FINAL APPRAISAL DOCUMENT

MANAGEMENT OPTIONS FOR PATIENTS WITH LOW BACK DISORDERS

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- Deep engagement throughout the appraisal process with all stakeholders through an external Evidence Review Group, which includes patients, clinicians, manufacturers, purchasers, and payers

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REPORT OF KEY FINDINGS

Introduction

Low back pain is an exceedingly common complaint, with a lifetime prevalence ranging from 11-84% (Walker, 2000). Chronic low back pain may be seen in as many as 75% of patients 6-12 months after an initial episode (Wahlgren, 1997). The economic impact of low back pain is also substantial. It is the fifth most common reason for all physician visits in the U.S. (Deyo, 2002; Hart, 1995), and is responsible for direct medical costs that approach $30 billion annually (Luo, 2003). In addition, low back pain is a major cause of lost productivity; it is estimated that up to 2% of the U.S. work force is compensated for back pain or injury each year (Taylor, 1985).

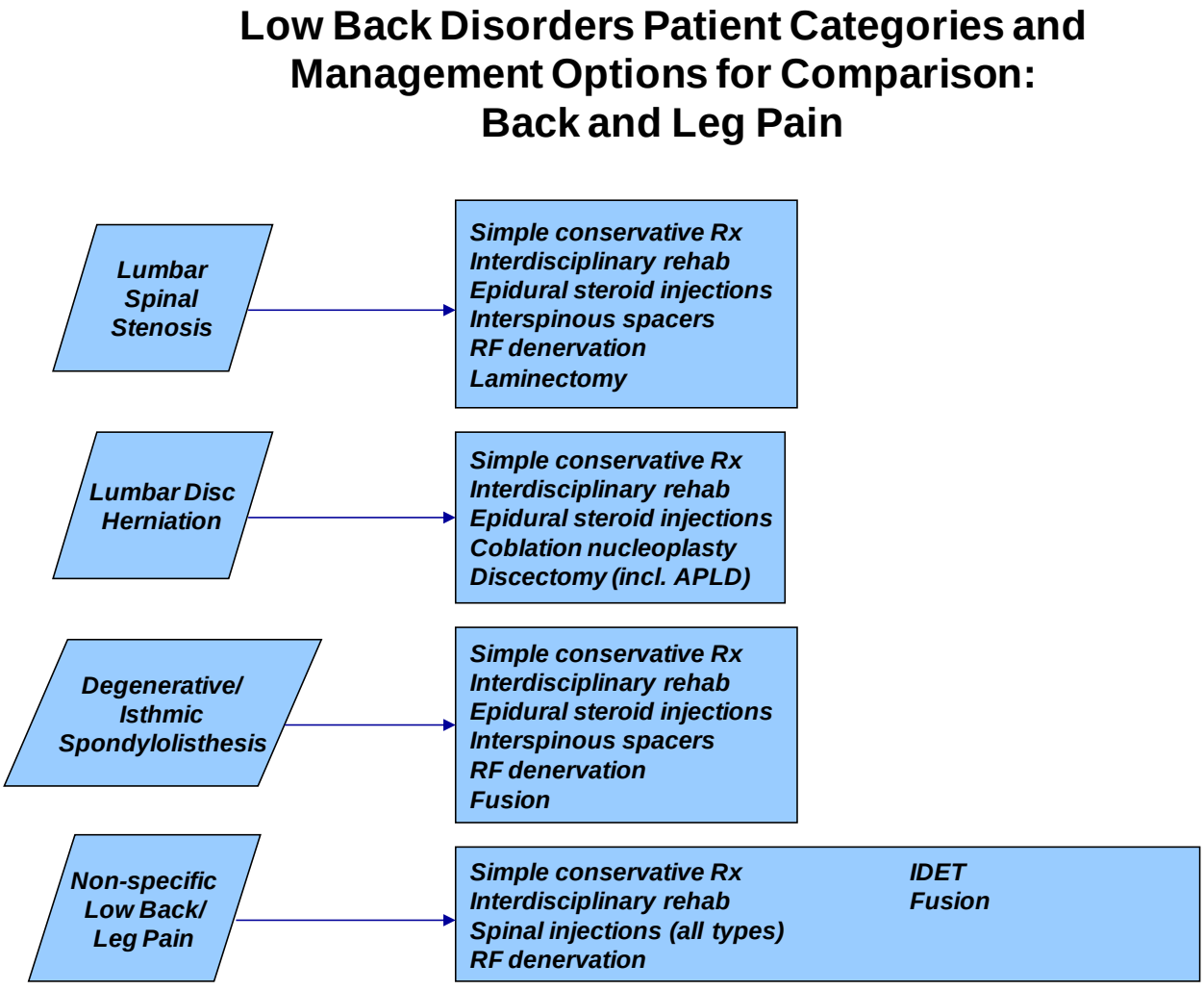
Low back pain can be caused by various specific and nonspecific conditions, which differ in prevalence and affect different age groups. Lumbar disc herniation occurs when an intervertebral disc ruptures and pushes outside its normal boundary (Heliovaara, 1988). Lumbar spinal stenosis refers to the narrowing of the spinal canal, which compresses the spinal cord and surrounding nerves (Kalichman, 2009). Spinal stenosis can occur alone or with spondylolisthesis, a condition caused by the shifting of a vertebra out of proper position and onto the one below it. Spondylolisthesis may be caused by intervertebral fracture ("isthmic" type) or by degeneration of the intervertebral disc ("degenerative" type).

While herniation, stenosis, and spondylolisthesis as confirmed through imaging are relatively prevalent conditions, imaging results are often weakly associated with the presence of symptoms. It has been estimated that up to 90% of cases of low back and/or leg pain cannot be tied to a specific anatomic cause (Manek, 2005). As a result, many patients presenting to primary care physicians with low back pain are classified as having pain that is nonspecific (Chou, 2010).

A variety of options are available to manage low back disorders. While some options are used exclusively in certain patient populations, they can be generally characterized as follows:

- Simple, unimodal conservative treatment: medications, physical and/or exercise therapy, behavioral therapy, chiropractic, alternative therapy (e.g., acupuncture, yoga)
- Interdisciplinary rehabilitation: intensive, multimodal rehabilitation that is physician-directed and may include workplace, exercise, educational, and/or behavioral interventions
- Spinal injections (e.g., epidural steroids, facet joint)
- Minimally-invasive procedures (e.g., radiofrequency denervation, intradiscal electrothermal therapy)
- Surgery (e.g., discectomy, spinal fusion)

This appraisal sought to evaluate the comparative clinical effectiveness and comparative value of multiple management options for 4 distinct patient populations. Populations and interventions of interest are presented in the Figure below:



RF: Radiofrequency; IDET: Intradiscal electrothermal therapy; DS: Degenerative spondylolisthesis; IS: Isthmic spondylolisthesis; APLD: Automated percutaneous lumbar discectomy

The population for this appraisal included patients with subacute or chronic low back and/or leg pain who have continued symptoms following a minimum of 4-6 weeks of simple conservative management. Therefore, while conservative care remained an important comparator for the interventions of interest, detailed analyses of conservative management options were considered outside the scope of the appraisal. Similarly, while the appropriateness of early imaging for low back disorders continues to be an important clinical and economic issue for many stakeholders, in consultation with our Evidence Review Group (ERG) convened for this appraisal it was decided that a new evidence review would add little information to the existing body of evidence reviews, clinical guidelines, and policy tools related to low back imaging.

This appraisal included evidence based on systematic review and synthesis of published peer-reviewed studies. Because several clinical societies and other decision-making bodies have conducted high-quality systematic reviews of many of the interventions of interest, *de novo* abstraction of studies was reserved for studies published after the literature search timeframe of these systematic reviews. Reviews were selected that met criteria for high quality (Oxman, 1991), have been widely cited, and have been influential in the development of clinical practice guidelines and/or policy decision-making. Selected reviews included:

- ***Spinal injections*:** Hashimoto R, et al. Spinal Injections: Health Technology Assessment. Spectrum Research, Inc., November 2010.

- ***Surgical interventions:*** Chou R, et al. Surgery for low back pain: a review of the evidence for an American Pain Society practice guideline. *Spine* 2009;34:1094-1109.

- ***Non-surgical minimally-invasive interventions:*** Chou R, et al. Nonsurgical interventional therapies for low back pain: a review of the evidence for an American Pain Society practice guideline. *Spine* 2009;34:1078-93.

We used standardized, back-pain specific criteria (Oxman, 1991) focused on study design, reporting, and minimization of bias to rate the quality of each included RCT or systematic review (see Appendix B). General criteria were employed to assess the quality of observational studies, using the categories "good", "fair", or "poor", based on criteria employed by the U.S. Preventive Services Task Force (AHRQ, 2008). Finally, we followed the approach used by AHRQ in evaluating the overall strength of evidence for each management option (AHRQ, 2011), which considers the following domains in making summary judgments:

- *Risk of bias* (study design and quality)
- *Consistency* (narrow range of effect sizes, uniform direction of effect)
- *Directness* (direct comparisons of interventions, direct link of intervention to key health outcomes)
- *Precision* (degree of certainty around estimates of effectiveness and/or harm)

Each management option was then assessed in relation to its relevant comparator(s) based on considerations of (a) relative certainty provided by the strength of the body of evidence; and (b) the magnitude of the comparative net health benefit observed. This assessment was performed separately for each measure of interest (e.g., pain, function, return to work); it is therefore possible that different ratings would be given for different outcome measures. Importantly, level of certainty in these rating is directly tied to the amount and quality of available RCT evidence. Management options for which there were only one or no RCTs for a given population were automatically rated as "I: Insufficient" across all measures.

In addition to the systematic review, a decision-analytic model tailored specifically for the 4 patient populations and management options of interest was developed to assess the comparative value of each intervention and provide additional clinical insights.

Evidence on Comparative Clinical Effectiveness

Data Quality

Of the 71 studies newly-identified and abstracted, the most abundant data identified were for non-specific low back pain (37 studies; N=14,741), followed by lumbar disc herniation (27 studies; N=51,216), lumbar spinal stenosis (4 studies; N=2,851) and degenerative or isthmic spondylolisthesis (3 studies; N=1,836). A total of 19 of 28 RCTs and 14 of 21 systematic reviews were identified as higher quality; the majority of these were in lumbar disc herniation and non-specific low back pain. Note that for the purposes of this analysis, observational studies rated as "good" or "fair" were deemed to be "higher-quality". Of the 22 observational studies abstracted, 15 were classified as "higher quality".

As noted previously, a significant degree of clinical heterogeneity has been observed in studies of patients with low back disorders. Even among studies of patients with a particular condition, such as lumbar disk herniation, comparisons across interventions within each patient population are problematic for multiple reasons. For one, there is a dearth of direct comparisons between the interventions of interest. More troubling is the variable nature of the comparator populations in these studies, making even indirect comparisons difficult if not impossible. As shown in Table ES1 below for lumbar disc herniation and nonspecific low back pain, the characteristics of patients randomized to "conservative" or "usual" nonoperative management differ substantially by patient population and intervention.

Table ES1. Baseline characteristics of patients randomized to conservative or other nonoperative management, by patient population and intervention.

		Comparator			
		Mean	Mean	Physical Function	Back Pain
Population/Intervention	Comparator	Age [Yrs]	% Female	Mean ODI	Mean VAS
Lumbar Disc Herniation					
Epidural Steroid Injections	Sham Placebo	45.2	58.6%	30.8	80.8
Discectomy	Conservative Care	42.0	33.6%	45.4	38.9
Non-Specific Low Back Pain					
IRP	Conservative Care	43.1	65.0%	49.6	57.5
IDET	Sham Placebo	40.1	34.8%	37.2	65.0
Spinal Fusion	Conservative Care	43.0	35.5%	45.1	64.7

IRP: Interdisciplinary Rehabilitation Program; IDET: Intradiscal Electrothermal Therapy; ODI: Oswestry Disability Index; VAS: Visual Analogue Scale

It should be further noted that, despite our intent to focus on studies evaluating patients presenting for treatment after attempts at short-term (4-6 weeks) conservative management, symptom duration was much longer at baseline in nearly all studies of interest. For example, mean symptom duration in RCTs of interventions for lumbar spinal stenosis, degenerative spondylolisthesis, and non-specific low back pain ranged from one to 5, one to 5, and 2 to 8 years respectively; in fact, a duration of symptoms of <6 months was a protocol *exclusion* in many of these studies. Only in lumbar disc herniation did the patient population approximate our initial target, as most patients had experienced symptoms for <6 months at study entry.

Effectiveness: Lumbar Disc Herniation

A table providing an overall summary of clinical benefit among the management options of focus for lumbar disc herniation can be found on the following page (Table ES2). An examination of findings for each management option can be found below. A single RCT was available for coblation nucleoplasty. No RCT data were available for automated percutaneous lumbar discectomy or interdisciplinary rehabilitation specifically for this patient population.

Discectomy

"Treatment Success"

Limited data are available on the impact of discectomy on measures of clinical success or improvement; those data that were obtainable suggest that discectomy results higher rates of success in the short term, but over time, treatment effects are diminished. For example, in an RCT of microdiscectomy vs. conservative care in 283 patients who were followed for 1 year (Peul, 2007), the median time to near-complete or complete recovery as assessed by a 7-point Likert scale was significantly shorter in the surgery group (4.0 vs. 12.1 weeks for conservative care, p<.001). However, by month 12 of follow-up, approximately 95% of patients in both groups had reported near-complete or complete recovery.

Pain and Function

A total of 7 RCTs reported pain and/or functional outcomes of open or microdiscectomy; 4 of these compared surgery to nonoperative care, and 3 compared alternative approaches to discectomy. In studies comparing surgery to nonoperative care, findings were generally consistent in favor of surgery up to month 6 of follow-up, but were not materially different at later timepoints. For example, intention-to-treat results from the SPORT trial indicated significant improvement on the Oswestry Disability Index (ODI) at 3 months (***Treatment Effect [TE]:*** -4.7; 95% CI: -9.3, -0.2), but no significant differences at 1 or 2 years of follow-up (Weinstein, 2006); this trend continued through 4-year follow-up (Weinstein, 2008). In contrast, significant treatment effects favoring surgery for both the ODI and low back pain scale were noted at 2, 3, and 4 years of follow-up in an "as-treated" analysis that combined data from both the randomized cohort and a separate observational cohort that allowed patients to select their management option (Weinstein, 2008). Observational findings suggesting a significant treatment effect favoring surgery on back pain, leg pain, and

Table ES2. Results Summary: *Lumbar Disc Herniation*

Comparison Set	Function	Pain	HRQoL	Return to Work	Responder %	Major Harms	Additional Procedures/ Reoperation
Discectomy vs. CC	≤12 mo: **B** >12 mo: **C**	≤12 mo: **B** >12 mo: **C**	≤12 mo: **B** >12 mo: **C**	≤12 mo: **C** >12 mo: **C**	>12 mo: **C**	0-4%	>12 mo: **C**
APLD vs. CC	**I**	**I**	**I**	**I**	**I**	0-4%	**I**
Coblation nucleoplasty vs. CC	**I**	**I**	**I**	**I**	**I**	**I**	**I**
ESI vs. other injections/CC	≤12 mo: **C** >12 mo: **C**	≤12 mo: **C** >12 mo: **C**	≤12 mo: **C** >12 mo: **C**	**I**	≤12 mo: **C** >12 mo: **C**	<1%	>12 mo: **C**
IRP vs. CC/surgery	**I**	**I**	**I**	**I**	**I**	<1%	**I**

Legend: Ratings of *Comparative* Clinical Effectiveness (vs. Comparator[s] of Interest)

A: "Superior": High certainty of moderate-to-large health benefit
B: "Incremental": High certainty of a small health benefit
C: "Comparable": High certainty of a comparable health benefit
D: "Inferior": High certainty of an inferior health benefit

U/P: "Unproven with Potential": Moderate certainty of small or moderate-large health benefit:
*High certainty health benefit is at least comparable, OR
*Moderate certainty of small or moderate-large health benefit

I: "Insufficient": The available evidence does not provide high certainty that the health benefit is at least comparable to that provided by the comparator(s)

CC: Conservative care; APLD: Automated percutaneous lumbar discectomy; ESI: Epidural steroid injections; IRP: Interdisciplinary rehabilitation programs

function as assessed by the Roland Morris Disability Questionnaire (RDQ) were also available from a 10-year study conducted in Maine (Atlas, 2005).

In RCTs comparing alternative forms of discectomy, significant improvements from baseline in pain and function were observed for all discectomy approaches, with no significant treatment effects favoring a specific approach.

Quality of Life

Available RCT data suggest that, as with the other outcome measures, quality of life improved substantially for both surgical and nonoperative patients. In the SPORT trial, a significant treatment effect favoring surgery on physical function was observed in the intention-to-treat population at 3 months (+2.8; 95% CI: +2.5, +8.1), but no similar effects were observed at 1-4 years of follow-up (Weinstein, 2006 and 2008). There were no significant effects on bodily pain at any timepoint. In the "as-treated" analysis of the combined randomized and observational cohorts, significant treatment effects favoring surgery were observed at 2, 3, and 4 years for both SF-36 subdomains. Similar patterns were observed in the above-described Peul RCT over 1 year of follow-up (Peul, 2007).

Return to Work

RCT-based data on working status for discectomy studies was available only from the SPORT trial. No significant treatment effects on working status were observed in either cohort at any timepoint, ranging from 3 months to 4 years of follow-up (Weinstein, 2006 and 2008). Findings from the previously-described cohort study reporting 10-year outcomes in patients receiving discectomy or conservative care showed similar proportions who were employed at baseline still working at year 10 (81% vs. 75% for surgical and nonsurgical care respectively, p=.43) (Atlas, 2005). In both studies, the authors speculate that the relative impact of such factors as workplace accommodations, job characteristics, and local economic factors may have a greater influence on return-to-work measures than the effects of specific interventions.

Coblation Nucleoplasty

"Treatment Success"

Findings from an RCT of 90 patients with image-confirmed lumbar disc herniation randomized to coblation nucleoplasty or up to 2 epidural steroid injections (Gerszten, 2010) indicated that significantly more nucleoplasty patients attained "literature-based" minimum clinically-important changes in VAS leg pain (≥25 points; 49% vs. 21%, p=.007) and VAS back pain (≥12 points; 49% vs. 22%, p=.017) during the 6-month randomized portion of the study; improvements remained significant through 2 years of observational follow-up. While the percentage of patients achieving a ≥13-point improvement of the ODI did not significantly differ at 6 months of follow-up, a higher percentage of nucleoplasty patients achieved this improvement during the observational period (30% vs. 10% at 2 years, p=.026).

In a separate, lower-quality systematic review identified in this appraisal (Manchikanti, 2009), a total of 5 coblation nucleoplasty series were identified. Rates of pain relief ranged

between 59-85% and 56-88% at 6 and 12 months of follow-up respectively, although this measure was variably defined.

Pain and Function

RCT findings indicated a statistically-significant difference in the magnitude of improvement on VAS leg pain (mean change: 47 vs. 21 at 6 months, p<.001), VAS back pain (21 vs. 0.4, p=.002), and ODI (14 vs. 4, p=.002) among patients receiving coblation nucleoplasty vs. epidural steroid injections (Gerszten, 2010). Findings from the 5 above-described coblation nucleoplasty case series (Manchikanti, 2009) suggest substantial improvements in VAS or numeric rating scales over 6-12 months of follow-up, ranging from 50-60%. One of these series evaluated changes in the ODI, reporting a decrease from a mean of 42.2 at baseline to 24.8 at 6 months.

Quality of Life

The Gerszten RCT observed significantly (p<.05) greater improvement in the physical function, bodily pain, and social function subdomains of the SF-36 as well as the physical component summary score at 6 months among patients randomized to coblation nucleoplasty (Gerszten, 2010). No data on quality of life were reported in available systematic reviews and case series of coblation nucleoplasty.

Return to Work

No differences were noted between treatment groups in the percentage of patients working full- or part-time at 6 months in the above-described RCT (Gerszten, 2010). No data on return to work were reported in available systematic reviews and case series of coblation nucleoplasty.

Epidural Steroid Injections (ESI)

"Treatment Success"

The systematic review used as a basis for our analysis of spinal injections (Hashimoto, 2010) included 2 RCTs with information on clinical improvement. Both RCTs involved fluoroscopic guidance. Evidence on this outcome was mixed. One RCT found a statistically-significant treatment effect favoring ESI vs. saline/anesthetic injections in the proportion of patients achieving >50% pain relief at 6 months, but no difference at 12 months or at earlier timepoints (Manchikanti, 2010). Findings from these and other studies conducted by this group should be interpreted with caution, however, as significant percentages of patients had data imputed at multiple timepoints because of missed assessments; in addition, the conclusions of many of these studies are described as positive because patients receiving both active and control therapy experienced improvement, despite the fact that no major differences between treatment groups were observed.

In the other RCT, pain relief >50% was reported in 54% of patients at 1 month vs. 7-21% in multiple control groups (p<.05) (Ghahreman, 2010), but was only measured at later timepoints for treatment failures.

Pain and Function

Combined data from the 2 spinal injection systematic reviews used as a basis for this appraisal (Chou, 2009b; Hashimoto, 2010) indicate a total of 23 RCTs of ESI that measured short-term (i.e., <3 months) pain and/or function in patients with lumbar disc herniation. Findings in favor of ESI were observed for pain in 8 of 23, no incremental benefit was observed in 10 of 23, and findings were unclear in the remaining 5. An identical breakdown of findings was seen in measures of function.

Long-term benefits were measured in a total of 12 studies. Results favoring ESI were observed for pain in 1 of 12, no incremental benefit was observed in 9 of 12, and findings were unclear in the remaining 2. Similarly, functional improvement favoring ESI was observed in 2 of 12 studies, no incremental benefit was observed in 8 of 12, and findings were unclear in the remaining 2 studies. Neither short-term nor long-term findings appeared to be correlated with whether fluoroscopic guidance was used.

Quality of Life

Data on quality of life were not found in RCTs or observational studies of ESI specifically for lumbar disc herniation.

Return to Work

Employment status was tracked in 2 recent RCTs of fluoroscopically-guided ESI over 12 months of follow-up (Manchikanti, 2008 and 2010). In both RCTs, the proportion employed full-time at 12 months was higher in the ESI group, but the rates of employment differed at baseline and no statistical testing was done on the change in employment during follow-up.

Interdisciplinary Rehabilitation

No RCTs or observational studies of interdisciplinary rehabilitation programs were identified with data on the effectiveness measures of interest in a specific population with lumbar disc herniation.

Effectiveness: Lumbar Spinal Stenosis

A table providing an overall summary of clinical benefit among the management options of focus for lumbar spinal stenosis can be found on the following page (Table ES3). An examination of findings for each management option can be found below. No RCT data were available for radiofrequency denervation or interdisciplinary rehabilitation specifically for this patient population.

Laminectomy with or without Spinal Fusion

"Treatment Success"

Among the major trials comparing laminectomy with or without spinal fusion to nonoperative care for patients with lumbar spinal stenosis, a global measure of treatment

Table ES3. Results Summary: *Lumbar Spinal Stenosis*

Comparison Set	Function	Pain	HRQoL	Return to Work	Responder %	Major Harms	Additional Procedures/ Reoperation
Laminectomy vs. CC	≤12 mo: **B** >12 mo: **B**	≤12 mo: **B** >12 mo: **B**	≤12 mo: **B** >12 mo: **B**	**I**	>12 mo: **C**	0-5%	**I**
Interspinous spacers vs. CC	**I**	**I**	**I**	**I**	**I**	0-6%	**I**
RF denervation vs. CC	**I**	**I**	**I**	**I**	**I**	**I**	**I**
ESI vs. other injections /CC	≤12 mo: **C** >12 mo: **C**	≤12 mo: **C** >12 mo: **C**	**I**	>12 mo: **C**	≤12 mo: **C** >12 mo: **C**	<1%	>12 mo: **C**
IRP vs. CC/surgery	**I**	**I**	**I**	**I**	**I**	<1%	**I**

Legend: Ratings of *Comparative* Clinical Effectiveness (vs. Comparator[s] of Interest)

A: "Superior": High certainty of moderate-to-large health benefit
B: "Incremental": High certainty of a small health benefit
C: "Comparable": High certainty of a comparable health benefit
D: "Inferior": High certainty of an inferior health benefit

U/P: "Unproven with Potential": Moderate certainty of small or moderate-large health benefit:
*High certainty health benefit is at least comparable, OR
*Moderate certainty of small or moderate-large health benefit

I: "Insufficient": The available evidence does not provide high certainty that the health benefit is at least comparable to that provided by the comparator(s)

CC: Conservative care; RF: Radiofrequency; ESI: Epidural steroid injections; IRP: Interdisciplinary rehabilitation program

success was only available from the SPORT trial (Weinstein, 2008b). In this trial, approximately 90% of patients in both the randomized and observational cohorts received laminectomy alone. The proportion of patients recording "major improvement" in their condition was examined at each study timepoint. No significant treatment effects were observed in this measure at any timepoint in the intention-to-treat analysis. In the as-treated analysis of the combined cohorts, surgery was associated with a significantly greater likelihood of self-reported major improvement at all timepoints; at 2 years, estimates were 62.9% and 28.7% for surgery and nonoperative care respectively (TE: 34.1%; 95% CI: 25.6%, 42.6%).

Pain and Function

In the intention-to-treat analysis of the SPORT trial, no significant treatment effects on ODI were observed at any timepoint through the 2-year follow-up. However, significant treatment effects favoring surgery on ODI were seen at 2 years in the as-treated analysis of both the randomized cohort alone (TE: -8.7; 95% CI: -13.3, -4.0) and the combined randomized and observational cohorts (TE: -11.2; 95% CI: -14.1, -8.3). In contrast, findings from another RCT conducted in Finland (Malmivaara, 2007) indicated significant treatment effects favoring surgery in the intention-to-treat population for the ODI, leg pain, and back pain at all timepoints over 2 years of follow-up.

Quality of Life

In the SPORT trial (Weinstein, 2008b), the intention-to-treat analysis indicated no significant short-term effect of surgery on SF-36 bodily pain, but a significant effect favoring surgery at 2 years (TE: 7.8; 95% CI: 1.5, 14.1). No benefit was observed for SF-36 physical function at any timepoint in this analysis. In contrast, long-term benefits were observed favoring surgery on both of these domains in as-treated analyses of the randomized cohort alone and the randomized and observational cohorts combined.

Return to Work

Data on return to work were not found in available RCTs or observational studies of laminectomy and/or spinal fusion specifically for lumbar spinal stenosis.

Interspinous Spacers

"Treatment Success"

Findings from a lower-quality RCT of interspinous spacers vs. nonoperative care were based on the 3 components of the Zurich Claudication Questionnaire (Zucherman, 2004). Patients with statistically significant improvements on the physical function, symptom severity, and satisfaction with treatment were considered successes. Treatment success was rated at 59% vs. 12% for spacers and nonoperative care respectively at 1 year ($p<.05$); corresponding results at 2 years were 48% and 5% (significance not reported).

Pain and Function

The Zucherman RCT used the Zurich Claudication Questionnaire (ZCQ) to evaluate the impact of treatment on physical function and symptom severity (Zucherman, 2004).

Significantly more patients were reported to be pain-free and have improved function in the spacer group at 6 weeks, 6 months, and 1 year of follow-up; these measures are difficult to compare to more widely-used indices, however, as the level of correlation between the ZCQ and other measures has not been extensively evaluated.

Quality of Life

The Zucherman RCT evaluated the impact of spacers vs. nonoperative care on all 8 subdomains of the SF-36. Significant differences favoring spacers were observed at 6 weeks, 6 months, and 1 year for all 8 subdomains (i.e., bodily pain, physical function, role physical, general health, vitality, social function, role emotional, and mental health).

Return to Work

Data on return to work were not found in RCTs or observational studies of interspinous spacers specifically for lumbar spinal stenosis.

Radiofrequency Denervation

No RCTs or observational studies of radiofrequency (RF) denervation were identified with data on the effectiveness measures of interest in a specific population with lumbar spinal stenosis.

Epidural Steroid Injections (ESI)

"Treatment Success"

The Hashimoto systematic review (Hashimoto, 2010) included 1 RCT of caudal ESI vs. saline/local anesthetic (Manchikanti, 2008) in which the percentage of patients achieving pain relief >50% did not significantly differ between groups at 3, 6, or 12 months, and was in fact numerically lower at each timepoint in the ESI group. However, as noted previously, results of this and other studies conducted by this group should be interpreted with caution.

Pain and Function

Combined data from the 2 spinal injection systematic reviews used as a basis for this appraisal (Chou, 2009b; Hashimoto, 2010) indicate a small number of RCTs (n=6) of ESI that measured short-term (i.e., <3 months) pain and/or function in patients with lumbar spinal stenosis. No incremental benefit of ESI was observed in all 6 of these studies. Long-term benefits were measured in a total of 3 studies; again, no benefit for ESI on either pain or function was observed in any of these studies.

Quality of Life

Data on quality of life were recorded in a single RCT of ESI for spinal stenosis (Koc, 2009), which involved comparison of ESI to both physical therapy and control injections. The Nottingham Health Profile (NHP) was used to measure quality of life. No significant between-group differences were noted on any domain of the NHP at 2 weeks, 1 month, 3 months, and 6 months of follow-up.

Return to Work

Data on working status were available for 2 RCTs of ESI for patients with spinal stenosis. Unfortunately, in these RCTs (Manchikanti, 2008 and 2010), baseline data were carried forward for patients who did not respond to queries on working status at 12 months of follow-up. Regardless, 12-month working status did not significantly differ between ESI and control patients in either study.

Interdisciplinary Rehabilitation

No RCTs or observational studies of interdisciplinary rehabilitation programs were identified with data on the effectiveness measures of interest in a specific population with lumbar spinal stenosis.

Effectiveness: Degenerative Spondylolisthesis

A table providing an overall summary of clinical benefit among the management options of focus for degenerative spondylolisthesis can be found on the following page (Table ES4). Detailed summaries for each outcome of interest can be found on the following pages. Available evidence is extremely limited; only 2 RCTs of spinal fusion and 1 RCT of interspinous spacers were identified specifically for this indication. No RCT data were available for radiofrequency denervation, epidural steroid injections, or interdisciplinary rehabilitation specifically for this patient population.

Spinal Fusion

"Treatment Success"

In the SPORT trial, approximately 95% of patients in both the randomized and observational cohorts received spinal fusion; 75% of these procedures were performed with instrumentation. The proportion of patients recording "major improvement" in their condition was examined only in the as-treated analysis of the combined randomized and observational cohorts; surgery was associated with a statistically significantly greater likelihood of improvement at all timepoints. The proportions reporting major improvement at 2 years were 74.1% and 24.1% for surgery and nonoperative care respectively (TE: 50.0%; 95% CI: 42.2%, 57.9%).

Pain and Function

RCT-based evidence on surgery comes from the SPORT trial (Weinstein, 2007) as well as the Finnish RCT (Malmivaara, 2007). While the latter RCT was conducted in a population with lumbar spinal stenosis, 42% of patients in the study were found to have "significant" spondylolisthesis (i.e., spondylolisthetic slips ≥3 mm) in a radiographic subgroup analysis.

In the intention-to-treat analysis of the SPORT trial, no significant treatment effects on ODI were observed at any timepoint through the 2-year follow-up. However, significant treatment effects favoring surgery on ODI were seen at 3 months, 1 year, and 2 years in the as-treated analysis of the combined randomized and observational cohorts (2-year TE: -16.7;

Table ES4. Results Summary: *Degenerative Spondylolisthesis*

Comparison Set	Function	Pain	HRQoL	Return to Work	Responder %	Major Harms	Additional Procedures/ Reoperation
Fusion vs. CC	≤12 mo: **B** >12 mo: **B**	≤12 mo: **B** >12 mo: **B**	≤12 mo: **B** >12 mo: **B**	**I**	>12 mo: **B**	0-5%	**I**
Interspinous spacers vs. CC	**I**	**I**	**I**	**I**	**I**	0-6%	**I**
RF denervation vs. CC	**I**	**I**	**I**	**I**	**I**	**I**	**I**
ESI vs. other injections/CC	**I**	**I**	**I**	**I**	**I**	<1%	**I**
IRP vs. CC/surgery	**I**	**I**	**I**	**I**	**I**	<1%	**I**

Legend: Ratings of *Comparative* Clinical Effectiveness (vs. Comparator[s] of Interest)

A: "Superior": High certainty of moderate-to-large health benefit
B: "Incremental": High certainty of a small health benefit
C: "Comparable": High certainty of a comparable health benefit
D: "Inferior": High certainty of an inferior health benefit

U/P: "Unproven with Potential": Moderate certainty of small or moderate-large health benefit:
*High certainty health benefit is at least comparable, OR
*Moderate certainty of small or moderate-large health benefit

I: "Insufficient": The available evidence does not provide high certainty that the health benefit is at least comparable to that provided by the comparator(s)

CC: Conservative care; RF: Radiofrequency; ESI: Epidural steroid injections; IRP: Interdisciplinary rehabilitation program

95% CI: -19.5, -13.9). In addition, significant treatment effects were observed in this analysis for two secondary outcomes, 6-point scales indicating levels of bothersomeness from leg pain (2-year TE: -1.5; 95% CI: -1.8, -1.1) and low back pain (2-year TE: -1.0; 95% CI: -1.3, -0.7). While stratified analyses by diagnosis were not available in the Malmivaara RCT, findings were stratified by type of surgery. At 2 years, significant treatment effects in the intention-to-treat analysis of patients receiving spinal fusion (the treatment approach for 90% of spondylolisthetic patients in this study) were noted for leg pain (TE: -2.4; 95% CI: -4.5, -0.3), but not for back pain or the ODI. In a separate on-treatment analysis, significant treatment effects were noted for all 3 measures.

Quality of Life

Data on the impact of decompressive surgery on quality of life were available from the SPORT trial (Weinstein, 2007). In this population, the intention-to-treat analysis indicated no significant treatment effects on bodily pain or physical function at any timepoint. In contrast, significant and stable treatment effects favoring surgery were noted across all time periods in the as-treated analysis of bodily pain (2-year TE: 18.1; 95% CI: 14.5, 21.7) and physical function (2-year TE: 18.3; 95% CI: 14.6, 21.9).

Return to Work

Data on return to work were not found in RCTs or observational studies of laminectomy and/or spinal fusion specifically for degenerative spondylolisthesis.

Interspinous Spacers

"Treatment Success"

Findings from one higher-quality RCT of interspinous spacers vs. nonoperative care were based on a 15-point or greater improvement in the combined physical function and symptom severity scores from the ZCQ, a final ZCQ-based satisfaction score <2.5 (lower scores indicate better satisfaction), and no requirements for further surgery (Anderson, 2006). Overall "treatment success" was observed in 63.4% of X-STOP patients vs. 12.9% of those randomized to nonoperative care ($p<.05$).

Pain and Function

In the above-mentioned RCT (Anderson, 2006), the ZCQ scores for physical function and symptom severity were combined. At 2 years, the combined score had improved significantly for patients in the X STOP group (mean [SD] 50.40 [2.04] vs. 23.05 [3.14] at baseline and 2 years respectively, $p<.05$), while no significant change in this measure was observed in the nonoperative group.

Quality of Life

In the Anderson RCT, a 10-point improvement in the physical component summary score of the SF-36 was noted in the X-STOP group (mean [SD] 31.53 vs. 41.19 at baseline and 2 years respectively, $p<.05$) (Anderson, 2006), while no change was observed in the nonoperative group. In contrast, no significant change was observed on the mental

component summary in either group; in addition, mean mental component summary scores were similar to norms obtained from healthy individuals.

Return to Work
Data on return to work were not found in RCTs or observational studies of interspinous spacers specifically for degenerative spondylolisthesis.

Radiofrequency Denervation, Epidural Steroid Injections, & Interdisciplinary Rehabilitation

No RCTs or observational studies of these management options were identified with data on the effectiveness measures of interest in a specific population with degenerative spondylolisthesis.

Effectiveness: Non-Specific Low Back Pain

A table providing an overall summary of clinical benefit among the management options of focus for non-specific low back pain can be found on the following page (Table ES5). Detailed summaries for each outcome of interest can be found below and on the following pages.

Spinal Fusion

There have been 4 major RCTs published comparing spinal fusion to nonoperative care among patients with non-specific low back pain. Three of these studies compared fusion to interdisciplinary rehabilitation with a cognitive-behavioral component (Brox, 2003; Brox, 2006; Fairbank, 2005), while control therapy in the remaining RCT was at the discretion of the treating physician, and mainly involved non-intensive physical therapy (Fritzell, 2001). While patients undergoing spinal fusion had similar levels of improvement in pain and function over 1-2 years of follow-up across all 4 RCTs, statistically-significant treatment effects favoring fusion were only noted in the RCT comparing fusion to non-intensive physical therapy (Fritzell, 2001). Comparisons across these RCTs are further complicated by differences in study design, methods, and crossover rates (Mirza, 2007). These limitations, as well as a higher observed rate of major harms with fusion vs. nonoperative care, should be considered when reviewing the results presented in the sections that follow.

"Treatment Success"
Two available RCTs of spinal fusion vs. interdisciplinary rehabilitation programs (IRP) defined clinical success on the basis of patient ratings of "excellent", "good", or "fair" on the Global Back Disability Questionnaire (Brox, 2003; Brox, 2006). At 1 year, the percentage of patients recording success (Brox, 2003: 71% vs. 63%; Brox, 2006: 50% vs. 48%) did not statistically differ between groups. A third RCT comparing fusion to physical therapy (Fritzell, 2001) defined treatment success based on patient ratings of their symptoms as

Table ES5. Results Summary: *Non-specific Low Back Pain*

Comparison Set	Function	Pain	HRQoL	Return to Work	Responder %	Major Harms	Additional Procedures/ Reoperation
Fusion vs. CC	≤12 mo: **C** >12 mo: **C**	≤12 mo: **C** >12 mo: **C**	≤12 mo: **C** >12 mo: **C**	>12 mo: **C**	>12 mo: **C**	0-5%	>12 mo: **C**
IDET vs. CC	≤12 mo: **U/P**	≤12 mo: **U/P**	≤12 mo: **U/P**	**I**	≤12 mo: **U/P**	<1%	**I**
RF denervation vs. CC	≤12 mo: **C** >12 mo: **I**	≤12 mo: **C** >12 mo: **I**	**I**	≤12 mo: **C**	≤12 mo: **C**	**I**	>12 mo: **C**
IRP vs. CC	≤12 mo: **C** >12 mo: **U/P**	≤12 mo: **C** >12 mo: **C**	≤12 mo: **U/P** >12 mo: **U/P**	>12 mo: **U/P**	≤12 mo: **U/P**	<1%	**I**
IRP vs. PT	≤12 mo: **C** >12 mo: **C**	≤12 mo: **C** >12 mo: **C**	≤12 mo: **C** >12 mo: **C**	>12 mo: **C**	≤12 mo: **C**	<1%	**I**
Spinal injections vs. CC/other injections							
ESI	≤12 mo: **C** >12 mo: **C**	≤12 mo: **C** >12 mo: **C**	**I**	≤12 mo: **C** >12 mo: **C**	≤12 mo: **C** >12 mo: **C**	<1%	>12 mo: **C**
SSI	**I**	**I**	**I**	**I**	**I**	<1%	**I**
ISI	≤12 mo: **C**	≤12 mo: **C**	**I**	**I**	**I**	<1%	**I**
BB	≤12 mo: **C** >12 mo: **C**	≤12 mo: **C** >12 mo: **C**	**I**	**I**	>12 mo: **C**	<1%	**I**

Legend: Ratings of *Comparative* Clinical Effectiveness (vs. Comparator[s] of Interest)

A: "Superior": High certainty of moderate-to-large health benefit
B: "Incremental": High certainty of a small health benefit
C: "Comparable": High certainty of a comparable health benefit
D: "Inferior": High certainty of an inferior health benefit

U/P: "Unproven with Potential": Moderate certainty of small or moderate-large health benefit:
*High certainty health benefit is at least comparable, OR
*Moderate certainty of small or moderate-large health benefit

I: "Insufficient": The available evidence does not provide high certainty that the health benefit is at least comparable to that provided by the comparator(s)

CC: Conservative care; IDET: Intradiscal electrothermal therapy; RF: Radiofrequency; ESI: Epidural steroid injections; SSI: Sacroiliac steroid injections; ISI: Intradiscal steroid injections: BB: Branch blocks; IRP: Interdisciplinary rehabilitation program

"better" or "much better". At 2 years, a significant difference favoring surgery was observed (63% vs. 29% for nonsurgical therapy, p<.0001).

Pain and Function

RCT-based evidence on surgery comes from the 3 above-described RCTs in Norway and Sweden as well as an RCT comparing fusion or graf ligamentoplasty to IRP (Fairbank, 2005). In the Norwegian RCTs, no significant treatment effects were observed for pain (as measured by a 100-point VAS scale) or the ODI at 1 year of follow-up. In the Swedish RCT, however, significant differences favoring surgery were noted in the mean change from baseline for both the 100-point VAS (-21.0 vs. -4.3 for physical therapy, p=.0002) and the ODI (-11.6 vs. -2.8, p=.015) (Fritzell, 2001). A significant difference in the ODI favoring surgery at 2 years was also observed in the UK RCT of surgery and IRP (TE: -4.1; 95% CI: -8.1, -0.1; p=.045); no specific pain measure was employed in this study.

Quality of Life

Data on the impact of spinal fusion on quality of life were available only from the Fairbank RCT vs. IRP (Fairbank, 2005). No statistically significant differences were noted at 24 months for the SF-36 mental or physical component summary scores, nor were differences observed in any specific subdomain.

Return to Work

Data on the impact of spinal fusion on return to work come from the Brox and Fritzell studies. In the former, the percentage of employed individuals who returned to work was numerically higher in the IRP control group, but did not reach statistical significance. In contrast, the percentage of individuals in the Fritzell RCT not able to work at baseline due to back pain who returned to work was significantly higher in the spinal fusion group (39% vs. 23% for physical therapy, p=.049). The "net" rate of back to work (i.e., subtracting those who stopped working during follow-up) was also significantly higher in the surgery group (36% vs. 13% for physical therapy, p=.002).

Intradiscal Electrothermal Therapy (IDET)

"Treatment Success"

Successful clinical outcome was measured in a single RCT of IDET vs. sham placebo (Freeman, 2005), and was defined based on the combination of no neurologic deficit, an improvement of at least 7 points on the 75-point Low Back Outcome Score, and improvement of at least 1 standard deviation beyond the mean in the bodily pain and physical function scales of the SF-36. No patient in either study arm met all of these criteria; when criteria were evaluated individually, no statistically-significant differences between groups were observed.

Pain and Function

Evidence on pain and function is mixed in the 2 available RCTs of IDET. In the previously-mentioned Freeman RCT, the ODI score improved only slightly in the IDET group at 6 months, and no significant treatment effect was observed. In a second RCT of IDET vs.

sham placebo (Pauza, 2004), positive findings at 6 months were observed on both the ODI (mean [SD] change from baseline -11 [11] vs. -4 [12] for sham, p=.05) and on a 10-point VAS scale for pain (mean [SD] change from baseline -2.4 [2.3] vs. 1.1 [2.6] for sham, p=.045); the latter RCT appeared to involve a highly selected patient population, however, as only 64 of 1,360 potentially-eligible patients were randomized.

Quality of Life

In the 2 available RCTs of IDET (Pauza, 2004; Freeman, 2005), no significant differences were observed between groups for changes in SF-36 physical or mental component summary scores or subdomain scores for bodily pain and physical function.

Return to Work

Neither of the 2 IDET RCTs measured return to work as a primary or secondary outcome. Findings from a prospective series of 53 worker's compensation patients receiving IDET suggested a significant increase in the percentage of patients working at some level (i.e., full duty, light duty, w/lifting restrictions) at 4.5 years of follow-up relative to baseline (47.2% vs. 5.3%, p<.0001).

RF Denervation

"Treatment Success"

A single RCT comparing RF denervation to sham placebo also included a measure of "treatment success", defined based on reductions in VAS back pain, resumption of daily activities, and/or decreases in analgesic use. No significant differences in this outcome were noted at 3 months; in addition, Kaplan-Meier analysis of time to treatment success suggested no differences in treatment success at any point up to 1 year after treatment. In a separate 10-year case series examining the proportion of patients with "good-to-excellent" pain relief (Gofeld, 2007), the percentages were 96%, 43%, and 2% for durations of 6-12 months, 12-24 months, and >24 months respectively.

Pain and Function

Evidence on RF denervation comes from 3 systematic reviews (Chou, 2009b; Niemisto, 2010; Henschke, 2010), all of which reached similar conclusions. For presumed lumbar facet joint pain, there was mixed evidence from 3 RCTs regarding a short-term (i.e., 4 weeks) benefit of RF denervation on VAS pain and ODI vs. sham placebo. No evidence of benefit was observed with longer-term follow-up. A single RCT of RF denervation was conducted in patients with presumed discogenic pain. No significant differences were observed for any outcome measure.

Quality of Life

Data on quality of life were not found in RCTs or observational studies of RF denervation focused on patients with non-specific low back pain.

Return to Work
Measures of return to work were available in a single RCT of RF denervation (Leclaire, 2001). In this study, 8 patients in each of the RF denervation and placebo groups were not working at baseline; all patients in both groups returned to work by the end of the 3-month follow-up.

Spinal Injections

"Treatment Success"
Two RCTs comparing fluoroscopically-guided ESI to local anesthetic injections defined "treatment success" based on ≥50% improvement on both a 10-point numeric rating scale for pain and the ODI (Manchikanti, 2008; Manchikanti, 2010). The number of weeks of "total relief" did not materially differ between treatment groups in either study at any timepoint up to 12 months after study initiation. In another RCT of therapeutic medial branch blocks (BB) vs. local anesthetic injections (Manchikanti 2010b), separate analyses were conducted of improvement ≥50% on pain scores and ≥40% on the ODI. There were no material differences in these rates in either the short term (3 months) or long term (24 months); statistical significance was not reported. Again, studies conducted by this group should be interpreted with caution given the limitations previously described.

Pain and Function
Combined data from the 2 spinal injection systematic reviews used as a basis for this appraisal (Chou, 2009b; Hashimoto, 2010) indicate no evidence of benefit on pain or function in the short- or long-term for RCTs of ESI (n=12), intradiscal steroid injections (ISI) (n=7) or therapeutic medical branch blocks (BB) (n=5). A single RCT of sacroiliac steroid injections (SSI) (Lukkainen, 2002) vs. local anesthetic injections indicated significant improvement on both a 100-point VAS scale (median change from baseline -40 vs. -13, p=.046) and a 12-point pain index (median change from baseline -3 vs. 0, p=.017).

Quality of Life
Data on quality of life were not found in RCTs or observational studies of spinal injections of any type focused on patients with non-specific low back pain.

Return to Work
Data on return to work were available from a single RCT of ESI (Manchikanti, 2010). Rates of part-time employment, full-time employment, unemployment, and unemployment due to pain did not materially change in either group, and did not numerically differ between groups (although this was not tested statistically).

Interdisciplinary Rehabilitation

"Treatment Success"
Measures of "successful clinical outcome" were varied in studies of interdisciplinary rehabilitation programs (IRP), including changes on the EQ-5D or RDQ as well as patient

perception of improvement. No significant differences favoring IRP were noted for any of these measures.

Pain and Function

Function was evaluated in 8 of the 11 available RCTs of interdisciplinary rehabilitation programs including the Fairbank study described above. Function was measured by the RDQ in 6 RCTs and the ODI in 2. Significant treatment effects favoring IRP were observed in 2 RCTs. One was a comparison of IRP to usual care (Lambeek, 2010); effects on the RDQ were reported at 12 months (TE: -2.86; 95% CI: -4.9, -0.9, p=.01). The other RCT compared IRP to an intensive exercise program (Dufour, 2010); effects on the RDQ were reported at 24 months (mean [SD] change from baseline: 3.2 [6.4] vs. 1.4 [5.4] for control, p=.003). No significant treatment effects on pain were observed in any of these RCTs over durations of follow-up ranging from 4 months to 2 years.

Two observational studies were available that documented the long-term effects of IRP on pain and function. In one study (Lee, 2003), large and statistically significant improvements from baseline were noted on a 10-point VAS (mean [SD] change: -3.2 [3.0], p=.001) and the RDQ (mean [SD] change: -6.6 [7.5], p=.001) at 4 years of follow-up. In the other study, however, changes from baseline in a 10-point VAS essentially plateaued at 5 months and remained constant through 2 years of follow-up (Bontoux, 2009).

Quality of Life

Measures of quality of life were reported in a total of 5 RCTs of interdisciplinary rehabilitation programs. Significant findings favoring IRP were noted in 2 of these RCTs. In one, the previously-described RCT of IRP and individualized exercise (Dufour, 2010), a significant treatment effect was noted at all timepoints on the physical functioning subdomain and the physical component summary score. In the other, a comparison of a combined physical and cognitive-behavioral therapy program vs. usual care in Sweden (Jensen, 2005), a significant treatment effect was observed at 3 years on the SF-36 global score, but this effect was only noted in females following a post hoc subgroup analysis by sex.

Return to Work

Surprisingly, despite the inclusion of workplace interventions in many IRP studies, only 6 of the 11 RCTs in our sample measured return to work as an outcome. Positive findings in favor of IRP were observed in 3 of the 6 RCTs. In one comparison of IRP to usual care (Lambeek, 2010), the median duration of sick leave in the year following randomization was significantly lower in the IRP group (88 vs. 208 days for usual care, p=.003). In a comparison of IRP to usual care in Sweden (Jensen, 2005), the likelihood of return to work, based on Cox proportional hazards regression, was significantly better in the IRP group vs. usual care (HR=1.9; 95% CI: 1.3, 3.5), but only among female employees. Finally, in a comparison of a workplace intervention, a graded activity program, the combination of the two, and usual care in the Netherlands (Anema, 2007), the workplace intervention was associated with a lower number of days of sick leave (median 77 vs. 104 for usual care, p=.02) and an increased likelihood of return to work (HR: 1.7; 95% CI: 1.2, 2.3; p=.002).

Analysis of Interdisciplinary Rehabilitation Programs

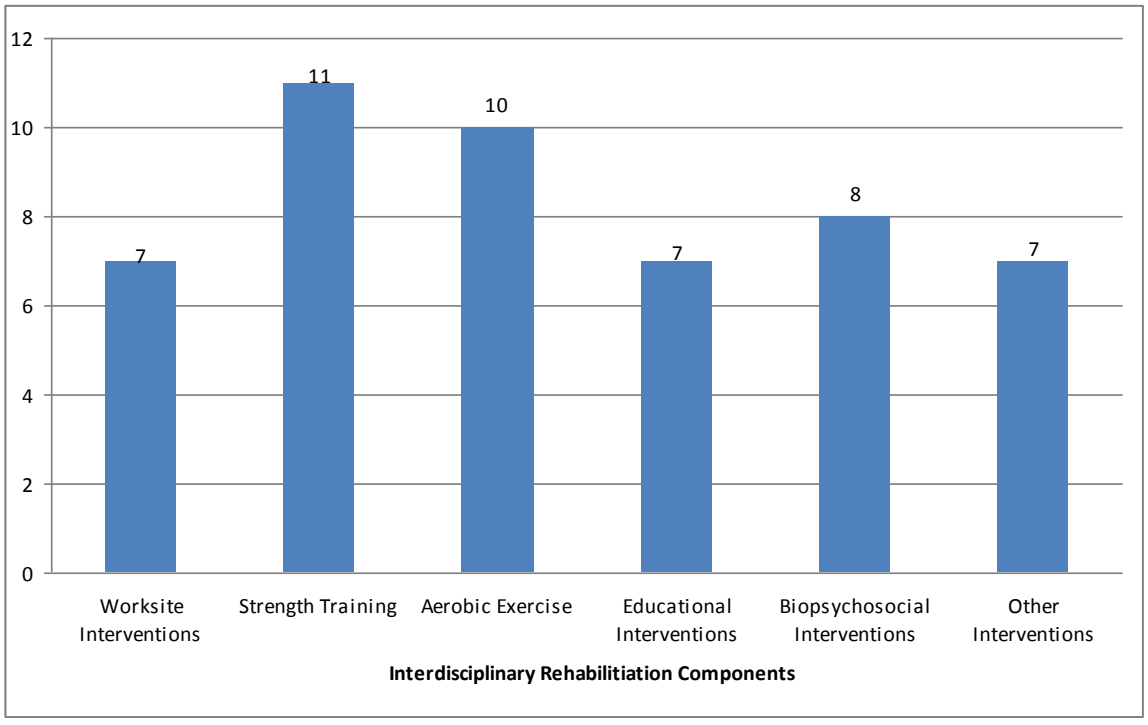
The purpose of this section is to characterize the programs that have been described in the literature and identify those program elements associated with the highest levels of effectiveness. Consistent with the criteria employed in other systematic reviews, IRP was defined based on the following minimum criteria:

- Physician direction of program
- Physical/exercise component
- At least *one* of the following components:
  - Psychological (e.g., CBT, individual counseling)
  - Social (e.g., social worker/case manager intervention)
  - Occupational (e.g., worksite assessment, vocational therapy)
  - Educational (e.g., anatomy, self-care)

IRP studies were abstracted regardless of whether program components were delivered by different disciplines or by individual therapists with multidisciplinary training.

We identified a total of 11 RCTs published since 2000 that describe truly interdisciplinary programs. Program intensity ranged widely, from 5 to 150 hours. As can be seen in Figure ES1 below, all programs had a muscle strengthening component, and nearly all involved aerobic exercise. These components varied widely in their definition, however (see Table 7 on page 152 of Section 7). For example, muscle strengthening was based on individualized goals in some cases, and involved defined exercises for spinal stability/mobility in others.

Figure ES1. Components of abstracted interdisciplinary rehabilitation programs (n=11).



Another area of variation was the comparator treatment involved. In 4 of these RCTs, a physical therapy regimen was employed (Roche, 2007; Dufour, 2010; Kaapa, 2006; van der Roer, 2008) in another, the comparator was spine stabilization surgery (Fairbank, 2005). A "usual care" control arm involving no specific protocol was used in only 3 of these RCTs.

Evidence is mixed on the effects of IRP vs. usual care. In one RCT, significant treatment effects in favor of IRP were observed in terms of function on the RDQ (Treatment Effect [TE]: -2.86 at 12 months; 95% CI: -4.9, -0.9, p=.01) and median number of days of sick leave over 12 months (82 vs. 175 for usual care, p=.003) (Lambeek, 2010). In another, no significant treatment effects on function, pain, or quality of life were observed (Vollenbroek-Hutten, 2004); in fact, only 30-50% of patients in the IRP group showed improvement on any effectiveness measure over 6 months of follow-up. In the third RCT, some improvement was noted on total sick leave days and SF-36 global health ratings, but only in the "per-protocol" analysis and was noted only for female patients (Jensen, 2005).

The potential reasons for these discrepant findings are not easily discernible. One possible explanation might involve working status at baseline. All of the patients in the positive Lambeek RCT were sick-listed at baseline, while working status was used only to balance groups during randomization in the Vollenbroek-Hutten RCT. However, RDQ-assessed functional status was worse in the latter RCT; as noted in many studies previously, work status may not be an adequate proxy for symptom severity or the likelihood of treatment success.

Findings from those RCTs comparing IRP to some form of physical therapy were relatively consistent, in that no significant treatment effects favoring IRP were observed for any primary outcome measure. In all of these cases, substantial improvements in pain, disability, and function were observed in both treatment groups.

The components of effective IRP programs that showed some level of effectiveness vs. usual or non-intensive care (i.e., 4 of the 6 studies not comparing IRP to PT or structured exercise) are summarized in Table ES6 on the following page. Worksite interventions and aerobic exercises were employed in 3 of the 4 studies, and strength training was a component of all 4 studies. Educational, biospsychosocial, and other types of interventions were less frequently employed.

A number of systematic reviews of IRP have also been published in this timeframe, focusing on studies published in the late 1980s and 1990s (Tveito, 2004; van Geen, 2007; Ravenek, 2010), and including 2 Cochrane reviews conducted using the methods recommended by the Cochrane Back Review Group (Guzman, 2001, 2006; Karjalainen, 2008). As with the individual studies described above, these systematic reviews are marked by heterogeneity in the studies examined, interpretation of the evidence, and determination of the IRP components associated with benefit. These reviews focused attention on studies of IRP in working-age adults, but most did not find that IRP increased rates of return to work, even in those reviews that featured studies with workplace interventions (Tveito, 2004; Ravenek, 2010). One review found that intensive IRP (>100 hours) was associated

Table ES6. Components of interdisciplinary rehabilitation programs showing some effectiveness vs. usual or non-intensive care.

Study	Worksite Interventions	Strength Training	Aerobic Exercise	Educational Interventions	Biopsychosocial Interventions	Other Interventions
Anema 2007	●	●	●			
Jensen 2005	●	●	●	●	●	
Lambeek 2010	●	●	●			
Ribiero 2008		●		●	●	●

Note: use of acetaminophen (at prescribed doses) allowed in Ribiero 2008

with clinically-important improvement in function (Guzman, 2001, 2006), while others did not find an association between program intensity and clinical benefit (van Geen, 2007; Ravenek, 2010). Nevertheless, despite differences in methods, included studies, and conclusions, all of these reviews concluded that there was least moderate evidence that IRP conferred some level of incremental benefit over usual care in at least one of the domains of interest this appraisal (i.e., pain, function, patient satisfaction, or return to work).

Conclusion

As described above, the literature on interdisciplinary rehabilitation programs, stretching over 2 decades, is marked by significant heterogeneity in study populations, program content, intensity, setting, and comparators, and is not generally of high quality. Despite this variability, most studies of IRP show modest incremental benefit over usual care in at least one domain (e.g., pain, function, return to work). However, the specific components of IRP associated with the greatest level of benefit remain unclear, as does whether IRP offers any benefit over a well-designed, active physical therapy and exercise regimen. Finally, further research is necessary to determine the specific types of patients who would be most likely to respond to IRP.

Potential Harms

Information on potential harms is presented on the following page (Table ES7). Good evidence on the true rates of serious harms is not available from published RCTs of treatments for low back disorders. Individual studies are too small to capture reliable data on complications that occur infrequently, and the relatively low rate of serious complications has led to standards for research reporting that often do not include formal reports on all complications. Other contributing factors to the dearth of data on complications include the general exclusion of high-risk patients from many RCTs, possible publication bias that disfavors reports of unsuccessful outcomes, and the short-term nature of most studies, which can fail to detect adverse outcomes associated with surgical interventions that do not manifest until later years (Chou, 2005).

Table ES7. Reported ranges of harms in randomized controlled trials and observational studies, by management option.

Intervention	30-day Mortality	Major Complications	Minor Complications	Subsequent Treatment
Conservative Care	NR	NR	NR	Surgery: 9-50%
Interdisciplinary Rehabilitation	NR	NR	<1%	Surgery: 1-28%
Spinal Injections	NR	<1%	2-16%	# Injections: 2-4* Surgery: 14-36%
Coblation Nucleoplasty	NR	NR	11%†	Surgery: 4-27%†
Radiofrequency Denervation	NR	NR	4-14%	Repeat: 15.8%‡ Surgery: 11.9%**
Intradiscal Electrothermal Therapy	NR	<1%	1-10%	Surgery: 2-6%
Interspinous Spacers	NR	0-6%	3-6%	Surgery: 6-12%
Discectomy	<0.1%	0-4%	2-21%	Surgery: 3-25%
Laminectomy and Fusion	<1%	0-5%	10-16%	Surgery: 2-11%

NOTE: "NR" used to indicate no reported events for intervention across body of evidence
*"# Injections" refers to average number of spinal injections per year; "Surgery" refers to need for subsequent surgery following injection(s)
†Data from one RCT and one observational study assessing minor harms and secondary procedures following nucleoplasty
‡Data from single observational study assessing repeat denervation procedures
**Data from a single observational study assessing long-term outcome following RF denervation

Information from the observational studies examined in this review suggests that risks of minimally-invasive and surgical interventions may be higher than reported in RCTs. For example, no cases of peri-operative mortality were reported in any surgical RCT examined for this appraisal; in contrast, rates of in-hospital and 30-day mortality from observational studies, while <1%, were certainly nonzero (Deyo, 1992; Deyo, 2010). Also, a significant

percentage of RCTs of epidural steroid injections report very low complication rates or do not mention harms at all (Chou, 2009). While data are not directly comparable, information from analyses of closed malpractice claims indicate that epidural steroid injections are associated with 40% of all claims for chronic pain management, and that in two-thirds of cases, injury was not apparent until after discharge from the treatment facility (Fitzgibbon, 2004).

Subsequent Treatment

Data on subsequent treatment includes information on both the need for repeat attempts of the initial procedure as well as requirements for subsequent treatment (typically surgery). Rates of subsequent surgery in studies involving conservative care or interdisciplinary rehabilitation were highly variable and heavily influenced by study protocol and patient population. For example, rates of subsequent surgery in the SPORT trial ranged from 40-50% over 2 years across all patient populations (Weinstein, 2006; Weinstein, 2007; Weinstein, 2008b). In contrast, lower rates (9-10%) were observed in available RCTs conducted in Finland and Sweden (Malmivaara, 2007; Fritzell, 2001). In the Fritzell RCT, surgical intervention was reserved for patients meeting a clinical definition of "exacerbation of symptoms".

Rates of subsequent surgery in studies of minimally-invasive interventions were also highly variable, and were also influenced by study protocol, patient population, and duration of follow-up. For example, rates of subsequent surgery in studies of spinal injections ranged from 14-36%, but were measured infrequently as most injection RCTs were of 3 months' duration or less. Rates of subsequent surgery in studies of coblation nucleoplasty, RF denervation, and IDET ranged from 2-12% over 6 – 21 months of follow-up, and were measured in a total of 4 studies.

Finally, data from RCTs and observational studies of surgical interventions suggest that subsequent surgery and/or reoperation is relatively common among all surgical procedures. Rates of subsequent surgery for patients in the 2 available interspinous spacer RCTs ranged from 6-12% over 2 years of follow-up (Zucherman, 2004; Anderson, 2006).

Requirements for subsequent surgery ranged relatively tightly in RCTs and shorter-term observational studies of discectomy, laminectomy, and fusion (2-11%). Available longer-term data suggest that as many as 25% of patients initially receiving discectomy for lumbar disc herniation undergo another surgical procedure within 10 years (Atlas, 2005).

Data on repeat procedures were most commonly available for spinal injections. Findings from the systematic review used as the basis for this appraisal (Hashimoto, 2010) included information from health-care claims. The number of injection claims received averaged 2-4 per patient per year, and between 27-88% of patients had more than 1 injection attempt on the same day. A single observational study examining the rate of repeat RF denervation attempts found that 16% of patients had another denervation attempt within 1.5 months of the initial procedure (Mikeladze, 2003).

30-Day Mortality

Data are sparse on the rate of peri-procedure or peri-operative mortality. No deaths attributable to treatment were reported in any RCT or systematic review in our sample. Observational data are limited to hospital discharge and Medicare claims analyses for discectomy, laminectomy, and fusion. Peri-operative mortality for discectomy is rare; in an analysis of hospital discharge data, a total of 5 deaths were identified among nearly 11,000 discharges (<0.1%) (Deyo, 1992). While mortality is also rare for laminectomy and fusion, there is evidence that mortality risk increases with increasing surgical complexity. In an analysis of data for over 30,000 Medicare beneficiaries undergoing decompressive surgery, 30-day mortality for laminectomy, simple fusion, and complex fusion was 0.3%, 0.5%, and 0.6% respectively (Deyo, 2010).

Major Complications

Information on major complications was also rarely reported except in studies of surgical interventions. Among minimally-invasive procedures, data on major complications were only reported in studies of spinal injection and IDET; rates were <1% for both interventions. Major complication rates ranged from 0-6% in studies of interspinous spacers, discectomy, and laminectomy and/or fusion. Types of major complications varied by intervention. The most common major complication in studies of interspinous spacers was fracture of the spinous process. In RCTs of discectomy, laminectomy, and fusion, most major complications involved nerve root or vascular injuries as well as respiratory distress. Regarding laminectomy and fusion, observational data on major complications suggest, as with mortality, that rates increase with increasing surgical complexity. In the above-described Medicare study, rates of life-threatening complications were 2.1%, 4.7%, and 5.2% for laminectomy, simple fusion, and complex fusion respectively (Deyo, 2010).

Minor Complications

Minor complications were more frequently reported among all interventions. Among minimally-invasive interventions, rates ranged from 1-16%. Again, complication types differed somewhat by intervention. In spinal injection studies, complications primarily involved site reactions, numbness, minor bleeding, and headache. In RF denervation studies, minor complications were mostly associated with treatment-related pain, site reactions, and transient lower limb weakness. The most common minor complication in IDET studies was radiculopathy, but numbness, foot drop, and headache also were reported.

The most common minor complication across all forms of surgery was dural tear. In addition, studies of interspinous spacers and spinal fusion also reported cases of device malpositioning.

Analysis of Comparative Value

We used data from the systematic review on clinical effectiveness, as well as information from the literature and other sources, to inform a primary decision-analytic model of a variety of management strategies for low back disorders. Patients were assumed to have persistent low back and/or leg pain despite 4-6 weeks of "simple" conservative management (e.g., medications, physical therapy). Separate cohorts of patients were evaluated based on imaging findings and symptoms. Specific patient populations and modeled strategies can be found below:

- *45 year old male patient with lumbar disc herniation (LDH):*
    - Conservative care
    - Discectomy

- *65 year old male patient lumbar spinal stenosis (LSS):*
    - Conservative care
    - Interspinous spacers
    - Laminectomy

- *65 year old male patient with degenerative spondylolisthesis (DS):*
    - Conservative care
    - Interspinous spacers
    - Fusion

- *45 year old male patient with chronic low back pain (CLBP):*
    - Conservative care
    - Interdisciplinary rehabilitation
    - Fusion

Note that the strategies above do not comprise the full list of relevant strategies evaluated in the systematic review. Interventions without clear and consistent evidence of benefit, as well as those studied in highly selected or otherwise nongeneralizable populations were excluded from consideration for modeling (see further detail in Section 8).

Probabilities of clinical outcomes used were derived from the systematic review, peer-reviewed publications, US life tables, US vital statistics, and input from the ERG. Health related quality of life for patients with LDH, LSS, and DS was estimated from the quality of life reported directly in available RCTs. Quality of life in CLBP was estimated using low back dysfunction on the ODI as measure of magnitude of quality of life reduction below age and sex norms of quality of life in the US from the Medical Expenditure Panel Survey (MEPS). Costs of direct medical services were estimated using the 2010 Medicare fee schedule for payments for hospital care for procedures based on MS-DRGs with additional payments for physician, anesthesia, and surgeon fees for procedures. The Medicare payments used to estimate cost of the major interventions for the LBD conditions treatments in the clinical and economic analysis are as follows: conservative care ($2,400 for

a 6-8 week regimen), intensive interdisciplinary rehabilitation ($8,500 for a 6-8 week program), interspinous spacers ($8,500), discectomy ($11,100), laminectomy ($10,700), simple fusion ($23,900) and complex fusion ($32,800). Model outcomes were evaluated over a 2-year timeframe.

Although there are many important assumptions that were made as part of the model, 3 additional issues stood out as potentially of greatest impact and controversy. These 3 areas involved (1) the impact of crossovers (i.e., from non-operative to surgical treatment and vice versa) in RCTs in estimating the clinical effectiveness and costs of LBD interventions; (2) the importance of work loss costs in relation to the magnitude of medical care costs for LBD patients; (3) and the impact of the increased costs and increased risk of complications from complex fusion compared to simple fusion for LBD. These 3 assumptions provided the basis for *a priori* alternative scenarios that were analyzed for this review.

Other key assumptions for the model are listed in Table ES8 below and continuing onto the following page. For brevity, only those overarching assumptions regarding low back disorders and the course of the disease are listed; other strategy-specific assumptions can be found in Section 8.

Table ES8. Key assumptions, low back disorders treatment and outcomes.

Assumptions	Rationale & Source
Low Back Disorders	
• Patients' have had an initial evaluation and do not have indications for urgent interventions. • Patients have persistent pain and dysfunction after 4-6 weeks, and are classified as having LDH, LSS, DS or CLBP on basis of initial evaluation, treatment and imaging.	Chou, 2007
Clinical Outcome Measures	
• Back Pain: The primary back pain measure in the model was the SF-36 bodily pain (BP) subscale.	Bombardier, 2000
• The Visual Analogue Scale (VAS), (0 to 100 scale) was used when the SF-36 BP was not available.	Bombardier, 2000
• A change in SF-36 BP > 10 is a moderate effect and > 20 is a large/substantial effect.	Ostelo, 2008 Chou, 2009
• Back Function: The primary back function measure in the model was the Oswestry Disability Index (ODI), on a 0-100 scale (100 = maximum back dysfunction).	RDQ, ODI and methods citations
• The Roland Morris Disability Questionnaire (RDQ) on a 0-24 scale, 24 = maximum dysfunction was mapped to a 0-100 scale to compare with the ODI in the model.	Bombardier, 2000

Employment, Work Loss and Cost of Work Loss	
• Working FT/PT. Working status is defined as working full time or part time at baseline in RCTs.	Assumption based on available data in randomized controlled trials
• Work Days per Year: We assume 48 work weeks x 5 days per week = 240 working days per year.	Assumption
• We assume annual daily wage of $165.	Bureau of Labor Statistics, Report LEU025289100, 2010
• Work loss estimated from patient's perspective as product of work loss (days) x wages per day.	Assumption
• In the RCT of microdiscectomy compared to conservative care for LDH, "full recovery" on a 7 point Likert scale was interpreted as return to work.	Peul, 2007
Quality of Life	
• EQ-5D is the measure for quality of life in the analysis. Age-specific norm for EQ-5D (US scoring, males) for US non-institutionalized population used	Bombardier, 2000 Tosteson, 2000
• VAS, general health, may be used for quality of life when a EQ-5D is not reported.	Tosteson, 2000
• The SF-36 subscales may be mapped to EQ-5D	Ara, 2008
Adjustment for Baseline Differences	
• In comparisons across studies, back pain (SF-36 BP, 0-100 scale) and back function (ODI 0 to 100 scale or RDQ transformed to 0 to 100 scale) were adjusted to the baseline of the conservative care group. The adjustment used the reported value of the measure (0 to 100 scale) and proportion of maximum potential gain to avoid ceiling/floor effects and overestimation that might occur from simple linear adjustment.	Assumption

Summary Model Results

Model results are presented on the pages that follow separately for each patient population. Summary findings for both the "intention-to-treat" (i.e., including crossovers) and "as-treated" (excluding crossovers) analyses are displayed in detail in Section 8; for brevity, presentation of selected tabular findings in this summary are limited to intention-to-treat analyses only. For continuous and event-based measures, 95% confidence intervals are presented to facilitate interpretation of uncertainty around model-generated means.

Across all populations, differences were noted between strategies in individual outcomes as well as both medical care and work-loss costs. On a summary basis, however, differences in effectiveness (as measured by QALYs) were modest for most comparisons.

Lumbar Disc Herniation: Conservative Care or Discectomy

Intention-to-treat (ITT) findings for the LDH model are presented in Table ES9 on the following page. The LDH patients had the most severe back pain (SF-36 BP mean: 23.9 on

Table ES9. 2-year outcomes, costs, and cost-effectiveness of management strategies for lumbar disc herniation (intention-to-treat findings only).

	Conservative Care			Discectomy		
		95% CI			95% CI	
	Mean	Lower	Upper	Mean	Lower	Upper
Clinical Outcomes						
Back Pain (SF BP)	78.4	74.4	82.3	83.2	78.8	87.6
Back Function (ODI)	14.6	10.5	18.6	13.0	9.1	16.8
Work Loss						
Work Loss (Based on Work FT/PT), days	85.8	60.8	109.9	42.4	17.0	71.7
Complications						
Minor Complications	5.4%	4.1%	6.8%	12.7%	10.7%	14.9%
Major Complications	0.8%	0.3%	1.4%	2.0%	1.2%	2.9%
Process of Care						
Surgery within 2 Years	39%	36%	42%	91%	90%	93%
Health Services						
Surgical Procedures	0.4	0.4	0.5	1.0	1.0	1.0
Other Procedures	0.0	0.0	0.0	0.0	0.0	0.0
Visits	19.6	19.3	20.0	13.5	13.3	13.8
Costs						
Total Costs	$7,533	$774	$27,187	$13,553	$1,591	$60,425
Surgery	$4,539	$4	$23,209	$10,794	$9	$55,155
Procedures	$0	$0	$0	$0	$0	$0
Complications	$539	$401	$696	$1,281	$1,057	$1,495
Visits	$2,454	$39	$11,159	$1,478	$23	$6,460
Cost of Work Loss						
Work Loss (Work FT/PT)	$14,151	$10,036	$18,130	$6,997	$2,805	$11,835
Quality of Life (QALYs)	1.41	1.35	1.48	1.46	1.39	1.53
Cost per QALY Gained (vs. Cons. Care)*	N/A			$115,992		

SF BP: Short-form 36 Bodily Pain subscale; ODI: Oswestry Disability Index; FT/PT: Full-time/Part-time; QALY: Quality-adjusted life year

*Based on medical care costs only

0-100 scale, lower values = more severe pain) and lowest back function (RDQ mean: 16.3 on 0-23 scale, higher values = worse function) of the 4 LBD conditions. Data for both interventions assessed in this model were obtained from a large RCT of microdiscectomy vs. prolonged conservative care (Peul, 2007).

In the ITT analysis, 91% of patients intending to have microdiscectomy actually received surgery, and 39% of patients initially receiving conservative care ultimately received surgery by 2 years. Both treatment pathways produced substantial improvements in back pain and back function, and a very high proportion of patients in both pathways returned to work. The microdiscectomy strategy results in fewer work loss days (42 days compared to 86 days for conservative care), lower costs due to work loss ($6,997 compared to $14,151), and slightly higher quality of life (1.46 QALYs compared to 1.41 QALYs) than conservative care. The microdiscectomy strategy has higher direct medical care costs than the conservative care strategy ($13,553 compared to $7,533) due to the higher costs of surgery compared to conservative care.

The as-treated (AT) analysis of this population has identical effectiveness findings, as no as-treated results were generated in the source RCT. However, no crossovers are assumed to occur in the AT analysis, which affects estimates of cost and harm. In the absence of crossover, the difference in 2-year cost for surgery and conservative care is larger the ($13,699 and $2,325 for microdiscectomy and conservative care respectively).

In the ITT analysis, microdiscectomy is more expensive and marginally more effective than conservative care and has an incremental cost-effectiveness ratio (ICER) of $116,000 per QALY gained. In the AT analysis, the difference in costs between management strategies is greater in the absence of crossover, but the QALY gain is identical to that in the ITT analysis. Therefore, the ICER of microdiscectomy compared to conservative care in the AT analysis is higher ($233,000 per QALY gained).

As-treated analyses of data from other RCTs of discectomy such as SPORT show substantially better outcomes as compared to intention-to-treat findings. It is likely that a similar trend would be observed if such data were made available in the Peul RCT. Findings from a cost-effectiveness analysis using data from the combined randomized and observational LDH cohorts in SPORT suggest that surgery would be associated with an additional 2.5 months of quality-adjusted life expectancy over 2 years, which resulted in a lower cost-effectiveness ratio (~$69,000 per QALY gained) than that observed in our analysis (Tosteson, 2008). The estimates of effectiveness, costs, and cost-effectiveness presented in this appraisal therefore represent a "lower boundary" around the estimate of benefit that would be expected in an as-treated population.

Lumbar Spinal Stenosis: Conservative Care, Interspinous Spacers, or Laminectomy

Data on LSS management options were derived from an RCT of laminectomy with or without fusion vs. nonoperative care ("SPORT", Weinstein ,2008) and a separate RCT of the X-STOP interspinous spacer system vs. nonoperative care (Zucherman, 2004). Our analysis assumed that baseline back pain and back function was the same as in the conservative care arm of the SPORT RCT (Weinstein, 2008). The X STOP trial did not use the same measure of back function as the SPORT RCT; no back function outcome was therefore produced for this strategy in the model. The clinical effectiveness of surgical interventions in the SPORT

LSS study have not been stratified by surgical procedure, but 90% of surgical patients received laminectomy alone; we therefore assumed effectiveness and costs consistent with laminectomy. The effectiveness of interspinous spacers was adjusted to account for the greater severity of pain and back dysfunction in the X STOP trial relative to the SPORT LSS RCT. ITT findings are presented on the following page in Table ES10.

Note that the model results for interspinous spacers are presented distinctly from the results for conservative care and laminectomy. Whereas direct comparative data are available for these latter management options, we can only make much more tenuous, indirect assumptions of the magnitude of the clinical benefits of interspinous spacers vs. conservative care. For this reason the ERG advised highlighting the significantly greater uncertainty regarding the model results for interspinous spacers. Findings for the spacers strategy are therefore shaded to distinguish them from direct comparative results.

In the SPORT LSS RCT there were large and differential crossovers between study arms (43% to surgery and 34% to conservative care). Laminectomy produces greater reductions in back pain and back dysfunction compared to conservative care. Based on available RCT data, interspinous spacers produce greater reduction is back pain than laminectomy or fusion. Surgical management strategies have higher costs than conservative care. The higher quality of life of interspinous spacers compared to laminectomy should be interpreted cautiously, as quality of life was not directly measured in the clinical trial of interspinous spacers and was estimated using change in the physical function subscale of the Zurich Claudication Questionnaire.

In the AT analysis of the LSS strategies, the effectiveness of laminectomy in reducing back pain and back dysfunction is higher and the effectiveness of conservative care is lower relative to the ITT analysis. While, as expected, differences in costs and complication rates between surgery and conservative care are higher in the AT analyses, differences in QALYs are also somewhat greater due to the greater treatment effects seen in the AT population.

Regarding cost-effectiveness, interspinous spacers are more expensive and somewhat more effective than conservative care and have an ICER of $51,000. Laminectomy is more expensive and slightly more effective than conservative care and has an ICER of $258,000. Crossovers impacted cost-effectiveness findings in this population. Corresponding ICERs in the AT analysis were $90,000 and $101,000 per QALY gained for interspinous spacers and laminectomy respectively. In particular, the QALY gain for fusion relative to conservative care was tenfold higher in the AT vs. ITT analyses (0.12 vs. 0.01 QALYs respectively).

Table ES10. 2-year outcomes, costs, and cost-effectiveness of management strategies for lumbar spinal stenosis (intention-to-treat findings only).

	Conservative Care			Laminectomy			Interspinous Spacers		
		95% CI			95% CI			95% CI	
	Mean	Lower	Upper	Mean	Lower	Upper	Mean	Lower	Upper
Clinical Outcomes									
Back Pain (SF BP)	47.7	43.0	52.2	55.0	49.9	60.0	67.5	62.7	72.5
Back Function (ODI)	29.8	25.9	33.6	26.6	22.5	30.7	---	---	---
Complications									
Minor Complications	0.2%	0.0%	0.5%	8.8%	7.1%	10.6%	3.3%	2.2%	4.5%
Major Complications	0.1%	0.0%	0.3%	1.5%	0.7%	2.3%	2.0%	1.2%	3.0%
Process of Care									
Surgery within 2 Years	42%	40%	45%	65%	63%	68%	65%	63%	68%
Health Services									
Surgical Procedures	0.4	0.4	0.5	0.7	0.7	0.7	0.7	0.7	0.7
Other Procedures	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Visits	18.2	17.8	18.6	16.6	16.1	17.0	14.7	14.3	15.0
Costs									
Total Costs	$7,344	$523	$27,373	$10,478	$1,428	$39,160	$10,534	$1,668	$36,807
Surgery	$4,612	$2	$24,097	$7,391	$76	$35,542	$5,716	$51	$28,792
Procedures	$0	$0	$0	$0	$0	$0	$0	$0	$0
Complications	$25	$0	$61	$819	$661	$988	$516	$364	$679
Visits	$2,509	$47	$12,172	$2,269	$53	$10,084	$4,302	$260	$14,255
Quality of Life (QALYs)	1.22	1.18	1.25	1.23	1.20	1.27	1.28	1.25	1.32
Cost per QALY Gained (vs. Cons. Care)*	N/A			$257,705			$50,877		

SF BP: Short-form 36 Bodily Pain subscale; ODI: Oswestry Disability Index; FT/PT: Full-time/Part-time; QALY: Quality-adjusted life year

*Based on medical care costs only

Degenerative Spondylolisthesis: Conservative Care, Interspinous Spacers, or Fusion

The key published studies used as a basis for the DS population were the SPORT RCT (Weinstein, 2007) and the above-described Zucherman X-STOP RCT (Zucherman, 2004). Our analysis assumed a baseline back pain, and back dysfunction observed in the conservative care arm of the SPORT RCT (Weinstein, 2007). We assumed that crossovers in the X STOP trial of interspinous spacers are similar to crossovers in the surgical interventions in the SPORT DS study. As with the LSS analyses, data for interspinous spacers are presented separately, as the comparison of this management option to conservative care required indirect analyses based on results from RCTs with widely differing "usual care" results. ITT findings are presented on the following page in Table ES11.

Table ES11. 2-year outcomes, costs, and cost-effectiveness of management strategies for degenerative spondylolisthesis (intention-to-treat findings only).

	Conservative Care			Fusion			Interspinous Spacers		
		95% CI			95% CI			95% CI	
	Mean	Lower	Upper	Mean	Lower	Upper	Mean	Lower	Upper
Clinical Outcomes									
Back Pain (SF BP)	49.6	46.6	52.9	54.4	51.3	57.6	65.8	62.2	69.5
Back Function (ODI)	24.3	21.7	26.6	25.4	23.0	28.0	---	---	---
Complications									
Minor Complications	6.6%	5.2%	8.1%	8.6%	6.8%	1.4%	3.4%	2.3%	4.6%
Major Complications	2.5%	1.6%	3.5%	3.3%	2.2%	4.5%	2.1%	1.3%	3.0%
Process of Care									
Surgery within 2 Years	47%	45%	50%	62%	59%	65%	62%	59%	65%
Use of Health Services									
Surgical Procedures	0.5	0.5	0.5	0.7	0.6	0.7	0.7	0.6	0.7
Other Procedures	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Visits	18.3	17.9	18.7	17.5	17.1	18.0	17.5	17.1	18.0
Costs									
Total Costs	$14,198	$1,111	$65,825	$17,639	$1,395	$84,370	$8,841	$1,155	$31,649
Surgery	$11,416	$7	$63,855	$14,881	$10	$82,070	$6,246	$105	$29,036
Procedures	$0	$0	$0	$0	$0	$0	$0	$0	$0
Complications	$811	$640	$987	$1,054	$863	$1,245	$522	$394	$672
Visits	$1,971	$83	$9,241	$1,703	$18	$7,779	$475	$5	$2,255
Quality of Life (QALYs)	1.24	1.20	1.27	1.22	1.18	1.25	1.24	1.20	1.27
Cost per QALY Gained (vs. Cons. Care)*	N/A			†			‡		

SF BP: Short-form 36 Bodily Pain subscale; ODI: Oswestry Disability Index; FT/PT: Full-time/Part-time; QALY: Quality-adjusted life year

*Based on medical care costs only

†Cost-effectiveness not reported--fusion more expensive and less effective than conservative care

‡Cost-effectiveness not reported--spacers less expensive than conservative care and equally effective

In the ITT analyses, there were a large number of crossovers (47% to surgery and 38% to conservative care). All strategies produced moderate or better improvements in pain and function in this population, but improvements were better on average in the interspinous spacer and fusion strategies. The costs of fusion ($17,639) are higher than the costs of the interspinous spacers ($8,841) and conservative care ($14,198) strategies; costs for the latter largely reflect crossover to surgery. The quality of life is similar across all treatment pathways, but is slightly lower for fusion as compared to conservative care or interspinous spacers.

For the AT analysis, in the absence of crossovers, the effectiveness of the fusion and interspinous spacers strategies is higher and the effectiveness of the conservative care strategy is lower than in the ITT analysis.

Costs of conservative care in this analysis are much lower, and the costs of interspinous spacers and surgery are higher than in the ITT analysis. QALYs substantially increase in

the AT analysis for interspinous spacers and fusion, and decrease for conservative care (1.29-1.31 vs. 1.15).

In the ITT analyses, interspinous spacers are cost-saving relative to conservative care, given the high degree of crossover, and appear to be equally effective. Fusion is more expensive and less effective than conservative care. In both of these situations, an incremental cost-effectiveness ratio could not be generated. In the AT analysis, interspinous spacers become more expensive in the absence of crossovers and remain more effective than conservative care with an ICER of $71,000. Fusion is both much more expensive and more effective than conservative care and has an ICER of $163,000.

Chronic Non-Specific Low back Pain: Conservative Care, Interdisciplinary Rehabilitation or Fusion

The key published studies used as a basis for the clinical and economic model for CLBP management are the Swedish Spine Study (Fritzell, 2001) which was an RCT of fusion compared to conservative care, and an RCT of interdisciplinary rehabilitation compared to intensive back strengthening (Dufour, 2010). Our analysis assumed a baseline back pain, back dysfunction, and employment status observed in the conservative care arm of the Swedish Spine Study (Fritzell, 2001). Interdisciplinary rehabilitation (IRP) was studied in a population with more severe back pain and back dysfunction, so changes in these measures were adjusted to the uniform baseline severity as described above. The crossovers from interdisciplinary rehabilitation to fusion were assumed to occur in the same proportion as in the conservative care strategy. Quality of life was not directly measured and was estimated based on change in back function across all 4 chronic back pain conditions to facilitate comparisons within the CLBP interventions. As with the previous patient populations, data for interdisciplinary rehabilitation are presented separately because of this indirect comparison. Findings are presented on the following page in Table ES12.

In the ITT analyses, a small amount of crossover was generated in this model relative to the other populations (9% to surgery and 8% to conservative care or IRP). On average, improvements in back pain are small, moderate, and substantial for conservative care, IRP, and fusion respectively, while improvements in function are substantial for both IRP and fusion. The costs of fusion are substantially higher than the costs of IRP and conservative care. Note that work loss costs are substantially higher than medical care costs in this population, that work loss was similar in conservative care ($60,000) and IRP ($61,000), and that work losses in both of the nonsurgical interventions are higher than in fusion ($45,000). Quality of life overall was low (due in part to the different method of estimating quality of life in CLBP compared to other low back disorders).

Table ES12. 2-year outcomes, costs, and cost-effectiveness of management strategies for chronic nonspecific low back pain (intention-to-treat findings only).

	Conservative Care			Fusion			Interdisciplinary Rehab		
		95% CI			95% CI			95% CI	
	Mean	Lower	Upper	Mean	Lower	Upper	Mean	Lower	Upper
Clinical Outcomes									
Back Pain (SF BP)	49.0	44.2	53.8	61.9	59.4	64.6	55.8	51.3	60.6
Back Function (ODI)	42.1	36.8	47.5	37.8	35.1	40.3	36.0	31.6	40.6
Work Loss									
Work Loss (Based on Work FT/PT), days	364.2	341.5	387.4	271.0	258.2	283.0	373.0	350.5	396.3
Complications									
Minor Complications	1.1%	0.5%	1.8%	12.5%	10.6%	14.8%	1.1%	0.5%	1.8%
Major Complications	0.4%	0.1%	0.9%	4.8%	3.5%	6.2%	0.4%	0.1%	0.9%
Process of Care									
Surgery within 2 Years	9%	7%	10%	92%	90%	94%	9%	7%	10%
Use of Health Services									
Surgical Procedures	0.1	0.1	0.1	1.0	0.9	1.0	0.1	0.1	0.1
Other Procedures	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Visits	19.4	19.3	19.6	9.4	9.2	9.6	87.5	86.9	88.0
Costs									
Total Costs	$4,404	$241	$16,947	$23,208	$1,709	$114,175	$10,208	$328	$41,028
Surgery	$1,877	$1	$9,559	$21,282	$11	$112,541	$1,877	$1	$9,559
Procedures	$0	$0	$0	$0	$0	$0	$0	$0	$0
Complications	$136	$69	$209	$1,549	$1,321	$1,794	$136	$69	$209
Visits	$2,391	$6	$12,789	$377	$7	$1,477	$8,186	$4	$38,192
Cost of Work Loss									
Work Loss (Work FT/PT)	$60,097	$56,342	$63,920	$44,722	$42,601	$46,687	$61,546	$57,827	$65,391
Quality of Life (QALYs) Based on ODI	0.88	0.84	0.91	0.94	0.90	0.97	0.96	0.93	1.00
Cost per QALY Gained (vs. Cons. Care)*	N/A			$328,168			$67,098		

SF BP: Short-form 36 Bodily Pain subscale; ODI: Oswestry Disability Index; FT/PT: Full-time/Part-time; QALY: Quality-adjusted life year

*Based on medical care costs only

Given the low rate of crossover, findings did not change dramatically in the AT analysis. Differences in medical care costs and QALYs were similar across analyses. Cost-effectiveness findings based on the ITT analysis suggested that IRP was more expensive and more effective than conservative care and had an ICER of $67,000. Fusion was substantially more expensive and more effective than conservative care and had an ICER of $328,000. QALY gains in the AT analysis for IRP and fusion resulted in ICERs of $32,000 and $181,000 respectively.

Alternative Scenarios

Inclusion of Work Loss Costs

Additional analyses were conducted examining the impact of inclusion of work loss costs in analyses of the two working-age populations of interest (LDH and CLBP). For LDH, microdiscectomy was found to substantially reduce work loss in both the ITT and AT analyses. Not surprisingly, cost-effectiveness improved when these costs were included. In the ITT analyses, microdiscectomy produced an ICER of $116,000 per QALY gained; when work-loss costs were included, surgery became cost-saving. Similarly, inclusion of work-loss costs in the AT analyses reduced the ICER for microdiscectomy from $233,000 to $88,000 per QALY gained.

For CLBP, in which estimated work loss was much more substantial, inclusion of these costs slightly increased the ICERs for IRP (from $67,000 to $84,000 in the ITT analysis and from $32,000 to $40,000 in the AT analysis). This is not surprising, as IRP did not have an impact on return to work in the RCT of focus for the model (Dufour, 2010).

Spinal fusion does substantially reduce work loss relative to either conservative care or IRP in the CLBP model, however, based on the Fritzell RCT results (Fritzell, 2001). As a result, ICERs are reduced for fusion vs. conservative care when work-loss costs are included in both the ITT (from $328,000 to $60,000) and AT (from $181,000 to $59,000) analyses.

Simple Fusion vs. Complex Fusion

Modifications were also made to analyses of spinal fusion in the DS and CLBP populations. Higher costs and higher complication rates were assumed for complex fusion, while measures of effectiveness were unchanged. Findings are presented for the ITT analyses only. For chronic low back pain, the effect on the ICER was dramatic ($1.2 million vs. $328,000 per QALY gained for complex vs. simple fusion). Because no difference in effectiveness was assumed for simple vs. complex fusion, both forms of surgery remained more expensive and slightly less effective than conservative care in the DS population; an ICER could therefore not be generated.

ICER Evidence Review Group Deliberation

The ICER Evidence Review Group deliberation (see section starting on page 54 for membership and details) focused on many important issues regarding the evidence provided by the ICER review. Major points of discussion are shown in the numbered points below.

1) *Additional context is required to adequately examine issues of variability in training and reporting of harms.* While the initial draft appraisal document characterized, as other systematic reviews have, the reporting of procedure-related harms as suboptimal, it was felt that additional context should be provided. Specifically, findings from long-term observational studies, database analyses, and analyses of malpractice claims should be highlighted to provide additional information on the most common types of harms, trends in complication rates for emerging procedures, and other concerns. A separate but related concern is the lack of uniform training standards (which can contribute to variability in rates of harm). Both of these concerns have been highlighted, and additional evidence provided, in Section 7 of the revised report.

2) *The draft color-coded "stop sign" method for summarizing the evidence on comparative clinical effectiveness can be misleading*. In the initial draft appraisal, a color scheme was employed to summarize the available evidence on the effectiveness of a given management option for each measure of interest vs. the relevant comparator(s) within a given population:

    - Green→"Reasonable evidence of incremental benefit"
    - Yellow→"Conflicting evidence of incremental benefit"
    - Red→"No incremental benefit"
    - Black→"Insufficient evidence"

    This system was felt by most on the ERG to be misleading. For one, the colors used were felt to imply a recommendation or guideline, even though this was not intended. In addition, the green, yellow, and red assignments did not allow for any measurement of the uncertainty underlying these designations, as evidence of benefit could have been observed from a single RCT or 20 RCTs and would still be summarized using a green symbol. We have replaced the previous system with one that is similar to ICER's Integrated Evidence Rating system in that both the presence of benefit and the level of certainty from the evidence are addressed.

3) *Given the amount of focus applied to the Spine Patient Outcomes Research Trial (SPORT) in both the systematic review and decision-analytic model, additional justification for this focus should be provided.* ICER made the decision not to systematically review the literature on decompressive surgery, as such a review would contribute little to the already-large body of evidence on this intervention. Instead, several key studies were identified based on study size, recency, frequent citation, or other important features. SPORT was selected as a key study because of its unique design (inclusion

of both randomized and observational cohorts) and relatively large size. This justification has been added to the "Key Studies" subsection of Section 7.

4) *Limitations of available evidence should be explicitly stated, such as evidence for spinal fusion in non-specific low back pain and spinal injections for all indications.* The revised appraisal document includes new language explaining the limitations of the available RCT evidence for fusion in non-specific low back pain, as benefit was demonstrated in only one of 4 available RCTs, and issues with study design and analysis that make conclusions across studies problematic. In addition, specific issues with studies of spinal injections, including both methodologic concerns as well as questions regarding interpretation of findings, have been described in the revised report.

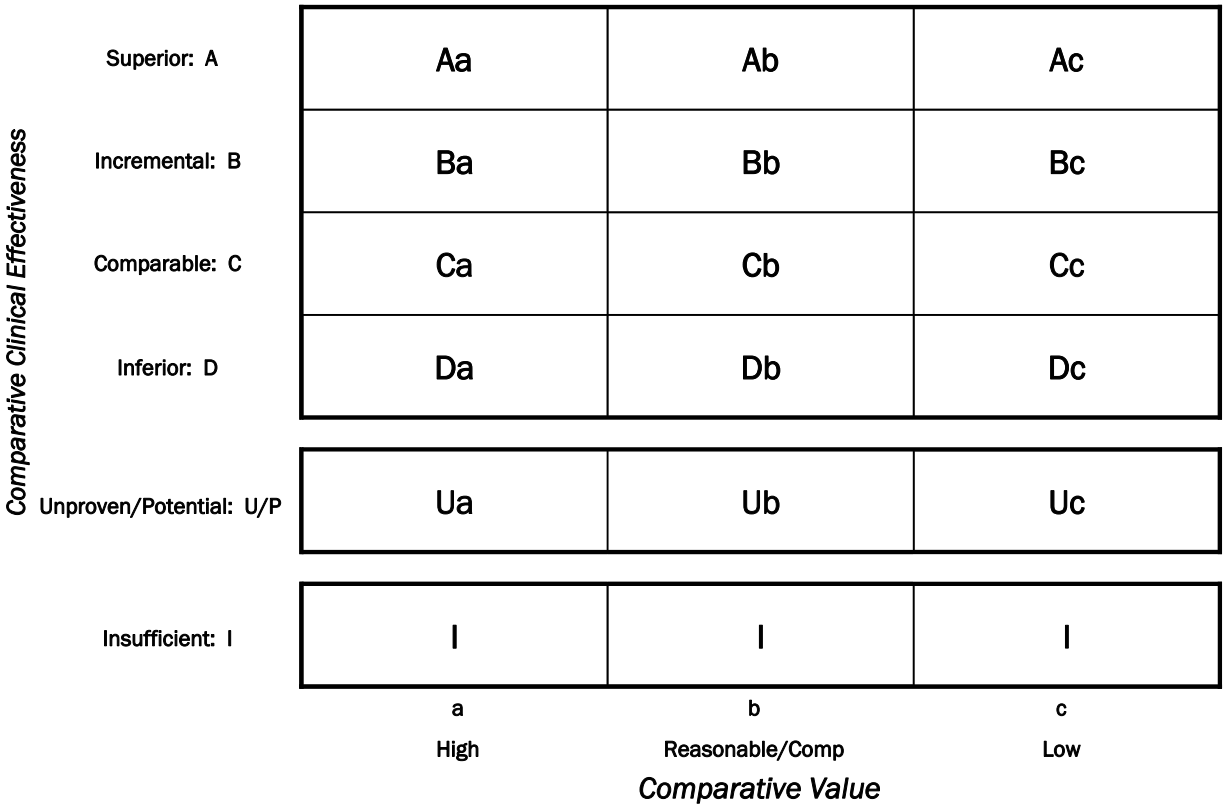
5) *Additional effort should be undertaken to identify the "correct" set of studies of interdisciplinary rehabilitation.* It was pointed out that, while the "de novo" abstraction strategy employed in this appraisal did not include studies published prior to 2000, there is a relative abundance of evidence on interdisciplinary rehabilitation (IRP) from studies published in the 1990s that has informed the conclusions of recent systematic reviews. However, it was also suggested that additional scrutiny should be applied to studies that may use the term "interdisciplinary" or "multidisciplinary" but are not truly so. While some on the ERG felt that no program could really be considered interdisciplinary without specific components (e.g., cognitive-behavioral intervention, workplace intervention), it should be noted that major systematic reviews of this topic have only required that these programs be physician-directed, include an exercise dimension, and at least one additional dimension (i.e., psychological, social, educational, and/or occupational) (Karjalainen, 2008; Guzman, 2001, 2006; Tveito, 2004; van Geen, 2007; Ravenek, 2010). These criteria were applied in the revised appraisal report, and findings concerning earlier studies of IRP were also summarized.

6) *Uncertainty in model outputs should be further characterized.* A suggestion was made to include confidence intervals for selected outputs from the decision-analytic model (rather than standard deviations or standard errors) to better characterize uncertainty in model findings. This change has been applied in the revised report.

7) *Model results arising from indirect comparisons of data from multiple studies should be presented separately.* The presentation of model results that mixed direct comparisons of data (e.g., decompressive surgery vs. conservative care in SPORT trial) with indirect comparisons (e.g., data from an RCT of interspinous spacers adjusted to SPORT baseline levels) was criticized as misleading. While the ability to make indirect comparisons is one of the key benefits of modeling, identification of situations in which indirect comparisons occurred was nevertheless included in the revised report.

ICER Integrated Evidence Ratings™: Management Options for Low Back Disorders

The ICER integrated evidence rating matrix is shown below; a detailed explanation of the methodology underpinning this rating system can be found beginning on page 50. Ratings for each patient population and management option of interest are shown on the following pages rather than illustrated in the body of the matrix figure itself. Although the input of the Evidence Review Group helps inform ICER's consideration of the evidence, the final ratings are ultimately a judgment made solely by ICER, and individual members of the ERG should not be viewed in any way as having endorsed the ratings described below.



ICER Integrated Evidence Ratings for Lumbar Disc Herniation (vs. Simple Conservative Care):

- **Discectomy: Bb**
- **Epidural Steroid Injections: Cc**
- **Coblation Nucleoplasty: I**
- **Interdisciplinary Rehabilitation: I**

Comparative Clinical Effectiveness. While the evidence on open and microdiscectomy indicates no long-term benefit relative to conservative treatment, there is consistent evidence demonstrating faster symptom recovery and early improvement in function among patients opting for surgery, which led ICER to make the judgment that there is a high level of certainty in a rating of "incremental" net health benefit for discectomy vs. conservative care. The equivalent longer-term benefits and small but not inconsequential rate of major harms with this type of surgery prevented a rating of "superior" net health benefit, however.

While there are multiple RCTs of epidural steroid injections for lumbar disc herniation, there has been no clear demonstration of incremental benefit over conservative treatment, as approximately equal numbers of studies have shown no advantage and small benefit, which led to ICER's rating of high certainty that epidural steroid injections were "comparable" but not better than conservative care alone.

Finally, the presence of only a single RCT of coblation nucleoplasty, despite the positive findings from this study (Gerszten, 2010), led ICER to conclude that evidence was still "insufficient" to determine with reasonable certainty whether this procedure was superior or inferior to conservative treatment. Because no RCTs of IRP were identified specifically for lumbar disc herniation, the evidence on this treatment option was also rated as "insufficient".

Comparative Value. The comparative value rating of "reasonable/comparable" for discectomy was determined based on the model findings of relatively modest incremental 2-year costs as well as modest incremental benefit in the intention-to-treat population. Some stakeholders may consider discectomy as a "high" value option in cases where early recovery may speed return to work; indeed, our own analyses with work-loss costs included suggested discectomy may be cost-saving over a 2-year timeframe relative to conservative care. Epidural steroid injections, while not modeled explicitly, would be considered a "low" value service because the costs of these injections would be considered additive to and not a replacement for conservative care costs, and no clinical net benefit is assumed for this management option. Finally, we do not typically model management options with insufficient evidence of benefit, and hence no comparative value rating was applied.

ICER Integrated Evidence Ratings for Lumbar Spinal Stenosis (vs. Simple Conservative Care):

- **Laminectomy: Bb**
- **Interspinous Spacers: I**
- **Epidural Steroid Injections: Cc**
- **Radiofrequency Denervation: I**
- **Interdisciplinary Rehabilitation: I**

Comparative Clinical Effectiveness. The evidence on laminectomy for lumbar spinal stenosis suggests that clinical benefits vs. conservative treatment are maintained for at least 1-2 years; because these benefits are moderate, however, and such surgery has the potential for major harm, ICER judged the comparative clinical effectiveness to be "incremental". The evidence on epidural steroid injections for lumbar spinal stenosis suggests no incremental benefit in comparison to conservative treatment alone. Finally, evidence for interspinous spacers (one RCT only), radiofrequency (RF) denervation (no RCTs), and IRP (no RCTs) for lumbar spinal stenosis was considered "insufficient" to make any determination of benefit.

Comparative Value. Information from the ICER model regarding laminectomy suggests moderate QALY gains over 2 years with increased costs that produce an incremental cost-effectiveness ratio of approximately $250,000; however, the ICER is reduced to approximately $100,000 when as-treated results are considered. With this in mind, and the potential for work productivity gains for some younger patients factored in, we judged surgery to represent a "reasonable/comparable" value intervention. As with lumbar disc herniation, the incremental cost associated with epidural steroid injections coupled with no evidence of benefit over conservative care led to a "low" value rating. Note that, while interspinous spacers were modeled on an exploratory basis, no formal rating of value was applied given our overall judgment that there is insufficient evidence with which to have reasonable certainty in comparative clinical outcomes. In addition, while small numbers of patients in surgical RCTs for lumbar spinal stenosis received laminectomy *with* spinal fusion, clinical effectiveness findings were not separately available for these patients. However, given what is known about the higher rates of major complications with fusion procedures and their higher cost, as well as uncertainty regarding whether the addition of fusion provides any incremental clinical benefit, it is likely that fusion would be considered a "low" value service for this indication.

ICER Integrated Evidence Ratings for Degenerative Spondylolisthesis (vs. Simple Conservative Care):

- **Fusion: Bb**
- **Interspinous Spacers: I**
- **Epidural Steroid Injections: I**
- **Radiofrequency Denervation: I**
- **Interdisciplinary Rehabilitation: I**

Comparative Clinical Effectiveness. As with lumbar spinal stenosis, decompressive surgery for stenosis with degenerative spondylolisthesis (primarily spinal fusion) is associated with moderate clinical benefits when compared to conservative care at 1-2 years. However, given a higher rate of complications with increasing levels of fusion complexity, ICER judged the balance of evidence on comparative clinical effectiveness to represent an "incremental" comparative advantage. Evidence was judged to be insufficient to determine whether the remaining options for degenerative spondylolisthesis were associated with any comparative clinical benefit, given that only one RCT of interspinous spacers was performed in this indication, and no RCTs of epidural steroid injections, RF denervation, or IRP were identified.

Comparative Value. Both fusion and interspinous spacers were initially modeled. However, no comparative value rating for spacers was assigned given the decision to rate the evidence on comparative clinical effectiveness to be "insufficient". The results of the ICER model suggest that, on an intention-to-treat basis, the fusion pathway produces somewhat higher costs than conservative care, but is essentially equally effective. When the model was run on an "as-treated" basis, fusion was found to produce more substantial clinical benefits at 2 years (2 additional months of quality-adjusted life expectancy), but at a significantly higher marginal cost. Still, we have judged that the resulting incremental cost-effectiveness ratio, complemented by the possibility of savings from improved work productivity for younger patients, suggests that fusion is a "reasonable/comparable" value in this patient population.

ICER Integrated Evidence Ratings for Non-Specific Low Back Pain (vs. Simple Conservative Care):

- **Fusion:**
  - **vs. Interdisciplinary Rehabilitation Dc**
  - **vs. Conservative Care Cc**
- **Spinal Injections:**
  - **Epidural Steroid Cc**
  - **Sacroiliac Steroid I**
  - **Intradiscal Steroid Cc**
  - **Branch Block Cc**
- **Radiofrequency Denervation: Cc**
- **Intradiscal Electrothermal Therapy: U***
- **Interdisciplinary Rehabilitation:**
  - **vs. Active Physical Therapy Cc**
  - **vs. Conservative Care Ub**

In a highly selected patient population

Comparative Clinical Effectiveness. One of 4 major RCTs of fusion in patients with non-specific low back pain showed a modest clinical benefit vs. conservative treatment, while the remaining 3 RCTs showed no evidence of benefit in comparison to interdisciplinary rehabilitation. Given the potential for major procedure-related harm in comparison to these non-invasive management options, ICER judged the net benefit of fusion vs. IRP to be "inferior" (no clinical benefit with greater potential for harm), and the net benefit of fusion vs. conservative care to be "comparable" (small clinical benefit offset by potential for harm).

The evidence on all forms of spinal injection suggested benefits only "comparable" to conservative care except for sacroiliac steroid injections, which were assigned an "insufficient" rating based on the availability of just a single RCT. Data from RCTs of RF denervation were mostly short-term in nature and showed no incremental benefits relative to sham or conservative treatment.

Two RCTs were available for intradiscal electrothermal therapy (IDET) vs. sham procedures, and were conducted in highly selected patient populations (e.g., positive discography; observed benefit from injections; exclusion of patients with comorbidity, history of radicular pain, or history of surgery). One of these RCTs showed no clinical benefits at 6 months (Freeman, 2005), while the other showed significant improvements in pain and function (Pauza, 2004). While this evidence provided only moderate certainty, ICER judged a rating of "unproven with potential" to be appropriate, as clinical benefit appeared to be at least comparable in these circumstances. We continue to qualify this rating, however, as applicable only to highly selected patients as described above.

Finally, as noted previously, IRP programs featured 2 major types of comparators: active physical therapy or structured exercise, and conservative or "usual" care. For comparisons to active physical therapy/exercise, ICER judged the available evidence for IRP to indicate only a "comparable" clinical effectiveness, given the lack of consistently demonstrated additional benefit in available RCTs. While comparisons to conservative/usual care were more varied in their outcome, the evidence was felt to indicate a level of benefit that was at least comparable to or perhaps moderately incremental, leading to a rating of "unproven with potential".

Comparative Value. Findings from the ICER model suggested that, even under assumptions based on the sole positive RCT of fusion in non-specific low back pain (Fritzell, 2001), fusion would result in very modest clinical improvement at a substantially increased cost, leading to a rating of "low" value. Low-value ratings were also applied to spinal injections, RF denervation, and IRP as compared to physical therapy, as all of these interventions would be expected to increase costs of care without providing any incremental clinical benefit. When compared to conservative or usual care, however, ICER model findings indicated that IRP would provide a "reasonable" value for the benefits achieved.

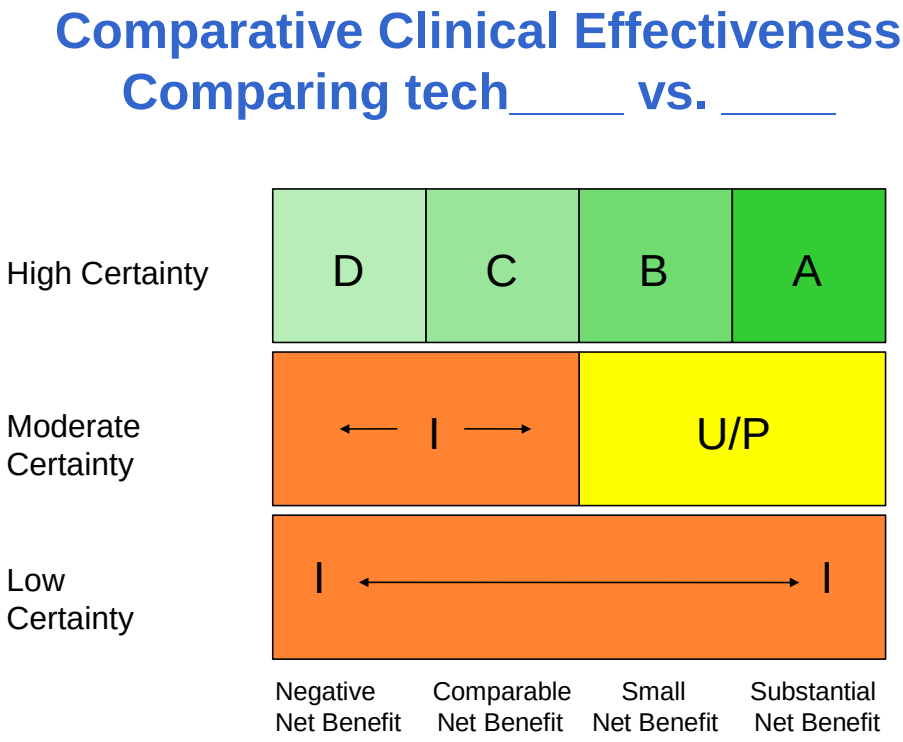
Note that no comparative value rating was assigned to IDET, as the clinical effectiveness rating was changed from "insufficient" to "unproven with potential" during report finalization without sufficient time to estimate relevant parameters for the model.

Methodology: ICER Integrated Evidence Rating™

The ICER Integrated Evidence Rating™ is shown on page 53. It is constructed as a matrix, with a vertical axis denoting the possible categories for a rating of comparative clinical effectiveness, and the horizontal axis divided into 3 possible rating categories for comparative value (Ollendorf, 2010). It is important to note that these ratings are specified as comparing specific uses of medical interventions; that is, there may be different ratings for different uses of a test, treatment, or other intervention depending on the specified indication and patient population(s).

Level of Certainty in a Comparative Net Health Benefit

The underlying approach to ICER's rating of comparative clinical effectiveness mirrors that developed by the United States Preventive Services Task Force (USPSTF) in its most recent methods documents, and is dependent upon a joint judgment of the level of certainty provided by the body of evidence and a categorical judgment of the magnitude of the comparative net health benefit (Sawaya, 2007). To render this 2-part judgment both explicit and transparent, ICER uses a "Comparative Clinical Effectiveness Matrix" very similar to that used by the USPSTF. This matrix, depicted below, was developed independently (although with some overlap in participants with the USPSTF effort) and pilot-tested specifically for comparative clinical effectiveness assessments by a multistakeholder evidence-based medicine roadmap group (Berger, 2009; Forum, 2006).



A = "Superior" - High certainty of a moderate-large net health benefit
B = "Incremental" - High certainty of a small net health benefit
C = "Comparable" - High certainty of a comparable net health benefit
D = "Inferior" - High certainty of an inferior net health benefit
U/P = "Unproven with Potential" - Moderate certainty of a small or moderate-large net health benefit
This category is meant to reflect technologies whose evidence provides:

1) High certainty of *at least* comparable net health benefit
2) Moderate certainty suggesting a small or moderate-large net health benefit

I = "Insufficient" - The evidence does not provide high certainty that the net health benefit of the technology is at least comparable to that provided by the comparator(s).

The vertical axis of the comparative clinical effectiveness matrix rates the level of certainty that the evidence provides in the precision of the net health benefit. There are 3 categories: high, moderate, and low, the same categories used by the USPSTF. While the vertical axis represents a judgment of certainty, the horizontal axis of the Comparative Clinical Effectiveness Matrix displays gradients of the estimated net health benefit provided by a health intervention compared with the net health benefit of the selected comparator intervention. The categories for comparative net health benefit begin at the far left with "negative"; as the estimate of net health benefit increases, the rating moves to "comparable," then to "small net benefit," and culminates with a rating of "substantial" comparative net health benefit.

The term comparative "net" health benefit is used because of the importance attached to an explicit judgment of the overall balance of benefits and risks between an intervention and its selected comparator(s). The rating of net health benefit on the horizontal axis of the Comparative Clinical Effectiveness Matrix represents the best conceptual "point estimate" ICER can make given its interpretation of the existing evidence. As with the approach taken by the USPSTF, ICER has at this time no set definition of the boundaries between "comparable," "small," and "substantial" comparative net health benefit. For example, if the results of the appraisal include an estimate of a small lifetime quality-adjusted life year (QALY) advantage for one intervention compared with another, balanced against known greater short-term risks, whether or not these findings should be judged as conferring a comparative net health benefit will depend on many features of the relative certainty of the benefits and harms, as well as value judgments of the importance to patients of small QALY gains over a lifetime.

Despite the variability that will attend these judgments, presenting a categorical judgment of net health benefit serves an important goal: it enhances understanding of the underlying evidence by forcing the review team to justify its rating. The review team must describe more concretely than they might otherwise their view of how the disparate findings of a systematic review and decision model sum up. The review team's justification can be debated and disagreed with, but in all cases it will give decision makers a more clear insight into the key issues they should consider when summing up the evidence and applying it to particular clinical actions or policies.

Summary Rating of Comparative Clinical Effectiveness
As shown in the figure above, the Comparative Clinical Effectiveness Matrix maps the 3 categories of certainty upon the categories of comparative net health benefit to define a summary rating of comparative clinical effectiveness. Here, the relationship between level of certainty and magnitude of net health benefit comes into sharper relief. With a high level of certainty, the point estimate of net health benefit in one category is relatively assured, and therefore each cell in the matrix on the row of high certainty has a distinct label. A technology whose evidence base provides high certainty of a moderate-to-high net health benefit is rated to have "superior" comparative clinical effectiveness. As the net health benefit diminishes, the rating of comparative clinical effectiveness shifts to "incremental," then "comparable," and finally "inferior."

When the level of certainty in the comparative net health benefit is only moderate, however, uncertainty about either benefits or harms is such that the precision of the net health benefit is significantly reduced. This lack of precision is akin to a broader "conceptual confidence interval," and is illustrated in the matrix by the broader summary categories of Unproven with Potential (U/P) and Insufficient (I).

The U/P category is a particularly important element of the Comparative Clinical Effectiveness Matrix. This category is intended to indicate a judgment that the available evidence can only yield moderate certainty in the comparative net health benefit at the population level, but that the best estimate is that there is either a small or substantial net benefit. Moderate certainty implies that the point estimate of net health benefit is unlikely to shift more than one category in either direction; thus, a U/P rating implies a judgment that there is relatively high certainty that the comparative net health benefit is comparable or better, and a correspondingly relatively small possibility that future evidence would demonstrate that the true net comparative benefit of the intervention being assessed is inferior to its comparator.

The final summary category of comparative clinical effectiveness is the "I" category that sweeps from the moderate certainty of a point estimate of comparable or inferior net health benefit into the entire bottom row in which certainty in net health benefit is so low that there remains a reasonable probability that the true net health benefit is inferior; in other words, that the intervention being evaluated produces a net harm for many or most patients.

Rating Comparative Value
The rating of comparative clinical effectiveness can stand alone, to be discussed and applied by decision makers, but it also forms the first of the 2 parts of the ICER Integrated Evidence Rating. The second component is a rating of "comparative value." ICER rates the use of interventions for particular patient populations as having "high," "reasonable or comparable," or "low" comparative value.

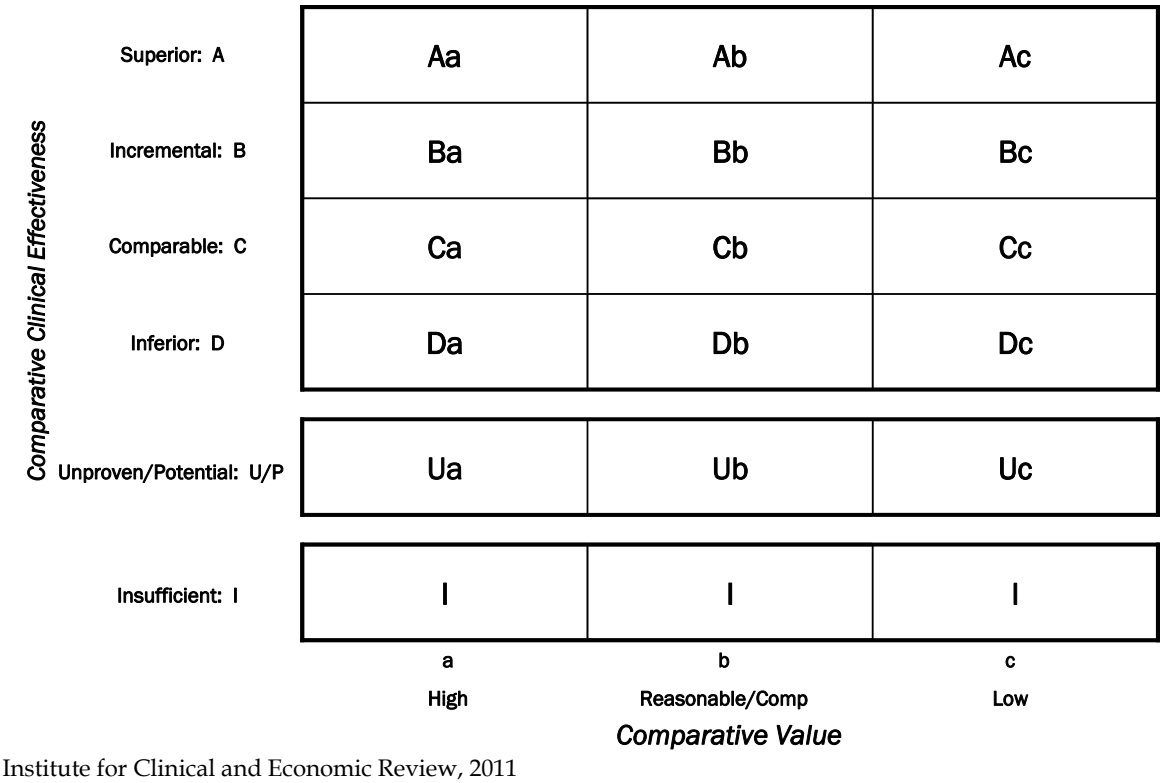
ICER does not employ a single measure of cost effectiveness, such as the incremental cost-effectiveness ratio, for assignment of a rating of comparative value, and therefore does not

rely on a formal cost-effectiveness threshold. Instead, the rating of comparative value is informed by multiple measures of potential economic impact.

To determine a final rating of "high," "reasonable/ comparable," or "low" value, ICER considers all of the economic findings, including the relative uncertainty of model findings as explored through multiple deterministic sensitivity analyses and a probabilistic sensitivity analysis. To aid transparency, ICER provides general guidance that incremental cost per QALY ratios of less than approximately $50,000 will often be considered as indicative of a "high" value intervention; incremental cost per QALYs from about $50,000 to $150,000 would often fit within a designation as "reasonable" values; and incremental cost per QALYs above $150,000 would be more likely to suggest "low" value interventions. This general guidance is based upon previous academic work benchmarks modified by ICER's interpretation of evidence on the role medical inflation and societal willingness to pay should have in creating cost-effectiveness thresholds (Braithwaite, 2008; King, 2005). While there is a limited normative or empiric basis for the loose boundaries ICER presents, these boundaries also reflect input from stakeholders in today's health care system on how best to present incremental cost-effectiveness ratios within broad categories that can be widely understood, gain relative consensus, and be actionable.

Integrated Ratings

The ICER Integrated Evidence Rating™ combines the individual ratings given for comparative clinical effectiveness and comparative value. The overall purpose of the integrated ratings is to highlight the separate considerations that go into each element but to combine them for the purposes of conveying that clinical benefits provided by technologies come at varying relative values based on their cost and their impact on the outcomes of care and the health care system (Ollendorf, 2010).



Evidence Review Group Members

The Evidence Review Group (ERG) is an independent group brought together by ICER and composed of academic experts, patients, clinicians, epidemiologists, ethicists, and medical policy representatives of stakeholder groups including health plans and manufacturers.

The purpose of the ERG is to guide and help interpret the entire appraisal process. Members of the ERG are first convened to function as a "scoping committee" for the appraisal. During this phase the key questions for the appraisal are outlined, including elements such as the appropriate comparator technologies, patient outcomes of interest, patient subpopulations for which clinical and cost-effectiveness may vary systematically, time horizon for outcomes, and key aspects of the existing data that must be taken into account during the appraisal. The ERG may be divided into sub-committees that advise the ICER appraisal team at the mid-point of the appraisal on the early findings and challenges encountered. All of the ERG members listed below participated in scoping and/or mid-cycle activities, but not all were able to participate in the final ERG meeting.

At the final ERG meeting, members are asked to declare any interests in the technology or its comparator(s), or other potential influences on their expertise. The ERG meeting allows for in-depth deliberation on the findings of the ICER appraisal document and provides an opportunity for comment on the determination of the ICER integrated evidence rating. Although the ERG helps guide the final determination of the ICER Integrated Evidence Rating™, the final rating is ultimately a judgment made by ICER, and individual members of the ERG should not be viewed in any way as having endorsed this appraisal.

ERG Participant Name and Affiliation	**Potential Influences on Judgment**
Steven Atlas, MD, MPH Director, MGH Primary Care Quality Improvement Program and Practice Based Research Network Associate Physician, Massachusetts General Hospital Associate Professor of Medicine, Harvard Medical School	Editor of back pain guidelines for Foundation for Informed Medical Decision Making (FIMDM); recipient of grant funding from NIH and AHRQ; consultant to UpToDate
Christopher M. Bono, MD Chief, Orthopaedic Spine Service, Brigham & Women's Hospital Associate Professor of Orthopaedic Surgery, Harvard Medical School	Deputy editor of Spine journal; member of North American Spine Society (NASS)
Donald E. Casey, Jr., MD, MPH, MBA, FACP (ex officio) Vice President of Quality & Chief Medical Officer Atlantic Health	Member of American College of Physicians (ACP); employed by hospital that performs spine surgery; member of ICER advisory board

ERG Participant Name and Affiliation	Potential Influences on Judgment
Daniel C. Cherkin, PhD Senior Scientific Investigator Group Health Research Institute	Bias from 25 years of research experience showing a need for new models of diagnosis and treatment of low back pain
Roger Chou, MD, FACP Scientific Director, Oregon Evidence-Based Practice Center Associate Professor, Departments of Medicine and Medical Informatics/Clinical Epidemiology Oregon Health & Science University	Involved in development of back pain guidelines for ACP and American Pain Society (APS); member of editorial board of Cochrane Back Review Group; receives grant funding from AHRQ
Anthony Delitto, PhD, PT, FAPTA Vice President for Education and Research, Center for Rehab Services, University of Pittsburgh Medical Center Professor and Chair, Department of Physical Therapy Associate Dean of Research, Health and Rehabilitation Sciences University of Pittsburgh	Consultant to University of Pittsburgh Medical Center health plan
Richard A. Deyo, MD, MPH Director, Community and Practice-Based Research, Oregon Clinical and Translational Research Institute Kaiser Permanente Professor of Evidence-Based Family Medicine Departments of Family Medicine and Internal Medicine Oregon Health & Science University Deputy Editor, Spine	Involved in development of FIMDM back pain guidelines; consultant to UpToDate; receives grant funding from AHRQ, NIH, and Robert Wood Johnson Foundation (RWJF)
Gilbert J. Fanciullo, MD, MS Director, Pain Management Center Dartmouth-Hitchcock Medical Center Professor of Anesthesiology, Dartmouth Medical School	Practices pain medicine exclusively; did not receive industry funding in past year
Mariann Farrell Patient Representative	Has had chronic back pain for 26 years; runs Pittsburgh-area chronic pain support group
Christina Farup, MD (ex officio) Vice President, Evidence-Based Medicine DePuy, Inc. (a Johnson & Johnson company)	An employee of a manufacturer of devices for spinal surgery

ERG Participant Name and Affiliation	Potential Influences on Judgment
Theodore G. Ganiats, MD Executive Director, University of California at San Diego (UCSD) Health Services Research Center Professor and Interim Chair, Department of Family & Preventive Medicine UCSD School of Medicine	Did not attend meeting
Jason Kemner Director of Health Economics, Spine Medtronic, Inc.	An employee of a manufacturer of devices for spinal surgery; previous work experience in pharmaceuticals, devices, and health plans
Carolyn S. Langer, MD, JD, MPH Medical Director, Medical Management and Quality Harvard Pilgrim Health Care Instructor, Occupational Health Harvard University School of Public Health	Background and training in occupational health; makes coverage decisions as an employee of a private health plan
John D. Loeser, MD Professor Emeritus, Neurological Surgery, Anesthesiology, and Pain Medicine University of Washington	Previous head of hospital pain center; funding from every major manufacturer at some point
William Meeker, DC, MPH President, Palmer College of Chiropractic – West Campus	Did not attend meeting
Sohail K. Mirza, MD, MPH Professor and Chair, Department of Orthopaedics Dartmouth-Hitchcock Medical Center and Dartmouth Medical School	Chair of hospital orthopedic department; funding from NIH, AHRQ, and Wellpoint
Glenn Pransky, MD, MOccH Director, Center for Disability Research Liberty Mutual Research Institute for Safety	Employee of a disability insurer dealing with work-related back pain; has L5 radiculopathy himself
Lisa A. Prosser, PhD Research Associate Professor Child Health Evaluation and Research Unit, Division of General Pediatrics University of Michigan Health System	Has been involved in development of models for previous ICER appraisals; interest in novel approaches to characterize uncertainty

ERG Participant Name and Affiliation	Potential Influences on Judgment
Richard W. Rosenquist, MD Director, Pain Medicine Division Professor of Anesthesia, University of Iowa	Involved in multiple committees of American Society of Anesthesiologists (ASA), including economics; incoming chair of pain medicine at Cleveland Clinic
Christopher S. Stanley, MD, MBA Senior Medical Director United Healthcare of Colorado	Did not attend meeting
Steven P. Stanos, DO Medical Director, Center for Pain Management Rehabilitation Institute of Chicago Assistant Program Director, Multidisciplinary Pain Fellowship Assistant Professor, Department of Physical Medicine and Rehabilitation Northwestern University Feinberg School of Medicine	Leader of interdisciplinary pain program, speaker and consultant for pharmaceutical manufacturers

APPRAISAL OVERVIEW

MANAGEMENT OPTIONS FOR LOW BACK DISORDERS

The overview is written by members of ICER's research team. The overview summarizes the evidence and views that have been considered by ICER and highlights key issues and uncertainties.

Final Scope

Low back disorders are highly prevalent and result in high rates of chronic disability and work loss as well as substantial costs to the U.S. medical system. Given their prevalence as well as the variety of management options available for low back disorders, evaluating the comparative effectiveness of these options is a top priority for patients, clinicians, and policymakers. To provide a comprehensive evaluation of the major management options for low back disorders, the scope of this appraisal includes conservative care, interdisciplinary rehabilitation, multiple minimally-invasive procedures (e.g., spinal injections, radiofrequency denervation), and multiple surgical interventions (e.g., interspinous spacer devices, spinal fusion). The final scope of this appraisal, described using the Populations, Interventions, Comparators, Outcomes, Timing, and Setting (PICOTS) format (Counsell, 1997), is described in detail in the sections that follow. Four distinct patient populations were identified according to the presumed source of pain through imaging:

- Lumbar disc herniation
- Lumbar spinal stenosis
- Degenerative spondylolisthesis (with or without spinal stenosis)
- Non-specific low back disorders (i.e., no identifiable anatomic source of pain)

Objective and Methods:
The objective of this report is to appraise the comparative clinical effectiveness and comparative value of multiple management options for low back disorders. To support this appraisal we report the results of a systematic review of published randomized controlled trials, systematic reviews, and observational studies as well as the findings from a *de novo* decision analysis. From the outset of this effort the research team has been aided by in the input of a national Evidence Review Group (ERG) composed of clinical and methodological experts, patient experts, and representatives from private insurers and manufacturers. Input from the ERG was used to help identify the patient populations and comparisons that serve as the focus for this review.

Key Areas of Focus

1) The impact of management options for low back disorders on rates of clinically-important improvement as well as improvements on multiple individual outcomes, including pain, function, quality of life, and return to work

2) The relative rates of complications and side effects between management options

3) The components of interdisciplinary rehabilitation programs that appear to be associated with the highest levels of effectiveness

4) The cost-effectiveness and budget impact of multiple management options for low back disorders relative to conservative care

Key Considerations Highlighted by the Evidence Review Group:

1. Key outcomes: An outcome of focus for this review should be the rate of repeat procedures and/or subsequent surgery within 2 years of initial treatment, as rates are high for many management options

2. Long-term data: Any review of long-term data on outcomes for patients with low back disorders should be performed with care, as findings may be influenced by (a) the proportion of patients who are satisfied and continue with care; and/or (b) the proportion of dissatisfied patients who continue to search for solutions.

3. Key subpopulations: Patients with prior surgery and those with workers' compensation or disability issues are of particular interest because they are among the most expensive patients to treat. However, these groups are often excluded from clinical trials powered to identify a treatment effect with one or more individual outcome measures.

4. Model considerations: If feasible, the model should be constructed to evaluate the impact of each management option on both short-term relief and long-term effectiveness.

5. Ethical considerations: At the outset of the appraisal there appeared to be no distinctive ethical issues regarding the patient populations or the interpretation of results from cost-effectiveness analyses.

1. Background

1.1 The Condition

Low back pain is an exceedingly common complaint, with a lifetime prevalence ranging from 11-84% (Walker, 2000). Chronic low back pain may be seen in as many as 75% of patients 6-12 months after an initial episode (Wahlgren, 1997). The economic impact of low back pain is also substantial. It is the fifth most common reason for all physician visits in the U.S. (Deyo, 2002; Hart, 1995), and is responsible for direct medical costs that approach $30 billion annually (Luo, 2003). In addition, low back pain is a major cause of lost productivity; it is estimated that up to 2% of the U.S. work force is compensated for back pain or injury each year (Taylor, 1985).

Low back pain can be caused by various specific and nonspecific conditions, which differ in prevalence and affect different age groups. Lumbar disc herniation occurs when an intervertebral disc ruptures and pushes outside its normal boundary (Heliovaara, 1988). Studies have shown that, while the prevalence of *symptomatic* lumbar disc herniation is between 1-3% (Andersson, 1997), between 20-80% of asymptomatic individuals have been found to have some degree of disc bulge or protrusion when examined on MRI (Battie, 2004).

Lumbar spinal stenosis refers to the narrowing of the spinal canal, which compresses the spinal cord and surrounding nerves. It affects 2-13% of the U.S. population, and the prevalence increases with age; most of those affected are over the age of 50 (Kalichman, 2009). Spinal stenosis can occur alone or with spondylolisthesis, a condition caused by the shifting of a vertebra out of proper position and onto the one below it. The condition is classified as "isthmic" when the shift is due to a fracture in the bone that connects the 2 vertebrae. "Degenerative" spondylolisthesis occurs when the shift is caused by a degeneration of the intervertebral disc. As with spinal stenosis, the prevalence of degenerative spondylolisthesis increases with age. Studies have shown an overall prevalence of spondylolisthesis around 2-12% in the adult population, increasing after the age of 60 to between 17-42% (Fredrickson, 1984; Virta, 1992; Kalichman, 2009).

While many cases of back and/or leg pain resolve within 30 days of initial onset, chronic low back disorders are not uncommon and can become debilitating. A significant percentage (42-75%) of patients still report some degree of pain 12 months after initial onset, and a considerable proportion may have varying levels of disability as much as 4 years after diagnosis (Manek, 2005). The long-term course of low back/leg pain is made complicated by other factors, as the influence of depressive symptoms and other psychological concerns, fear-avoidance beliefs, and sleep dysfunction may outweigh the effects of pain and disability in patients with long-term symptoms (Burton, 2004). Even patients with aggressive initial treatment may be at risk of persistent low back pain, as initial surgery is subject to high rates of reoperation, with declining success rates after each successive surgery. It is estimated that as many as 80,000 cases of so-called "failed back surgery syndrome" are seen in the U.S. each year (Ragab, 2008).

Various organizations and medical societies have outlined specific guidelines for diagnosing and treating low back disorders. Diagnosis and subsequent treatment typically involves an initial history and physical examination by a clinician. Depending on the presentation, the clinician might prescribe various self-care therapies or will perform a diagnostic exam to check the patient's pain tolerance, functional capabilities, and reflexes. Symptoms may subside within a month, so clinicians will typically prescribe conservative treatments as an initial strategy (Pengel, 2003). If the condition becomes chronic (> 6 weeks duration), then diagnostic imaging may be considered, following which treatment options may include continued conservative management, more intensive rehabilitation options, and minimally-invasive and surgical procedures (ICSI, 2008; Chou, 2007).

While herniation, stenosis, and spondylolisthesis are confirmed through imaging, imaging results are often weakly associated with the presence of symptoms. It has been estimated that up to 90% of cases of low back and/or leg pain cannot be tied to a specific anatomic cause (Manek, 2005). As a result, many patients presenting to primary care physicians with low back pain are classified as having pain that is nonspecific (Chou, 2010), and there is no evidence that plain radiography in patients with nonspecific low back pain is associated with better patient outcomes (Deyo, 1987; Kendrick, 2001; Kerry, 2002). Therefore, imaging is not recommended as a primary diagnostic strategy. While the American College of Physicians and American Pain Society recommend imaging only for patients who have severe neurologic deficits or a severe, specific underlying condition (Chou, 2007), imaging is nevertheless used extensively and accounts for a significant portion of the $90 billion in U.S. health care expenditures attributable to low back pain (Luo, 2004; Chou, 2011).

Due to the prevalence of low back disorders and the varying nature of the underlying conditions, numerous management options are available. These options vary substantially in their intensity, degree of invasiveness, and most importantly, level of evidence regarding their effectiveness in the diverse sub-populations of patients with low back disorders. Not surprisingly, there is significant interest on the part of patients, clinicians, policymakers, and other stakeholders in evaluating the clinical and economic impact of the major management options for low back disorders.

2. The Alternative Management Strategies

A plethora of management options is available for patients with low back disorders, from a number of conservative approaches, to a wide variety of minimally invasive procedures, to several surgical options. This wide variety of options for management is described in detail below.

2.1 "Simple" Conservative Treatment

What we are calling "simple" conservative treatment for chronic low back pain consists of a number of pharmacological and non-pharmacological therapies as well as self-care interventions (Chou, 2007). Often used as an initial treatment strategy for patients presenting with low back pain, the individual options can take many forms. They include, but are not limited to:

Self-Care

- Advice to remain active
- Books, handouts

Pharmacologic Therapy

- Acetaminophen
- NSAIDs
- Antidepressants (TCA)
- Benzodiazepines
- Tramadol, opioids

Non-pharmacologic Therapy

- Spinal manipulation
- Exercise therapy
- Massage
- Acupuncture
- Yoga
- Cognitive-behavioral therapy
- Progressive relaxation

2.2 Interdisciplinary Rehabilitation Programs

Interdisciplinary rehabilitation programs (IRPs) are interventions that combine and coordinate physical, vocational, and behavioral components (Schonstein, 2003). IRPs are typically physician-directed, with care provided by multiple health care professionals with different clinical backgrounds. The intensity and content of interdisciplinary therapy varies widely; duration of treatment may be as short as 1 week or as long as 15 weeks and activity levels range from 1 to 8 hours on any given day. IRPs are usually held in groups of up to 10.

IRPs vary not only in duration and intensity, but also in the types of components provided. Worksite interventions, strength training, aerobic exercises, educational interventions, and psychological interventions are all examples of components that can constitute an IRP. These individual interventions can include:

Worksite Interventions

- Ergonomic evaluation
- Specific workplace-based interventions

Strength Training

- General muscle strengthening
- Spine stabilization exercises

Aerobic Exercises

- Treadmill walking
- Cycling
- Rowing

Educational Interventions

- Books, handouts
- Back schools

Psychological interventions

- Cognitive Behavioral Therapy
- Psychological Counseling

Adverse events are rare in IRPs. However, barriers to this type of treatment strategy include relatively high costs, unavailability in some areas, and limited insurance coverage. In addition, because these programs vary in terms of scope and components, it is difficult to assess the structure of the most effective programs as well as their associated cost-effectiveness.

2.3 Minimally-Invasive Procedures

Spinal Injections

Spinal injections deliver medication to the anatomic location that has been identified as the likely source of pain (Falco, 1998). Several spinal injections are used in practice today. They can be classified as either intraspinal injections or injections outside the spine. Intraspinal injections are further categorized into either intraspinal steroid injections or chemonucleolysis (Chou, 2009). These include:

Intraspinal injections

- Intraspinal steroid injections
  - Epidural steroid injection

  - Facet joint steroid injection
  - Sacroiliac joint steroid injection
  - Intradiscal steroid injection

- Nerve blocks
  - Medial branch blocks
  - Sympathetic nerve blocks
  - Selective nerve root blocks

- Chemonucleolysis

Injections outside the spine

- Botulinum toxin injections
- Local injections
- Prolotherapy

Intraspinal injections

Epidural steroid injections (ESIs) deliver the steroid into the epidural space, the space between the dura and the spine. The injection typically includes both a long-lasting steroid and a local anesthetic. ESIs may be delivered in three different ways. The transforaminal approach delivers the needle to the neural foramen, the space through which nerve roots exit the spinal canal to form the peripheral nerves. Interlaminar (or translaminar) injections deliver steroid directly into the epidural space. Finally, caudal injections approach the epidural space by going through the sacral opening.

Additional types of steroid injections have other anatomic targets. Facet joint steroid injections deliver corticosteroids into the facet joints, joints that are located between and behind adjacent vertebrae. Sacroiliac joint steroid injections are corticosteroid injections into or around the sacroiliac joint, the joint that connects the sacrum to the pelvis. Intradiscal steroid injections involve injecting a corticosteroid into an intervertebral disc to treat discogenic pain.

Nerve block injections include an anesthetic and may also include a corticosteroid. These injections are intended to target specific areas thought to be the source of pain, temporarily blocking pain signals. Most commonly, these injections target the medial branch nerves, which emanate from the facet joints and in turn carry pain signals from these joints. Nerve-blocking injections may also target the sympathetic nervous system, which control some of the body's involuntary functions. Nerve blocks may target selective nerve roots. These injections are intended primarily to diagnose the source of pain, not to treat it.

Chemonucleolysis uses a proteolytic enzyme, usually chymopapain, to dissolve the inner part of a herniated disc, in an effort to resolve radicular pain.

Increasingly, intraspinal injections are being performed with the assistance of imaging technology. An image-guided spinal injection involves the use of fluoroscopy or computed

tomography to facilitate placement of the injection needle for diagnostic or therapeutic purposes (Manchikanti, 2004). Proponents of imaging guidance feel that use of imaging guidance enhances injection accuracy relative to the exact source of pain (Watanabe, 2002), and also reduces the risk of serious complications such as subarachnoid puncture and inadvertent injection into the intrathecal or intravascular spaces (Manchikanti, 2004). Concerns have been raised, however, regarding whether there is clear evidence of improved outcomes through imaging guidance as well as the level of radiation dose to the physician performing the procedure (Murtagh, 2000).

Injections outside the spine

Injections that take place outside of the spine target the muscles or the soft tissues of the back. Botulinum toxin (Botox) injections are injected into the muscles of the back to control muscle spasms. Local injections utilize a local anesthetic, injected into the muscles or soft tissues of the back. These are used to treat inflammation in small areas of the back. Prolotherapy is a procedure in which a chemical irritant is injected into the soft tissues of the back. This promotes an inflammatory response, which is thought to lead to a natural healing that will strengthen the injured soft tissue and thus, reduce back pain. Also known as sclerotherapy, it is used to treat sciatica and degenerative disc disease.

Each type of injection procedure may last between 15 and 30 minutes. The patient lies on an X-ray table and the skin in the lower back area is cleaned and numbed with a local anesthetic. Spinal injections are best done under fluoroscopic (live X-ray) guidance. Once the needle is in the proper position, a contrast dye is injected to confirm the position of the needle. Following confirmation, the steroid/anesthetic solution is injected.

Risks associated with these procedures include misplacement of the needle (either advancing the needle too deeply or placing it in the wrong position). The outcomes of incorrect needle position include nerve damage, infection, bleeding, and headaches. Risks associated with the medications include elevated blood sugars, arthritis, stomach ulcers, and weight gain. Chemonucleolysis may also cause anaphylactic reactions in some patients.

One risk specifically associated with epidural steroid injections is wet tap, in which the needle penetrates the spinal sac and enters the cerebrospinal fluid. This causes the fluid to leak, resulting in severe headaches. Other rare complications associated with epidural steroid injections include epidural hematoma and abscess.

Spinal injections have come under intense scrutiny because of the exponential increase in their use as well as doubts regarding the most appropriate timing, interval, active ingredients, and anatomic site for these injections in patients with low back disorders. In addition, the effectiveness of spinal injections in preventing or delaying more invasive procedures is not well-understood.

Radiofrequency Denervation
Radiofrequency denervation (also known as radiofrequency neurotomy) is a type of procedure that uses heat to cauterize the affected nerve(s) thought to be associated with back pain (Niemisto, 2003). This procedure attempts to interrupt pain signals from these nerves, thereby reducing pain perception by the brain.

On the day of the procedure, patients are advised to avoid engaging in any strenuous activities. Patients may continue to take their normal medications except for blood-thinning medications. The patient lies face down on an X-ray table. The skin over the lower back is cleaned and numbed. The physician uses fluoroscopy to help advance the placement of the needle into the desired location. A small amount of current is passed through the needle to ensure that it is next to the target nerve; this may briefly cause facet joint or sacroiliac pain. The nerves are then numbed to minimize facet or sacroiliac joint pain while the lesion is being created. The process is repeated for up to 1-5 additional nerves. The entire procedure can last between 30 and 90 minutes and is performed in an outpatient setting. Patients are usually able to resume their normal activities in a short period. Risks associated with this procedure include pain or discomfort around the injection site, worsened facet or sacroiliac joint pain, permanent nerve pain, infection, and bleeding.

Intradiscal Electrothermal Therapy (IDET)
IDET involves the insertion of a probe into the disc(s) thought to be the source of pain and application of heat through a catheter in the disc. Proposed mechanisms of action include thermal destruction of nerve endings in the posterior disc wall; thickening of the collagen, which changes its form, thus destroying the painful nerves near the disc; stimulation of new collagen formation; and destruction of inflammatory or pain mediators within the disc tissue (Urrutia, 2007).

Using X-ray guidance, an electrothermal catheter is inserted through a needle and guided into the proper position. The temperature of the catheter is slowly increased to 90° Celsius (195° Fahrenheit). The heat shrinks and repairs the tears in the disc wall. The catheter is removed and the disc is then injected with small amounts of antibiotic and anesthetic to reduce the risk of infection and diminish discomfort, respectively. The procedure is performed on an outpatient basis. Several discs may be treated during a single session.

The most common complaint is mild irritation at the needle insertion site after the local anesthetic has worn off. Other risks associated with the procedure include bleeding, infection, and nerve damage.

Coblation Nucleoplasty
Coblation nucleoplasty (also known as percutaneous disc decompression) is a relatively new minimally-invasive procedure used to treat lumbar disc herniation. The procedure uses radiofrequency energy to create small channels within the herniated disc, which is

then thermally treated, producing an area of thermal coagulation. Channels are then formed in the nucleus in order to decompress the herniated discs (Singh, 2002).

Similar to previously mentioned minimally-invasive strategies, this procedure usually takes 20 to 30 minutes and is performed in an outpatient setting. Patients are typically able to resume normal activity within a short time after the procedure.

Proponents of RF denervation, IDET, and coblation nucleoplasty argue that these procedures can provide long-term pain relief in many patients. Others feel that multiple repeat attempts may be required for treatment success, and a significant proportion of patients require surgical intervention within 6-12 months.

2.4 Invasive Procedures

Interspinous Spacer Devices

Interspinous spacer devices are implanted between two spinous processes. They hold the spine in a slight flexion position, in an effort to allow for decompression of the spinal cord or nerve roots. Consequently, they may limit spinal extension (Kabir, 2010). However, the implants do not restrict rotation or lateral bending. Interspinous spacer devices are used in the treatment of lumbar spinal stenosis. This procedure serves as an alternative to spinal fusion and laminectomy.

The implantation of interspinous spacer devices is performed in an outpatient setting under local anesthesia. The patient may lay face down or on his side while the area is cleaned. A small incision is made in the back and an opening is created in the ligaments at the rear of the spine. Under fluoroscopic guidance, the surgeon uses a sizing distractor to create a space between the spinous processes. If the patient is conscious, he may be asked to bend his or her back to help create more space between the processes. After the implantation, the incision is closed and a bandage is applied. Strenuous activity should be avoided or limited for up to 6 weeks post-procedure. Physical therapy may be required in some cases.

Some potential complications include incorrect positioning of implant, spinous process fracture, implant dislodgement, allergic reaction, and mechanical failure of the implant.

The X-STOP® Interspinous Process Decompression System is currently the only interspinous spacer system that has been approved by the U.S. Food and Drug Administration (FDA). The labeled indication for the device is for patients ages 50 and older or patients who are experiencing neurogenic intermittent claudication secondary to a confirmed diagnosis of lumbar spinal stenosis. The device has been approved for implantation at one or two lumbar levels. Contraindications to X-STOP include titanium or titanium alloy allergies, significant instability of the lumbar spine, cauda equina syndrome, and osteoporosis.

Laminectomy
A lumbar laminectomy (also known as open decompression) is a surgical procedure used to alleviate pain that is believed to be caused by neural impingement resulting from spinal stenosis and, in some cases, disc herniation (Mayo Clinic, 2009). The surgery involves the removal of the lamina bone, a thin bony layer that covers and protects both the spinal canal and spinal cord. Surgeons may also remove bone spurs from the facet joints during laminectomy; this also helps to remove pressure from the spinal nerves.

Laminectomies are usually performed under general anesthesia. First, an incision is made over the lower back. The surgeon uses a retractor to spread the muscles and fatty tissues of the spine apart to expose the lamina. After the laminectomy, the patient is moved to a recovery room for observation. Hospital stays may range from one to 3 days. Activities such as lifting and bending should be avoided for a few weeks after the laminectomy.

Spinal Fusion
In addition to a laminectomy, a spinal fusion may be performed in order to achieve adequate decompression of the nerve root. The spine is stabilized by fusing two or more vertebrae together, using metal rods, bone grafts, or screws (American Academy of Orthopaedic Surgeons, June 2010). There are a number of potential reasons to fuse vertebrae. These include treatment of a fractured vertebra; correction of spinal deformities; elimination of pain from painful motion; and treatment of spinal instability. Spinal fusions are classified as either simple (1 or 2 disc levels or a single surgical approach) or complex (more than 2 disc levels or a combined anterior and posterior approach). Fusion may or may not use instrumentation such as screws, plates, or cages. Instrumentation is generally used as an internal splint to hold the vertebrae together while the bone grafts heal. Bone or bone substitutes are used to help fuse the vertebrae together. The bone may be taken from another bone in the patient (autograft) or from a bone bank (allograft).

During the operation, the surgeon removes the lamina to help relieve the pressure on the nerve. The surgeon then removes any additional bone that may impinge upon the affected nerve. Bone grafts are then added to the spine; these will eventually fuse with the spine to form a solid bone. Instrumentation may be added to provide additional stability while the grafts heal. There is generally more discomfort experienced after fusion surgery compared to other procedures and recovery takes much longer. Patients usually stay in the hospital for at least 3-4 days post-procedure. Substantial bone healing takes some time to achieve and the healing process varies from person to person. The indication of bone healing, as evidenced by an X-ray, is not attempted until approximately 6 weeks post-procedure. During this time, the patient's activity must be limited. The surgeon may recommend a post-operative rehabilitation program (Mayo Clinic, May 2010).

Risks associated with laminectomy and spinal fusion include nerve root damage, bowel or bladder incontinence, cerebrospinal fluid leakage, bleeding, and infection. While the major risks are relatively rare, the odds of injury increase with increasing complexity of

surgical approach and use of instrumentation (Deyo, 2010). Other complications, common to all types of major surgery, may include blood clots, myocardial infarction, pulmonary embolism, and pneumonia.

Discectomy

Lumbar discectomy is a surgical procedure to remove part of a bulging or herniated disc in an attempt to alleviate pressure on the surrounding nerve roots (American Academy of Orthopaedic Surgeons, June 2010). Open discectomy involves making a small incision in the skin over the spine, removing some of the ligament and bone to access the disc, and removing some of the disc material.

Open discectomy is performed under general anesthesia and typically requires a one-day hospital stay. The patient lies face down or is in a kneeling position. The surgeon makes an incision in the skin over the affected area of the spine. The muscle is removed from the bone. Retractors are used to hold the muscle and skin away from the surgical site so that the surgeon may have clear access to the problem disc. In some cases, ligaments and bone must be removed in order to have better access to the disc without damaging the nerve. Once the surgeon can visualize the lamina, disc, and other surrounding structures, he or she will remove the section of the disc that is protruding from the disc wall. No material is used to replace the removed disc. The incision is then closed and the patient is taken to a recovery room. After the procedure, patients should avoid strenuous activity and heavy lifting for some time. Sedentary work may be resumed within 1-2 weeks.

In addition to the open procedure, there are several alternative approaches to discectomy. Microdiscectomy is a form of discectomy where only the ruptured portion of the disc is removed. To perform this procedure, the surgeon utilizes a surgical microscope. Alternatively, the surgeon may use an endoscope to help guide the surgical approach. With microdiscectomy, the surgeon makes a very small incision in the lower back over the problem disc. A small portion of the vertebra is removed. An X-ray is used to help guide the surgeon to the right disc. Once the bony material has been removed, the surgeon locates the area near the pinched nerve root. With the aid of a microscope or endoscope, the ruptured portion of the disc is removed as well as any disc fragments that have broken off in the process.

Automated percutaneous lumbar discectomy (APLD) is a minimally-invasive form of discectomy. Using a posterolateral approach on the symptomatic side, the physician places a cannula in the center of disc under fluoroscopic guidance. An automated cutting and aspiration device is then inserted through the cannula, and the disc is then aspirated until nuclear material is completely obtained (Pfeiffer, 1990). This procedure can be performed using local anesthesia with or without conscious sedation.

Discectomy is generally a safe procedure but it is associated with some risks. These risks include infection, bleeding, injury to surrounding blood vessels or nerves, leaking cerebrospinal fluid, and injury to the dura mater, the outer layer of the spinal cord. An

open or microdiscectomy typically requires an overnight hospital stay, while APLD is typically performed on an outpatient basis.

Proponents of surgical intervention feel that, in appropriate patients, these approaches are best equipped to eliminate the root cause of low back and/or leg pain. Others feel that the inability to precisely diagnose the causes of low back disorders has led to unnecessary surgery in many patients, high re-operation rates, and increased morbidity.

2.5 Emerging Management Options

Transaxial Anterior Lumbar Interbody Fusion
Transaxial anterior lumbar interbody fusion is a minimally invasive spinal fusion procedure used to treat patients with chronic lower back pain. This procedure is an alternative to traditional fusion techniques that utilize anterior or posterior approaches to directly expose the lumbosacral spine. In the case of transaxial anterior lumbar interbody fusion the spine is accessed percutaneously via the anterior surface of the sacrum.

Laparoscopic Anterior Lumbar Interbody Fusion (Laparoscopic ALIF)
Laparoscopic anterior lumbar interbody fusion involves another minimally-invasive approach for placement of interbody fusion devices with smaller incisions and potentially lower rates of bowel irritation and post–operative ileus. Laparoscopic ALIF represents an alternative to standard open transperitoneal approaches.

Minimally-invasive Transforaminal Lumbar Interbody Fusion (TLIF)
Minimally-invasive transforaminal lumbar interbody fusion (TLIF) involves inserting bone graft, or a bone graft substitute, in between vertebrae from a side approach instead of a back approach, which is the standard technique used in posterior lumbar interbody fusion (PLIF). In addition, spinal instrumentation, such as screws and rods are used to hold the spine in position and help promote successful fusion. In recent years, many surgeons have begun to use a TLIF in preference to a PLIF because the nerve roots are moved less during the procedure and may reduce the damage to the nerve roots.

discTrode™
The discTrode™ procedure, similar to IDET, involves a radiofrequency electrode, which reduces the bulge of the disc material and desensitizes the pain sensors of the affected disc. While the IDET procedure involves applying thermal heat to the inner part of the disc, the discTrode™ procedure inserts the electrode into the outer disc area.

Disc regeneration by injection
Disc regeneration by injection involves injecting medications and nutritional supplements such as glucosamine into the disc area. The intent is to promote the healing of injured discs through the injection of these substances into the center of the disc, which in turn stimulates the growth of new collagen fibers and increases the strength of the painful disc.

3. Clinical Guidelines

3.1 Simple Conservative Care

- American Society of Anesthesiologists Task Force on Chronic Pain Management and the American Society of Regional Anesthesia and Pain Medicine (2010) http://journals.lww.com/anesthesiology/Fulltext/2010/04000/Practice_Guidelines_for_Chronic_Pain_Management_.13.aspx
  - Evidence suggests acupuncture may be considered as an adjuvant to conventional therapy (e.g., drugs, physical therapy, and exercise) in the treatment of nonspecific, non-inflammatory low back pain
  - Pharmacologic Management:
    - Anticonvulsants should be used as part of a multimodal strategy for patients with neuropathic pain
    - Antidepressants and serotonin-norepinephrine reuptake inhibitors should be used as part of a multimodal strategy for a variety of patients with chronic pain
    - As part of a multimodal pain management strategy, extended-release oral opioids should be used for neuropathic or back pain patients, and transdermal, sublingual, and immediate-release oral opioids may be used.
    - For selected patients, NMDA (ionotropic) receptor antagonists (*e.g.*, neuropathic pain), NSAIDs (*e.g.*, back pain), and topical agents (*e.g.*, peripheral neuropathic pain) may be used, and benzodiazepines and skeletal muscle relaxants may be considered.
    - A strategy for monitoring and managing side effects, adverse effects, and compliance should be in place before prescribing any long-term pharmacologic therapy.
  - Physical or restorative therapy may be used as part of a multimodal strategy for patients with low back pain.
  - Cognitive Behavioral Therapy, biofeedback or relaxation training may be used as part of a multimodal strategy for low back pain. Support psychotherapy, group therapy, or counseling may be considered as part of a multimodal strategy for chronic pain management

- American College of Physicians and American Pain Society (2007) http://www.annals.org/content/147/7/478.full.pdf+html?sid=8f9f962b-1f68-4795-ba23-7f4239901aae
  - Evidence suggests that clinicians should provide patients with evidence-based information on low back pain, advise patients to remain active, and provide information about effective self-care options
  - In conjunction with self-care recommendations, clinicians should consider the use of medications with proven benefits. Before starting therapy, clinicians should assess severity of baseline pain and functional deficits, potential

benefits, risks, and relative lack of long-term efficacy and safety data. For most patients, first-line medication options are acetaminophen or NSAIDs
    - For patients who do not improve with self-care options, clinicians should consider the addition of non-pharmacologic therapy with proven benefits for chronic low back pain, such as exercise therapy, acupuncture, massage therapy, spinal manipulation, yoga, cognitive-behavioral therapy, or progressive relaxation.

- National Institute for Health and Clinical Excellence (NICE, 2009)
  http://www.nice.org.uk/nicemedia/live/11887/44334/44334.pdf
  Based on evidence regarding simple conservative treatments, NICE recommends:
    - Providing people with educational advice that includes information on nonspecific low back pain and encourages the person to be physically active.
    - Including an educational component as part of other interventions, but not as a stand-alone program
    - Offering an exercise program, a course of manual therapy, or a course on acupuncture
    - Regarding physical activity and exercise, clinicians should advise patients with low back pain that staying physically active is beneficial
    - Offering a structured exercise program
    - Offering a course of manual therapy, including spinal manipulation
    - Offering a course of acupuncture needling
    - Advising person to take regular paracetamol (acetaminophen) as the first medication option. When paracetamol is insufficient for pain relief, NICE recommends offering NSAIDs or weak opioids while taking into account the risk of side effects.
    - Offering antidepressants if other medications provide insufficient pain relief
    - Offering strong opioids for short-term use to people in severe pain
    - Not offering selective serotonin reuptake inhibitors for treating pain

3.2 Interdisciplinary Rehabilitation Programs

- American Society of Anesthesiologists Task Force on Chronic Pain Management and the American Society of Regional Anesthesia and Pain Medicine (2010)
  http://journals.lww.com/anesthesiology/Fulltext/2010/04000/Practice_Guidelines_for_Chronic_Pain_Management_.13.aspx
  The evidence indicates that multidisciplinary treatment programs when compared to conventional treatment programs is effective in reducing the intensity of pain for 4 months to 1 year. Multimodal interventions should be part of the treatment strategy for patients with chronic pain. Furthermore, periodic follow-up evaluations should be incorporated as part of the overall treatment strategy.

- The American Pain Society (APS, 2009)
  http://journals.lww.com/spinejournal/Abstract/2009/05010/Interventional_Therapies,_Surgery,_and.14.aspx
  There is insufficient evidence to recommend interdisciplinary rehabilitation for persistent radiculopathy or symptomatic spinal stenosis. It is recommended that interdisciplinary rehabilitation be considered as a treatment option for persistent, disabling low back pain that does not respond to usual, non-interdisciplinary therapies.

- National Institute for Health and Clinical Excellence (NICE, 2009)
  http://www.nice.org.uk/nicemedia/live/11887/44343/44343.pdf
  A combined physical and psychological treatment program is recommended for patients suffering from low back pain who:
  - have received at least one less intensive treatment
  - have high disability and/or significant psychological distress

  The program should comprise around 100 hours over a maximum of 8 weeks.

3.3 Minimally-Invasive Procedures

Spinal Injections

- American Society of Anesthesiologists Task Force on Chronic Pain Management and the American Society of Regional Anesthesia and Pain Medicine (2010)
  http://journals.lww.com/anesthesiology/Fulltext/2010/04000/Practice_Guidelines_for_Chronic_Pain_Management_.13.aspx
  Intra-articular facet joint injections may be used for symptomatic relief of facet-mediated pain. Sacroiliac joint injections may be considered for symptomatic relief of sacroiliac joint pain. Medial branch blocks may be used for treatment of facet-mediated pain. Epidural steroid injections with or without local anesthetics may be used as part of a multimodal treatment regimen in select patients with radiculopathy.

- The American Pain Society (APS, 2009)
  http://journals.lww.com/spinejournal/Abstract/2009/05010/Interventional_Therapies,_Surgery,_and.14.aspx
  In patients with persistent non-radicular low back pain, facet joint corticosteroid injection and intradiscal corticosteroid injection are not recommended because randomized trials consistently found them to be no more effective than sham therapies. In patients with persistent radiculopathy due to a herniated lumbar disc, it is recommended that clinicians discuss the risks and benefits of epidural steroid injection as a treatment option. It is also recommended that any shared decision-making regarding epidural steroid injection include a specific discussion about inconsistent evidence showing moderate short-term benefits and the lack of long-

term benefits. There is little evidence to sufficiently assess the benefits and harms of epidural steroid injection for spinal stenosis.

- American Society of Interventional Pain Physicians (ASIPP, 2009)
  http://www.painphysicianjournal.com/2009/july/2009;12;699-802.pdf
  Based on the quality of evidence, the use of therapeutic lumbar facet joint nerve blocks for both short-term and long-term relief is strongly recommended. For those with either lumbar spinal pain with disc herniation and radiculitis, or discogenic pain without disc herniation, or radiculitis, the use of epidural steroid injections is strongly recommended. For those with disc herniation and radiculitis, lumbar interlaminar epidural injections are strongly recommended for short-term relief, although this recommendation may change when higher quality evidence becomes available. Interlaminar epidural injections are not highly recommended for long- term relief. For those with spinal stenosis and discogenic pain without disc herniation and radiculitis, the use of lumbar intralaminar epidural injection is not highly recommended. For managing chronic low back and lower extremity pain, the use of transforaminal epidural injections is strongly recommended.

- American Association of Neurological Surgeons/Congress of Neurological Surgeons Joint Section on Disorders of the Spine and Peripheral Nerves (AANS/CNS, 2005)
  http://www.spinesection.org/fusion_guidelines.php
  The use of facet epidural injections or lumbar epidural injections is not recommended for long-term treatment of low back pain. The use of lumbar epidural injections is recommended, however, as a treatment option that provides temporary, symptomatic relief in selected patients with low back pain.

Radiofrequency Denervation

- American Society of Anesthesiologists Task Force on Chronic Pain Management and the American Society of Regional Anesthesia and Pain Medicine (2010)
  http://journals.lww.com/anesthesiology/Fulltext/2010/04000/Practice_Guidelines_for_Chronic_Pain_Management_.13.aspx
  Radiofrequency ablation of the medial branch nerves to the facet joint should be performed for low back pain when previous therapeutic injections have provided temporary relief. Radiofrequency ablation of the dorsal root ganglion should not be routinely used in the treatment of lumbar radicular pain.

- The American Pain Society (APS, 2009)
  http://journals.lww.com/spinejournal/Abstract/2009/05010/Interventional_Therapies,_Surgery,_and.14.aspx
  There is insufficient evidence to adequately evaluate the benefits of radiofrequency denervation for patients with persistent non-radicular low back

pain. The evidence supporting the use of radiofrequency denervation for low back pain is limited. Though radiofrequency denervation appears to be safe, there appears to be a trend towards increased pain immediately after the procedure as compared to sham denervation.

- American Society of Interventional Pain Physicians (ASIPP, 2009)
  http://www.painphysicianjournal.com/2009/july/2009;12;699-802.pdf
  The level of evidence for lumbar radiofrequency neurotomy is limited. Despite the limited evidence for radiofrequency neurotomy, the procedure is strongly recommended for the management of low back pain.

Intradiscal Electrothermal Therapy

- American Society of Anesthesiologists Task Force on Chronic Pain Management and the American Society of Regional Anesthesia and Pain Medicine (2010)
  http://journals.lww.com/anesthesiology/Fulltext/2010/04000/Practice_Guidelines_for_Chronic_Pain_Management_.13.aspx
  IDET may be considered for young active patients with early single-level degenerative disc disease and well-maintained disc height.

- The American Pain Society (APS, 2009)
  http://journals.lww.com/spinejournal/Abstract/2009/05010/Interventional_Therapies,_Surgery,_and.14.aspx
  There is insufficient evidence to evaluate adequately the benefits of IDET for patients with persistent non-radicular low back pain.

- American Society of Interventional Pain Physicians (ASIPP, 2009)
  http://www.painphysicianjournal.com/2009/july/2009;12;699-802.pdf
  The level of evidence for IDET is limited. Based on this level of evidence, the procedure is not recommended for treatment of low back pain.

Coblation Nucleoplasty

- American College of Occupational and Environmental Medicine (ACOEM, 2007)
  http://www.guideline.gov/content.aspx?id=12540&search=coblation+nucleoplasty
  There is insufficient evidence regarding the efficacy of coblation nucleoplasty. Therefore, it is not recommended for treatment of chronic low back pain.

- American Society of Anesthesiologists Task Force on Chronic Pain Management and the American Society of Regional Anesthesia and Pain Medicine (2010)
  http://journals.lww.com/anesthesiology/Fulltext/2010/04000/Practice_Guidelines_for_Chronic_Pain_Management_.13.aspx

Minimally-invasive spinal procedures, such as coblation nucleoplasty, may be used for the treatment of pain related to vertebral compression fractures.

- The American Pain Society (APS, 2009)
  http://journals.lww.com/spinejournal/Abstract/2009/05010/Interventional_Therapies,_Surgery,_and.14.aspx
  There is insufficient evidence to evaluate coblation nucleoplasty for patients with persistent due to lumbar disc herniation.

- American Society of Interventional Pain Physicians (ASIPP, 2009)
  http://www.painphysicianjournal.com/2009/july/2009;12;699-802.pdf
  The level of evidence for coblation nucleoplasty is limited. Therefore, the procedure is not recommended for treatment of radicular low back pain due to contained disc herniation.

3.4 Invasive Procedures

Laminectomy

- American Pain Society (APS, 2009)
  http://journals.lww.com/spinejournal/Abstract/2009/05010/Interventional_Therapies,_Surgery,_and.14.aspx
  For patients with persistent and disabling leg pain due to spinal stenosis, either with or without degenerative spondylolisthesis, decompressive laminectomy is associated with moderate benefits compared to nonsurgical therapy through 1 to 2 years. However, effects appear to diminish with long-term follow-up.

- North American Spine Society (NASS, 2007)
  http://www.spine.org/Pages/PracticePolicy/ClinicalCare/ClinicalGuidlines/Default.aspx
  At long-term follow-up (8-10 years) compared to medical/interventional treatment, surgical decompression treatment of spinal stenosis is consistently supported. In patients with severe symptoms of lumbar spinal stenosis, decompressive surgery alone is effective about 80% of the time while medical/interventional treatment alone is effective about 33% of the time. In patients with severe symptoms of lumbar spinal stenosis, surgery is more effective than medical/interventional treatment.

Spinal Fusion

- National Institute for Health and Clinical Excellence (NICE, 2009)
  http://www.nice.org.uk/nicemedia/live/11887/44334/44334.pdf
  - Consider referral for an opinion on spinal fusion for people who:
    - Have completed an optimal package of care including a combined physical and psychological treatment programme, and
    - Still have severe nonspecific low back pain for which the patient would consider surgery
  - Offer anyone with psychological distress appropriate treatment for this before referral for an opinion on spinal fusion.

- North American Spine Society (NASS, 2007)
  http://www.spine.org/Pages/PracticePolicy/ClinicalCare/ClinicalGuidlines/Default.aspx
  For patients with spinal stenosis and spondylolisthesis, decompression with fusion results in better surgical outcomes than for patients who undergo decompression alone. For patients with lumbar spinal stenosis without spondylolisthesis or instability, there is no evidence to support the addition of fusion.

- American Association of Neurological Surgeons/Congress of Neurological Surgeons Joint Section on Disorders of the Spine and Peripheral Nerves (AANS/CNS, 2005)
  http://www.spinesection.org/fusion_guidelines.php
  - Lumbar fusion is not recommended following disc excision in patients with a herniated lumbar disc causing radiculopathy. However, spinal fusion is recommended as a potential supplemental procedure in patients with a herniated disc in whom there is evidence of preoperative lumbar spinal deformity or instability. It is also recommended as a potential surgical adjunct in patients with chronic axial low back pain associated with radiculopathy due to a herniated disc.
  - Posterolateral fusion (PLF) is recommended for patients with spinal stenosis and associated degenerative spondylolisthesis who require decompression. Pedical screw fixation added to lumbar PLF should be considered as a treatment option for those with spinal stenosis and spondylolisthesis in which there is preoperative evidence of spinal instability.

Discectomy

- The American Pain Society (APS, 2009)
  http://journals.lww.com/spinejournal/Abstract/2009/05010/Interventional_Therapies,_Surgery,_and.14.aspx
  For those with persistent and disabling radiculopathy due to a herniated lumbar disc, standard open discectomy and microdiscectomy are associated with moderate short-term (6-12 weeks) benefits compared to nonsurgical therapy. However, differences in outcomes in some trials are diminished or are nonexistent after 1-2 years.

- American Society of Interventional Pain Physicians, Interventional Pain Management Guidelines (ASIPP-IPM, 2009)
  http://www.painphysicianjournal.com/2009/july/2009;12;699-802.pdf
  - The recommendations for automated percutaneous lumbar discectomy (APLD) and percutaneous lumbar laser discectomy (PLLD) are strong but may change with higher quality evidence (1C/strong recommendation). The indications for APLD and PLLD are:
    1. Unilateral leg pain greater than back pain.
    2. Radicular symptoms in a specific dermatomal distribution that correlates with MRI findings.
    3. Positive straight leg raising test or positive bowstring sign, or both.
    4. Neurologic findings or radicular symptoms.
    5. No improvement after 6 weeks of conservative therapy.
    6. Imaging studies (CT, MRI, discography) indicating a subligamentous contained disc herniation.
    7. Well maintained disc height of 60%.

- American College of Occupational and Environmental Medicine (ACOEM, 2004)
  http://www.guideline.gov/content.aspx?id=12540&search=discectomy
  Lumbar discectomy is recommended for radiculopathy due to ongoing nerve root compression with continued significant pain and functional limitation after 4 to 6 weeks and appropriate conservative treatment. Percutaneous discectomy (nucleoplasty), laser discectomy, and disc coblation therapy is *not* recommended for any back or radicular pain syndrome. Similarly, discectomy is *not* recommended for acute, subacute, or chronic LBP without radiculopathy.

Interspinous Spacer Devices

- The American Pain Society (APS, 2009)
  http://journals.lww.com/spinejournal/Abstract/2009/05010/Interventional_Therapies,_Surgery,_and.14.aspx
  Use of an interspinous spacer device is more effective compared to nonsurgical therapy for spinal stenosis. However, the results are only applicable to patients with either 1- or 2-level stenosis. Data on long-term follow-up are lacking.

- North American Spine Society (NASS, 2007)
  http://www.spine.org/Pages/PracticePolicy/ClinicalCare/ClinicalGuidlines/Default.aspx
  At two-year follow-up, use of an interspinous spacer device in patients with mild-to- moderate symptoms of lumbar spinal stenosis was more effective than medical/interventional treatment. However, this is based upon only one high quality randomized controlled trial and until more evidence is published, no recommendation can be made.

4. Medicare and Representative Private Insurer Coverage Policies

4.1 Simple Conservative Treatment

Centers for Medicare and Medicaid Services (CMS): Medicare currently does not have a National Coverage Determination for most simple conservative management therapies regarding low back pain. However, limits on coverage of chiropractic services were documented in the Medicare national coverage policy manual. The limitations are:

- A chiropractor must be licensed or legally authorized
- Coverage extends only to treatment by means of manual manipulation of the spine to correct a subluxation provided such treatment is legal in the state where performed.
- There is no coverage or payment for X-ray services used in chiropractic treatment or for any other diagnostic or therapeutic service ordered or furnished by the chiropractor.
- In addition, in performing manual manipulation of the spine, some chiropractors use manual devices that are hand-held with the thrust of the force of the device being controlled manually. While such manual manipulation may be covered, there is no separate payment permitted for use of this device.

Aetna: Aetna considers needle acupuncture medically necessary for chronic low back pain. However, maintenance treatment, where the patient's symptoms are neither regressing nor improving, is considered not medically necessary.

Aetna considers chiropractic services medically necessary when all of the following criteria are met:

1. The member has a neuromusculoskeletal disorder;
2. The medical necessity for treatment is clearly documented; *and*
3. Improvement is documented within the initial 2 weeks of chiropractic care.

If no improvement is documented within the initial 2 weeks, additional chiropractic treatment is considered not medically necessary unless the chiropractic treatment is modified. Once the maximum therapeutic benefit has been achieved, continuing chiropractic care is considered not medically necessary.

CIGNA: Under many CIGNA benefit plans, acupuncture and chiropractic care are specifically excluded.

However, if coverage is available for acupuncture, CIGNA covers acupuncture as an adjunct to standard conservative therapy for the treatment of low back pain when other conservative methods of treatment have failed.

If coverage for chiropractic care is available, the following conditions of coverage apply. CIGNA covers chiropractic manipulation and adjunct therapeutic

procedures/modalities (e.g., mobilization, therapeutic exercise, traction) as medically necessary when ALL of the following conditions are met:

- A neuromusculoskeletal condition is diagnosed that may be relieved by standard chiropractic treatment in order to restore optimal function.
- The individual is involved in a treatment program with clear documentation of the goals, frequency, duration, and results.

Humana: Humana members **MAY** be eligible under their benefit plan for chiropractic care, for the following indications:

- The patient must have a significant neuromusculoskeletal condition, creating a functional impairment, necessitating an appropriate, medically necessary evaluation and treatment services;
- There must be a reasonable expectation of recovery or improvement in function to support the onset and continuation of a therapeutic level care plan;
- The services should be reflective of an acute care model and episodic in nature. Ongoing care after the condition has stabilized or a patient's condition has reached a clinical plateau, called maximum medical improvement (MMI), may not qualify as "medically necessary" covered services.

UnitedHealthCare: Of the various forms of complementary and alternative medicine, UnitedHealthCare covers acupuncture with the following restrictions:

1. The acupuncture benefit applies to:
   a. Pain therapy when another method of pain management has failed, and
   b. Nausea that is related to surgery, pregnancy or chemotherapy.
2. The benefit is limited to 10 visits per year.

4.2 Interdisciplinary Rehabilitation Programs

Centers for Medicare and Medicaid Services (CMS): Medicare currently does not have a National Coverage Determination for interdisciplinary rehabilitation programs.

Local Coverage Determinations regarding *rehabilitation services* have been made by the Medicare contractor in Florida (First Coast Service Options, Inc.). The policy states that outpatient therapy services shall be furnished under a *plan* established by:

- A physician/NPP (consultation with the treating physical therapist, occupational therapist, or speech-language pathologist is recommended. Only a physician may establish a plan of care in a comprehensive outpatient rehabilitation facility);
- The physical therapist who will provide the physical therapy services;
- The occupational therapist who will provide the occupational therapy services; or

- The speech-language pathologist who will provide the speech-language pathology services.

It is acceptable to treat under two separate plans of care when different physician's/NPPs refer a patient for different conditions. It is also acceptable to *combine the plans of care into one plan* covering both conditions if one or the other referring physician/NPP is willing to certify the plan for both conditions.

Aetna: Aetna covers both outpatient and inpatient pain management programs of multidisciplinary nature when certain criteria are met. Outpatient multidisciplinary programs are deemed medically necessary when all of the following criteria are met:

1. If a surgical procedure or acute medical treatment is indicated, it has been performed prior to entry
2. Member has experienced non-malignant pain for greater than 6 months
3. Member ahs failed conservative care treatments
4. Member has undergone psychiatric evaluation and has been treated appropriately
5. Member's work or lifestyle has been impaired due to pain
6. Referral from a primary care physician; and
7. The cause of the pain is unknown or attributable to a physical cause

CIGNA: CIGNA covers an interdisciplinary rehabilitation program when all of the following criteria are met:

1. The individual requires comprehensive, coordinated, skilled rehabilitation treatment from a multidisciplinary team consisting of at least two therapies
2. The individual is medically stable and is capable and willing to participate in intensive therapy for several hours per day, three to five days per week.
3. The rehabilitation program is expected to result in significant therapeutic improvement over a clearly defined period of time.
4. The rehabilitation program is individualized, and documentation outlines quantifiable, attainable treatment goals.; and
5. Rehabilitation is not required in an inpatient rehabilitation facility.

4.3 Minimally-Invasive Procedures

Spinal Injections

Centers for Medicare and Medicaid Services (CMS): Medicare currently does not have a National Coverage Determination (NCD) for spinal injections.

Local Coverage Determinations (LCDs) regarding multiple types of spinal injections have been made by Noridian, the Medicare contractor for Alaska, Arizona, Montana, North Dakota, Oregon, South Dakota, Utah, Washington,

and Wyoming. Epidural or subarachnoid injections of corticosteroids/local anesthetics are considered medically necessary for certain indications under the following conditions:

- A multi-disciplinary or collaborative comprehensive evaluation is performed prior to initiating a trial of these injections for pain relief;
- Epidural steroid injections should not exceed a series of 3 within a 6-month period when used as treatment for a pain disorder. These may be performed at intervals of one week or greater for each subsequent injection.
- Appropriate reasons for a repeat injection are: (a) significant improvement in the patient's symptoms, even if relapsed, or (b) technical reasons indicating need for a repeat the procedure even if no prior improvement.
- In the absence of a compelling technical reason, it is not appropriate to repeat a procedure a third time if there has been no improvement from the two preceding.
- If a previous series of epidural injections gave lasting relief of pain and the pain reoccurs within 6 months of the last injection, a repeat series of epidural injections may be performed.
- If steroids are used, consideration should be given to the potential complications of repetitive steroid dosing.

LCDs have been made regarding *facet joint injections* by the Medicare contractor for Colorado, Oklahoma, New Mexico, and Texas (TrailBlazer Health Enterprises, LLC). Facet joint blocks are considered to be reasonable and necessary for chronic pain (persistent pain for 3 months or greater) suspected to originate from the facet joint. Facet joint block is one of the methods used to document/confirm suspicions of posterior element biomechanical pain of the spine. Hallmarks of posterior element biomechanical pain are as follows:

- The pain does not have a strong radicular component.
- There is no associated neurological deficit and the pain is aggravated by hyperextension, rotation or lateral bending of the spine, depending on the orientation of the facet joint at that level.

LCDs have been made regarding *epidural and transforaminal epidural injections* by the Medicare contractor for Nebraska, Wisconsin, Illinois, Michigan, Minnesota, Iowa, Kansas, and Missouri (Noridian Administrative Services, LLC). Epidural steroid injections, both interlaminar/translaminar and transforaminal may be used for acute/sub acute and chronic pain syndrome with radiculopathy, along with various other conditions. Therapeutic transforaminal epidural injections are appropriate for the following purposes:

- Radicular pain resistant to more conservative measures or when surgery is contraindicated.
- Post-decompressive radiculitis or post surgical scarring

- Monoradicular pain, confirmed by diagnostic block in which a surgically correctible lesion cannot be identified

LCDs regarding *sacroiliac (SI) joint injections* have been made by the Medicare contractor for Wisconsin, Illinois, Michigan, Minnesota, Iowa, Kansas, Missouri, and Nebraska (Noridian Administrative Services, LLC). Medicare will consider the injection procedure of the SI joint medically necessary when an injection is given for therapeutic indications, such as injection of an anesthetic and/or steroid, to block the joint for immediate and potentially lasting pain relief. When therapeutic injections of the SI joint are performed, it would be expected that the record reflects noninvasive treatments (i.e., rest, physical therapy, NSAIDs, etc.) have failed.

LCDs regarding *transforaminal epidural, paravertebral facet and sacroiliac joint injections* have been made by the Medicare contractor for Delaware, the District of Columbia, Maryland, New Jersey, and Pennsylvania (Highmark Medicare Services). Transforaminal epidural injections may be appropriate for the following therapeutic situations:

- When radicular pain is resistant to or there is a patient with a contraindication to other therapeutic measures (such as non-narcotic analgesic, physical therapy, etc)
- When surgery is contraindicated
- When post-decompressive radiculitis or post–surgical scarring exists
- When there is monoradicular pain, confirmed by diagnostic blockade, in which a surgically correctable lesion cannot be identified
- When treatment of acute herpes zoster pain or post-herpetic neuralgia is needed
- When there is reflex sympathetic dystrophy, causalgia or a complex regional pain syndrome I and II, in lieu of a sympathetic blockade

The standard of care for all transforaminal epidural injections in the treatment of chronic pain requires that these procedures be performed under imaging guidance. Therefore, injections for chronic pain performed without imaging guidance are considered not reasonable or necessary.

For performance of paravertebral facet joint injections, pain must have been present for greater than 3 months. A detailed pain history is essential and must provide information about prior treatments and responses which may include, but not be limited to, analgesics and physical therapy. Imaging guidance must be used for both diagnostic and therapeutic injections to assure that the injection is properly placed.

Sacroiliac joint injection can be done diagnostically or therapeutically. Imaging guidance ensures optimal access to the SI joint space in diagnostic procedures but may not be necessary for therapeutic SI injections. Imaging confirmation of intra-articular needle positioning is required.

Washington State Health Care Authority: In a health technology assessment concluded in April, 2011 the Washington State HTA program concluded that there is limited evidence to support the use of spinal injections for back pain Epidural spine injections and sacroiliac joint injections were judged to have slightly stronger evidence of short-term pain relief; therefore, these injections are to be covered under certain conditions. A draft coverage decision is available: (http://www.hta.hca.wa.gov/documents/draft_findings_decision_spinal_injections_031811.pdf)
Nerve block, intradiscal, and facet injections are *not* a covered benefit. Epidural injections are covered under the following conditions:

- With fluoroscopic or CT guidance
- After failure of conservative therapy
- For treatment of radicular pain
- No more than 2 without clinically meaningful improvement in pain and function, and no more than 3 in 6 months

Sacroiliac injections are also covered if performed with fluoroscopic or CT guidance and after failure of conservative therapy, but are limited to no more than one injection without clinically meaningful improvement as above.

Aetna: Aetna considers any of the following injections or procedures medically necessary for the treatment of back pain; provided, however, that only one invasive modality or procedure will be considered medically necessary at a time.

- Epidural steroid injections are considered medically necessary when:
  1. Intraspinal tumor or other space-occupying lesion has been ruled out as a cause of pain; and
  2. The patient has failed to improve after two or more weeks using conservative measures; and
  3. Epidural steroid injections beyond the first set of three injections are provided as part of a comprehensive pain management program.
- Selective nerve root blocks are considered medically necessary in the treatment of persons with radiculopathy when non-invasive measures have failed and when any of the following conditions are met:
  1. Radicular pain is due to post-surgical or post-traumatic scarring; or
  2. Radicular pain when a surgically correctable lesion cannot be identified; or
  3. Radicular pain in persons with surgically correctable lesions but who are not surgical candidates.

Humana: Humana members may be eligible for epidural steroid injections for back and neck pain when all of the following criteria are met:

1. Failure to improve after six weeks of conservative therapy; and
2. Pain is radicular in nature; and
3. With low back pain, radicular pain radiates below the knee.

Members may be eligible for lumbar facet joint injections or medical branch nerve blocks when all of the following criteria are met:

1. Absence of radiculopathy; and
2. Since initial diagnosis, back pain is not responsive to conservative therapy; and
3. There are no more than three levels of facet joint injections per side, per region; and
4. Pain is aggravated by rotation, extension, or lateral bending of the spine and is not associated with neurological deficits.

UnitedHealthCare:

1. Facet joint injections are unproven for the treatment of chronic spinal pain.
2. Epidural steroid injections are proven for the treatment of sub-acute sciatica or low back radicular pain caused by disc herniation or degenerative changes in the vertebrae, when pain has been unresponsive to conservative treatment.

Radiofrequency Denervation

Centers for Medicare and Medicaid Services (CMS): Medicare currently does not have a National Coverage Determination (NCD) for radiofrequency denervation. An identified local coverage determination for paravertebral facet joint denervation by the Medicare contractor for California, Nevada, Hawaii, and the Pacific territories (Palmetto GBA) indicates that this procedure is appropriate provided:

1. Diagnosis of facet syndrome is confirmed from previous paravertebral facet joint blockage; and
2. The procedure is performed under fluoroscopic guidance.

Aetna: Radiofrequency facet denervation is considered medically necessary for treatment of members with back pain with or without sciatica in the outpatient setting when all of the following criteria are met:

1. The member has experienced severe pain-limiting activities of daily living for at least 6 months; and
2. Member has not had prior spinal fusion surgery; and
3. Neuroradiologic studies have failed to confirm disc herniation; and
4. There is no significant narrowing of the vertebral canal or presence of spinal instability requiring surgery; and
5. The member has tried and failed conservative treatment options; and
6. A trial of facet joint injections has been successful in relieving pain.

CIGNA: Radiofrequency ablation of chronic spinal pain is covered when all of the following criteria are met:

1. Severe pain that is unresponsive to at least 6 months of conservative medical treatment; and
2. The pain is of face joint origin and medial branch block/injection of the fact joint with local anesthetic results in either the elimination of marked decrease in the intensity of pain; and
3. Clinical findings do not suggest any other obvious source of the pain.

Humana: Members may be eligible for facet denervation for the following indications:

1. Severe neck or back pain; and
2. Must be at least 3 months since the initial diagnosis of neck or back pain that has not responded to conservative therapy; and
3. A diagnostic, temporary facet joint injection(s) that has been performed and has provided significant pain reduction; and
4. No more than three levels of facet joints per side, per region may be treated during a session.

UnitedHealthCare: Radiofrequency ablation is proven for the treatment of chronic thoracic and low back pain when confirmed by medial branch block injection with subsequent improvement. However, it is unproven in the treatment of all other sources of spinal or orthopedic pain for negative response to medial blocks and specific causes of spinal pain (e.g. disc herniation).

Intradiscal Electrothermal Therapy (IDET)

Centers for Medicare and Medicaid Services (CMS): Effective September 29, 2008, CMS made a National Coverage Determination (NCD) that thermal intradiscal procedures (TIPs), including IDET, are not reasonable and necessary for the treatment of low back pain.

Aetna: Aetna considers thermal intradiscal procedures (TIPs) experimental and investigational for the relief of discogenic pain or other indications.

CIGNA: CIGNA does not cover intradiscal electrothermal annuloplasty (e.g., IDET) because it is considered experimental, investigational, or unproven.

UnitedHealthCare: United Health Care considers IDET and percutaneous intradiscal radiofrequency thermocoagulation (PIRFT) to be unproven for the treatment of low back pain caused by a herniated intervertebral disc.

Coblation Nucleoplasty

Centers for Medicare and Medicaid Services (CMS): Effective September 29, 2008, CMS made a National Coverage Determination (NCD) that thermal intradiscal procedures (TIPs), including coblation nucleoplasty, are not reasonable and necessary for the treatment of low back pain.

Aetna: Aetna considers coblation percutaneous disc decompression (or coblation nucleoplasty) experimental and investigational for relief of discogenic pain or other indications.

CIGNA: CIGNA does not cover coblation nucleoplasty because it is considered experimental, investigational or unproven.

Humana: Coblation nucleoplasty is considered experimental/investigational as it is not identified as widely used and generally accepted for the proposed use as reported in nationally recognized peer reviewed medical literature.

UnitedHealthCare: United Health Care considers coblation nucleoplasty for the treatment of discogenic low back pain to be unproven.

4.4 Invasive Procedures

Laminectomy

Centers for Medicare and Medicaid Services (CMS): Medicare does not have a National Coverage Determination (NCD) or current local coverage determinations for laminectomy.

Aetna: Lumbar laminectomy is considered medically necessary for individuals with a herniated disc when all of the following criteria are met:

1. The member's daily living activities are limited by persistent pain radiating from the back down to the lower extremity;
2. Physical findings of nerve root tension are present;
3. Demonstrated presence of neurological abnormalities;
4. Imaging studies which indicate and correspond to clinical findings of specific affected nerve root;
5. Members have failed at least 6 weeks of conservative therapy; and
6. All other sources of pain have been ruled out.

Spinal Fusion

Centers for Medicare and Medicaid Services (CMS): Medicare currently does not have a National Coverage Determination (NCD) for spinal fusion surgery. A meeting of the Medicare Evidence Development and Coverage Advisory Committee (MedCAC) meeting was held in November 2006 to discuss this topic. The results of the voting demonstrate a need for better evidence to conclude that lumbar spinal fusion leads to better health outcomes for patients with low back pain due to degenerative disc disease.

Aetna: Lumbar fusion is considered medically necessary for the following (but not necessarily limited to): spinal fracture, spondylolisthesis with segmental instability, and spinal stenosis with unremitting pain, all as confirmed by imaging studies.

CIGNA: CIGNA covers lumbar fusion with or without spinal instrumentation for multiple adjacent spinal segment levels for a number of conditions including progressive neurological impairment, spinal deformity, and neural compression after spinal fracture. CIGNA covers lumbar fusion with or without spinal instrumentation for up to 2 adjacent spinal segment levels for either:

1. Chronic low back pain when both pain and disability has failed to respond to at least six consecutive months of conservative treatment; or
2. Degenerative disc disease has been demonstrated on appropriate imaging studies.

CIGNA also covers lumbar fusion as treatment for spinal instability with persistent pain and disability. CIGNA does not cover anterior interbody fusion, extreme lateral interbody fusion, or axial interbody fusion, as they are considered experimental.

Humana: Members are eligible under the plan for lumbar fusion surgery for any of the following (but not limited to) spinal stenosis associated with spondylolisthesis, spinal fracture with instability or neural compression, or failure of three months of conservative treatment.

United Health Care: United Health Care covers spinal fusion, with the addition of instrumentation, imaging, and discectomy (when performed). United Health Care considers the following spinal fusion techniques to be unproven: laparoscopic anterior lumbar interbody fusion (LALIF), minimally- invasive transforaminal lumbar interbody fusion (MITLIF), and axial lumbar interbody fusion via a pre-sacral approach (AxiaLIF).

Discectomy

Centers for Medicare and Medicaid Services (CMS): Medicare does not have a National Coverage Determination (NCD) or any current local coverage determinations (LCDs) for discectomy, microdiscectomy, or automated percutaneous lumbar discectomy (APLD).

Aetna: Percutaneous lumbar discectomy is considered medically necessary when all the following conditions are met:

1. Member is otherwise a candidate for open discectomy; and
2. Has failed 6 months of conservative treatment; and
3. Diagnostic studies show that the nuclear bulge of the disc is contained within the annulus; and
4. Member has not had previous surgery or chemonucleolysis of the disc being treated; and
5. Members must have clinical symptoms that are consistent with the level of disc involvement.

CIGNA: CIGNA does not cover automated percutaneous lumbar discectomy, laser discectomy (percutaneous or laparoscopic), laser-assisted disc decompression (LADD), or laser disc decompression as they are considered to be experimental, investigational, or unproven.

Humana: Member may be eligible for lumbar discectomy for the following indications:

1. Rapidly progressive neurologic signs/symptoms of lumbar spine compression confirmed by imaging studies; or
2. Spinal fractures confirmed by imaging studies; or
3. Herniated disc, confirmed by imaging studies, radicular neck, or back pain that has persisted despite conservative treatment.

UnitedHealthCare: United Health Care considers percutaneous disc decompression, automated percutaneous lumbar discectomy (APLD) and percutaneous laser disc decompression (PLDD) unproven for the treatment of low back pain cause by a herniated intervertebral disc.

Interspinous Spacer Devices

Centers for Medicare and Medicaid Services (CMS): Medicare currently does not have a National Coverage Determination (NCD) for interspinous spacer devices. However, in August 2006, CMS approved a pass-through payment for X-STOP procedures, allowing for additional device payments when the X-STOP device is performed in a hospital outpatient setting. Local coverage

determinations (LCDs) around interspinous process decompression have been made by the Medicare contractor for Florida, Arkansas, Louisiana, and Mississippi (First Coast Service Options, Inc.). Medicare considers interspinous process decompression medically reasonable and necessary for those who meet all of the following criteria:

1. Aged 50 or older suffering from intermittent neurogenic claudication secondary to a confirmed diagnosis of lumbar spinal stenosis;
2. Those with moderately impaired physical function who experience relief in flexion from their symptoms of leg/buttock/groin pain, with or without back pain; and
3. Patients who have undergone at least 6 months of non operative treatment

Aetna: Aetna considers interspinous distraction devices experimental and investigational.

CIGNA: CIGNA does not cover interspinous spacer devices because they are considered experimental, investigational, or unproven.

Humana: Members are not eligible for the implantation of interspinous decompression spacers, as the technology is considered experimental.

5. Previous Systematic Reviews/Tech Assessments

5.1 Simple Conservative Treatment

The Cochrane Collaboration (2011)
http://www2.cochrane.org/reviews/en/ab008112.html
There is no clinically relevant difference between spinal manipulation therapy and other interventions for reducing pain and improving function in patients with chronic low-back pain.

Medications (Chou, 2010)
http://adisonline.com/drugs/Abstract/2010/70040/Pharmacological_Management_of_Low_Back_Pain.2.aspx
For nonspecific low back pain, several medications are effective for short-term relief of acute or chronic symptoms, including NSAIDs, skeletal muscle relaxants, and tricyclic antidepressants, although each is associated with a unique set of risks and benefits. Evidence is limited on the benefits and harms associated with long-term use of medications for low back pain.

The Cochrane Collaboration (2008)
http://www2.cochrane.org/reviews/en/ab001703.html
There is no clear evidence that antidepressants are more effective than placebo in the management of patients with chronic low back pain.

The Cochrane Collaboration (2008)
http://www2.cochrane.org/reviews/en/ab001929.html
Massage might be beneficial for patients with subacute and chronic nonspecific low-back pain, especially when combined with exercises and education. The evidence suggests that acupuncture massage is more effective than classic massage, but this need confirmation.

Annals of Internal Medicine (Chou, 2007)
http://www.annals.org/content/147/7/492.abstract
Non-pharmacologic therapies with good evidence of moderate efficacy for chronic or subacute low back pain are cognitive-behavioral therapy, exercise, and spinal manipulation. For acute low back pain, the only therapy with good evidence of efficacy is superficial heat.

The Cochrane Collaboration (2007)
http://www2.cochrane.org/reviews/en/ab001929.html
Evidence suggests the benefits of opioids in clinical practice for the long-term management of chronic LBP remain questionable.

The Cochrane Collaboration (2003)
http://www2.cochrane.org/reviews/en/ab001351.html
For chronic low-back pain, acupuncture is more effective for pain relief and functional improvement than no treatment or sham treatment immediately after treatment and in the short-term only. Acupuncture is not more effective than other conventional and "alternative" treatments. The data suggest that acupuncture and dry-needling may be useful adjuncts to other therapies for chronic low-back pain.

5.2 Interdisciplinary Rehabilitation Programs

The Cochrane Collaboration (2003)
http://www2.cochrane.org/reviews/en/ab002193.htmlT
Multidisciplinary biopsychosocial rehabilitation programs (including workplace visits) seem to offer some benefit for adults with subacute low back pain, but further research on effectiveness and cost-effectiveness is needed.

British Medical Journal (Guzman, 2001)
http://www.bmj.com.ezp-prod1.hul.harvard.edu/content/322/7301/1511.long
There is evidence that intensive multidisciplinary biopsychosocial rehabilitation with functional restoration reduces pain and improves function in patients with chronic low back pain. Less intensive interventions did not show improvements in clinically relevant outcomes.

Spine (Karjalainen, 2001)
http://journals.lww.com/spinejournal/Abstract/2001/02010/Multidisciplinary_Biopsychosocial_Rehabilitation.11.aspx
There was moderate scientific evidence showing that multidisciplinary rehabilitation, which includes a workplace visit or more comprehensive occupational health care intervention, helps patients to return to work faster, results in fewer sick leaves and alleviates subjective disability.

5.3 Minimally-Invasive Procedures

Spinal Injections

National Institute for Health and Clinical Excellence (NICE, 2010)
http://guidance.nice.org.uk/IP/609
Epidural steroid injections do not fall within the program's remit because they are considered standard clinical practice with a well-established safety and efficacy.

Canadian Agency for Drugs and Technologies in Health (CADTH, 2007)
http://www.cadth.ca/media/pdf/I3003_tr_Facet_Joint_Injections_e.pdf
Facet joint injections should be used as an adjunct to other forms of conservative treatment, such as physical exercise, rather than as a stand-alone treatment.

The Cochrane Collaboration (2009)
http://www2.cochrane.org/reviews/en/ab001824.html
There is not enough evidence to recommend the use of injection therapy for sub- acute and chronic low back pain.

Institute for Clinical Systems improvement (2004)
http://www.icsi.org/technology_assessment_reports_-_active/ta_fluoroscopically_guided_transforaminal_epidural_steroid_injections_for_lumbar_radicular_pain.html
When performed by an experienced physician, fluoroscopically-guided epidural steroid injections are generally safe. There is limited information, however, to comment on the short- or long-term efficacy of epidural steroid injections.

Radiofrequency Denervation

National Institute for Health and Clinical Excellence (NICE, 2004)
http://www.nice.org.uk/nicemedia/live/11115/31119/31119.pdf
The current evidence on the safety and efficacy of percutaneous intradiscal radiofrequency thermocoagulation for low back pain is not adequate to support the use of the procedure without special consideration.

Canadian Agency for Drugs and Technologies in Health (CADTH, 2007)
http://www.cadth.ca/media/pdf/I3003_tr_Facet_Joint_Injections_e.pdf
Facet joint injections should be used as an adjunct to other forms of conservative treatment, such as physical exercise, rather than as a stand-alone treatment.

The Cochrane Collaboration (2009)
http://www2.cochrane.org/reviews/en/ab001824.html
There is not enough evidence to recommend the use of injection therapy for sub- acute and chronic low back pain.

Institute for Clinical Systems improvement (2004)
http://www.icsi.org/technology_assessment_reports_-_active/ta_fluoroscopically_guided_transforaminal_epidural_steroid_injections_for_lumbar_radicular_pain.html
When performed by an experienced physician, fluoroscopically-guided epidural steroid injections are generally safe. There is limited information, however, to comment on the short- or long-term efficacy of epidural steroid injections.

Intradiscal Electrothermal Therapy

National Institute for Health and Clinical Excellence (NICE, 2009)
http://www.nice.org.uk/nicemedia/live/11055/46396/46396.pdf
This procedure should only be used with special arrangements for clinical governance, as the current evidence on safety and efficacy for low back pain is inconsistent.

California Technology Assessment Forum (CTAF, 2003)
http://www.ctaf.org/content/assessment/detail/551
IDET with either the radionics RF system or the Oratec IDET system does not meet CTAF criteria 1-5.

Coblation Nucleoplasty

National Institute for Health and Clinical Excellence (NICE, 2006)
http://www.nice.org.uk/nicemedia/live/11147/31277/31277.pdf
Current evidence suggests that there is no major safety concerns associated with the use of percutaneous disc decompression using coblation for lower back pain. There is some evidence of short-term efficacy; however, this is not sufficient to support the use of this procedure without special arrangements for consent and for audit or research.

5.4 Invasive Procedures

Laminectomy

There are no recent technology assessments or systematic reviews of laminectomy for low back disorders.

Spinal Fusion

National Institute for Health and Clinical Excellence (NICE, 2011)
http://www.nice.org.uk/nicemedia/live/13025/53631/53631.pdf
While the evidence surrounding transaxial interbody lumbosacral fusion is limited, short-term symptom relief is shown in some patients. However, there is a risk of rectal perforation.

National Institute for Health and Clinical Excellence (NICE, 2009)
http://www.nice.org.uk/nicemedia/live/12138/46410/46410.pdf
The evidence regarding lateral interbody fusion in the lumbar spine is lacking and of low quality.

Agency for Healthcare Research and Quality (AHRQ, 2006)
http://www.cms.gov/determinationprocess/downloads/id41ta.pdf
The amount of evidence on lumbar spinal fusion does not demonstrate either short- or long-term benefits when compared with non-surgical treatment, especially for patients over 65 years of age, or for those with degenerative disc disease.

Discectomy

National Institute for Health and Clinical Excellence (NICE, 2005)
http://www.nice.org.uk/nicemedia/live/11179/31406/31406.pdf
While the evidence suggests that there are no major risks associated with automated percutaneous lumbar discectomy (APLD), its efficacy is uncertain.

National Institute for Health and Clinical Excellence (NICE, 2009)
http://www.nice.org.uk/nicemedia/live/12073/44256/44256.pdf
There is little evidence regarding the safety and efficacy of percutaneous endoscopic lumbar discectomy.

California Technology Assessment Forum (CTAF, 2008)
http://www.ctaf.org/content/assessment/detail/869
Laser discectomy is not recommended for the treatment of symptomatic lumbar disc prolapse, as it does not meet CTAF criteria 2-5 for safety, efficacy, and improvement in health outcomes. Automated percutaneous lumbar discectomy has been used for a number of years but has not been clinically evaluated in trials comparing to percutaneous lumbar disc decompression.

Interspinous Spacer Devices

National Institute for Health and Clinical Excellence (NICE, 2010)
http://guidance.nice.org.uk/IPG365
The evidence on interspinous distraction procedures shows that these surgical interventions are efficacious for carefully selected patients in the short- and medium-term, although failure may occur and further surgery may be needed. There are no major safety concerns.

California Technology Assessment Forum (CTAF, 2006)
http://www.ctaf.org/content/assessment/detail/528
The use of the X-STOP interspinous process distractor device meets CTAF criteria 1-5 for safety, effectiveness, and improvement in health outcomes when used in the following patient population:

1. Age>50 years old;
2. Moderate impairment of physical function, symptomatic lumbar spinal stenosis at no more than 2 levels;
3. Failed ≥6 months of non-operative, conservative care;
4. No evidence of radiculopathy; and
5. Image evidence of spinal stenosis.

6. Ongoing Clinical Studies

Ongoing Research (from www.clinicaltrials.gov)

6.1 Simple Conservative Treatment

Trial Sponsor, NCT ID Number/Title	Design	Primary Outcomes	Populations	Variables	Estimated Study Completion Date
Department of Veterans Affairs; University of California, San Diego, NCT00608530/Telehealth Outreach for Chronic Back Pain	RCT	Function: N/S Pain: NRS	• N=130 • Age: 18 to 75 years	CBT vs. Rogerian psychotherapy	July 2011
Department of Veterans Affairs	RCT	Pain: NRS Function: RMS QoL: SF-36	• N=230 • Age: 18 years or older	Face to Face CBT vs. Interactive Voice Response CBT	June 2013
University of Kentucky, NCT01147120/Chronic Low Back Pain and Primary Health Care	RCT	Function: ODI QoL: SF-36	• N=138 • Age: 21 years or older	Progressive Muscle Relaxation vs. Clinical Massage Therapy	July 2012

6.2 Interdisciplinary Rehabilitation Programs

Trial Sponsor, NCT ID Number/Title	Design	Primary Outcomes	Populations	Variables	Estimated Study Completion Date
Ullevaal University Hospital, NCT00840697/Effect of Interventions in Return to Work for Patients With Neck and Low Back Pain	RCT	Return-to-work	• 18 to 65 Years	Interdisciplinary Rehabilitation vs. Conservative Care	April 2013
Helsinki University, NCT00908102/Managing Non-acute Low Back Symptoms in Occupational Health: Two Trials	RCT	Sickness absence days Pain: Visual Analog Scale (VAS) Disability: Roland-Morris Disability Questionnaire (RDQ) Quality of Life: 15-D	• 18 to 56 Years • N=505	Interdisciplinary Rehabilitation vs. Conservative Care	September 2010
University Hospital, Gentofte, Copenhagen, NCT00256373/Treatment of Chronic Low Back Pain: A Trial Comparing Traditional Back School and Individual Therapist-Assisted Exercise	RCT	Pain: Visual Analog Scale (VAS)	• 18 to 60 years • N=286	Interdisciplinary Rehabilitation vs. Conservative Care	November 2005 (on-going)

6.3 Minimally-Invasive Procedures

Spinal Injections

Trial Sponsor, NCT ID Number/Title	Design	Primary Outcomes	Populations	Variables	Estimated Study Completion Date
Franklin Pierce University|University of Colorado, Denver, NCT00786981/Epidural Steroid Injection Versus Epidural Steroid Injection and Manual Physical Therapy and Exercise in the Management of Lumbar Spinal Stenosis; a Randomized Clinical Trial	RCT	Change in disability as measured by the Modified Oswestry Disability Index	• 50 Years to 90 Years • N=80	Epidural steroid injection plus physical therapy vs. Epidural steroid injection	May 2011
Coastal Orthopedics & Sports Medicine|Vertos Medical, Inc., NCT00995371/Study of Epidural Steroid Injection (ESI) Versus Minimally Invasive Lumbar Decompression (MILD®) in Patients With Symptomatic Lumbar Central Canal Stenosis	RCT	Changes in back pain (as by Visual Analog Scale; Changes in quality of life on SF-12; change in function as measured by the Oswestry Disability Index and Zürich Claudication Questionnaire	• 18 Years and older • N=40	MILD® (Minimally Invasive Lumbar Decompression) vs. Epidural Steroid Injection	June 2011
Pain Management Center of Paducah, NCT01053273/A Randomized, Equivalence Trial of Percutaneous Lumbar Adhesiolysis and Caudal Epidural Steroid Injections	RCT	Numeric rating scale (NRS), Oswestry Disability Index (ODI), duration of significant pain relief, opioid intake, and return to work	• 18 Years and older • N=120	Caudal Epidural Injection vs. percutaneous adhesiolysis	January 2014

Radiofrequency Denervation

Trial Sponsor, NCT ID Number/Title	Design	Primary Outcomes	Populations	Variables	Estimated Study Completion Date
Maastricht University Medical Center|ZOL Hospital Genk Belgium|Sint Jozef Hospital Bornem en Willebroek Belgium, NCT00991237/ PRFTreatment for Patients With Chronic Lumbosacral Radicular Pain Compared to Conventional Medical Management	Comparative Cohort	Pain reduction at 2 months post-treatment	• 18 Years and older N=29	Pulsed Radiofrequency Denervation vs. Historical Control	March 2014
Coastal Orthopedics & Sports Medicine, NCT00802997/Trial Assessing Cooled Radiofrequency Denervation as a Treatment for Sacroiliac Joint Pain Using the Sinergy System	RCT	Pain: Visual Analog Scale (VAS)	• 18 Years and older • N=51	Cooled Radiofrequency denervation vs. placebo	June 2012

Intradiscal Electrothermal Therapy

There are no current trials of IDET identified through clintrials.gov.

Coblation Nucleoplasty

Trial Sponsor, NCT ID Number/Title	Design	Primary Outcomes	Populations	Variables	Estimated Study Completion Date
ArthroCare Corporation | ArthroCare Europe, NCT00940810/Plasma Disc Decompression Versus Conservative Care	RCT	Pain status change assessed using a visual analogue scale (VAS) for radicular pain intensity	• 18 to 65 Years old • N = 46	Plasma Disc Decompression (Coblation Nucleoplasty) Versus Conservative Care	November 2011

6.4 Invasive Procedures

Laminectomy

There are no current trials of laminectomy identified through clinicaltrials.gov.

Spinal Fusion

Trial Sponsor/Title	Design	Primary Outcomes	Populations	Variables	Estimated Study Completion Date
Jyväskylä Central Hospital|Tampere University Hospital|University of Tampere, NCT00834015/Spinal Fusion Study	RCT	Pain disability quality of life	• 20 Years and older • N = 100	Lumbar spinal fusion patients and postoperative exercise therapy vs. Lumbar spinal fusion patients without postoperative exercise therapy	December 2012
Interventional Spine, Inc., NCT00878579/Percutaneous Dynamic Stabilization (PDS) System Versus Fusion for Treating Degenerative Disc Disease	RCT	Improvement in Oswestry Disability Index (ODI)	• 18 Years to 70 Years • N = 292	Percutaneous Dynamic Stabilization System vs. TLIF with Autograft and Pedicle Screws	TBD

Discectomy

Trial Sponsor, NCT ID Number/Title	Design	Primary Outcomes	Populations	Variables	Estimated Study Completion Date
Norwegian University of Science and Technology, NCT00546949/Treatment of Lumbar Spinal Stenosis; Comparison of Two Different Surgical Methods; Mini-invasive Decompression to X-stop	RCT	Zürich Claudication Questionnaire	• 50 Years to 85 Years • N=180	Minimal invasive decompression vs. X-stop	December 2010
Medtronic Spine LLC, NCT00905359/Neurogenic Intermittent Claudication Evaluation Study	RCT	Zürich Claudication Questionnaire	• 21 Years and older • N=280	Aperius™ PercLID™ System and Standalone Decompressive Surgery vs. Standalone Decompressive Surgery	October 2015
Coastal Orthopedics & Sports Medicine | Vertos Medical, Inc., NCT00995371/Study of Epidural Steroid Injection (ESI) Versus Minimally Invasive Lumbar Decompression (MILD®) in Patients With Symptomatic Lumbar Central Canal Stenosis	RCT	10-point visual analog scale and pain medication requirements, Oswestry Disability, Zürich Claudication Questionnaire, Work Production Index, Quality of Life Physical Component Score (PCS) on SF-12	• 18 Years and older • N=40	MILD® (Minimally Invasive Lumbar Decompression) vs. Epidural Steroid Injection	June 2011

Interspinous Spacer Devices

Trial Sponsor, NCT ID Number/Title	Design	Primary Outcomes	Populations	Variables	Estimated Study Completion Date
Norwegian University of Science and Technology, NCT00546949/Treatment of Lumbar Spinal Stenosis; Comparison of Two Different Surgical Methods; Mini-invasive Decompression to X-STOP	RCT	Zürich Claudication Questionnaire	• 50 Years to 85 Years • N=180	Minimal invasive decompression vs. Interspinous device	December 2010
VertiFlex, Incorporated, NCT00692276/ Investigating Superion™ In Spinal Stenosis [ISISS]	RCT	Effectiveness will be determined based on Zürich Claudication Questionnaire	• 45 Years and older • N=400	Superion™ Interspinous Spacer vs. X-STOP® IPD® Device	June 2011
Synthes Spine, NCT00697827/A Study of the In-Space Device for Treatment of Moderate Spinal Stenosis	RCT	Zürich Claudication Questionnaire	• 50 Years and older • N=500	In-Space vs. X-STOP®	December 2011

7. The Evidence

Objectives
The primary objectives of the systematic review were to:

- Evaluate and compare the published evidence on the effects of interdisciplinary rehabilitation, minimally-invasive interventions (e.g., spinal injections, radiofrequency denervation), and surgical management (e.g., discectomy, fusion) on pain, function, and health-related quality of life in patients with subacute or chronic low back and/or leg pain arising from disc herniation, spinal stenosis, spondylolisthesis, or non-specific causes;

- Evaluate and compare the clinical benefits of these therapies in terms of other outcomes, including rates of return to work, rates of "successful" outcomes, and subsequent patient management;

- Evaluate and compare the potential harms of these therapies, including procedure-related fatalities and major and minor complications; and

- Classify the major components of interdisciplinary rehabilitation programs and identify those program components associated with the greatest degree of effectiveness.

As discussed in greater detail in sections below, the target population for this appraisal was patients who have failed a trial of "simple conservative management" – the use of one or more non-invasive management modalities (e.g., medication, exercise, alternative therapies) without the overarching coordination that is inherent in interdisciplinary rehabilitation. We therefore did not include these individual modalities in our review of the evidence.

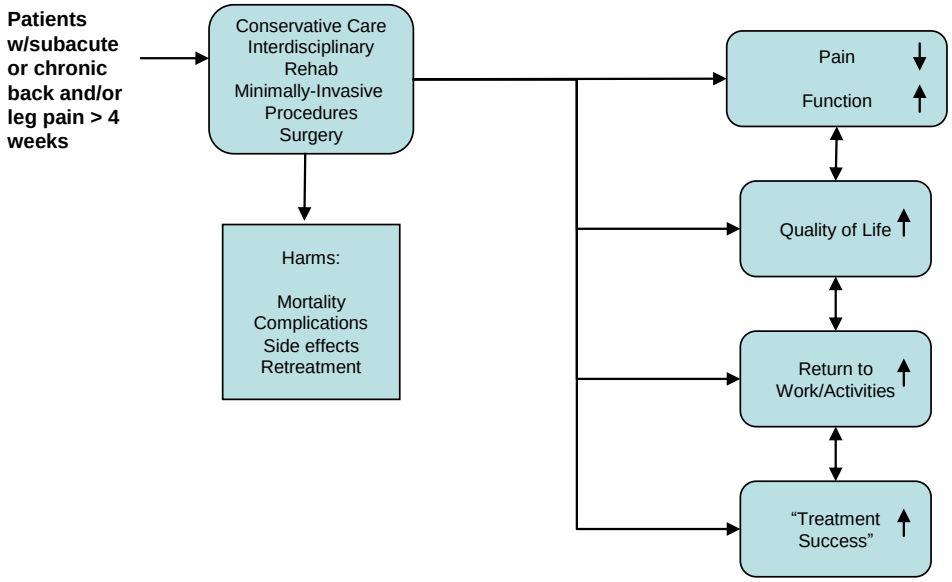
Our recording of data on potential harms of either minimally-invasive or invasive surgical procedures included "peri-procedure" fatalities occurring during the procedure or within 30 days following. While the types of major and minor complications differed somewhat by management approach, we generally defined major complications as those requiring reoperation or other major intervention to correct, while we defined minor complications as transient conditions or those requiring minimal intervention.

While not part of the systematic review, published studies of the economic impact of the management options of focus are summarized in Section 8 to provide additional context for the ICER clinical and economic model.

Analytic Framework

The analytic framework for this review is shown in the Figure below. Note that the figure is intended to convey the conceptual links involved in evaluating outcomes of these management alternatives, and are not intended to depict a clinical pathway through which all patients would flow. This framework also does not represent the clinical pathways as they were constructed for the decision analytic model (see Section 8).

Analytic Framework: Management Options for Low Back Disorders



There are little to no data directly demonstrating the impact of most LBD management strategies on summary measures of "treatment success" or "successful clinical outcome", so judgments about the effectiveness of these interventions must rest almost exclusively upon consideration of multiple and potentially overlapping measures (e.g., pain, function, quality of life) as well as evaluation of treatment-associated risks. In addition, various stakeholders will by nature be more interested in certain outcomes than others. For example, payers and employers may be most interested in functional improvement and/or return to work, while clinicians and patients may focus more on relief of symptoms.

There is considerable debate about how much credence to place in comparisons across studies of multiple outcome measures for the management of LBD. Patient populations may differ significantly in terms of baseline severity of their condition and degree of impairment, which can then in turn affect the sensitivity of measurement instruments to detect clinically important differences, even when these instruments are standardized and validated (Carey, 2007). In addition, the primary research questions and goals of management may differ substantially by approach. For example, interventions with a goal of functional restoration may show little to no effects on pain and quality of life measures. Finally, study comparators may vary considerably across populations and interventions.

For example, the term "usual care" may relate to typical general practitioner-directed care in a surgical study and to active physical therapy in a study of interdisciplinary rehabilitation.

Differences across interventions and patient populations are not surprising, as the construct of "low back pain" is a poorly-defined clinical entity that is difficult to differentiate in terms of severity, degree of impairment, and root cause (Pransky, 2010). As a result, LBD studies vary substantially in terms of their entry criteria, as there is no agreed-upon standard with which to delineate specific patient cohorts, even with the use of imaging. In addition, as mentioned before, interventions may have differential effects on the outcomes of primary interest in LBD studies, including pain, function, quality of life, satisfaction, and work status. Finally, RCTs of fundamentally different interventions (e.g., surgery for pain relief vs. rehabilitation for functional restoration) may have difficulty enrolling and randomizing patients, resulting in many studies with inadequate statistical power or other quality concerns (e.g., high dropout and/or crossover rates). It is therefore important to keep these challenges in mind during the evaluation of management options for each LBD condition of interest.

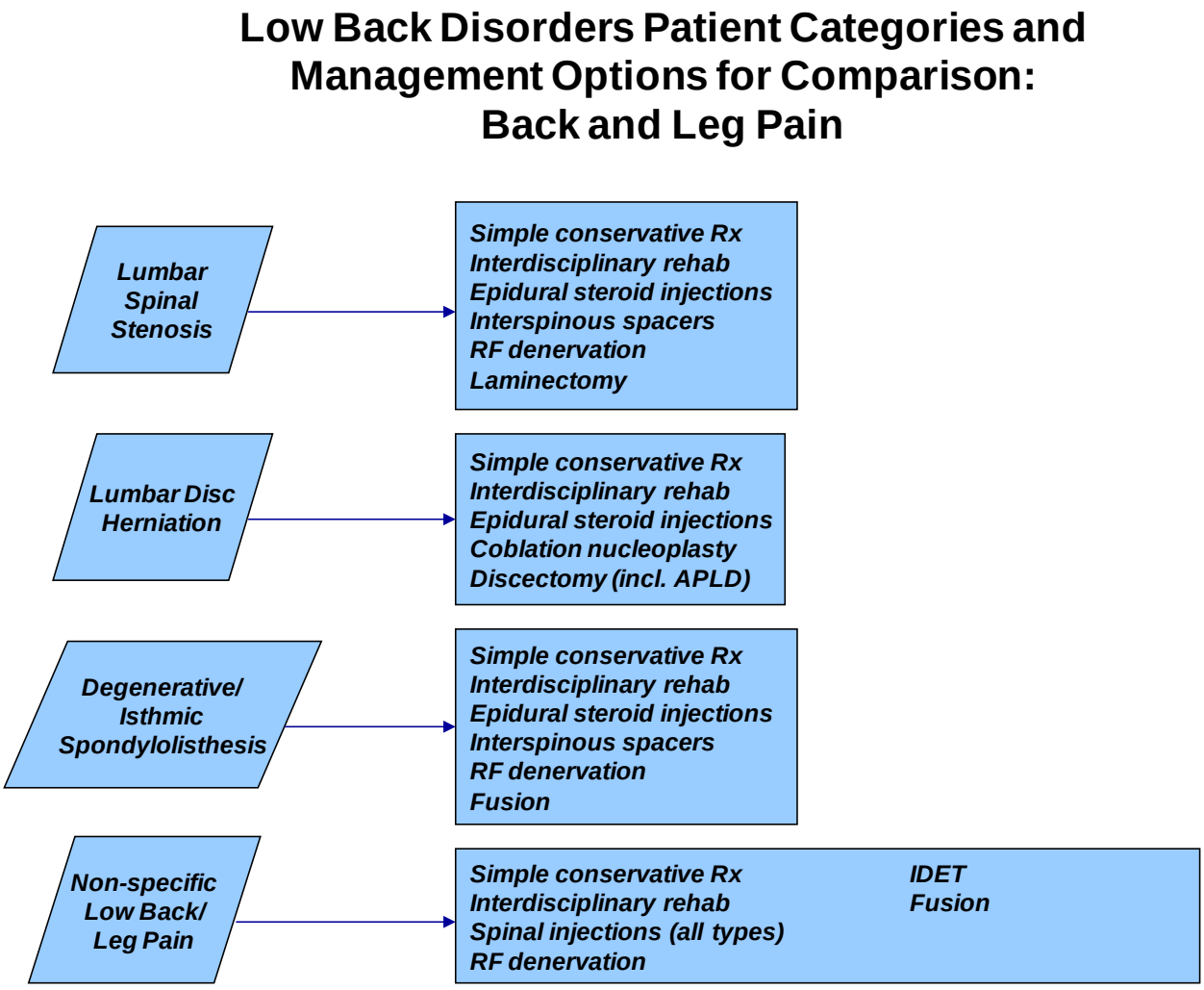
7.1 Patient Populations

The focus of this appraisal was on patients with subacute or chronic low back and/or leg pain. With input from the Evidence Review Group (ERG) we defined this patient population as those who have continued pain following a minimum of an initial 4-6 week course of conservative treatment (e.g., medications, exercise). We excluded data from studies on patients with low back pain associated with acute major trauma, cancer, infection, the cauda equina syndrome, fibromyalgia, and osteoporosis or vertebral compression fracture, as well as studies focusing specifically on failed back surgery syndrome. Within this overall patient population, we organized our review to analyze evidence relevant to 4 specific patient groups:

- Lumbar disc herniation
- Lumbar spinal stenosis
- Degenerative spondylolisthesis
- Non-specific low back pain (patients either not imaged or imaged with findings not placing them into one of the other diagnostic categories)

The literature search was conducted separately for these 4 patient populations. Data on multiple populations from individual studies or systematic reviews were abstracted for each population studied if feasible. We evaluated differences in treatment outcomes stratified by work capacity and/or disability coverage and by patients' demographic characteristics.

The 4 patient populations and list of comparator interventions are shown in the Figure below. It is important to note that the listed interventions represent those judged to be of most interest to multiple stakeholders for each patient population by the members of the ERG, and do *not* reflect any assumptions regarding the associated level of evidence.



RF: Radiofrequency; IDET: Intradiscal electrothermal therapy; DS: Degenerative spondylolisthesis; IS: Isthmic spondylolisthesis; APLD: Automated percutaneous lumbar discectomy

7.2 Interventions

The list of management alternatives for each population was derived in consultation with the ERG among options that were believed to represent common choices for patients and clinicians, as well as interventions for which the evidentiary base was considered controversial. As described previously, the population for this appraisal included patients with subacute or chronic low back and/or leg pain who have continued symptoms following a minimum of 4-6 weeks of simple conservative management. The scope of the

appraisal therefore did not include analysis of the evidence comparing the effectiveness of individual conservative management modalities (e.g., medications, exercise, alternative therapies). Similarly, evidence regarding the clinical value of imaging was not a specific focus of this appraisal. While the appropriateness of early imaging for low back disorders continues to be an important clinical and economic issue for many stakeholders, in consultation with our ERG we decided that a new evidence review would add little information to the existing body of evidence reviews, clinical guidelines, and policy tools related to low back imaging.

Several additional decisions were made to further limit the number of management options analyzed in the appraisal in order to produce a feasible scope. Among surgical techniques, artificial disc replacement was not evaluated, in part because Medicare's 2006 national coverage decision considering the procedure non-covered remains in force (Center for Medicare and Medicaid Services, 2006 [updated August 2007]). In addition, while spinal fusion and laminectomy were considered part of the scope of this appraisal, the available evidence on these longstanding procedures was considered to be sufficiently robust to permit judgments on their comparative effectiveness without requiring a *de novo* literature search.

Several non-surgical minimally-invasive interventions also were excluded from consideration. These included prolotherapy, chemonucleolysis, spinal cord stimulation, and vertebroplasty. In addition, studies of the use of spinal injections solely for diagnostic purposes also were excluded.

7.3 Comparators

The universal comparator for all of the management options described previously was the continuation of simple conservative treatment, including medications, exercise and/or physical therapy, spinal manipulation, alternative therapies (e.g., acupuncture, yoga), and cognitive-behavioral therapy.

7.4 Outcomes

In order to adequately compare effectiveness across management options within each patient population, we selected for abstraction data from the most widely-used and validated outcome instruments. These measures are described in more detail on the following pages, by type. Wherever feasible, both short-term and long-term outcomes were reported. While the duration of follow-up differed by population and intervention, short-term outcomes were generally defined as those occurring within 12 months of follow-up, while long-term outcomes were reported at timepoints >12 months.

Pain
Pain outcomes were evaluated based on visual analogue (VAS), numeric, or Likert rating scales, as well as the Brief Pain Inventory where available. Data were abstracted as recorded, including repeated-measures means and standard deviations at multiple timepoints, "change scores" (i.e., mean or median change from baseline), and both univariate and multivariate measures of treatment effect. The statistical significance of all findings was also abstracted as reported. While data were abstracted as reported for the systematic review, data transformations were performed for modeling if warranted. For example, VAS results using a different scale (e.g., 10 mm) may have been converted to 100mm scales for the purpose of consistency (see Section 8).

Functional Status
Findings with regard to patient functional status were assessed from studies employing one of 2 well-known indices for measuring function in low back disorders, the Oswestry Disability Index (ODI) or the Roland-Morris Disability Questionnaire (RDQ). Data were abstracted as described above for pain. In addition, as these indices are scaled differently (0-100 for the ODI; 0-24 for the RDQ), transformations of data were considered in modeling where warranted (see Section 8).

Health-related Quality of Life
Generic health-related quality of life was recorded from studies using the Medical Outcomes Study Short Form 36 (SF-36) or the EuroQol EQ-5D, as both of these instruments have been found to correlate well with LBD-specific functional and other questionnaires (Kovacs, 2004). Data were abstracted as described for pain and function above. Most studies employing the SF-36 focused only on specific subdomains; we abstracted data on the bodily pain and physical function subdomains as well as the physical and mental component summary scores. In addition, studies recording data on all 8 subdomains of the SF-36 were sought for modeling purposes given their feasibility for determining utility values (see Section 8).

Successful Clinical Outcome
The frequency or likelihood of "successful clinical outcome" or "treatment success" was abstracted where reported. Because these measures do not typically follow a standard definition, the approach used to measure this outcome was also abstracted in free-text format.

Return to Work
Multiple measures of return to work were recorded, including the frequency of successful return to work and total amount of sick leave/absenteeism. Where available, time-to-event measures of return to part- or full-time employment were also recorded.

Potential Harms

Peri-Procedure Mortality and Complications

Peri-procedure deaths were classified as those occurring during the procedure or within 30 days following. Procedure-related complications were recorded as "major" or "minor" based on a discrete list of complication types as reported in the studies that comprised our sample; a specific classification scheme (e.g., Clavien) was *not* used, as such schemes were infrequently employed in the studies we evaluated. Major complications were those that were felt to require re-exploration of the intervention site or a significant new clinical intervention; examples included:

- Discitis/abscess
- Nerve root injury
- Osteolysis of spinous process
- Major hemorrhage
- Spinous process fracture
- Loss of fixation
- Deep vein thrombosis and/or pulmonary embolism

Minor complications were recorded as a single category based on classification as "minor" or "not requiring major invasive treatment" in comparative studies or case series. Examples of minor complications as recorded in the studies of focus included:

- Dural tears and/or incidental durotomy
- Dyesthesia
- Superficial wound infection
- Neuropathic pain

Retreatment

Rates of repeat treatment with the initial procedure were abstracted where reported, most commonly for minimally-invasive interventions (e.g. spinal injections, radiofrequency denervation). Rates of subsequent treatment with other interventions (typically surgery) also were abstracted where available. Finally, the related but distinct issue of "crossover" (i.e., use of the alternative treatment instead of the one to which patients were randomized) was abstracted on a time-varying basis as data permitted.

7.5 Timeframe

The timeframe for evaluation of clinical benefits and potential harms differed by study design (see Section 7.7 below). Data from RCTs were considered from baseline through 2 years of follow-up. Use of observational studies was focused on longer durations of follow-up, from 2-10 years following study initiation.

7.6 Study Designs

Data from both RCTs and observational studies were considered. However, only data from RCTs comparing the management options of interest to some form of active or sham treatment were used to evaluate measures of clinical effectiveness, given the significant risks of selection bias and placebo effects inherent in other study designs. Use of observational studies was limited to (a) evaluation of measures of effectiveness and the stability of clinical benefit more than 2 years after treatment initiation; (b) examination of data on potential harms; and (c) patterns of resource use, including subsequent treatment requirements.

7.7 Literature Search and Retrieval

Because several clinical societies and other decision-making bodies have conducted high-quality systematic reviews of many of these interventions, we sought to build on these efforts in two ways. First, we abstracted data from studies published after the search timeframe of the reviews of interest. Second, since the selected reviews included data from randomized controlled trials only, we conducted a supplemental search focusing on observational studies. The general timeframe for literature search and retrieval was January 2000 – February 2011.

Systematic reviews were selected that met criteria for high quality (Oxman, 1991), have been widely cited, and have been influential in the development of clinical practice guidelines and/or policy decision-making. Selected reviews included:

- ***Spinal injections*:** Hashimoto R, et al. Spinal Injections: Health Technology Assessment. Spectrum Research, Inc., November 2010.

- ***Surgical interventions:*** Chou R, et al. Surgery for low back pain: a review of the evidence for an American Pain Society practice guideline. *Spine* 2009;34:1094-1109.

- ***Non-surgical minimally-invasive interventions:*** Chou R, et al. Nonsurgical interventional therapies for low back pain: a review of the evidence for an American Pain Society practice guideline. *Spine* 2009;34:1078-93.

Importantly, we did <u>not</u> rely on a single previous systematic review to serve as the evidentiary basis for our analysis of interdisciplinary rehabilitation, given our interest in evaluating the components of these programs in detail. All individual studies and systematic reviews on interdisciplinary rehabilitation programs that met eligibility criteria were therefore sought across the entire literature search timeframe.

Major study eligibility criteria included:

- Minimum of 3 months of follow-up post-intervention
- English-language only
- Randomized controlled studies without active or sham placebo arm
- Effectiveness studies: ≥25 patients per study arm
- Retrospective cohort studies for harms: ≥50 study subjects

The electronic databases we searched as part of the systematic review included MEDLINE, EMBASE, and *The Cochrane Library* (including the Database of Abstracts of Reviews of Effects [DARE]) for health technology assessments (HTAs), systematic reviews, and primary studies. Reference lists of all eligible studies were also searched. The strategies used for MEDLINE, EMBASE, and *The Cochrane Library* are shown in Appendix A.

Studies were not further restricted by instrumentation, manufacturer, or treatment approach. Figure 1 on the following page shows a flow chart of the results of all searches for RCTs (n=28), systematic reviews (n=21), and observational studies (n=22).

Study Quality

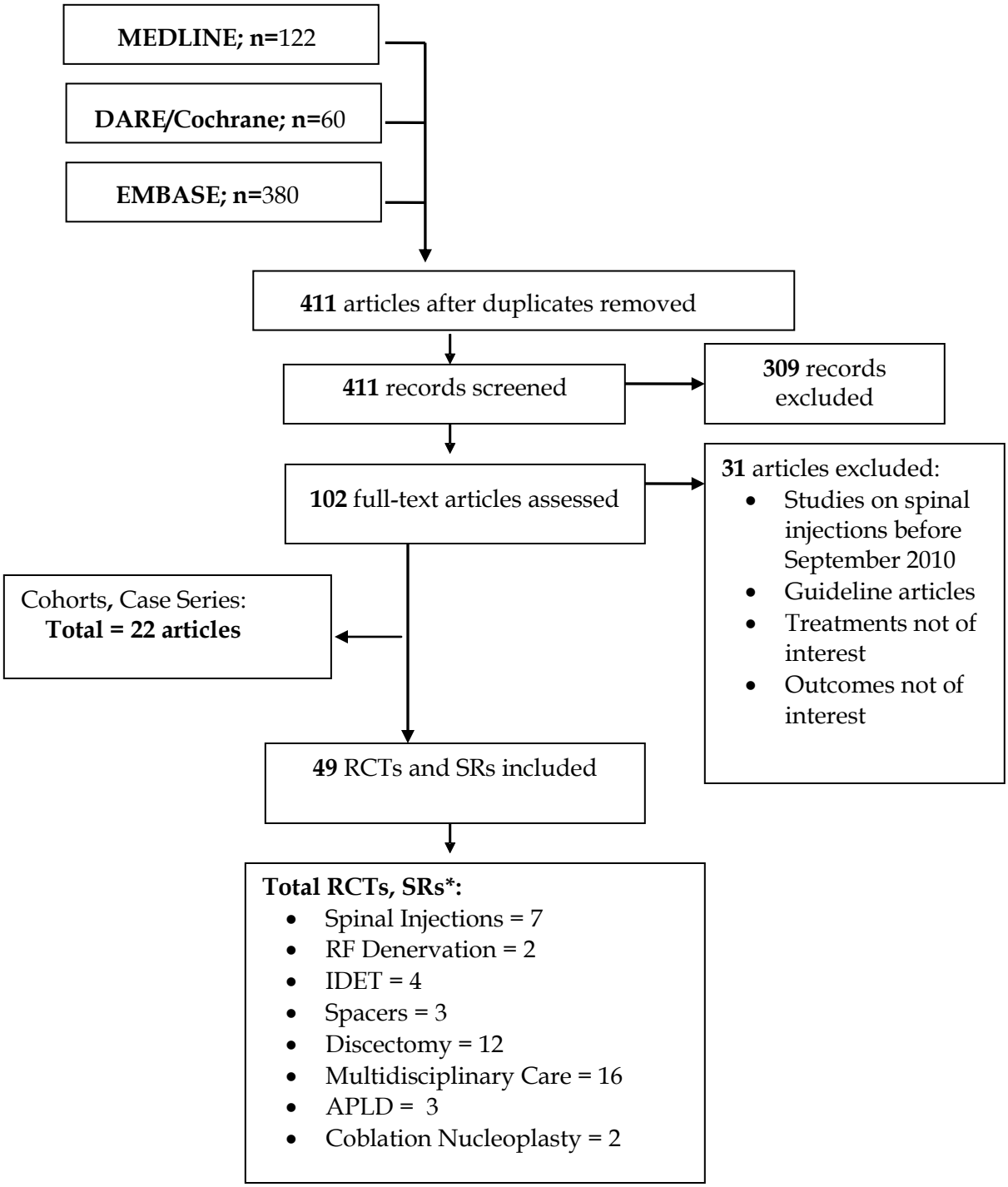
We used standardized criteria specific to previous systematic reviews in back pain to rate the quality of each included RCT or systematic review. These criteria, which related to issues in study design, reporting, and minimization of bias, are presented in Appendix B. RCTs meeting a majority of criteria (i.e., 6 of 10) were deemed to be "higher quality", as were systematic reviews with an overall global rating of 5 or higher. Finally, we used general criteria to assess the quality of observational studies, using the categories "good", "fair", or "poor". Our methods were based on the criteria employed by the U.S. Preventive Services Task Force (AHRQ, 2008), as described below:

- ***Good:*** Comparable groups (for comparative studies) are assembled initially and maintained throughout the study (follow-up of at least 80%); reliable and valid measurement instruments are used and applied equally to the groups; interventions are spelled out clearly; important outcomes are considered; and appropriate attention to confounders in analysis.

- ***Fair:*** Generally comparable groups are assembled initially but some question remains whether minor/moderate differences occurred in follow-up; measurement instruments are acceptable (although not the best) and generally applied equally; some but not all important outcomes are considered; and some but not all potential confounders are accounted for.

- ***Poor:*** Any of the following problems exist: (1) groups assembled initially are not close to being comparable or maintained throughout the study; (2) unreliable or invalid measurement instruments are used or not applied at all equally among groups (including not masking outcome assessment); and (3) key confounders are given little or no attention.

Figure 1. PRISMA flow chart showing results of literature search.



RF: Radiofrequency; IDET: Intradiscal electrothermal therapy; APLD: Automated percutaneous lumbar discectomy

Importantly, studies of any type that were considered "lower quality" were nevertheless abstracted and included in evidence tables. However, the focus of attention in the presentation of results was on higher-quality studies where available.

Data Synthesis

Due to the high degree of patient and study heterogeneity within and across interventions within a given population, no attempt was made to quantitatively synthesize treatment effects through meta-analysis or other techniques. For the same reason, meta-analysis was not performed in any of the key systematic reviews used as the foundation for this appraisal. Detailed evidence tables, which are presented in Appendix C of this document and summarized graphically and in text in this section, served as the basis for the review and interpretation of findings on effectiveness and harms.

Descriptive comparisons of comparative clinical effectiveness are also provided in summary tables for each patient population on the pages that follow. We followed the approach used by AHRQ in evaluating the overall strength of evidence for each management option (AHRQ, 2011), which considers the following domains in making summary judgments:

- *Risk of bias* (study design and quality)
- *Consistency* (narrow range of effect sizes, uniform direction of effect)
- *Directness* (direct comparisons of interventions, direct link of intervention to key health outcomes)
- *Precision* (degree of certainty around estimates of effectiveness and/or harm)

Other domains that were considered in evaluating strength of evidence included dose-response association for effect estimates, underestimation of effect size due to confounding, magnitude of effect size, and presence of publication bias.

Each management option is assessed in relation to its relevant comparator(s) based on considerations of (a) relative certainty provided by the strength of the body of evidence; and (b) the magnitude of the comparative net health benefit observed. This assessment is performed separately for each measure of interest (e.g., pain, function, return to work); it is therefore possible that different ratings would be given for different outcome measures. For example, a body of evidence with consistent findings of small comparative improvements in function but without any measurement of pain outcomes would be rated as "B: Incremental" for function and "I: Insufficient" for pain.

Importantly, level of certainty in these rating is directly tied to the amount and quality of available RCT evidence. Management options for which there were only one or no RCTs for a given population were automatically rated as "I: Insufficient" across all measures.

7.8 Results

Evidence Quality

Of the 71 studies newly-identified and abstracted, the most abundant data identified were for non-specific low back pain (37 studies; N=14,741), followed by lumbar disc herniation (27 studies; N=51,216), lumbar spinal stenosis (4 studies; N=2,851) and degenerative or isthmic spondylolisthesis (3 studies; N=1,836).

Study quality is presented in Table 1 below by population and study type. A total of 19 RCTs and 14 systematic reviews were identified as higher quality; the majority of these were in lumbar disc herniation and non-specific low back pain. Note that for the purposes of this table, observational studies rated as "good" or "fair" were deemed to be "higher-quality".

Table 1. Study quality, by population, type of study, and intervention (de novo abstraction only).

	Study Type		
	Systematic Reviews	Randomized Controlled Trials	Observational Studies
Lumbar Disc Herniation			
Higher	4	8	6
Lower	3	2	4
Lumbar Spinal Stenosis			
Higher	1	0	2
Lower	0	1	0
Degenerative/Isthmic Spondylolisthesis			
Higher	2	0	0
Lower	0	1	0
Non-specific Low Back Pain			
Higher	7	11	7
Lower	4	5	3

As noted previously, a significant degree of clinical heterogeneity has been observed in studies of patients with low back disorders. Even among studies of patients with a particular condition, such as lumbar disk herniation, comparisons across interventions within each patient population are problematic for multiple reasons. For one, there is a dearth of direct comparisons between the interventions of interest. More troubling is the variable nature of the comparator populations in these studies, making even indirect comparisons difficult if not impossible. As shown in Table 2 on the following page, the characteristics of patients randomized to "conservative" or "usual" nonoperative management differ substantially by patient population and intervention. Note that the

table is limited to the lumbar disk herniation and non-specific low back pain populations due to a paucity of identified studies of different interventions in the lumbar spinal stenosis and degenerative spondylolisthesis populations.

Table 2. Baseline characteristics of patients randomized to conservative or other nonoperative management, by patient population and intervention.

		Comparator			
Population/Intervention	Comparator	Mean Age [Yrs]	Mean % Female	Physical Function Mean ODI	Back Pain Mean VAS
Lumbar Disc Herniation					
Epidural Steroid Injections	Sham Placebo	45.2	58.6%	30.8	80.8
Discectomy	Conservative Care	42.0	33.6%	45.4	38.9
Non-Specific Low Back Pain					
IRP	Conservative Care	43.1	65.0%	49.6	57.5
IDET	Sham Placebo	40.1	34.8%	37.2	65.0
Spinal Fusion	Conservative Care	43.0	35.5%	45.1	64.7

IRP: Interdisciplinary Rehabilitation Program; IDET: Intradiscal Electrothermal Therapy; ODI: Oswestry Disability Index; VAS: Visual Analogue Scale

It should be further noted that, despite our intent to focus on studies evaluating patients presenting for treatment after attempts at short-term (4-6 weeks) conservative management, symptom duration was much longer at baseline in nearly all studies of interest. For example, mean symptom duration in RCTs of interventions for lumbar spinal stenosis, degenerative spondylolisthesis, and non-specific low back pain ranged from one to 5, one to 5, and 2 to 8 years respectively; in fact, a duration of symptoms of <6 months was a protocol *exclusion* in many of these studies. Only in lumbar disc herniation did the patient population approximate our initial target, as most patients had experienced symptoms for <6 months at study entry.

RCT data are very limited for many of the management options we sought to evaluate, including coblation nucleoplasty, IDET, RF denervation, automated percutaneous lumbar discectomy (APLD), and selected types of spinal injections. There are primarily case series data available on the outcomes of these interventions, limiting the direct and indirect comparisons with other LBD management options that can be made. In addition, the data that are available for these interventions are marked by variability in technical approach, lack of standardized timing and reporting of outcome measures, and a relatively brief duration of follow-up (3-6 months in most circumstances).

While RCT data as well as other comparative data were more widely available for surgical procedures and interdisciplinary rehabilitation, these data were not without limitations. As with minimally-invasive procedures, variability in technique, approach, and patient populations made it difficult to draw conclusions across studies. For example, fluoroscopic guidance was used in some RCTs of spinal injections, not used in others, and not reported in yet another set of studies. In addition, studies comparing surgery to nonoperative management were marked by varying degrees of crossover between treatment arms. This has in turn provoked a variety of reactions from the clinical community. Some feel that limited conclusions can be drawn regarding treatment effect in studies with relatively high crossover rates, as these threaten the internal validity of the study design and findings (Angevine, 2007). Others argue that allowing crossover between invasive and non-invasive management best represents reality when there is sufficient clinical equipoise and a reasonably well-educated patient population (Vaccaro, 2007). Finally, with the exception of a single trial comparing interdisciplinary rehabilitation (IRP) to spinal fusion, IRP trials involved some form of usual or single-discipline care as the comparator. However, the level of intensity of usual care varied substantially by study, from standard GP-directed care with no specific protocol to guideline-driven individualized exercise programs with specific treatment goals, which may in turn have influenced the potential treatment effect realized for IRP (see Section 7.9).

Training Standards and Relationship to Outcomes

The benefits and harms associated with all procedures vary to some extent according to the skills of the operator. This is certainly true for many of the treatment options for low back disorders. Unfortunately, the relative importance of training and experience on patient outcomes has been little studied. Moreover, whatever impact training and skill differences has on the outcomes reported in the published literature, it is likely that even broader variations are seen in general clinical practice.

There are few widely-accepted training standards for the specific procedures evaluated in this report, despite calls for such standards. For example, in a letter responding to a case report of paralysis following transforaminal epidural steroid injection, Raghavendra and Patel argue for standardized training and minimum levels of experience with these injections, given the number of variables that must be considered to ensure patient safety (e.g., number of injection attempts, needle type and gauge, injectate volume, needle positioning) (Raghavendra, 2005).

Studies examining the relation of procedure volume to outcome in low back disorders are relatively few in number, and have produced conflicting findings. A recent evaluation of data from the National Inpatient Sample indicated that hospitals and surgeons in the highest quartile of decompressive surgery volume had lower mortality and complication rates compared to those in the lowest quartile (Farjoodi, 2011). In an examination of Medicare inpatient data, Taylor and colleagues observed lower mortality rates at hospitals performing a high volume of back and neck procedures (Taylor, 1997). However, data from the Maine Lumbar Spine Study suggested that improvements in disability, patient satisfaction, and quality-of-life scores were statistically-significantly greater for patients

managed by surgeons located in the region of the state performing the *lowest* volume of surgical procedures for lumbar disc herniation and spinal stenosis (Keller, 1999).

Key Studies
Despite the variability in the quality of available data, several studies will be described here as "key" studies on the basis of their citation in multiple editorials and reviews. These studies are considered notable due to some combination of high quality study design, size and representativeness of patient population, and recent publication date. Summaries of their key findings are on the following pages.

Of note, the Spine Patient Outcomes Research Trial (SPORT) is highlighted in the sections that follow as having produced key evidence on interventions for multiple indications. While interpretations of the results of this trial have been somewhat controversial because of high observed rates of crossover, we felt that its large sample size, broadly representative patient population, the rigor of patient characterization and follow-up, and the presentation of data from both randomized and observational cohorts combined to make the results of this study particularly relevant and persuasive.

LUMBAR DISC HERNIATION

Discectomy: *Weinstein, the SPORT Trial (2006 and 2008):* This NIH-funded study involved a unique design in which a total of 501 patients (mean age: 42) with image-confirmed herniation were randomized to either surgical discectomy or nonoperative management, defined as a minimum of active physical therapy, education/counseling with home education instruction, and NSAIDs. A separate cohort of 743 patients who declined to be randomized but selected their own treatment were enrolled in an observational study following the same protocol. Crossover rates were high in the randomized cohort: 42% of patients randomized to surgery had not undergone the procedure at 2 years, while 43% of those randomized to nonoperative management had undergone surgery. Not surprisingly, those crossing over to surgery reported more pain and disability at baseline than those crossing over to nonoperative care.

Among patients in the randomized cohort, no statistically significant treatment effects were consistently observed for measures of pain, function, return to work, or patient satisfaction over up to 4 years of follow-up, as substantial improvement was noted for both patient groups. Some differences were noted in favor of surgery in function (as measured by the ODI), level of bothersomeness from sciatica, and satisfaction with symptoms at 3 months, but these differences were no longer present at later timepoints. However, in an "as-treated" analysis of the combined randomized and observational cohorts, statistically significant treatment effects in favor of surgery were noted for all clinical measures at 2 years of follow-up, all of which persisted at 4 years of follow-up. No benefit was observed for work status, however, suggesting that the effects of surgery on pain and function do not directly translate to a favorable impact on return-to-work. The authors theorize that,

without clear expectation-setting and articulated treatment goals related to employment, this link will remain tenuous at best (Weinstein, 2008).

Discectomy: *Peul (2007):* In this study, a multicenter RCT conducted in the Netherlands, a total of 283 patients (mean age: 43 years) with image-confirmed herniation were randomized to microdiscectomy or nonoperative care (GP-directed education, pain medication, and physical therapy as necessary) and followed for 1 year. Microdiscectomy was scheduled within 2 weeks of randomization; additionally, patients in the nonoperative group with persistent sciatica after 6 months were offered surgery. The early surgery protocol resulted in a low crossover rate, as 89% of patients randomized to surgery were operated on within 2 weeks. In contrast, nearly 40% of nonoperative care patients received surgery by 12 months of follow-up.

Study findings were reported on an intention-to-treat basis alone. As with the SPORT trial described above substantial improvement was noted in both groups. Statistically significant differences were observed in favor of surgery at 8 weeks for function (as measured by the RDQ), VAS scores for back and leg pain, SF-36 scores for bodily pain, and global patient perceptions of recovery as assessed by Likert scale. However, differences in these measures became nonsignificant in all cases, as early as week 26 of follow-up for some measures.

Discectomy: *Atlas (2005).* Data from this prospective observational study feature 10-year outcomes among 400 patients (imaging confirmation unknown) treated surgically or nonoperatively in community practices throughout Maine. Surgical patients reported more severe symptoms and worse functional status at baseline. By year 10 of follow-up, 25% of surgically-treated patients had received at least 1 additional surgical procedure, and a similar proportion of nonoperative patients had received surgery. Nevertheless, statistically-significant differences favoring surgery were noted in the proportion of patients reporting reduced or eliminated pain, improved function on the RDQ, and satisfaction with current status at 10 years, even after multivariate adjustment for differences between groups. However, as with the SPORT trial, no benefits were observed regarding work and/or disability status at any point during follow-up.

Epidural Steroid Injections: *Manchikanti (2010).* A recent RCT cited in the systematic review used as a foundation for this appraisal (Hashimoto, 2010) compared interlaminar epidural steroid injections to saline/local anesthetic injections in 120 patients who were followed for 12 months (imaging confirmation unknown). The proportion of patients achieving "treatment success", defined in this case as >50% improvement in pain on a 100-mm VAS, was statistically-significantly higher in favor of ESI at 6 months, but not at 12 months or earlier timepoints. In terms of changes in pain and function scores, no statistically significant differences between groups were noted at any timepoint for pain. Changes in ODI scores were significantly in favor of ESI at 12 months, but the proportion of patients with >50% improvement on ODI did not statistically differ.

Coblation Nucleoplasty: *Gerszten (2010).* The only published RCT of coblation nucleoplasty randomized a total of 90 patients with image-confirmed lumbar disc herniation to receive this procedure or up to 2 epidural steroid injections and followed patients for 6 months (a separate observational component tracked patients for an additional 18 months after the RCT ended). Patients receiving coblation nucleoplasty had statistically significantly reduced VAS leg pain, VAS back pain, and ODI scores at 6 months. Significant improvements were also noted in favor of nucleoplasty on the physical function, bodily pain, and social function component scores of the SF-36. Kaplan-Meier estimates of freedom from requirements for secondary procedures were also significantly in favor of nucleoplasty at 2 years (52% vs. 17% for ESI, p=.02).

Interdisciplinary Rehabilitation Programs: No key studies with specific data for this indication

LUMBAR SPINAL STENOSIS

Laminectomy/Fusion: *Weinstein, the SPORT Trial (2008)*: In this component of the SPORT trial, a total of 289 patients, mean age 66 years, were randomized to receive either surgery (laminectomy: 89%; spinal fusion: 11%) or nonoperative management as described previously. Another 365 patients were enrolled in the observational cohort. Crossover rates also were high in this population, as 33% of surgical patients had not undergone surgery by 2 years, and 43% of nonoperative patients received surgery by this timepoint. As in the LDH cohort, significant differences in favor of surgery for primary effect measures, in this case the SF-36 bodily pain and physical function scales as well as the ODI, were observed at early timepoints in the intention-to-treat population. However, at 2 years of follow-up, the only significant treatment effect that remained was SF-36 bodily pain. In the combined "as-treated" analysis, statistically significant treatment effects in favor of surgery were noted at all timepoints for primary measures.

Interspinous Spacers: *Zucherman (2004):* This was the first reported trial of the X STOP® (Medtronic, Inc.) interspinous process distraction system. A total of 200 patients were randomized to receive the X STOP implant or nonoperative management (defined as at least one epidural steroid injection plus NSAIDs, analgesics, and physical therapy as needed) and were followed for 2 years. Nine patients in the nonoperative group withdrew shortly after randomization. Patients in the X STOP group were significantly ($p<.05$) improved vs. nonoperative care at 1 and 2 years on both the bodily pain and physical function scales of the SF-36, as well as the symptom severity, physical function, and satisfaction scales of the Zurich Claudication Questionnaire (ZCQ). By 2 years, 6% of patients in the X STOP group required subsequent laminectomy vs. 22% in the nonoperative group ($p<.05$).

Epidural Steroid Injections: *Manchikanti (2008):* A recent RCT cited in the systematic review used as a basis for this appraisal (Hashimoto, 2010) randomized 61 patients to receive epidural steroid injections or saline/anesthetic injections; patients were followed for

12 months. At 3 months, no statistically-significant differences were observed in changes in numeric rating scale-based pain scores or function as measured by the ODI. In addition, no statistically-significant differences in opioid analgesic use were observed. Twelve-month data were excluded by this review because >20% of long-term results were carried forward from the 3-month timepoint.

RF Denervation: *Guerts (2003):* As described in systematic review of non-interventional therapies that served as the basis for this appraisal (Chou, 2009b), this was a higher-quality RCT of denervation of the dorsal root ganglions as compared to sham treatment in 83 patients with chronic lumbosacral radicular pain who were followed for 3 months. No statistically-significant differences in the proportion of patients achieving clinical success, quality of life as measured by the SF-36, or use of analgesics were observed. In fact, there was a statistical trend toward a higher percentage of patients in the *sham* group reporting >50% improvement in VAS-measured pain (42% vs. 21% for RF denervation, p=.051).

Interdisciplinary Rehabilitation Programs: No key studies with specific data for this indication

<u>DEGENERATIVE SPONDYLOLISTHESIS</u>

Laminectomy/Fusion: *Weinstein, the SPORT Trial (2007):* In the spondylolisthesis component of the SPORT trial, a total of 304 patients, mean age 66 years, were randomized to receive surgical intervention (spinal fusion: 94%; laminectomy: 6%) or nonoperative management as described previously; 303 additional patients were enrolled in the observational cohort. As in the other SPORT population, crossover rates were substantial. By year 2 of follow-up, 36% of those randomized to surgery had not undergone any surgical procedure, while 49% of patients in the nonoperative group had received surgery. Study findings also echoed those of other SPORT populations. In the intention-to-treat analysis of the randomized cohort, no statistically significant treatment effects were observed on the SF-36 bodily pain or physical function scales as well as the ODI. In the "as-treated" analysis of the combined randomized and observational cohorts, however, statistically significant differences were observed at all timepoints for all primary effect measures, as well as for bothersomeness indices relating to stenosis, leg pain, and back pain, as well as multiple satisfaction scales. Finally, over 3 times as many surgical patients rated their progress as significant at 2 years vs. those receiving nonoperative care (74% vs. 24%, p<.05).

Interspinous Spacers: *Anderson (2006)*: A later multicenter RCT of the X STOP interspinous spacer implant conducted in the US followed 75 patients (mean age: 70 years) for 2 years. Implant patients were compared to those receiving nonoperative care, defined as at least one epidural steroid injection plus NSAIDs, analgesics, and physical therapy as needed. Statistically significant treatment effects were observed in favor of the X STOP at all study timepoints in the ZCQ, patient satisfaction, and the SF-36 physical component summary score. No significant improvement in the mental summary score was noted for either

group. The rate of clinical success, defined as a >15 point improvement in the ZCQ, >2.5 point change in patient satisfaction, and no requirement for subsequent surgery, was significantly higher in the X STOP group (63% vs. 13% in the nonoperative group, p<.0001). This finding was driven primarily by ZCQ and patient satisfaction changes, as the rate of subsequent surgery did not differ by treatment group (12% in each).

Epidural Steroid Injections: No key studies with specific data for this indication

RF Denervation: No key studies with specific data for this indication

Interdisciplinary Rehabilitation Programs: No key studies with specific data for this indication

NON-SPECIFIC LOW BACK PAIN

Fusion/Interdisciplinary Rehabilitation: *Fairbank (2005):* This large multicenter RCT conducted in the UK was notable for its comparison of an interdisciplinary rehabilitation program (IRP) to surgical intervention. A total of 349 patients with chronic low back pain were randomized to receive surgery (spinal fusion or graf ligamentoplasty) or a mean of 75 hours (range: 60-110) of IRP, including daily muscle strengthening and aerobic exercise, cognitive behavioral therapy, and hydrotherapy. Over one-quarter of patients randomized to IRP had surgery by 2 years, but only 4% of those randomized to surgery crossed over to IRP. Both groups showed substantial improvement from baseline in all effect measures. A significant treatment effect in the change in ODI from baseline to year 2 was noted in favor of surgery (-4.1, 95% CI: -8.1, -0.1, p=.045). No significant treatment effects were noted for improvements on a shuttle walking test or any of the SF-36 subdomains or component summary scores. A separate multiple imputation analysis was conducted to carry forward values for patients who crossed over or were lost to follow-up; this did not materially affect any primary findings.

Fusion: *Fritzell, the Swedish Lumbar Spine Study (2001):* This Swedish RCT randomized a total of 294 patients to spinal fusion (noninstrumented posterolateral, instrumented posterolateral, or instrumented circumferential) or non-intensive physical therapy and followed them for up to 2 years. Crossover rates in either direction were relatively low (<10%). At 2 years of follow-up, significant differences in changes from baseline were noted in favor of surgery for VAS pain scores (-21.0 vs. -4.3 for non-intensive PT, p=.0002), ODI (-11.6 vs. -2.8, p=.015), and an overall rating of "better" or "much better" (63% vs. 29%, p<.0001). Findings from a later cost-effectiveness analysis indicated that fusion surgery, despite direct medical care costs twice those of control treatment, would likely be cost-effective from a societal perspective based on improvements in pain, function, and return to work (Fritzell, 2004).

Interdisciplinary Rehabilitation: *Dufour (2010).* This large RCT, conducted in Denmark, randomized a total of 286 patients to receive a 12-week, 85-hour interdisciplinary

rehabilitation program (consisting of aerobic and muscle strengthening exercise, light exercise and occupational therapy, and an educational intervention) or a 12-week personal training program consisting of 2 hours of exercise per week. Patients were followed for 2 years. A total of 39 patients did not start treatment or dropped out of the study (14%). Improvements on all measures were noted in both groups. At 2 years of follow-up, significant treatment effects favoring the IRP program were noted on the RDQ (mean [SD] change from baseline: -3.2 [6.4] vs. -1.4 [5.4] for control therapy, p=.003) and the physical function subdomain of the SF-36 (mean [SD] change from baseline: 11.2 [23.3] vs. 1.6 [20.4] for control therapy, p<.0001), but not for any other SF-36 subdomain or VAS-measured pain., ability to work, or patients' global perceptions of clinical improvement.

RF Denervation: *Leclaire (2001).* This RCT, conducted in Canada, randomized a total of 70 patients with low back pain of >3 months' duration and positive response to facet joint injections to receive RF denervation or a sham procedure. Patients were assessed for changes in pain and function at one and 3 months. At one month, a significant treatment effect favoring RF denervation was noted on the RDQ (TE: -6.2; 95% CI: -13.8, -1.3; p=.05); however, changes in ODI and VAS pain scores were not significant. At 3 months, no significant treatment effects were observed on any measure of pain or function.

Spinal Injections: *Lukkainen (2002).* This RCT, conducted in Finland, randomized 24 patients with low back pain of >3 months' duration to receive sacroiliac methylprednisolone plus lidocaine injections or lidocaine injections alone and were followed for one month. Pain intensity was measured on both a 100-point VAS and a 12-point pain index, which was completed by clinicians based on a variety of mobility tests. At one month, significant treatment effects favoring the methylprednisolone plus lidocaine injection were noted for both VAS pain (median change from baseline: -40 vs. -13 for control therapy, p=.046) and the pain index (median change from baseline: -3 vs. 0, p=.017).

IDET: *Pauza (2004).* This U.S.-based RCT compared IDET to sham treatment in 64 patients with positive discography findings who were followed for 6 months. Statistically-significant differences were observed in the mean change from baseline to 6 months on a 10-point VAS scale (2.4 vs. 1.1 for sham, p=.045) and the ODI (11 vs. 4, p=.05), but not on either the bodily pain or physical function subscales of the SF-36. In the 56 patients remaining in the study for full follow-up (the "per protocol" analysis), statistically significant differences also were noted on the proportions of patients with a VAS change >2.0 and reporting pain relief >75%. Interestingly, this RCT appears to have been conducted in a highly selected population, as only 64 of 1,360 patients initially considered to be eligible were randomized.

Clinical Benefits

Findings are organized by patient population and management option in the sections that follow. As noted before, while conservative care is mentioned as a management option of interest in all 4 populations, data were not systematically abstracted for conservative management approaches. References to conservative care are only in relation to the comparator arms of relevant RCTs and observational studies.

1. *Lumbar Disc Herniation*:

- **Conservative care**
- **Discectomy (all approaches)**
- **Coblation nucleoplasty**
- **Epidural Steroid Injections**
- **Interdisciplinary rehabilitation**

A table providing an overall summary of clinical benefit among the management options of focus for lumbar disc herniation can be found on the following page (Table 3). Detailed summaries for each management option and outcome of interest can be found in the pages following.

Discectomy (all approaches)

"Treatment Success"
Two RCTs of discectomy reported rates of "clinical success" or "clinically-important change". In the previously-described Peul trial (Peul, 2007), the likelihood of symptom recovery, defined as complete or near-complete disappearance of symptoms on a 7-point Likert scale, was significantly greater for surgery over the 1-year course of the trial (Hazard Ratio [HR]: 1.97; 95% CI: 1.7, 2.2). Median time to recovery, as shown in Figure 2 on page 117, was 4.0 weeks in the surgical group vs. 12.1 weeks among nonoperative patients ($p<.001$). However, the difference in the percentage of patients reporting complete or near-complete recovery declined at each timepoint, and was not materially different by month 12 (approximately 95% in both groups). A second RCT comparing full-endoscopic discectomy to microdiscectomy showed a similar rate of complete freedom from leg pain at 2 years (76.5% and 73%, respectively) (Ruetten, 2009). Finally, a lower-quality systematic review focused on APLD (Hirsch, 2009) describes the findings only of older RCTs (i.e., pre-2000) as negative for long-term pain relief.

Pain and Function
A total of 7 RCTs reported pain and/or functional outcomes of open or microdiscectomy; 4 of these compared surgery to nonoperative care, and 3 compared alternative approaches to discectomy. In studies comparing surgery to nonoperative care, findings were generally

Table 3. Comparative Clinical Effectiveness: *Lumbar Disc Herniation*

Comparison Set	Function	Pain	HRQoL	Return to Work	Responder %	Major Harms	Additional Procedures/ Reoperation
Discectomy vs. CC	≤12 mo: **B** >12 mo: **C**	≤12 mo: **B** >12 mo: **C**	≤12 mo: **B** >12 mo: **C**	≤12 mo: **C** >12 mo: **C**	>12 mo: **C**	0-4%	>12 mo: **C**
APLD vs. CC	**I**	**I**	**I**	**I**	**I**	0-4%	**I**
Coblation nucleoplasty vs. CC	**I**	**I**	**I**	**I**	**I**	**I**	**I**
ESI vs. other injections/CC	≤12 mo: **C** >12 mo: **C**	≤12 mo: **C** >12 mo: **C**	≤12 mo: **C** >12 mo: **C**	**I**	≤12 mo: **C** >12 mo: **C**	<1%	>12 mo: **C**
IRP vs. CC/surgery	**I**	**I**	**I**	**I**	**I**	<1%	**I**

Legend: Ratings of *Comparative* Clinical Effectiveness (vs. Comparator[s] of Interest)

A: "Superior": High certainty of moderate-to-large health benefit
B: "Incremental": High certainty of a small health benefit
C: "Comparable": High certainty of a comparable health benefit
D: "Inferior": High certainty of an inferior health benefit

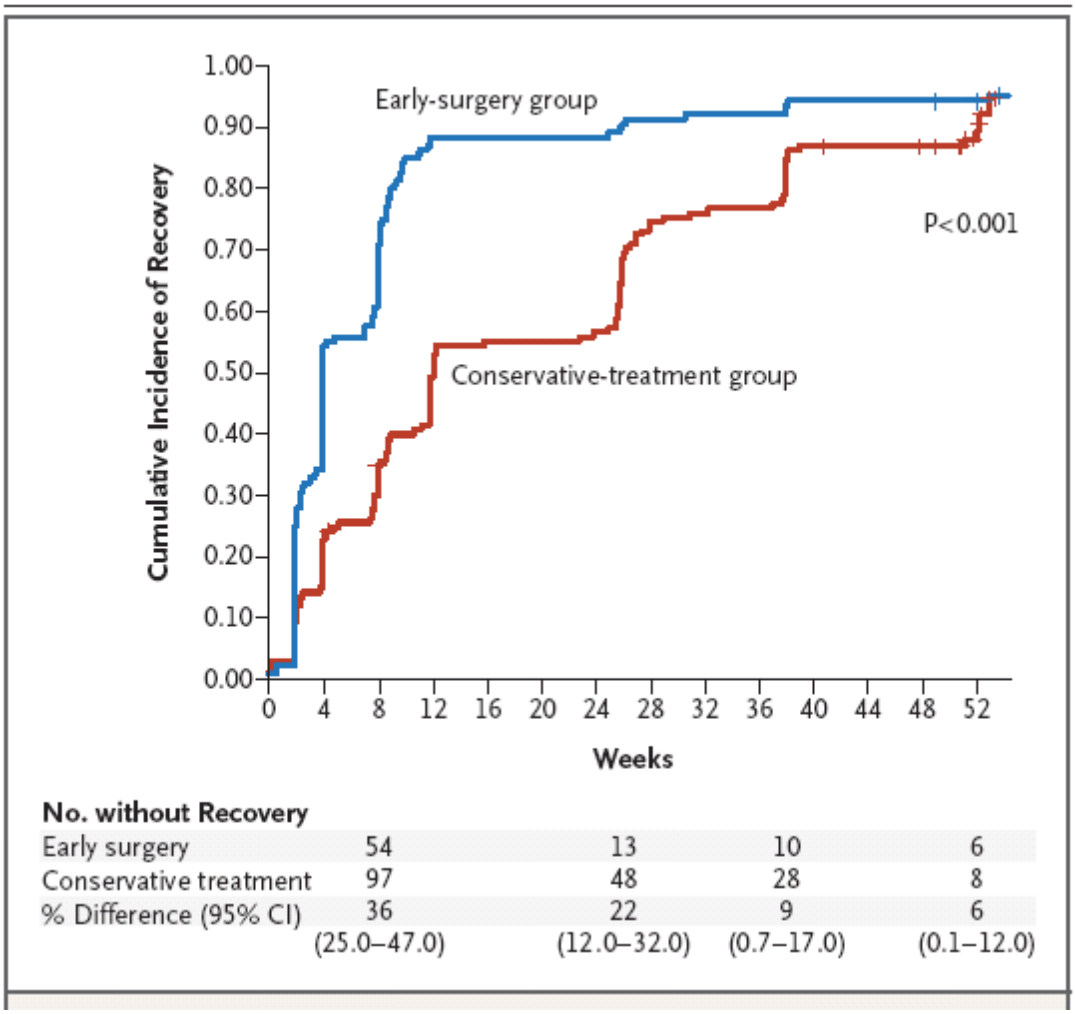
U/P: "Unproven with Potential": Moderate certainty of small or moderate-large health benefit:
*High certainty health benefit is at least comparable, OR
*Moderate certainty of small or moderate-large health benefit

I: "Insufficient": The available evidence does not provide high certainty that the health benefit is at least comparable to that provided by the comparator(s)

CC: Conservative care; APLD: Automated percutaneous lumbar discectomy; ESI: Epidural steroid injections; IRP: Interdisciplinary rehabilitation programs

consistent in favor of surgery up to month 6 of follow-up, but were not materially different at later timepoints. For example, intention-to-treat results from the SPORT trial indicated significant improvement on the ODI at 3 months (***Treatment Effect [TE]:*** -4.7; 95% CI: -9.3, -0.2), but no significant differences at 1 or 2 years of follow-up (Weinstein, 2006); this trend continued through 4-year follow-up (Weinstein, 2008). Level of bother from low back pain, assessed via a 6-point Likert scale, was only reported at 2 to 4 years of follow-up, and was not associated with significant treatment effects at any of these timepoints in the intention-to-treat population (Weinstein, 2008). In contrast, significant treatment effects favoring surgery for both the ODI and low back pain scale were noted at 2, 3, and 4 years of follow-up in the as-treated analysis of the combined randomized and observational cohorts.

Figure 2. Time to full symptom recovery for patients receiving early microdiscectomy vs. nonoperative care (n=283).



No. without Recovery				
Early surgery	54	13	10	6
Conservative treatment	97	48	28	8
% Difference (95% CI)	36 (25.0–47.0)	22 (12.0–32.0)	9 (0.7–17.0)	6 (0.1–12.0)

Source: Peul et al., N Engl J Med 2007;356:2245-56.

In a separate analysis of the SPORT as-treated population, stratified by whether patients were receiving worker's/disability compensation (Atlas, 2009), significant treatment effects

favoring surgery were seen in the ODI at 6 weeks regardless of compensation status. These benefits did not persist over time among patients receiving worker's compensation, however, while they remained significant in patients not on worker's compensation.

Other RCTs have echoed the findings seen in the SPORT intention-to-treat population. In the Peul RCT, significant treatment effects were observed in favor of surgery up to month 6 of follow-up for a VAS scale measuring leg pain, and up to week 8 for the RDQ and a VAS scale measuring back pain (Peul, 2007). All treatment effects were non-significant by month 12 of follow-up, however. In another small (n=58) RCT, no significant treatment effects were observed over 2 years of follow-up in the ODI or back/leg pain numeric rating scales (Osterman, 2006).

In the 3 available RCTs comparing alternative forms of discectomy, improvements in pain were noted in both arms of each study (Ruetten, 2009; Katayama, 2005; Teli, 2010). Significance testing was only performed on the change from baseline in one of these RCTs, and showed no significant differences over 2 years of follow-up (Teli, 2010). Similarly, improvements in function (as measured by the ODI) were observed in both arms of 2 of these RCTs (Ruetten, 2009; Teli, 2010); no significant differences in ODI changes over 2 years were noted in the Teli RCT, however. Finally, the systematic review on APLD does not report any discrete measures of pain or function in the one included RCT (Hirsch, 2009). Data from a recent observational study of APLD (n=55) described improvement on a 10-point VAS scale from a mean of 7.6 to a mean of 2.0 at 2 years, although this change was not statistically tested.

Long-term observational data on pain and function was available from a prospective, comparative cohort study comparing discectomy to nonsurgical management; patients were followed for up to 10 years (Atlas, 2005). Significant treatment effects regarding surgery were identified for low back and leg pain as well as a modified form of the RDQ ($p<.01$ in all cases), despite worse pain and function at baseline in these individuals.

Quality of Life

Data were available from 2 RCTs on the impact of discectomy on quality of life, the SPORT trial (Weinstein, 2006 and 2008) and the Peul RCT. As with the other outcome measures, quality of life improved substantially for both surgical and nonoperative patients. In the SPORT trial, a significant treatment effect favoring surgery on physical function was observed in the intention-to-treat population at 3 months (+2.8; 95% CI: +2.5, +8.1), but no similar effects were observed at one to 4 years of follow-up. There were no significant effects on bodily pain at any timepoint. In the "as-treated" analysis of the combined randomized and observational cohorts, significant treatment effects favoring surgery were observed at 2, 3, and 4 years for both SF-36 subdomains. In the analysis of the SPORT as-treated population stratified by worker's/disability compensation status (Atlas, 2009), changes in SF-36 bodily pain and physical function favoring surgery were noted only for non-compensation patients after 3 months of follow-up.

Similar patterns were observed in the Peul RCT; significant treatment effects were observed in favor of surgery for bodily pain (+8.4; 95% CI: +3.2, +13.5) and physical function (+9.3; 95% CI: +4.4, +14.2) at week 8 of follow-up, but all comparisons were nonsignificant thereafter. Improvements were also seen on the bodily pain and physical function subdomains in 2 case series of APLD (Peng, 2010) and microdiscectomy (Boskovic, 2010) respectively. In the former, scores steadily improved by 40-100% over 2 years of follow-up. In the latter, however, while three- to fourfold improvements were seen over 6 months of follow-up, no further improvement was observed when patients were evaluated again at 4 years.

Return to Work

RCT-based data on working status for discectomy studies were available only from the SPORT trial. Working status at baseline was 64.3% and 73.6% for the intention-to-treat and as-treated populations respectively. As described in the "Key Studies" section, in contrast to findings for pain, function, and quality of life, no significant treatment effects on working status were observed in either cohort at any timepoint, ranging from 3 months to 4 years of follow-up (Weinstein, 2006 and 2008). In the separate analysis of the as-treated population stratified by worker's compensation status (Atlas, 2009), no effect of surgery was observed in either the worker's compensation or noncompensation groups at any timepoint.

Findings from the previously-described cohort study reporting 10-year outcomes in patients receiving discectomy or conservative care showed similar proportions who were employed at baseline still working at year 10 (81% vs. 75% for surgical and nonsurgical care respectively, p=.43) (Atlas, 2005). As in the SPORT trial, the authors speculate that the relative impact of such factors as workplace accommodations, job characteristics, and local economic factors may have a greater influence on return-to-work measures than the effects of specific interventions.

Coblation Nucleoplasty

"Treatment Success"

Findings from the previously-mentioned Gerszten RCT indicated that significantly more nucleoplasty patients attained "literature-based" minimum clinically-important changes in VAS leg pain (≥25 points; 49% vs. 21%, p=.007) and VAS back pain (≥12 points; 49% vs. 22%, p=.017) during the randomized portion of the study; improvements remained significant through 2 years of observational follow-up. While the percentage of patients achieving a ≥13-point improvement of the ODI did not significantly differ at 6 months of follow-up, a higher percentage of nucleoplasty patients achieved this improvement during the observational period (30% vs. 10% at 2 years, p=.026).

In a separate, lower-quality systematic review identified in this appraisal (Manchikanti, 2009), a total of 5 coblation nucleoplasty series were identified that met study entry criteria (e.g., 50+ patients, follow-up 6+ months). Rates of pain relief ranged between 59-85% and 56-88% at 6 and 12 months of follow-up respectively, although this measure was variably

defined – representing patient satisfaction in some cases, changes in pain or function beyond a defined threshold in others, and discontinuation of analgesics in still other cases.

Pain and Function

As noted previously, findings from the Gerszten RCT indicated a statistically-significant difference in the magnitude of improvement on VAS leg pain (mean change: 47 vs. 21 at 6 months, p<.001), VAS back pain (21 vs. 0.4, p=.002), and ODI (14 vs. 4, p=.002) among patients receiving coblation nucleoplasty vs. epidural steroid injections (Gerszten, 2010).

Findings from the 5 above-described coblation nucleoplasty case series (Manchikanti, 2009) suggest substantial improvements in VAS or numeric rating scales over 6 to 12 months of follow-up, ranging from 50-60%. One of these series evaluated changes in the ODI, reporting a decrease from a mean of 42.2 at baseline to 24.8 at 6 months.

Quality of Life

The Gerszten RCT observed significantly (p<.05) greater improvement in the physical function, bodily pain, and social function subdomains of the SF-36 as well as the physical component summary score at 6 months among patients randomized to coblation nucleoplasty (Gerszten, 2010). No data on quality of life were reported in available systematic reviews and case series of coblation nucleoplasty.

Return to Work

No differences were noted between treatment groups in the percentage of patients working full- or part-time at 6 months in the above-described RCT (Gerszten, 2010). No data on return to work were reported in available systematic reviews and case series of coblation nucleoplasty.

Epidural Steroid Injections

"Treatment Success"

The Hashimoto systematic review (Hashimoto, 2010) included 2 RCTs with information on clinical improvement in addition to those previously summarized in the systematic review by Chou et al. (Chou, 2009b). Both RCTs involved fluoroscopic guidance. As in the Chou review, evidence on this outcome was mixed. One RCT comparing interlaminar epidural steroid injections to saline/local anesthetic injections found a statistically-significantly greater percentage of patients achieving pain relief >50% at 6 months (89% vs. 63%, p<.02), but no difference at 12 months or at earlier timepoints (Manchikanti, 2010). Findings from these and other studies conducted by this group should be interpreted with caution, however, as significant percentages of patients had data imputed at multiple timepoints because of missed assessments; in addition, the conclusions of many of these studies are described as positive because patients receiving both active and control therapy experienced improvement, despite the fact that no major differences between treatment groups were observed.

In the second RCT, comparing transforaminal epidural steroid injections to local anesthetic or saline injections, pain relief >50% was reported in 54% of patients at 1 month vs. 7-21% in the other control groups ($p<.05$) (Ghahreman, 2010). Pain relief was only measured at later timepoints for treatment failures.

Pain and Function

Combined data from the 2 spinal injection systematic reviews used as a basis for this appraisal (Chou, 2009b; Hashimoto, 2010) identify a total of 23 RCTs of epidural steroid injections that measured short-term (i.e., <3 months) pain and/or function in patients with lumbar disc herniation. Findings in favor of ESI were observed for pain in 8 of 23, no incremental benefit was observed in 10 of 23, and findings were unclear in the remaining 5. An identical breakdown of findings was seen in measures of function. Long-term benefits were measured in a total of 12 studies. Results favoring ESI were observed for pain in 1 of 12, no incremental benefit was observed in 9 of 12, and findings were unclear in the remaining 2. Similarly, functional improvement favoring ESI was observed in 2 of 12 studies, no incremental benefit was observed in 8 of 12, and findings were unclear in the remaining 2 studies. Neither short-term nor long-term findings appeared to be correlated with whether fluoroscopic guidance was used.

Quality of Life

Data on quality of life were not found in RCTs or observational studies of epidural steroid injections specifically for lumbar disc herniation.

Return to Work

Findings from the systematic review of spinal injections (Hashimoto, 2010) showed that employment status was tracked in 2 RCTs of fluoroscopically-guided epidural steroid injections over 12 months of follow-up (Manchikanti, 2008 and 2010). In both RCTs, the proportion employed full-time at 12 months was higher in the ESI group, but the rates of employment differed at baseline and no statistical testing was done on the change in employment during follow-up.

Interdisciplinary Rehabilitation

No RCTs or observational studies of interdisciplinary rehabilitation programs were identified with data on the effectiveness measures of interest in a specific population with lumbar disc herniation.

2. *Lumbar Spinal Stenosis*:

- **Conservative care**
- **Laminectomy with or without Spinal Fusion**
- **Spinal fusion**
- **Interspinous spacers**
- **Radiofrequency denervation**
- **Epidural steroid injections**
- **Interdisciplinary rehabilitation**

A table providing an overall summary of clinical benefit among the management options of focus for lumbar spinal stenosis can be found on the following page (Table 4). Detailed summaries for each outcome of interest are given on the following pages. While laminectomy studies were not a focus of our data abstraction, the major RCTs are nevertheless summarized.

Laminectomy with or without Spinal Fusion

"Treatment Success"

Among the major trials comparing laminectomy with or without spinal fusion to nonoperative care for patients with lumbar spinal stenosis, a global measure of treatment success was only available from the SPORT trial (Weinstein, 2008b). In this trial, approximately 90% of patients in both the randomized and observational cohorts received laminectomy alone. The proportion of patients recording "major improvement" in their condition was examined at each study timepoint. No significant treatment effects were observed in this measure at any timepoint in the intention-to-treat analysis. In the as-treated analysis of the combined cohorts, surgery was associated with a significantly greater likelihood of self-reported major improvement at all timepoints. The proportions reporting major improvement at 2 years were 62.9% and 28.7% for surgery and nonoperative care respectively (TE: 34.1%; 95% CI: 25.6%, 42.6%).

Pain and Function

RCT-based evidence on laminectomy and fusion comes from the SPORT trial (Weinstein, 2008b) as well as a smaller RCT conducted in Finland (Malmivaara, 2007). In the intention-to-treat analysis of the SPORT trial, no significant treatment effects on ODI were observed at any timepoint through the 2-year follow-up. However, significant treatment effects favoring surgery on ODI were seen at 2 years in the as-treated analysis of both the randomized cohort alone (TE: -8.7; 95% CI: -13.3, -4.0) and the combined randomized and observational cohorts (TE: -11.2; 95% CI: -14.1, -8.3).

Table 4. Comparative Clinical Effectiveness: *Lumbar Spinal Stenosis*

Comparison Set	Function	Pain	HRQoL	Return to Work	Responder %	Major Harms	Additional Procedures/ Reoperation
Laminectomy vs. CC	≤12 mo: **B** >12 mo: **B**	≤12 mo: **B** >12 mo: **B**	≤12 mo: **B** >12 mo: **B**	**I**	>12 mo: **C**	0-5%	**I**
Interspinous spacers vs. CC	**I**	**I**	**I**	**I**	**I**	0-6%	**I**
RF denervation vs. CC	**I**	**I**	**I**	**I**	**I**	**I**	**I**
ESI vs. other injections /CC	≤12 mo: **C** >12 mo: **C**	≤12 mo: **C** >12 mo: **C**	**I**	>12 mo: **C**	≤12 mo: **C** >12 mo: **C**	<1%	>12 mo: **C**
IRP vs. CC/surgery	**I**	**I**	**I**	**I**	**I**	<1%	**I**

Legend: Ratings of *Comparative* Clinical Effectiveness (vs. Comparator[s] of Interest)

A: "Superior": High certainty of moderate-to-large health benefit
B: "Incremental": High certainty of a small health benefit
C: "Comparable": High certainty of a comparable health benefit
D: "Inferior": High certainty of an inferior health benefit

U/P: "Unproven with Potential": Moderate certainty of small or moderate-large health benefit:
*High certainty health benefit is at least comparable, OR
*Moderate certainty of small or moderate-large health benefit

I: "Insufficient": The available evidence does not provide high certainty that the health benefit is at least comparable to that provided by the comparator(s)

CC: Conservative care; RF: Radiofrequency; ESI: Epidural steroid injections; IRP: Interdisciplinary rehabilitation program

In the Malmivaara RCT, a total of 94 patients were randomized to decompressive surgery (primarily laminectomy alone) or nonoperative care and followed for 2 years. Relatively low rates of crossover (4 of 50 surgical patients did not have surgery, while 4 of 44 nonoperative patients received surgery) were observed. In contrast to intention-to-treat findings from SPORT, significant treatment effects favoring surgery were observed at all timepoints on the ODI as well as on numeric scales measuring leg pain and low back pain during walking. Findings were similar in a separate on-treatment analysis.

Quality of Life

Data on the impact of decompressive surgery on quality of life were available from the SPORT trial (Weinstein, 2008b). In this population, the intention-to-treat analysis indicated no significant short-term effect of surgery on SF-36 bodily pain, but a significant effect favoring surgery at 2 years (TE: 7.8; 95% CI: 1.5, 14.1). No benefit was observed for SF-36 physical function at any timepoint in this analysis. In contrast, long-term benefits were observed favoring surgery on both of these domains in as-treated analyses of the randomized cohort alone and the randomized and observational cohorts combined.

Return to Work

Data on return to work were not found in available RCTs or observational studies of laminectomy and/or spinal fusion specifically for lumbar spinal stenosis.

Interspinous Spacers

"Treatment Success"

Findings from a lower-quality RCT of interspinous spacers vs. nonoperative care were based on the 3 components of the Zurich Claudication Questionnaire (Zucherman, 2004). Patients with statistically significant improvements on the physical function, symptom severity, and satisfaction with treatment were considered successes. Treatment success was rated at 59% vs. 12% for spacers and nonoperative care respectively at 1 year ($p<.05$); corresponding results at 2 years were 48% and 5% (significance not reported).

Pain and Function

The Zucherman RCT used the Zurich Claudication Questionnaire (ZCQ) to evaluate the impact of treatment on physical function and symptom severity (Zucherman, 2004). Significantly more patients were reported to be pain-free and have improved function in the spacer group at 6 weeks, 6 months, and 1 year of follow-up; these measures are difficult to compare to more widely-used indices, however, as the level of correlation between the ZCQ and other measures has not been extensively evaluated.

Quality of Life

The Zucherman RCT evaluated the impact of spacers vs. nonoperative care on all 8 subdomains of the SF-36. Significant differences favoring spacers were observed at 6 weeks, 6 months, and 1 year for all 8 subdomains (i.e., bodily pain, physical function, role physical, general health, vitality, social function, role emotional, and mental health).

Return to Work
Data on return to work were not found in RCTs or observational studies of interspinous spacers specifically for lumbar spinal stenosis.

Radiofrequency Denervation

No RCTs or observational studies of radiofrequency (RF) denervation were identified with data on the effectiveness measures of interest in a specific population with lumbar spinal stenosis.

Epidural Steroid Injections

"Treatment Success"
The Hashimoto systematic review (Hashimoto, 2010) included 1 RCT with information on clinical improvement in addition to those previously summarized in the previous systematic review by Chou et al. (Chou, 2009b). This RCT involved a comparison of fluoroscopically-guided caudal epidural steroid injections vs. saline/local anesthetic injections (Manchikanti, 2008). The percentage of patients achieving pain relief >50% did not significantly differ between groups at 3, 6, or 12 months, and was in fact numerically lower at each timepoint in the ESI group. However, as noted previously, results of this and other studies conducted by this group should be interpreted with caution.

Pain and Function
Combined data from the 2 spinal injection systematic reviews used as a basis for this appraisal (Chou, 2009b; Hashimoto, 2010) indicate a small number of RCTs (n=6) of epidural steroid injections that measured short-term (i.e., <3 months) pain and/or function in patients with lumbar spinal stenosis. No incremental benefit of ESI was observed in all 6 of these studies. Long-term benefits were measured in a total of 3 studies; again, no benefit for ESI on either pain or function was observed in any of these studies.

Quality of Life
Data on quality of life were recorded in a single RCT of epidural steroid injections for spinal stenosis (Koc, 2009), which involved comparison of ESI to both physical therapy and control injections. The Nottingham Health Profile (NHP) was used to measure quality of life. No significant between-group differences were noted on any domain of the NHP at 2 weeks, 1 month, 3 months, and 6 months of follow-up.

Return to Work
Data on working status were available for 2 RCTs of epidural steroid injections for patients with spinal stenosis. Unfortunately, in these RCTs (Manchikanti, 2008 and 2010), baseline data were carried forward for patients who did not respond to queries on working status at 12 months of follow-up. Regardless, 12-month working status did not significantly differ between ESI and control patients in either study.

Interdisciplinary Rehabilitation

No RCTs or observational studies of interdisciplinary rehabilitation programs were identified with data on the effectiveness measures of interest in a specific population with lumbar spinal stenosis.

3. *Degenerative Spondylolisthesis*:

- **Conservative care**
- **Spinal fusion**
- **Interspinous spacers**
- **Radiofrequency denervation**
- **Epidural steroid injections**
- **Interdisciplinary rehabilitation**

A table providing an overall summary of clinical benefit among the management options of focus for degenerative spondylolisthesis can be found on the following page (Table 5). Detailed summaries for each outcome of interest can be found on the following pages. Available evidence is extremely limited; for example, only 2 RCTs of spinal fusion and 1 RCT of interspinous spacers were identified specifically for this indication.

Spinal Fusion

"Treatment Success"

Among the major trials comparing spinal fusion to nonoperative care for patients with degenerative spondylolisthesis, a global measure of treatment success was only available from the SPORT trial (Weinstein, 2007). In this trial, approximately 95% of patients in both the randomized and observational cohorts received spinal fusion; 75% of these procedures were performed with instrumentation. The proportion of patients recording "major improvement" in their condition was examined at each study timepoint. Between-group differences were not reported for the intention-to-treat cohort. In the as-treated analysis of the combined cohorts, surgery was associated with a significantly greater likelihood of self-reported major improvement at 3 months, 1 year, and 2 years. The proportions reporting major improvement at 2 years were 74.1% and 24.1% for surgery and nonoperative care respectively (TE: 50.0%; 95% CI: 42.2%, 57.9%).

Table 5. Comparative Clinical Effectiveness: *Degenerative Spondylolisthesis*

Comparison Set	Function	Pain	HRQoL	Return to Work	Responder %	Major Harms	Additional Procedures/ Reoperation
Fusion vs. CC	≤12 mo: **B** >12 mo: **B**	≤12 mo: **B** >12 mo: **B**	≤12 mo: **B** >12 mo: **B**	**I**	>12 mo: **B**	0-5%	**I**
Interspinous spacers vs. CC	**I**	**I**	**I**	**I**	**I**	0-6%	**I**
RF denervation vs. CC	**I**	**I**	**I**	**I**	**I**	**I**	**I**
ESI vs. other injections/CC	**I**	**I**	**I**	**I**	**I**	<1%	**I**
IRP vs. CC/surgery	**I**	**I**	**I**	**I**	**I**	<1%	**I**

Legend: Ratings of *Comparative* Clinical Effectiveness (vs. Comparator[s] of Interest)

A: "Superior": High certainty of moderate-to-large health benefit
B: "Incremental": High certainty of a small health benefit
C: "Comparable": High certainty of a comparable health benefit
D: "Inferior": High certainty of an inferior health benefit

U/P: "Unproven with Potential": Moderate certainty of small or moderate-large health benefit:
*High certainty health benefit is at least comparable, OR
*Moderate certainty of small or moderate-large health benefit

I: "Insufficient": The available evidence does not provide high certainty that the health benefit is at least comparable to that provided by the comparator(s)

CC: Conservative care; RF: Radiofrequency; ESI: Epidural steroid injections; IRP: Interdisciplinary rehabilitation program

Pain and Function

RCT-based evidence on surgery comes from the SPORT trial (Weinstein, 2007) as well as a smaller RCT conducted in Finland (Malmivaara, 2007). While the latter RCT was conducted in a population with lumbar spinal stenosis, 42% of patients in the study were found to have "significant" spondylolisthesis (i.e., spondylolisthetic slips ≥3 mm) in a radiographic subgroup analysis.

In the intention-to-treat analysis of the SPORT trial, no significant treatment effects on ODI were observed at any timepoint through the 2-year follow-up. However, significant treatment effects favoring surgery on ODI were seen at 3 months, 1 year, and 2 years in the as-treated analysis of the combined randomized and observational cohorts (2-year TE: -16.7; 95% CI: -19.5, -13.9). In addition, significant treatment effects were observed in this analysis for two secondary outcomes, 6-point scales indicating levels of bothersomeness from leg pain (2-year TE: -1.5; 95% CI: -1.8, -1.1) and low back pain (2-year TE: -1.0; 95% CI: -1.3, -0.7).

Unfortunately, neither primary nor subgroup analyses in the Malmivaara RCT differentiated between spinal stenosis patients with and without spondylolisthesis. However, analyses of primary outcome measures were stratified by the type of surgery received. Significant treatment effects were noted for patients receiving fusion (the management approach for 90% of spondylolisthetic patients in this study), however. At 2 years, significant treatment effects in the intention-to-treat analysis of fused patients were noted for leg pain (TE: -2.4; 95% CI: -4.5, -0.3), but not for back pain or the ODI. In the on-treatment analysis, significant treatment effects were noted for all 3 measures.

Quality of Life

Data on the impact of decompressive surgery on quality of life were available from the SPORT trial (Weinstein, 2007). In this population, the intention-to-treat analysis indicated no significant treatment effects on bodily pain or physical function at any timepoint. In contrast, significant and stable treatment effects favoring surgery were noted across all time periods in the as-treated analysis of bodily pain (2-year TE: 18.1; 95% CI: 14.5, 21.7) and physical function (2-year TE: 18.3; 95% CI: 14.6, 21.9).

Return to Work

Data on return to work were not found in RCTs or observational studies of laminectomy and/or spinal fusion specifically for degenerative spondylolisthesis.

Interspinous Spacers

"Treatment Success"

Findings from a higher-quality RCT of interspinous spacers vs. nonoperative care were based on a 15-point or greater improvement in the combined physical function and symptom severity scores from the ZCQ, a final ZCQ-based satisfaction score <2.5 (lower scores indicate better satisfaction), and no requirements for further surgery (Anderson, 2006). Overall "treatment success" was observed in 63.4% of X-STOP patients vs. 12.9% of those randomized to nonoperative care ($p<.05$).

Pain and Function

In the previously-described RCT of interspinous spacers (Anderson, 2006), the ZCQ scores for physical function and symptom severity were combined. At 2 years, the combined score had improved significantly for patients in the X STOP group (mean [SD]: 50.40 [2.04] vs. 23.05 [3.14] at baseline and 2 years respectively, $p<.05$), while no significant change in this measure was observed in the nonoperative group.

Quality of Life

The Anderson RCT of interspinous spacers evaluated the impact of spacers vs. nonoperative care on the physical and mental component summary scores of the SF-36 (Anderson, 2006). A 10-point improvement in the physical component summary was noted in the X-STOP group (mean [SD]: 31.53 [1.68] vs. 41.19 [1.97] at baseline and 2 years respectively, $p<.05$), while no change was observed in the nonoperative group. In contrast, no significant change was observed on the mental component summary in either group; in addition, mean mental component summary scores were similar to norms obtained from healthy individuals.

Return to Work

Data on return to work were not found in RCTs or observational studies of interspinous spacers specifically for degenerative spondylolisthesis.

Radiofrequency Denervation

No RCTs or observational studies of RF denervation were identified with data on the effectiveness measures of interest in a specific population with degenerative spondylolisthesis.

Epidural Steroid Injections

No RCTs or observational studies of epidural steroid injections were identified with data on the effectiveness measures of interest in a specific population with degenerative spondylolisthesis.

Interdisciplinary Rehabilitation

No RCTs or observational studies of interdisciplinary rehabilitation programs were identified with data on the effectiveness measures of interest in a specific population with degenerative spondylolisthesis.

4. *Non-specific Low Back Pain*:

- **Conservative care**
- **Spinal fusion**
- **Intradiscal electrothermal therapy**
- **RF denervation**
- **Spinal injections**
- **Interdisciplinary rehabilitation**

A table providing an overall summary of clinical benefit among the management options of focus for non-specific low back pain can be found on the following page (Table 6). Detailed summaries for each outcome of interest can be found on the following pages.

Spinal Fusion

There have been 4 major RCTs published comparing spinal fusion to nonoperative care among patients with non-specific low back pain. Three of these studies compared fusion to interdisciplinary rehabilitation with a cognitive-behavioral component (Brox, 2003; Brox, 2006; Fairbank, 2005), while control therapy in the remaining RCT was at the discretion of the treating physician, and mainly involved non-intensive physical therapy (Fritzell, 2001). While patients undergoing spinal fusion had similar levels of improvement in pain and function over one to 2 years of follow-up across all 4 RCTs, statistically-significant treatment effects favoring fusion were only noted in the RCT comparing fusion to non-intensive physical therapy (Fritzell, 2001). Comparisons across these RCTs are further complicated by differences in study design, methods, and crossover rates (Mirza, 2007). These limitations, as well as a higher observed rate of major harms with fusion vs. nonoperative care, should be considered when reviewing the results presented in the sections that follow.

"Treatment Success"

Among the major trials of spinal fusion in patients with nonradicular low back pain, 2 RCTs comparing instrumented posterolateral fusion with interdisciplinary rehabilitation in Norway included a measure of "treatment success". These RCTs, which were conducted by the same group (Brox, 2003; Brox, 2006) defined this measure on the basis of patient ratings of "excellent", "good", or "fair" on the Global Back Disability Questionnaire. At 1 year, the percentage of patients recording success (Brox, 2003: 71% vs. 63%; Brox, 2006: 50% vs. 48%) did not statistically differ between groups. A third RCT, the Swedish Lumbar Spine Study (Fritzell, 2001), compared 3 forms of spinal fusion (noninstrumented posterolateral, instrumented posterolateral, or instrumented circumferential) to non-intensive physical therapy. Treatment success was defined based on patient ratings of their symptoms as "better" or "much better". At 2 years, a significant difference favoring surgery was observed (63% vs. 29% for nonsurgical therapy, $p<.0001$). It should be noted that the crossover rate was ≤10% in either arm in all 3 of these studies.

Table 6. Comparative Clinical Effectiveness: *Non-specific Low Back Pain*

Comparison Set	Function	Pain	HRQoL	Return to Work	Responder %	Major Harms	Additional Procedures/ Reoperation
Fusion vs. CC	≤12 mo: **C** >12 mo: **C**	≤12 mo: **C** >12 mo: **C**	≤12 mo: **C** >12 mo: **C**	>12 mo: **C**	>12 mo: **C**	0-5%	>12 mo: **C**
IDET vs. CC	≤12 mo: **U/P**	≤12 mo: **U/P**	≤12 mo: **U/P**	**I**	≤12 mo: **U/P**	<1%	**I**
RF denervation vs. CC	≤12 mo: **C** >12 mo: **I**	≤12 mo: **C** >12 mo: **I**	**I**	≤12 mo: **C**	≤12 mo: **C**	**I**	>12 mo: **C**
IRP vs. CC	≤12 mo: **C** >12 mo: **U/P**	≤12 mo: **C** >12 mo: **C**	≤12 mo: **U/P** >12 mo: **U/P**	>12 mo: **U/P**	≤12 mo: **U/P**	<1%	**I**
IRP vs. PT	≤12 mo: **C** >12 mo: **C**	≤12 mo: **C** >12 mo: **C**	≤12 mo: **C** >12 mo: **C**	>12 mo: **C**	≤12 mo: **C**	<1%	**I**
Spinal injections vs. CC/other injections							
ESI	≤12 mo: **C** >12 mo: **C**	≤12 mo: **C** >12 mo: **C**	**I**	≤12 mo: **C** >12 mo: **C**	≤12 mo: **C** >12 mo: **C**	<1%	>12 mo: **C**
SSI	**I**	**I**	**I**	**I**	**I**	<1%	**I**
ISI	≤12 mo: **C**	≤12 mo: **C**	**I**	**I**	**I**	<1%	**I**
BB	≤12 mo: **C** >12 mo: **C**	≤12 mo: **C** >12 mo: **C**	**I**	**I**	>12 mo: **C**	<1%	**I**

Legend: Ratings of *Comparative* Clinical Effectiveness (vs. Comparator[s] of Interest)

A: "Superior": High certainty of moderate-to-large health benefit
B: "Incremental": High certainty of a small health benefit
C: "Comparable": High certainty of a comparable health benefit
D: "Inferior": High certainty of an inferior health benefit

U/P: "Unproven with Potential": Moderate certainty of small or moderate-large health benefit:
*High certainty health benefit is at least comparable; OR
*Moderate certainty of small or moderate-large health benefit

I: "Insufficient": The available evidence does not provide high certainty that the health benefit is at least comparable to that provided by the comparator(s)

CC: Conservative care; IDET: Intradiscal electrothermal therapy; RF: Radiofrequency; ESI: Epidural steroid injections; SSI: Sacroiliac steroid injections; ISI: Intradiscal steroid injections: BB: Branch blocks; IRP: Interdisciplinary rehabilitation program; PT: Physical therapy

Pain and Function

RCT-based evidence on surgery comes from the 3 above-described RCTs in Norway and Sweden (Brox, 2003; Brox, 2006; Fritzell, 2001) as well as an RCT comparing fusion (85% of patients or graf ligamentoplasty (15%) to interdisciplinary rehabilitation in the UK (Fairbank, 2005). In the Norwegian RCTs, no significant treatment effects were observed for pain (as measured by a 100-point VAS scale) or the ODI at 1 year of follow-up. In the Swedish RCT, however, significant differences favoring surgery were noted in the mean change from baseline for both the 100-point VAS (-21.0 vs. -4.3 for physical therapy, p=.0002) and the ODI (-11.6 vs. -2.8, p=.015) (Fritzell, 2001). A significant difference in the ODI favoring surgery was also observed in the UK RCT of surgery and IRP (TE: -4.1; 95% CI: -8.1, -0.1; p=.045); no specific pain measure was employed in this study.

Quality of Life

Data on the impact of spinal fusion on quality of life were available only from the Fairbank RCT vs. IRP (Fairbank, 2005). No statistically significant differences were noted at 24 months for the SF-36 mental or physical component summary scores, nor were differences observed in any specific subdomain.

Return to Work

Data on the impact of spinal fusion on return to work come from the Brox and Fritzell studies. In the former, the percentage of employed individuals who returned to work was numerically higher in the IRP control group, but did not reach statistical significance. In contrast, the percentage of individuals in the Fritzell RCT not able to work at baseline due to back pain who returned to work was significantly higher in the spinal fusion group (39% vs. 23% for physical therapy, p=.049). The "net" rate of back to work (i.e., subtracting those who stopped working during follow-up) was also significantly higher in the surgery group (36% vs. 13% for physical therapy, p=.002).

Intradiscal Electrothermal Therapy (IDET)

"Treatment Success"

Successful clinical outcome was measured in a single RCT of IDET vs. sham placebo (Freeman, 2005), and was defined based on the combination of no neurologic deficit, an improvement of at least 7 points on the 75-point Low Back Outcome Score, and improvement of at least 1 standard deviation beyond the mean in the bodily pain and physical function scales of the SF-36. No patient in either study arm met all of these criteria; when criteria were evaluated individually, no statistically-significant differences between groups were observed.

Pain and Function

Evidence on pain and function is mixed in the 2 available RCTs of IDET. In the previously-mentioned Freeman RCT, the ODI score improved only slightly in the IDET group at 6 months, and no significant treatment effect was observed. In a second RCT of IDET vs. sham placebo (Pauza, 2004), positive findings at 6 months were observed on both the ODI (mean [SD] change from baseline -11 [11] vs. -4 [12] for sham, p=.05) and on a 10-point VAS scale for pain (mean [SD] change from baseline -2.4 [2.3] vs. 1.1 [2.6] for sham, p=.045).

Quality of Life
In the 2 available RCTs of IDET (Pauza, 2004; Freeman, 2005), no significant differences were observed between groups for changes in SF-36 physical or mental component summary scores or subdomain scores for bodily pain and physical function.

Return to Work
Neither of the 2 IDET RCTs measured return to work as a primary or secondary outcome. Findings from a prospective series of 53 worker's compensation patients receiving IDET suggested a significant increase in the percentage of patients working at some level (i.e., full duty, light duty, w/lifting restrictions) at 4.5 years of follow-up relative to baseline (47.2% vs. 5.3%, $p<.0001$).

RF Denervation

"Treatment Success"
A single RCT comparing RF denervation to sham placebo also included a measure of "treatment success", defined based on either (a) a reduction in the back VAS score of at least 50%, with no reduction in daily activities or rise in analgesic use; or (b) a reduction in the back VAS score of at least 25%, a rise in daily activity levels of at least 25%, and a reduction in analgesic use of at least 25%. No significant differences in this outcome were noted at 3 months; in addition, Kaplan-Meier analysis of time to treatment success suggested no differences in treatment success at any point up to 1 year after treatment. In a separate 10-year case series of RF denervation examining the proportion of patients with "good-to-excellent" pain relief (Gofeld, 2007), the percentages reporting this level of relief were 96%, 43%, and 2% for durations of 6 to 12 months, 12 to 24 months, and >24 months respectively.

Pain and Function
Evidence on RF denervation comes from the key systematic review on non-surgical interventional therapies (Chou, 2009b) as well as two additional higher-quality systematic reviews (Niemisto, 2010; Henschke, 2010). All of these reviews reached similar conclusions. For presumed lumbar facet joint pain, there was mixed evidence from 3 RCTs regarding a short-term (i.e., 4 weeks) benefit of RF denervation on VAS pain and ODI vs. sham placebo. No evidence of benefit was observed with longer-term follow-up. A single RCT of RF denervation was conducted in patients with presumed discogenic pain. No significant differences were observed for any outcome measure.

Quality of Life
Data on quality of life were not found in RCTs or observational studies of RF denervation focused on patients with non-specific low back pain.

Return to Work
Measures of return to work were available in a single RCT of RF denervation (Leclaire, 2001). In this study, 8 patients in each of the RF denervation and placebo groups were not

working at baseline; all patients in both groups returned to work by the end of the 3-month follow-up.

Spinal Injections

"Treatment Success"

Evidence on spinal injections was available for epidural steroid injections (ESI) and therapeutic branch blocks (BB). Two RCTs comparing fluoroscopically-guided ESI to local anesthetic injections defined "treatment success" based on ≥50% improvement on both a 10-point numeric rating scale for pain and the ODI (Manchikanti, 2008; Manchikanti, 2010). The number of weeks of "total relief" did not materially differ between treatment groups in either study at any timepoint up to 12 months after study initiation (statistical significance was not reported). Relief also was not impacted by the number of injections received (up to 4 were allowed). In another RCT of therapeutic medial branch blocks vs. local anesthetic injections (Manchikanti 2010b), separate analyses were conducted of improvement ≥50% on pain scores and ≥40% on the ODI. There were no material differences in these rates in either the short term (3 months) or long term (24 months); statistical significance was not reported. Again, studies conducted by this group should be interpreted with caution given the limitations previously described.

Pain and Function

Combined data from the 2 spinal injection systematic reviews used as a basis for this appraisal (Chou, 2009b; Hashimoto, 2010) indicate no evidence of benefit on pain or function in the short- or long-term for RCTs of epidural steroid injections (n=12), intradiscal steroid injections (n=7) or therapeutic medical branch blocks (n=5). A single RCT of sacroiliac steroid injections (Lukkainen, 2002) vs. local anesthetic injections indicated significant improvement on both a 100-point VAS scale (median change from baseline -40 vs. -13, p=.046) and a 12-point pain index (median change from baseline -3 vs. 0, p=.017).

Quality of Life

Data on quality of life were not found in RCTs or observational studies of spinal injections of any type focused on patients with non-specific low back pain.

Return to Work

Data on return to work were available from a single RCT of epidural steroid injections (Manchikanti, 2010). Rates of part-time employment, full-time employment, unemployment, and unemployment due to pain did not materially change in either group, and did not numerically differ between groups (although this was not tested statistically).

Interdisciplinary Rehabilitation

"Treatment Success"

Measures of "successful clinical outcome" were varied in studies of interdisciplinary rehabilitation programs (IRP). In one RCT defining success based on *any* improvement on the EQ-5D or RDQ at 6 months (Vollenbroek-Hutten, 2004), no significant differences were noted for either measure between IRP and the usual-care control arm. In another RCT measuring success in terms of patients' perceptions of their conditions as "improved", "unchanged", or "worsened" (Dufour, 2010), the percentage reporting improved outcome did not statistically differ between IRP patients and those in the individualized physical therapy control arm. Interestingly, although numeric differences in this measure were noted at later timepoints up to 2 years of follow-up, statistical testing was only done at 3 months. Finally, in a third RCT, "treatment success" was defined based on patient's perceptions of improved clinical status (van der Roer, 2008). While the rate of perceived improvement was numerically higher with IRP at 12 months vs. guideline-based physical therapy, these findings were not statistically significant.

Pain and Function

Function was evaluated in 8 of the 11 available RCTs of interdisciplinary rehabilitation programs including the Fairbank study described above. Function was measured by the RDQ in 6 RCTs and the ODI in 2. Significant treatment effects favoring IRP were observed in 2 RCTs. One was a comparison of IRP to usual care (Lambeek, 2010); effects on the RDQ were reported at 12 months (TE: -2.86; 95% CI: -4.9, -0.9, p=.01). The other RCT compared IRP to an intensive exercise program (Dufour, 2010); effects on the RDQ were reported at 24 months (mean [SD] change from baseline: 3.2 [6.4] vs. 1.4 [5.4] for control, p=.003). As mentioned above, the Fairbank RCT noted a significant treatment effect in favor of surgery vs. IRP at 24 months (Fairbank, 2005). No significant treatment effects on function were noted in the remaining 5 RCTs.

Pain was also evaluated in 8 of 11 RCTs of IRP, although this did not include the Fairbank RCT (which did not employ a separate pain measure beyond the SF-36 bodily pain measure). Nearly all of these studies used a 10- or 100-point VAS for pain measurement. No significant treatment effects on pain were observed in any of these RCTs over durations of follow-up ranging from 4 months to 2 years.

Two observational studies were available that documented the long-term effects of IRP on pain and function. In one study (Lee, 2003), large and statistically significant improvements from baseline were noted on a 10-point VAS (mean [SD] change: -3.2 [3.0], p=.001) and the RDQ (mean [SD] change: -6.6 [7.5], p=.001) at 4 years of follow-up. In the other study, however, changes from baseline in a 10-point VAS essentially plateaued at 5 months and remained constant through 2 years of follow-up (Bontoux, 2009).

Quality of Life

Measures of quality of life were reported in a total of 5 RCTs of interdisciplinary rehabilitation programs; 4 of these used various scores from the SF-36, and one used the EQ-5D. Significant findings favoring IRP were noted in 2 of these RCTs. In one, the

previously-described RCT of IRP and invidualized exercise (Dufour, 2010), a significant treatment effect was noted at all timepoints on the physical functioning subdomain (mean [SD] change from baseline: 11.2 [23.3] vs. 1.6 for control, p<.001) and the physical component summary score (mean [SD] change from baseline: 5.0 [8.2] vs. 1.7 [7.8] for control, p=.001). In the other, a comparison of a combined physical and cognitive-behavioral therapy program vs. usual care in Sweden (Jensen, 2005), a significant treatment effect was observed at 3 years on the SF-36 global score, but this effect was only noted in females following a post hoc subgroup analysis by sex (TE: 7.3; 95% CI: 0.6, 14.0, p<.05).

Return to Work

Surprisingly, despite the inclusion of workplace interventions in many IRP studies, only 6 of the 11 RCTs in our sample measured return to work as an outcome. Positive findings in favor of IRP were observed in 3 of the 6 RCTs. In one comparison of IRP to usual care (Lambeek, 2010), the median duration of sick leave in the year following randomization was significantly lower in the IRP group (88 vs. 208 days for usual care, p=.003). In a comparison of IRP to usual care in Sweden (Jensen, 2005), the likelihood of return to work, based on Cox proportional hazards regression, was significantly better in the IRP group vs. usual care (HR=1.9; 95% CI: 1.3, 3.5); however, this increased likelihood was only observed among female employees. Finally, in a multi-level comparison of a workplace intervention, a graded activity program, the combination of the two, and usual care in the Netherlands (Anema, 2007), the workplace intervention was associated with a lower number of days of sick leave (median 77 vs. 104 for usual care, p=.02) and an increased likelihood of return to work (HR: 1.7; 95% CI: 1.2, 2.3; p=.002). However, neither the graded activity program nor the combination of the two programs was associated with a significant return-to-work benefit. In the remaining RCTs, no significant differences in return-to-work measures were observed between groups.

7.9 Analysis of Interdisciplinary Rehabilitation Programs

Specific clinical benefits and harms of interdisciplinary rehabilitation programs (IRP) are described in other parts of Section 7. The purpose of this section is to characterize the programs that have been described in the literature and identify those program elements associated with the highest levels of effectiveness. Consistent with the criteria employed in other systematic reviews, IRP was defined based on the following minimum criteria:

- Physician direction of program
- Physical/exercise component
- At least *one* of the following components:
  - Psychological (e.g., CBT, individual counseling)
  - Social (e.g., social worker/case manager intervention)
  - Occupational (e.g., worksite assessment, vocational therapy)
  - Educational (e.g., anatomy, self-care)

IRP studies were abstracted regardless of whether program components were delivered by different disciplines or by individual therapists with multidisciplinary training.

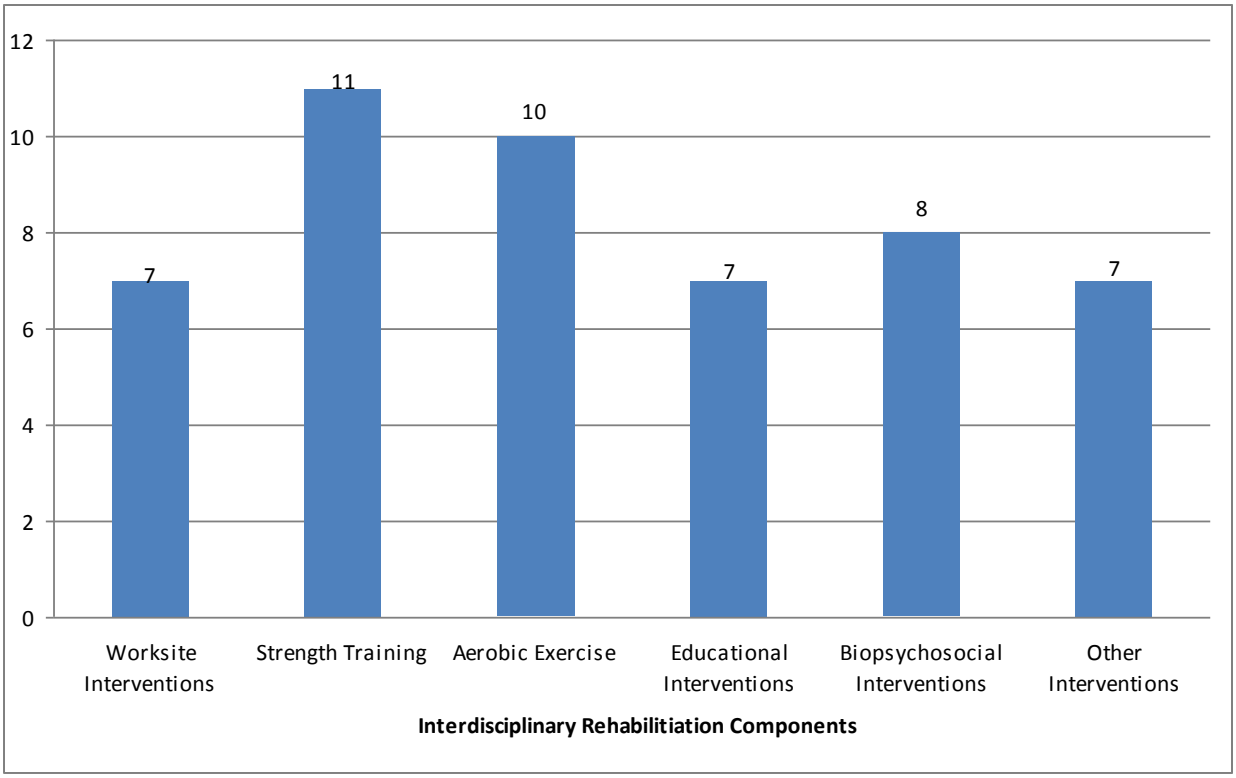
We identified a total of 11 RCTs published since 2000 that describe interdisciplinary programs, nearly all of which were conducted in European settings. Two additional RCTs were identified of multi-component rehabilitation (Fritz, 2005 and Friedrich, 2005), but these were not physician-directed. Components of the selected programs are presented in detail on Table 7 on page 151. Program intensity ranged widely, from 5 to 150 hours. As can be seen in Figure 3 on the following page, all programs had a muscle strengthening component, and nearly all involved aerobic exercise.

As is illustrated in Table 7, however, these components varied widely in their definition. For example, muscle strengthening was based on individualized goals in some cases, and involved defined exercises for spinal stability and mobility in others.

Biopsychosocial interventions also varied widely. In half of the programs reporting use of this type of intervention, individual counseling or unspecified relaxation techniques were reported. In the other studies, interventions focused on stress management, belief modification, and coping exercises or fear avoidance. When used, worksite interventions tended to be fairly intensive, involving ergonomic assessment (often including the patient), work skills training, and clinical observation. Educational interventions generally focused on back anatomy, function, and posture, and included details on treatment options in some circumstances. Other interventions included hydrotherapy, dietary consultation, medication, and telephone hotline support.

Another area of variation was the comparator treatment involved. In 4 of these RCTs, a physical therapy regimen was employed (Roche, 2007; Dufour, 2010; Kaapa, 2006; van der Roer, 2008) in another, the comparator was spine stabilization surgery (Fairbank, 2005). A "usual care" control arm involving no specific protocol was used in only 3 of these RCTs.

Figure 3. Components of abstracted interdisciplinary rehabilitation programs (n=11).



Comparisons to control therapy of varying intensity can be problematic in making determinations about the impact of interdisciplinary rehabilitation on measures of clinical effectiveness, as treatment effects may be less pronounced as control therapy becomes more intense.

Evidence is mixed on the effects of IRP vs. usual care. In one RCT, significant treatment effects in favor of IRP were observed in terms of function on the RDQ (Treatment Effect [TE]: -2.86 at 12 months; 95% CI: -4.9, -0.9, p=.01) and median number of days of sick leave over 12 months (82 vs. 175 for usual care, p=.003) (Lambeek, 2010). In another, no significant treatment effects on function, pain, or quality of life were observed (Vollenbroek-Hutten, 2004); in fact, only 30-50% of patients in the IRP group showed improvement on any effectiveness measure over 6 months of follow-up. In the third RCT, some improvement was noted on total sick leave days and SF-36 global health ratings, but only in the "per-protocol" analysis and was noted only for female patients (Jensen, 2005).

The potential reasons for these discrepant findings are not easily discernible. Of the 3 RCTs, 2 were conducted at different sites in the Netherlands (Vollenbroek-Hutten, 2004; Lambeek, 2010). As mentioned above, benefits were found for IRP in 1 of these studies but not the other. One possible explanation might involve working status at baseline. All of the patients in the positive Lambeek RCT were sick-listed at baseline, while working status was used only to balance groups during randomization in the Vollenbroek-Hutten RCT.

Table 7. Characteristics of randomized controlled trials of interdisciplinary rehabilitation programs

				Components						
First Author	Year	Comparator	Study Quality	Worksite Interventions	Strength Training	Aerobic Exercise	Educational Interventions	Biopsychosocial Interventions	Other Interventions	Program Intensity (Total Hours)
Fairbank	2005	Spinal stabilization surgery	7/10		Muscle stretching Spinal flexibility Gen'l strength Spine stability	Various cardiovascular endurance exercises		Fear avoidance Belief modification	Hydrotherapy	60-110
Roche	2007	Active physical therapy	7/10	OT work simulation	Muscle stretching Isotonic training Proprioception Balneotherapy Weight lifting	Jogging Walking Cycling Ball sports	Weekly clinic with physiatrist	Individual psychological counseling	Dietician consultation as needed	150
Vollenbroek-Hutten	2004	Usual care	6/10	Unspecified occupational therapy Occupational intervention as needed	Unspecified physical therapy	Unspecified conditioning Swimming		Psychological counseling as needed	Dietician consultation as needed	63
Jensen	2005	Usual care	6/10	Rehabilitation planning	Individual goal-oriented exercises	Cycling Pool training	Ergonomics Medical/psych aspects of pain	Activity planning Goal setting Applied relaxation Cognitive coping		136
Anema	2007	Education/coping training GP consult	6/10	Patient/clinician assessment Ergonomic review Clinical observation	Individual goal-oriented exercises	Individual goal-oriented exercises				26

Table 7. Characteristics of randomized controlled trials of interdisciplinary rehabilitation programs (cont'd)

				Components						
First Author	Year	Comparator	Study Quality	Worksite Interventions	Strength Training	Aerobic Exercise	Educational Interventions	Biopsychosocial Interventions	Other Interventions	Program Intensity (Total Hours)
Ribeiro	2008	Weekly MD visits Acetaminophen	6/10		Unspecified abdominal and back exercises		Anatomy Ergonomics	Unspecified relaxation exercises	Acetaminophen	5
Dufour	2010	Intensive muscle training	6/10		Unspecified abdominal and back exercises	Ball sports Ball stick training	Anatomy Posture Pain mgmt		Hydrotherapy	85
Lambeek	2010	Usual care	6/10	Patient/clinician assessment Ergonomic review Clinical observation	Individual goal-oriented exercises	Individual goal-oriented exercises				26
Ewert	2009	General physical exercise	5/10	Ergonomic analysis/advice Posture/lifting training	Segmental stabilization General strength/ stretching	Low-impact aerobics Goal: HR 130	Anatomy Back function	Belief modification Stress mgmt Communication skills	Telephone hotline support	32
van der Roer	2008	Guideline-based physical therapy	5/10		Unspecified operant-conditioning exercises	Unspecified operant-conditioning exercises	Unspecified operant-conditioning exercises	Unspecified operant-conditioning exercises	Start/end goal evaluation	30
Kaapa	2006	Passive/active physical therapy	5/10	Ergonomic adjustments Video task review	Muscle strengthening Spinal mobility Balance	Cycling Step aerobics	Anatomy Back function Treatment options	Stress mgmt Applied relaxation Belief modification		70

GP: General practitioner; HR: Heart rate

However, RDQ-assessed functional status was worse in the latter RCT; as noted in many studies previously, work status may not be an adequate proxy for symptom severity or the likelihood of treatment success.

Findings from those RCTs comparing IRP to some form of physical therapy were relatively consistent, in that no significant treatment effects favoring IRP were observed for any primary outcome measure. In all of these cases, substantial improvements in pain, disability, and function were observed in both treatment groups. In one RCT, IRP was associated with improved measures of endurance, anxiety, and depression relative to control therapy, but not for measures of pain intensity, daily activities, or work/leisure activities (Roche, 2007). In another, IRP was associated with improvements in function on the RDQ and physical function on the SF-36, but not in measures of pain or work ability (Dufour, 2010). A fifth RCT comparing IRP to a general physical exercise program also showed no material differences between groups in any measure of pain or quality of life (Ewert, 2009).

The remaining RCTs involved multiple types of comparisons. In the large RCT comparing IRP and spine stabilization surgery, a significant treatment effect favoring surgery was found on the ODI at 2 years (TE: -4.1; 95% CI: -8.1, -0.1, p=.045), but not on any other measure of pain, quality of life, or walking ability (Fairbank, 2005). In a comparison of a workplace intervention, a graded activity physical therapy regimen, and a combination program, the workplace intervention alone was associated with a significant increase in the likelihood of return to work (Hazard Ratio [HR}: 1.7; 95% CI=1.2, 2.3; p=.02), and no interventions had a significant impact on measures of pain or function (Anema, 2007). Finally, a comparison of an interdisciplinary "back school" program to a regimen of weekly physician visits indicated a significant treatment effect favoring the IRP program on the SF-36 general health domain at 4 months (p=.018), as well as a significant reduction in the percentage of patients receiving anti-inflammatory medication (11.5% vs. 34.5% at 4 months, p=.046) (Ribiero, 2008). However, no significant differences in pain, function, anxiety, or depression were observed.

The components of effective IRP programs that showed some level of effectiveness vs. usual or non-intensive care (i.e., 4 of the 6 studies not comparing IRP to PT or structured exercise) are summarized in Table 8 on the following page. Worksite interventions and aerobic exercises were employed in 3 of the 4 studies, and strength training was a component of all 4 studies. Educational, biospychosocial, and other types of interventions were less frequently employed.

A number of systematic reviews of IRP have also been published in this timeframe, focusing on studies published in the late 1980s and 1990s (Tveito, 2004; van Geen, 2007; Ravenek, 2010), and including 2 Cochrane reviews conducted using the methods recommended by the Cochrane Back Review Group (Guzman, 2001, 2006; Karjalainen, 2008). As with the individual studies described above, these systematic reviews are marked by heterogeneity in the studies examined, interpretation of the evidence, and determination of the IRP components associated with benefit. These reviews focused attention on studies

Table 8. Components of interdisciplinary rehabilitation programs showing some effectiveness vs. usual or non-intensive care.

Study	Worksite Interventions	Strength Training	Aerobic Exercise	Educational Interventions	Biopsychosocial Interventions	Other Interventions
Anema 2007	●	●	●			
Jensen 2005	●	●	●	●	●	
Lambeek 2010	●	●	●			
Ribiero 2008		●		●	●	●

Note: use of acetaminophen (at prescribed doses) allowed in Ribiero 2008

of IRP in working-age adults, but most did not find that IRP increased rates of return to work, even in those reviews that featured studies with workplace interventions (Tveito, 2004; Ravenek, 2010). One review found that intensive IRP (>100 hours) was associated with clinically-important improvement in function (Guzman, 2001, 2006), while others did not find an association between program intensity and clinical benefit (van Geen, 2007; Ravenek, 2010). Nevertheless, despite differences in methods, included studies, and conclusions, all of these reviews concluded that there was at least moderate evidence that IRP conferred some level of incremental benefit over usual care in at least one of the domains of interest in this appraisal (i.e., pain, function, patient satisfaction, or return to work).

Conclusion

As described above, the literature on interdisciplinary rehabilitation programs, stretching over 2 decades, is marked by significant heterogeneity in study populations, program content, intensity, setting, and comparators, and is not generally of high quality. Despite this variability, most studies of IRP show modest incremental benefit over usual care in at least one domain (e.g., pain, function, return to work). However, the specific components of IRP associated with the greatest level of benefit remain unclear, as does whether IRP offers any benefit over a well-designed active physical therapy and exercise regimen. Finally, further research is necessary to determine the specific types of patients who would be most likely to respond to IRP.

Potential Harms

The management options evaluated in this appraisal are associated with a number of different harms, some of which are common to multiple interventions and others of which are unique to particular strategies. Relevant harms, as well as the range of reported rates in the set of studies evaluated for this appraisal, are listed for each intervention in Table 9 on page 158. Note that the relative rates of repeat procedures and need for subsequent treatment are also presented; while not technically patient harms, they nevertheless represent the potential for additional clinical risks and inconvenience, and are outcomes that play an important role in patient- and clinician decision-making.

Data on harms are presented for all management options, including non-invasive interventions. While reported complications were rare in these populations, data do exist on requirements for subsequent treatment. For both minimally-invasive as well as surgical procedures, we have categorized complications as major vs. minor: major complications were considered to be those that required a major procedure or intervention to correct (e.g., nerve root injury, major hemorrhage), while minor complications represented those that required a minor procedure or intervention (e.g., dural tear, superficial wound infection) or resolved on their own.

Good evidence on the true rates of serious harms is not available from published RCTs of treatments for low back disorders. Individual studies are too small to capture reliable data on complications that occur infrequently, and the relatively low rate of serious complications has led to standards for research reporting that often do not include formal reports on all complications. Other contributing factors to the dearth of data on complications include the general exclusion of high-risk patients from many RCTs, possible publication bias that disfavors reports of unsuccessful outcomes, and the short-term nature of most studies, which can fail to detect adverse outcomes associated with surgical interventions that do not manifest until later years (Chou, 2005).

Information from the observational studies examined in this review suggests that risks of minimally-invasive and surgical interventions may be higher than reported in RCTs. For example, no cases of peri-operative mortality were reported in any surgical RCT examined for this appraisal; in contrast, rates of in-hospital and 30-day mortality from observational studies, while <1%, were certainly nonzero (Deyo, 1992; Deyo, 2010). Also, a significant percentage of RCTs of epidural steroid injections report very low complication rates or do not mention harms at all (Chou, 2009). While data are not directly comparable, information from analyses of closed malpractice claims indicate that epidural steroid injections are associated with 40% of all claims for chronic pain management, and that in two-thirds of cases, injury was not apparent until after discharge from the treatment facility (Fitzgibbon, 2004).

Information on harms is presented separately for each management option in the sections that follow. Note that, unlike findings for clinical effectiveness, harms are not presented separately for each patient population, as these data are not typically stratified by indication for interventions that are used for multiple indications.

Conservative Care

Information on harms for conservative care has been gleaned from the comparator arms of the RCTs and observational studies evaluated for this appraisal. No attempt has been made to systematically evaluate potential harms (e.g., medication side effects) from studies focused specifically on conservative management modalities.

Conservative treatment in these studies was typically not subject to a specific protocol, and may have included medications, physical or exercise therapy, and alternative treatments (e.g., acupuncture, massage). This construct does not include the multi-modal care inherent in interdisciplinary rehabilitation programs, which are summarized in a separate section. In addition, the comparator arms of most studies of spinal injections or minimally-invasive procedures were not considered equivalent to conservative care, as they typically involved some form of active treatment or sham procedure.

30-day Mortality
No cases of mortality attributable to conservative or non-operative care have been reported in any systematic review, RCT, or observational study in our sample.

Complications
There were no reported complications of conservative or non-operative care in any RCT or comparative observational study available in our sample.

Subsequent Treatment
Data on the rates of subsequent surgery among patient randomized to conservative care in RCTs of discectomy, laminectomy, spinal fusion, interspinous spacers, and interdisciplinary rehabilitation vary widely (range: 9-50%), and are influenced by patient population and study protocol.

Rates of subsequent surgery among patients initially receiving conservative care varied widely in available RCTs, and were heavily influenced by patient population and study protocol. In the SPORT trials of surgery vs. non-operative care for lumbar disc herniation, lumbar spinal stenosis, and degenerative spondylolisthesis (Weinstein, 2006; Weinstein, 2007; Weinstein, 2008), a uniform protocol was employed in all populations. Not surprisingly, rates of subsequent surgery were similar across populations, ranging from 40-50% at 2 years. Findings from the Peul study of early microdiscectomy for lumbar disc herniation yielded a similar rate at one year of follow-up (39%) (Peul, 2007). Lower rates of subsequent surgery (9-10%) were reported in the Finnish RCT of laminectomy or fusion for lumbar spinal stenosis (Malmivaara, 2007) as well as the Swedish RCT of fusion for nonspecific low back pain (Fritzell, 2001). No obvious reason for the lower rates was discernible upon examination of study entry criteria or baseline characteristics, although subsequent surgery in the Fritzell study was employed as a result of "exacerbation of symptoms", which may have represented a clinical decision as opposed to patient preference.

Table 9. Reported ranges of harms in randomized controlled trials and observational studies, by management option.

Intervention	30-day Mortality	Major Complications	Minor Complications	Subsequent Treatment
Conservative Care	NR	NR	NR	Surgery: 9-50%
Interdisciplinary Rehabilitation	NR	NR	<1%	Surgery: 1-28%
Spinal Injections	NR	<1%	2-16%	# Injections: 2-4* Surgery: 14-36%
Coblation Nucleoplasty	NR	NR	11%†	Surgery: 4-27%†
Radiofrequency Denervation	NR	NR	4-14%	Repeat: 15.8%‡ Surgery: 11.9%**
Intradiscal Electrothermal Therapy	NR	<1%	1-10%	Surgery: 2-6%
Interspinous Spacers	NR	0-6%	3-6%	Surgery: 6-12%
Discectomy	<0.1%	0-4%	2-21%	Surgery: 3-25%
Laminectomy and Fusion	<1%	0-5%	10-16%	Surgery: 2-11%

NOTE: "NR" used to indicate no reported events for intervention across body of evidence
*"# Injections" refers to average number of spinal injections per year; "Surgery" refers to need for subsequent surgery following injection(s)
† Data from one RCT and one observational study assessing minor harms and secondary procedures following nucleoplasty
‡Data from single observational study assessing repeat denervation procedures
**Data from a single observational study assessing long-term outcome following RF denervation

In the available RCTs of interspinous spacers, requirements for subsequent laminectomy were tracked in both treatment arms. A higher rate of subsequent laminectomy was reported among patients randomized to conservative care (22% vs. 6% for X-STOP) in an RCT focused on lumbar spinal stenosis (Zucherman, 2004), although this difference was not statistically tested. The rate of subsequent laminectomy in another RCT involving patients with degenerative spondylolisthesis was 12% in both groups (Anderson, 2006).

Finally, a rate of subsequent treatment was reported in 1 RCT comparing IRP to conservative care in nonspecific low back pain (Lambeek, 2010). The rate was based on a composite endpoint of surgery or any inpatient stay during the 12-month follow-up. Rates were 12% and 5% for conservative care and IRP, respectively, and were not tested statistically.

Interdisciplinary Rehabilitation Programs

30-day Mortality
No cases of mortality attributable to interdisciplinary rehabilitation programs have been reported in any systematic review, RCT, or observational study in our sample.

Major Complications
No major complications attributable to interdisciplinary rehabilitation programs have been reported in any systematic review, RCT, or observational study in our sample.

Minor Complications
Data on complications were obtainable from a single RCT, in which a single minor complication was reported among 129 patients (<1%).

In an RCT comparing IRP to a 12-week personal training program (Dufour, 2010), a minor concussion was reported in 1 patient randomized to the IRP group (<1%).

Subsequent Treatment
Rates of subsequent treatment were infrequently reported in IRP studies, appearing in only 3 RCTs involving patients with nonspecific low back pain. These rates also varied substantially (1-28%), and were heavily influenced by study design and comparator.

In the only IRP RCT with surgery as a comparator (Fairbank, 2005), among 173 patients randomized to IRP, 48 (28%) received spinal fusion by 2 years of follow-up. In another RCT comparing IRP to an individualized exercise program, a single patient in the IRP group (<1%) sought surgery for a herniated disc. Mention was made in this study of surgery requirements as one of the reasons for study dropout; however, only the overall dropout rate was reported (27% for IRP vs. 29% for personal training, significance not tested). In addition, the rate of subsequent care (inpatient visit or surgery) in the above-described Lambeek RCT was 5% in the IRP arm; this rate was lower than the 12% rate seen in the conservative care arm of the study (not tested for statistical significance).

Spinal Injections

30-day Mortality

No cases of mortality attributable to spinal injections of any type have been reported in any systematic review, RCT, or observational study in our sample.

Major Complications

The incidence of major complications of spinal injections is considered to be rare, but complication rates are inadequately reported in many injection studies. The best estimates available suggest that the rate of major complications is <1%.

Combined results from the systematic reviews used as a basis for this appraisal (Chou, 2009b; Hashimoto, 2010) suggest that the rate of major complications is extremely rare, but also suboptimally reported in RCTs. For example, 10 of the 20 RCTs used by Chou in evaluating epidural steroid injections did not report any data on harms at all. In more recent data evaluated by Hashimoto, a total of 3 major complications (dural puncture, subarachnoid puncture, and angina pectoris) were noted among 1,406 injections (0.2%) in available RCTs. Rates from over 10,000 injections included in observational studies were lower (0.01%).

Minor Complications

A more frequent rate of minor complications of spinal injections, including site reactions, numbness, minor bleeding, headache, and vasovagal reactions, has been reported in RCTs and observational studies, but the issue of reporting bias remains. The best available data suggest a rate of reported minor complications in RCTs of approximately 2%. Reported rates in observational studies ranged from 3-16%.

As noted above, the Chou review highlighted the reporting bias associated with both major and minor complication rates. In addition to the complication types mentioned above, cases of nausea and dysmenorrhea have also been reported. Most minor complications appeared to be self-limiting. In the more recent systematic review, a total of 34 minor complications were noted among 1,406 injections (2.4%) (Hashimoto, 2010). Higher rates of minor complications were seen in observational studies. Overall, 176 complications were observed among 3,041 injections (5.8%); complication rates in each study ranged from 2.7%-16.3% (Hashimoto, 2010).

Subsequent Treatment

Two measures of subsequent treatment are available for spinal injections: repeat injections and requirements for subsequent invasive treatment. Data from RCTs and observational studies suggest that the average number of lumbar spinal injections per patient ranges from 2-4 on an annual basis, and that up to 90% of patients receiving these injections require a repeat injection during the initial session. Data on subsequent treatment requirements are sparser, but indicate that the need for surgical intervention arises in 14-36% of patients with nonspecific low back pain, lumbar disc herniation, or foraminal stenosis by 12 months following initial injection.

Data on repeat injections come from the Hashimoto systematic review, and include information gleaned from RCTs as well as retrospective database analyses of the Washington Health Care Authority's member claims activity (Hashimoto, 2010). Available RCT data suggest that the number of lumbar spinal injections of any type ranges from 2 to 4 annually; no significant differences in these rates were observed or reported in comparisons to control or sham injections.

In the retrospective claims analysis, between 27-88% of injection records involved claims for multiple injections on the same day, depending on the program and location of injection (epidural, foraminal, or paravertebral). Over 12 months of follow-up, the total number of claims for injections ranged between 1.7 and 3.2 per member. Data from a separate observational study of 81 patients receiving epidural steroid injections who were followed for a mean of 17 months suggest that 54% of patient required at least one repeat injection during the period of follow-up.

Limited data are available on requirements for surgical intervention after spinal injections. In one RCT, a comparison of 150 patients with nonspecific lumbar radicular pain who were randomized to 2 steroid groups (transforaminal epidural or intramuscular), 2 saline groups using the same approaches, or 1 transforaminal epidural anesthetic under fluoroscopic guidance, the incidence of surgery required as rescue treatment or injection failure ranged between 21% and 36% after 12 months of follow-up (Ghahreman, 2010). Between-group differences were not tested statistically. In another RCT, a comparison of 150 patients with lumbar disc herniation or foraminal stenosis who were randomized to receive transforaminal epidural methylprednisolone plus local anesthetic vs. local anesthestic alone (Tafazal, 2009), the rates of any surgery at 12 months of follow-up were 14.1% in the steroid plus anesthetic group and 21.5% in the anesthetic alone group (significance not reported).

Coblation Nucleoplasty

Data on coblation nucleoplasty are extremely limited due to the paucity of RCT evidence and quality observational data on this procedure.

30-day Mortality
No data on mortality attributable to coblation nucleoplasty have been reported in any RCT, systematic review or observational study in our sample.

Major Complications
No data on major complications attributable to coblation nucleoplasty have been reported in any RCT, systematic review or observational study in our sample.

Minor Complications
Data from the single available RCT suggest a rate of minor complications of 11%. No data on minor complications attributable to coblation nucleoplasty have been reported in any systematic review or observational study in our sample.

Procedure-attributable adverse events were reported in the available RCT comparing coblation nucleoplasty to epidural steroid injections (Gerszten, 2010). Events in both groups were considered to be minor and transient, and included pain at the injection site, worsening radicular and/or back pain, muscle spasm, and lightheadedness. The rate of minor complications was lower in the nucleoplasty arm (11% vs. 18% for ESI), although this difference was not statistically tested.

Subsequent Treatment

Data on subsequent treatment from the available RCT suggest that as many as one-quarter of patients receiving coblation nucleoplasty require secondary treatment for unresolved symptoms at 6 months following initial treatment. Information from a single observational study reports a requirement for surgery in 2 of 52 patients with lumbar disc herniation (3.8%).

During the randomized portion of the above-described RCT (Gerszten, 2010), 12 of 45 coblation nucleoplasty patients (26.7%) had unresolved symptoms requiring a secondary procedure, vs. 8/40 in the ESI group (20%, difference not statistically tested). When the observational period was included, however, a higher percentage of ESI patients required secondary treatment (44.4% vs. 70% for ESI, difference not statistically tested). Kaplan-Meier estimates of freedom from secondary treatment at 2 years were 52% and 17% for nucleoplasty and ESI respectively (p=.02). Secondary procedures included additional ESI, RF denervation, microdiscectomy, and spinal fusion.

A lower-quality systematic review (Manchikanti, 2009) reports data from a single observational study with information on requirements for subsequent treatment among patients with lumbar disc herniation. Two patients of 52 in the series (3.8%) were operated on 7 and 10 days following nucleoplasty because of continuation of severe pain. No information on subsequent treatment is available from the other 4 observational studies included in this review.

Radiofrequency (RF) Denervation

Data on RF denervation are also extremely limited, as data on harm or subsequent treatment were infrequently reported in RCTs or observational studies.

30-day Mortality

No data on mortality attributable to RF denervation have been reported in any systematic review, RCT, or observational study in our sample.

Major Complications

No data on major complications attributable to RF denervation have been reported in any systematic review, RCT, or observational study in our sample.

Minor Complications

Limited data on the rate of minor complications with RF denervation suggest relatively low rates of these complications (4-14%), which appear to be related to pain from treatment, numbness or irritability at procedure site, and lower limb weakness and were self-limiting in all cases.

Limited data exist with which to evaluate the rate of minor complications with RF denervation. Data from two systematic reviews (Chou, 2009b; Niemisto, 2010) suggest that adverse events were only reported in 3 RCTs. Rates ranged from 4-14%, and included a single case of lower limb weakness that resolved within two weeks as well as rates of treatment-related pain and numbness/irritability at the procedure site; these latter measures, which ranged from 5-14% in frequency, were not found to differ significantly from rates observed with sham procedures.

Subsequent Treatment

Data on subsequent treatment are limited to 2 observational studies; one of these reports a repeat RF denervation rate of ~16% in patients with nonspecific, nonradicular lumbar pain. The other study documents requirements for subsequent surgery in ~12% of patients receiving RF denervation for nonspecific, nonradicular lumbar pain.

Data on subsequent treatment comes from a series of 114 RF denervation patients with nonspecific lumbar pain without radicular symptoms who had a positive response to medial branch block injections (Mikeladze, 2003). Patients were assessed for pain reduction 1.5 months after the procedure. Those with <50% reduction in pain on a 100-point VAS were offered a repeat denervation procedure. The procedure was repeated in 18 patients (15.8%).

In a separate retrospective cohort analysis of 42 patients with nonspecific back pain >3 months without radicular symptoms or moderate-to-severe disc protrusion who had failed conservative treatment (Manejias, 2008), a total of 5 patients underwent surgery (11.9%) 5 to 21 months after the RF denervation procedure; 1 of these 5 patients expressed dissatisfaction with pain relief from the initial denervation attempt.

Intradiscal Electrothermal Therapy (IDET)

30-day Mortality

No data on mortality attributable to IDET have been reported in any systematic review, RCT, or observational study in our sample.

Major Complications

No major complications were observed in the 2 available RCTs of IDET. Data from observational studies suggest that the incidence of major complications is rare (<1%).

No major complications or adverse events attributable to IDET were observed in either available RCT of this intervention (Pauza, 2004; Freeman, 2005). While major complications of this procedure include vertebral osteonecrosis, cauda equina syndrome, and discitis, data

on these complications come from individual case reports (Freeman, 2006). In one registry of 1,675 IDET recipients, totals of 1 unresolved nerve root injury and 6 new-onset disc herniations were reported (0.4%) (Eckel, 2002).

Minor Complications

The rate of minor complications was reported in 1 of the 2 available RCTs of IDET, and was limited to cases of transient radiculopathy (10%). Data from observational studies suggest that the incidence of minor complications is relatively infrequent but ranges widely (1-10%).

A total of 4 cases (10.5%) of transient radiculopathy were reported in one of the available RCTs of IDET (Freeman, 2005), as compared to 1 case in the sham procedure group (5.3%). The statistical significance of this difference was not tested. No complications or adverse events attributable to IDET were observed in the other RCT (Pauza, 2004).

In the registry described above, minor complications included 19 catheter breakages and 5 transient cases of neuropathy among 1,675 patients (1.4%) (Eckel, 2002). In another series of 79 patients, a total of 8 patients had complications (10.1%) (Cohen, 2003). These complications, most of which were transient in nature, included radicular pain, paraesthesia and numbness, foot drop, and headache.

Subsequent Treatment

Data on repeat and subsequent treatment with IDET are limited to information from small case series. Data on repeat IDET were limited to a single case series (4%) in chronic discogenic pain. Information on subsequent treatment was available from 3 case series; rates for subsequent surgery ranged from 2-4%, while rates for other procedures ranged from 4-6%.

Information on repeat IDET was available in a single case series of 51 patients in New York who presented with chronic discogenic pain without radiographic evidence of a compressive lesion were followed for 2 years following the initial procedure (Lee, 2003). Two patients (3.9%) underwent repeat IDET at unspecified times during a mean of 34 months of follow-up.

Data on subsequent treatment were available from 3 case series. In one series of 56 IDET patients with chronic discogenic pain who had failed >6 months of conservative treatment and did not have radicular symptoms (Maurer, 2008), 2 patients required subsequent spine surgery for symptom relief over a mean of 20.5 months of follow-up (3.6%). In another, a series of 58 patients with persistent low back pain for >6 months, without radiographic evidence of compressive lesions or radicular symptoms who were followed for a mean of 28 months (Saal, 2002), 1 patient required lumbar interbody fusion at 6 months post-IDET (1.7%). In the above-mentioned Lee series, 2 of the 51 patients (3.9%) underwent spinal fusion after IDET.

The Lee series also evaluated the use of other minimally-invasive procedures. In addition to the cases of repeat IDET and spinal fusion, 2 and 3 patients respectively underwent coblation nucleoplasty (3.9%) and RF denervation (5.8%) following IDET.

Interspinous Spacers

30-day Mortality

No data on mortality attributable to interspinous spacers have been reported in any systematic review, RCT, or observational study in our sample.

Major Complications

In the 2 available RCTs of interspinous spacers, major complications were rarely reported, ranging from 0-3%. Data from a single observational study suggest a somewhat higher rate of major complications (6%), all of which were spinous process fractures.

Data from the earlier RCT of interspinous spacers identified 3 cases of major complications in 100 randomized patients (3%): 1 case each of spinous process fracture, coronary ischemia, and respiratory distress (Zucherman, 2004). The later RCT did not identify any major complications (Anderson, 2006).

In a series of 69 patients receiving the X-STOP in Italy, a total of 4 patients (5.8%) had spinous process fractures over a mean follow-up duration of 23 months (Barbagallo, 2009). The authors note that these complications appeared to occur in patients with unusual anatomic characteristics in the interspinous space.

Minor Complications

The rate of minor complications was in the 2 available RCTs of interspinous spacers ranged from 3-5%. The rate of minor complications in the single observational study identified was approximately 6%, and comprised cases of device malpositioning.

In the earlier RCT of interspinous spacers, a total of 3 minor complications were identified, including 1 case each of pulmonary edema, device malpositioning, and implant dislodgment among 100 patients (Zucherman, 2004). In the later RCT, 2 minor complications were identified in 42 patients (4.8%), including 1 case of superficial wound infection and device malpositioning (Anderson, 2006).

In the above-described observational study in Italy, a total 4 cases of device dislocations were identified (5.8%) (Barbagallo, 2009).

Subsequent Treatment

No data on repeat interspinous spacer procedures was available from RCTs or observational studies. Data from the 2 RCTs of interspinous spacers indicate that the rate of subsequent requirements for surgical intervention ranged from 6% in lumbar spinal stenosis to 12% in degenerative spondylolisthesis.

No information was available on the rate of repeat interspinous spacer procedures in either RCTs or observational studies. In the Zucherman RCT for lumbar spinal stenosis, the rate of subsequent laminectomy was reported to be significantly lower in the X-STOP group vs. non-operative care (6% vs. 22%, p<.05) (Zucherman, 2004). In contrast, the rate of subsequent laminectomy or fusion did not differ between groups in the Anderson RCT for degenerative spondylolisthesis (12% in each group) (Anderson, 2006).

Discectomy (all approaches)

30-day Mortality

No data on peri-operative mortality attributable to open, micro-, or automated percutaneous lumbar discectomy have been reported in any systematic review, RCT, or observational study in our sample. Data from older studies suggest that inpatient mortality related to discectomy is <0.1%.

No information on intra- or peri-operative mortality was available from any RCT, systematic review, or observational study in our sample. Findings from older studies suggest that peri-operative mortality with discectomy alone is rare. For example, in an analysis of 10,755 patients hospitalized for discectomy alone (Deyo, 1992), a total of 5 deaths occurring during the hospital stay that were attributable to the procedure was reported (0.05%).

Major Complications

In 7 available RCTs of discectomy, the incidence of major complications was low, ranging from 0-4% in most studies; most of these complications related to nerve root or vascular injuries. Limited available data suggest that major complication rates do not materially differ by surgical approach.

A total of 7 RCTs reported information on the incidence of major complications with discectomy. In the 4 RCTs comparing various forms of discectomy to non-operative care, the reported rate of major complications ranged between 0% and 3.6%. In 2 key RCTs (Weinstein, 2006; Peul, 2007), very low rates of major complications were reported. In the SPORT trial, a single case of intra-operative vascular injury was reported among the 243 patients in the randomized cohort (0.4%) (Weinstein, 2006). In the latter RCT, no major complications were identified (Peul, 2007).

Among those RCTs comparing different approaches to discectomy, no major complications were noted in 2 RCTs (Katayama, 2005; Ruetten, 2009). Some numeric differences were noted in the RCT comparing micro-endoscopic discectomy, microdiscectomy, and open discectomy (Teli, 2010), with rates ranging between 0% for open discectomy and 7.1% for micro-endoscopic discectomy; complication types for the latter group included nerve root injury, discitis, and worsening motor deficit. Statistical testing across all 3 treatment groups for each specific type of complication yielded no significant differences.

Data on complication rates with APLD are limited to those cited in the lower-quality systematic review included in the appraisal (Hirsch, 2009). Very low complication rates were reported in the observational studies included in this review (all less than 1%).

Additional observational data for discectomy were available from a retrospective analysis of 113 patients receiving a combination of endoscopic discectomy and IDET who were followed for a mean of 31.3 months (Tsou, 2004). A single case of thrombophlebitis was observed (0.9%).

Minor Complications

The rate of minor complications varied widely, ranging from 2-21% in 6 available RCTs. The most frequently reported minor complication was dural tears. As with major complications, limited data suggest that the rate of minor complications does not materially differ by discectomy approach.

Among the 3 RCTs reporting information on minor complications in studies comparing discectomy to non-operative care (Weinstein, 2006; Peul, 2007; Pearson, 2008), rates of minor complications ranged from 2.1%-10.3%. In the Peul RCT of early microdiscectomy, 2 cases of dural tear and 1 hematoma were observed over 1 year of follow-up in 141 patients (2.1%). In the SPORT trial, minor complications included 10 dural tears, 4 superficial wound infections, and 11 complications classified as "other" among 243 patients in the randomized cohort (10.3%). In a follow-up study examining all SPORT patients receiving surgery (i.e., including randomized, observational, and crossover patients), 23 and 18 cases of dural tear and wound infection were observed over 2 years of follow-up (5.3%).

In the 3 RCTs comparing various forms of discectomy, a single case of superficial wound infection was noted among 62 patients receiving macro-endoscopic discectomy (1.6%), while no complications were observed among 57 patients receiving microdiscectomy (Katayama, 2005); this difference was not tested statistically. In another RCT comparing these 2 approaches, a statistically significant difference was observed in favor of the macro-endoscopic approach (6% vs. 21% for microdiscectomy, $p<.05$) in patients followed for 2 years (Ruetten, 2009); most cases were related to transient post-operative dyesthesia in both groups. However, in the above-mentioned Teli RCT comparing 3 surgical approaches, no statistical differences were noted by technique (7.1%, 8.3%, and 8.6% for open, microscopic, and micro-endoscopic discectomy respectively) (Teli, 2010).

As mentioned above, the systematic review used to evaluate data on APLD reported very low complication rates of all types (<1%) in a limited set of observational studies (Hirsh, 2009). In the above-described observational study of endoscopic discectomy plus IDET (Tsou, 2004), 3 cases of dyesthesia were observed (2.7%).

Subsequent Treatment

Data from available RCTs indicate that requirements for additional surgery, primarily reoperation for recurrence of herniation symptoms, range from 3-11% over 2 to 4 years of follow-up. Long-term information from observational studies suggests that the rate of

reoperation continues to rise, and may affect as many as one-quarter of patients after 10 years.

Information on reoperation or subsequent surgery was available from a total of 8 RCT reports. In the 5 RCT reports involving comparisons of discectomy to conservative care for lumbar disc herniation, rates of reoperation due to re-herniation ranged from 2% to 7% over 2 to 4 years of follow-up, while rates of additional surgery for all reasons ranged from 3% to 11%. In the SPORT RCT, rates of reoperation due to re-herniation and all reasons in the randomized cohort were 3.3% and 5.3% respectively at 2 years of follow-up (Weinstein, 2006); these rates grew to 5.1% and 8.7% by year 4 of follow-up (Weinstein, 2008). Examination of all patients receiving surgery in SPORT (i.e., randomized, observational, and crossovers) indicated that 4.9% and 6.2% received subsequent surgery for re-herniation and all causes respectively (Pearson, 2008). Finally, an analysis of reoperation by workmen's compensation status in SPORT suggested that the overall 2-year reoperation rate did not differ (7% in each group) (Atlas, 2009). Data from the Peul RCT indicate that the total rate of reoperation due to recurrence of herniation symptoms at 1 year was 3.2% (Peul, 2007).

Similar findings were observed in the 3 RCTs comparing alternative approaches to discectomy. Rates of reoperation in the Teli comparison of 3 approaches ranged from 3% for open discectomy to 11.4% for micro-endoscopic discectomy (Teli, 2010); differences were not statistically significant. In the comparison of microdiscectomy to full endoscopic discectomy, rates were 7.1% and 4.4% respectively at 2 years (statistical significance not tested) (Ruetten, 2009). Finally, 2 patients in the microdiscectomy group required reoperation at 3-4 years of follow-up in the Katayama RCT (3.5%), while no patients in the macro-endocsopic discectomy group had this requirement.

Data from a total of 6 observational studies suggest that the need for reoperation or additional surgery grows over time. Reported rates ranged between 2% and 25% over 2 to 10 years of follow-up. It should be noted that the lowest rate reported (2%) was based on a rate of "early" reoperation; it is unclear whether later reoperation was evaluated in assessment of outcome after a mean of 34 months of follow-up (Shick, 2009). At the other end of the reported range, 10-year results from the Maine Lumbar Spine Study suggest that 25% of patients receiving surgery for lumbar disc herniation had additional lumbar spine surgery, at a median of 2 years following the initial procedure (Atlas, 2005).

Laminectomy and Fusion

30-day Mortality

No data on peri-operative mortality attributable to laminectomy or fusion have been reported in any systematic review or RCT. Findings from an analysis of Medicare claims suggest that that rate of peri-operative mortality is <1% regardless of the type of surgery.

No peri-operative deaths were reported in any RCT or systematic review used for this appraisal. In an analysis of 2007 Medicare claims among over 30,000 beneficiaries

undergoing decompressive surgery for lumbar spinal stenosis, 30-day mortality rates were reported to be 0.3%, 0.5%, and 0.6% for laminectomy, simple fusion, and complex fusion respectively (Deyo, 2010).

Major Complications

Rates of reported major complications in available RCTs were very low, ranging from 0-4%. Observational findings suggest that the rate of life-threatening complications increases with surgical complexity, ranging from 2-5%.

Data from the SPORT trial for lumbar spinal stenosis (Weinstein, 2008b) indicate no major intra- or post-operative complications in a population primarily undergoing laminectomy. In the SPORT trial report for degenerative spondylolisthesis, only intra-operative complications were reported; 1 case of vascular injury was noted (0.6%) in a population primarily undergoing fusion (Weinstein, 2007).

In the Malmivaara RCT comparing decompressive surgery to conservative care in patients with lumbar spinal stenosis with or without degenerative spondylolisthesis, 1 case each of neural dysfunction and respiratory distress were observed (4.0%) (Malmivaara, 2007). Finally, in the Fairbank RCT comparing spinal fusion to interdisciplinary rehabilitation for nonspecific low back pain, a total of 7 major complications were observed among 176 patients (4.0%) (Fairbank, 2005); these were primarily excessive bleeding and vascular injuries.

The above-described Medicare claims analysis examined the rate of life-threatening medical complications, including cardiac and pulmonary complications (e.g., conditions requiring intubation or resuscitation) as well as stroke. Observed rates were calculated up to 30 days post-operatively. The rates of such complications increased with increasing surgical complexity, and were reported to be 2.1%, 4.7%, and 5.2% for laminectomy, simple fusion, and complex fusion respectively (Deyo, 2010).

Minor Complications

Minor surgical complications were reported more frequently, ranging from 10-16% in available RCTs. The most frequently-reported complications were dural tears and difficulties with surgical implants and/or hardware.

Minor complications of surgery were relatively frequently reported in available RCTs. In the SPORT lumbar spinal stenosis RCT (Weinstein, 2008b), a total of 18 minor complications were reported among 153 patients (11.8%), 13 of which were dural tears (8.4%). In the degenerative spondylolisthesis RCT, 19 dural tears (11%) and 3 "other" complications were reported intra-operatively in 172 patients (12.8%) (Weinstein, 2007).

A total of 8 complications (16%) were observed in the surgical arm of the Malmivaara RCT, including 7 cases of dural tear (14%) and 1 misplaced transpedicular screw (2%). In the Fairbank RCT, a total of 18 minor complications (10.2%), primarily dural tears and problems with surgical implants (2.8% each), were noted.

The above-described Medicare claims analysis did not examine minor complications other than wound complications. As with major complications, the incidence of these increased with increasing surgical complexity, ranging from 0.9% for laminectomy to 2.2% for complex fusion (Deyo, 2010).

Subsequent Treatment

Data from available RCTs indicate that requirements for additional surgery vary widely in both reported rate and indication for such surgery. Reoperation in lumbar spinal stenosis populations ranged from 2-7% at 2 years, primarily for recurrent stenosis. A higher reoperation rate (11%) was observed in an RCT for degenerative spondylolisthesis, primarily for complications of the initial procedure.

Information from the SPORT trials yielded different rates and conclusions regarding the reason for reoperation. In the spinal stenosis RCT, 10 of 155 patients (6.5%) required additional surgery by 2 years; 6 of these 10 repeat procedures were for recurrent stenosis (Weinstein, 2008b). In contrast, a higher rate of reoperation was reported in the degenerative spondylolisthesis RCT (10.5%); 13 of the 18 additional procedures were for complications of the initial procedure (Weinstein, 2007).

In the Malmivaara spinal stenosis RCT, 1 patient required new decompressive surgery 1 year after the initial procedure (2.0%); no reason for the reoperation was given (Malmivaara, 2007). In the Fairbank RCT of spinal fusion for nonspecific low back pain, 11 of 176 patients (6.3%) required additional surgery within 2 years; no reasons for the additional surgery were given (Fairbank, 2005).

8. Clinical and Economic Model

8.1 Overview

The objective of the decision analytic model was to compare the outcomes, costs, and cost-effectiveness of management strategies for patients with low back disorders, with a particular focus on lumbar disk herniation (LDH), lumbar spinal stenosis (LSS), degenerative spondylolisthesis (DS), and chronic nonspecific back pain (CLBP)--those patient populations identified through our appraisal process as of greatest interest to patients, clinicians, and policymakers.

In the creation of a decision analytic model we have focused on the management of patients with persistent low back pain after an initial 4-6 week period of initial conservative treatment. In order to frame the patient populations in accordance with available evidence on the effectiveness of different interventions, patients were assumed to have had an imaging procedure and were classified as having one of the four conditions: LDH, LSS, DS, or CLBP. We further assumed that patients did not have any comorbid conditions or physical findings that would require urgent or emergent interventions.

In the model the management strategy for each condition begins with an initial approach, and patients whose low back pain and functional limitations do not respond may receive another, generally more invasive, treatment. Patients may also cross over from a plan for an initial invasive treatment approach to conservative care and vice versa. Our strategies are designed to represent the most common sequence of interventions for each condition but are not exhaustive. We have selected interventions for the clinical and economic model based on input from our ERG on those interventions for which there is evidence of effectiveness and/or specific controversy over appropriate use.

The analysis presented here provides a summary of the clinical outcomes and medical care costs and work loss resulting from each management strategy in hypothetical cohorts of patients with each of the LBD conditions. The clinical measures of pain, back pain-related dysfunction, work loss, procedural complications, medical care costs, and quality of life are summarized in tables to facilitate comparisons of interventions for each of the low back disorder conditions.

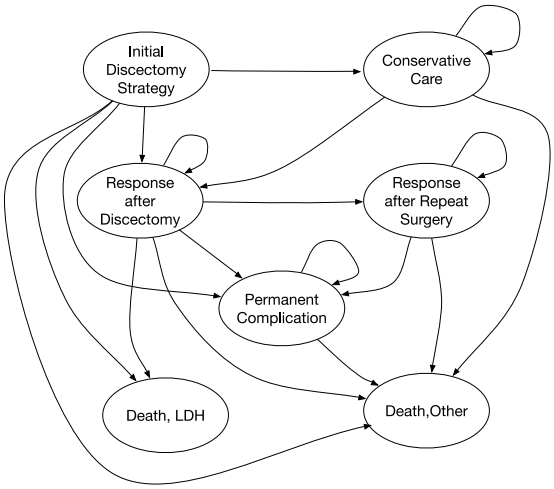
The presentation of results focused on the following initial interventions for each condition: (1) lumbar disc herniation: conservative care or discectomy; (2) lumbar spinal stenosis: conservative care, interspinous spacers, laminectomy, or fusion; (3) degenerative spondylolisthesis: conservative care, spacers, or fusion; and (4) chronic nonspecific low back pain: conservative care, interdisciplinary rehabilitation, or fusion.

8.2 Methods

Approach

The decision analytic model is a discrete state, discrete time, state transition model (Markov model). In the Markov model, patients' clinical status in each time interval is classified into discrete, mutually exclusive states. The disease states describe important clinical status such as initial treatment, response after initial treatment, response after repeat surgery, permanent disability due to complication of an intervention, death due to intervention for low back disorders, and death due to other causes (see Figure 4 below). In the model, patients transition between clinical states at 3-month intervals over an initial two-year period from the onset of an episode of low back pain. Treatments such as conservative care, procedures, or surgery result in transitions to new states. During the time in each state the clinical outcomes of back pain and function, work status, use of health care services, medical care costs, work loss costs, and quality of life are accrued. The analysis summarizes these outcomes for each management strategy for each of the 4 conditions.

Figure 4. Representative Low Back Disorders Markov Disease State Diagram

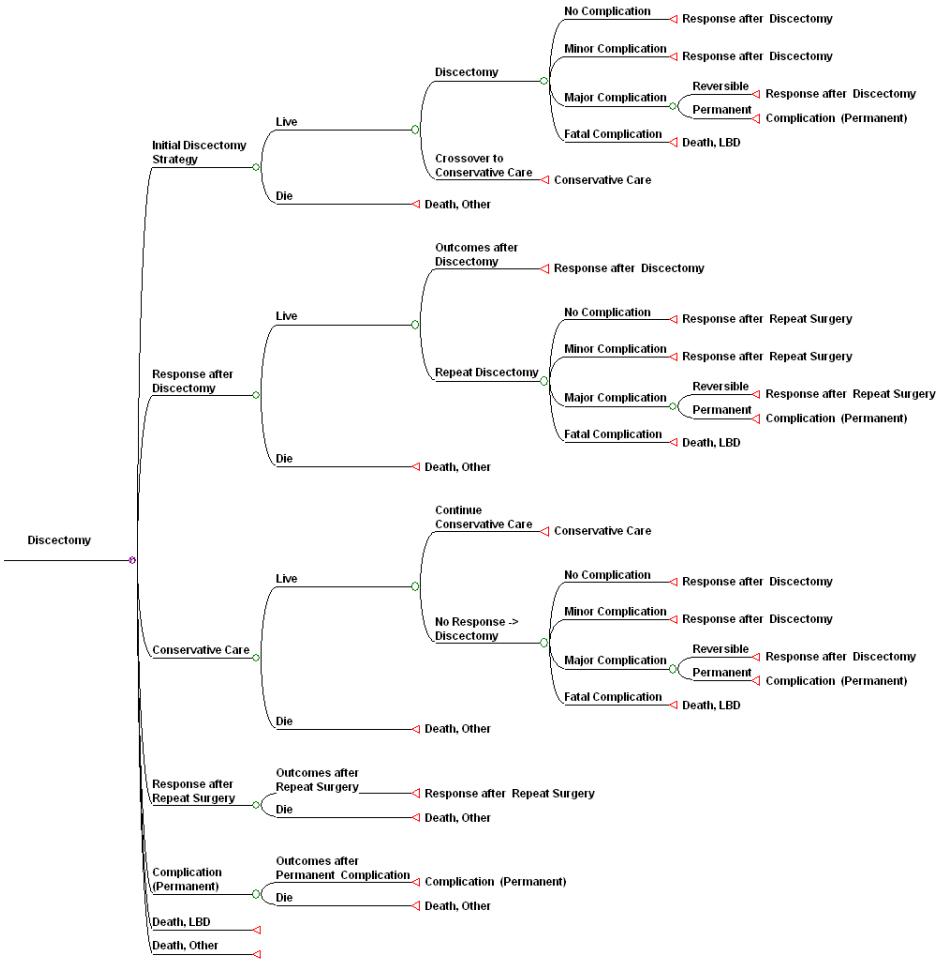


The decision analytic model is modeled as a decision tree, a graphic summary of the sequence of events that occur in the transitions between states. A representative decision tree of the discectomy strategy for lumbar disc herniation is shown in Figure 5 on the following page.

Perspective

We adopted a public payer perspective for the base case which includes capital expenditures in its reimbursement framework, thus following the majority of recommendations from the Panel on Cost-Effectiveness in Health and Medicine (Gold, 1996). As we did not address societal questions of the full return on investment for various treatment strategies, however, some recommendations were not relevant to this analysis (e.g., caregiver burden, other indirect costs).

Figure 5. Decision tree for discectomy strategy for lumbar disc herniation.



Medicare payment rates for fiscal 2010 were used to estimate direct medical care costs. We estimated the impact of LBD and the effect of treatments on patient productivity by estimating lost wages for patients in the work force (LDH and CLBP patients, with mean age 45) but not for older patients (LSS and LDH, with mean age 65). Other than lost wages, we did not take patient time in therapy or other patient time costs into account in this model given what we perceived to be serious limitations in our ability to estimate these elements.

Time Horizon

A clinical course of LBD treatments over a 2-year time horizon was adopted as the primary approach to summarize clinical outcomes, health related quality of life, and costs because the majority of clinical trials have reported 1-2 year outcomes.

Outcome Measures

The analysis summarizes clinical outcomes of back pain, back function, work status, the use of minimally invasive procedures, surgery (initial surgery and recurrent surgery), and

deaths. Costs include medical care costs for ambulatory visits, procedures, surgery, complications, and work loss costs estimated as lost wages. Quality adjusted life years (QALYs) were also estimated.

Microsimulation and Probabilistic Sensitivity Analysis
The clinical outcomes, work status and work loss, costs, and quality adjusted life years, and total costs and components of costs over the 2–year time horizon were calculated in a Markov cohort analysis of each strategy for each condition. Two major sources of uncertainty are accounted for in the model design and analysis. The first source of uncertainty results from variability among patients within each LBD condition and within groups of patients that receive a specific intervention. This "first order" variability between patients and the selection of patients for clinical trials is addressed with a microsimulation that evaluates the outcome in a sample of 1,000 patients with similar baseline characteristics for each strategy.

The second source of uncertainty results from variability in estimates of the effectiveness of specific interventions reported in the published medical literature, as well as uncertainty in the measurements of clinical outcomes, costs, and quality of life. This "second order" variability between strategies is addressed in a probabilistic sensitivity analysis that represents the key model data as probability distributions and analyzes the outcome of 1,000 samples for the set of distributions for the model parameters. The first order microsimulation with 1,000 "patient" samples is nested within each of the 1,000 parameter samples (total of one million samples) in the probabilistic sensitivity analysis. The summary measures of these outcomes have inherent variation due to sampling and should be interpreted cautiously when differences between strategies are small.

The clinical outcomes of back pain and back function, status, work loss, use of medical services, costs, and quality of life and their 95% confidence intervals are summarized for each condition. The primary outcomes were costs and quality-adjusted life years, both discounted at a 3% annual rate. The analysis was conducted using TreeAge Pro 2009 (TreeAge Software, Williamstown, MA).

Patient Populations and Low Back Disorder Conditions
The focus of the model, as in the systematic review, was on patients with subacute or chronic low back and/or leg pain. With input from the Evidence Review Group (ERG) we defined this patient population as those who have continued pain following a minimum of an initial 4-6 week course of conservative treatment (e.g., medications, exercise). Patients were assumed *not* to have low back pain arising from systemic disease, neurologic causes, or pregnancy, or to have failed back surgery syndrome. Patients were assumed to have persistent pain limitations in function that met indications for imaging, and were classified on the basis of clinical history, examination and imaging findings into one of the following four LBD conditions, with the noted management options that emerged with some degree of evidentiary support from the systematic review on clinical effectiveness:

- *45 year old male patient with lumbar disc herniation (LDH):*
    - Conservative care

    - Discectomy
- *65 year old male patient lumbar spinal stenosis (LSS):*
    - Conservative care
    - Interspinous spacers
    - Laminectomy

- *65 year old male patient with degenerative spondylolisthesis (DS):*
    - Conservative care
    - Interspinous spacers
    - Fusion

- *45 year old male patient with chronic low back pain (CLBP):*
    - Conservative care
    - Interdisciplinary rehabilitation
    - Fusion

8.3 Model Structure & Assumptions

The model follows hypothetical cohorts of simulated patients transitioning between the LBD clinical states at fixed 3-month intervals from the onset of their initial management with each strategy through a 2-year course of treatment. The base case analysis assumed male gender, as data from modern cohort studies suggest that interventions for specific low back disorders (e.g., disc herniation, spinal stenosis) occur somewhat more commonly in males (Stromqvist, 2008; Shabat, 2005).

Management Strategies
Detailed evaluation of each of the modeled interventions for the 4 patient populations of interest is available in the systematic review (Section 7). It should be noted that interventions without clear evidence of benefit were *not* included in the modeling framework; other interventions also were excluded based on study-specific concerns (e.g., measurement instruments employed, population selection). In this section we highlight those aspects of the individual studies that influenced the selection of interventions and the specific studies that served as the basis of the design of the management strategy and as major sources for the base case parameter estimates of effectiveness of the interventions.

1. *Lumbar Disc Herniation*
    a. Management strategies
        - Conservative care:
            1. Assumed continuation of initial 4-6 week regimen of conservative care
            2. A percentage of patients will opt for immediate discectomy over conservative care (Peul, 2007)
            3. Pathway includes initial physician office visit, a course of physical therapy 3 times per week for 6 weeks, and

prescriptions for NSAIDs and skeletal muscle relaxants (assumption)
4. Patients attempting conservative care who "fail" will receive discectomy (assumption)

- Discectomy:
  1. A percentage of patients will opt for conservative care instead of discectomy (Peul, 2007)
  2. Pathway assumes an average stay in hospital of 3.5 days, a follow-up physician visit and 6 physical therapy visits within 3 months of surgery, and an annual physician visit thereafter (Center for Medicare and Medicaid Services, assumption)
  3. Patients who do not respond to discectomy receive one or more repeat discectomies (assumption)

b. Rationale for interventions included: Randomized controlled trials of microdiscectomy (Peul, 2007) and discectomy (the SPORT trial, Weinstein, 2006) provide evidence of effectiveness of discectomy compared to conservative care for LDH. While the latter study involved direct collection of quality of life data, the only publicly-available information was for the combined randomized and observational cohorts. The Peul study therefore represented the best opportunity to use intention-to-treat data that represented a comparison of discectomy and conservative care.

c. Rationale for interventions excluded: Epidural steroid injections (ESI), coblation nucleoplasty, and interdisciplinary rehabilitation were excluded from the model. As noted in the systematic review, there is no consistent evidence of benefit for ESI among patients with LDH. In addition, there was insufficient RCT evidence for coblation nucleoplasty and interdisciplinary rehabilitation among patients with LDH.

2. *Lumbar Spinal Stenosis*
   a. Management strategies
      - Conservative care:
        1. Assumed continuation of initial 4-6 week regimen of conservative care
        2. A percentage of patients will opt for immediate laminectomy over conservative care (Weinstein, 2008b)
        3. Pathway assumes initial physician office visit, a course of physical therapy 3 times per week for 6 weeks, and prescriptions for NSAIDs and skeletal muscle relaxants (assumption)
        4. Patients attempting conservative care who "fail" will receive laminectomy; a 2nd failure requires spinal fusion (assumption)

- Interspinous spacers:
    1. A percentage of patients will opt for conservative care instead of spacers (assumption: identical to Weinstein, 2008b)
    2. Pathway assumes an outpatient procedure, a follow-up physician visit and 6 physical therapy visits within 3 months of surgery, and an annual physician visit thereafter (Center for Medicare and Medicaid Services, assumption)
    3. Patients who do not respond to spacers receive laminectomy; a 2nd failure requires spinal fusion (Zucherman, 2004, assumption)

- Laminectomy:
    1. A percentage of patients will opt for conservative care instead of laminectomy (Weinstein, 2008b)
    2. Pathway assumes an average stay in hospital of 3.5 days, a follow-up physician visit and 6 physical therapy visits within 3 months of surgery, and an annual physician visit thereafter (Center for Medicare and Medicaid Services, assumption)
    3. Patients who do not respond to laminectomy receive repeat laminectomy; a 2nd failure requires spinal fusion (assumption)

b. Rationale for interventions included: The effectiveness of surgical treatment (laminectomy and fusion) compared to conservative care for LSS has been evaluated in the SPORT RCT (Weinstein, 2008); this was selected for use in the model because it was a large trial with a design intended to approximate real-world practice, and data were reported on both an intention-to-treat and as-treated basis. A single RCT comparing the X-STOP interspinous spacer device to conservative care in LSS has been published (Zucherman, 2004), and was therefore also included for modeling purposes.

c. Rationale for interventions excluded: Epidural steroid injections (ESI), radiofrequency (RF) denervation, and interdisciplinary rehabilitation were excluded from the model. As noted in the systematic review, there is no consistent evidence of benefit for ESI among patients with LSS. In addition, there were no available RCTs of RF denervation or interdisciplinary rehabilitation among patients with LSS.

3. *Degenerative Spondylolisthesis.*
    a. Management Strategies
        - Conservative care:
            1. Assumed continuation of initial 4-6 week regimen of conservative care
            2. A percentage of patients will opt for immediate spinal fusion over conservative care (Weinstein, 2007)

3. Pathway assumes initial physician office visit, a course of physical therapy 3 times per week for 6 weeks, and prescriptions for NSAIDs and skeletal muscle relaxants (assumption)
4. Patients attempting conservative care who "fail" will receive one or more spinal fusions (assumption)

- Interspinous spacers:
  1. A percentage of patients will opt for conservative care instead of spacers (assumption: identical to Weinstein, 2007)
  2. Pathway assumes an outpatient procedure, a follow-up physician visit and 6 physical therapy visits within 3 months of surgery, and an annual physician visit thereafter (Center for Medicare and Medicaid Services, assumption)
  3. Patients who do not respond to spacers receive one more spinal fusions (Anderson, 2006, assumption)

- Spinal fusion:
  1. A percentage of patients will opt for conservative care instead of spinal fusion (Weinstein, 2007)
  2. Pathway assumes an average stay in hospital of 4.0 days, a follow-up physician visit and 6 physical therapy visits within 3 months of surgery, a follow-up visit with imaging to assess fusion healing, and an annual physician visit thereafter (Center for Medicare and Medicaid Services, assumption)
  3. Patients who do not respond to spinal fusion receive one or more repeat fusions (assumption)

b. Rationale for interventions included: The effectiveness of surgical treatment (nearly 95% of which was spinal fusion) compared to conservative care for DS has been evaluated in the SPORT RCT (Weinstein, 2007). As noted for LSS, this RCT was selected for use in the DS model because it was a large trial with a design intended to approximate real-world practice, and data were reported on both an intention-to-treat and as-treated basis. While a single RCT is available examining the X-Stop interspinous spacer device in DS (Anderson, 2006), outcomes were measured using instruments that do not map to the standard instruments of focus for the model. The decision was therefore made to use the other available X-Stop RCT for LSS (Zucherman, 2004) as the basis for the model.
.
c. Rationale for interventions excluded: Epidural steroid injections (ESI), radiofrequency (RF) denervation, and interdisciplinary rehabilitation were excluded from the model. As noted in the systematic review, there were no available RCTs of ESI, RF denervation, or interdisciplinary rehabilitation among patients with DS.

4. *Chronic Nonspecific Low Back Pain*
    a. Management Strategies
        - Conservative care
            1. Assumed continuation of initial 4-6 week regimen of conservative care
            2. A percentage of patients will opt for immediate spinal fusion over conservative care (Fritzell, 2001)
            3. Pathway assumes initial physician office visit, a course of physical therapy 3 times per week for 6 weeks, and prescriptions for NSAIDs and skeletal muscle relaxants (assumption)
            4. Patients attempting conservative care who "fail" will receive one or more spinal fusions (assumption)

        - Interdisciplinary rehabilitation
            1. A percentage of patients will opt for immediate spinal fusion over interdisciplinary rehabilitation (assumption: identical to conservative care in Fritzell, 2001)
            2. Pathway assumes an initial physician visit, 60 hours of physical and supervised exercise therapy, 16 hours of work conditioning and workplace assessment, 10 hours of cognitive-behavioral therapy, and a final physician assessment visit (88 hours) (Kaapa, 2006)
            3. Patients attempting interdisciplinary rehabilitation who "fail" will receive one or more spinal fusions (assumption)

        - Spinal fusion
            1. A percentage of patients will opt for conservative care instead of spinal fusion (Fritzell, 2001)
            2. Pathway assumes an average stay in hospital of 4.0 days, a follow-up physician visit and 6 physical therapy visits within 3 months of surgery, a follow-up visit with imaging to assess fusion healing, and an annual physician visit thereafter (Center for Medicare and Medicaid Services, assumption)
            3. Patients who do not respond to spinal fusion receive one or more repeat fusions (assumption)

    b. Rationale for interventions included: Direct RCT evidence comparing the effects of spinal fusion and conservative care in CLBP is available from a large RCT in Sweden with measurement of the outcomes of interest and 2-year follow-up (Fritzell, 2001). Data from an RCT comparing interdisciplinary rehabilitation to an individualized exercise program was selected for long-term follow-up and similar pain and function at baseline to the Fritzell RCT (Dufour, 2010).

c. Rationale for interventions excluded: Spinal injections, radiofrequency (RF) denervation, and intradiscal electrothermal therapy (IDET) were excluded from the model. As noted in the systematic review, there was no consistent evidence of benefit for any category of spinal injection in CLBP. While RCT data are available in this population for RF denervation and IDET (Leclaire, 2001; Pauza, 2004), these RCTs were conducted in highly selected populations, putting their generalizability to the broader CLBP population in question.

Key Alternative Scenarios Identified for the Clinical and Economic Model

Although there are many important assumptions that were made as part of the model, during the creation of the model three issues stood out as potentially of greatest impact and controversy. These three areas involved (1) the impact of crossovers in RCTs in estimating the clinical effectiveness and costs of LBD interventions; (2) the importance of work loss costs in relation to the magnitude of medical care costs for LBD patients; (3) the impact of the increased costs and increased risk of complications from complex fusion compared to simple fusion for LBD. Our rationale for base case assumptions is presented on the following pages for the overall disease process and by treatment strategy, but these three assumptions provided the basis for *a priori* alternative scenarios that analyzed for this review.

1. Impact of crossovers in RCTs in estimating the effectiveness of LBD interventions
2. Importance of work loss costs in comparison to medical care costs
3. The impact of the increased costs and increased risk of complications of complex fusion compared to simple fusion.

Key Assumptions in the Clinical and Economic Model

Major assumptions of the model as well as relevant sources and justification are presented in the Tables on the following pages. Our model was based on the work of previously published decision analysis models of management of LBD (Shvartzman, 1992 and Kuntz, 2000) and CEA of LBD conducted as part of RCTs (Fritzell, 2004 ; Rivero-Arias, 2005 ; Hansson, 2007 ; Soegaard, 2007 ; Herman, 2008 ; Tosteson, 2008a ; Tosteson 2008b ; and Burnett, 2010).

Key Assumptions – Low Back Disorders

Assumptions	Rationale & Source
Low Back Disorders	
• Patients' have had an initial evaluation and do not have indications for urgent interventions. • Patients have persistent pain and dysfunction after 4-6 weeks, and are classified as having LDH, LSS, DS or CLBP on basis of initial evaluation, treatment and imaging.	Chou, 2007
Clinical Outcome Measures	
• Back Pain: The primary back pain measure in the model was the SF-36 bodily pain (BP) subscale.	Bombardier, 2000
• The Visual Analogue Scale (VAS), (0 to 100 scale) was used when the SF-36 BP was not available.	Bombardier, 2000
• A change in SF-36 BP > 10 is a moderate effect and > 20 is a large/substantial effect.	Ostelo, 2008 Chou, 2009
• Back Function: The primary back function measure in the model was the Oswestry Disability Index (ODI), on a 0-100 scale (100 = maximum back dysfunction).	RDQ, ODI and methods citations
• The Roland Morris Disability Questionnaire (RDQ) on a 0-24 scale, 24 = maximum dysfunction was mapped to a 0-100 scale to compare with the ODI in the model.	Bombardier, 2000
Employment, Work Loss and Cost of Work Loss	
• Working FT/PT. Working status is defined as working full time or part time at baseline in RCTs.	Assumption based on available data in randomized controlled trials
• Work Days per Year: We assume 48 work weeks x 5 days per week = 240 working days per year.	Assumption
• We assume annual daily wage of $165.	Bureau of Labor Statistics, Report LEU025289100, 2010
• Work loss estimated from patient's perspective as product of work loss (days) x wages per day.	Assumption
• In the RCT of microdiscectomy compared to conservative care for LDH, "full recovery" on a 7 point Likert scale was interpreted as return to work.	Peul, 2007
Quality of Life	
• EQ-5D is the measure for quality of life in the analysis. Age-specific norm for EQ-5D (US scoring, males) for US non-institutionalized population used	Bombardier, 2000 Tosteson, 2000
• VAS, general health, may be used for quality of life when a EQ-5D is not reported.	Tosteson, 2000
• The SF-36 subscales may be mapped to EQ-5D	Ara, 2008
Adjustment for Baseline Differences	
• In comparisons across studies, back pain (SF-36 BP, 0-100 scale) and back function (ODI 0 to 100 scale or RDQ transformed to 0 to 100 scale) were adjusted to the baseline of the conservative care group. The adjustment used the reported value of the measure (0 to 100 scale) and proportion of maximum potential gain to avoid ceiling/floor effects and overestimation that might occur from simple linear adjustment.	Assumption

Key Assumptions: Lumbar Disc Herniation

Assumptions	Rationale & Source
Conservative Care	
• Assume effectiveness of strategy in as-treated (AT) analysis same as in intention-to-treat (ITT) analysis.	As-treated analysis not reported in Peul, 2007
• Quality of life was estimated from SF-36 subscales.	Ara, 2008
• Work status by time was estimated from a 7-point Likert scale indicating full recovery.	Peul, 2007
Microdiscectomy	
• Assume effectiveness of strategy in as-treated analysis same as in intention-to-treat analysis.	As-treated analysis not reported in Peul, 2007
• Quality of life was estimated from SF-36 subscales.	Ara, 2008
• Work status by time was estimated from a 7-point Likert scale indicating full recovery.	Peul, 2007

Key Assumptions: Lumbar Spinal Stenosis`

Assumptions	Rationale & Source
Conservative Care	
• In ITT analyses, the probability of crossover by time was derived from the cumulative crossovers by time in the RCT patient flow diagram	Weinstein, 2008
• The baseline back pain and back function in the conservative care strategy were used as the baseline for all patients	Assumption
• The reported change in SF-36 bodily pain and Oswestry Disability Index in the ITT and AT analyses (Tables and Figures) were used in the model.	Weinstein, 2008
Interspinous Spacers	
• The effectiveness of interspinous spacers in reducing on back pain is based on SF-36 BP subscale. with LSS	Zucherman, 2004
• Crossovers observed in the fusion strategy in the SPORT RCT were assumed for the interspinous spacers strategy	Weinstein, 2008
• The baseline SF-36 and ODI are adjusted for the conservative care baseline in the SPORT LSS RCT	Control for baseline differences between studies
Laminectomy	
• Laminectomy is assumed to have risks of fatal, major, and minor complications	Deyo, 2010
• In ITT analyses, the probability of crossover by time was derived from the cumulative crossovers by time in the RCT patient flow diagram	Weinstein, 2008

Key Assumptions: Degenerative Spondylolisthesis

Assumptions	Rationale & Source
Conservative Care	
• In ITT analyses, the probability of crossover by time was derived from the cumulative crossovers by time in the RCT patient flow diagram	Weinstein, 2007
• The baseline back pain and back function in the conservative care strategy were used as the baseline for all patients	Assumption
• The reported change in SF-36 bodily pain and Oswestry Disability Index in the ITT and AT analyses (Tables and Figures) were used in the model	Weinstein, 2007
Interspinous Spacers	
• The effectiveness interspinous spacers in LSS as measured by SF-36 BP subscale were used for DS. The effectiveness of interspinous spacers in DS is based on aggregate measures of SF-36 PCS and MCS scales. SF-36 BP subscale is not reported	Zucherman, 2004 Anderson, 2006
• The ZCQ physical function subscale was used to estimate the impact of spacers on quality of life	Quality of life not reported in Zucherman, 2004
• Crossovers observed in the fusion strategy in the SPORT RCT were assumed for the interspinous spacers strategy	Weinstein, 2007
• The baseline SF-36 and ODI were adjusted for the conservative care baseline in the SPORT DS RCT	*Post hoc* adjustment of Zucherman, 2004 and Weinstein, 2007
Fusion	
• In ITT analyses, the probability of crossover by time was derived from the cumulative crossovers by time in the RCT patient flow diagram	Weinstein, 2007

Key Assumptions: Chronic Low Back Pain

Assumptions	Rationale & Source
Conservative Care	
• Back Pain estimated from VAS	Fritzell, 2001
• AT values reported in tables and statistical analysis based on ITT. ITT values are estimated from AT values reported in tables on entire population and characteristics of crossover patients	Control for differences in back pain and back function in patients who crossover to other intervention
Interdisciplinary Rehabilitation	
• Back function adjusted for baseline in conservative care group in Swedish Lumbar Spine Study (Fritzell, 2001) based on measured ODI	Dufour, 2010 Control for baseline differences
• Crossovers from interdisciplinary rehabilitation to fusion were assumed to occur in the same proportion as crossovers from conservative care to fusion	Fritzell, 2001
• Back function reported for AT and ITT analysis. Back Pain SF-36 BP adjustment for AT and ITT based on VAS change in AT and ITT analyses	Fritzell, 2001; VAS but not SF-36 BP reported in ITT and AT analyses
Fusion	
• Back Pain estimated from VAS	Fritzell, 2001
• AT values reported. ITT values estimated from AT values and crossovers	Control for differences in back pain and back function in patients who crossover to other intervention

Model Outcome Measures

Clinical Outcomes

The clinical outcomes measured used to evaluate each strategy are back pain (SF-36 bodily pain or VAS) Back Function (ODI, or RDQ mapped to the ODI), total life years from onset of treatment through death, total number of visits to healthcare providers, total number of surgical procedures (discectomy, interspinous spacers, laminectomy, and fusion), other procedures, complications (fatal complications, major complications, major complication with permanent sequelae, and minor complications), and deaths due to other non-LBD-related causes. Quality adjusted life years (QALYs) were used as a summary measure for clinical outcomes.

Economic Outcomes

The cost measures used to evaluate each strategy are payments for direct medical care estimated from Medicare fee schedules and expressed in 2010 US dollars. The costs were further categorized as surgical costs, procedure costs, ambulatory visit costs, adverse event costs (complications of surgery and other procedures), and work loss costs. Total costs are used as a summary measure for economic outcomes.

Model Inputs
All variable inputs for the model are shown in Appendix D. Some of the key parameter inputs are described in the paragraphs below.

Patient Population
The patient population variables include patient age, sex, and classification of low back disorder as LDH, LSS, DS, and CLBP. Patients with LDH and CLBP were assumed to be working age (45 years), while patients with LSS and DS were assumed to be retired (65 years).

Probabilities of Clinical Outcomes
Probabilities of clinical outcomes used in the model are shown in Table A. These inputs were derived from the ICER systematic review, peer-reviewed publications, US life tables, US vital statistics, and input from the ERG. The probabilities of death due to treatments for LBD were obtained from published peer-reviewed studies. US vital statistics and life tables were used to calculate the probabilities of death due other causes. Transition probabilities between disease states are converted to 3-month probabilities for the 3-month cycle time of the Markov model. All rates were converted to probabilities.

Quality of Life
The quality of life variables are listed in Table B. The health related quality of life for patients with LBD with LSS and DS were estimated from the quality of life reported in the SPORT LDH trial (Tosteson, 2008). The quality of life of patients with LDH were estimated from SF-36 values published in the RCT of early microdiscectomy vs. prolonged conservative for LDH (Peul, 2007) and compared well with the quality of life estimates reported in the as-treated analyses of the combined SPORT RCT and observational cohort studies (Tosteson, 2008). Quality of life in CLBP was estimated using low back dysfunction on the ODI as measure of magnitude of quality of life reduction below age and sex norms of quality of life in the US from the Medical Expenditure Panel Survey (MEPS), a national survey of the US non-institutionalized population, using the EuroQoL (EQ-5D) measure with US population norms for scoring. The MEPS provides representative age and sex specific quality of life measures for the population.

Short term morbidity associated with procedures, complications, and adverse events was estimated by using the average Medicare Severity (MS)-DRG length of stay in days for the duration of morbidity and assumed short term disutilities.

Costs
The cost variables are provided in Table C. Costs of direct medical services were estimated using the 2010 Medicare fee schedule for payments for hospital care for procedures based on CMS 2010 MS-DRGs with additional payments for physician, anesthesia, and surgeon fees for procedures. The Medicare payments used to estimate cost of the major interventions for the LBD conditions treatments in the clinical and economic analysis are conservative care ($2,400 for a 6-8 week regimen), intensive interdisciplinary rehabilitation ($8,500 for a 6-8 week program), interspinous spacers ($8,500), discectomy ($11,100), laminectomy ($10,700), simple fusion ($23,900) and complex fusion ($32,800).

8.4 Results

In this section we present the findings of the clinical and economic model of interventions for the 4 LBD conditions. For each LBD condition, the clinical and economic model results based on the intention-to-treat (ITT) analysis from RCTs are presented first, and then the model results from the as-treated (AT) analysis are presented to facilitate an understanding of the impact of crossover on model findings. For continuous and event-based measures, 95% confidence intervals are presented to facilitate interpretation of uncertainty around model-generated means. The cost-effectiveness analyses are then presented. In general, while differences were noted for individual outcomes and costs between interventions, summary measures of effectiveness (e.g., QALYs, proportion of patients with substantial improvement) differed only moderately.

Lumbar Disc Herniation: Conservative Care or Discectomy

Patient Characteristics and Effectiveness of Interventions

The baseline back pain, back function, and work status of patients used as a basis for the clinical and economic model of the LDH management was derived from randomized controlled trial of early microdiscectomy compared to prolonged conservative care (Peul, 2007). The LDH patients had the most severe back pain (SF-36 BP mean: 23.9 on 0-100 scale, lower values = more severe pain) and lowest back function (RDQ mean: 16.3 on 0-23 scale, higher values = worse function) of the 4 LBD conditions.

LDH Intention-to-treat Analysis

The ITT analysis of microdiscectomy compared to conservative care is summarized in Table 10 on the following page. In the ITT analysis, 91% of patients intending to have microdiscectomy actually received surgery, and 39% of patients initially receiving conservative care ultimately received surgery. Both treatment pathways produced substantial improvements in back pain and back function (100% had substantial/large improvement [>20-point change] in back pain and back function and a very high proportion of patients in both pathways returned to work). The microdiscectomy strategy results in less work loss (42 days compared to 86 days for conservative care), lower costs due to work loss ($6,997 compared to $14,151), and higher quality of life (1.46 QALYs compared to 1.41 QALYs) than conservative care. The microdiscectomy strategy had higher direct medical care costs than conservative care ($13,553 compared to $7,533) due to a higher proportion of patients who receive microdiscectomy and the higher costs of surgery compared to conservative care.

Table 10. Clinical outcomes and costs of management options for lumbar disc herniation (intention-to-treat analysis).

	Conservative Care			Discectomy		
		95% CI			95% CI	
	Mean	Lower	Upper	Mean	Lower	Upper
Clinical Outcomes						
Back Pain (SF BP)	78.4	74.4	82.3	83.2	78.8	87.6
Back Function (ODI)	14.6	10.5	18.6	13.0	9.1	16.8
Change in Clinical Outcomes						
Change in Back Pain > 10 SF BP, %	100%			100%		
Change in Back Pain > 20 SF BP, %	100%			100%		
Change in Back Function > 10 ODI, %	100%			100%		
Change in Back Function > 20 ODI, %	100%			100%		
Work Status						
Working (FT/PT)	94%			96%		
Change in Work Status						
Change in Work FT/PT > 20 days, %	100%			100%		
Work Loss						
Work Loss (Based on Work FT/PT), days	85.8	60.8	109.9	42.4	17.0	71.7
Complications						
Minor Complications	5.4%	4.1%	6.8%	12.7%	10.7%	14.9%
Major Complications	0.8%	0.3%	1.4%	2.0%	1.2%	2.9%
Major Permanent Complications	0.1%	0.0%	0.3%	0.2%	0.0%	0.5%
Fatal Complications	0.0%	0.0%	0.1%	0.0%	0.0%	0.1%
Process of Care						
Surgery within 2 Years	39%	36%	42%	91%	90%	93%
Health Services						
Surgical Procedures	0.4	0.4	0.5	1.0	1.0	1.0
Other Procedures	0.0	0.0	0.0	0.0	0.0	0.0
Visits	19.6	19.3	20.0	13.5	13.3	13.8
Costs						
Total Costs	$7,533	$774	$27,187	$13,553	$1,591	$60,425
Surgery	$4,539	$4	$23,209	$10,794	$9	$55,155
Procedures	$0	$0	$0	$0	$0	$0
Complications	$539	$401	$696	$1,281	$1,057	$1,495
Visits	$2,454	$39	$11,159	$1,478	$23	$6,460
Cost of Work Loss						
Work Loss (Work FT/PT)	$14,151	$10,036	$18,130	$6,997	$2,805	$11,835
Quality of Life (QALYs)	1.41	1.35	1.48	1.46	1.39	1.53

SF BP: Short-form 36 Bodily Pain subscale; ODI: Oswestry Disability Index; FT/PT: Full-time/Part-time; QALY: Quality-adjusted life year

LDH As-treated Analysis

The AT analysis of microdiscectomy compared to conservative care is summarized in Table 11 on the following page. It should be noted that, because the RCT used for this model (Peul, 2007) did not feature an AT analysis, changes in effectiveness measures are identical to those in the ITT analysis. However, no crossovers are assumed to occur in the AT analysis, which affects estimates of cost and harm. In the absence of crossover, the difference in 2-year costs for surgery and conservative care is larger than in the ITT analysis ($13,699 and $2,359 for microdiscectomy and conservative care, respectively). In addition, the percentage of patients with treatment complications is higher for surgical patients. QALYs do not differ between analyses, because as noted previously, effectiveness outcomes were identical in the ITT and AT analyses for LDH.

Cost-Effectiveness of Microdiscectomy Compared to Conservative Care for LDH

In the ITT analysis, microdiscectomy is more expensive and more effective than conservative care and has an incremental cost-effectiveness ratio (ICER) of $116,000 per QALY gained (Table 12 at top of page 190). In the AT analysis, the difference in costs between management strategies is greater in the absence of crossover, but the QALY gain is identical to that in the ITT analysis. Therefore, the ICER of microdiscectomy compared to conservative care in the AT analysis is higher ($233,000 per QALY gained).

As-treated analyses of data from other RCTs of discectomy such as SPORT show substantially better outcomes as compared to intention-to-treat findings. It is likely that a similar trend would be observed if such data were made available in the Peul RCT. Findings from a cost-effectiveness analysis using data from the combined randomized and observational LDH cohorts in SPORT suggest that surgery would be associated with an additional 2.5 months of quality-adjusted life expectancy over 2 years, which resulted in a lower cost-effectiveness ratio (~$69,000 per QALY gained) than that observed in our analysis (Tosteson, 2008). The estimates of effectiveness, costs, and cost-effectiveness presented in this appraisal therefore represent a "lower boundary" around the estimate of benefit that would be expected in an as-treated population.

Table 11. Clinical outcomes and costs of management options for lumbar disc herniation (as-treated analysis).

	Conservative Care			Discectomy		
		95% CI			95% CI	
	Mean	Lower	Upper	Mean	Lower	Upper
Clinical Outcomes						
Back Pain (SF BP)	78.3	74.3	82.3	83.1	78.8	87.5
Back Function (ODI)	14.5	10.5	18.5	13.0	9.1	17.1
Change in Clinical Outcomes						
Change in Back Pain > 10 SF BP, %	100%			100%		
Change in Back Pain > 20 SF BP, %	100%			100%		
Change in Back Function > 10 ODI, %	100%			100%		
Change in Back Pain > 20 SF ODI, %	100%			100%		
Work Status						
Working (FT/PT)	94%			96%		
Change in Work Status						
Change in Work FT/PT > 20 days, %	100%			100%		
Work Loss						
Work Loss (Based on Work FT/PT), days	86.4	57.4	110.4	43.5	16.8	70.4
Complications						
Minor Complications	0.0%	0.0%	0.0%	13.9%	11.9%	16.1%
Major Complications	0.0%	0.0%	0.0%	2.1%	1.3%	3.1%
Major Permanent Complications	0.0%	0.0%	0.0%	0.2%	0.0%	0.5%
Fatal Complications	0.0%	0.0%	0.0%	0.0%	0.0%	0.1%
Process of Care						
Surgery within 2 Years	0%	0%	0%	100%	100%	100%
Health Services						
Surgical Procedures	0.0	0.0	0.0	1.1	1.1	1.1
Other Procedures	0.0	0.0	0.0	0.0	0.0	0.0
Visits	19.0	18.9	19.0	12.6	12.4	12.7
Costs						
Total Costs	$2,359	$1	$12,004	$13,699	$1,497	$62,528
Surgery	$0	$0	$0	$10,976	$7	$58,368
Procedures	$0	$0	$0	$0	$0	$0
Complications	$0	$0	$0	$1,399	$1,176	$1,635
Visits	$2,359	$1	$12,004	$1,324	$1	$7,069
Cost of Work Loss						
Work Loss (Work FT/PT)	$14,249	$9,474	$18,223	$7,181	$2,774	$11,611
Quality of Life (QALYs)	1.41	1.35	1.48	1.46	1.39	1.53

SF BP: Short-form 36 Bodily Pain subscale; ODI: Oswestry Disability Index; FT/PT: Full-time/Part-time; QALY: Quality-adjusted life year

Table 12. Cost-effectiveness of microdiscectomy compared to conservative care for LDH (intention-to-treat & as-treated analyses).

Strategy	Costs ($)	Incremental Costs ($)	Effectiveness (QALYs)	Incremental Effectiveness (QALYs)	ICER ($/QALYs)
Intention To Treat Analysis					
Conservative Care	$7,533		1.41		
Discectomy	$13,553	$6,020	1.46	0.05	$115,992
As Treated Analysis					
Conservative Care	$2,359		1.41		
Discectomy	$13,699	$11,340	1.46	0.05	$233,333

QALY: Quality-adjusted life year; ICER: Incremental cost-effectiveness ratio

Lumbar Spinal Stenosis: Conservative Care, Interspinous Spacers, or Laminectomy

Patient Characteristics and Effectiveness of Interventions

Data on LSS management options were derived from the SPORT randomized trial (Weinstein ,2008) and the X STOP randomized trial (Zucherman, 2004). Our analysis assumed that patients' mean age was 65, and assumed that the baseline back pain and back function was the same as in the conservative care arm of the SPORT RCT (Weinstein, 2008). The X STOP trial did not use the same measure of back function as the SPORT RCT; no back function outcome was therefore produced for this strategy in the model. The effectiveness of interspinous spacers was adjusted to account for the greater severity of pain and back dysfunction in the X STOP trial relative to the SPORT LSS RCT. In our analysis we assume that crossover rates in the interspinous spacers strategy are the same as rates among the surgical interventions in the SPORT LSS trial. Finally, as with the Peul RCT, the X STOP RCT does not include an as-treated analysis. Effectiveness findings were therefore identical for the ITT and AT analyses of interspinous spacers.

LSS Intention-to-Treat Analysis

The clinical outcomes, costs, and quality of life in the intention-to-treat analysis are shown in Table 13 on the following page. Note that the model results for interpsinous spacers are presented distinctly from the results for conservative care and laminectomy. Whereas direct comparative data are available for these latter management options, we can only make much more tenuous, indirect assumptions of the magnitude of the clinical benefits of interspinous spacers vs. conservative care. For this reason the ERG advised highlighting the significantly greater uncertainty regarding the model results for interspinous spacers. Findings for the spacers strategy are therefore shaded to distinguish them from direct comparative results.

The comparative data for laminectomy vs. conservative care come directly from the SPORT LSS RCT in which there were large and differential crossovers between study arms (42% to surgery and 34% to conservative care). The surgical interventions produce greater reductions in back pain and back dysfunction compared to conservative care and a higher proportion of patients have a moderate or larger improvement in back pain (but not back function) compared to conservative care. Interspinous spacers produce greater reduction in back pain than laminectomy. In the model essentially all patients treated with interspinous spacers would have large/substantial improvements in back pain, in contrast to approximately 90% of patients who receive laminectomy. Surgical management strategies have higher costs than conservative care. Interspinous spacers result in higher quality of life than conservative care, but the higher quality of life of interspinous spacers compared to laminectomy and fusion should be interpreted cautiously, as quality of life was not directly measured in the spacers trial and was estimated using change in physical function.

Table 13. Clinical outcomes and costs of management options for lumbar spinal stenosis (intention-to-treat analysis).

	Conservative Care			Laminectomy			Interspinous Spacers		
		95% CI			95% CI			95% CI	
	Mean	Lower	Upper	Mean	Lower	Upper	Mean	Lower	Upper
Clinical Outcomes									
Back Pain (SF BP)	47.7	43.0	52.2	55.0	49.9	60.0	67.5	62.7	72.5
Back Function (ODI)	29.8	25.9	33.6	26.6	22.5	30.7	---	---	---
Change in Clinical Outcomes									
Change in Back Pain > 10 SF BP, %	99%			99%			100%		
Change in Back Pain > 20 SF BP, %	4%			90%			100%		
Change in Back Function > 10 ODI, %	92%			98%			---		
Change in Back Function > 20 ODI, %	0%			0%			---		
Complications									
Minor Complications	0.2%	0.0%	0.5%	8.8%	7.1%	10.6%	3.3%	2.2%	4.5%
Major Complications	0.1%	0.0%	0.3%	1.5%	0.7%	2.3%	2.0%	1.2%	3.0%
Major Permanent Complications	0.0%	0.0%	0.1%	0.1%	0.0%	0.4%	0.1%	0.0%	0.4%
Fatal Complications	0.0%	0.0%	0.1%	0.2%	0.0%	0.5%	0.0%	0.0%	0.1%
Process of Care									
Surgery within 2 Years	42%	40%	45%	65%	63%	68%	65%	63%	68%
Health Services									
Surgical Procedures	0.4	0.4	0.5	0.7	0.7	0.7	0.7	0.7	0.7
Other Procedures	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Visits	18.2	17.8	18.6	16.6	16.1	17.0	14.7	14.3	15.0
Costs									
Total Costs	$7,344	$523	$27,373	$10,478	$1,428	$39,160	$10,534	$1,668	$36,807
Surgery	$4,612	$2	$24,097	$7,391	$76	$35,542	$5,716	$51	$28,792
Procedures	$0	$0	$0	$0	$0	$0	$0	$0	$0
Complications	$25	$0	$61	$819	$661	$988	$516	$364	$679
Visits	$2,509	$47	$12,172	$2,269	$53	$10,084	$4,302	$260	$14,255
Quality of Life (QALYs)	1.22	1.18	1.25	1.23	1.20	1.27	1.28	1.25	1.32

NOTE: Laminectomy and conservative care estimates based on direct RCT-based comparison; estimates for interspinous spacers based on indirect comparisons of RCT results
SF BP: Short-form 36 Bodily Pain subscale; ODI: Oswestry Disability Index; FT/PT: Full-time/Part-time; QALY: Quality-adjusted life year

LSS As-treated Analysis

In the as-treated analysis of the LSS strategies there are no crossovers and the effectiveness of laminectomy in reducing back pain and back dysfunction is higher and the effectiveness of conservative care is lower relative to the ITT analysis (Table 14 below). Laminectomy produces large/substantial reductions in back pain in all patients and large/substantial changes in back function in 65% of patients vs. 0% for conservative care. While, as expected, differences in costs and complication rates between surgery and conservative care are higher in the AT analyses, differences in QALYs are also somewhat greater due to the greater treatment effects seen in the AT population.

Table 14. Clinical outcomes and costs of management options for lumbar spinal stenosis (as-treated analysis).

	Conservative Care			Laminectomy			Interspinous Spacers		
		95% CI			95% CI			95% CI	
	Mean	Lower	Upper	Mean	Lower	Upper	Mean	Lower	Upper
Clinical Outcomes									
Back Pain (SF BP)	45.0	40.5	49.5	58.8	53.7	63.6	67.6	62.4	72.5
Back Function (ODI)	33.4	29.6	37.3	21.8	17.6	26.0	---	---	---
Change in Clinical Outcomes									
Change in Back Pain > 10 SF BP, %	92%			99%			100%		
Change in Back Pain > 20 SF BP, %	0%			99%			100%		
Change in Back Function > 10 ODI, %	32%			99%			---		
Change in Back Function > 20 ODI, %	0%			65%			---		
Complications									
Minor Complications	0.0%	0.0%	0.0%	13.5%	11.3%	15.7%	5.1%	3.8%	6.6%
Major Complications	0.0%	0.0%	0.0%	2.2%	1.4%	3.2%	3.1%	2.1%	4.1%
Major Permanent Complications	0.0%	0.0%	0.0%	0.2%	0.0%	0.5%	0.2%	0.0%	0.5%
Fatal Complications	0.0%	0.0%	0.0%	0.3%	0.0%	0.7%	0.0%	0.0%	0.1%
Process of Care									
Surgery within 2 Years	0%	0%	0%	100%	99%	100%	100%	99%	100%
Health Services									
Surgical Procedures	0.0	0.0	0.0	1.0	1.0	1.1	1.0	1.0	1.1
Other Procedures	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Visits	18.9	18.8	19.0	8.8	8.7	8.9	20.7	20.6	20.8
Costs									
Total Costs	$2,430	$2	$12,429	$14,122	$1,670	$65,129	$11,064	$1,200	$42,995
Surgery	$0	$0	$0	$11,567	$117	$61,444	$8,897	$87	$39,028
Procedures	$0	$0	$0	$0	$0	$0	$0	$0	$0
Complications	$0	$0	$0	$1,259	$1,063	$1,462	$792	$625	$957
Visits	$2,430	$2	$12,429	$1,296	$7	$6,496	$1,375	$7	$7,073
Quality of Life (QALYs)	1.18	1.15	1.22	1.30	1.26	1.33	1.28	1.25	1.31

NOTE: Laminectomy and conservative care estimates based on direct RCT-based comparison; estimates for interspinous spacers based on indirect comparisons of multiple RCTs

SF BP: Short-form 36 Bodily Pain subscale; ODI: Oswestry Disability Index; FT/PT: Full-time/Part-time; QALY: Quality-adjusted life year

Cost-Effectiveness of Laminectomy and Interspinous Spacers compared to Conservative Care for LSS

In the ITT analysis, interspinous spacers are more expensive and more effective than conservative care and have an ICER of $50,877 (Table 15 below). Laminectomy is more expensive but only minimally more effective than conservative care and has an ICER of $257,705.

In the AT analysis, interspinous spacers are more expensive and more effective than conservative care, with an ICER of $89,844. Laminectomy is more expensive and much more effective than conservative care with an ICER of $101,229. These findings suggest that crossovers in the published RCTs have a major impact on the cost-effectiveness of interventions for LSS.

Table 15. Cost-effectiveness of laminectomy and interspinous spacers compared to conservative care for lumbar spinal stenosis

Strategy	Costs ($)	Incremental Costs ($)	Effectiveness (QALYs)	Incremental Effectiveness (QALYs)	ICER ($/QALYs)
Intention To Treat Analysis					
Conservative Care	$7,344		1.22		
Interspinous Spacers	$10,534	$3,190	1.28	0.06	$50,877
Conservative Care	$7,334		1.22		
Laminectomy	$10,478	$3,144	1.23	0.01	$257,705
As Treated Analysis					
Conservative Care	$2,430		1.18		
Interspinous Spacers	$11,064	$8,634	1.28	0.10	$89,844
Conservative Care	$2,430		1.18		
Laminectomy	$14,122	$11,692	1.30	0.12	$101,229

NOTE: Laminectomy and conservative care estimates based on direct RCT-based comparison; estimates for interspinous spacers based on indirect comparisons of multiple RCTs
QALY: Quality-adjusted life year; ICER: Incremental cost-effectiveness ratio

Degenerative Spondylolisthesis: Conservative Care, Interspinous Spacers, or Fusion

Patient Characteristics and Effectiveness of Interventions

The key published studies used as a basis for the DS clinical and economic model included the SPORT randomized trial (Weinstein, 2007) and the randomized trial of the X STOP device (Zucherman, 2004). Our analysis assumed that patients' mean age was 65, and assumed a baseline back pain, and back dysfunction observed in the conservative care arm

of the SPORT RCT (Weinstein, 2007). We assumed that crossovers in the X STOP trial of interspinous spacers were similar to crossovers in the surgical interventions in the SPORT LSS study. Finally, as noted above, the X STOP RCT does not include an as-treated analysis. Effectiveness findings were therefore identical for the ITT and AT analyses of interspinous spacers. As with the LSS analyses, data for interspinous spacers are shaded, as the comparison of this management option to conservative care required indirect analyses based on results from RCTs with widely differing results in the nonoperative care arms.

DS Intention-to-treat Analysis

The intention-to-treat analysis of management strategies of degenerative spondylolisthesis is shown in Table 16 below. There are a large number of crossovers (47% to surgery and 38% to conservative care). Conservative care produced moderate improvement in back

Table 16. Clinical outcomes and costs of management options for degenerative spondylolisthesis (intention-to-treat analysis).

	Conservative Care			Fusion			Interspinous Spacers		
		95% CI			95% CI			95% CI	
	Mean	Lower	Upper	Mean	Lower	Upper	Mean	Lower	Upper
Clinical Outcomes									
Back Pain (SF BP)	49.6	46.6	52.9	54.4	51.3	57.6	65.8	62.2	69.5
Back Function (ODI)	24.3	21.7	26.6	25.4	23.0	28.0	---	---	---
Change in Clinical Outcomes									
Change in Back Pain > 10 SF BP, %	99%			99%			100%		
Change in Back Pain > 20 SF BP, %	45%			98%			100%		
Change in Back Function > 10 ODI, %	99%			99%			---		
Change in Back Function > 20 ODI, %	3%			0%			---		
Complications									
Minor Complications	6.6%	5.2%	8.1%	8.6%	6.8%	1.4%	3.4%	2.3%	4.6%
Major Complications	2.5%	1.6%	3.5%	3.3%	2.2%	4.5%	2.1%	1.3%	3.0%
Major Permanent Complications	0.1%	0.0%	0.3%	0.1%	0.0%	0.4%	0.0%	0.0%	0.1%
Fatal Complications	0.3%	0.0%	0.6%	0.3%	0.0%	0.7%	0.0%	0.0%	0.2%
Process of Care									
Surgery within 2 Years	47%	45%	50%	62%	59%	65%	62%	59%	65%
Use of Health Services									
Surgical Procedures	0.5	0.5	0.5	0.7	0.6	0.7	0.7	0.6	0.7
Other Procedures	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Visits	18.3	17.9	18.7	17.5	17.1	18.0	17.5	17.1	18.0
Costs									
Total Costs	$14,198	$1,111	$65,825	$17,639	$1,395	$84,370	$8,841	$1,155	$31,649
Surgery	$11,416	$7	$63,855	$14,881	$10	$82,070	$6,246	$105	$29,036
Procedures	$0	$0	$0	$0	$0	$0	$0	$0	$0
Complications	$811	$640	$987	$1,054	$863	$1,245	$522	$394	$672
Visits	$1,971	$83	$9,241	$1,703	$18	$7,779	$475	$5	$2,255
Quality of Life (QALYs)	1.24	1.20	1.27	1.22	1.18	1.25	1.24	1.20	1.27

NOTE: Fusion and conservative care estimates based on direct RCT-based comparison; estimates for interspinous spacers based on indirect comparisons of multiple RCTs

SF BP: Short-form 36 Bodily Pain subscale; ODI: Oswestry Disability Index; FT/PT: Full-time/Part-time; QALY: Quality-adjusted life year

pain in all patients with large/substantial improvement in 45% of patients, and moderate improvement in back function in all patients. The fusion strategy produced large or substantial improvements in back pain in all patients and moderate improvement in back function in almost all patients. The interspinous spacers strategy produces large/substantial improvements in back pain in all patients. In the ITT analysis with a large proportion of crossovers, the costs of fusion ($17,639) are higher than the costs of the interspinous spacers ($8,841) and conservative care ($14,198) strategies; costs for the latter largely reflect crossover to surgery. The quality of life for the fusion (1.22) is slightly lower than the quality of life for the conservative care strategy (1.24) and the quality of life of interspinous spacers is essentially the same as the conservative care strategy.

DS As-treated Analysis

The as-treated analysis of management strategies of degenerative spondylolisthesis is shown in Table 17 on the following page. In the absence of crossovers, the effectiveness of the fusion strategy is higher and the effectiveness of the conservative care strategy is lower than in the ITT analysis.

Conservative care produces moderate improvement in back pain but not in back function. Interspinous spacers produce a large/substantial improvement in back pain. Fusion produces a large/substantial improvement in back pain and back function in all patients. Costs of conservative care in this analysis are much lower, and the costs of interspinous spacers and surgery are higher than in the ITT analysis. The quality of life of fusion (1.31) and interspinous spacers (1.29) is somewhat larger than the quality of life of the conservative care strategy.

Cost-Effectiveness of Laminectomy, Fusion and Interspinous Spacers, compared to Conservative Care for DS

The cost-effectiveness of the interventions for DS is summarized in Table 18 on page 197. In the intention-to-treat analysis, interspinous spacers are less expensive and have essentially the same effectiveness as conservative care. Fusion is more expensive and slightly less effective than conservative care. In the as-treated analysis, interspinous spacers are more expensive and more effective than conservative care with an ICER of $70,555. Fusion is both much more expensive and more effective than conservative care and has an ICER of $162,874.

Table 17. Clinical outcomes and costs of management options for degenerative spondylolisthesis (as-treated analysis).

	Conservative Care			Fusion			Interspinous Spacers		
		95% CI			95% CI			95% CI	
	Mean	Lower	Upper	Mean	Lower	Upper	Mean	Lower	Upper
Clinical Outcomes									
Back Pain (SF BP)	46.6	43.7	49.7	60.8	57.6	63.8	65.7	62.0	69.3
Back Function (ODI)	34.2	31.7	36.8	17.2	14.6	19.7	---	---	---
Change in Clinical Outcomes									
Change in Back Pain > 10 SF BP, %	100%			99%			100%		
Change in Back Pain > 20 SF BP, %	0%			99%			99%		
Change in Back Function > 10 ODI, %	0%			99%			---		
Change in Back Function > 20 ODI, %	0%			99%			---		
Complications									
Minor Complications	0.0%	0.0%	0.0%	14.0%	11.5%	16.3%	5.7%	4.3%	7.2%
Major Complications	0.0%	0.0%	0.0%	5.4%	4.1%	6.8%	3.4%	2.3%	4.6%
Major Permanent Complications	0.0%	0.0%	0.0%	0.2%	0.0%	0.6%	0.0%	0.0%	0.2%
Fatal Complications	0.0%	0.0%	0.0%	0.5%	0.1%	1.0%	0.1%	0.0%	0.2%
Process of Care									
Surgery within 2 Years	0%	0%	0%	100%	99%	100%	100%	99%	100%
Use of Health Services									
Surgical Procedures	0.0	0.0	0.0	1.1	1.1	1.1	1.1	1.1	1.1
Other Procedures	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Visits	18.9	18.9	19.0	9.0	8.9	9.1	9.1	8.9	9.2
Costs									
Total Costs	$2,334	$2	$12,129	$27,384	$1,853	$148,571	$12,374	$1,401	$49,866
Surgery	$0	$0	$0	$25,460	$14	$146,823	$10,354	$212	$47,890
Procedures	$0	$0	$0	$0	$0	$0	$0	$0	$0
Complications	$0	$0	$0	$1,734	$1,496	$1,970	$875	$697	$1,069
Visits	$2,334	$2	$12,129	$190	$0	$884	$1,145	$4	$6,228
Quality of Life (QALYs)	1.15	1.12	1.19	1.31	1.27	1.34	1.29	1.26	1.33

NOTE: Fusion and conservative care estimates based on direct RCT-based comparison; estimates for interspinous spacers based on indirect comparisons of multiple RCTs
SF BP: Short-form 36 Bodily Pain subscale; ODI: Oswestry Disability Index; FT/PT: Full-time/Part-time; QALY: Quality-adjusted life year

Table 18. Cost-effectiveness of laminectomy and interspinous spacers compared to conservative care for degenerative spondylolisthesis.

Strategy	Costs ($)	Incremental Costs ($)	Effectiveness (QALYs)	Incremental Effectiveness (QALYs)	ICER ($/QALYs)
Intention To Treat Analysis					
Conservative Care *	$14,198		1.24		
Interspinous Spacers *	$8,841	-$5,357	1.24	0.00	---
Conservative Care**	$14,812		1.24		
Fusion**	$17,639	$2,827	1.22	-0.02	---
As Treated Analysis					
Conservative Care	$2,334		1.15		
Interspinous Spacers	$12,374	$10,040	1.29	0.14	$70,555
Conservative Care	$2,334		1.15		
Fusion	$27,384	$25,050	1.31	0.15	$162,874

*Cost-effectiveness not reported—spacers less expensive and equally effective vs. conservative care
**Cost-effectiveness not reported—fusion more expensive and less effective than conservative care
NOTE: Fusion and conservative care estimates based on direct RCT-based comparison; estimates for interspinous spacers based on indirect comparisons of multiple RCTs
QALY: Quality-adjusted life year; ICER: Incremental cost-effectiveness ratio

Chronic Non-Specific Low back Pain: Conservative Care, Interdisciplinary Rehabilitation or Discectomy

Patient Characteristics and Effectiveness of Interventions

The key published studies used as a basis for the clinical and economic model for CLBP management are the Swedish Spine Study (Fritzell, 2001) which was a randomized controlled trial of fusion compared to conservative care, and a randomized controlled trial of interdisciplinary rehabilitation compared to intensive back strengthening (Dufour, 2010). Our analysis assumed that patients' mean age was 45, and assumed a baseline back pain, back dysfunction, and employment observed in the conservative care arm of the Swedish Spine Study (Fritzell, 2001). Interdisciplinary rehabilitation was studied in a population with more severe back pain and back dysfunction, and the effectiveness of interdisciplinary rehabilitation was adjusted to the baseline severity of back pain and back dysfunction as described above. The crossovers from interdisciplinary rehabilitation to fusion were assumed to occur in the same proportion as the conservative care strategy. As with the previous patient populations, data for interdisciplinary rehabilitation are presented separately because of this indirect comparison.

Quality of life was not directly measured and was estimated based on change in back function chronic back pain conditions to facilitate comparisons within the CLBP interventions. Comparisons of quality of life between the other low back disorder conditions (LDH, LSS, and DS) and chronic low back pain used in this analysis must be considered cautiously because of the different approach to estimating quality of life in the chronic low back pain patients.

CLBP Intention-to-treat Analysis

The ITT analysis of clinical outcomes, employment, cost and quality of life are shown in Table 19 on the following page. A small amount of crossover was generated in this model (9% to surgery and 8% to conservative care or IRP). Conservative care resulted in small/slight overall improvements in back pain and back function. Interdisciplinary rehabilitation resulted in overall moderate improvement in back pain in almost all patients and in back function in approximately 85% of patients. Under the most beneficial effectiveness scenario available (i.e., the Fritzell RCT), fusion results in large /substantial improvement in back pain in approximately 80% and small/moderate improvement in back function of 67%. The costs of fusion are substantially higher than the costs of IRP and conservative care. Note that work loss costs are substantially higher than medical care costs in this population, that work loss was similar in conservative care ($60,000) and interdisciplinary rehabilitation ($61,000), and that work losses in both of the nonsurgical interventions are higher than in fusion ($45,000). Quality of life overall was low (due in part to the different method of estimating quality of life in CLBP compared to other low back disorders), but the quality of life with interdisciplinary rehabilitation (0.96) and fusion (0.94) was higher than with conservative care. (0.88).

Table 19. Clinical outcomes and costs of management options for chronic nonspecific low back pain (intention-to-treat analysis).

	Conservative Care			Fusion			Interdisciplinary Rehab		
		95% CI			95% CI			95% CI	
	Mean	Lower	Upper	Mean	Lower	Upper	Mean	Lower	Upper
Clinical Outcomes									
Back Pain (SF BP)	49.0	44.2	53.8	61.9	59.4	64.6	55.8	51.3	60.6
Back Function (ODI)	42.1	36.8	47.5	37.8	35.1	40.3	36.0	31.6	40.6
Change in Clinical Outcomes									
Change in Back Pain > 10 SF BP, %	20%			99%			98%		
Change in Back Pain > 20 SF BP, %	0%			76%			2%		
Change in Back Function > 10 ODI, %	9%			67%			85%		
Change in Back Function > 20 ODI, %	0%			0%			0%		
Work Status									
Working (FT/PT), %	13%			35%			11%		
Change in Work Status									
Change in Work FT/PT > 20 days, %	0%			88%			0%		
Work Loss									
Work Loss (Based on Work FT/PT), days	364.2	341.5	387.4	271.0	258.2	283.0	373.0	350.5	396.3
Complications									
Minor Complications	1.1%	0.5%	1.8%	12.5%	10.6%	14.8%	1.1%	0.5%	1.8%
Major Complications	0.4%	0.1%	0.9%	4.8%	3.5%	6.2%	0.4%	0.1%	0.9%
Major Permanent Complications	0.0%	0.0%	0.1%	0.2%	0.0%	0.5%	0.0%	0.0%	0.1%
Fatal Complications	0.0%	0.0%	0.2%	0.5%	0.1%	0.9%	0.0%	0.0%	0.2%
Process of Care									
Surgery within 2 Years	9%	7%	10%	92%	90%	94%	9%	7%	10%
Use of Health Services									
Surgical Procedures	0.1	0.1	0.1	1.0	0.9	1.0	0.1	0.1	0.1
Other Procedures	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Visits	19.4	19.3	19.6	9.4	9.2	9.6	87.5	86.9	88.0
Costs									
Total Costs	$4,404	$241	$16,947	$23,208	$1,709	$114,175	$10,208	$328	$41,028
Surgery	$1,877	$1	$9,559	$21,282	$11	$112,541	$1,877	$1	$9,559
Procedures	$0	$0	$0	$0	$0	$0	$0	$0	$0
Complications	$136	$69	$209	$1,549	$1,321	$1,794	$136	$69	$209
Visits	$2,391	$6	$12,789	$377	$7	$1,477	$8,186	$4	$38,192
Cost of Work Loss									
Work Loss (Work FT/PT)	$60,097	$56,342	$63,920	$44,722	$42,601	$46,687	$61,546	$57,827	$65,391
Quality of Life (QALYs) Based on ODI	0.88	0.84	0.91	0.94	0.90	0.97	0.96	0.93	1.00

NOTE: Fusion and conservative care estimates based on direct RCT-based comparison; estimates for interdisciplinary rehabilitation based on indirect comparisons of multiple RCTs
SF BP: Short-form 36 Bodily Pain subscale; ODI: Oswestry Disability Index; FT/PT: Full-time/Part-time; QALY: Quality-adjusted life year

CLBP As-treated Analysis

The as-treated analysis of clinical outcomes, employment, cost and quality of life are shown in Table 20 on the following page. Results associated with conservative care yield essentially no improvement overall in back pain and back dysfunction. Interdisciplinary

rehabilitation results in moderate improvement in back pain and back dysfunction. Fusion results in moderate improvement in back pain in essentially all patients and with large/substantial reductions in back pain in 65% of patients. Fusion results in moderate improvement in back function in approximately 90% of patients.

Table 20. Clinical outcomes and costs of management options for chronic nonspecific low back pain (as-treated analysis).

	Conservative Care			Fusion			Interdisciplinary Rehab		
		95% CI			95% CI			95% CI	
	Mean	Lower	Upper	Mean	Lower	Upper	Mean	Lower	Upper
Clinical Outcomes									
Back Pain (SF BP)	45.3	40.5	50.1	61.5	59.1	63.9	56.1	51.4	60.9
Back Function (ODI)	45.4	40.0	50.7	36.7	34.1	39.3	33.4	28.7	38.3
Change in Clinical Outcomes									
Change in Back Pain > 10 SF BP, %	1%			99%			99%		
Change in Back Pain > 20 SF BP, %	0%			65%			2%		
Change in Back Function > 10 ODI, %	0%			91%			98%		
Change in Back Function > 20 ODI, %	0%			0%			2%		
Work Status									
Working (FT/PT)	13%			35%			11%		
Change in Work Status									
Change in Work FT/PT > 20 days, %	0%			88%			0%		
Work Loss									
Work Loss (Based on Work FT/PT), days	364.3	343.1	387.2	271.0	258.7	283.8	373.1	349.4	397.3
Complications									
Minor Complications	0.0%	0.0%	0.0%	13.7%	11.5%	16.0%	0.0%	0.0%	0.0%
Major Complications	0.0%	0.0%	0.0%	5.2%	3.9%	6.6%	0.0%	0.0%	0.0%
Major Permanent Complications	0.0%	0.0%	0.0%	0.2%	0.0%	0.5%	0.0%	0.0%	0.0%
Fatal Complications	0.0%	0.0%	0.0%	0.5%	0.1%	1.0%	0.0%	0.0%	0.0%
Process of Care									
Surgery within 2 Years	0%	0%	0%	100%	100%	100%	0%	0%	0%
Use of Health Services									
Surgical Procedures	0.0	0.0	0.0	1.1	1.0	1.1	0.0	0.0	0.0
Other Procedures	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Visits	19.0	18.9	19.0	8.6	8.5	8.6	87.9	87.7	88.0
Costs									
Total Costs	$2,555	$2	$13,615	$25,297	$1,779	$113,358	$8,479	$5	$40,363
Surgery	$0	$0	$0	$23,392	$28	$111,404	$0	$0	$0
Procedures	$0	$0	$0	$0	$0	$0	$0	$0	$0
Complications	$0	$0	$0	$1,687	$1,458	$1,944	$0	$0	$0
Visits	$2,555	$2	$13,615	$218	$0	$1,125	$8,479	$5	$40,363
Cost of Work Loss									
Work Loss (Work FT/PT)	$60,101	$56,611	$63,881	$44,721	$42,692	$46,832	$61,555	$57,652	$65,560
Quality of Life (QALYs) Based on ODI	0.82	0.79	0.86	0.95	0.92	0.98	1.01	0.97	1.04

NOTE: Fusion and conservative care estimates based on direct RCT-based comparison; estimates for interdisciplinary rehabilitation based on indirect comparisons of multiple RCTs
SF BP: Short-form 36 Bodily Pain subscale; ODI: Oswestry Disability Index; FT/PT: Full-time/Part-time; QALY: Quality-adjusted life year

Costs of conservative care and interdisciplinary rehabilitation are somewhat lower than their costs in the ITT analysis because they do not include any costs of surgery. The costs of fusion are substantially higher than the cost of rehabilitation, which in turn is substantially higher than the cost of conservative care. The costs of work loss in the AT analysis are not adjusted for crossovers and therefore are similar to the costs in the ITT analysis. Quality of life did not appreciably change between the ITT and AT analyses; quality of life was higher for interspinous spacers (1.01) and fusion (0.95) than for conservative care (0.82).

Cost-Effectiveness of Fusion and Interdisciplinary Rehabilitation, compared to Conservative Care for Chronic Low Back Pain

In the cost-effectiveness analysis based on the ITT analysis, interdisciplinary rehabilitation was more expensive and more effective than conservative care and had an ICER of $67,098 (Table 21 below). Fusion was substantially more expensive and more effective than conservative care and had an ICER of $328,168. In the AT analysis interdisciplinary rehabilitation was more expensive and much more effective than conservative care and had an ICER of $32,178. Fusion was much more expensive and much more effective than conservative care and had an ICER of $181,211.

Table 21. Cost-effectiveness of interdisciplinary rehabilitation and fusion compared to conservative care for chronic low back pain.

Strategy	Costs ($)	Incremental Costs ($)	Effectiveness (QALYs)	Incremental Effectiveness (QALYs)	ICER ($/QALYs)
Intention To Treat Analysis					
Conservative Care	$4,404		0.88		
Interdisciplinary Rehabilitation	$10,208	$5,804	0.96	0.09	$67,098
Conservative Care	$4,404		0.88		
Fusion	$23,208	$18,804	0.94	0.06	$328,168
As Treated Analysis					
Conservative Care	$2,555		0.82		
Interdisciplinary Rehabilitation	$8,479	$5,924	1.01	0.18	$32,178
Conservative Care	$2,555		0.82		
Fusion	$25,297	$22,742	0.95	0.13	$181,211

NOTE: Fusion and conservative care estimates based on direct RCT-based comparison; estimates for interdisciplinary rehabilitation based on indirect comparisons of multiple RCTs
QALY: Quality-adjusted life year; ICER: Incremental cost-effectiveness ratio

Alternative Assumption Scenarios

Analyses Including Work Loss Costs

Lumbar Disc Herniation

In the ITT cost-effectiveness analysis based on medical care costs alone, microdiscectomy is more expensive and effective and has an ICER of $116,000. A cost-effectiveness analysis using total costs consisting of medical care costs and work loss costs is shown in Table 22. When work loss costs are included, microdiscectomy saves $1,134 and is more effective compared to conservative care.

In the AT analysis where there are no crossovers between interventions the work loss costs of conservative care ($14,249) were much larger than the medical care costs ($2,359) because conservative care does not include any surgical costs, and the work loss costs of microdiscectomy ($7,181) are smaller than the medical care costs ($13,699), because all patients incur the surgical costs. In the cost-effectiveness analysis based on medical care costs alone, microdiscectomy is more expensive and effective and has an ICER of $233,000. In the cost-effectiveness analysis including medical care costs *and* work loss costs, microdiscectomy remains more expensive and more effective, but the ICER is reduced to approximately $88,000 (Table 22 below).

Table 22. Cost-effectiveness analysis of management options for lumbar disc herniation based on medical care costs and work loss costs.

Strategy	Costs ($)	Incremental Costs ($)	Effectiveness (QALYs)	Incremental Effectiveness (QALYs)	ICER ($/QALYs)
Intention To Treat Analysis					
Conservative Care	$21,684		1.41		
Discectomy	$20,550	-$1,134	1.46	0.05	---
As Treated Analysis					
Conservative Care	$16,608		1.41		
Discectomy	$20,880	$4,272	1.46	0.05	$87,901

QALY: Quality-adjusted life year; ICER: Incremental cost-effectiveness ratio

Chronic Low Back Pain

In the ITT analysis for chronic low back pain there were fewer crossovers between interventions (9%to surgery and 8% to conservative care). The work loss costs of interdisciplinary rehabilitation and conservative care were substantially larger than the medical care costs. In the cost-effectiveness analysis based on medical care costs alone interdisciplinary rehabilitation is more expensive and effective than conservative care and has an ICER of $67,098. A cost-effectiveness analysis using total costs consisting of medical

care costs and work loss costs is shown in Table 23 below. When work loss costs are included interdisciplinary rehabilitation is still more expensive and more effective and has an ICER of $83,850. The minimal change in the cost-effectiveness of interdisciplinary rehabilitation that results from inclusion of work loss costs results from the failure of interdisciplinary rehabilitation to increase full-time or part-time employment in the clinical trial (Dufour, 2010).

In the AT analysis, the work loss costs of interdisciplinary rehabilitation and conservative care are also substantially larger than the medical care costs. In the cost-effectiveness analysis based on medical care costs only, interdisciplinary rehabilitation is more expensive and effective than conservative care and has an ICER of $32,178. In the cost-effectiveness analysis based on medical care costs and work loss costs, interdisciplinary rehabilitation remains somewhat more expensive and much more effective than conservative care, and has an ICER of approximately $40,000.

Table 23. Cost-effectiveness analysis of management options for chronic low back pain based on medical care costs and work loss costs.

Strategy	Costs ($)	Incremental Costs ($)	Effectiveness (QALYs)	Incremental Effectiveness (QALYs)	ICER ($/QALYs)
Intention To Treat Analysis					
Conservative Care	$64,501		0.88		
Interdisciplinary Rehabilitation	$71,754	$7,253	0.96	0.09	$83,850
Conservative Care	$64,501		0.88		
Fusion	$67,930	$3,429	0.94	0.06	$59,843
As Treated Analysis					
Conservative Care	$62,656		0.82		
Interdisciplinary Rehabilitation	$70,034	$7,378	1.01	0.18	$40,076
Conservative Care	$62,656		0.82		
Fusion	$70,018	$7,362	0.95	0.13	$58,661

NOTE: Fusion and conservative care estimates based on direct RCT-based comparison; estimates for interdisciplinary rehabilitation based on indirect comparisons of multiple RCTs
QALY: Quality-adjusted life year; ICER: Incremental cost-effectiveness ratio

In the cost-effectiveness analysis based on medical care costs alone, fusion is more expensive and more effective and has an ICER of ~$328,000. When work loss costs are included, fusion is more expensive and more effective compared to conservative care but the ICER falls to $59,843, resulting in a more desirable ratio. This lower ICER is due to the

benefits of fusion in increasing the proportion of patients who are working full-time or part-time.

In the AT analysis based on medical care costs alone, fusion is more expensive and effective than conservative care and has an ICER of approximately $180,000. In the cost-effectiveness analysis based on medical care costs and work loss costs, fusion is more expensive and more effective than conservative care but the ICER is approximately $59,000. Again, this lower ICER is due to the benefits of fusion in increasing the proportion of patients who return to work.

Simple Fusion vs. Complex Fusion for Degenerative Spondylolisthesis and Chronic Low Back Pain

Complex fusion has higher costs and complication rates compared to simple fusion. In the analyses comparing complex fusion to simple fusion, the effectiveness of complex fusion was assumed to be the same as the effectiveness of simple fusion as there are no stratifications of effectiveness by type of fusion in the published RCTs used as the basis for the ICER clinical and economic analysis of DS and CLBP.

Simple Fusion or Complex Fusion vs. Conservative Care for Degenerative Spondylolisthesis
In the intention-to-treat analysis for degenerative spondylolisthesis the medical care costs of simple fusion ($17,639) were higher than conservative care ($14,812) and the medical care costs of complex fusion ($25,714) were approximately 50% higher (see Table 24 below). The incremental costs of simple fusion compared to conservative care ($2,827) were lower than the incremental costs of complex fusion compared to conservative care ($5,425), while the incremental effectiveness of simple or complex fusion were assumed to be the same and were slightly less than the quality of life of conservative care. Thus for both simple fusion and complex fusion for degenerative spondylolisthesis, the intention-to-treat analysis found that either form of surgery was more expensive and less effective than conservative care.

Table 24. Cost-effectiveness of simple fusion or complex fusion compared to conservative care for degenerative spondylolisthesis.

Strategy	Costs ($)	Incremental Costs ($)	Effectiveness (QALYs)	Incremental Effectiveness (QALYs)	ICER ($/QALYs)
Simple Fusion vs. Conservative Care					
Conservative Care	$14,812		1.24		
Simple Fusion	$17,639	$2,827	1.22	-0.02	---
Complex Fusion vs. Conservative Care					
Conservative Care	$20,289		1.24		
Complex Fusion	$25,714	$5,425	1.22	-0.02	---

QALY: Quality-adjusted life year; ICER: Incremental cost-effectiveness ratio

Simple Fusion or Complex Fusion vs. Conservative Care for Chronic Low Back Pain
In the ITT analysis for chronic low back pain, the medical care costs of simple fusion ($23,208) were higher than for conservative care ($4,404); the medical care costs of complex fusion ($34,768) are higher still (see Table 25 below). The incremental costs of simple fusion compared to conservative care ($18,804) were lower than the incremental costs of complex fusion compared to conservative care ($29,540) while the incremental effectiveness was slightly worse. The ICER for complex fusion compared to conservative care was approximately $1.2 million per QALY gained, which was fourfold higher than the ICER of simple fusion compared to conservative care ($328,168); these findings therefore indicate a substantial cost for a modest benefit in both cases.

Table 25. Cost-effectiveness of simple fusion or complex fusion compared to conservative care for chronic low back pain.

Strategy	Costs ($)	Incremental Costs ($)	Effectiveness (QALYs)	Incremental Effectiveness (QALYs)	ICER ($/QALYs)
Simple Fusion vs. Conservative Care					
Conservative Care	$4,404		0.88		
Simple Fusion	$23,208	$18,804	0.94	0.06	$328,168
Complex Fusion vs. Conservative Care					
Conservative Care	$5,228		0.88		
Complex Fusion	$34,768	$29,540	0.90	0.02	$1,210,656

QALY: Quality-adjusted life year; ICER: Incremental cost-effectiveness ratio

8.5 Comparison of Results to Prior Health Economic Evaluations

Lumbar Disc Herniation

Previous economic evaluations of discectomy vs. conservative care that were based on RCTs or other prospective comparative studies produced estimates of cost-effectiveness for surgery that ranged from $17,000-$69,000 per QALY gained over 2-10 year timeframes (Malter, 1996; Hansson, 2007; Tosteson, 2008). Another study provided sufficient data to estimate the cost-effectiveness of discectomy to be approximately $47,000 per QALY based on a retrospective cohort of male truck drivers (Shvartzman, 1992).

In contrast, our cost-effectiveness analysis of early microdiscectomy compared to conservative care for lumbar disc herniation was based on a recent RCT (Peul, 2007), and estimated an incremental cost of $116,000 per QALY based on an intention-to-treat analysis (which experienced crossovers between study arms), and an incremental cost per QALY of $233,000 based on an analysis that assumed no crossovers. We used SF-36 scores to estimate quality of life. The study did not directly report as-treated outcomes, and the impact on quality of life is likely to have been underestimated. Perhaps most importantly, the short

duration (one year) of the RCT and the associated smaller gain in incremental QALYs may in part explain the higher ICERs observed in our analysis as compared to the other studies above.

Lumbar Spinal Stenosis with or without Degenerative Spondylolisthesis

We used clinical and cost-effectiveness information from the published data in the 2 year follow-up reports from the SPORT randomized controlled trial and observational cohort studies for lumbar spinal stenosis alone (Weinstein, 2007; Tosteson, 2008) and lumbar spinal stenosis with degenerative spondylolisthesis (Weinstein, 2008; Tosteson, 2008), as well as an RCT of the X-STOP interspinous spacer device (Zucherman, 2004) to estimate the cost-effectiveness of surgery and interspinous spacers compared to conservative care in both intention-to-treat and as-treated contexts. In our cost-effectiveness analysis for lumbar spinal stenosis, interspinous spacers had an incremental cost per QALY of $51,000 in the intention-to-treat analysis and $90,000 in the as-treated analysis vs. conservative care. Corresponding estimates for laminectomy were $258,000 and $101,000, respectively.

For degenerative spondylolisthesis the intention-to-treat analysis found that interspinous spacers were less expensive and had virtually the same effectiveness as conservative care. In contrast, fusion was more expensive and less effective than conservative care. In the as-treated analyses compared to conservative care, interspinous spacers had an incremental cost per QALY of $70,555 and fusion had an incremental cost per QALY of $163,000.

An economic evaluation was also conducted alongside the SPORT trial for lumbar spinal stenosis with and without degenerative spondylolisthesis (Tosteson, 2008), based on clinical, economic, and quality-of-life data obtained from the combined randomized and observational cohorts. Using our as-treated results as a guide for comparison, the incremental gain in QALYs for laminectomy and fusion over 2 years was slightly less than that generated by the SPORT model. Nevertheless, the 2-year cost-effectiveness ratios were similar for laminectomy in lumbar spinal stenosis alone ($101,000 vs. $78,000 in our analysis vs. SPORT) and fusion in lumbar spinal stenosis with degenerative spondylolisthesis ($163,000 vs. $116,000, respectively).

Another evaluation considered the cost-effectiveness of laminectomy, interspinous spacers, and nonsurgical care for lumbar spinal stenosis over a 2-year timeframe, using meta-analysis of SF-36 data in the literature to estimate the response to treatment (Burnett, 2010). As in our analysis, costs were estimated using Medicare reimbursements. Interestingly, for 1-level spinal stenosis, the incremental cost-effectiveness for spacers vs. conservative care in this study was essentially identical to our intention-to-treat estimate (~$51,000 per QALY gained). However, based on the method used in this study, laminectomy was found to be much more effective than either interspinous spacers or conservative care. In contrast, our study found spacers to be more effective than laminectomy based on the RCT data employed. As a result, the Burnett model found that, for 1-level disease, laminectomy produced ICERs in the $50,000-$100,000 range for comparisons to either conservative care or interspinous spacers. For 2-level disease, laminectomy was found to dominate spacers.

Chronic Low Back Pain

In our study of conservative care, interdisciplinary rehabilitation, or fusion for patients with chronic low back pain, we found that interdisciplinary rehabilitation had an incremental cost per QALY of $67,098 and fusion had an incremental cost per QALY of $328,168 in the intention-to-treat analysis. In the as-treated analysis, corresponding estimates were $32,178 and $181,211 per QALY respectively.

Unfortunately, the only other major cost-effectiveness analysis for this indication, while based on the same RCT used for our analysis, did not report effectiveness in terms of QALYs (Fritzell, 2004). Instead, findings were reported in terms of unit improvements in pain, function, patients' perceptions of improvement, and return to work. A re-analysis of data from our model for selected outcomes shows similar findings. For example, the Fritzell model reported an incremental cost-effectiveness for fusion, based on a societal perspective, of 11,300 Swedish kroner (SEK) ($1,366) per 1-point change on the ODI; data from our analysis suggests this value would be $2,614 ($846 with work-loss costs included). Similarly, the cost per 1% improvement in return to work was 4,100 SEK ($496) in the Fritzell study, and would have been $1,034 in ours ($335 with work-loss costs included). This similarity is not surprising, given that the 2 models share the same source of effectiveness data, and would therefore differ primarily in terms of estimation of costs.

9. Recommendations for Future Research

As documented in this appraisal report, despite the high prevalence, clinical significance, and economic impact of low back disorders, syntheses of all the available medical literature continue to highlight many notable areas of uncertainty that hinder comparisons of the clinical effectiveness and value of major management options. In part the uncertainty is driven by the fact that "low back pain" is not a specific disease or condition; it is a symptom experienced by most adults at some time and reflects a wide spectrum of often-intersecting physical and emotional features. The symptoms patients experience in the lower back, sometimes including pain in the sciatic distribution of the hips and legs, are poorly correlated with specific physical or radiological findings. Given that it is often difficult to pinpoint the exact pathophysiology of low back pain and functional disability, and that symptoms are often linked to psychosocial factors and work environments that differ widely across communities, it is challenging to identify studies of "comparable" populations of patients to allow evidence synthesis to make generalizable conclusions about treatment effectiveness.

The ability to study the comparative effectiveness of treatments for low back disorders is also complicated by the fact that the natural history of low back pain and disability is one of general improvement for many patients. If most patients are getting better no matter what is done for them, it becomes difficult to demonstrate that any intervention is better than usual care, even if that intervention seems to work much better for some patients. In addition, patients in clinical trials who do not improve on the first treatment option they receive often try other interventions. Such complexities mean that comparative studies must be very large and of long duration in order to have any hope of evaluating clinically-meaningful differences in patient outcomes, while the presence of high rates of crossover to other interventions creates an intractable problem in interpreting the results of even the best comparative studies.

These challenges make low back disorders one of the most difficult of common conditions to evaluate in clinical trials. But progress has been hindered by another factor as well: the lack of collaboration among clinical investigators, manufacturers, payers, and patients to create standards for definitions of patient characteristics and clinical outcome measures that will allow robust comparisons across studies of different interventions. Too often the clinical characteristics of enrolled patients are recorded in ways that make it impossible to judge whether two studies had "comparable" patients. Also common are differences in the timing of the measurement of patient outcomes, creating a mixed bag of studies that have outcomes at different points of time, creating another barrier to attempts to merge or even compare results across trials. Perhaps the most consequential research recommendation of this appraisal, therefore, is that efforts are needed to bring all stakeholders together to forge a new consensus moving forward around what will be considered high-quality research designs and standards for consistent definitions of patient characteristics, outcome measures, and for the timing and mechanism of outcome measurement. If these kinds of standards can be achieved it will go a long way toward improving the future bodies of evidence that will support decisions by patients, clinicians, and policy makers.

General Recommendations for All Research on Low Back Disorders

Informed by the evidence gaps highlighted by our systematic review, and also guided by input from our national Evidence Review Group, we present below high-level recommendations for all research on low back disorders.

1. Efforts should be initiated to bring all stakeholders together at the inception of the planning of a research program in order to clarify the scope and goals of the research and to come to broad consensus on: 1) the methods to characterize patients at the time of recruitment; 2) the minimum duration of time over which to measure meaningful outcomes; 3) the timing of outcome measurement to enable pooling of data from disparate studies; and 4) the outcome measures to be used, including some version of a dichotomous patient-reported outcome of "satisfactory/unsatisfactory results."

2. All trials should directly assess quality of life by validated instruments such as the EQ-5D.

3. Whenever possible, studies should capture healthcare utilization and cost outcomes.

4. More trials are needed of different methods of early stratification of patients to enable better evaluation of the relative benefits of treatments for specific patient subpopulations.

5. More trials are needed of treatment "pathways" or "algorithms" that would characterize care for patients who need more than an initial form of treatment. In particular, more trials are needed of combinations of non-surgical interventions for all forms of low back disorders.

6. Guidelines are needed to define the characteristic components of "interdisciplinary" rehabilitation programs so that research on different approaches can be categorized and compared with greater confidence.

7. More trials are needed of patient preferences for different types of treatment options and how these preferences correlate with treatment outcomes.

8. More trials are needed in more broadly representative patient populations, including patients with low back pain of shorter duration (2-6 months) and among clinical providers in the community, not just the elite practitioners at top academic sites.

9. Long-term observational registries and other studies are necessary to gain a better understanding of treatment-related harms, requirements for retreatment and additional treatment, and real-world healthcare utilization.

Specific research recommendations: Lumbar disc herniation

1. Randomized controlled trials are needed to evaluate automated percutaneous lumbar discectomy and interdisciplinary rehabilitation for this patient population. Further RCTs of coblation nucleoplasty are needed as well. Comparator arms of such trials can include either well-defined "usual care" that mirrors community practice, or it may include sham interventions. Both forms of RCTs provide valuable information for patients, clinicians, and policy makers. If usual care is the comparator, patients should be selected for randomization before they are at a stage at which they feel that they have "failed" usual care already.

2. The evidence on epidural steroid injections is very heterogeneous and does not suggest comparative benefit beyond 3-6 months. If further studies of ESI for disc herniation are performed, it will be important to measure all key outcomes for a minimum of 1-2 years.

Specific research recommendations: Lumbar **spinal stenosis**

1. Trials are needed evaluating the effectiveness of interdisciplinary rehabilitation programs among patients with milder forms of spinal stenosis.

2. Randomized controlled trials are needed of laminectomy plus posterolateral fusion versus interbody fusion for degenerative spinal stenosis and spondylolisthesis.

3. Randomized controlled trials of interspinous spacers versus laminectomy are needed. At a minimum, future trials of spacer systems should employ entry criteria similar to those employed in the seminal laminectomy studies.

4. Studies are needed that are large enough for subgroup analyses that can help identify predictors of "success" with certain interventions for specific subgroups of patients. For example:
    a. Which clinical characteristics predict greater success of surgery vs. non-surgical treatment for spinal stenosis? Does success correlate with physical characteristics (e.g. degree of stenosis) and/or with psychosocial characteristics (e.g. patient expectations)?

Specific research recommendations: Degenerative spondylolisthesis

1. Randomized controlled trials are needed of laminectomy plus posterolateral fusion versus interbody fusion for degenerative spinal stenosis and spondylolisthesis.

2. RCTs of instrumented vs. non-instrumented fusion for degenerative spondylolisthesis would be ideal but may not be practical. Clinical registries with careful notation of clinical and psychosocial patient characteristics prior to surgery

could be useful in understanding patient characteristics associated with better overall outcomes with various techniques.

3. Randomized controlled trials of interspinous spacers versus fusion are needed. At a minimum, future trials of spacer systems should employ entry criteria similar to those employed in the seminal laminectomy studies.

Specific research recommendations: Chronic non-specific low back pain

1. A critical issue that requires further study is the role of screening protocols in triaging patients toward targeted treatments. For example, evidence exists to demonstrate that patients with poorer physical function and, in particular, those with psychological factors such as increased fear of activity, psychological distress, and negative feelings about back pain, are more disabled by their pain, and are more likely to have a poor outcome with conservative care. Randomized controlled trials and large clinical registries could both play a part in helping to evaluate the outcomes of systems of patient identification and treatment targeting.

2. Studies are needed that capture the long-term outcomes associated with narcotic use for patients with chronic low back pain syndromes.

3. Randomized controlled trials are needed of educational interventions for patients with chronic non-specific low back pain. Extensive research literature addresses the education of adults using a wide variety of techniques, but studies of patient education for people with low back pain have focused almost exclusively on written information. Little evidence is available as to whether such materials are the most effective way to deliver educational goals. Interdisciplinary projects combining educational and healthcare research methodologies should:
    a. identify appropriate goals and techniques for the education of people with low back pain;
    b. determine efficacy in achieving educational goals;
    c. determine effects on clinical outcomes, including pain, distress and disability.

4. As noted earlier, studies are needed of defined protocols of sequential therapies (manual therapy, exercise and acupuncture) compared with single interventions with respect to pain, functional disability and psychological distress in people with chronic non-specific low back pain. It is unclear whether there is added health gain for this subgroup from either multiple or sequential use of therapies. Research should test the effect of providing a subsequent course of a different therapy (manual therapy, exercise or acupuncture) in the management of persistent non-specific low back pain, when the first-choice therapy has been inadequately effective.

5. More research is required to develop relevant assessments of physical capacity and functional performance in patients with chronic non-specific low back pain, in order to better understand the relationship between self-rated disability, physical capacity and physical impairment.

6. Further research is needed to evaluate specific components of treatments commonly used by physical therapists, by comparing their individual and combined use. The combination of certain passive physical treatments for symptomatic pain relief with more "active" treatments aimed at reducing disability (e.g. massage, hot packs or TENS together with exercise therapy) should be further investigated. The application of cognitive behavioral principles to physiotherapy in general needs to be evaluated.

7. The effectiveness of specific types of exercise therapy needs to be further evaluated. This includes the evaluation of spinal stabilization exercises, McKenzie exercises, and other popular exercise regimens that are often used but inadequately researched. The optimal intensity, frequency and duration of exercise should be further researched, as should the issue of individual versus group exercises. The "active ingredient" of exercise programs remains largely unknown.

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APPENDIX A

LITERATURE SEARCH STRATEGY

De Novo Abstraction Search Strategy (OVID)

Databases:

- Ovid Medline(R) 1996 to Present with Daily Update
- Ovid MEDLINE(R) 1950 to Present with Daily Update
- Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations

The Disorder –Low Back Pain

1. (((low$ adj2 back) or (low$ adj2 lumbar) or (low$ adj2 spin$)) adj pain).mp.
2. exp Low Back Pain/
3. 1 or 2
4. limit 3 to (english language and humans and yr="2000 -Current")

To cross-reference with all of the following:

A. Spinal Injections

5. spinal injections.mp. or exp Injections, Spinal/
6. ((Intra-spin$ or Intraspin$) adj4 (Inject$ or steroid$)).mp.
7. (epidural$ adj4 (steroid$ or inject$)).mp.
8. (facet$ adj4 (steroid$ or inject$)).mp.
9. ((sacro-iliac or sacroiliac) adj4 (steroid$ or inject$)).mp.
10. ((intra-disc$ or intradisc$) adj4 (steroid$ or inject$)).mp.
11. nerve block$.mp. or exp Nerve Block/
12. (medial$ adj4 block$).mp.
13. (sympathetic adj4 block$).mp.
14. (select$ adj4 block$).mp.
15. exp Intervertebral Disk Chemolysis/
16. (Chemo-nucleo$ or chemonucleo$).mp.
17. 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16
18. 4 and 17
19. remove duplicates from 18

B. RF Denervation

5. exp Denervation/
6. ((radio-freq$ or radiofreq$) adj4 denerv$).mp.
7. 5 or 6
8. 4 and 7
9. remove duplicates from 8

C. IDET

5. ((intra-disc$ or intradisc$) adj4 (electrotherm$ or electro-therm$)).mp.
6. 4 and 5
7. remove duplicates from 6

D. Interspinous Spacers

5. ((inter-spin$ or interspin$) adj4 (spacer$ or device$ or implant$)).mp.
6. 4 and 5
7. remove duplicates from 6

E. Discectomy

5. discectomy.mp. or exp Diskectomy/
6. $discectom$.mp.
7. $diskectom$.mp.
8. 5 or 6 or 7
9. 4 and 8
10. remove duplicates from 9

F. Multi-disciplinary Care Program

5. ((multidisciplin$ or multi-disciplin$) adj7 (therap$ or care$ or program$ or rehab$)).mp.
6. ((interdisciplin$ or inter-disciplin$) adj7 (therap$ or care$ or program$ or rehab$)).mp.
7. (integrat$ adj7 (therap$ or care$ or program$ or rehab$)).mp.
8. (intens$ adj7 (therap$ or care$ or program$ or rehab$)).mp.
9. 5 or 6 or 7 or 8
10. 4 and 9
11. remove duplicates from 10

G. Pathways of Care

5. ((treatment$ or care$ or therap$ or clinical$) adj4 (pathway$ or algorithm$)).mp.
6. 4 and 5
7. remove duplicates from 6

De Novo Abstraction Search Strategy (EMBASE)

Database:

- EMBASE

The Disorder –Low Back Pain

1. low* AND ('back'/exp OR back) AND ('pain'/exp OR pain)
2. 'low back pain'/exp OR 'low back pain'
3. low* NEXT/2 back OR low* NEXT/2 lumbar OR low* NEXT/2 spin*
4. #1 OR #2 OR #3
5. #4 AND [humans]/lim AND [english]/lim AND [2000-2011]/py

To cross-reference with all of the following:

A. Spinal Injections

6. spinal AND injection*
7. spin* AND inject*
8. intraspin* NEXT/4 (inject* OR steroid*)
9. (intraspinous OR 'intra spinous') NEXT/4 (inject* OR steroid*)
10. (intraspinal OR 'intra spinal') NEXT/4 (inject* OR steroid*)
11. epidural NEXT/4 (steroid* OR inject*)
12. facet* NEXT/4 (inject* OR steroid*)
13. ('sacro iliac' OR sacroiliac) NEXT/4 (inject* OR steroid*)
14. (intradiscal OR 'intra-discal') NEXT/4 (inject* OR steroid*)
15. (intradiskal OR 'intra diskal') NEXT/4 (inject* OR steroid*)
16. 'nerve block'/exp OR 'nerve block'
17. medial* NEXT/4 block*
18. sympathetic NEXT/4 block*
19. select* NEXT/4 block*
20. 'intervertebral disk chemolysis'/exp OR 'intervertebral disk chemolysis'
21. chemonucleo*
22. chemo AND nucleo*
23. #6 OR #7 OR #8 OR #9 OR #11 OR #12 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22
24. #5 AND #23

B. RF Denervation

6. 'denervation'/exp OR denervation
7. 'radiofrequency'/exp OR radiofrequency AND ('denervation'/exp OR denervation)
8. 'radiofrequency denervation'
9. radiofreq* NEXT/4 denerv*
10. radio* NEXT/4 denerv*
11. #6 OR #7 OR #8 OR #9 OR #10
12. #5 AND #11

C. IDET

6. 'intradiscal electrothermal therapy'/exp OR 'intradiscal electrothermal therapy'
7. intra* NEXT/4 electro*
8. #6 OR #7
9. #5 AND #8

D. Interspinous Spacers

6. 'interspinous spacers'
7. inter* NEXT/4 spacer*
8. inter* NEXT/4 device*
9. inter* NEXT/4 implant*
10. #6 OR #7 OR #8 OR #9
11. #5 AND #10

E. Discectomy

6. 'diskectomy intervertebral'/exp OR 'diskectomy intervertebral'
7. 'discectomy'/exp OR 'discectomy'
8. #6 OR #7
9. #5 AND #8

F. Multi-disciplinary Care Program

6. ('multi-disciplinary' OR multidisciplinary) NEXT/7 (therap* OR care* OR program* OR rehab*)
7. ('multi-disciplined' OR multidisciplined) NEXT/7 (therap* OR care* OR program* OR rehab*)
8. ('multi-discipline' OR multidiscipline) NEXT/7 (therap* OR care* OR program* OR rehab*)
9. ('inter-disciplinary' OR interdisciplinary) NEXT/7 (therap* OR care* OR program* OR rehab*)
10. ('inter-disciplined' OR interdisciplined) NEXT/7 (therap* OR care* OR program* OR rehab*)
11. ('inter-discipline' OR interdiscipline) NEXT/7 (therap* OR care* OR program* OR rehab*)
12. integrat* NEXT/7 (therap* OR care* OR program* OR rehab*)
13. intens* NEXT/7 (therap* OR care* OR program* OR rehab*)
14. #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13
15. #5 AND #14

G. Pathways of Care

6. (treat* OR care* OR therap* OR clinical*) NEXT/4 (pathway* OR algorithm*)
7. #5 AND #6

De Novo Abstraction Search Strategy (EBM Reviews)

Databases:

- EBM Reviews - Cochrane Database of Systematic Reviews 2005 to October 2010
- EBM Reviews - Database of Abstracts of Reviews of Effects 3rd Quarter 2010
- EBM Reviews - Health Technology Assessment 4th Quarter 2010
- EBM Reviews - Cochrane Central Register of Controlled Trials 4th Quarter 2010
- EBM Reviews - NHS Economic Evaluation Database 4th Quarter 2010

The Disorder –Low Back Pain

1. (Low$ adj2 (back or spin$ or vert$ or lumbar)).mp.
2. (((low$ adj3 back) or (low$ adj3 lumbar) or (low$ adj3 spin$)) adj7 (pain or disorder$)).mp.
3. 1 or 2
4. limit 3 to (english language and humans and yr="2000 -Current")

[Limit not valid in CDSR,DARE,CCTR; records were retained]

To cross-reference with all of the following:

A. Spinal Injections

5. (spin$ adj7 inject$).mp.
6. ((Intra-spin$ or Intraspin$) adj4 (Inject$ or steroid$)).mp.
7. (epidural$ adj4 (steroid$ or inject$)).mp.
8. (facet$ adj4 (steroid$ or inject$)).mp.
9. ((sacro-iliac or sacroiliac) adj4 (steroid$ or inject$)).mp.
10. ((intra-disc$ or intradisc$) adj4 (steroid$ or inject$)).mp.
11. (nerve adj7 block$).mp.
12. (medial$ adj4 block$).mp.
13. (sympathetic adj4 block$).mp.
14. (select$ adj4 block$).mp.
15. ((Inter-verteb$ or Interverteb$) adj7 Dis$ adj7 Chemo$).mp.
16. (Chemo-nucleo$ or chemonucleo$).mp.
17. 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16
18. 4 and 17
19. remove duplicates from 18

B. RF Denervation

5. denerv$.mp.
6. ((radio-freq$ or radiofreq$) adj4 denerv$).mp.
7. 5 or 6
8. 4 and 7
9. remove duplicates from 8

C. IDET

5. ((intra-disc$ or intradisc$) adj7 (electrotherm$ or electro-therm$)).mp.
6. 4 and 5
7. remove duplicates from 6

D. Interspinous Spacers

5. ((inter-spin$ or interspin$) adj4 (spacer$ or device$ or implant$)).mp.
6. 4 and 5
7. remove duplicates from 6

E. Discectomy

5. (discectomy or diskectomy).mp.
6. $diskectom$.mp.
7. $discectom$.mp.
8. 5 or 6 or 7
9. 4 and 8
10. remove duplicates from 9

F. Multi-disciplinary Care Program

5. ((multidisciplin$ or multi-disciplin$) adj7 (therap$ or care$ or program$ or rehab$)).mp.
6. ((interdisciplin$ or inter-disciplin$) adj7 (therap$ or care$ or program$ or rehab$)).mp.
7. (integrat$ adj7 (therap$ or care$ or program$ or rehab$)).mp.
8. (intens$ adj7 (therap$ or care$ or program$ or rehab$)).mp.
9. 5 or 6 or 7 or 8
10. 4 and 9
11. remove duplicates from 10

G. Pathways of Care

5. ((treatment$ or care$ or therap$ or clinical$) adj4 (pathway$ or algorithm$)).mp.
6. 4 and 5
7. remove duplicates from 6

Systematic Review Search Strategy (OVID)

Databases:

- Ovid Medline(R) 1996 to Present with Daily Update
- Ovid MEDLINE(R) 1950 to Present with Daily Update
- Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations

The Disorder –Low Back Pain

1. (((low$ adj2 back) or (low$ adj2 lumbar) or (low$ adj2 spin$)) adj pain).mp.
2. exp Low Back Pain/
3. 1 or 2
4. limit 3 to (english language and humans and yr="2000 -Current")

To cross-reference with all of the following:

A. Laminectomy

5. laminectomy.mp. or exp Laminectomy/
6. exp Decompression, Surgical/ or open decompression.mp.
7. 5 or 6
8. 4 and 7
9. meta-analysis.mp. or exp Meta-Analysis/
10. (cochrane or medline).tw.
11. search$.tw.
12. 9 or 10 or 11
13. "Review Literature as Topic"/ or systematic review.mp.
14. 12 or 13
15. 8 and 14
16. remove duplicates from 15

B. Spinal Fusion

5. spinal fusion.mp. or exp Spinal Fusion/
6. (verteb$ adj3 fusion).mp.
7. 5 or 6
8. 4 and 7
9. meta-analysis.mp. or exp Meta-Analysis/
10. (cochrane or medline).tw.
11. search$.tw.
12. 9 or 10 or 11
13. "Review Literature as Topic"/ or systematic review.mp.
14. 12 and 13
15. 8 and 14
16. remove duplicates from 15

C. Conservative Care

5. (conservative adj4 (care or manage$ or treat$)).mp. [mp=ti, ab, tx, kw, ct, ot, sh, hw]
6. (yoga or acupuncture or cognitive behavioral therap$ or physical therap$ or spin$ manipulat$ or progressive relax$ or exercise therap$ or massage or function$ restorat$ or (Complement$ adj2 Alternat$) or non-pharm$ or nonpharm$).mp.
7. (pharm$ or acetaminophen or NSAIDs or (antidepress$ or anti-depress$) or benzodiazepin$ or (antiepilep$ or anti-epilep$) or (musc$ adj3 relax$) or (opioid adj2 analgesic$) or tramadol or (systemic adj2 corticosteroid$) or ((dual-medicat$ or dualmedicat$) adj2 therap$)).mp.
8. 5 or 6 or 7
9. 4 and 8
10. meta-analysis.mp. or exp Meta-Analysis/
11. (cochrane or medline).tw.
12. search$.tw.
13. 10 or 11 or 12
14. "Review Literature as Topic"/ or systematic review.mp.
15. 13 or 14
16. 9 and 15
17. remove duplicates from 16

Systematic Review Search Strategy (EBM Reviews)

Databases:

- EBM Reviews - Cochrane Database of Systematic Reviews 2005 to October 2010
- EBM Reviews - Database of Abstracts of Reviews of Effects 3rd Quarter 2010
- EBM Reviews - Health Technology Assessment 4th Quarter 2010
- EBM Reviews - Cochrane Central Register of Controlled Trials 4th Quarter 2010
- EBM Reviews - NHS Economic Evaluation Database 4th Quarter 2010

The Disorder –Low Back Pain

1. (Low$ adj2 (back or spin$ or vert$ or lumbar)).mp.
2. (((low$ adj3 back) or (low$ adj3 lumbar) or (low$ adj3 spin$)) adj7 (pain or disorder$)).mp.
3. 1 or 2
4. limit 3 to (english language and humans and yr="2000 -Current")

[Limit not valid in CDSR,DARE,CCTR; records were retained]

To cross-reference with all of the following:

A. Laminectomy

5. laminectomy.ti,ab.
6. (open adj4 decompress$).ti,ab.
7. decompress$.ti,ab.
8. 5 or 6 or 7
9. 4 and 8
10. remove duplicates from 9

B. Spinal Fusion

5. ((spin$ or verteb$ or lumbar) adj4 fus$).ti,ab.
6. 4 and 5
7. remove duplicates from 6

C. Conservative Care

5. (conservative adj4 (care or manage$ or treat$)).ti,ab.
6. (yoga or acupuncture or cognitive behavioral therap$ or physical therap$ or spin$ manipulat$ or progressive relax$ or exercise therap$ or massage or function$ restorat$ or (Complement$ adj2 Alternat$) or non-pharm$ or nonpharm$).ti,ab.
7. (pharm$ or acetaminophen or NSAIDs or (antidepress$ or anti-depress$) or benzodiazepin$ or (antiepilep$ or anti-epilep$) or (musc$ adj3 relax$) or (opioid adj2 analgesic$) or tramadol or (systemic adj2 corticosteroid$) or ((dual-medicat$ or dualmedicat$) adj2 therap$)).ti,ab.
8. 5 or 6 or 7
9. 4 and 8
10. remove duplicates from 9

Background Information Search Strategy (OVID)

Databases:

- Ovid Medline(R) 1996 to Present with Daily Update
- Ovid MEDLINE(R) 1950 to Present with Daily Update
- Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations

The Disorder –Low Back Pain

1. (((low$ adj2 back) or (low$ adj2 lumbar) or (low$ adj2 spin$)) adj pain).mp.
2. exp Low Back Pain/
3. 1 or 2
4. limit 3 to (english language and humans and yr="2000 -Current")

To cross-reference with all of the following:

A. Episodes of Care

5. episode$ of care.mp. or exp "Episode of Care"/
6. 4 and 5
7. remove duplicates from 6

Background Information Search Strategy (EMBASE)

Database:

- EMBASE

The Disorder –Low Back Pain

1. low* AND ('back'/exp OR back) AND ('pain'/exp OR pain)
2. 'low back pain'/exp OR 'low back pain'
3. low* NEXT/2 back OR low* NEXT/2 lumbar OR low* NEXT/2 spin*
4. #1 OR #2 OR #3
5. #4 AND [humans]/lim AND [english]/lim AND [2000-2011]/py

To cross-reference with all of the following:

A. Episodes of Care

6. episode AND of AND care
7. episode* NEXT/4 care
8. #6 OR #7
9. #5 AND #8

Background Information Search Strategy (EBM Reviews)

Databases:

- EBM Reviews - Cochrane Database of Systematic Reviews 2005 to October 2010
- EBM Reviews - Database of Abstracts of Reviews of Effects 3rd Quarter 2010
- EBM Reviews - Health Technology Assessment 4th Quarter 2010
- EBM Reviews - Cochrane Central Register of Controlled Trials 4th Quarter 2010
- EBM Reviews - NHS Economic Evaluation Database 4th Quarter 2010

The Disorder –Low Back Pain

1. (Low$ adj2 (back or spin$ or vert$ or lumbar)).mp.
2. (((low$ adj3 back) or (low$ adj3 lumbar) or (low$ adj3 spin$)) adj7 (pain or disorder$)).mp.
3. 1 or 2
4. limit 3 to (english language and humans and yr="2000 -Current")

[Limit not valid in CDSR,DARE,CCTR; records were retained]

To cross-reference with all of the following:

A. Episodes of Care

5. (episode$ adj4 care).ti,ab.
6. 4 and 5

APPENDIX B

STUDY QUALITY RATING CRITERIA

Quality Rating System for Systematic Reviews*

Criteria for Assessing Scientific Quality of Research Reviews*	Operationalization of Criteria
	The purpose of this index is to evaluate the scientific quality (i.e., adherence to scientific principles) of research overviews (review articles) published in the medical literature. It is not intended to measure literary quality, importance, relevance, originality, or other attributes of overviews.
	The index is for assessing overviews of primary ("original") research on pragmatic questions regarding causation, diagnosis, prognosis, therapy, or prevention. A research overview is a survey of research. The same principles that apply to epidemiologic surveys apply to overviews: A question must be clearly specified; a target population identified and accessed; appropriate information obtained from that population in an unbiased fashion; and conclusions derived, sometimes with the help of formal statistical analysis, as is done in meta-analyses. The fundamental difference between overviews and epidemiologic studies is the unit of analysis, not the scientific issues that the questions in this index address.
1. Were the search methods reported? *Were the search methods used to find evidence (original research) on the primary questions stated?* "Yes" if the review states the databases used, date of most recent searches, and some mention of search terms.	Because most published overviews do not include a methods section, it is difficult to answer some of the questions in the index. Base your answers, as much as possible, on information provided in the overview. If the methods that were used are reported incompletely relative to a specific question, score it as "can't tell," unless there is information in the overview to suggest that the criterion was or was not met.
2. Was the search comprehensive? *Was the search for evidence reasonably comprehensive?* "Yes" if the review searches at least 2 databases and looks at other sources (e.g., reference lists, hand searches, queries of experts).	
3. Were the inclusion criteria reported? *Were the criteria used for deciding which studies to include in the overview reported?*	
4. Was selection bias avoided? *Was bias in the selection of studies avoided?* "Yes" if the review reports how many studies were identified by searches, numbers excluded, and appropriate reasons for excluding them (usually because of predefined inclusion/exclusion criteria).	
5. Were the validity criteria reported? *Were the criteria used for assessing the validity of the included studies reported?*	
6. Was validity assessed appropriately? *Was the validity of all the studies referred to in the text assessed by using appropriate criteria (either in selecting studies for inclusion or in analyzing the studies that are cited)?* "Yes" if the review reports validity assessment and did some type of analysis with it (e.g., sensitivity analysis of results according to quality ratings, excluded low-quality studies).	
7. Were the methods used to combine studies reported? *Were the methods used to combine the findings of the relevant studies (to reach a conclusion) reported?* "Yes" for studies that did qualitative analysis if report mentions that quantitative analysis was not possible and reasons that it could not be done, or if "best evidence" or some other grading of evidence scheme used.	
8. Were the findings combined appropriately? *Were the findings of the relevant studies combined appropriately relative to the primary question the overview addresses?* "Yes" if the review performs a test for heterogeneity before pooling or does appropriate subgroup testing, appropriate sensitivity analysis, or other such analysis.	For question 8, if no attempt has been made to combine findings, and no statement is made regarding the inappropriateness of combining findings, check "No." If a summary (general) estimate is given anywhere in the abstract, the discussion, or the summary section of the paper, and it is not reported how that estimate was derived, mark "No" even if there is a statement regarding the limitations of combining the findings of the studies reviewed. If in doubt, mark "Can't tell."
9. Were the conclusions supported by the reported data? *Were the conclusions made by the author(s) supported by the data and/or analysis reported in the overview?*	For an overview to be scored as "Yes" in question 9, data (not just citations) must be reported that support the main conclusions regarding the primary question(s) that the overview addresses.
10. What was the overall scientific quality of the overview? *How would you rate the scientific quality of this overview?*	The score for question 10, the overall scientific quality, should be based on your answers to the first 9 questions. The following guidelines can be used to assist with deriving a summary score: If the "Can't tell" option is used 1 or more times on the preceding questions, a review is likely to have minor flaws at best and it is difficult to rule out major flaws (i.e., a score ≤4). If the "No" option is used on question 2, 4, 6, or 8, the review is likely to have major flaws (i.e., a score ≤3, depending on the number and degree of the flaws).

Scoring: Each Question Is Scored as Yes, Partially/Can't Tell, or No

Extensive Flaws		Major Flaws		Minor Flaws		Minimal Flaws
1	2	3	4	5	6	7

* Operationalization of the Oxman criteria (19), adapted from reference (20).

*Adapted from American Pain Society/American College of Physicians Clinical Practice Guidelines on Low Back Pain (Chou 2007)

Quality Rating System for Randomized, Controlled Trials*

Criteria List for Assessment of Methodologic Quality†	Operationalization of Criteria	Score
A. Was the method of randomization adequate?	A random (unpredictable) assignment sequence. An example of adequate methods is a computer-generated random-number table and use of sealed opaque envelopes. Methods of allocation using date of birth, date of admission, hospital numbers, or alternation should not be regarded as appropriate.	Yes/No/Don't Know
B. Was the treatment allocation concealed?	Assignment generated by an independent person not responsible for determining the eligibility of the patients. This person has no information about the persons included in the trial and has no influence on the assignment sequence or on the decision about eligibility of the patient.	Yes/No/Don't Know
C. Were the groups similar at baseline regarding the most important prognostic factors? *"Yes", if similar:* *Age and sex* *Description of type of pain* *Intensity, duration, or severity of pain*	To receive a "yes," groups have to be similar at baseline regarding demographic factors, duration or severity of symptoms, percentage of patients with neurologic symptoms, and value of main outcome measure(s).	Yes/No/Don't Know
D. Was the patient blinded to the intervention?	The reviewer determines whether enough information about the blinding is given in order to score a "yes." Use the author's statement on blinding, unless there is a differing statement/reason not to (no need for explicit information on blinding).	Yes/No/Don't Know
E. Was the care provider blinded to the intervention?		Yes/No/Don't Know
F. Was the outcome assessor blinded to the intervention?		Yes/No/Don't Know
G. Were co-interventions avoided or similar?	Co-interventions should be avoided in the trial design or similar between the index and control groups.	Yes/No/Don't Know
H. Was adherence acceptable in all groups?	The reviewer determines whether adherence to the interventions is acceptable, based on the reported intensity, duration, number, and frequency of sessions for both the index intervention and control intervention(s).	Yes/No/Don't Know
I. Was the dropout rate described and acceptable? *≤15% dropout rate is acceptable*	The number of participants who are included in the study but did not complete the observation period or were not included in the analysis must be described and reasons given. If the percentage of withdrawals and dropouts does not exceed 15% and does not lead to substantial bias, a "yes" is scored.	Yes/No/Don't Know
J. Was the timing of the outcome assessment in all groups similar?	Timing of outcome assessment should be identical for all intervention groups and for all important outcome assessments.	Yes/No/Don't Know
K. Did the analysis include an intention-to-treat analysis? *"Yes," if <5% of randomly assigned patients excluded*	All randomly assigned patients are reported/analyzed in the group they were allocated to by randomization for the most important moments of effect measurement (minus missing values), irrespective of nonadherence and co-interventions.	Yes/No/Don't Know

* This list includes only the 11 internal validity criteria that refer to characteristics of the study that might be related to selection bias (criteria A and B), performance bias (criteria D, E, G, and H), attrition bias (criteria I and K), and detection bias (criteria F and J). The internal validity criteria should be used to define methodological quality in the meta-analysis.
† Adapted from methods developed by the Cochrane Back Review Group (24).

*Adapted from American Pain Society/American College of Physicians Clinical Practice Guidelines on Low Back Pain (Chou 2007)

APPENDIX C

SYSTEMATIC REVIEW EVIDENCE TABLES

Table 1a: Study characteristics and main outcomes of systematic reviews for the herniated disc population, by type of treatment

Treatment Type	Author	Year	# of Studies	Eligibility Criteria	Main Results	Quality Rating	Comments
APLD	Hirsch	2009	80	Inclusion: LBP >=3 months; Treatment with APLD; >= 12 months follow-up; >= 50 patients included in observational studies	Based on USPSTF criteria, the indicated evidence for APLD is Level II-2 for short- and long-term relief	5	
	Singh	2009	33	Inclusion: LBP >= 3 months; treatment with percutaneous laser disc decompression; >= 12 month follow-up; >= 50 patients included in observational studies	Based on USPSTF criteria, the indicated evidence for percutaneous lumbar laser discectomy (PLLD) is II-2 for short- and long-term relief	5	
	Watters	2009	25	Inclusion: Patients with primary lumbar disc herniation with radiculopathy	Fair Evidence: conservative discectomy results in shorter operating times and quicker return-to-work then aggressive discectomy; similar pain levels at discharge, similar 6-month functional status, and similar 2-year incidence of persistent/recurrent back pain Poor Evidence: conservative discectomy will result in a lower incidence of recurrent back pain beyond 2 years post-operatively	4	
Coblation Nucleoplasty	Manchikanti	2009	16	Inclusion: LBP >= 3 months duration; mechanical disc decompression with nucleoplasty; >= 12 month follow-up; >= 50 patients included in observational studies	Based on USPSTF criteria, the level of evidence for nucleoplasty is Level II-3 in managing predominantly lower extremity pain due to contained disc herniation	4	

APLD: Automated Percutaneous Lumbar Discectomy; USPSTF: United States Preventive Services Task Force; LBP: Low Back Pain

Table 1a: Study characteristics and main outcomes of systematic reviews for the herniated disc population, by type of treatment

Treatment Type	Author	Year	# of Studies	Eligibility Criteria	Main Results	Quality Rating	Comments
Discectomy	Gibson	2007	42	Inclusion: All RCTs or quasi-RCTs pertinent to the surgical management of lumbar disc prolapse; Patients with lumbar disc prolapse who have indications for surgical intervention.	Discectomy produces better clinical outcomes than chemonucleolysis, and that in turn is better than placebo. Microdiscectomy gives broadly comparable results to standard discectomy. There is insufficient evidence about the effect on clinical outcomes. There is insufficient evidence on other percutaneous discectomy techniques to draw firm conclusions. Three small RCTs of laser discectomy do not provide conclusive evidence on its efficacy. There are no published RCTs of coblation therapy or transforaminal endoscopic discectomy	4	
	Chou	2009	84	Inclusion: LBP of any duration, alone or with leg pain; evaluated surgery for nonradicular LBP with common degenerative changes, radiculopathy with herniated lumbar disc, or symptomatic spinal stenosis (with or without degenerative spondylolisthesis); reported at least one of the following outcomes: back specific function, generic health status, pain, work disability, or patient satisfaction	For radiculopathy with herniated lumbar disc, there is good evidence that standard open discectomy and microdiscectomy are moderately superior to nonsurgical therapy for improvement in pain and function through 2 to 3 months	7	

APLD: Automated Percutaneous Lumbar Discectomy; USPSTF: United States Preventive Services Task Force; LBP: Low Back Pain

Table 1a: Study characteristics and main outcomes of systematic reviews for the herniated disc population, by type of treatment

Treatment Type	Author	Year	# of Studies	Eligibility Criteria	Main Results	Quality Rating	Comments
Spinal Injections	Chou	2009	135	Inclusion: Low back pain of any duration, alone or with leg pain; evaluated a target injection or other interventional therapy; reported at least 1 of the following outcomes: back specific function, generic health status, pain, work disability, or patient satisfaction; Exclusion: LBP associated with major trauma, cancer, infection, cauda equina syndrome, fibromyalgia, spondyloarthropathy, and osteoporosis or vertebral compression fracture	For prolapsed lumbar disc with radiculopathy, there is good evidence that chemonucleolysis is moderately superior to placebo injection but inferior to surgery, and fair evidence that ESIs are moderately effective for short-term (but not long-term) symptom relief. There is good or fair evidence that prolotherapy, facet joint injection, intradiscal steroid injection, and percutaneous intradiscal radiofrequency thermocoagulation are not effective; There is insufficient evidence from randomized trials to reliably evaluate other interventional therapies, such as local injections, botulinum toxin injection, therapeutic medial branch block, sacroiliac joint injection, RFD, IDET, and coblation nucleoplasty	7	

APLD: Automated Percutaneous Lumbar Discectomy; USPSTF: United States Preventive Services Task Force; LBP: Low Back Pain

Table 2a: Characteristics of studies for the herniated disc population, by type of treatment
Study Type: Randomized Controlled Trials, Systematic Reviews, and Meta-Analysis

Treatment Type	Author	Year	Study Design	Comparator	Sample Size	Follow-up (Months)	Eligibility Criteria	Quality Rating	Comments
Discectomy	Katayama	2006	RCT	Microdiscectomy	119	Mean: 32	Consecutive patients undergoing primary surgery for lumbar disc herniation	6	
	Osterman	2006	RCT	Conservative Care	56	Actual: 24	Inclusion: below the knee radicular pain of 6-12 weeks duration at randomization; CT finding of intervertebral disc extrusion or sequester and at least one specific physical finding; Exclusion: previous back surgery; spondylolisthesis; symptomatic spinal stenosis; over 3 months of continuous sick due to low back pain or leg pain preceding randomization	6	
	Weinstein	2006	RCT	mary lumbar disc her	472	Actual: 24	Inclusion: intervertebral disk herniation and persistent symptoms despite nonoperative treatment for >= 6 months; radicular pain; evidence of nerve-root irritation; Exclusion: prior lumbar surgery, cauda equina syndrome, vertebral fractures, inflammatory spondyloarthropathy,comorbid conditions contraindicating surgery or unwillingness to have surgery within 6 months	6	
	Peul	2007	RCT	Conservative Care	283	Actual: 12	Inclusion: radiologically confirmed disc herniation; incapacitating lumbosacral radicular syndrome that had lasted for 6-12 weeks; Exclusion: patients presenting with cauda equina syndrome, muscle paralysis, or insufficient strength to move against gravity; occurrence of another episode of symptoms similar to those of the current episode during the previous 12 months, previous spine surgery, bony stenosis, spondylolisthesis	6	
	Pearson	2008	RCT	Conservative Care	1191	Actual: 48	Inclusion: patients with radicular pain with a positive nerve root tension sign or neurologic deficit; presence of symptoms for at least 6 weeks; Exclusion: cauda equina syndrome, malignancy, significant deformity, prior back surgery and other established contraindications to elective surgery	6	

APLD: Automated Percutaneous Lumbar Discectomy; IDET: Intradiscal Electrothermal Therapy; RCT: Randomized Controlled Trial; SR: Systematic Review; META: Meta-Analysis; N/A: Not Applicable

Table 2a: Characteristics of studies for the herniated disc population, by type of treatment
Study Type: Randomized Controlled Trials, Systematic Reviews, and Meta-Analysis

Treatment Type	Author	Year	Study Design	Comparator	Sample Size	Follow-up (Months)	Eligibility Criteria	Quality Rating	Comments
Discectomy	Atlas	2009	RCT	Conservative Care	886	Actual: 24	Inclusion: symptoms and signs of lumbar radiculopathy for >= 6 weeks; Exclusion: restricted enrollment to patients without prior spine surgery for whom surgery was deemed elective	6	
	Ruetten	2009	RCT	Microdiscectomy	87	Actual: 24	Inclusion: Patients who had undergone previous conventional discectomy; acute occurrence of radicular leg symptoms on the same side after a pain-free interval and who showed a recurrent disc herniation in the same level in a MRI	4	
	Teli	2010	RCT	Microdiscectomy	212	Actual: 24	Inclusion: pain and/or neurological signs lasting with over 6 weeks of conservative treatment; Exclusion: < 6 weeks of pain duration, cauda equina symptoms, foraminal or extra-foraminal herniation, lumbar spinal stenosis of any etiology, malignancy, previous spine surgery, spinal deformity including spondylolisthesis of any etiology, concurrent infections and rheumatic disease	8	
	Weinstein	2008	RCT	Conservative Care	1192	Actual: 48	Inclusion: below the knee radicular pain of 6-12 weeks' duration at randomization, a CT finding of intervertebral disc extrusion or sequester and at least one specific physical finding; Exclusion: previous back surgery; spondylolisthesis; symptomatic spinal stenosis; over 3 months' continuous sick leave because of low back pain or leg pain preceding randomization; a condition confounding evaluation of treatment outcomes or a contraindication to conservative treatment	6	
Spinal Injections	Steppan	2010	META	N/A	12	N/A	Exclusion: outcome scales that could not be converted to one of the standard scales analyzed; studies that did not provide sufficient data or provide data that could not be estimated with a statistically sound method; those that were discussions of oxygen/ozone treatment without results from clinical studies	N/A	

APLD: Automated Percutaneous Lumbar Discectomy; RCT: Randomized Controlled Trial; SR: Systematic Review; META: Meta-Analysis; N/A: Not Applicable

Table 2a: Characteristics of studies for the herniated disc population, by type of treatment
Study Type: Randomized Controlled Trials, Systematic Reviews, and Meta-Analysis

Treatment Type	Author	Year	Study Design	Comparator	Sample Size	Follow-up (Months)	Eligibility Criteria	Quality Rating	Comments
Coblation Nucleoplasty	Gerszten	2010	RCT	Epidural steroid injections	90	6 (RCT) 24 (observational)	Inclusion: Age 18-75, BMI <40, radicular pain 50+ on 100 mm VAS, received epidural steroid injection 3 wks - 6 mo previously. Normal neurological function, imaging evidence of focal lumbar disc protrusion and disc height >50%. Exclusion: sciatica from >1 level, back pain worse than leg pain, cauda equina, severe spondylosisthesis or stenosis, previous spinal surgery, other urgent symptoms, Worker's comp/litigation, ongoing antipsychotic treatment.	4	

APLD: Automated Percutaneous Lumbar Discectomy; RCT: Randomized Controlled Trial; SR: Systematic Review; META: Meta-Analysis; N/A: Not Applicable

Table 3a: Patient Characteristics in studies of the herniated disc population, by type of treatment
Study Type: Randomized Controlled Trials, Systematic Reviews, and Meta-Analysis

Treatment Type	Author	Year	Study Design	Interventions	Age (Yrs)	Female: n (%)	Race: White n (%)	Disability Coverage n (%)	Employment Status n (%)	Psychological Comorbidity n (%)	Imaging Used n (%)	Comments
Discectomy	Katayama	2006	RCT	Microdiscectomy	Mean (Range): 34 (14-62)	19 (33.3%)	N/R	N/R	N/R	N/R	N/R	
				Macrodiscectomy	Mean (Range): 41 (18-65)	24 (38.7%)	N/R	N/R	N/R	N/R	N/R	
	Osterman	2006	RCT	Microdiscectomy	Mean (SD): 37 (7)	13 (46.0%)	N/R	N/R	Employed: 26 (93.0%)	N/R	N/R	
				Conservative Care	Mean (SD): 38 (7)	9 (32.0%)	N/R	N/R	Employed: 22 (79.0%)	N/R	N/R	
	Weinstein	2006	RCT	Open Discectomy	Mean (SD): 41.7 (11.8)	101 (44.0%)	197 (85.0%)	N/R	Employed: 142 (61.0%)	30 (13.0%)	MRI: (97.0%)	
				Conservative Care	Mean (SD): 43 (11.3)	93 (39.0%)	202 (84.0%)	N/R	Employed: 148 (62.0%)	32 (13.0%)	MRI: (97.0%)	
	Peul	2007	RCT	Microdiscectomy	Mean (SD): 41.7 (9.9)	52 (37.0%)	N/R	N/R	N/R	N/R	N/R	
				Conservative Care	Mean (SD): 43.4 (9.6)	45 (32.0%)	N/R	N/R	N/R	N/R	N/R	
	Pearson	2008	RCT	Open Discectomy	Mean (SD): 40.7 (10.8)	338 (44.0%)	683 (88.0%)	WC: 157 (20.0%)	FT: 380 (49.0%)	N/R	MRI: 775 (100%)	
				Conservative Care	Mean (SD): 43.8 (12.1)	169 (41%)	350 (84%)	WC: 51 (12.0%)	FT: 235 (56.0%)	N/R	MRI: 416 (100%)	
	Weinstein	2008	RCT	Open Discectomy	Mean (SD): 40.7 (10.8)	340 (43.0%)	694 (88.0%)	N/R	Employed: 455 (58%)	93 (12%)	MRI: (97.0%)	
				Conservative Care	Mean (SD): 43.9 (12.2)	167 (41.0%)	339 (84.0%)	N/R	Employed: 267 (66%)	48 (12%)	MRI: (97.0%)	

APLD: Automated Percutaneous Lumbar Discectomy; RCT: Randomized Controlled Trial; SR: Systematic Review; WC: Worker's Compensation Insurance; NWC: Patients without Worker's Compensation Insurance; FT: Full-time; N/R: Not Reported

Table 3a: Patient Characteristics in studies of the herniated disc population, by type of treatment
Study Type: Randomized Controlled Trials, Systematic Reviews, and Meta-Analysis

Treatment Type	Author	Year	Study Design	Interventions	Age (Yrs)	Female: n (%)	Race: White n (%)	Disability Coverage n (%)	Employment Status n (%)	Psychological Comorbidity n (%)	Imaging Used n (%)	Comments
Discectomy	Atlas	2009	RCT	Open Discectomy: WC	Mean (SD): 36.9 (8.3)	18 (22.0%)	62 (78.0%)	WC: 80 (100%)	Employed: 63 (79.0%)	N/R	N/R	
				Conservative Care: WC	Mean (SD): 41 (10.4)	5 (18.0%)	20 (71.0%)	WC: 28 (100%)	Employed: 19 (68%)	N/R	N/R	
				Open Discectomy: NWC	Mean (SD): 40.7 (9.8)	197 (43.0%)	410 (89.0%)	WC: 0	Employed: 358 (78.0%)	N/R	N/R	
				Conservative Care: NWC	Mean (SD): 41 (10.2)	130 (41.0%)	279 (87.0%)	WC: 0	Employed: 246 (77.0%)	N/R	N/R	
	Ruetten	2009	RCT	Microdiscectomy Discectomy	Mean (Range): 39 (23-59)	44	N/R	N/R	N/R	N/R	N/R	
	Teli	2010	RCT	Microendoscopic Discectomy	Mean (SD): 39 (12)	25 (36.0%)	N/R	N/R	N/R	N/R	MRI/CT: 70 (100%)	
				Microdiscectomy	Mean (SD): 40 (12)	24 (33.0%)	N/R	N/R	N/R	N/R	MRI/CT: 72 (100%)	
				Open Discectomy	Mean (SD): 39 (12)	24 (34.0%)	N/R	N/R	N/R	N/R	MRI/CT: 70 (100%)	
Coblation Nucleoplasty	Gerszten	2010	RCT	Coblation Nucleoplasty	Mean (SD): 46 (12)	24 (53.0%)	N/R	N/R	Employed: 28 (62%)	N/R	MRI/CT: 100%	
				Epidural Steroid Injections	Mean (SD): 42 (11)	19 (48.0%)	N/R	N/R	Employed: 26 (65%)	N/R	MRI/CT: 100%	

APLD: Automated Percutaneous Lumbar Discectomy; RCT: Randomized Controlled Trial; SR: Systematic Review; WC: Worker's Compensation Insurance; NWC: Patients without Worker's Compensation Insurance; FT: Full-time; N/R: Not Reported

Table 4a: Functional outcomes for the herniated disc population, by type of treatment
Study Type: Randomized Controlled Trials, Systematic Reviews, and Meta-Analysis

Intervention	Author	Year	Study Design	Comparator	Index	Time (Months)	Measure	Intervention Outcome	Comparator Outcome	Comments
Discectomy	Osterman	2006	RCT	Conservative Care	ODI	0	Mean (SD)	39 (15)	39 (14)	
						1.5	Mean (SD)	16 (16)	22 (16)	
						3	Mean (SD)	8 (11)	14 (14)	
						6	Mean (SD)	8 (12)	12 (15)	
						12	Mean (SD)	10 (13)	11 (14)	
						24	Mean (SD)	6 (9)	11 (16)	
	Weinstein	2006	RCT	Conservative Care	ODI	0	Mean (SD)	47.5 (21.4)	46.3 (20.6)	
						3	Mean Change (SD)	-26 (1.7)	-21.3 (1.6)	
						3	Treatment Effect (95% CI)	-4.7 (-9.3, -0.2)		
						12	Mean Change (SD)	-30.6 (1.7)	-27.4 (1.6)	
						12	Treatment Effect (95% CI)	-3.2 (-7.8, 1.3)		
						24	Mean Change (SD)	-31.4 (1.7)	-28.7 (1.7)	
						24	Treatment Effect (95% CI)	-2.7 (-7.4, 1.9)		
	Peul	2007	RCT	Conservative Care	RMS	0	Mean (SD)	16.5 (4.4)	16.3 (3.9)	
						0.5	Mean (SD)	13 (0.5)	14.4 (0.5)	
						0.5	Treatment Effect (95% CI)	-1.6 (-2.8, -0.3)		
						2	Mean (SD)	6.1 (0.5)	9.2 (0.5)	
						2	Treatment Effect (95% CI)	3.1 (1.7, 4.3)		
						6	Mean (SD)	4 (0.5)	4.8 (0.5)	
						6	Treatment Effect (95% CI)	0.8 (-0.5, 2.1)		
						12	Mean (SD)	3.3 (0.5)	3.7 (0.5)	
						12	Treatment Effect (95% CI)	0.4 (-0.9, 1.7)		
	Weinstein	2008	RCT	Conservative Care	ODI	0	Mean (SD)	54.9 (19.6)	38.8 (20.4)	
						24	Mean Change (SD)	-31.5 (1.7)	-28.8 (1.7)	
						24	Treatment Effect (95% CI)	-2.8 (-7.5, 1.9)		
						36	Mean Change (SD)	-31.5 (1.7)	-27.2 (1.7)	
						36	Treatment Effect (95% CI)	-4.3 (-9.1, 0.6)		
						48	Mean Change (SD)	-31.2 (1.8)	-27.6 (1.8)	
						48	Treatment Effect (95% CI)	-3.6 (-8.6, 1.4)		

RCT: Randomized Controlled Trial; META: Meta-Analysis; ODI: Oswestrey Disability Index; RMS: Roland-Morris Scale; WC: Worker's Compensation Insurance; NWC: Patients without Worker's Compensation Insurance; N/R: Not Reported; N/A: Not Applicable

Table 4a: Functional outcomes for the herniated disc population, by type of treatment
Study Type: Randomized Controlled Trials, Systematic Reviews, and Meta-Analysis

Intervention	Author	Year	Study Design	Comparator	Index	Time (Months)	Measure	Intervention Outcome	Comparator Outcome	Comments
Discectomy	Atlas	2009	RCT	Conservative Care	ODI	0	Mean (SD)	60.2 (17)	50.1 (19.4)	WC
						1.5	Treatment Effect (95% CI)	-11.3 (-17.3 to -5.4)		WC
						3	Treatment Effect (95% CI)	-9.4 (-15.8 to -2.9)		WC
						6	Treatment Effect (95% CI)	-4.8 (-1.8-2.2)		WC
						12	Treatment Effect (95% CI)	-2.2 (-9.9-5.5)		WC
						24	Treatment Effect (95% CI)	-2 (-10.3-6.3)		WC
						0	Mean (SD)	53.1 (19.3)	36.7 (19.9)	NWC
						1.5	Treatment Effect (95% CI)	-15.5 (-17.6 to -13.3)		NWC
						3	Treatment Effect (95% CI)	-16.1 (-18.5 to -13.6)		NWC
						6	Treatment Effect (95% CI)	-15.6 (-18.2 to -13)		NWC
						12	Treatment Effect (95% CI)	-14.4 (-17 to -11.8)		NWC
						24	Treatment Effect (95% CI)	-12.5 (-15.2 to -9.9)		NWC
	Ruetten	2009	RCT	Microdiscectomy	ODI	0	Mean	80	84	
						3	Mean	22	18	
						6	Mean	24	19	
						12	Mean	18	23	
						24	Mean	20	21	
	Teli	2010	RCT	Microendoscopic Discectomy	ODI	0	Mean (SD)	39 (4)	40(4)	
						6	Mean (SD)	12 (4)	12 (4)	
						12	Mean (SD)	13 (4)	14 (4)	
						24	Mean (SD)	15 (3)	14 (6)	
						24	p-value	0.81		
				Microdiscectomy	ODI	0	Mean (SD)	39 (4)	41 (4)	
						6	Mean (SD)	12 (4)	12 (4)	
						12	Mean (SD)	13 (4)	13 (4)	
						24	Mean (SD)	15 (3)	16 (5)	
						24	p-value	0.81		
Spinal Injections	Steppan	2010	META	N/A	ODI	N/R	Mean Change (SD)	21 (14.14, 27.94)	N/A	

RCT: Randomized Controlled Trial; META: Meta-Analysis; ODI: Oswestrey Disability Index; RMS: Roland-Morris Scale; WC: Worker's Compensation Insurance; NWC: Patients without Worker's Compensation Insurance; N/R: Not Reported; N/A: Not Applicable

Table 4a: Functional outcomes for the herniated disc population, by type of treatment
Study Type: Randomized Controlled Trials, Systematic Reviews, and Meta-Analysis

Intervention	Author	Year	Study Design	Comparator	Index	Time (Months)	Measure	Intervention Outcome	Comparator Outcome	Comments
Coblation Nucleoplasty	Gerszten	2010	RCT	Epidural Steroid Injections	ODI	0	Mean (SD)	42 (14)	43 (17)	
						1.5	Mean Change (SE)*	-11 (3)	4 (2)	p=.02
						3	Mean Change (SE)*	-10 (3)	2 (2)	p=.03
						6	Mean Change (SE)*	-12 (3)	-4 (2)	p=.03

*From GEE Model

RCT: Randomized Controlled Trial; META: Meta-Analysis; ODI: Oswestrey Disability Index; RMS: Roland-Morris Scale; WC: Worker's Compensation Insurance; NWC: Patients without Worker's Compensation Insurance; N/R: Not Reported; N/A: Not Applicable

Table 5a: Pain outcomes in studies of the herniated disc population, by type of treatment
Study Type: Randomized Controlled Trials, Systematic Reviews, and Meta-Analysis

Intervention	Author	Year	Study Design	Comparator	Scale	Time (Months)	Measure	Intervention Outcome	Comparator Outcome	Comments
Discectomy	Katayama	2006	RCT	Microdiscectomy	VAS	0	Mean (SD)	8.5 (0.7)	7.6 (0.9)	
						8	Mean (SD)	1.6 (0.7)	1.2 (0.4)	
	Osterman	2006	RCT	Conservative Care	VAS	0	Mean (SD)	53 (25)	47 (28)	
						1.5	Mean (SD)	21 (25)	28 (24)	
						3	Mean (SD)	15 (20)	22 (23)	
						6	Mean (SD)	17 (23)	20 (28)	
						12	Mean (SD)	19 (25)	17 (23)	
						24	Mean (SD)	11 (18)	21 (27)	
	Peul	2007	RCT	Conservative Care	VAS	0	Mean (SD)	33.8 (29.6)	30.8 (27.7)	
						0.5	Mean (SD)	33.3 (2.1)	34.9 (2.1)	
						2	Mean (SD)	14.4 (2.1)	25.7 (2.1)	
						6	Mean (SD)	15.5 (2.2)	17.8 (2.1)	
						12	Mean (SD)	14.2 (2.2)	16.5 (2.1)	
	Pearson	2008	RCT	Conservative Care	PLS	0	Mean (SD)	4.1 (1.8)	3.6 (1.9)	
						3	Mean Change (SD)	-2.2 (0.1)	-1.3 (0.1)	
						3	Treatment Effect (95% CI, p-value)	-0.9 (-1.2--0.7, <0.001)		
						12	Mean Change (SD)	-2.1 (0.1)	-1.4 (0.1)	
						12	Treatment Effect (95% CI, p-value)	-0.7 (-0.9--0.4, <0.001)		
						24	Mean Change (SD)	-2 (0.1)	-1.5 (0.1)	
						24	Treatment Effect (95% CI, p-value)	-0.5 (-0.7--0.3, <0.001)		
	Weinstein	2008	RCT	Conservative Care	PLS	24	Mean Change(SD)	-1.9 (0.2)	-1.8 (0.2)	
						24	Treatment Effect (95% CI)	-0.1 (-0.6-0.3)		
						36	Mean Change(SD)	-1.9 (0.2)	-1.6 (0.2)	
						36	Treatment Effect (95% CI)	-0.3 (-0.7-0.2)		
						48	Mean Change(SD)	-1.8 (0.2)	-1.7 (0.2)	
						48	Treatment Effect (95% CI)	-0.1 (-0.6-0.3)		
	Ruetten	2009	RCT	Microdiscectomy	VAS	0	Mean	14	15	
						3	Mean	14	13	
						6	Mean	12	12	
						12	Mean	16	15	
						24	Mean	15	14	

RCT: Randomized Controlled Trial; SR: Systematic Review; META: Meta-Analysis; VAS: Visual Analog Scale; PLS: Pain Likert Scale; NRS: Numeric Rating Scale

Table 5a: Pain outcomes in studies of the herniated disc population, by type of treatment
Study Type: Randomized Controlled Trials, Systematic Reviews, and Meta-Analysis

Intervention	Author	Year	Study Design	Comparator	Scale	Time (Months)	Measure	Intervention Outcome	Comparator Outcome	Comments
Discectomy	Teli	2010	RCT	Microendoscopic Discectomy	VAS	0	Mean (SD)	3 (1)	3 (1)	
						6	Mean (SD)	1 (1)	2 (1)	
						12	Mean (SD)	1(1)	1(1)	
						24	Mean (SD)	1 (1)	2 (1)	
						24	p-value	0.75		
				Microdiscectomy	VAS	0	Mean (SD)	3 (1)	4 (1)	
						6	Mean (SD)	1 (1)	2 (1)	
						12	Mean (SD)	1(1)	1(1)	
						24	Mean (SD)	1 (1)	2 (1)	
						24	p-value	0.75		
Spinal Injections	Steppan	2010	META	N/A	VAS	N/R	Mean (95% CI)	3.9 (3.21-4.45)	N/A	
Coblation Nucleoplasty	Gerszten	2010	RCT	Epidural Steroid Injections	VAS	0	Mean (SD)	44 (24)	53 (23)	
						1.5	Mean Change (SE)*	-16 (4)	2 (3)	p=.0002
						3	Mean Change (SE)*	-15 (4)	7 (3)	p<.0001
						6	Mean Change (SE)*	-16 (4)	0.2 (4)	p=.004

*From GEE Model

RCT: Randomized Controlled Trial; SR: Systematic Review; META: Meta-Analysis; VAS: Visual Analog Scale; PLS: Pain Likert Scale; NRS: Numeric Rating Scale

Table 6a: Quality of life outcomes in studies of herniated disc population, by type of treatment
Study Type: Randomized Controlled Trials, Systematic Reviews, and Meta-Analysis

Intervention	Author	Year	Study Design	Comparator	Scale	Component	Time (Months)	Measure	Intervention Outcome		Comparator Outcome	Comments
Discectomy	Weinstein	2006	RCT	Conservative Care	SF36	BP	0	Mean (SD)	27.1 (18.5)		26.7 (17.4)	
							3	Mean Change(SD)	30.5 (1.9)		27.6 (1.8)	
							3	Treatment Effect (95% CI)		2.9 (-2.2-8)		
							12	Mean Change(SD)	39.7 (1.8)		36.9 (1.8)	
							12	Treatment Effect (95% CI)		2.8 (-2.3-7.8)		
							24	Mean Change(SD)	40.3 (1.9)		37.1 (1.9)	
							24	Treatment Effect (95% CI)		3.2 (-2-8.4)		
						PF	0	Mean (SD)	39.7 (24.9)		39.2 (25.7)	
							3	Mean Change(SD)	27.7 (1.9)		24.9 (1.9)	
							3	Treatment Effect (95% CI)		2.8 (-2.5-8.1)		
							12	Mean Change(SD)	36.4 (1.9)		35.2 (1.9)	
							12	Treatment Effect (95% CI)		1.2 (-4.1-6.5)		
							24	Mean Change(SD)	35.9 (2)		35.9 (1.9)	
							24	Treatment Effect (95% CI)		0 (-5.4-5.5)		
	Peul	2007	RCT	Conservative Care	SF36	BP	0	Mean (SD)	21.9 (16.6)		23.9 (18.1)	
							2	Mean (SD)	62.8 (2.1)		54.4 (2)	
							2	Treatment Effect (95% CI)		-8.4 (-13.5--3.2)		
							6	Mean (SD)	76.1 (1.1)		72.8 (1.9)	
							6	Treatment Effect (95% CI)		-3.3 (-8.4-1.8)		
							12	Mean (SD)	81.2 (2)		78.5 (1.9)	
							12	Treatment Effect (95% CI)		-2.7 (-7.9-2.6)		
						PF	0	Mean (SD)	33.9 (19.6)		34.6 (19)	
							2	Mean (SD)	71.2 (1.7)		61.9 (1.9)	
							2	Treatment Effect (95% CI)		-9.3 (-14.2--4.4)		
							6	Mean (SD)	79.1 (1.9)		77.6 (1.7)	
							6	Treatment Effect (95% CI)		-1.5 (-6.4-3.4)		
							12	Mean (SD)	84.2 (1.8)		82 (1.9)	
							12	Treatment Effect (95% CI)		-2.2 (-7.2-2.8)		

RCT: Randomized Controlled Trial; SF36: Short Form - 36; BP: Bodily Pain; PF: Physical Function; MCS: Mental Component Summary; N/R: Not Reported; WC: Worker's Compensation Insurance; NWC: Patients without Non-Worker's Compensation Insurance

Table 6a: Quality of life outcomes in studies of herniated disc population, by type of treatment
Study Type: Randomized Controlled Trials, Systematic Reviews, and Meta-Analysis

Intervention	Author	Year	Study Design	Comparator	Scale	Component	Time (Months)	Measure	Intervention Outcome		Comparator Outcome	Comments
Discectomy	Weinstein	2008	RCT	Conservative Care	SF36	BP	0	Mean (SD)	22.3 (16.2)		32.9 (19.7)	
							24	Mean Change(SD)	40.5 (1.9)		37.5 (1.9)	
							24	Treatment Effect (95% CI)		3.1 (-2.2-8.4)		
							36	Mean Change(SD)	39.6 (2)		36.2 (2)	
							36	Treatment Effect (95% CI)		3.4 (-2.1-8.9)		
							48	Mean Change(SD)	41.3 (2.1)		36.8 (2.1)	
							48	Treatment Effect (95% CI)		4.5 (-1.2-10.3)		
						PF	0	Mean (SD)	32.3 (23.4)		48.2 (26.3)	
							24	Mean Change(SD)	36.2 (2)		35.7 (2)	
							24	Treatment Effect (95% CI)		0.5 (-4.9-6)		
							36	Mean Change(SD)	37.2 (2)		34.1 (2)	
							36	Treatment Effect (95% CI)		3.1 (-2.5-8.8)		
							48	Mean Change(SD)	36.6 (2.1)		34.4 (2.1)	
							48	Treatment Effect (95% CI)		2.2 (-3.7-8)		

RCT: Randomized Controlled Trial; SF36: Short Form - 36; BP: Bodily Pain; PF: Physical Function; MCS: Mental Component Summary; N/R: Not Reported; WC: Worker's Compensation Insurance; NWC: Patients without Non-Worker's Compensation Insurance

Table 6a: Quality of life outcomes in studies of herniated disc population, by type of treatment
Study Type: Randomized Controlled Trials, Systematic Reviews, and Meta-Analysis

Intervention	Author	Year	Study Design	Comparator	Scale	Component	Time (Months)	Measure	Intervention Outcome	Comparator Outcome	Comments
Discectomy	Atlas	2009	RCT	Conservative Care	SF36	BP	0	Mean (SD)	23.2 (13.3)	19.3 (16)	WC
							1.5	Treatment Effect (95% CI)	10.8 (3.1-18.5)		WC
							3	Treatment Effect (95% CI)	11.8 (3.5-20.1)		WC
							6	Treatment Effect (95% CI)	7.3 (-1.7-16.3)		WC
							12	Treatment Effect (95% CI)	2.2 (-7.7-12.2)		WC
							24	Treatment Effect (95% CI)	-5.9 (-16.7-4.9)		WC
							0	Mean (SD)	24.1 (16.3)	34.5 (19.8)	NWC
							1.5	Treatment Effect (95% CI)	10.8 (8-13.5)		NWC
							3	Treatment Effect (95% CI)	17.8 (14.7-21)		NWC
							6	Treatment Effect (95% CI)	15.7 (12.4-19)		NWC
							12	Treatment Effect (95% CI)	12.2 (8.9-15.5)		NWC
							24	Treatment Effect (95% CI)	11 (7.7-14.4)		NWC
						PF	0	Mean (SD)	27.3 (20.1)	37.5 (22.8)	WC
							1.5	Treatment Effect (95% CI)	10.9 (3.8-18)		WC
							3	Treatment Effect (95% CI)	12.4 (4.7-20.1)		WC
							6	Treatment Effect (95% CI)	5.3 (-3-13.6)		WC
							12	Treatment Effect (95% CI)	5 (-4.2-14.2)		WC
							24	Treatment Effect (95% CI)	5(-4.9-15)		WC
							0	Mean (SD)	34 (23.3)	51.5 (26)	NWC
							1.5	Treatment Effect (95% CI)	13.8 (11.2-16.4)		NWC
							3	Treatment Effect (95% CI)	18.1 (15.1-21.1)		NWC
							6	Treatment Effect (95% CI)	19 (16-22.3)		NWC
							12	Treatment Effect (95% CI)	16.4 (13.3-19.5)		NWC
							24	Treatment Effect (95% CI)	13.4 (10.3-16.5)		NWC
Coblation Nucleoplasty	Gerszten	2010	RCT	Epidural Steroid Injections	SF36	BP	0	Mean (SD)	31 (6)	32 (6)	NS
							6	Mean (SD)	44 (N/R)	35 (N/R)	p<.0001
						PF	0	Mean (SD)	31 (9)	32 (9)	NS
							6	Mean (SD)	45 (N/R)	34 (N/R)	p<.0001

RCT: Randomized Controlled Trial; SF36: Short Form - 36; BP: Bodily Pain; PF: Physical Function; MCS: Mental Component Summary; N/R: Not Reported; WC: Worker's Compensation Insurance; NWC: Patients without Non-Worker's Compensation Insurance

Table 7a: Employment status outcomes in studies of the herniated disc population, by type of treatment
Study Type: Randomized Controlled Trials, Systematic Reviews, and Meta-Analysis

Intervention	Author	Year	Study Design	Comparator	Work Status Outcome	Time (Months)	Measures	Intervention Outcome	Comparator Outcome	Comments
Discectomy	Weinstein	2006	RCT	Conservative Care	% Employed	3	Percentage (SD)	69.4 % (3.1 %)	63.4 % (3.3 %)	
						12	Percentage (SD)	77 % (2.8 %)	76.4 % (2.9 %)	
						24	Percentage (SD)	76.4 % (3.0 %)	74.2 % (3.1 %)	
	Weinstein	2008	RCT	Conservative Care	% Employed	36	Percentage	71.0%	74.5%	
					% Employed	48	Percentage	71.4%	75.1%	
	Atlas	2009	RCT	Conservative Care	% Employed	0	n (%)	63 (79.0%)	19 (68.0%)	
						1.5	Treatment Effect (95% CI)	-35.1 (-59.6 to -10.7)		WC
						3	Treatment Effect (95% CI)	-17.4 (-39.1-4.3)		WC
						6	Treatment Effect (95% CI)	-2.4 (-21.4-16.6)		WC
						12	Treatment Effect (95% CI)	13.3 (-9-35.6)		WC
						24	Treatment Effect (95% CI)	7.7 (-14.6-30.1)		WC
					% Employed	0	n (%)	358 (78.0%)	246 (77.0%)	NWC
						1.5	Treatment Effect (95% CI)	-20.8 (-26.8 to -14.9)		NWC
						3	Treatment Effect (95% CI)	-3.4 (-8.4-1.6)		NWC
						6	Treatment Effect (95% CI)	-0.5 (-4.3-3.3)		NWC
						12	Treatment Effect (95% CI)	1.9 (-2.2-6)		NWC
						24	Treatment Effect (95% CI)	0.8 (-3.4-5)		NWC
Coblation Nucleoplasty	Gerszten	2010	RCT	Epidural Steroid Injections	% Employed	0	Percentage	62%	65%	p=0.98
						6	Percentage	69%	70%	NS

RCT: Randomized Controlled Trial; SR: Systematic Review; META: Meta-Analysis; N/R: Not Reported; N/A: Not Applicable; WC: Worker's Compensation Insurance; NWC: Patients without Worker's Compensation Insurance

Table 8a: Measures of clinical improvement in studies of the herniated disc population, by type of treatment
Study Type: Randomized Controlled Trials, Systematic Reviews, and Meta-Analysis

Intervention	Author	Year	Study Design	Comparator	Time (Months)	Measure	Intervention Outcome	Comparator Outcome	Definition	Comments
Discectomy	Ruetten	2009	RCT	Microdiscectomy	24	Percent No Pain	76.0%	82.0%	N/R	Determined by VAS scores
					24	Percent Occasional Pain	17.0%	16.0%	N/R	Determined by VAS scores
					24	Percent No Change	7.0%	2.0%	N/R	Determined by VAS scores

RCT: Randomized Controlled Trial; SR: Systematic Review; META: Meta-Analysis; N/R: Not Reported; N/A: Not Applicable

Table 9a: Mortality and other harms in studies of the herniated disc population, by type of treatment
Study Type: Randomized Controlled Trials, Systematic Reviews, and Meta-Analysis

Harm Category	Intervention	Author	Year	Study Design	Comparator	Measure	Intervention Outcome	Comparator Outcome	Comments
30-day Mortality	Discectomy	Teli	2010	RCT	Microendoscopic Discectomy	n (%)	0 (0%)	0 (0%)	
					Microdiscectomy	n (%)	0 (0%)	0 (0%)	
	Discectomy	Pearson	2008	RCT	Conservative Care	n (%)	0 (0%)	N/R	
Major	Discectomy	Teli	2010	RCT	Microendoscopic Discectomy	n (%)	5 (7.1%)	N/R	
					Microdiscectomy	n (%)	1 (1.4%)	N/R	
					Open Discectomy	n (%)	0 (0%)	N/R	
	Discectomy	Ruetten	2009	RCT	Microdiscectomy	n (%)	0 (0%)	0 (0%)	
	Discectomy	Weinstein	2006	RCT	Conservative Care	n (%)	1 (0.4%)	N/R	
Minor	Discectomy	Teli	2010	RCT	Microendoscopic Discectomy	n (%)	6 (8.6%)	N/R	
					Microdiscectomy	n (%)	6 (8.3%)	N/R	
					Open Discectomy	n (%)	5 (7.1%)	N/R	
	Discectomy	Ruetten	2009	RCT	Microdiscectomy	n (%)	1 (1.2%)	9 (8.8%)	
	Discectomy	Pearson	2008	RCT	Conservative Care	n (%)	41 (5.3%)	N/R	
	Discectomy	Peul	2007	RCT	Open Discectomy	n (%)	3 (2.1%)	N/R	
	Discectomy	Katayama	2006	RCT	Microdiscectomy	n (%)	1 (1.6%)	0 (0%)	
	Discectomy	Osterman	2006	RCT	Conservative Care	n (%)	1 (3.6%)	N/R	
	Discectomy	Weinstein	2006	RCT	Conservative Care	n (%)	25 (11%)	N/R	
	Coblation Nucleoplasty	Gerszten	2010	RCT	Epidural Steroid Injections	n (%)	5 (11%)	7 (18%)	

N/R: Not Reported

Table 10a: Characteristics of studies for the herniated disc population, by type of treatment
Study Type: Comparative studies, Case-Series: Non-comparative studies

Treatment Type	Author	Year	Study Design	Comparator	Sample Size	Follow-up (Months)	Eligibility Criteria	Quality Rating	Comments
APLD	Peng	2010	Prospective Cohort	N/A	55	Mean: 36	Inclusion: patients with percutaneous endoscopic discectomy performed for herniated intervertebral disc at our institution had data collected prospectively; patients who had radicular symptoms due to discogenic lumbar nerve root compression and failed conservative therapy and had the diagnosis of lumbar disc herniation made on MRI were offered discectomy;	Poor	
Discectomy	Veresciagina	2010	Prospective Cohort	Control	200	Actual: 48	Inclusion: chronic pain, occurring daily, for>=t 3 months, and >= 20 hours a day, refractory to >6 weeks of conservative treatment; chief complaint of pain and/or numbness in the lumbar spine, buttock, and/or lower extremity; age >21 years and < 76 years; duration of current episode < 16 days; symptoms extending distal to the knee; stiffness in the lumbar spine from segmental mobility testing; signs consistent with nerve root compression, including any one of the following: reproduction of LB or leg pain with straight leg raise > 45 degrees, muscle weakness involving a major muscle group of the lower extremity, diminished lower extremity muscle stretch reflex, diminished or absence of sensation to pinprick in any lower extremity dermatome; MRI or CT demonstrating anatomical unilateral LDH correlating with patients symptoms; Exclusion: prior lumbar surgery, segmental instability, vertebral fractures and spinal infections, other types of DDD, tumors, and pregnancy	Fair	

LDH: Lumbar Disc Herniation; DDD: Degenerative Disc Disease; LBP: Low Back Pain; N/A: Not Applicable

Table 10a: Characteristics of studies for the herniated disc population, by type of treatment
Study Type: Comparative studies, Case-Series: Non-comparative studies

Treatment Type	Author	Year	Study Design	Comparator	Sample Size	Follow-up (Months)	Eligibility Criteria	Quality Rating	Comments
Discectomy	Schick	2009	Prospective Cohort	Sequestrectomy	200	Actual: 34	Inclusion: all patients suffered from lumbar back pain and radicular pain resistant to>= 3 weeks of conservative treatment; MRI studies revealed herniation in all cases; clinical symptoms were referable to a segmental level; all patients were proficient enough in the german language to complete the self-assessment questionnaires; Exclusion: all patients undergoing a lateral spinal approach, with prior operation at the same level, significant spinal stenosis or articular cysts were excluded; non underwent instrumentation for spondylolisthesis	Fair	
	Atlas	2005	Prospective Cohort	Conservative Care	400	Actual: 120	Inclusion: diagnoses of sciatica resulting from intervertebral disc herniation based on physicians assessment, no radiographic findings required; Exclusion: prior lumbar spine surgery, cauda equina syndrome, developmental spine deformities, vertebral fractures, spine infection or tumor, inflammatory spondylopathy, pregnancy, or severe comorbid conditions	Good	
	Fisher	2004	Prospective Cohort	N/A	82	Actual: 12	Inclusion: lumbar disc herniation causing lower-extremity radiculopathy; Exclusion: previously undergone spine surgery at the same level, suffered severe comorbidity that would influence outcomes, exhibitted spinal deformity	Fair	

LDH: Lumbar Disc Herniation; DDD: Degenerative Disc Disease; LBP: Low Back Pain; N/A: Not Applicable

Table 10a: Characteristics of studies for the herniated disc population, by type of treatment
Study Type: Comparative studies, Case-Series: Non-comparative studies

Treatment Type	Author	Year	Study Design	Comparator	Sample Size	Follow-up (Months)	Eligibility Criteria	Quality Rating	Comments
Discectomy	Asch	2002	Prospective Cohort	N/A	212	Mean: 24	Inclusion: unremitting sciatica, with or without back pain, and/or a neurological deficit that correlated with appropriate level and side of neural compression revealed on CT or MR imaging; patients who presented with other spinal degenerative conditions such as stenosis or arthritis were not excluded provided their diagnosis indicated that there primary cause for complaint(s) was deemed a herniated disc; patients were also not excluded because of age, sex, compensation claims, diabetes, obesity, or other medical conditions that would not preclude surgery in general	Fair	
	Tsou	2004	Retrospective Cohort	N/A	113	Mean: 31	Inclusion: Preoperative diagnosis of chronic LBP who failed to respond to nonoperative treatment	Poor	
	Marks	2000	Retrospective Cohort	N/A	103	Mean (SD): 31 (18)	Inclusion: All had LBP with or without radiation to one or both lower extremities, and unsuccessful rigorous trial of conservative care	Poor	
Microdiscectomy	Boskovic	2010	Prospective Cohort	N/A	50	Actual: 48	Inclusion: patients with discal genesis lumbar radiculopathy who had undergone a lumbar microdiscectomy	Fair	
	Kim	2007	Retrospective Cohort	Percutaneous Transforaminal Endoscopic Discectomy	915	Actual: 23.6	Inclusion: disc herniation and 3 to 6 weeks of conservative treatment that failed to improve major motor weaknes, intractable leg pain, and functional imapirments; intractable radicular symptoms such as sciatica, a positive straight-leg raising test, and sensory and/or motor disturbances; Exclusion: recurrent hernaition, spinal stenosis, and segmetnal instability including spondylolisthesis	Poor	

LDH: Lumbar Disc Herniation; DDD: Degenerative Disc Disease; LBP: Low Back Pain; N/A: Not Applicable

Table 11a: Mortality and other harms in studies of the herniated disc population, by type of treatment
Study Type: Comparative studies, Case-Series: Non-comparative studies

Harm Category	Intervention	Author	Year	Study Design	Comparator	Time (Months)	Measure	Intervention Outcome	Comparator Outcome	Comments
30-day Mortality	No Studies with outcomes >= 24 months reported									
Major	Discectomy	Tsou	2004	Retrospective Cohort	N/A	31.3	n (%)	1 (0.9%)	N/A	
Minor	Discectomy	Tsou	2004	Retrospective Cohort	N/A	31.3	n (%)	3 (2.7%)	N/A	

N/A: Not Applicable

Table 12a: Functional outcomes for the herniated disc population, by type of treatment
Study Type: Comparative studies, Case-Series: Non-comparative studies

Intervention	Author	Year	Study Design	Comparator	Scale	Time (Months)	Measure	Intervention Outcome	Comparator Outcome	Comments
Discectomy	Asch	2002	Prospective Cohort	N/A	ODI	0	Median	47	N/A	
						1.5	Median	26	N/A	
						6	Median	18	N/A	
						25	Median	14	N/A	
	Atlas	2005	Prospective Cohort	Conservative Care	RMS	0	Mean Change (SD)	-5.8 (7.6)	-11.7 (7.2)	
						120	Mean (SD)	3.5 (2)	4.2 (2)	

ODI: Oswestrey Disability Index; RMS: Roland-Morris Scale; N/R: Not Reported; N/A: Not Applicable

Table 13a: Pain outcomes in studies of the herniated disc population, by type of treatment
Study Type: Comparative studies, Case-Series: Non-comparative studies

Intervention	Author	Year	Study Design	Comparator	Scale	Time (Months)	Measure	Intervention Outcome	Comparator Outcome	Comments
APLD	Peng	2010	Prospective Cohort	N/A	VAS	0	Mean	7.6	N/A	
						6	Mean	3.1	N/A	
						24	Mean	2	N/A	
Discectomy	Atlas	2005	Prospective Cohort	Conservative Care	7NRS	0	Mean (SD)	3.5 (2)	4.2 (2)	
						120	Mean Change (SD)	-1.2 (2.4)	-2.3 (2.5)	
	Schick	2009	Prospective Cohort	Sequestrectomy	VAS	0	Mean	7.81	7.86	
						34	Mean	3.7	3.3	

VAS: Visual Analog Scale; NRS: Numeric Rating Scale; 7NRS: 7-point Numeric Rating Scale; N/R: Not Reported; N/A: Not Applicable

Table 14a: Quality of life outcomes in studies of the herniated disc population, by type of treatment
Study Type: Comparative studies, Case-Series: Non-comparative studies

Intervention	Author	Year	Study Design	Comparator	Scale	Subdomain	Time (Months)	Measure	Intervention Outcome	Comparator Outcome	Comments
APLD	Peng	2010	Prospective Cohort	N/A	SF36	BP	0	Mean	35.5	N/A	
							6	Mean	57.9	N/A	
							24	Mean	74.4	N/A	
						PF	0	Mean (SD)	56.2	N/A	
							6	Mean (SD)	65.8	N/A	
							24	Mean (SD)	80.9	N/A	
Discectomy	Veresciagina	2010	Prospective Cohort	Conservative Care	SF36	MCS	0	Mean (SD)	18.1 (1)	35.57 (1)	
							48	Mean (SD)	18.1 (1)	25.42 (2)	
Microdiscectomy	Boskovic	2010	Prospective Cohort	N/A	SF36	BP	0	Mean	15.4	N/A	
							3	Mean	53.6	N/A	
							6	Mean	72	N/A	
							48	Mean	69	N/A	
					SF36	PF	0	Mean	23	N/A	
							3	Mean	65.3	N/A	
							6	Mean	80	N/A	
							48	Mean	78.4	N/A	

APLD: Automated Percutaneous Lumbar Discectomy; SF36: Short Form-36; BP: Bodily Pain; PF: Physical Functioning; MCS: Mental Component Summary; N/R: Not Reported; N/A: Not Applicable

Table 15a: Employment status outcomes in studies of the herniated disc population, by type of treatment
Study Type: Comparative studies, Case-Series: Non-comparative studies

Intervention	Author	Year	Study Design	Comparator	Work Status Outcome	Time (Months)	Measures	Intervention Outcome	Comparator Outcome	Comments
Discectomy	Asch	2002	Prospective Cohort	N/A	% Return to work	25	n (%)	130 (61%)	N/A	
	Atlas	2005	Prospective Cohort	Conservative Care	% Employed	120	n (%)	91 (42%)	90 (49%)	
	Veresciagina	2010	Prospective Cohort	Control	% Return to work	48	n (%)	64 (64%)	N/R	
	Marks	2000	Retrospective Cohort	N/A	% Return to work	30.7	n (%)	28(27%)	N/A	

N/R: Not Reported; N/A: Not Applicable

Table 16a: Measures of clinical improvement in studies of the herniated disc population, by type of treatment
Study Type: Comparative studies, Case-Series: Non-comparative studies

Intervention	Author	Year	Study Design	Comparator	Time (Months)	Measure	Intervention Outcome	Comparator Outcome	Definition
Discectomy	Asch	2002	Prospective Cohort	N/A	25	% Improvement	164 (77.0%)	N/A	Determined by VAS scores
					25	% Improvement	166 (78.0%)	N/A	Determined by ODI scores
	Atlas	2005	Prospective Cohort	N/A	120	% Improvement	146 (68.9%)	105 (58.7%)	Back Pain severity was reported to be improved if the response was "better" to "completely gone" the same if the response
					120	% No Change	43 (20.3%)	50 (27.9%)	
					120	% Worse	23 (10.9%)	14 (13.4%)	
	Marks	2000	Retrospective Cohort		30.7	% Excellent Outcome	33.0%	N/A	Excellent Outcome: Back and/or leg pain completely relieved; No further surgical intervention required at involved level; Return to previous employment; no restriction on physical activities; no medications
					30.7	% Good Outcome	30.0%	N/A	Good Outcome: significant relief of back and/or leg pain; return to previous employment; few restrictions on physical activity; occasional use of non-steroidal anti-inflammatory or mild analgesic meds
					30.7	% Fair Outcome	20.0%	N/A	Fair Outcome: Some back and/or leg pain; return to lighter duty of work; moderate restrictions on physical activities; regular use of non-steroidal anti-inflammatory or mild analgesic meds; patient feels relief was adequate; pain and life-style, although not as good as hoped for pre-operatively is acceptable; patient wishes no further surgical treatment
					30.7	% Poor Outcome	17.0%	N/A	Poor Outcome: little or no relief of back and/or leg pain; unable to return to work; severe restrictions on physical activities; occasional or regular use of narcotic pain meds

APLD: Automated Percutaneous Lumbar Discectomy; IDET: Intradiscal Electrothermal Therapy; N/R: Not Reported; N/A: Not Applicable

Table 16a: Measures of clinical improvement in studies of the herniated disc population, by type of treatment
Study Type: Comparative studies, Case-Series: Non-comparative studies

Intervention	Author	Year	Study Design	Comparator	Time (Months)	Measure	Intervention Outcome	Comparator Outcome	Definition
Discectomy	Tsou	2004	Retrospective Cohort		31.3	% Excellent Outcome	15.0%	N/A	Surgeon's Assessment
					31.3	% Good Outcome	28.3%	N/A	Surgeon's Assessment
					31.3	% Fair Outcome	30.1%	N/A	Surgeon's Assessment
					31.3	% Poor Outcome	26.5%	N/A	Surgeon's Assessment

N/R: Not Reported; N/A: Not Applicable

Table 17a: Subsequent treatment in studies of the herniated disc population, by type of initial treatment
Study Type: Randomized Controlled Trials, Comparative studies, Case-Series: Non-comparative studies

Intervention	Author	Year	Study Design	Comparator	Subsequent Treatment Type	Time (Months)	Measures	Intervention Outcome	Comparator Outcome	Comments
APLD	Peng	2012	Prospective Cohort	N/A	Additional Discectomy	12	n(%)	2 (3.5%)	N/A	
					Additional Fusion	12	n(%)	3 (5.0%)	N/A	
Discectomy	Teli	2010	RCT	Microendoscopic Discectomy	Recurrent Herniation (operated)	24	n(%)	2 (3.0%)	8 (11.4%)	
				Microdiscectomy	Recurrent Herniation (operated)	24	n(%)	3 (3.0%)	3 (4.2%)	
	Atlas	2009	RCT	Conservative Care	Reoperation	24	n(%)	35 (7.0%)	6 (7.0%)	
	Ruetten	2009	RCT	Microdiscectomy	Subsequent Fusion/Laminectomy	12	n (%)	2 (4.4%)	3 (7.1%)	
	Schick	2009	Prospective Cohort	Sequestrectomy	Recurrence	34	n(%)	2 (2.0%)	1 (1.0%)	
	Pearson	2008	RCT	Conservative Care	Reoperation	12	n(%)	36 (4.6%)	N/R	
					Reoperation	24	n(%)	48 (6.2%)	N/R	
					Reoperation due to Reherniation	12	n(%)	36 (4.6%)	N/R	
					Reoperation due to Reherniation	24	n(%)	38 (4.9%)	N/R	
	Weinstein	2008	RCT	Conservative Care	Reoperation	12	n(%)	46 (6.0%)	N/R	
					Reoperation	24	n(%)	63 (8.0%)	N/R	
					Reoperation	36	n(%)	70 (9.0%)	N/R	
					Reoperation	48	n(%)	81 (10.0%)	N/R	
					Reoperation due to Reherniation	48	n(%)	49 (6.0%)	N/R	
					Reoperation due to Other Complication	48	n(%)	21 (3.0%)	N/R	
					Reoperation due to a New Condition	48	n(%)	9 (1.0%)	N/R	
	Kim	2007	Retrospective Cohort	Microscopic Discectomy	Recurrence	23.6	n(%)	41 (45.1%)	19 (42.2%)	
	Peul	2007	RCT	Conservative Care	Reoperation	12	n (%)	4 (3.2%)	N/R	
	Katayama	2006	RCT	Microdiscectomy	Subsequent Fusion/Fenestration Surgery	48	n (%)	0 (0%)	2 (3.5%)	
	Weinstein	2006	RCT	Conservative Care	Additional Surgery	12	n(%)	9 (4.0%)	N/R	
					Additional Surgery	24	n(%)	13 (5.0%)	N/R	
					Reoperation due to Reherniation	12	n(%)	5 (2.0%)	N/R	
					Reoperation due to Reherniation	24	n(%)	8 (3.0%)	N/R	
					Reoperation due to Other Complication	12	n(%)	4 (2.0%)	N/R	
					Reoperation due to Other Complication	24	n(%)	4 (2.0%)	N/R	

APLD: Automated Percutaneous Lumbar Discectomy; N/R: Not Reported; N/A: Not Applicable

Table 17a: Subsequent treatment in studies of the herniated disc population, by type of initial treatment
Study Type: Randomized Controlled Trials, Comparative studies, Case-Series: Non-comparative studies

Intervention	Author	Year	Study Design	Comparator	Subsequent Treatment Type	Time (Months)	Measures	Intervention Outcome	Comparator Outcome	Comments
Discectomy	Atlas	2005	Prospective Cohort	Conservative Care	Reoperation	120	n(%)	51 (25.0%)	N/A	
	Fisher	2004	Prospective Cohort	N/A	Reoperation	12	n(%)	6 (8.0%)	N/A	
	Tsou	2004	Retrospective Cohort	N/A	Additional Fusion	31.3	n(%)	8 (7.1%)	N/A	
					Additional Laminectomy	31.3	n(%)	3 (2.7%)	N/A	
					Reoperation	31.3	n(%)	7 (6.2%)	N/A	
	Marks	2000	Retrospective Cohort	N/A	Reoperation	30.7	n(%)	10 (9.7%)	N/A	
					Additional Posterolateral interbody fusion	30.7	n(%)	1 (0.97%)	N/A	
					Additional anterolateral interbody fusion	30.7	n(%)	5 (4.9%)	N/A	
					Additional 360 degree fusion	30.7	n(%)	3 (2.9%)	N/A	
					Additional micro-laminectomy	30.7	n(%)	1 (0.97%)	N/A	
Coblation Nucleoplasty	Gerszten	2010	RCT	Epidural Steroid Injections	Freedom from Secondary Procedures	6	K-M	67.7%	75.3%	
					Freedom from Secondary Procedures	12	K-M	57.9%	29.0%	
					Freedom from Secondary Procedures	24	K-M	52.1%	16.6%	

N/R: Not Reported; N/A: Not Applicable

Table 1b: Study Characteristics and Main Outcomes of Systematic Reviews for the spinal stenosis population, by type of treatment

Treatment Type	Author	Year	# of Studies	Eligibility Criteria	Main Results	Quality Rating	Comments
Spinal Injections	Chou	2009	135	Inclusion: LBP of any duration, alone or with leg pain; evaluated a target injection or other interventional therapy; reported at least 1 of the following outcomes: back specific function, generic health status, pain, work disability, or patient satisfaction; Exclusion: LBP associated with major trauma, cancer, infection, cauda equina syndrome, fibromyalgia, spondyloarthropathy, and osteoporosis or vertebral compression fracture	There is evidence on the efficacy of epidural injections for spinal stenosis.	7	

LBP: Low Back Pain

Table 2b: Characteristics of studies for the spinal stenosis population, by type of treatment
Study Type: Randomized Controlled Trials and Meta-Analysis

Treatment Type	Author	Year	Study Design	Comparator	Sample Size	Follow-up (Months)	Eligibility Criteria	Quality Rating	Comments
Interspinal Spacers	Zucherman	2004	RCT	Conservative Care	191	Actual: 12	Inclusion: be able to sit for 50 minutes without pain; walk 50 feet or more; completed at least 6 months of non-operative therapy; Exclusion: fixed motor deficit, cauda equina syndrome, significant lumbar instability, previous lumbar surgery, significant peripheral neuropathy or acute denervation secondary to radiculopathy, scoliotic Cobb angle greater than 25 degree, spondylolisthesis greater than grade 1.0 at the affected level, sustained pathologic fractures, or severe osteoporosis of the vertebrae and/or hips, obesity, active infection or systemic disease, Paget's disease or metastasis to the vertebrae, or steroid use for more than 1 month within 12 months preceding the study	4	

RCT: Randomized Controlled Trial

Table 3b: Functional outcomes for the spinal stenosis population, by type of treatment
Study Type: Randomized Controlled Trials, Systematic Reviews, and Meta-Analysis

Treatment Type	Author	Year	Study Design	Interventions	Age (Yrs)	Female: n (%)	Race: White n (%)	Disability Coverage n (%)	Employment Status n (%)	Psychological Comorbidity n (%)	Imaging Used n (%)	Comments
Interspinal Spacers	Zucherman	2004	RCT	Interspinous Spacers	69.9	43 (43.0%)	N/R	N/R	N/R	N/R	N/R	
				Conservative Care	68.6	48 (48.0%)	N/R	N/R	N/R	N/R	N/R	

RCT: Randomized Controlled Trial; N/R: Not Reported

Table 4b: Functional outcomes for the spinal stenosis population, by type of treatment
Study Type: Randomized Controlled Trials and Meta-Analysis

Intervention	Author	Year	Study Design	Comparator	Index	Time (Months)	Measure	Intervention Outcome	Comparator Outcome	Comments
No Studies reported										

Table 5b: Pain outcomes in studies of the spinal stenosis population, by type of treatment
Study Type: Randomized Controlled Trials and Meta-Analysis

Intervention	Author	Year	Study Design	Comparator	Scale	Time (Months)	Measure	Intervention Outcome	Comparator Outcome	Comments
No Studies reported										

Table 6b: Quality of life outcomes in studies of spinal stenosis population, by type of treatment
Study Type: Randomized Controlled Trials and Meta-Analysis

Intervention	Author	Year	Study Design	Comparator	Scale	Component	Time (Months)	Measure	Intervention Outcome	Comparator Outcome	Comments
Interspinal Spacers	Zucherman	2004	RCT	Conservative Care	SF36	PF	0	Mean	31.7	33	
							12	Mean	62.2	42.7	
						BP	0	Mean	24.5	28.2	
							12	Mean	56.1	36.9	

RCT: Randomized Controlled Trial; SF36: Short Form - 36; BP: Bodily Pain; PF: Physical Function

Table 7b: Employment status outcomes in studies of the spinal stenosis population, by type of treatment
Study Type: Randomized Controlled Trials and Meta-Analysis

Intervention	Author	Year	Study Design	Comparator	Work Status Outcome	Time (Months)	Measures	Intervention Outcome	Comparator Outcome	Comments
No Studies reported										

Table 8b: Measures of clinical improvement in studies of the spinal stenosis population, by type of treatment
Study Type: Randomized Controlled Trials and Meta-Analysis

Intervention	Author	Year	Study Design	Comparator	Time (Months)	Measure	Intervention Outcome	Comparator Outcome	Definition	Comments

No Studies reported

Table 9b: Mortality and other harms in studies of the spinal stenosis population, by type of treatment
Study Type: Randomized Controlled Trials and Meta-Analysis

Harm Category	Intervention	Author	Year	Comparator	Study Design	Time (Months)	Measure	Intervention Outcome	Comparator Outcome	Comments
30-day mortality					No Studies reported					
Major					No Studies reported					
Minor					No Studies reported					

Table 10b: Characteristics of studies for the spinal stenosis population, by type of treatment
Study Type: Comparative studies, Case-Series: Non-comparative studies

Treatment Type	Author	Year	Study Design	Comparator	Sample Size	Follow-up (Months)	Eligibility Criteria	Quality Rating	Comments
Interspinous Spacers	Sobottke	2009	Retrospective Cohort	N/A	129	Mean (SD): 18 (13)	Inclusion: Patients who felt relief in flexion and were treated with an interspinous spacer device	Fair	
Spinal Injections	Hebl	2010	Retrospective Cohort	N/A	937	Actual: 180	Inclusion: the medical records of all patients with history of spinal stenosis or lumbar disk disease who underwent a subsequent spinal or epidural anesthetic during a 15-year study period were retrospectively reviewed; patients were identified if 'spinal stenosis' or 'lumbar disk disease' was entered on their master diagnosis list within Mayo clinic database; neurologic diagnosis were limited to abnormalities of the spinal canal and did not include patients with primary central nervous systems disorders such as MS, amyotrophic lateral sclerosis, or postpolio syndrome; all neurologic diagnoses were confirmed by clinical exam and radiographic imaging by a neurologist or neurosurgeon before study inclusion	Fair	

N/A: Not Applicable

Table 11b: Mortality and other harms in studies of the spinal stenosis population, by type of treatment
Study Type: Comparative studies, Case-Series: Non-comparative studies

Harm Category	Intervention	Author	Year	Comparator	Study Design	Time (Months)	Measure	Intervention Outcome	Comparator Outcome	Comments
30-day Mortality	No Studies with outcomes >= 24 months reported									
Major	No Studies with outcomes >= 24 months reported									
Minor	No Studies with outcomes >= 24 months reported									

Table 12b: Functional outcomes for the spinal stenosis population, by type of treatment
Study Type: Comparative studies, Case-Series: Non-comparative studies

Intervention	Author	Year	Study Design	Comparator	Time (Months)	Scale	Measure	Intervention Outcome	Comparator Outcome	Comments

No Studies with outcomes >= 24 months reported

Table 13b: Pain outcomes in studies of the spinal stenosis population, by type of treatment
Study Type: Comparative studies, Case-Series: Non-comparative studies

Intervention	Author	Year	Study Design	Comparator	Time (Months)	Scale	Measure	Intervention Outcome	Comparator Outcome	Comments

No Studies with outcomes >= 24 months reported

Table 14b: Quality of life outcomes in studies of the spinal stenosis population, by type of treatment
Study Type: Comparative studies, Case-Series: Non-comparative studies

Intervention	Author	Year	Study Design	Comparator	Time (Months)	Scale	Subdomain	Measure	Intervention Outcome	Comparator Outcome	Comments

No Studies with outcomes >= 24 months reported

Table 15b: Employment status outcomes in studies of the spinal stenosis population, by type of treatment
Study Type: Comparative studies, Case-Series: Non-comparative studies

Intervention	Author	Year	Comparator	Study Design	Time (Months)	Work Status Outcome	Measures	Intervention Outcome	Comparator Outcome	Comments

No Studies with outcomes >= 24 months reported

Table 16b: Measures of clinical improvement in studies of the spinal stenosis population, by type of treatment
Study Type: Comparative studies, Case-Series: Non-comparative studies

Intervention	Author	Year	Study Design	Comparator	Time (Months)	Measure	Intervention Outcome	Comparator Outcome	Definition	Comments
Spinal Injections	Hebl	2010	Retrospective Cohort	N/A	180	Percent Success	911 (97.2%)	N/A	Patient reported success	
					180	Percent Failure	16 (1.7%)	N/A	Patient reported failure	

N/R: Not Reported; N/A: Not Applicable

Table 17b: Subsequent treatment in studies of the spinal stenosis population, by type of initial treatment
Study Type: Randomized Controlled Trials, Comparative studies, Case-Series: Non-comparative studies

Intervention	Author	Year	Comparator	Study Design	Subsequent Treatment Type	Time (Months)	Measures	Intervention Outcome	Comparator Outcome	Comments

No Studies reported

Table 1c: Study characteristics and main outcomes of systematic reviews for degenerative spondylolisthesis/isthmic spondylolisthesis population, by type of treatment

Treatment Type	Author	Year	# of Studies	Eligibility Criteria	Main Results	Quality Rating	Comments
Injections	Chou	2009	135	Inclusion: Low back pain of any duration, alone or with leg pain; evaluated a target injection or other interventional therapy; reported at least 1 of the following outcomes: back specific function, generic health status, pain, work disability, or patient satisfaction; Exclusion: LBP associated with major trauma, cancer, infection, cauda equina syndrome, fibromyalgia, spondyloarthropathy, and osteoporosis or vertebral compression fracture	Three placebo-controlled trials evaluated intradiscal steroid injection for degenerative disc disease; 2 (1 high quality) found no significant difference between intradiscal steroid and control injections for pain relief or improvement in functional status; third lower quality trial found discography plus intradiscal steroid injection found discography plus intradiscal steroid superior to discography alone online in the subgroup of patients with inflammatory endplate changes on MRI	7	
Spacers	Chou	2009	84	Inclusion: LBP of any duration, alone or with leg pain; evaluated surgery for nonradicular LBP with common degenerative changes, radiculopathy with herniated lumbar disc, or symptomatic spinal stenosis (with or without degenerative spondylolisthesis); reported at least one of the following outcomes: back specific function, generic health status, pain, work disability, or patient satisfaction	There is fair evidence that fusion is no better than intensive rehabilitation with a cognitive-behavioral emphasis for improvement in pain or function but slightly to moderately superior to standard nonsurgical therapy; Less than half of patients experience optimal outcomes following fusion; Clinical benefits of instrumented versus noninstrumented fusion are unclear; There is good evidence that decompressive surgery is moderately superior to nonsurgical therapy through q to 2 years; There is fair evidence that artificial disc replacement is similarly effective compared to fusion for single level degenerative disc disease and that an interspinous spacer device is superior to nonsurgical therapy for 1- or 2-level spinal stenosis with symptoms relieved with forward flexion; There is insufficient evidence to judge long-term harms or benefits	7	

LBP: Low Back Pain

Table 2c: Characteristics of studies for the Degenerative spondylolisthesis/Isthmic spondylolisthesis population, by type of treatment
Study Type: Randomized Controlled Trials and Meta-Analysis

Treatment Type	Author	Year	Study Design	Comparator	Sample Size	Follow-up (Months)	Eligibility Criteria	Quality Rating	Comments
Interspinous Spacers	Anderson	2006	RCT	Conservative Care	42	Actual: 24	Inclusion: Symptoms must be relieved by sitting or flexion; completed at least a 6-month course of nonoperative treatment; Exclusion: could not walk at least 50 feet and/or were unable to sit for at least 50 minutes, or if anterior translation great than 25% was seen on imaging studies	3	

RCT: Randomized Controlled Trial

Table 3c: Patient Characteristics in studies of the Degenerative spondylolisthesis/Isthmic spondylolisthesis population, by type of treatment
Study Type: Randomized Controlled Trials and Meta-Analysis

Treatment Type	Author	Year	Study Design	Interventions	Age (Yrs)	Female: n (%)	Race: White n (%)	Disability Coverage n (%)	Employment Status n (%)	Psychological Comorbidity n (%)	Imaging Used n (%)	Comments
Interspinous Spacers	Anderson	2006	RCT	Interspinous Spacers	Mean (Range): 71.4 (52-82)	23 (54.8%)	N/R	WC: (2.4%)	Retired: (64.3%)	N/R	N/R	
				Conservative Care	Mean (Range): 68.5 (50-88)	22 (66.7%)	N/R	WC: (3.0%)	Retired: (60.6%)	N/R	N/R	

RCT: Randomized Controlled Trial; WC: Worker's Compensation Insurance; N/R: Not Reported

Table 4c: Functional outcomes for the Degenerative spondylolisthesis/Isthmic spondylolisthesis population, by type of treatment
Study Type: Randomized Controlled Trials and Meta-Analysis

Intervention	Author	Year	Study Design	Comparator	Index	Time (Months)	Measure	Intervention Outcome	Comparator Outcome	Comments
No Studies reported										

Table 5c: Pain outcomes in studies of the Degenerative spondylolisthesis/Isthmic spondylolisthesis population, by type of treatment
Study Type: Randomized Controlled Trials and Meta-Analysis

Intervention	Author	Year	Study Design	Comparator	Scale	Time (Months)	Measure	Intervention Outcome	Comparator Outcome	Comments
No Studies reported										

Table 6c: Quality of life outcomes in studies of Degenerative spondylolisthesis/Isthmic spondylolisthesis population, by type of treatment
Study Type: Randomized Controlled Trials and Meta-Analysis

Intervention	Author	Year	Study Design	Comparator	Scale	Component	Time (Months)	Measure	Intervention Outcome	Comparator Outcome	Comments
Interspinous Spacers	Anderson	2006	RCT	Conservative Care	SF36	MCS	0	Mean (SD)	52.06 (1.76)	49.92 (1.78)	
							24	Mean (SD)	56.29 (1.25)	49.66 (2.22)	

RCT: Randomized Controlled Trial; SF36: Short Form - 36; MCS: Mental Component Summary

Table 7c: Employment status outcomes in studies of the Degenerative spondylolisthesis/Isthmic spondylolisthesis population, by type of treatment
Study Type: Randomized Controlled Trials and Meta-Analysis

Intervention	Author	Year	Study Design	Comparator	Work Status Outcome	Time (Months)	Measures	Intervention Outcome	Comparator Outcome	Comments
No Studies reported										

RCT: Randomized Controlled Trial; N/R: Not Reported

Table 8c: Measures of clinical improvement in studies of Degenerative spondylolisthesis/Isthmic spondylolisthesis population, by type of treatment
Study Type: Randomized Controlled Trials and Meta-Analysis

Intervention	Author	Year	Study Design	Comparator	Time (Months)	Measure	Intervention Outcome	Comparator Outcome	Definition	Comments

No Studies reported

Table 9c: Mortality and other harms in studies of the Degenerative spondylolisthesis/Isthmic spondylolisthesis population, by type of treatment
Study Type: Randomized Controlled Trials and Meta-Analysis

Harm Category	Intervention	Author	Year	Study Design	Comparator	Measure	Intervention Outcome	Comparator Outcome	Comments
30-day Mortality					No Studies reported				
Major					No Studies reported				
Minor					No Studies reported				

Table 10c: Characteristics of studies for the Degenerative spondylolisthesis/Isthmic spondylolisthesis population, by type of treatment
Study Type: Comparative studies, Case-Series: Non-comparative studies

Treatment Type	Author	Year	Study Design	Comparator	Sample Size	Follow-up (Months)	Eligibility Criteria	Quality Rating	Comments

No Studies with outcomes >= 24 months reported

Table 11c: Mortality and other harms in studies of Degenerative spondylolisthesis/Isthmic spondylolisthesis population, by type of treatment
Study Type: Comparative studies, Case-Series: Non-comparative studies

Harm Category	Intervention	Author	Year	Study Design	Comparator	Measure	Intervention Outcome	Comparator Outcome	Comments
30-day Mortality				No Studies with outcomes >= 24 months reported					
Major				No Studies with outcomes >= 24 months reported					
Minor				No Studies with outcomes >= 24 months reported					

Table 12c: Functional outcomes for the Degenerative spondylolisthesis/Isthmic spondylolisthesis population, by type of treatment
Study Type: Comparative studies, Case-Series: Non-comparative studies

Intervention	Author	Year	Study Design	Comparator	Scale	Time (Months)	Measure	Intervention Outcome	Comparator Outcome	Comments

No Studies with outcomes >= 24 months reported

Table 13c: Pain outcomes in studies of Degenerative spondylolisthesis/Isthmic spondylolisthesis population, by type of treatment
Study Type: Comparative studies, Case-Series: Non-comparative studies

Intervention	Author	Year	Study Design	Comparator	Scale	Time (Months)	Measure	Intervention Outcome	Comparator Outcome	Comments

No Studies with outcomes >= 24 months reported

Table 14c: Quality of life outcomes in studies of Degenerative spondylolisthesis/Isthmic spondylolisthesis population, by type of treatment
Study Type: Comparative studies, Case-Series: Non-comparative studies

Intervention	Author	Year	Study Design	Comparator	Scale	Subdomain	Time (Months)	Measure	Intervention Outcome	Comparator Outcome	Comments

No Studies with outcomes >= 24 months reported

Table 15c: Employment status outcomes in studies of Degenerative spondylolisthesis/Isthmic spondylolisthesis population, by type of treatment
Study Type: Comparative studies, Case-Series: Non-comparative studies

Intervention	Author	Year	Study Design	Comparator	Time (Months)	Work Status Outcome	Measures	Intervention Outcome	Comparator Outcome	Comments

No Studies with outcomes >= 24 months reported

Table 16c: Measures of clinical improvement in studies of Degenerative spondylolisthesis/Isthmic spondylolisthesis population, by type of treatment
Study Type: Prospective Trials, Cohorts, Case-Control

Intervention	Author	Year	Study Design	Comparator	Time (Months)	Measure	Intervention Outcome	Comparator Outcome	Definition	Comments

No Studies with outcomes >= 24 months reported

Table 17c: Subsequent treatment of Degenerative spondylolisthesis/Isthmic spondylolisthesis population, by type of initial treatment
Study Type: RCTs, Comparative studies, Case-Series: Non-comparative studies

Intervention	Author	Year	Comparator	Study Design	Subsequent Treatment Type	Time (Months)	Measures	Intervention Outcome	Comparator Outcome	Comments
No Studies reported										

RCT: Randomized Controlled Trial

Table 1d: Study characteristics and main outcomes of systematic reviews for the non-specific low back pain population, by type of treatment

Treatment Type	Author	Year	# of Studies	Eligibility Criteria	Main Outcomes	Quality Rating	Comments
IRP	Guzman	2001	10	Inclusion: adults with disabling LBP >= 3 months; patients had to be assessed and treated by qualified professionals according to a plan that addresses physical and at least one of psychological and social/occupational dimensions; Excluded education back school literature	There is evidence that intensive multidisciplinary biopsychosocial rehabilitation with functional restoration reduces pain and improves function in patients with chronic low back pain; Less intensive interventions did not show improvements in clinically relevant outcomes	5	
	Tveito	2004	10	Inclusion: Controlled workplace interventions with employees as participants aiming to prevent or treat	Only exercise, comprehensive multidisciplinary, and treatment interventions have a documented effect on LBP	3	
	Karjalainen	2008	2	Inclusion: Chronic LBP >4 weeks and < 3 months; defined multidisciplinary as consisting of a physician's consultation plus either a psychological, social or vocational intervention, or a combination; patients LBP could not be due to acute trauma, neoplasms, and inflammatory or neurologic diseases, osteoporosis	There was moderate scientific evidence showing that multidisciplinary rehabilitation, which includes a workplace visit or more comprehensive occupational health care intervention, helps patients to return to work faster, results in fewer sick leaves and alleviates subjective disability	7	
	Ravenek	2010	12	Inclusion: RCT or controlled clinical trial; Participants were working age adults experiencing work-related CLBP (>= 12 weeks duration); Intervention evaluated was multidisciplinary; Employment outcome measured	There is conflicting evidence for the effectiveness of multidisciplinary programs to improve employment outcomes in CLBP	3	
IDET	Andersson	2006	18	Inclusion: disc degeneration or disruption must be the primary indication for IDET; follow-up outcome data included evaluations of back pain severity, condition-specific functional impairment and/or health-related quality-of-life	Median % improvement in pain severity after IDET was 51%, in back function 41%, and in quality-of-life 43%; Adverse events were rarely experienced with the IDET procedure (Median: 0%, range: 0% to 16%, n=14 studies).	3	
	Helm	2009	18	Inclusion: LBP >= 6 months duration; Treatment with annuloplasty procedure using IDET or radiofrequency annuloplasty; >= 6 month follow-up	Based on USPSTF criteria, the indicated evidence for IDET is Level II-3 in reducing low back pain in patients with intradiscal disorders	5	

IDET: Intradiscal Electrothermal Therapy; IRP: Interdisciplinary Rehabilitation Program; RFD: Radiofrequency Denervation; LBP: Low Back Pain

Table 1d: Study characteristics and main outcomes of systematic reviews for the non-specific low back pain population, by type of treatment

Treatment Type	Author	Year	# of Studies	Eligibility Criteria	Main Outcomes	Quality Rating	Comments
IDET	Freeman	2006	14	Inclusion: all IDET studies with at least one of the four specified primary outcome measures; pain intensity as assessed by VAS, global measurement of overall improvement, back specific functional status such as ODI, and return to work.	There were eleven prospective cohort studies with Level II evidence. Overall, these studies showed a mean improvement in the VAS for back pain of 3.4 (range 1.4-6.5); There were 5 retrospective studies with Level III evidence, which showed that between 13% and 23% of patients subsequently underwent surgery for low back pain within the study period. Two RCTs have been reported on IDET. One showed an advantage of 1.3 points on the VAS and seven points on the ODI when compared to sham placebo. The second RCT showed no benefit from IDET over sham placebo. Overall, there is weak evidence for the efficacy of IDET.	2	
	Waseem	2011	3	Inclusion: non-specific LBP and/or sciatica; patients with acute subacute or chronic LBP were included	There is low quality evidence that botulinum toxin injections are effective in treating LBP and sciatica	7	
RFD	Niemisto	2003	7	Inclusion: RCTs of radiofrequency denervation for musculoskeletal pain disorders	There is conflicting evidence for RFDs effectiveness for lumbar zygapophysial joint pain; There is limited evidence suggesting that intradiscal RFD may not be effective in relieving discogenic LBP	5	
	Henschke	2010	27	Inclusion: only RCTs with <= 1 day of follow-up were considered; participants must fulfill the following: adults with chronic (>12 weeks) LBP; Exclusion: trials including subjects with specific LBP caused by pathological entities, such as vertebral spinal stenosis, ankylosing spondylitis, scoliosis, or coccydynia; post-operative studies; prevention studies; abstracts or non-published studies	Because of heterogeneity, only two comparisons could be pooled. Overall, there is only low to very low quality evidence to support the use of injection therapy and denervation procedures over placebo or other treatments for patients with chronic LBP	6	

IDET: Intradiscal Electrothermal Therapy; IRP: Interdisciplinary Rehabilitation Program; RFD: Radiofrequency Denervation; LBP: Low Back Pain

Table 1d: Study characteristics and main outcomes of systematic reviews for the non-specific low back pain population, by type of treatment

Treatment Type	Author	Year	# of Studies	Eligibility Criteria	Main Outcomes	Quality Rating	Comments
Spinal Injections	Chou	2009	135	Inclusion: Low back pain of any duration, alone or with leg pain; evaluated a target injection or other interventional therapy; reported at least 1 of the following outcomes: back specific function, generic health status, pain, work disability, or patient satisfaction; Exclusion: LBP associated with major trauma, cancer, infection, cauda equina syndrome, fibromyalgia, spondyloarthropathy, and osteoporosis or vertebral compression fracture	There is good evidence that prolotherapy is ineffective for nonspecific low back pain and intradiscal corticosteroid injection is ineffective for presumed discogenic back pain. There is fair evidence that intra-articular facet joint steroid injection is not effective.	7	

IDET: Intradiscal Electrothermal Therapy; IRP: Interdisciplinary Rehabilitation Program; RFD: Radiofrequency Denervation; LBP: Low Back Pain

Table 2d: Characteristics of studies for the non-specific back pain population, by type of treatment
Study Type: Randomized Controlled Trials, Systematic Reviews, and Meta-Analysis

Treatment Type	Author	Year	Study Design	Comparator	Sample Size	Follow-up (Months)	Eligibility Criteria	Quality Rating	Comments
IRP	Vollenbroek-Hutten	2004	RCT	Conservative Care	142	Actual: 6	Inclusion: Pain longer than 3 mos., no back surgery in the pat 3 mos.; Exclusion: structural pathology, medical contraindication for physical training	6	
	Fairbank	2005	RCT	Spinal Fusion	349	Actual: 24	Inclusion: > 12 months history of chronic LBP with or without referred pain and irrespective of whether they had had previous root decompression or discectomy; Exclusion: inflammatory disease, tumors, fractures, psychiatric disease, inability or unwillingness to complete the trial questionnaires or pregnancy; previous surgical stabilization surgery of the spine	7	
	Friedrich	2005	RCT	Conservative Care	56	Actual: 60	Exclusion: specific LBP; 3 or more of 5 nonorganic physical signs; patients involved in disability pension proceedings or private insurance litigation	3	
	Jensen	2005	RCT	Conservative Care	186	Actual: 3	Inclusion: long term non-specific spinal pain; currently and continuously sick-listed for spinal pain at least 1 month and a max of 6 months; Exclusion: serious spinal pathology exposure to physical trauma within 6 months before examination	6	
	Kaapa	2006	RCT	Conservative Care	120	Actual: 24	Exclusion: acute disc prolapse with nerve root entrapment < 3 months, >= 6 months since back surgery, severe cardiovascular or other disorder interfering with active rehab, specific back disorder, severe mental illness, more than 90 days off work because of LBP during the preceding year, pension in the near future (within 2 yrs), pregnancy, ongoing or planned LBP rehab.	5	
	Anema	2007	RCT	Conservative Care	308	Actual: 12	Excluded LBP due to cardiovascular, psychiatric, or surgical contraindications; and sick leave due to LBP < 1 month before the current episode of sick leave	6	

IDET: Intradiscal Electrothermal Therapy; IRP: Interdisciplinary Rehabilitation Program; RCT: Randomized Controlled Trial; META: Meta-Analysis; LBP: Low Back Pain

Table 2d: Characteristics of studies for the non-specific back pain population, by type of treatment
Study Type: Randomized Controlled Trials, Systematic Reviews, and Meta-Analysis

Treatment Type	Author	Year	Study Design	Comparator	Sample Size	Follow-up (Months)	Eligibility Criteria	Quality Rating	Comments
IRP	Roche	2007	RCT	Conservative Care	132	Actual: 5	Inclusion: LBP at least 3 mos.; patients on sick leave or at risk of work disability and not in temporary employment; Exclusion: patients with malignant, traumatic, infectious, or inflammatory LBP; acute LBP or sciatica, spondylolisthesis, or cardiac or respiratory insufficiency; articular or neurologic impairment incompatible with a physical exercise program; psychiatric disorders precluding participation in group therapy; receiving disability pensions or refusing to participate in the study	7	
	Ribeiro	2008	RCT	Conservative Care	55	Actual: 4	Inclusion: chronic non-specific low back pain lasting more than 3 months; Exclusion: previous back surgery, spinal tumor, spinal fracture, pregnancy, fibromyalgia, inflammatory or infectious spinal diseases and litigant patients	6	
	van der Roer	2008	RCT	Conservative Care	114	Actual: 12	Inclusion: Non-specific LBP > 12 months, inability to resume daily activities in the last 3 weeks, health insurance with one insurance company who was willing to reimburse the intense training protocol	5	
	Ewert	2009	RCT	Conservative Care	169	Actual: 12	Inclusion: at least one LBP episode in the previous 2 years; Exclusion: doctor's note for sick leave as the result of acute or chronic LBP, surgery to treat back pain 6 months before the study, or insufficient fitness to participate in the GPE	5	
	Dufour	2010	RCT	Conservative Care	272	Actual: 12	Inclusion: LBP lasting >= 12 weeks with or without radiating leg pain; Exclusion: patients with symptoms of an acute herniated disc accompanied by nerve root entrapment, unstable spondylolisthesis, spondylitis, health conditions that prevented them from performing strenuous exercise	6	

IDET: Intradiscal Electrothermal Therapy; IRP: Interdisciplinary Rehabilitation Program; RCT: Randomized Controlled Trial; META: Meta-Analysis; LBP: Low Back Pain

Table 2d: Characteristics of studies for the non-specific back pain population, by type of treatment
Study Type: Randomized Controlled Trials, Systematic Reviews, and Meta-Analysis

Treatment Type	Author	Year	Study Design	Comparator	Sample Size	Follow-up (Months)	Eligibility Criteria	Quality Rating	Comments
IRP	Lambeek	2010	RCT	Conservative Care	134	Actual: 12	Inclusion: LBP >12 weeks; employed at least 8 hrs per week; absent or partially absent from work; Exclusion: absent from work for more than 2 years, had worked temporarily for an employment agency without detachment, had specific LBP due to infection, tumor, osteoporosis, rheumatoid arthritis, fracture, or inflammatory process; had undergone spinal surgery or invasive exams within three months; had serious psych. or cardio. illness	6	
IDET	Pauza	2004	RCT	Sham Placebo	64	Actual: 6	Inclusion: low back greater than leg pain present for greater than 6 months; failure to improve after >= 6 weeks of nonoperative care; a score less than 20 on the beck depression scale; no surgical interventions within the previous 3 months; Exclusion: previous lumbar spine surgery, abnormal neurological exam other than ankle reflex changes, radicular pain by history or exam, structural deformities; intervertebral disc herniation; uncontrolled or acute medical illnesses	9	
	Freeman	2005	RCT	Sham Placebo	57	Actual: 6	Inclusion: Symptoms of degenerative lumbar disc disease of at least 3 months; failure to improve with a minimum of 6 week of conservative treatment; present with marked functional limitation; present with predominant low back pain with or without referred leg pain; Exclusion: Evidence of large contained or sequestered herniation; loss of more than 50% disc height at the target level; severely disrupted disc; previous back surgery at any level of the lumbar spine; spondylolisthesis at a symptomatic disc level; psychological disorders that may impact treatment outcome; medical condition that could interfere with follow-up care or evaluation	8	

IDET: Intradiscal Electrothermal Therapy; IRP: Interdisciplinary Rehabilitation Program; RCT: Randomized Controlled Trial; META: Meta-Analysis; LBP: Low Back Pain

Table 2d: Characteristics of studies for the non-specific back pain population, by type of treatment
Study Type: Randomized Controlled Trials, Systematic Reviews, and Meta-Analysis

Treatment Type	Author	Year	Study Design	Comparator	Sample Size	Follow-up (Months)	Eligibility Criteria	Quality Rating	Comments
Spinal Injections	Luukkainen	2002	RCT	Sham Placebo	24	Actual: 1	Inclusion: pain at least for 3 months in the region of the Sacroiliac Joint; positive results on at least one of the following tests: Gaenslen's test, Patrick's test or thigh flexion test; no allergy to lidocaine; no signs of infections or neoplasms; no radiological signs of sacroilitis and no signs of spondyloarthropathy;	3	
	Manchikanti	2010	RCT	Injections	140	Actual: 12	Inclusion: patients with history of chronic function-limiting low back pain with or without lower extremity pain of at least 6 months duration (post-surgery), with surgery performed at least 6 months earlier; Exclusion: a positive response to controlled comparative local anesthetic blocks, uncontrollable or unstable opiod use, uncontrolled psychiatric disorders, uncontrolled medical illness, any conditions that could interfere with the interpretation of the outcome assessments, and history of potential for adverse reactions to local anesthetic or steroids	8	

IDET: Intradiscal Electrothermal Therapy; IRP: Interdisciplinary Rehabilitation Program; RCT: Randomized Controlled Trial; META: Meta-Analysis; LBP: Low Back Pain

Table 3d: Patient Characteristics in studies of the non-specific back pain population, by type of treatment
Study Type: Randomized Controlled Trials, Systematic Reviews, and Meta-Analysis

Treatment Type	Author	Year	Study Design	Interventions	Age (Yrs)	Female: n (%)	Race: White n (%)	Disability Coverage n (%)	Employment Status n (%)	Psychological Comorbidity n (%)	Imaging Used n (%)	Comments
IRP	Vollenbroek-Hutten	2004	RCT	IRP	Mean (SD): 38.5 (9.8)	N/R	N/R	N/R	N/R	N/R	N/R	
				CC	Mean (SD): 39.5 (9.9)	N/R	N/R	N/R	N/R	N/R	N/R	
	Fairbank	2005	RCT	IRP	Range: 18-55	80 (46.2%)	N/R	N/R	Employed: 94 (54.3%)	N/R	N/R	
				Spinal Fusion	Range: 18-55	97 (55.1%)	N/R	N/R	Employed: 88 (50.0%)	N/R	N/R	
	Friedrich	2005	RCT	IRP	Mean (SD): 51.4 (10.9)	12 (0.4)	N/R	N/R	N/R	N/R	N/R	
				CC	Mean (SD): 47.5 (10.6)	13 (0.5)	N/R	N/R	N/R	N/R	N/R	
	Jensen	2005	RCT	CC	Mean (SD): 44 (11)	28 (58.0%)	N/R	N/R	Employed: 44 (94.0%)	N/R	N/R	
				Physical Therapy	Mean (SD): 43 (9)	37 (68.0%)	N/R	N/R	Employed: 42 (78.0%)	N/R	N/R	
				CBT	Mean (SD): 44 (10)	22 (45.0%)	N/R	N/R	Employed: 42 (86.0%)	N/R	N/R	
				IRP	Mean (SD): 43 (12)	30 (48.0%)	N/R	N/R	Employed: 52 (84.0%)	N/R	N/R	
	Kaapa	2006	RCT	IRP	Mean (SD): 46 (7.9)	118 (98.0%)	N/R	N/R	N/R	N/R	N/R	
				CC	Mean (SD): 46.5 (7)	118 (98.0%)						
	Anema	2007	RCT	Workplace	Mean (SD): 44 (8.6)	45 (46.9%)	N/R	N/R	N/R	N/R	N/R	
				No Workplace	Mean (SD): 41.2 (10.7)	67 (67.0%)	N/R	N/R	N/R	N/R	N/R	
										N/R	N/R	
				Graded Activity	Mean (SD): 41.3 (9.2)	36 (65.5%)	N/R	N/R	N/R	N/R	N/R	
				No Graded Activity	Mean (SD): 43.4 (8.3)	31 (54.4%)	N/R	N/R	N/R			
	Roche	2007	RCT	IRP	Mean (SD): 40.8 (7.4)	22 (32.4%)	N/R	N/R	Employed: (100%)	16 (23.5%)	N/R	
				CC	Mean (SD): 38.7 (6.1)	24 (37.5%)	N/R	N/R	Employed: (100%)	11 (17.2%)	N/R	

RCT: Randomized Controlled Trial; IDET: Intradiscal Electrothermal Therapy; IRP: Interdisciplinary Rehabilitation Program; CC: Conservative Care; CBT: Cognitive Behavioral Therapy; FT: Full-Time; PT: Part-Time; N/R: Not Reported

Table 3d: Patient Characteristics in studies of the non-specific back pain population, by type of treatment
Study Type: Randomized Controlled Trials, Systematic Reviews, and Meta-Analysis

Treatment Type	Author	Year	Study Design	Interventions	Age (Yrs)	Female: n (%)	Race: White n (%)	Disability Coverage n (%)	Employment Status n (%)	Psychological Comorbidity n (%)	Imaging Used n (%)	Comments
IRP	Ribeiro	2008	RCT	IRP	Mean (SD): 48.1 (14.1)	19 (73.1%)	12 (46.2%)	N/R	N/R	N/R	N/R	
				CC	Mean (SD): 52.8 (10)	26 (89.7%)	20 (69%)	N/R	N/R	N/R	N/R	
	van der Roer	2008	RCT	IRP	Mean (SD): 41.5 (8.8)	33 (55%)	N/R	N/R	Employed: 42 (70%)	N/R	N/R	
				CC	Mean (SD): 42.0 (9.9)	26 (48%)	N/R	N/R	Employed: 31 (57%)	N/R	N/R	
	Ewert	2009	RCT	IRP	Mean (SD): 37.9 (11.6)	84 (91.3%)	N/R	N/R	N/R	N/R	N/R	
				CC	Mean (SD): 41.1 (10.8)	85 (93.4%)	N/R	N/R	N/R	N/R	N/R	
	Dufour	2010	RCT	IRP	Mean (SD): 41.2 (10)	73 (56.6%)	N/R	N/R	Employed: 73 (56.6%)	N/R	N/R	
				CC	Mean (SD): 40.6 (9.1)	80 (55.9%)	N/R	N/R	Employed: 79 (55.2%)	N/R	N/R	
IDET	Pauza	2004	RCT	IDET	Mean (SD): 42 (10)	18 (49.0%)	N/R	Disability: 3 (11%)	Employed: 30 (81.0%)	N/R	N/R	
				Sham Placebo	Mean (SD): 40 (8)	16 (59.0%)	N/R	Disability: 4 (15%)	Employed: 17 (63.0%)	N/R	N/R	
	Freeman	2005	RCT	IDET	Mean (SD, Range): 37.49 (7.82, 20.38-54.68)	13 (34.2%)	N/R	N/R	N/R	N/R	MRI: 38 (100%)	
				Sham Placebo	Mean (SD, Range): 40.2 (8.38, 27.13-54.13)	2 (10.5%)	N/R	N/R	N/R	N/R	MRI: 19 (100%)	

RCT: Randomized Controlled Trial; IDET: Intradiscal Electrothermal Therapy; IRP: Interdisciplinary Rehabilitation Program; CC: Conservative Care; CBT: Cognitive Behavioral Therapy; FT: Full-Time; PT: Part-Time; N/R: Not Reported

Table 3d: Patient Characteristics in studies of the non-specific back pain population, by type of treatment
Study Type: Randomized Controlled Trials, Systematic Reviews, and Meta-Analysis

Treatment Type	Author	Year	Study Design	Interventions	Age (Yrs)	Female: n (%)	Race: White n (%)	Disability Coverage n (%)	Employment Status n (%)	Psychological Comorbidity n (%)	Imaging Used n (%)	Comments
Spinal Injections	Luukkainen	2002	RCT	Injections	Mean (Range): 50.3 (38-68)	10 (77.0%)	N/R	N/R	N/R	N/R	N/R	
				Sham Placebo	Mean (Range): 49.3 (32-70)	7 (64.0%)	N/R	N/R	N/R	N/R	N/R	
	Manchikanti	2010	RCT	Injections	Mean (SD): 52.4 (14.1)	43 (61.0%)	N/R	N/R	FT: 8 (11.4%) PT: 1 (1.4%)	N/R	N/R	
				Injections	Mean (SD): 48 (12.3)	34 (49.0%)	N/R	N/R	FT: 11 (15.7%) PT: 2 (2.9%)	N/R	N/R	

RCT: Randomized Controlled Trial; IDET: Intradiscal Electrothermal Therapy; IRP: Interdisciplinary Rehabilitation Program; CC: Conservative Care; CBT: Cognitive Behavioral Therapy; FT: Full-Time; PT: Part-Time; N/R: Not Reported

Table 4d: Functional outcomes for the non-specific back pain population, by type of treatment
Study Type: Randomized Controlled Trials, Systematic Reviews, and Meta-Analysis

Intervention	Author	Year	Study Design	Comparator	Index	Time (Mos.)	Measure	Intervention Outcome	Comparator Outcome	Comments
IRP	Vollenbroek-Hutten	2004	RCT	CC	RMS	0	Mean (SD)	13 (4)	13 (4)	
						2	Mean (SD)	11 (5)	13 (5)	
						6	Mean (SD)	10 (5)	11 (5)	
	Fairbank	2005	RCT	Spinal Fusion	ODI	0	Mean SD)	46.5 (14.6)	44.8 (14.8)	
						24	Mean SD)	34 (21.1)	36.1 (20.6)	
						24	Treatment Effect (95% CI, p-value)	-4.1 (-8.1 to -0.1, 0.045)		
	Kaapa	2006	RCT	CC	ODI	0	Mean (SD)	25.4 (10.6)	23.8 (11.7)	
						2	Mean (SD)	20.9 (10.1)	21.6 (11.4)	Intervention: RTW Comparator: Did not RTW
						6	Mean (SD)	20.4 (11.6)	18 (11.5)	Intervention: RTW Comparator: Did not RTW
						12	Mean (SD)	18.9 (12.8)	18.5 (12.4)	Intervention: RTW Comparator: Did not RTW
						24	Mean (SD)	19.7 (14.3)	19.3 (13.1)	Intervention: RTW Comparator: Did not RTW
	van der Roer	2008	RCT	CC	RMS	0	Mean	11.6	12.1	
						1.5	Mean	10.2	10.2	
						3	Mean	7.9	7.5	
						6	Mean	7.4	7.7	
						12	Mean	6.7	7.1	

IDET: Intradiscal Electrothermal Therapy; IRP: Interdisciplinary Rehabilitation Program; RCT: Randomized Controlled Trial; CC: Conservative Care; ODI: Oswestrey Disability Index; RMS: Roland-Morris Scale; RTW: Return to work; N/R: Not Reported; N/A: Not Applicable

Table 4d: Functional outcomes for the non-specific back pain population, by type of treatment
Study Type: Randomized Controlled Trials, Systematic Reviews, and Meta-Analysis

Intervention	Author	Year	Study Design	Comparator	Index	Time (Mos.)	Measure	Intervention Outcome	Comparator Outcome	Comments
IRP	Anema	2007	RCT	CC	RMS	0	Mean (SD)	14.9 (4.2)	13.8 (4.6)	Workplace Intervention vs. Not
						12	Mean Change (SD)	9.0 (6.2)	8.1 (5.7)	Workplace Intervention vs. Not
						12	Treatment Effect (95% CI)	-0.25 (-1.57 to 1.06)		Workplace Intervention vs. Not
					RMS	0	Mean (SD)	14.4 (4.5)	15.8 (3.2)	Graded Activity vs. Not
						12	Mean Change (SD)	7.3 (6.2)	9.9 (6.1)	Graded Activity vs. Not
						12	Treatment Effect (95% CI)	1.74 (0.07 to 3.42)		Graded Activity vs. Not
					RMS	12	Mean Change (SD)	8.3 (7.9)	8.7 (6.0)	Combined Intervention vs. Not
						12	Treatment Effect (95% CI)	1.49 (-0.33 to 3.31)		Combined Intervention vs. Not
	Ribeiro	2008	RCT	CC	RMS	0	Mean (SD, 95% CI)	11.46 (4.71, 9.65-13.26)	11.48 (4.46, 9.77-9.65)	
						1	Mean (SD, 95% CI)	9.07 (5.26, 7.09-11.05)	9.89 (4.82, 8.02-7.09)	
						2	Mean (SD, 95% CI)	7.38 (5.33, 5.33-9.43)	8.13 (5.09, 6.19-5.33)	
						4	Mean (SD, 95% CI)	8.15 (5.99, 5.87-10.43)	8.24 (5.62, 6.08-5.87)	
IDET	Pauza	2004	RCT	Sham Placebo	ODI	0	Mean (SD)	32 (10)	33 (11)	
						6	Mean (SD)	20 (12)	28 (15)	
						6	Mean Change (SD)	11 (11)	4 (12)	
						6	p-value	0.05		
	Freeman	2005	RCT	Sham Placebo	ODI	0	Mean (SD)	41.42 (14.8)	40.74 (11.84)	
						6	Mean (SD)	39.77 (16.28)	41.58 (11.29)	
						6	Treatment Effect (95% CI, p-value)	-2.156 (-8.369-4.056, 0.489)		
Injections	Manchikanti	2010	RCT	Injections	ODI	0	Mean (SD)	29.1 (4.5)	30.5 (4.6)	
						3	Mean (SD)	16.8 (6.8)	17.8 (6.7)	
						6	Mean (SD)	16.3 (7)	17.7 (6.9)	
						12	Mean (SD)	16.5 (7)	17.8 (7.1)	

IDET: Intradiscal Electrothermal Therapy; IRP: Interdisciplinary Rehabilitation Program; RCT: Randomized Controlled Trial; CC: Conservative Care; ODI: Oswestrey Disability Index; RMS: Roland-Morris Scale; RTW: Return to work; N/R: Not Reported; N/A: Not Applicable

Table 5d: Pain outcomes in studies of the non-specific back pain population, by type of treatment
Study Type: Randomized Controlled Trials, Systematic Reviews, and Meta-Analysis

Intervention	Author	Year	Study Design	Comparator	Scale	Time (Mos.)	Measure	Intervention Outcome	Comparator Outcome	Comments
IRP	Kaapa	2006	RCT	Conservative Care	NRS	0	Mean (SD)	4.6 (1.9)	5 (2.6)	
						2	Mean (SD)	3.3 (2.5)	3.4 (2.4)	
						6	Mean (SD)	3.3 (2.5)	3.4 (2.5)	
						12	Mean (SD)	3.6 (2.7)	3.4 (2.5)	
						24	Mean (SD)	3.5 (2.6)	4 (2.9)	
	Roche	2007	RCT	Conservative Care	VAS	0	Mean (SD)	4.7 (2.1)	4.5 (2.1)	
						12	Mean Change	-1.9	-1.5	
	Anema	2007	RCT	Conservative Care	VAS	0	Mean (SD)	6.5 (1.7)	6.3 (1.7)	Intervention: Return to work Comparator: Did not return to work
						12	Mean Change (SD)	3.3 (2.6)	2.9 (2.7)	Intervention: Return to work Comparator: Did not return to work
						12	Treatment Effect (95% CI)	-0.20 (-0.75 to 0.35)		Intervention: Return to work Comparator: Did not return to work
					VAS	0	Mean (SD)	6.6 (1.4)	6.7 (1.5)	Graded Activity vs. Not
						12	Mean Change (SD)	2.7 (2.6)	3.7 (2.6)	Graded Activity vs. Not
						12	Treatment Effect (95% CI)	0.67 (-0.05 to 1.38)		Graded Activity vs. Not
					VAS	12	Mean Change (SD)	2.9 (2.6)	3.3 (2.6)	Combined Intervention vs. Not
						12	Treatment Effect (95% CI)	0.47 (-0.42 to 1.35)		Combined Intervention vs. Not
	Ribeiro	2008	RCT	Conservative Care	VAS	0	Mean (SD, 95% CI)	5.26 (2.14, 4.36-6.17)	5.34 (2.4, 4.49-4.36)	
						1	Mean (SD, 95% CI)	3.46 (3.08, 2.31-4.6)	4.24 (2.74, 3.15-2.31)	
						2	Mean (SD, 95% CI)	3.53 (2.94, 2.39-4.68)	3.44 (2.88, 2.36-2.39)	
						4	Mean (SD, 95% CI)	3.34 (3.08, 2.13-4.56)	3.86 (3.09, 2.71-2.13)	
IRP	van der Roer	2008	RCT	Conservative Care	NRS	0	Mean	6.2	5.9	
						1.5	Mean	5.3	5.4	
						3	Mean	4.4	4.9	
						6	Mean	4.1	4.8	
						12	Mean	3.9	4.6	
IDET	Pauza	2004	RCT	Sham Placebo	VAS	0	Mean (SD)	6.5 (1.6)	6.5 (1.8)	
						6	Mean Change (SD)	2.4 (2.3)	1.1 (2.6)	

IDET: Intradiscal Electrothermal Therapy; IRP: Interdisciplinary Rehabilitation Program; RCT: Randomized Controlled Trial; VAS: Visual Analog Scale; NRS: Numeric Rating Scale; N/R: Not Reported; N/A: Not Applicable

Table 5d: Pain outcomes in studies of the non-specific back pain population, by type of treatment
Study Type: Randomized Controlled Trials, Systematic Reviews, and Meta-Analysis

Intervention	Author	Year	Study Design	Comparator	Scale	Time (Mos.)	Measure	Intervention Outcome	Comparator Outcome	Comments
Spinal Injections	Luukkainen	2002	RCT	Sham Placebo	VAS	0	Median (Range)	53 (27-84)	53 (20-83)	
						1	Median Change (Range)	-40(-57--1)	-13(-64-43)	
	Manchikanti	2010	RCT	Injections	NRS	0	Mean (SD)	7.8 (0.9)	7.9 (1)	
						3	Mean (SD)	4.1 (1.7)	4.2 (1.9)	
						6	Mean (SD)	4.1 (1.7)	4.4 (1.9)	
						12	Mean (SD)	4.2 (1.7)	4.5 (1.9)	

IDET: Intradiscal Electrothermal Therapy; IRP: Interdisciplinary Rehabilitation Program; RCT: Randomized Controlled Trial; VAS: Visual Analog Scale; NRS: Numeric Rating Scale; N/R: Not Reported; N/A: Not Applicable

Table 6d: Quality of life outcomes in studies of non-specific back pain population, by type of treatment
Study Type: Randomized Controlled Trials, Systematic Reviews, and Meta-Analysis

Intervention	Author	Year	Study Design	Comparator	Scale	Component	Time (Months)	Measure	Intervention Outcome	Comparator Outcome	Comments
IRP	Fairbank	2005	RCT	Spinal Fusion	SF36	BP	0	Mean (SD)	28.6 (17.3)	30 (16)	
							24	Mean (SD)	48.1 (26.4)	44.9 (25.1)	
					SF36	PF	0	Mean (SD)	33.6 (19)	39.5 (22.1)	
							24	Mean (SD)	50 (28.2)	49.8 (28.7)	
					SF36	MCS	0	Mean (SD)	43.2 (10.9)	44.2 (12.6)	
							24	Mean (SD)	47.4 (12.2)	48.1 (12.6)	
	Ribeiro	2008	RCT	Conservative Care	SF36	PF	0	Mean (SD, 95% CI)	45.38 (37.46, 30.48-60.28)	46.55 (38.22, 32.44-30.48)	
							1	Mean (SD, 95% CI)	66.34 (37.37, 51.74-80.95)	64.65 (36.91, 50.82-51.74)	
							2	Mean (SD, 95% CI)	69.11 (35.55, 54.41-83.81)	73.27 (38.92, 59.35-54.41)	
							4	Mean (SD, 95% CI)	68.26 (42.75, 51.16-85.37)	63.79 (44.11, 47.6-51.16)	
					SF36	BP	0	Mean (SD, 95% CI)	38.07 (18.41, 31.37-44.78)	38.44 (15.71, 32.1-31.37)	
							1	Mean (SD, 95% CI)	49.38 (21.1, 41.98-56.78)	44.1 (16.5, 37.09-41.98)	
							2	Mean (SD, 95% CI)	57.38 (24.67, 49.04-65.72)	46.86 (38.96-54.74)	
							4	Mean (SD, 95% CI)	54 (21.05, 46.28-61.71)	46.06 (38.76-53.37)	
	Ewert	2009	RCT	Conservative Care	SF36	MCS	0	Mean (SD)	49.99 (8.1)	48.09 (10.55)	
							3	Mean (SD)	49.8 (8.95)	50.38 (7.44	
							12	Mean (SD)	51.91 (7.17)	49.51 (10.23)	

IDET: Intradiscal Electrothermal Therapy; IRP: Interdisciplinary Rehabilitation Program; RCT: Randomized Controlled Trial; SF36: Short Form - 36; BP: Bodily Pain; PF: Physical Functioning; N/R: Not Reported; N/A: Not Applicable

Table 6d: Quality of life outcomes in studies of non-specific back pain population, by type of treatment
Study Type: Randomized Controlled Trials, Systematic Reviews, and Meta-Analysis

Intervention	Author	Year	Study Design	Comparator	Scale	Component	Time (Months)	Measure	Intervention Outcome	Comparator Outcome	Comments
IRP	Dufour	2010	RCT	Conservative Care	SF36	BP	0	Mean (SD)	29.7 (15.4)	29.1 (15.9)	
							3	Mean Change (SD)	15.2 (21)	9.5 (21.8)	
							6	Mean Change (SD)	13 (20.3)	9.7 (22.1)	
							12	Mean Change (SD)	14.6 (22.2)	9.8 (21.6)	
							24	Mean Change (SD)	15.2 (23.3)	11.4 (23.4)	
					SF36	PF	0	Mean (SD)	53.3 (21)	54.5 (18.9)	
							3	Mean Change (SD)	12.2 (21.2)	6 (17.7)	
							6	Mean Change (SD)	10.6 (22)	4.4 (18)	
							12	Mean Change (SD)	12.1 (24)	2 (19)	
							24	Mean Change (SD)	11.2 (23.3)	1.6 (20.4)	
					SF36	MCS	0	Mean (SD)	43.5 (11.1)	42.1 (12.1)	
							3	Mean Change (SD)	2.1 (10.7)	2.5 (10.2)	
							6	Mean Change (SD)	2.5 (10.2)	2.4 (10.8)	
							12	Mean Change (SD)	3.8 (11.2)	2.2 (11.5)	
							24	Mean Change (SD)	3.2 (11.6)	3.5 (11.6)	
IDET	Freeman	2005	RCT	Sham Placebo	SF36	PF	0	Mean (SD)	41.86 (23.01)	35 (15.37)	
							6	Mean Change (95% CI)	2.624 (-2.675-7.922)	1.579 (-6.416- 3.574)	
					SF36	BP	0	Mean (SD)	33.13 (15.97)	24.42 (13.45)	
							6	Mean (SD)	38.28 (21.37)	31.47 (15.29)	
					SF36	MCS	0	Mean (SD)	40.34 (12.76)	44.77 (8.29)	
							6	Mean (SD)	38.16 (13.29)	43.05 (11.07)	
	Pauza	2004	RCT	Sham Placebo	SF36	BP	0	Mean (SD)	35 (12)	35 (13)	
							6	Mean Change (SD)	17 (19)	9 (15)	
					SF36	PF	0	Mean (SD)	54 (24)	48 (21)	
							6	Mean Change (SD)	15 (27)	11 (17)	

IDET: Intradiscal Electrothermal Therapy; IRP: Interdisciplinary Rehabilitation Program; RCT: Randomized Controlled Trial; SF36: Short Form - 36; BP: Bodily Pain; PF: Physical Functioning; N/R: Not Reported; N/A: Not Applicable

Table 7d: Employment status outcomes in studies of the non-specific back pain population, by type of treatment
Study Type: Randomized Controlled Trials, Systematic Reviews, and Meta-Analysis

Intervention	Author	Year	Study Design	Comparator	Work Status Outcome	Time (Months)	Measures	Intervention Outcome	Comparator Outcome	Comments
IRP	Jensen	2005	RCT	CC	Total Days on Sick Leave	0	Mean (SD)	136 (64)	135 (60)	Physical Therapy
						36	Mean (SD)	542 (446)	572 (424)	Physical Therapy (Females)
						36	Treatment Effect (95%)	-39.9 (-225.4 to 145.6)		Physical Therapy (Females)
						0	Mean (SD)	153 (62)	135 (60)	CBT
						36	Mean (SD)	542 (446)	572 (424)	CBT (Females)
						36	Treatment Effect (95%)	-53.3 (-263.9 to 157.2)		CBT (Females)
						0	Mean (SD)	162 (61)	135 (60)	IRP
						36	Mean (SD)	439 (329)	572 (424)	IRP (Females)
						36	Treatment Effect (95%)	-134.2 (-327.5 to 59.1)		IRP (Females)
					Total Days on Sick Leave	0	Mean (SD)	136 (64)	135 (60)	Physical Therapy
						36	Mean (SD)	541 (446)	479 (408)	Physical Therapy (Males)
						36	Treatment Effect (95%)	-12.6 (-273.2 to 247.9)		Physical Therapy (Males)
						0	Mean (SD)	153 (62)	135 (60)	CBT
						36	Mean (SD)	629 (379)	479 (408)	CBT (Males)
						36	Treatment Effect (95%)	104.6 (-124.9 to 336.1)		CBT (Males)
						0	Mean (SD)	162 (61)	135 (60)	IRP
						36	Mean (SD)	494 (375)	479 (408)	IRP (Males)
						36	Treatment Effect (95%)	-65.1 (-290.3 to 160.2)		IRP (Males)
	Kaapa	2006	RCT	CC	Duration of Sick Leave: 0 days	12	Actual: n (%)	38 (61.5%)	34 (56.4%)	
					Duration of Sick Leave: 0 days	24	Actual: n (%)	40 (68%)	39 (63.8%)	
					Duration of Sick Leave: 1-30 days	12	Actual: n (%)	19 (32.7%)	21 (34.6%)	
					Duration of Sick Leave: 1-30 days	24	Actual: n (%)	12 (20%)	16 (25.6%)	
					Duration of Sick Leave: > 30 days	12	Actual: n (%)	3 (5.8%)	5 (9%)	
					Duration of Sick Leave: > 30 days	24	Actual: n (%)	7 (12%)	6 (10.6%)	
	Roche	2007	RCT	CC	% Return to work	52	Actual: n (%)	51 (85.7%)	53 (86.8%)	

IDET; Intradiscal Electrothermal Therapy; IRP: Interdisciplinary Rehabilitation Program; RCT: Randomized Controlled Trial; CC: Conservative Care; N/R: Not Reported; N/A: Not Applicable

Table 7d: Employment status outcomes in studies of the non-specific back pain population, by type of treatment
Study Type: Randomized Controlled Trials, Systematic Reviews, and Meta-Analysis

Intervention	Author	Year	Study Design	Comparator	Work Status Outcome	Time (Months)	Measures	Intervention Outcome	Comparator Outcome	Comments
Spinal Injections	Manchikanti	2010	RCT	Injections	Employed: Part Time	0	Actual: n (%)	1 (1.4%)	2 (2.9%)	
					Employed: Part Time	12	Actual: n (%)	1 (1.4%)	2 (2.9%)	
					Employed: Full Time	0	Actual: n (%)	8 (11.4%)	11 (15.7%)	
					Employed: Full Time	12	Actual: n (%)	11 (15.7%)	13 (18.6%)	
					Unemployed	0	Actual: n (%)	2 (2.9%)	2 (2.9%)	
					Unemployed	12	Actual: n (%)	1 (1.4%)	1 (1.4%)	
					Unemployed due to pain	0	Actual: n (%)	1 (1.4%)	2 (2.9%)	
					Unemployed due to pain	12	Actual: n (%)	0 (0%)	1 (1.4%)	

IDET; Intradiscal Electrothermal Therapy; IRP: Interdisciplinary Rehabilitation Program; RCT: Randomized Controlled Trial; CC: Conservative Care; N/R: Not Reported; N/A: Not Applicable

Table 8d: Measures of clinical improvement in studies of the non-specific back pain population, by type of treatment
Study Type: Randomized Controlled Trials, Systematic Reviews, and Meta-Analysis

Intervention	Author	Year	Study Design	Comparator	Time (Months)	Measure	Intervention Outcome	Comparator Outcome	Definition
IRP	Vollenbroek-Hutten	2004	RCT	Conservative Care	2	n (%) Improved	28 (41.0%)	22 (31.0%)	Percent of Improvement on EQ5D scale
					6	n (%) Improved	33 (48.0%)	32 (44.0%)	Percent of Improvement on EQ5D scale
					2	n (%) Improved	24 (35.0%)	17 (23.0%)	Percent of Improvement on RMS scale
					6	n (%) Improved	28 (41.0%)	31 (42.0%)	Percent of Improvement on RMS scale
	Dufour	2010	RCT	Conservative Care	3	n (%) Improved	83 (64.0%)	79 (55.0%)	Patient reported Global Perceived Outcome
					3	n (%) No Change	35 (27.0%)	53 (37.0%)	Patient reported Global Perceived Outcome
					3	n (%) Worse	5 (4.0%)	11 (8.0%)	Patient reported Global Perceived Outcome
RF Denervation	van Wijk	2005	RCT	Sham Placebo	3	n (%) Improved	11 (27.5 %)	12 (29.3 %)	Success defined by COM (components consist of VAS-back, physical activities, and analgesic intake)

IRP: Interdisciplinary Rehabilitation Program; RCT: Randomized Controlled Trial; N/R: Not Reported; N/A: Not Applicable

Table 9d: Mortality and other harms in studies of the non-specific low back pain population, by type of treatment
Study Type: Randomized Controlled Trials, Systematic Reviews, and Meta-Analysis

Harm Category	Intervention	Author	Year	Study Design	Comparator	Measure	Intervention Outcome	Comparator Outcome	Comments
30-day Mortality	IRP	van der Roer	2008	RCT	Conservative Care	n (%)	0 (0%)	N/R	
	Spinal Injections	Manchikanti	2010	RCT	Injections	n (%)	0 (0%)	N/R	
Major	IRP	Fairbank	2005	RCT	Spinal Fusion	n (%)	N/R	10 (5.6%)	
	IRP	van der Roer	2008	RCT	Conservative Care	n (%)	0 (0%)	N/R	
	Spinal Injections	Manchikanti	2010	RCT	Injections	n (%)	0 (0%)	N/R	
Minor	IRP	Fairbank	2005	RCT	Spinal Fusion	n (%)	N/R	6 (3.4%)	
	IRP	van der Roer	2008	RCT	Conservative Care	n (%)	0 (0%)	N/R	
	IRP	Dufour	2010	RCT	Conservative Care	n (%)	1	N/R	
	Spinal Injections	Manchikanti	2010	RCT	Injections	n (%)	0 (0%)	N/R	

IRP: Interdisciplinary Rehabilitation Program; RCT: Randomized Controlled Trial

Table 10d: Characteristics of studies for the non-specific back pain population, by type of treatment
Study Type: Comparative studies, Case-Series: Non-comparative studies

Treatment Type	Author	Year	Study Design	Comparator	Sample Size	Follow-up (Months)	Eligibility Criteria	Quality Rating	Comments
IRP	Buchner	2006	Prospective Cohort	N/A	231	Actual: 6	Inclusion: experienced chronic LBP as main symptom, which was defined as disabling pain of >= 3 months that led to patients being on sick leave for >= 6 weeks; Exclusion: specific etiology of LBP; patients with other pain locations as their main symptom and patients with multiple major pain locations were excluded	Fair	
	Bontoux	2009	Prospective Cohort	N/A	61	Actual: 24	Inclusion: presence of chronic LBP or lumbo-radiculopathy according to the criteria of the French health evaluation agency; presently employed with a permanent contract; on sick leave or having been on sick leave for > 6 months in the past 2 years; Exclusion: secondary LBP, osteoarthritis or neurological disease precluding physical exercise, cardiovascular disease and psychiatric disorders incompatible with the participation in a group program	Fair	
IDET	Assietti	2010	Prospective Cohort	N/A	50	Actual: 24	Inclusion: Chronic LBP and impaired physical function who were refractory to comprehensive conservative medical management, including physical therapy, or at least 6 months duration; all patients were initially examined and followed up through a neurosurgical consult and were determined to have sufficient symptom severity and duration to be candidates for either spinal fusion or total disc arthroplasty; patients providing informed consent were enrolled and were selected for IDET; eligible patients had single-level internal disc disruption demonstrated on MR imaging, provocative discography at the affected level, and >= 60% preserved disc height	Poor	

IRP: Interdisciplinary Rehabilitation Program; IDET: Intradiscal Electrothermal Therapy; LBP: Low Back Pain; N/A: Not Applicable

Table 10d: Characteristics of studies for the non-specific back pain population, by type of treatment
Study Type: Comparative studies, Case-Series: Non-comparative studies

Treatment Type	Author	Year	Study Design	Comparator	Sample Size	Follow-up (Months)	Eligibility Criteria	Quality Rating	Comments
IDET	Maurer	2008	Prospective Cohort	N/A	56	Mean (SD): 20.5 (4.4)	Inclusion: < 50% disc height loss evidenced on plain AP and lateral lumbar radiographs; posterior annular disruption such as radial and/or concentric fissure(s) to the outer annular fibers with maintenance of the anterior and lateral disc annulus evidenced by CT discogram; Exclusion: severe disc degeneration at one of more levels; extruded or sequestered herniated nucleus pulposus; previous back surgery (eg, laminectomy, descectomy, or fusion); chronic lower extremity radiculopathy; spinal canal stenosis > 30% evidenced by MRI or CT; spondylolisthesis or any translational instability of any lumbar segmental level	Fair	
	Nunley	2006	Prospective Cohort	N/A	53	Median (Range): 56 (29-72)	Inclusion: clinically established discogenic LBP with failure of improvement afer 4 to 6 weeks of pain management classes; Exclusion: patients with prior spine surgery, abnormal neurologic exam, structural deformities, and spinal stenosis are not considered for the procedure; a loss of more than 60% of the disc loss is exclusion; positive discography with control level is an essential requirement because this is accepted as the most reliable diagnostic test for LBP of discogenic origin	Fair	
	Lee	2003	Prospective Cohort	N/A	51	Mean (Range): 34 (24-47)	Inclusion: moderate to severe LBP > 6 months; sitting>standing pain; normal neurologic exam; failure of conservative care (trial of nonsteroidal anti-inflammatory, epidural injection, and a comprehensive spine rehab program); MRI or CT scan demonstrating no neural compressive lesion; positive discogram with post-CT image demonstrating internal disc disruption, focal annular tear with or without disc protrusion of <5mm; Exclusion: severe disc space narrowing >50%, disc extrusion or sequestered fragment; severe spinal stenosis; spondylolisthesis > grad1; and segmental instability	Fair	

IRP: Interdisciplinary Rehabilitation Program; IDET: Intradiscal Electrothermal Therapy; LBP: Low Back Pain; N/A: Not Applicable

Table 10d: Characteristics of studies for the non-specific back pain population, by type of treatment
Study Type: Comparative studies, Case-Series: Non-comparative studies

Treatment Type	Author	Year	Study Design	Comparator	Sample Size	Follow-up (Months)	Eligibility Criteria	Quality Rating	Comments
IDET	Saal	2002	Prospective Cohort	N/A	58	Actual: 24	Inclusion: persistent LBP >= 6 months; no satisfactory improvement with a comprehensively applied nonoperative care program for 6 months; normal neurologic exam findings; negative straight leg raising result; MR scan that did not demonstrate a neural compressive lesion; Exclusion: inflammatory arthritis; nonspinal conditions that could mimic lumbar pain; medical or metabolic disorder that would preclude appropriate follow-up and participation; prior surgery at the symptomatic level	Fair	
RFD	Mikeladze	2003	Retrospective Cohort	N/A	83	Actual: 1.5	Inclusion: Patients with a chief complaint of axial lumbar pain who denied radicular symptoms underwent; patients with positive response to diagnostic medial branch were included	Poor	
	Gofeld	2007	Prospective Cohort	N/A	174	Actual: 120	Inclusion: LBP >= 6 months duration with average pain score of more than 5 out of 10, with or without non-radicular radiation of the pain to the buttock, hip, and leg was considered; Exclusion: patients who exhibited a radicular pattern of pain, neurogenic claudication, and pain predominantly of the leg with or without neurological deficit, patient who had undergone previous back surgery	Poor	
Spinal Injections	Lee	2010	Retrospective Cohort	N/A	81	Range: 7-17	Inclusion: patients receiving interlaminar ESIs for axial LBP with selection criteria; patients with a numeric rating score of >5 on 10 pt. scale; Exclusion: previous lumbar operation; history of psychiatric disease; nerve root compression demonstrated on MR imaging or CT, by either disk; absence of initial ST follow-up data; initial ST follow-up >1 month after interlaminar ESI	Fair	

IRP: Interdisciplinary Rehabilitation Program; IDET: Intradiscal Electrothermal Therapy; LBP: Low Back Pain; N/A: Not Applicable

Table 11d: Mortality and other harms in studies of the non-specific low back population, by type of treatment
Study Type: Comparative studies, Case-Series: Non-comparative studies

Harm Category	Intervention	Author	Year	Study Design	Comparator	Time (Months)	Measure	Intervention Outcome	Comparator Outcome	Comments
30-day Mortality	No Studies with outcomes >= 24 months reported									
Major	No Studies with outcomes >= 24 months reported									
Minor	No Studies with outcomes >= 24 months reported									

IRP: Interdisciplinary Rehabilitation Program; N/R: Not Reported; N/A: Not Applicable

Table 12d: Functional outcomes for the non-specific low back pain population, by type of treatment
Study Type: Comparative studies, Case-Series: Non-comparative studies

Intervention	Author	Year	Study Design	Comparator	Scale	Time (Months)	Measure	Intervention Outcome	Comparator Outcome	Comments
IRP	Lee	2003	Prospective Cohort	N/A	RMS	0	Mean (SD)	15.4 (5.3)	N/A	
						48	Mean Change (SD)	-6.6 (7.5)	N/A	
						48	p-value	0.001	N/A	
IDET	Nunley	2006	Prospective Cohort	N/A	ODI	0	Mean	24.83	N/A	
						56	Mean (SE)	19.679 (1.907)	N/A	
	Assietti	2010	Prospective Cohort	N/A	ODI	0	Mean	59	N/A	
						12	Mean	27	N/A	
						24	Mean	20.1	N/A	

IRP: Interdisciplinary Rehabilitation Program; RMS: Roland-Morris Scale; ODI: Oswestrey Disability Index; N/R: Not Reported; N/A: Not Applicable

Table 13d: Pain outcomes in studies of the non-specific low back pain population, by type of treatment
Study Type: Comparative studies, Case-Series: Non-comparative studies

Intervention	Author	Year	Study Design	Comparator	Scale	Time (Months)	Measure	Intervention Outcome	Comparator Outcome	Comments
IRP	Lee	2003	Prospective Cohort	N/A	VAS	0	Mean (SD)	7.9 (1.3)	N/A	
						48	Mean Change (SD)	-3.2 (3)	N/A	
						48	p-value	0.001	N/A	
	Bontoux	2009	Prospective Cohort	N/A	VAS	0	Mean (SD)	4.85 (2)	N/A	
						3	Mean (SD)	3.35 (2.4)	N/A	
						12	Mean (SD)	3.46 (2.7)	N/A	
						24	Mean (SD)	3.83 (2.6)	N/A	
IDET	Bogduk	2002	Prospective Cohort	N/A	VAS	0	Median (IQR)	8 (5-8)	8 (7-9)	
						3	Median (IQR)	8 (7-8)	3.5 (1-5)	
						3	Treatment Effect (p-value)	0.071		
						6	Median (IQR)	N/R	3 (1-6)	
						6	Treatment Effect (p-value)	0.0001		
						12	Median (IQR)	7.5 (5-8)	3 (1-7)	
						12	Treatment Effect (p-value)	0.005		
						24	Median (IQR)	7.5 (4-8)	3 (1-7)	
						24	Treatment Effect (p-value)	0.028		
	Saal	2002	Prospective Cohort	N/A	VAS	0	Mean (SD)	6.57 (1.85)	N/A	
						6	Mean (SD)	3.71 (1.95)	N/A	
						12	Mean (SD)	3.52 (2.3)	N/A	
						24	Mean (SD)	3.41 (1.96)	N/A	
	Nunley	2006	Prospective Cohort	N/A	VAS	0	Mean	63.77	N/A	
						56	Mean (SE)	44.34 (5.55)	N/A	
	Assietti	2010	Prospective Cohort	N/A	NRS	0	Mean (SD)	7.6 (1.1)	N/A	
						12	Mean (SD)	3 (1.4)	N/A	
						24	Mean (SD)	2.4 (1.5)	N/A	

IRP: Interdisciplinary Rehabilitation Program; VAS: Visual Analog Scale; NRS: Numeric Rating Scale; N/A: Not Applicable

Table 14d: Quality of life outcomes in studies of the non-specific low back pain population, by type of treatment
Study Type: Comparative studies, Case-Series: Non-comparative studies

Intervention	Author	Year	Study Design	Comparator	Scale	Subdomain	Measure	Time (Months)	Intervention Outcome	Comparator Outcome	Comments

No Studies with outcomes >= 24 months reported

Table 15d: Employment status outcomes in studies of the non-specific low back pain population, by type of treatment
Study Type: Comparative studies, Case-Series: Non-comparative studies

Intervention	Author	Year	Study Design	Comparator	Time (Months)	Work Status Outcome	Measures	Intervention Outcome	Comparator Outcome	Comments
IDET	Nunley	2006	Prospective Cohort	N/A	56	% RTW: Full duty	Percentage	5.7%	N/A	
					56	% RTW: Restrictions	Percentage	17.0%	N/A	
					56	% RTW: Heavy Lifting Restrictions Only	Percentage	24.5%	N/A	
					56	% RTW: light duty	Percentage	52.8%	N/A	

IDET: Intradiscal Electrothermal Therapy; IRP: Interdisciplinary Rehabilitation Program; RTW: Return to work; N/A: Not Applicable

Table 16d: Measures of clinical improvement in studies of the non-specific back pain population, by type of treatment
Study Type: Randomized Controlled Trials, Systematic Reviews, and Meta-Analysis

Intervention	Author	Year	Study Design	Comparator	Time (Months)	Measure	Intervention Outcome	Comparator Outcome	Definition	Comments
RFD	Gofeld	2007	Prospective Cohort	N/A	6	n (%) Improvement	119 (68.4%)	N/A	Based on pain relief	
					12	n (%) Improvement	81 (96.4%)	N/A	12 months	
					24	n (%) Improvement	36 (42.8%)	N/A	12-24 months	
					120	n (%) Improvement	2 (2.4%)	N/A	greater than 24 months	

RFD: RF Denervation; N/R: Not Reported; N/A: Not Applicable

Table 17d: Subsequent treatment in studies of the non-specific low back pain population, by type of initial treatment
Study Type: Randomized Controlled Trials, Comparative studies, Case-Series: Non-comparative studies

Intervention	Author	Year	Study Design	Comparator	Subsequent Treatment Type	Time (Months)	Measures	Intervention Outcome	Comparator Outcome	Comments
IRP	Fairbank	2005	RCT	Spinal Fusion	Reoperation	24	n(%)	N/R	11 (6.25%)	
	Dufour	2010	RCT	Conservative Care	Additional Surgery for herniation	24	n(%)	1 (0.8%)	N/R	
IDET	Maurer	2008	Prospective Cohort	N/A	Additional surgery	20.5	n(%)	2 (0.9%)	N/A	
	Lee	2003	Prospective Cohort	N/A	Reoperation	12	n(%)	2 (4.0%)	N/A	
					Additional Therapeutic Procedure	12	n(%)	7 (14.0%)	N/A	
					Spinal Fusion procedure	12	n(%)	2 (4.0%)	N/A	
					Nucleoplasty decompression procedure	12	n(%)	2 (4.0%)	N/A	
					RFD procedure	12	n(%)	3 (6.0%)	N/A	
	Saal	2002	Prospective Cohort	N/A	Additional Fusion	6	n(%)	1 (1.7%)	N/A	
Spinal Injections	Lee	2010	Retrospective Cohort	N/A	Recurrent ESI	17	n(%)	34 (54.0%)	N/A	
RF Deneravtion	Mikeladze	2003	Retrospective Cohort	N/A	Reoperation	1.5	1.5	18 (15.8%)	N/A	

IDET: Intradiscal Electrothermal Therapy; IRP: Interdisciplinary Rehabilitation Program; RCT: Randomized Controlled Trial; ESI: Epidural Steroid Injection; N/R: Not Reported; N/A: Not Applicable

APPENDIX D

ECONOMIC MODEL OUTPUT

Table 1: LBD Clinical and Economic Model Parameters - Lumbar Disc Herniation, Intention To Treat

Parameter	Value	Source and Rationale
Patient Variables		
Age	45	
Sex	Male	Male. LDH more common in men
Model Parameters		
duration of Analysis, Years	2	RCTs provide 2 years of follow-up
SPY	4	Markov model 4 stages per year (3 months)
Annual Discount Rate	0.03	Gold, 1996
Work Days per Year	240	48 weeks x 5 days per week
LBD Clinical Status at Baseline		
Back Function	46.3 ± 20.6	Peul, 2007 Conservative Care
Back Pain	26.7 ± 17.4	Peul, 2007 Conservative Care
Working (FT/PT), proportion	0.61	Peul, 2007 Conservative Care
Working (FT/PT), Total number	232	Estimate Working SD
QoL	0.46 ± 0.246	SF-36 -> EQ5D. Peul, 2007, ARA, 2008
Costs		
Wages per day	$165	BLS Series Report LEU0252889100
Conservative Care		
LBD Clinical Outcomes *(By Time)*		
Back Function (Change in ODI)		Peul, 2007
Month 3	-30.4	
Month 6	-48.8	
Month 12	-53.3	
All months, SEM of mean cumulative change		
Back Pain (Change in SF-36 BP)		Peul, 2007
Month 3	30.5	
Month 6	48.9	
Month 12	54.6	
All months, SEM of mean cumulative change		
Employment, proportion		Peul, 2007. Based on "full recovery" on 7 point Likert Scale
Month 3	0.317	
Month 6	0.662	
Month 9	0.803	
Month 12	0.944	
All months, SEM proportion working (FT/PT)		
QoL		Peul, 2007, Ara, 2008 SF-36 -> EQ-5D
Month 3	0.686	
Month 6	0.824	
Month 12	0.864	
All months, SEM of QoL	0.02	
Adherence & Crossover *(By Time)*		
Probability of Surgery		Peul, 2007
Months 1-3	0.219	
Months 4-6	0.219	
Months 7-12	0	
Months 12-24	0	
Costs (Ambulatory Visit Costs)		
Initial cost of conservative care (first 3 months)	$2,400	CPT 99214 (office visit (1)), 97110 (PT) (72), Naprosen DR & cyclobenzaprine
Cost of conservative care (subsequent 3 months)	$0	
Visits		
Conservative Care, Initial 3 months	19	CPT 99214 (office visit), 97110 (PT)
Conservative Care, Annual Follow-up	0	

Table 1: LBD Clinical and Economic Model Parameters - Lumbar Disc Herniation, Intention To Treat

Parameter	Value	Source and Rationale
Quality of Life (QoL)	0.01	Assumption
QoL Disutility for Conservative Care		
Days of Disutility for Treatment		
Conservative Care	20	one day per visit
Initial Surgery (Discectomy)		
LBD Clinical Outcomes *(By Time)*		Peul, 2007
Back Function (Change in ODI)	-43.3	
Month 3	-52.1	
Month 6	-55	
Month 12	1.9	
All months, SEM of mean cumulative change		Peul, 2007
Back Pain (Change in SF-36 BP)	40.9	
Month 3	54.2	
Month 6	59.3	
Month 12	1.9	
All months, SEM of mean cumulative change		Peul, 2007. Based on "full recovery" on 7 point Likert Scale
Employment, proportion	0.617	
Month 3	0.908	
Month 6	0.929	
Month 9	0.958	
Month 12		
All months, SEM proportion working (FT/PT)		
QoL	0.770	SF-36 -> EQ-5D Peul, 2007, Ara, 2008
Month 3	0.849	
Month 6	0.883	
Month 12	0.02	
All months, SEM of QoL		
Adherence & Crossover *(By Time)*		Peul, 2007
Probability of Surgery	0.89	
Months 1-3	0	
Months 4-6	0	
Months 7-12	0	
Months 12-24		
		Peul, 2007
Probability of Recurrent Surgery	0.07	
Cumulative probability of recurrent surgery at 12 months	0.09	
Cumulative probability of recurrent surgery at 24 months		
Cost of Intervention	$11,100	MS-DRG 30 (no CC), 29 (CC), 28 (MCC), anesthesia=45 minutes=3 units, $9000 (DRG) + $1600 (CPT) + $500 (anesthesia)
Cost of discectomy (first 3 months)	$150	$900 first three months only
Cost of discectomy follow-up (after first 3 months)		
Visits	7	
Discectomy, Initial 3 months	1	
Discectomy, Annual Follow-up	2	
Major Complication, Permanent, Additional Visits		
Costs of Visits		
Discectomy Visits Costs, Initial 3 months	900	CPT 99215 (office visit 3); 97110 (PT 15 minutes, 24)
Discectomy Visits Costs, Annually	150	CPT 99215 (office visit 3)
Major Complication, Permanent		CPT 99215 (office visit, 3) (2), HCPCS L2114. Kuntz 2000
Quality of Life (QoL)	0.25	Assumption
QoL Disutility for Discectomy		
Days of Disutility from Interventions		
Days of Disutility from Discectomy	3.5	DRG LOS

Table 1: LBD Clinical and Economic Model Parameters - Lumbar Disc Herniation, Intention To Treat

Parameter	Value	Source and Rationale
Complications		
Complications of Surgery (Discectomy)	0.1300	
Probability of Minor Complication	0.0200	
Probability of Major Complication	0.1000	
Probability of Permanent Injury due to Major Complication	0.0001	
Probability of Death (Fatal Complication)		
Costs of Complications		
Cost of minor complication	$7,000	DRG with CC
Cost of major complication	$20,000	DRG with MCC
Cost of major permanent complication	$20,000	DRG with MCC (assume same as major complication)
Cost of fatal complication	0	Assumption
Quality of Life Disutility from Complications	0.01	
QoL reduction for minor complication	0.20	
QoL reduction for major complication	0.50	
QoL reduction for permanent disability from major complication	0.50	
QoL reduction for (acute) fatal complication		
Days of Disability from Complications	3	DRG LOS Increment
Days of disutility for minor complication	10	DRG LOS Increment
Days of disutility for major complication	10	DRG LOS Increment
Days of disutility for major permanent complication, initially	10	DRG LOS Increment
Days of disutility for acute fatal complication	0	

Table 2: LBD Clinical and Economic Model Parameters - Lumbar Spinal Stenosis, Intention To Treat

Parameter	Value	Source and Rationale
Patient Variables		
Age	65	Medicare eligible and approximate mean age in RCTs
Sex	Male	Male. LSS more common in men
Model Parameters		
Duration of Follow-up, years	2	RCTs provide 2 years of follow-up
SPY	4	Markov model 4 stages per year (3 months)
Annual Discount Rate	0.03	Gold, 1996
Work Days per Year	240	48 weeks x 5 days per week
LBD Clinical Status at Baseline		
Back Function	42.7 ± 17.9	Weinstein, 2008
Back Pain	31.9 + 17.5	
QoL	0.62 ± 0.20	Tosteson, 2008
Costs		
Wages per day	$165	BLS Series Report LEU0252889100
Conservative Care		
LBD Clinical Outcomes *(By Time)*		
Back Function (Change in ODI)		Weinstein, 2008
Month 3	-8.1	
Month 6	-13.7	
Month 12	-12.7	
Month 24	-12.9	
All months, SEM of mean cumulative change	1.9	
Back Pain (Change in SF-36 BP)		Weinstein, 2008
Month 3	11.1	
Month 6	16.1	
Month 12	17.5	
Month 24	15.6	
All months, SEM of mean cumulative change	2.3	
QoL		Tosteson, 2008
Month 3	0.690	
Month 6	0.713	
Month 12	0.700	
Month 24	0.768	
All months, SEM of mean cumulative change	0.010	
Adherence & Crossover *(By Time)*		
Probability of Surgery		Weinstein, 2008
Month 3	0.4200	3-month probability
Month 6	0.2000	3-month probability
Month 12	0.1070	3-month probability
Month 24	0.0025	3-month probability
Costs (ambulatory Visit Costs)		
Initial cost of conservative care (first 3 months)	$2,400	CPT 99214 (office visit (1)), 97110 (PT) (72), Naproxen DR & cyclobenzaprine
Cost of conservative care (subsequent 3 months)	$0	
Visits		
Conservative Care, Initial 3 months	19	
Conservative Care, Annual Follow-up	0	
Quality of Life (QoL)		
QoL Disutility for Conservative Care	0.01	Assumption
Days of Disutility for Treatment		
Conservative Care	19	one day per visit

Table 2: LBD Clinical and Economic Model Parameters - Lumbar Spinal Stenosis, Intention To Treat

Parameter	Value	Source and Rationale
Interspinous Spacers		
LBD Clinical Outcomes (*By Time*)		
Back Function (Change in ODI)		
Month 24	---	
All months, SEM of mean cumulative change		
Back Pain (Change in SF-36 BP)		Zucherman, 2004
Month 24	36	
All months, SEM of mean cumulative change	2.3	
QoL		
Month 24	0.763	Zucherman, 2004. QoL Estimated from Zurich Claudication Questionnaire physical function subscale and age- & sex-specific norm for EQ-5D
All months, SEM of mean cumulative change	0.01	
Adherence & Crossover *(By Time)*		Assume same as fusion & laminectomy Weinstein, 2008
Probability of Surgery		Weinstein, 2008
Months 1-3	0.4200	3-month probability
Months 4-6	0.2000	3-month probability
Months 7-12	0.1070	3-month probability
Months 12-24	0.0025	3-month probability
Probability of Recurrent Surgery		
Cumulative probability of recurrent surgery at 24 months	0.06	Zucherman, 2004
Cost of Intervention		
Cost of Interspinous spacers (first 3 months)	$8,500	$950 in visit costs, first 3 months
Cost of Interspinous spacers follow-up (after first 3 months)	$150	
Visits		
Interspinous spacers, Initial 3 months	7	
Interspinous spacers, annual follow-up	1	
Major Complication, Permanent, Additional Visits	2	
Costs of Visits		
Interspinous Spacers Visits Costs, Initial 3 months		CPT 99215 (office visit, 3);97110 (PT 15 min, 24); 77214 X-ray for fusion
Interspinous Visits Costs, Annually		(office visit, 1)
Major Complication, permanent		CPT 92115 (2), HCPCS L2114; Kuntz, 2000
Quality of Life (QoL)		
QoL Disutility for Interspinous spacers	0.2	Assumption. Less than laminectomy
Days of Disutility from Interventions		
Days of Disutility from Interspinous spacers	3.5	Assumption. Same as laminectomy
Complications		
Complications of Surgery (Interspinous spacers)		No Data. Assume similar to discectomy
Probability of Minor Complication	0.0450	
Probability of Major Complication	0.0300	
Probability of Permanent Injury due to Major Complication	0.0667	Chou, Systematic review, LBD surgery
Probability of Death (Fatal Complication)	0.0001	
Costs of Complications		DRG LOS No CC, CC, and MCC
Cost of minor complication	$7,000	
Cost of major complication	$14,000	
Cost of major permanent complication	$14,000	(additional $900/year for 2 complex visits & orthotics/year)
Cost of fatal complication		

Table 2: LBD Clinical and Economic Model Parameters - Lumbar Spinal Stenosis, Intention To Treat

Parameter	Value	Source and Rationale
Quality of Life Disutility from Complications		Assumption
QoL reduction for minor complication	0.01	
QoL reduction for major complication	0.20	
QoL reduction for permanent disability from major complication	0.50	
QoL reduction for (acute) fatal complication	0.50	
Days of Disability from Complications		DRG LOS
Days of disutility for minor complication	3	
Days of disutility for major complication	5	
Days of disutility for major permanent complication, initially	6	
Days of disutility for acute fatal complication	10	
Laminectomy		
LBD Clinical Outcomes *(By Time)*		
Back Function (Change in ODI)		Weinstein, 2008
Month 3	-7.6	
Month 6	-14.6	
Month 12	-14.9	
Month 24	-16.4	
All months, SEM of mean cumulative change		
Back Pain (Change in SF-36 BP)		Weinstein, 2008
Month 3	13.5	
Month 6	21	
Month 12	23	
Month 24	23.4	
All months, SEM of mean cumulative change		
All months, SEM proportion working (FT/PT)		
QoL		Tosteson, 2008
Month 3	0.72	
Month 6	0.74	
Month 12	0.74	
Month 24	0.75	
All months, SEM of QoL		
Adherence & Crossover *(By Time)*		
Probability of Surgery		Weinstein, 2008
Months 1-3	0.4200	3-month probability
Months 4-6	0.2000	3-month probability
Months 7-12	0.1070	3-month probability
Months 12-24	0.0025	3-month probability
Probability of Recurrent Surgery		
Cumulative probability of recurrent surgery at 12 months	0.04	Weinstein, 2008
Cumulative probability of recurrent surgery at 24 months	0.02	
Cost of Intervention		
Cost of laminectomy (first 3 months)	$10,700	
Cost of laminectomy follow-up (after first 3 months)	$150	
Visits		
Laminectomy, Initial 3 months	1	
Laminectomy, Annual Follow-up	7	
Major Complication, Permanent, Additional Visits	2	CPT 99215 (office visit 3)
Costs of Visits		
Laminectomy Visits Costs, Initial 3 months	$950	CPT 99215 (office visits, 3) (2) ;97110 (PT 15 min, 24); 77214 X-ray for fusion
Laminectomy Visits Costs, Annually	$150	(Office visit, 3)
Major Complication, Permanent	$900	CPT 92115 (2), HCPCS L2114; Kuntz, 2000
Quality of Life (QoL)		
QoL Disutility for Laminectomy	0.25	

Table 2: LBD Clinical and Economic Model Parameters - Lumbar Spinal Stenosis, Intention To Treat

Parameter	Value	Source and Rationale
Days of Disutility from Interventions		
Days of Disutility from Laminectomy	3.5	
Complications		
Complications of Surgery (Laminectomy)		
Probability of Minor Complication	0.1300	ICER Systematic review, midpoint of reported range
Probability of Major Complication	0.0200	Deyo, 2010
Probability of Permanent Injury due to Major Complication	0.1000	Chou, Systematic review. LBD surgery
Probability of Death (Fatal Complication)	0.0030	Deyo, 2010
Costs of Complications		DRG LOS No CC, CC, and MCC
Cost of minor complication	$7,000	
Cost of major complication	$20,000	
Cost of major permanent complication	$14,000	(additional $900/year for 2 complex visits & orthotics/year)
Cost of fatal complication	$0	
Quality of Life Disutility from Complications		Assumption
QoL reduction for minor complication	0.01	
QoL reduction for major complication	0.20	
QoL reduction for permanent disability from major complication	0.50	
QoL reduction for (acute) fatal complication	0.50	
Days of Disability from Complications		DRG LOS
Days of disutility for minor complication	3	
Days of disutility for major complication	5	
Days of disutility for major permanent complication, initially	6	
Days of disutility for acute fatal complication	10	
Fusion		
LBD Clinical Outcomes (*By Time*)		
Back Function (Change in ODI)		Weinstein, 2008
Month 3	-7.6	
Month 6	-14.6	
Month 12	-14.9	
Month 24	-16.4	
All months, SEM of mean cumulative change		
Back Pain (Change in SF-36 BP)		Weinstein, 2008
Month 3	13.5	
Month 6	21	
Month 12	23	
Month 24	23.4	
All months, SEM of mean cumulative change		
All months, SEM proportion working (FT/PT)		
QoL		Tosteson, 2008
Month 3	0.72	
Month 6	0.74	
Month 12	0.74	
Month 24	0.75	
All months, SEM of QoL	0.01	

Table 2: LBD Clinical and Economic Model Parameters - Lumbar Spinal Stenosis, Intention To Treat

Parameter	Value	Source and Rationale
Adherence & Crossover *(By Time)*		
Probability of Surgery		Weinstein, 2008
Months 1-3	0.42	3-month probability
Months 4-6	0.2	3-month probability
Months 7-12	0.107	3-month probability
Months 12-24	0.0025	3-month probability
Probability of Recurrent Surgery		Weinstein, 2008(LSS) & Weinstein, 2007 (DS)
Cumulative probability of recurrent surgery at 12 months	0.08	Recurrent surgery was higher in DS, where most of the initial surgical treatment was fusion
Cumulative probability of recurrent surgery at 24 months	0.03	
Cost of Intervention		
Cost of fusion (first 3 months)	$23,900	$32,800 for complex fusion. Addition $900 (simple fusion) or 1050 (complex fusion) in first 3 months.
Cost of fusion follow-up (after first 3 months)	150	$250 for complex fusion.
Visits		
Fusion, Initial 3 months	8	CPT 99215 (office visit,3) (3); 97110 (PT, 15 min, 24)
Fusion, Annual Follow-up	2	
Major Complication, Permanent, Additional Visits	2	
Costs of Visits		
Fusion Visits Costs, Initial 3 months	$1,050	CPT 99215 (office visit, 3);97110 (PT 15 min, 24); 77214 X-ray for fusion
Fusion Visits Costs, Annually	$150	(office visit, 1)
Major Complication, Permanent	$900	CPT 92115 (2), HCPCS L2114; Kuntz, 2000
Quality of Life (QoL)		
QoL Disutility for Fusion	0.5	Assumption
Days of Disutility from Interventions		
Days of Disutility from Fusion	4	DRG LOS
Complications		
Complications of Surgery (Fusion)		
Probability of Minor Complication	0.1300	RR 1.27 if complex fusion. Deyo, 2010
Probability of Major Complication	0.0500	RR 1.13 if complex fusion. Deyo, 2010
Probability of Permanent Injury due to Major Complication	0.0400	Chou, Systematic review, LBD surgery
Probability of Death (Fatal Complication)	0.0050	RR 1.33 if complex fusion. Deyo, 2010
Costs of Complications		
Cost of minor complication	$7,000	DRG with CC
Cost of major complication	$14,000	DRG with MCC ($28,000 if complex fusion)
Cost of major permanent complication	$14,000	DRG with MCC ($28,000 if complex fusion)
Cost of fatal complication	0	
Quality of Life Disutility from Complications		Assumption
QoL reduction for minor complication	0.01	
QoL reduction for major complication	0.20	
QoL reduction for permanent disability from major complication	0.50	
QoL reduction for (acute) fatal complication	0.50	
Days of Disability from Complications		DRG LOS
Days of disutility for minor complication	3	
Days of disutility for major complication	5	10 (for complex fusion)
Days of disutility for major permanent complication, initially	6	11 (for complex fusion)
Days of disutility for acute fatal complication	10	

Table 3: LBD Clinical and Economic Model Parameters - Degenerative Spondylolisthesis, Intention To Treat

Parameter	Value	Source and Rationale
Patient Variables		
Age	65	Medicare eligible and approximate mean age in RCTs
Sex	Male	Male. DS more common in men
Model Parameters		
Duration of Follow-up, years	2	RCTs provide 2 years of follow-up
SPY	4	Markov Model Stage per year
Annual Discount Rate	0.03	Gold, 1996
Work Days per Year	240	48 weeks x 5 days per week
LBD Clinical Status at Baseline		
Back Function	41.8 ± 16.5	Weinstein, 2007
Back Pain	30.7 ± 16.4	
QoL	0.65 ± 0.20	Tosteson, 2008
Costs		
Wages per day	$165	BLS Series Report LEU0252889100
Conservative Care		
LBD Clinical Outcomes (*By Time*)		
Back Function (Change in ODI)		Weinstein, 2007
Month 3	-7	
Month 12	-12.7	
Month 24	-17.6	
All months, SEM of mean cumulative change	1.9	
Back Pain (Change in SF-36 BP)		Weinstein, 2007
Month 3	10.2	
Month 12	21.7	
Month 24	22.8	
All months, SEM of mean cumulative change	2.3	
QoL		Tosteson, 2008
Month 3	0.7	
Month 6	0.69	
Month 12	0.69	
Month 24	0.69	
All months, SEM of QoL	0.01	
Adherence & Crossover *(By Time)*		
Probability of Surgery		Weinstein, 2007
Month 3	0.241	3-month probability
Month 6	0.182	3-month probability
Month 12	0.051	3-month probability
Month 24	0.022	3-month probability
Costs (Ambulatory Visit Costs)		
Initial cost of conservative care (first 3 months)	$2,400	CPT 99214 (office visit (1)), 97110 (PT) (72), Naprosen DR & cyclobenzaprine
Cost of conservative care (subsequent 3 months)	$0	
Visits		
Conservative Care, Initial 3 months	19	Office visit (1) & PT
Conservative Care, Annual Follow-up	0	
Quality of Life (QoL)		
QoL Disutility for Conservative Care	0.01	Assumption
Days of Disutility for Treatment		
Conservative Care	19	one day per visit

Table 3: LBD Clinical and Economic Model Parameters - Degenerative Spondylolisthesis, Intention To Treat

Parameter	Value	Source and Rationale
Interspinous Spacers		
LBD Clinical Outcomes *(By Time)*		
Back Function (Change in ODI)		
Month 24	---	
All months, SEM of mean cumulative change		
Back Pain (Change in SF-36 BP)		Zucherman, 2004
Month 24	35.3	
All months, SEM of mean cumulative change	2.3	
QoL		
Month 24	0.762	
		Zucherman, 2004. QoL Estimated from change in Zurich Claudication Questionnaire Physical Function subscale and age- & sex-specific norm for EQ-5D
All months, SEM of QoL	0.01	
Adherence & Crossover *(By Time)*		Assume same as fusion & laminectomy Weinstein, 2007
Probability of Surgery		Weinstein, 2007
Months 1-3	0.42	3-month probability
Months 4-6	0.2	3-month probability
Months 7-12	0.107	3-month probability
Months 12-24	0.0025	3-month probability
Probability of Recurrent Surgery		
Cumulative probability of recurrent surgery at 24 months	0.12	Zucherman, 2004
Cost of Intervention		
Cost of Interspinous spacers (first 3 months)	$8,500	APC 52 (APC ($6000), CPT ($2000), anesthesia ~$500
Cost of Interspinous spacers follow-up (after first 3 months)	$150	1 office visit
Visits		
Interspinous spacers, Initial 3 months	7	CPT 99215 (office visit,3) (2); 97110 (PT, 15 min, 24)
Interspinous spacers, annual follow-up	1	CPT 99215 (office visit 3)
Major Complication, Permanent, Additional Visits	2	CPT 99215, 2 visits, HCPCS L2114; Kuntz, 2000
Costs of Visits		
Interspinous Spacers Visits Costs, Initial 3 months	$950	CPT 99215 (office visit,3) (1); 97110 (PT, 15 min, 24)
Interspinous Visits Costs, Annually	$150	(office visit, 1)
Major Complication, Permanent	$900	CPT 92115 (2), HCPCS L2114; Kuntz, 2000
Quality of Life (QoL)		
QoL Disutility for Interspinous spacers	0.2	Assumption. Less than laminectomy
Days of Disutility from Interventions		
Days of Disutility from Interspinous spacers	1	Assumption. Same as laminectomy
Complications		
Complications of Surgery (Interspinous spacers)		No Data. Assume similar to discectomy
Probability of Minor Complication	0.0450	ICER Systematic review, midpoint of reported range
Probability of Major Complication	0.0300	Anderson, 2006; Zucherman, 2004
Probability of Permanent Injury due to Major Complication	0.0667	Chou, Systematic review, LBD surgery
Probability of Death (Fatal Complication)	0.0001	
Costs of Complications		
Cost of minor complication	$7,000	DRG with CC

Table 3: LBD Clinical and Economic Model Parameters - Degenerative Spondylolisthesis, Intention To Treat

Parameter	Value	Source and Rationale
Cost of major complication	$14,000	DRG with MCC
Cost of major permanent complication	$14,000	DRG with MCC
Cost of fatal complication	$0	
Quality of Life Disutility from Complications		Assumption
QoL reduction for minor complication	0.01	
QoL reduction for major complication	0.20	
QoL reduction for permanent disability from major complication	0.50	
QoL reduction for (acute) fatal complication	0.50	
Days of Disability from Complications		DRG LOS
Days of disutility for minor complication	3	
Days of disutility for major complication	5	
Days of disutility for major permanent complication, initially	6	
Days of disutility for acute fatal complication	10	
Fusion		
LBD Clinical Outcomes *(By Time)*		
Back Function (Change in ODI)		Weinstein, 2007
Month 3	-6.5	
Month 12	-14.3	
Month 24	-17.1	
All months, SEM of mean cumulative change		
Back Pain (Change in SF-36 BP)		Weinstein, 2007
Month 3	10.8	
Month 12	24.5	
Month 24	23.9	
All months, SEM of mean cumulative change		
All months, SEM proportion working (FT/PT)		
QoL		Tosteson, 2008
Month 3	0.73	
Month 6	0.73	
Month 12	0.73	
Month 24	0.74	
All months, SEM of QoL	0.01	
Adherence & Crossover *(By Time)*		
Probability of Surgery		Weinstein, 2007
Months 1-3	0.358	3-month probability
Months 4-6	0.265	3-month probability
Months 7-12	0.048	3-month probability
Months 12-24	0.039	3-month probability
Probability of Recurrent Surgery		Weinstein, 2008(LSS) & Weinstein, 2007 (DS)
Probability of recurrent surgery months 1-12 months	0.08	Recurrent surgery after surgery was higher in DS, where most of the initial surgical treatment was fusion
Probability of recurrent surgery months 12-24	0.03	
Cost of Intervention		
Cost of fusion (first 3 months)	$23,900	$32,800 for complex fusion.
Cost of fusion follow-up (after first 3 months)	150	$250 for complex fusion.
Visits		
Fusion, Initial 3 months	8	CPT 99215 (office visit,3) (2); 97110 (PT, 15 min, 24)
Fusion, Annual Follow-up	2	CPT 99215 (office visit 3)
Major Complication, Permanent, Additional Visits	2	CPT 99215, 2 visits, HCPCS L2114; Kuntz, 2000
Costs of Visits		

Table 3: LBD Clinical and Economic Model Parameters - Degenerative Spondylolisthesis, Intention To Treat

Parameter	Value	Source and Rationale
Fusion Visits Costs, Initial 3 months	$1,050	CPT 99215 (office visit, 3);97110 (PT 15 min, 24); 77214 X-ray for fusion
Fusion Visits Costs, Annually	$150	(office visit, 1)
Major Complication, Permanent	$900	CPT 92115 (2), HCPCS L2114; Kuntz, 2000
Quality of Life (QoL)		
QoL Disutility for Fusion	0.5	Assumption
Days of Disutility from Interventions		
Days of Disutility from Fusion	4	DRG LOS
Complications		
Complications of Surgery (Fusion)		
Probability of Minor Complication	0.13	RR 1.27 if complex fusion. Deyo, 2010
Probability of Major Complication	0.05	RR 1.13 if complex fusion. Deyo, 2010
Probability of Permanent Injury due to Major Complication	0.04	Chou, Systematic review, LBD surgery
Probability of Death (Fatal Complication)	0.005	RR 1.33 if complex fusion. Deyo, 2010
Costs of Complications		
Cost of minor complication	$7,000	DRG with CC
Cost of major complication	$14,000	DRG with MCC ($28,000 if complex fusion)
Cost of major permanent complication	$14,000	DRG with MCC ($28,000 if complex fusion)
Cost of fatal complication	0	
Quality of Life Disutility from Complications		Assumption
QoL reduction for minor complication	0.01	
QoL reduction for major complication	0.20	
QoL reduction for permanent disability from major complication	0.50	
QoL reduction for (acute) fatal complication	0.50	
Days of Disability from Complications		DRG LOS
Days of disutility for minor complication	3	
Days of disutility for major complication	5	10 (for complex fusion)
Days of disutility for major permanent complication, initially	6	11 (for complex fusion)
Days of disutility for acute fatal complication	10	

Table 4: LBD Clinical and Economic Model Parameters - Chronic Low Back Pain, Intention To Treat

Parameter	Value	Source and Rationale
Patient Variables		
Age	65	
Sex	Male	Male. CLBP more common in men
Model Parameters		
Duration of Follow-up, years	2	RCTs provide 2 years of follow-up
SPY	4	Markov Model Stage per year
Annual Discount Rate	0.03	Gold, 1996
Work Days per Year	240	48 weeks x 5 days per week
LBD Clinical Status at Baseline		
Back Function	48.4 ± 11.9	Fritzell, 2001
Back Pain	37.4 ± 14.3	
Working (FT/PT), proportion	0.2	
Working (FT/PT), Total number	56	
QoL	0.46 ± 0.246	Estimated based on back function, age & sex norm for EQ-5D, Hanmer, 2006
Costs		
Wages per day	$165	BLS Series Report LEU0252889100
Conservative Care		
LBD Clinical Outcomes *(By Time)*		
Back Function (Change in ODI)		Fritzell, 2001
Month 24	-6.35	
All months, SEM of mean cumulative change		
Back Pain (Change in SF-36 BP)		Fritzell, 2001
Month 24	7.98	
All months, SEM of mean cumulative change	1.3	
Work		
Month 24	0.13	Fritzell, 2001
All months, SEM proportion working (FT/PT)	0.015	
QoL		Estimated based on back function, age & sex norm for EQ-5D, Hanmer, 2006
Month 24	0.52	
All months, SEM of QoL		
Adherence & Crossover *(By Time)*		
Probability of Surgery		Fritzell, 2001
Month 12	0.58	Annual Probability (7/72)
Costs (ambulatory Visit Costs)		
Initial cost of conservative care (first 3 months)	$2,400	CPT 99214 (office visit (1)), 97110 (PT) (72), Naprosen DR & cyclobenzaprine
Cost of conservative care (subsequent 3 months)	$0	
Visits		
Conservative Care, Initial 3 months	19	CPT 99214 (office visit (1)), 97110 (PT) (72), Naprosen DR & cyclobenzaprine
Conservative Care, Annual Follow-up	0	
Quality of Life (QoL)		
QoL Disutility for Conservative Care	0.01	Assumption
Days of Disutility for Treatment		
Conservative Care	19	one per treatment day

Table 4: LBD Clinical and Economic Model Parameters - Chronic Low Back Pain, Intention To Treat

Parameter	Value	Source and Rationale
Interdisciplinary Rehabilitation		
LBD Clinical Outcomes *(By Time)*		
Back Function (Change in ODI)		Dufour, 2010
Months 3	-11.4	
Months 6	-11	
Month 12	-12.6	
Month 24	-12.2	
All months, SEM of mean cumulative change		
Back Pain (Change in SF-36 BP)		Dufour, 2010
Months 3	15.2	
Months 6	13.0	
Month 12	14.6	
Month 24	15.2	
All months, SEM of mean cumulative change	1.3	
Work		
Month 24	0.11	Dufour, 2010
All months, SEM proportion working (FT/PT)	0.028	
QoL		Estimated based on back function, age & sex norm for EQ-5D, Hanmer, 2006
Month 24	0.55	
All months, SEM of QoL		
Adherence & Crossover *(By Time)*		
Probability of Surgery		Fritzell, 2001
Month 12	0.10	Annual Probability (7/72)
Costs		
Initial cost of interdisciplinary rehabilitation (first 3 months)	$8,500	CPT 99214 (2), 97110 (240), 97537 (OT) (16), 90857 (CBT) (10)
Cost of interdisciplinary rehabilitation (subsequent 3 months)	$0	
Visits		
interdisciplinary rehabilitation, Initial 3 months	88	CPT 99214 (2), 97110 (240), 97537 (OT) (16), 90857 (CBT) (10)
interdisciplinary rehabilitation, Annual Follow-up	0	
Quality of Life (QoL)		
QoL Disutility for interdisciplinary rehabilitation	0.02	Assumption
Days of Disutility for Treatment		
interdisciplinary rehabilitation	88	one day per treatment day
Fusion		
LBD Clinical Outcomes *(By Time)*		
Back Function (Change in ODI)		Fritzell, 2001
Month 24	-10.58	
All months, SEM of mean cumulative change		
Back Pain (Change in SF-36 BP)		Fritzell, 2001
Month 24	21	
All months, SEM of mean cumulative change	2.4	
Work		
Month 24	0.35	Fritzell, 2001
All months, SEM proportion working (FT/PT)	0.015	
QoL		Estimated based on back function (Fritzell, 2001) and age & sex norm for EQ-5D, Hanmer, 2006
Month 24	0.55	
All months, SEM of QoL		
Adherence & Crossover *(By Time)*		
Probability of Surgery		

Table 4: LBD Clinical and Economic Model Parameters - Chronic Low Back Pain, Intention To Treat

Parameter	Value	Source and Rationale
Month 12	0.08	Annual Probability (18/222)
Probability of Recurrent Surgery		Fritzell, 2001
Probability of recurrent surgery at 3 months	0.06	
Probability of recurrent surgery months 3-6	0.02	
Probability of recurrent surgery after 6 months	0.00	
Cost of Intervention		
Cost of Fusion (first 3 months)	23900	32800 if complex fusion
Cost of Fusion follow-up (after first 3 months)		
Visits		
Fusion, Initial 3 months	7	8 if complex fusion
Fusion, Annual Follow-up	1	2 if complex fusion
Major Complication, Permanent, Additional Visits	2	
Quality of Life (QoL)		
QoL Disutility for Fusion	0.5	Assumption
Days of Disutility from Interventions		
Days of Disutility from Fusion	4	DRG LOS
Complications		
Complications of Surgery (Fusion)		
Probability of Minor Complication	0.1300	RR 1.27 if complex fusion ICER Systematic Review, Midpoint range
Probability of Major Complication	0.0500	RR 1.13 if complex fusion Deyo, 2010
Probability of Permanent Injury due to Major Complication	0.0400	RR 1.13 if complex fusion Chou Systematic review LBD Surgery
Probability of Death (Fatal Complication)	0.0050	RR 1.33 if complex fusion. Deyo, 2010
Costs of Complications		
Cost of minor complication	$7,000	DRG with CC
Cost of major complication	$14,000	DRG with MCC ($28,000 if complex fusion)
Cost of major permanent complication	$14,000	DRG with MCC ($28,000 if complex fusion)
Cost of fatal complication	0	
Quality of Life Disutility from Complications		Assumption
QoL reduction for minor complication	0.01	
QoL reduction for major complication	0.20	
QoL reduction for permanent disability from major complication	0.50	
QoL reduction for (acute) fatal complication	0.50	
Days of Disability from Complications		DRG LOS
Days of disutility for minor complication	5	
Days of disutility for major complication	5	10 if complex fusion
Days of disutility for major permanent complication, initially	5	10 if complex fusion
Days of disutility for acute fatal complication	7	