomy. Journal of Neurosurgery. 2000;92(1 Suppl):50-6.
21. Cohen SP, Larkin TM, Barna SA, Palmer WE, Hecht AC, Stojanovic MP. Lumbar discography: a comprehensive review of outcome studies, diagnostic accuracy, and principles. Regional Anesthesia & Pain Medicine. 2005;30(2):163-83.
22. Rengachary SS, Balabhadra RSV. Black disc disease: a commentary. Neurosurgical Focus. 2002;13(2):E14.

23. Resnick DK, Choudhri TF, Dailey AT, et al. Guidelines for the performance of fusion procedures for degenerative disease of the lumbar spine. Part 6: magnetic resonance imaging and discography for patient selection for lumbar fusion. Journal of Neurosurgery Spine. 2005;2(6):662-9.

24. Thalgott JS, Albert TJ, Vaccaro AR, et al. A new classification system for degenerative disc disease of the lumbar spine based on magnetic resonance imaging, provocative discography, plain radiographs and anatomic considerations. Spine Journal: Official Journal of the North American Spine Society. 2004;4(6 Suppl):167S-172S.

25. Carragee EJ, Barcohana B, Alamin T, van den Haak E. Prospective controlled study of the development of lower back pain in previously asymptomatic subjects undergoing experimental discography. Spine. 2004;29(10):1112-7.

26. Phelan EA, Deyo RA, Cherkin DC, et al. Helping patients decide about back surgery: a randomized trial of an interactive video program. Spine. 2001;26(2):206-11;discussion 212.

27. Kuklo TR, Rosner MK, Polly DW, Jr. Computerized tomography evaluation of a resorbable implant after transforaminal lumbar interbody fusion. Neurosurgical Focus. 2004;16(3):E10.

28. Lanman TH, Hopkins TJ. Lumbar interbody fusion after treatment with recombinant human bone morphogenetic protein-2 added to poly(L-lactide-co-D,L-lactide) bioresorbable implants. Neurosurgical Focus. 2004;16(3):E9.

29. Deyo RA. Gaps, tensions, and conflicts in the FDA approval process: implications for clinical practice. Journal of the American Board of Family Practice. 2004;17(2):142-9.

30. Fairbank JC, Pynsent PB. The Oswestry Disability Index.[see comment]. Spine. 2000;25(22):2940-52; discussion 2952.

31. Walsh TL, Hanscom B, Lurie JD, Weinstein JN. Is a condition-specific instrument for patients with low back pain/leg symptoms really necessary? The responsiveness of the Oswestry Disability Index, MODEMS, and the SF-36.[see comment]. Spine. 2003;28(6):607-15.

32. Pellise F, Vidal X, Hernandez A, Cedraschi C, Bago J, Villanueva C. Reliability of retrospective clinical data to evaluate the effectiveness of lumbar fusion in chronic low back pain. Spine. 2005;30(3):365-8.

33. Resnick DK, Choudhri TF, Dailey AT, et al. Guidelines for the performance of fusion procedures for degenerative disease of the lumbar spine. Part 4: radiographic assessment of fusion. Journal of Neurosurgery Spine. 2005;2(6):653-7.

34. Resnick DK, Choudhri TF, Dailey AT, et al. Guidelines for the performance of fusion procedures for degenerative disease of the lumbar spine. Part 5: correlation between radiographic and functional outcome. Journal of Neurosurgery Spine. 2005;2(6):658-61.

35. Deyo RA, Nachemson A, Mirza SK. Spinal-fusion surgery - the case for restraint.[see comment]. New England Journal of Medicine. 2004;350(7):722-6.

36. Errico TJ, Gatchel RJ, Schofferman J, et al. A fair and balanced view of spine fusion surgery. Spine Journal: Official Journal of the North American Spine Society. 2004;4(5 Suppl):S129-38.

37. Food and Drug Administration (FDA). Summary of Safety and Effectiveness Data for PRODISC-L Total Disc Replacement. 2006:1-23.

38. Gibson JNA, Waddell G. Surgery for degenerative lumbar spondylosis: updated Cochrane Review. Spine. 2005;30(20):2312-20.

39. Bono CM, Lee CK. The influence of subdiagnosis on radiographic and clinical outcomes after lumbar fusion for degenerative disc disorders: an analysis of the literature from two decades. Spine. 2005;30(2):227-34.

40. Tiusanen H, Seitsalo S, Osterman K, Soini J. Retrograde ejaculation after anterior interbody lumbar fusion. European Spine Journal. 1995;4(6):339-42.

41. Tiusanen H, Hurri H, Seitsalo S, Osterman K, Harju R. Functional and clinical results after anterior interbody lumbar fusion. European Spine Journal. 1996;5(5):288-92.

42. Sasso RC, Kenneth Burkus J, LeHuec J-C. Retrograde ejaculation after anterior lumbar interbody fusion: transperitoneal versus retroperitoneal exposure. Spine. 2003;28(10):1023-6.

43. Blumenthal S, McAfee PC, Guyer RD, 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.

44. Geisler FH, Blumenthal SL, Guyer RD, et al. Neurological complications of lumbar artificial disc replacement and comparison of clinical results with those related to lumbar arthrodesis in the literature: results of a multicenter, prospective, randomized investigational device exemption study of Charite intervertebral disc. Invited submission from the Joint Section Meeting on Disorders of the Spine and Peripheral Nerves, March 2004.[see comment]. Journal of Neurosurgery Spine. 2004;1(2):143-54.

45. Chung SK, Lee SH, Lim SR, et al. Comparative study of laparoscopic L5-S1 fusion versus open mini-ALIF, with a minimum 2-year follow-up. European Spine Journal. 2003;12(6):613-7.

46. Christensen FB, Hansen ES, Eiskjaer SP, et al. Circumferential lumbar spinal fusion with Brantigan cage versus posterolateral fusion with titanium Cotrel-Dubousset instrumentation: a prospective, randomized clinical study of 146 patients. Spine. 2002;27(23):2674-83.

47. Fritzell P, Hagg O, Wessberg P, Nordwall A, Swedish Lumbar Spine Study G. Chronic low back pain and fusion: a comparison of three surgical techniques: a prospective multicenter randomized study from the Swedish lumbar spine study group. Spine. 2002;27(11):1131-41.

48. Glassman S, Gornet MF, Branch C, et al. MOS short form 36 and Oswestry Disability Index outcomes in lumbar fusion: a multicenter experience. Spine Journal: Official Journal of the North American Spine Society. 2006;6(1):21-6.

49. Blumenthal SL, Ohnmeiss DD, Guyer RD, Hochschuler SH. Prospective study evaluating total disc replacement: preliminary results. Journal of Spinal Disorders & Techniques. 2003;16(5):450-4.

50. Bertagnoli R, Yue JJ, Fenk-Mayer A, Eerulkar J, Emerson JW. Treatment of symptomatic adjacent-segment degeneration after lumbar fusion with total disc arthroplasty by using the prodisc prosthesis: a prospective study with 2-year minimum follow up. Journal of Neurosurgery Spine. 2006;4(2):91-7.

51. Bertagnoli R, Yue JJ, Shah RV, et al. The treatment of disabling single-level lumbar discogenic low back pain with total disc arthroplasty utilizing the Prodisc prosthesis: a prospective study with 2-year minimum follow-up. Spine. 2005;30(19):2230-6.

52. Zigler JE. Clinical results with ProDisc: European experience and U.S. investigation device exemption study. Spine. 2003;28(20):S163-6.

53. Zigler JE. Lumbar spine arthroplasty using the ProDisc II. Spine Journal: Official Journal of the North American Spine Society. 2004;4(6 Suppl):260S-267S.

54. Le Huec JC, Mathews H, Basso Y, et al. Clinical results of Maverick lumbar total disc replacement: two-year prospective follow-up. Orthopedic Clinics of North America. 2005;36(3):315-22.

55. Zigler JE, Burd TA, Vialle EN, Sachs BL, Rashbaum RF, Ohnmeiss DD. Lumbar spine arthroplasty: early results using the ProDisc II: a prospective randomized trial of arthroplasty versus fusion. Journal of Spinal Disorders & Techniques. 2003;16(4):352-61.

56. Nachemson A. Lumbar discography--where are we today?[see comment]. Spine. 1989;14(6):555-7.

57. Kwon BK, Hilibrand AS, Malloy K, et al. A critical analysis of the literature regarding surgical approach and outcome for adult low-grade isthmic spondylolisthesis. Journal of Spinal Disorders & Techniques. 2005;18 Suppl:S30-40.

58. Resnick DK, Choudhri TF, Dailey AT, 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.

59. Wenger M, Sapio N, Markwalder T-M. Long-term outcome in 132 consecutive patients after posterior internal fixation and fusion for Grade I and II isthmic spondylolisthesis. Journal of Neurosurgery Spine. 2005;2(3):289-97.

60. Resnick DK, Choudhri TF, Dailey AT, 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.

61. Resnick DK, Choudhri TF, Dailey AT, et al. Guidelines for the performance of fusion procedures for degenerative disease of the lumbar spine. Part 17: bone growth stimulators and lumbar fusion. Journal of Neurosurgery Spine. 2005;2(6):737-40.

62. Resnick DK, Choudhri TF, Dailey AT, et al. Guidelines for the performance of fusion procedures for degenerative disease of the lumbar spine. Part 16: bone graft extenders and substitutes. Journal of Neurosurgery Spine. 2005;2(6):733-6.

63. Resnick DK, Choudhri TF, Dailey AT, et al. Guidelines for the performance of fusion procedures for degenerative disease of the lumbar spine. Part 12: pedicle screw fixation as an adjunct to posterolateral fusion for low-back pain. Journal of Neurosurgery Spine. 2005;2(6):700-6.

64. Resnick DK, Choudhri TF, Dailey AT, et al. Guidelines for the performance of fusion procedures for degenerative disease of the lumbar spine. Part 2: assessment of functional outcome. Journal of Neurosurgery Spine. 2005;2(6):639-46.

65. Resnick DK, Choudhri TF, Dailey AT, et al. Guidelines for the performance of fusion procedures for degenerative disease of the lumbar spine. Part 7: intractable low-back pain without stenosis or spondylolisthesis. Journal of Neurosurgery Spine. 2005;2(6):670-2.

66. Resnick DK, Choudhri TF, Dailey AT, et al. Guidelines for the performance of fusion procedures for degenerative disease of the lumbar spine. Part 8: lumbar fusion for disc herniation and radiculopathy. Journal of Neurosurgery Spine. 2005;2(6):673-8.

67. Resnick DK, Choudhri TF, Dailey AT, 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.

68. Resnick DK, Choudhri TF, Dailey AT, et al. Guidelines for the performance of fusion procedures for degenerative disease of the lumbar spine. Part 15:

electrophysiological monitoring and lumbar fusion. Journal of Neurosurgery Spine. 2005;2(6):725-32.

69. Resnick DK, Choudhri TF, Dailey AT, 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.

70. Resnick DK, Choudhri TF, Dailey AT, et al. Guidelines for the performance of fusion procedures for degenerative disease of the lumbar spine. Part 3: assessment of economic outcome. Journal of Neurosurgery Spine. 2005;2(6):647-52.

71. Moller H, Hedlund R. Surgery versus conservative management in adult isthmic spondylolisthesis--a prospective randomized study: part 1. Spine. 2000;25(13):1711-5.

72. Ekman P, Moller H, Hedlund R. The long-term effect of posterolateral fusion in adult isthmic spondylolisthesis: a randomized controlled study. Spine Journal: Official Journal of the North American Spine Society. 2005;5(1):36-44.

73. Matsudaira K, Yamazaki T, Seichi A, et al. Spinal stenosis in grade I degenerative lumbar spondylolisthesis: a comparative study of outcomes following laminoplasty and laminectomy with instrumented spinal fusion. Journal of Orthopaedic Science. 2005;10(3):270-6.

74. Thomsen K, Christensen FB, Eiskjaer SP, Hansen ES, Fruensgaard S, Bunger CE. The effect of pedicle screw instrumentation on functional outcome and fusion

rates in posterolateral lumbar spinal fusion: a prospective, randomized clinical study. Spine. 1997;22(24):2813-22.

75. Vaccaro AR, Patel T, Fischgrund J, et al. A pilot study evaluating the safety and efficacy of OP-1 Putty (rhBMP-7) as a replacement for iliac crest autograft in posterolateral lumbar arthrodesis for degenerative spondylolisthesis. Spine. 2004;29(17):1885-92.

76. Suk KS, Jeon CH, Park MS, Moon SH, Kim NH, Lee HM. Comparison between posterolateral fusion with pedicle screw fixation and anterior interbody fusion with pedicle screw fixation in adult spondylolytic spondylolisthesis. Yonsei Medical Journal. 2001;42(3):316-23.

77. Ghiselli G, Wang JC, Bhatia NN, Hsu WK, Dawson EG. Adjacent segment degeneration in the lumbar spine. Journal of Bone & Joint Surgery - American Volume. 2004;86-A(7):1497-503.

78. Cummins J, Lurie JD, Tosteson TD, et al. Descriptive epidemiology and prior healthcare utilization of patients in the Spine Patient Outcomes Research Trial's (SPORT) three observational cohorts: disc herniation, spinal stenosis, and degenerative spondylolisthesis. Spine. 2006;31(7):806-14.

79. Remes VM, Lamberg TS, Tervahartiala PO, et al. No correlation between patient outcome and abnormal lumbar MRI findings 21 years after posterior or posterolateral fusion for isthmic spondylolisthesis in children and adolescents. European Spine Journal. 2005;14(9):833-42.

80. Throckmorton TW, Hilibrand AS, Mencio GA, Hodge A, Spengler DM. The impact of adjacent level disc degeneration on health status outcomes following lumbar fusion.[see comment]. Spine. 2003;28(22):2546-50.

81. Ghiselli G, Wang JC, Hsu WK, Dawson EG. L5-S1 segment survivorship and clinical outcome analysis after L4-L5 isolated fusion. Spine. 2003;28(12):1275-80; discussion 1280.

82. Kornblum MB, Fischgrund JS, Herkowitz HN, Abraham DA, Berkower DL, Ditkoff JS. Degenerative lumbar spondylolisthesis with spinal stenosis: a prospective long-term study comparing fusion and pseudarthrosis. Spine. 2004;29(7):726-33; discussion 733-4.

83. Lamberg TS, Remes VM, Helenius IJ, et al. Long-term clinical, functional and radiological outcome 21 years after posterior or posterolateral fusion in childhood and adolescence isthmic spondylolisthesis. European Spine Journal. 2005;14(7):639-44.

84. Madan SS, Harley JM, Boeree NR. Anterior lumbar interbody fusion: does stable anterior fixation matter? European Spine Journal. 2003;12(4):386-92.

85. Lidar Z, Beaumont A, Lifshutz J, Maiman DJ. Clinical and radiological relationship between posterior lumbar interbody fusion and posterolateral lumbar fusion. Surgical Neurology. 2005;64(4):303-8; discussion 308.

86. Deyo RA, Ciol MA, Cherkin DC, Loeser JD, Bigos SJ. Lumbar spinal fusion. A cohort study of complications, reoperations, and resource use in the Medicare population. Spine. 1993;18(11):1463-70.

87. Kilincer C, Steinmetz MP, Sohn MJ, Benzel EC, Bingaman W. Effects of age on the perioperative characteristics and short-term outcome of posterior lumbar fusion surgery. Journal of Neurosurgery Spine. 2005;3(1):34-9.

88. Raffo CS, Lauerman WC. Predicting morbidity and mortality of lumbar spine arthrodesis in patients in their ninth decade. Spine. 2006;31(1):99-103.

89. Wang MY, Green BA, Shah S, Vanni S, Levi ADO. Complications associated with lumbar stenosis surgery in patients older than 75 years of age. Neurosurgical Focus. 2003;14(2):e7.

90. Carreon LY, Puno RM, Dimar JR, 2nd, Glassman SD, Johnson JR. Perioperative complications of posterior lumbar decompression and arthrodesis in older adults. Journal of Bone & Joint Surgery - American Volume. 2003;85-A(11):2089-92.

91. Glassman SD, Alegre G, Carreon L, Dimar JR, Johnson JR. Perioperative complications of lumbar instrumentation and fusion in patients with diabetes mellitus. Spine Journal: Official Journal of the North American Spine Society. 2003;3(6):496-501.

92. Fang A, Hu SS, Endres N, Bradford DS. Risk factors for infection after spinal surgery. Spine. 2005;30(12):1460-5.

93. Fritzell P, Hagg O, Nordwall A, Swedish Lumbar Spine Study G. Complications in lumbar fusion surgery for chronic low back pain: comparison of three surgical techniques used in a prospective randomized study. A report from the Swedish Lumbar Spine Study Group. European Spine Journal. 2003;12(2):178-89.

94. Hagg O, Fritzell P, Nordwall A, Swedish Lumbar Spine Study G. Sexual function in men and women after anterior surgery for chronic low back pain. European Spine Journal. 2006;15(5):677-82.

95. Villavicencio AT, Burneikiene S, Bulsara KR, Thramann JJ. Perioperative complications in transforaminal lumbar interbody fusion versus anterior-posterior reconstruction for lumbar disc degeneration and instability. Journal of Spinal Disorders & Techniques. 2006;19(2):92-7.

96. Sasso RC, Best NM, Mummaneni PV, Reilly TM, Hussain SM. Analysis of operative complications in a series of 471 anterior lumbar interbody fusion procedures. Spine. 2005;30(6):670-4.

97. Bezer M, Kocaoglu B, Aydin N, Guven O. Comparison of traditional and intrafascial iliac crest bone-graft harvesting in lumbar spinal surgery. International Orthopaedics. 2004;28(6):325-8.

98. Brau SA, Delamarter RB, Schiffman ML, Williams LA, Watkins RG. Vascular injury during anterior lumbar surgery.[see comment]. Spine Journal: Official Journal of the North American Spine Society. 2004;4(4):409-12.

99. Scaduto AA, Gamradt SC, Yu WD, Huang J, Delamarter RB, Wang JC. Perioperative complications of threaded cylindrical lumbar interbody fusion devices: anterior versus posterior approach. Journal of Spinal Disorders & Techniques. 2003;16(6):502-7.

100. Pappou IP, Papadopoulos EC, Sama AA, Girardi FP, Cammisa FP. Postoperative infections in interbody fusion for degenerative spinal disease. Clinical Orthopaedics & Related Research. 2006;444:120-8.

101. Burkus JK, Transfeldt EE, Kitchel SH, Watkins RG, Balderston RA. Clinical and radiographic outcomes of anterior lumbar interbody fusion using recombinant human bone morphogenetic protein-2. Spine. 2002;27(21):2396-408.

102. Haid RW, Jr., Branch CL, Jr., Alexander JT, Burkus JK. Posterior lumbar interbody fusion using recombinant human bone morphogenetic protein type 2 with cylindrical interbody cages. Spine Journal: Official Journal of the North American Spine Society. 2004;4(5):527-38; discussion 538-9.

103. Hsu C-J, Chou W-Y, Teng H-P, Chang W-N, Chou Y-J. Coralline hydroxyapatite and laminectomy-derived bone as adjuvant graft material for lumbar posterolateral fusion. Journal of Neurosurgery Spine. 2005;3(4):271-5.

104. Korovessis P, Koureas G, Zacharatos S, Papazisis Z, Lambiris E. Correlative radiological, self-assessment and clinical analysis of evolution in instrumented dorsal and lateral fusion for degenerative lumbar spine disease. Autograft versus coralline hydroxyapatite. European Spine Journal. 2005;14(7):630-8.

105. Castro FP, Jr. Role of activated growth factors in lumbar spinal fusions. Journal of Spinal Disorders & Techniques. 2004;17(5):380-4.

106. Cammisa FP, Jr., Lowery G, Garfin SR, et al. Two-year fusion rate equivalency between Grafton DBM gel and autograft in posterolateral spine fusion: a prospective controlled trial employing a side-by-side comparison in the same patient. Spine. 2004;29(6):660-6.

107. Weiner BK, Walker M. Efficacy of autologous growth factors in lumbar intertransverse fusions. Spine. 2003;28(17):1968-70; discussion 1971.

108. Hee HT, Majd ME, Holt RT, Myers L. Do autologous growth factors enhance transforaminal lumbar interbody fusion? European Spine Journal. 2003;12(4):400-7.

109. Jenis LG, Banco RJ, Kwon B. A prospective study of Autologous Growth Factors (AGF) in lumbar interbody fusion. Spine Journal: Official Journal of the North American Spine Society. 2006;6(1):14-20.

110. Burkus JK, Gornet MF, Dickman CA, Zdeblick TA. Anterior lumbar interbody fusion using rhBMP-2 with tapered interbody cages. Journal of Spinal Disorders & Techniques. 2002;15(5):337-49.

111. Greenough CG, Taylor LJ, Fraser RD. Anterior lumbar fusion: results, assessment techniques and prognostic factors. European Spine Journal. 1994;3(4):225-30.

112. Kuslich SD, Ulstrom CL, Griffith SL, Ahern JW, Dowdle JD. The Bagby and Kuslich method of lumbar interbody fusion. History, techniques, and 2-year follow-up results of a United States prospective, multicenter trial.[see comment]. Spine. 1998;23(11):1267-78; discussion 1279.

113. Penta M, Fraser RD. Anterior lumbar interbody fusion. A minimum 10-year follow-up.[see comment]. Spine. 1997;22(20):2429-34.

114. Trief PM, Ploutz-Snyder R, Fredrickson BE. Emotional health predicts pain and function after fusion: a prospective multicenter study. Spine. 2006;31(7):823-30.

115. Agazzi S, Reverdin A, May D. Posterior lumbar interbody fusion with cages: an independent review of 71 cases. Journal of Neurosurgery. 1999;91(2 Suppl):186-92.

116. Brantigan JW, Steffee AD, Lewis ML, Quinn LM, Persenaire JM. Lumbar interbody fusion using the Brantigan I/F cage for posterior lumbar interbody fusion and the variable pedicle screw placement system: two-year results from a Food and Drug Administration investigational device exemption clinical trial. Spine. 2000;25(11):1437-46.

117. Christensen F, Hansen E, Laursen M, Thomsen K, Bunger C. 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. 2002;27(12):1269-77.

118. DeBerard MS, Colledge AL, Masters KS, Schleusener RL, Schlegel JD. Outcomes of posterolateral versus BAK titanium cage interbody lumbar fusion in injured workers: a retrospective cohort study. Journal of the Southern Orthopaedic Association. 2002;11(3):157-66.

119. Folman Y, Lee S-H, Silvera JR, Gepstein R. Posterior lumbar interbody fusion for degenerative disc disease using a minimally invasive B-twin expandable spinal spacer: a multicenter study. Journal of Spinal Disorders & Techniques. 2003;16(5):455-60.

120. Freeman BJ, Licina P, Mehdian SH. Posterior lumbar interbody fusion combined with instrumented postero-lateral fusion: 5-year results in 60 patients. European Spine Journal. 2000;9(1):42-6.

121. Gepstein R, Werner D, Shabat S, Folman Y. Percutaneous posterior lumbar interbody fusion using the B-twin expandable spinal spacer. Minimally Invasive Neurosurgery. 2005;48(6):330-3.

122. Gertzbein SD, Betz R, Clements D, et al. Semirigid instrumentation in the management of lumbar spinal conditions combined with circumferential fusion. A multicenter study. Spine. 1996;21(16):1918-25; discussion 1925-6.

123. Hinkley BS, Jaremko ME. Effects of 360-degree lumbar fusion in a workers' compensation population. Spine. 1997;22(3):312-22; discussion 323.

124. Jang J-S, Lee S-H. Clinical analysis of percutaneous facet screw fixation after anterior lumbar interbody fusion. Journal of Neurosurgery Spine. 2005;3(1):40-6.

125. Lee CK, Vessa P, Lee JK. Chronic disabling low back pain syndrome caused by internal disc derangements. The results of disc excision and posterior lumbar interbody fusion. Spine. 1995;20(3):356-61.

126. Lettice JJ, Kula TA, Derby R, Kim B-J, Lee S-H, Seo KS. Does the number of levels affect lumbar fusion outcome? Spine. 2005;30(6):675-81.

127. Madan SS, Boeree NR. Comparison of instrumented anterior interbody fusion with instrumented circumferential lumbar fusion. European Spine Journal. 2003;12(6):567-75.

128. McKenna PJ, Freeman BJC, Mulholland RC, Grevitt MP, Webb JK, Mehdian SH. A prospective, randomised controlled trial of femoral ring allograft versus a titanium cage in circumferential lumbar spinal fusion with minimum 2-year clinical results. European Spine Journal. 2005;14(8):727-37.

129. Pavlov PW, Meijers H, van Limbeek J, et al. Good outcome and restoration of lordosis after anterior lumbar interbody fusion with additional posterior fixation. Spine. 2004;29(17):1893-9; discussion 1900.

130. Potter BK, Freedman BA, Verwiebe EG, Hall JM, Polly DW, Jr., Kuklo TR. Transforaminal lumbar interbody fusion: clinical and radiographic results and complications in 100 consecutive patients. Journal of Spinal Disorders & Techniques. 2005;18(4):337-46.

131. Pradhan BB, Nassar JA, Delamarter RB, Wang JC. Single-level lumbar spine fusion: a comparison of anterior and posterior approaches. Journal of Spinal Disorders & Techniques. 2002;15(5):355-61.

132. Schofferman J, Slosar P, Reynolds J, Goldthwaite N, Koestler M. A prospective randomized comparison of 270 degrees fusions to 360 degrees fusions (circumferential fusions). Spine. 2001;26(10):E207-12.

133. Dehoux E, Fourati E, Madi K, Reddy B, Segal P. Posterolateral versus interbody fusion in isthmic spondylolisthesis: functional results in 52 cases with a minimum follow-up of 6 years. Acta Orthopaedica Belgica. 2004;70(6):578-82.

134. Hackenberg L, Halm H, Bullmann V, Vieth V, Schneider M, Liljenqvist U. Transforaminal lumbar interbody fusion: a safe technique with satisfactory three to five year results. European Spine Journal. 2005;14(6):551-8.

135. Suk SI, Lee CK, Kim WJ, Lee JH, Cho KJ, Kim HG. Adding posterior lumbar interbody fusion to pedicle screw fixation and posterolateral fusion after decompression in spondylolytic spondylolisthesis. Spine. 1997;22(2):210-9; discussion 219-20.

136. Aiki H, Ohwada O, Kobayashi H, et al. Adjacent segment stenosis after lumbar fusion requiring second operation. Journal of Orthopaedic Science. 2005;10(5):490-5.

137. Chou W-Y, Hsu C-J, Chang W-N, Wong C-Y. Adjacent segment degeneration after lumbar spinal posterolateral fusion with instrumentation in elderly patients. Archives of Orthopaedic & Trauma Surgery. 2002;122(1):39-43.
138. Kanayama M, Hashimoto T, Shigenobu K, et al. Adjacent-segment morbidity after Graf ligamentoplasty compared with posterolateral lumbar fusion.[see comment]. Journal of Neurosurgery. 2001;95(1 Suppl):5-10.
139. Kuslich SD, Danielson G, Dowdle JD, et al. Four-year follow-up results of lumbar spine arthrodesis using the Bagby and Kuslich lumbar fusion cage. Spine. 2000;25(20):2656-62.
140. Booth KC, Bridwell KH, Eisenberg BA, Baldus CR, Lenke LG. Minimum 5-year results of degenerative spondylolisthesis treated with decompression and instrumented posterior fusion. Spine. 1999;24(16):1721-7.
141. Etebar S, Cahill DW. Risk factors for adjacent-segment failure following lumbar fixation with rigid instrumentation for degenerative instability. Journal of Neurosurgery. 1999;90(2 Suppl):163-9.
142. Buttermann GR, Garvey TA, Hunt AF, et al. Lumbar fusion results related to diagnosis. Spine. 1998;23(1):116-27.
143. Rahm MD, Hall BB. Adjacent-segment degeneration after lumbar fusion with instrumentation: a retrospective study. Journal of Spinal Disorders. 1996;9(5):392-400.
144. Frymoyer JW, Hanley EN, Jr., Howe J, Kuhlmann D, Matteri RE. A comparison of radiographic findings in fusion and nonfusion patients ten or more years following lumbar disc surgery. Spine. 1979;4(5):435-40.

145. Jansson K-A, Nemeth G, Granath F, Blomqvist P. Spinal stenosis re-operation rate in Sweden is 11% at 10 years--a national analysis of 9,664 operations.[see comment]. European Spine Journal. 2005;14(7):659-63.

146. Atlas SJ, Keller RB, Wu YA, Deyo RA, Singer DE. Long-term outcomes of surgical and nonsurgical management of sciatica secondary to a lumbar disc herniation: 10 year results from the Maine lumbar spine study. Spine. 2005;30(8):927-35.

147. Malter AD, McNeney B, Loeser JD, Deyo RA. 5-year reoperation rates after different types of lumbar spine surgery. Spine. 1998;23(7):814-20.

148. Johnsson B, Annertz M, Sjoberg C, Stromqvist B. A prospective and consecutive study of surgically treated lumbar spinal stenosis. Part II: Five-year follow-up by an independent observer. Spine. 1997;22(24):2938-44.

149. Greiner-Perth R, Boehm H, Allam Y, Elsaghir H, Franke J. Reoperation rate after instrumented posterior lumbar interbody fusion: a report on 1680 cases. Spine. 2004;29(22):2516-20.

150. Lai P-L, Chen L-H, Niu C-C, Fu T-S, Chen W-J. Relation between laminectomy and development of adjacent segment instability after lumbar fusion with pedicle fixation. Spine. 2004;29(22):2527-32; discussion 2532.

151. Okuda Sy, Iwasaki M, Miyauchi A, Aono H, Morita M, Yamamoto T. Risk factors for adjacent segment degeneration after PLIF. Spine. 2004;29(14):1535-40.

152. Gillet P. The fate of the adjacent motion segments after lumbar fusion. Journal of Spinal Disorders & Techniques. 2003;16(4):338-45.

153. Ishihara H, Osada R, Kanamori M, et al. Minimum 10-year follow-up study of anterior lumbar interbody fusion for isthmic spondylolisthesis. Journal of Spinal Disorders. 2001;14(2):91-9.

154. Kumar MN, Baklanov A, Chopin D. Correlation between sagittal plane changes and adjacent segment degeneration following lumbar spine fusion. European Spine Journal. 2001;10(4):314-9.

155. Kumar MN, Jacquot F, Hall H. Long-term follow-up of functional outcomes and radiographic changes at adjacent levels following lumbar spine fusion for degenerative disc disease. European Spine Journal. 2001;10(4):309-13.

156. Miyakoshi N, Abe E, Shimada Y, Okuyama K, Suzuki T, Sato K. Outcome of one-level posterior lumbar interbody fusion for spondylolisthesis and postoperative intervertebral disc degeneration adjacent to the fusion. Spine. 2000;25(14):1837-42.

157. Nakai S, Yoshizawa H, Kobayashi S. Long-term follow-up study of posterior lumbar interbody fusion. Journal of Spinal Disorders. 1999;12(4):293-9.

158. Wiltse LL, Radecki SE, Biel HM, et al. Comparative study of the incidence and severity of degenerative change in the transition zones after instrumented versus noninstrumented fusions of the lumbar spine. Journal of Spinal Disorders. 1999;12(1):27-33.

159. Hambly MF, Wiltse LL, Raghavan N, Schneiderman G, Koenig C. The transition zone above a lumbosacral fusion. Spine. 1998;23(16):1785-92.

160. Chen WJ, Niu CC, Chen LH, Shih CH. Survivorship analysis of DKS instrumentation in the treatment of spondylolisthesis. Clinical Orthopaedics & Related Research. 1997(339):113-20.

161. Seitsalo S, Schlenzka D, Poussa M, Osterman K. Disc degeneration in young patients with isthmic spondylolisthesis treated operatively or conservatively: a long-term follow-up. European Spine Journal. 1997;6(6):393-7.

162. Wimmer C, Gluch H, Krismer M, Ogon M, Jesenko R. AP-translation in the proximal disc adjacent to lumbar spine fusion. A retrospective comparison of mono- and polysegmental fusion in 120 patients. Acta Orthopaedica Scandinavica. 1997;68(3):269-72.

163. Pihlajamaki H, Bostman O, Ruuskanen M, Myllynen P, Kinnunen J, Karaharju E. Posterolateral lumbosacral fusion with transpedicular fixation: 63 consecutive cases followed for 4 (2-6) years. Acta Orthopaedica Scandinavica. 1996;67(1):63-8.

164. Aota Y, Kumano K, Hirabayashi S. Postfusion instability at the adjacent segments after rigid pedicle screw fixation for degenerative lumbar spinal disorders. Journal of Spinal Disorders. 1995;8(6):464-73.

165. Penta M, Sandhu A, Fraser RD. Magnetic resonance imaging assessment of disc degeneration 10 years after anterior lumbar interbody fusion. Spine. 1995;20(6):743-7.

166. Axelsson P, Johnsson R, Stromqvist B, Arvidsson M, Herrlin K. Posterolateral lumbar fusion. Outcome of 71 consecutive operations after 4 (2-7) years. Acta Orthopaedica Scandinavica. 1994;65(3):309-14.

167. Roy-Camille R, Benazet JP, Desauge JP, Kuntz F. Lumbosacral fusion with pedicular screw plating instrumentation. A 10-year follow-up. Acta Orthopaedica Scandinavica Supplementum. 1993;251:100-4.

168. Lehmann TR, Spratt KF, Tozzi JE, et al. Long-term follow-up of lower lumbar fusion patients. Spine. 1987;12(2):97-104.

169. Leong JC, Chun SY, Grange WJ, Fang D. Long-term results of lumbar intervertebral disc prolapse. Spine. 1983;8(7):793-9.

170. Glaser J, Stanley M, Sayre H, Woody J, Found E, Spratt K. A 10-year follow-up evaluation of lumbar spine fusion with pedicle screw fixation. Spine. 2003;28(13):1390-5.

171. Kim K-T, Lee S-H, Lee Y-H, Bae S-C, Suk K-S. Clinical outcomes of 3 fusion methods through the posterior approach in the lumbar spine. Spine. 2006;31(12):1351-7; discussion 1358.

172. Korovessis P, Papazisis Z, Koureas G, Lambiris E. Rigid, semirigid versus dynamic instrumentation for degenerative lumbar spinal stenosis: a correlative radiological and clinical analysis of short-term results. Spine. 2004;29(7):735-42.

173. McGuire RA, Amundson GM. The use of primary internal fixation in spondylolisthesis. Spine. 1993;18(12):1662-72.

174. Lai P-L, Chen L-H, Niu C-C, Chen W-J. Effect of postoperative lumbar sagittal alignment on the development of adjacent instability. Journal of Spinal Disorders & Techniques. 2004;17(5):353-7.

175. Sengupta DK, Truumees E, Patel CK, et al. Outcome of local bone versus autogenous iliac crest bone graft in the instrumented posterolateral fusion of the lumbar spine. Spine. 2006;31(9):985-91.

176. Block AR, Ohnmeiss DD, Guyer RD, Rashbaum RF, Hochschuler SH. The use of presurgical psychological screening to predict the outcome of spine surgery. Spine Journal: Official Journal of the North American Spine Society. 2001;1(4):274-82.