Appendix A. Search Strategy

Literature Search Methods

Electronic Database Searches

The following databases have been searched for relevant information:

Name	Date Limits	Platform/Provider
ClinicalTrials.gov	1995 through June 26, 2011	www.clinicaltrials.gov
The Cochrane Central Register of Controlled Trials (CENTRAL)	1995 through March 16, 2012	www.thecochranelibrary.com
The Cochrane Database of Methodology Reviews (Methodology Reviews)	1995 through March 16, 2012	www.thecochranelibrary.com
The Cochrane Database of Systematic Reviews (Cochrane Reviews)	1995 through March 16, 2012	www.thecochranelibrary.com
Database of Abstracts of Reviews of Effects (DARE)	1995 through March 16, 2012	www.thecochranelibrary.com
EMBASE (Excerpta Medica)	1995 through current	OVID
Health Technology Assessment Database (HTA)	1995 through March 20, 2012	www.ecri.org
MEDLINE	1995 through current	OVID
PubMed (In-process and Publisher records)	1995 through February 7, 2012	www.pubmed.gov
U.K. National Health Service Economic Evaluation Database (NHS EED)	1995 through March 16, 2012	www.thecochranelibrary.com
CINAHL	1995 through February 7, 2012	EBSCO
U.S. National Guideline Clearinghouse™ (NGC)	1995 through June 24, 2011	www.ngc.gov

Detailed search strategies are presented below.

Hand Searches of Journal and Nonjournal Literature

Journals and supplements maintained in ECRI Institute's collections were routinely reviewed. Nonjournal publications and conference proceedings from professional organizations, private agencies, and government agencies were also screened. Other mechanisms used to retrieve additional relevant information included review of bibliographies/reference lists from peer-reviewed and gray literature. (Grey literature consists of reports, studies, articles, and monographs produced by federal and local government agencies, private organizations, educational facilities, consulting firms, and corporations. These documents do not appear in the peer-reviewed journal literature).

Medical Subject Headings (MeSH), EMTREE, and Keywords

The search strategies employed combinations of freetext keywords as well as controlled vocabulary terms including (but not limited to) the concepts shown in the Topic-specific Search Terms table.

Search Strategies

The strategy below is presented in OVID syntax; the search was simultaneously conducted across EMBASE and MEDLINE. All MeSH and EMTREE controlled vocabulary terms were exploded (using the prefix exp) within individual search strings unless otherwise noted. A similar strategy was used to search the databases comprising PubMed, CINAHL and the Cochrane Library.

Search sets were structured to compare treatment alternatives to spinal fusion as well as various types of spinal fusion for patients with lumbar degenerative disc disease, lumbar stenosis and spondylolisthesis. These search results were further refined to capture specific patient outcomes, study designs and publication types. Final results for key questions 1-10 are represented in the aggregate in set 33 (below).

Topic-Specific Search Terms

EMBASE/MEDLINE OVID Syntax

Concept	*Controlled Vocabulary	Keywords
Non-surgical alternatives to spinal fusion (non-pharmacologic)	**MEDLINE (MeSH)** acupuncture therapy bed rest braces chiropractic cognitive therapy complementary therapies electric stimulation therapy exercise exercise movement techniques exercise therapy massage manipulation, chiropractic manipulation, osteopathic manipulation, spinal muscle stretching exercises musculoskeletal manipulations neurofeedback occupational therapy orthotic devices oxygen ozone phonophoresis physical therapy modalities psychotherapy recreation therapy rehabilitation rest sports therapeutic touch transcutaneous electric nerve stimulation yoga **EMBASE (EMTREE)**	acupunctur* aerobic athlet* bed rest biofeedback brace* chiroprac* cognitive therapy cold conservative complementary corset endurance e-stim exercise extension flexion heat holistic hot IDET intradiscal electrothermal therapy inversion isokinetic isometric manipulation massag* mobility muscle strength* muscle train* neurofeedback non-surgical nonsurgical non-operative

Concept	*Controlled Vocabulary	Keywords
	Acupuncture aerobic exercise alternative medicine bed rest brace chiropractic cognitive therapy electrostimulation exercise massage muscle stretching neurofeedback occupational therapy orthopedic manipulation orthotics oxygen therapy ozone ozone therapy physiotherapy psychotherapy recreational therapy rehabilitation rest sport stretching exercise traction therapy transcutaneous nerve stimulation yoga	nonoperative occupational orthos* orthotic* oxygen ozone phonophoresis physical therapy physiotherapy pilates psychotherap* range of motion range-of-motion recreational rehab* reiki rest stabilization exercis* strength train* stretch* sport* TENS Traction transcutaneous electric nerve stimulation wholistic yoga
Non-surgical alternatives to spinal fusion (over the-counter; pharmacologic)	**MEDLINE (MeSH)** acetaminophen analgesics, non-narcotic aspirin ibuprofen naproxen nonprescription drugs **EMBASE (EMTREE)** acetylsalicylic acid ibuprofen naproxen non prescription drug paracetamol	acetaminophen advil aleve aspirin celebrex celecoxib ibuprofen motrin naprosyn naproxen non-prescription nonprescription over the counter over-the-counter tylenol
Non-surgical alternatives to spinal fusion (prescription; pharmacologic)	**MEDLINE (MeSH)** adrenal cortex hormones analgesics analgesics, opioid antidepressive agents antidepressive agents, tricyclic anti-inflammatory agents anti-inflammatory agents, non-steroidal	adrenal cortex hormone* anaesthetic* analgesic* anesthetic* antidepressant* anti-inflammator* codeine corticosteroid*

Concept	*Controlled Vocabulary	Keywords
	drug therapy (floating subheading) carisoprodol codeine cortisone delayed-action preparations dextropropoxyphene diazepam drug therapy drug therapy, combination drug therapy (floating subheading) fluoxetine glucocorticoids hydrocodone injections injections, epidural methylprednisolone narcotics nerve block oxycodone paroxetine prednisone sertraline steroids tramadol **EMBASE (EMTREE)** analgesic agent antidepressive agent antiinflammatory agent carisoprodol codeine corticosteroid cortisone delayed release formulation dextropropoxyphene diazepam drug therapy epidural drug administration fluoxetine glucocorticoid hydrocodone injection methylprednisolone muscle relaxant agent narcotic agent nerve block nonsteroid antiinflammatory agent opiate oxycodone paroxetine prednisone	cortisone cyclobenzaprine darvocet drug* epidural* flexeril gabapentin hydrocodone inject* medication* medicin* methylprednisolone muscle relaxant* narcotic* nerve block* nerve root block* neurontin nonsteroidal NSAID opioid* oxycodone oxycontin paxil percocet pharmaceutical* pharmacotherap* prednisone prescription* propoxyphene prozac soma spinal block steroid* tramadol ultracet ultram valium vicodin zoloft

Concept	*Controlled Vocabulary	Keywords
	steroid tramadol	
Fusion techniques and instrumentation (techniques)	**MEDLINE (MeSH)** surgical procedures, minimally invasive **EMBASE (EMTREE)** anterior spine fusion minimally invasive surgery surgical technique	adjacen* ALIF Anteri anterilumbar interbody fusion anteroposteri approach* circumferential double-level image-guided instrument* laparoscopic* lateral level* method* micro* mini* minimally invasive mini-open MiTLIF Multilevel multi-level non-instrumented one-level open OTLIF PLIF Posterior posterior lumbar interbody fusion posterolateral postero-lateral posterolateral lumbar interbody fusion retroperitoneal segment* single-level standard technique* tthree-level TLIF traditional trans-foraminal transforaminal transforaminal lumbar interbody fusion transperitoneal transverse triple-level two-level unilateral
Fusion techniques and instrumentation	**MEDLINE (MeSH)** absorbable implant	arthrodesis cage

Concept	*Controlled Vocabulary	Keywords
(implants/hardware)	bone nails bone plates bone screws implantation instrumentation (floating subheading) internal fixators prostheses and implants prosthesis design prosthesis implantation **EMBASE (EMTREE)** bone nail bone plate bone screw cage collagen sponge fixation device implant instrumentation medical instrumentation pedicle screw plate fixation prosthesis	carbon cylindrical extender* hook* implant* instrumented interbody metal nail* noninstrumented non-instrumented ostaPek PEEK plate* prosthes* prosthetic* rigid rod* screw* semirigid semi-rigid sponge stainless steel threaded titanium
Fusion techniques and instrumentation (bone morphogenetic protein)	**MEDLINE (MeSH)** bone morphogenetic proteins bone morphogenetic protein 2 **EMBASE (EMTREE)** bone morphogenetic protein bone morphogenetic protein 2 recombinant bone morphogenetic protein 2	bone morphogenetic protein 2 bone morphogenetic protein-2 cage graft infuse infuse bone graft medtronic morphogenetic rhBMP-2 sponge
Fusion techniques and instrumentation (biocompatible materials/fillers)	**MEDLINE (MeSH)** biocompatible materials bone matrix bone transplantation **EMBASE (EMTREE)** Biocompatibility biomaterial bone allograft bone graft bone matrix bone prosthesis bone transplantation	actifuse allograft apatech autogenous autograft biocompatib* bioglass biologic* biomaterial* bone filler bone graft* bone growth stimulat* bone regeneration bone transplant* bone transplantation ceramic*

Concept	*Controlled Vocabulary	Keywords
		chromos collagen DBX demineralized bone matrix filler gel hydroxyapatite iliac crest matrix novabone OP-1 orthobiologic* osseoconduct* osseoinduct* osteogenic osteoprogenitor osteotech perioglas pliviopore polymer* putty recombinant resorbable resorption stryker synthetic*
Alternative surgical procedures (diskectomy)	**MEDLINE (MeSH)** arthroplasty arthroplasty, replacement discectomy diskectomy, percutaneous joint prosthesis laminectomy prostheses and implants prosthesis implantation total disc replacement **EMBASE (EMTREE)** arthroplasty intervertebral discectomy joint prosthesis laminectomy	activ-l AIDR arthroplasty artificial disc artificial disk artificial joint cadisc charite CL disc dekompress depuy disc arthroplasty disc prostheses disc prosthesis disc replacement discectomy disk arthroplasty disk prostheses disk prosthesis disk replacement diskectomy dynardi dynamic edisc facet replacement flexicore

Concept	*Controlled Vocabulary	Keywords
		freedom lumbar implant* "in motion" intersomatic joint prosthesis joint replacement kineflex maverick mobidisc nucleoplasty nucleotomy nucleus pulposus replacement nucleus replacement physio-l prodisc prodisc-l prosthes* prosthet* prosthetic disc prosthetic disc nucleus prosthetic disk prosthetic joint salubria spartacus TDR TFAS TOPS total disc replacement total facet arthroplasty system total posterior element replacement system truedisc welldisc-l
Alternative surgical procedures (dynamic stabilization)	**MEDLINE (MeSH)** N/A **EMBASE (EMTREE)** spine stabilization	accuflex bioflex CD Horizon DSS Dynesys dynamic flexible FlexPLUS graf ligament interspinous isobar nfix nflex satellite soft stabilimax stabilis* stabiliz*

Concept	*Controlled Vocabulary	Keywords
Alternative surgical procedures (pedicle screw implantation)	**MEDLINE (MeSH)** N/A **EMBASE (EMTREE)** pedicle screw	arx capless caplox CD horizon click'x diamondback fortex mantis mira pangea pathfinder pedicle screw* pedicular screw* pilot preference sequoia sextant silhouette ST360 TSRH viper 2 x90
Alternative surgical procedures (decompression)	**MEDLINE (MeSH)** decompression, surgical laminectomy **EMBASE (EMTREE)** decompression surgery laminectomy laminoplasty	coblation corpectom* decompress* facetectom* falena foraminectom* foraminotom* hemilaminectom* laminectom* laminoplast* laminotom* microdecompression microdiscectomy mild spinewand or vertos
Demographics/Risks/Outcomes	**MEDLINE (MeSH)** activities of daily living adverse effects (floating subheading) comorbidity convalescence disease progression disease susceptibility disability evaluation epidemiology health status health status disparities length of stay	activities of daily living ADL bend* blood loss course disabil* disable* drive* driving employ* epidemiol* fusion rate*

Concept	*Controlled Vocabulary	Keywords
	morbidity	"health status"
	mortality	housework
	nomograms	improve*
	incidence	improving
	outcome and process assessment (health care)	incidenc*
	outcome assessment (health care)	length of stay
	pain	morbidity
	pain measurement	mortality
	pain, postoperative	natural history
	patient satisfaction	nonunion
	postoperative complications	non-union
	predictive value of tests	ODI
	prevalence	oswestry
	prognosis	outcome*
	quality of life	pain*
	recovery of function	"patient satisfaction"
	reoperation	prevalen*
	risk factors	prognos*
		progress*
	EMBASE (EMTREE)	quality of life
	adl disability	recover*
	adverse outcome	reoperat*
	blood loss, surgical	re-operat*
	clinical effectiveness	risk factor*
	comorbidity	sit*
	convalescence	stand*
	daily life activity	surg* time
	disability	susceptib*
	disability severity	time factor*
	disease course	unemploy*
	disease predisposition	work*
	epidemiology	
	health status	
	"length of stay"	
	morbidity	
	mortality	
	incidence	
	oswestry disability	
	outcome assessment	
	outcome variable	
	patient assessment	
	patient satisfaction	
	physical disability	
	postoperative complication	
	postoperative pain	
	predictive validity	
	predictive value	
	prevalence	
	prognosis	
	quality of life	
	reoperation	

Concept	*Controlled Vocabulary	Keywords
	risk factor treatment outcome work disability	
Study designs/Publication types	**MEDLINE (MeSH)** cohort studies comparative effectiveness research controlled clinical trials as topic follow-up studies nomograms patient selection randomized controlled trials as topic regression analysis "validation studies as topic" **EMBASE (EMTREE)** cohort analysis comparative effectiveness controlled clinical trial "controlled clinical trial (topic)" controlled study evaluation research follow up nomogram patient selection "randomized controlled trial (topic)" regression analysis validation study	cohort* comparative study compare* compari* control* controlled clinical trial controlled trial evaluation studies "follow up*" meta-regression nomogram* patient selection random* randomized controlled trial validat* validation studies versus vs "vs."
Lumbar Fusion (lumbar)	**MEDLINE (MeSH)** low back pain lumbar vertebrae lumbosacral region zygapophyseal joint **EMBASE (EMTREE)** low back pain lumbar disk lumbar spinal cord lumbar spine lumbar vertebra zygapophyseal joint	facet low back lower back lumbar lumbopelvic lumbo-pelvic lumbosacral lumbo-sacral sacrolumbar sacro-lumbar thoracolumbar zygapophyseal
Lumbar Fusion (fusion)	**MEDLINE (MeSH)** Arthrodesis spinal fusion spine/surgery surgery (floating subheading) **EMBASE (EMTREE)** Arthrodesis spine fusion	arthrodes* fixation fuse* fusion*
Core Indication	**MEDLINE (MeSH)**	bulge*

Concept	*Controlled Vocabulary	Keywords
(degenerative disk/joint disease)	intervertebral disk degeneration **EMBASE (EMTREE)** intervertebral disk intervertebral disk degeneration intervertebral disk hernia lumbar disk hernia	degenerat* desiccate* disc* disk* fissure* hernia* joint* tear*
Core Indication (stenosis)	**MEDLINE (MeSH)** spinal canal spinal stenosis **EMBASE (EMTREE)** vertebral canal vertebral canal stenosis	lumbar stenosis narrow* spinal stenosis stenosis stenotic vertebral
Core Indication (spondylolisthesis)	**MEDLINE (MeSH)** spondylolisthesis **EMBASE (EMTREE)** spondylolisthesis	disc* disk* slip* spondylolisthesis
Exclusions (study designs/publication types, indications)	**MEDLINE (MeSH)** consensus development conferences as topic consensus development conferences as topic, NIH guideline adherence guidelines as topic health planning guidelines meta-analysis as (topic) neoplasms/major mesh practice guidelines as topic scoliosis/major **EMBASE (EMTREE)** consensus development neoplasm/major practice guideline scoliosis/major "systematic review" "meta analysis (topic)"	abscess* animal* autobiography biography bovine cadaver* cancer* canine carcinoma case report* case reports case stud* comment conference conference* congress consensus consensus development conference consensus development conference, NIH cyst* deform* editorial fracture* guideline guideline* hematoma* lectures letter meta analysis

Concept	*Controlled Vocabulary	Keywords
		meta-analysis metasta* mice mouse neoplas* news note oncolog* pig* porcine practice guideline proceeding proceeding* rat rats review rodent* sarcoma scoliosis systematic review trauma* tumor* tumour* video-audio media webcasts

OVID Conventions:

? or *	=	truncation character (wildcard)
.ab.	=	limit to abstract
ADJ*n*	=	search terms within a specified number (*n*) of words from each other in any order
exp/	=	"explodes" controlled vocabulary term (e.g., expands search to all more specific related terms in the vocabulary's hierarchy)
.de.	=	limit controlled vocabulary heading
.fs.	=	floating subheading
.hw.	=	limit to heading word
.mp.	=	combined search fields (default if no fields are specified)
.pt.	=	publication type
.ti.	=	limit to title
.tw.	=	limit to title and abstract fields

Search strategy conducted using EMBASE/MEDLINE OVID Syntax

Set #	Concept	Search Statement
1	Non-surgical alternatives to spinal fusion (non-pharmacologic)	exp acupuncture therapy/ or exp aerobic exercise/ or exp alternative medicine/ or exp bed rest/ or exp brace/ or exp braces/ or exp chiropractic/ or exp cognitive therapy/ or exp complementary therapies/ or exp electric stimulation therapy/ or exp electrostimulation/ or exp endurance training/ or exp exercise/ or exp exercise movement techniques/ or exp exercise therapy/ or exp manipulation, chiropractic/ or exp manipulation, orthopedic/ or exp manipulation, osteopathic/ or exp manipulation, spinal/ or exp massage/ or exp muscle stretching/ or exp muscle stretching exercises/ or exp musculoskeletal manipulations/ or exp neurofeedback/ or exp occupational therapy/ or exp orthopedic manipulation/ or exp orthotic devices/ or exp orthotics/ or exp oxygen/ or exp oxygen therapy/ or exp ozone/ or exp ozone therapy/ or exp phonophoresis/ or exp physical mobility/ or exp physical therapy modalities/ or exp physiotherapy/ or exp psychotherapy/ or exp range of motion/ or exp range of motion, articular/ or exp recreation therapy/ or exp recreational therapy/ or exp rehabilitation/ or exp rest/ or exp sport/ or exp sports/ or exp stretching exercise/ or exp therapeutic touch/ or exp traction/ or exp traction therapy/ or exp transcutaneous electric nerve stimulation/ or exp transcutaneous nerve stimulation/ or exp yoga/ or (acupunctur* or aerobic or athlet* or bed rest or biofeedback or brace* or chiroprac* or cold or cognitive therapy or conservative or complementary or chiroprac* or corset or endurance or e-stim or exercise or extension or flexion or heat or holistic or hot or IDET or intradiscal electrothermal therapy or inversion or isokinetic or isometric or manipulation or massag* or mobility or muscle strength* or muscle train* or neurofeedback or nonsurgical or non-surgical or nonoperative or non-operative or occupational or orthos* or orthotic* or oxygen or ozone or phonophoresis or physical therapy or physiotherap* or pilates or psychotherap* or range of motion or range-of-motion or recreational or rehab* or reiki or rest or stabilization exercis* or strength train* or stretch* or sport* or TENS or traction or transcutaneous electric nerve stimulation or wholistic or yoga).ti,ab.
2	Non-surgical alternatives to spinal fusion (non-prescription/over the-counter medication)	exp acetaminophen/ or exp acetylsalicylic acid/ or exp analgesics, non-narcotic/ or exp aspirin/ or exp ibuprofen/ or exp naproxen/ or exp non prescription drug/ or exp nonprescription drugs/ or exp paracetamol/ or (acetaminophen or advil or aleve or aspirin or celebrex or celecoxib or ibuprofen or motrin or naprosyn or naproxen or non-prescription or nonprescription or over the counter or over-the-counter or tylenol).ti,ab.

Set #	Concept	Search Statement
3	Non-surgical alternatives to spinal fusion (prescription medication)	dt.fs. or exp adrenal cortex hormones/ or exp analgesic agent/ or exp analgesics, opioid/ or exp analgesics/ or exp antidepressant agent/ or exp antidepressive agents/ or exp antidepressive agents, tricyclic/ or exp antiinflammatory agent/ or exp anti-inflammatory agents, non-steroidal/ or exp anti-inflammatory agents/ or exp carisoprodol/ or exp codeine/ or exp corticosteroid/ or exp cortisone/ or exp delayed release formulation/ or exp delayed-action preparations/ or exp dextropropoxyphene/ or exp diazepam/ or exp drug therapy, combination/ or exp drug therapy/ or exp epidural drug administration/ or exp fluoxetine/ or exp glucocorticoid/ or exp glucocorticoids/ or exp hydrocodone/ or exp injection/ or exp injections/ or exp injections, epidural/ or exp methylprednisolone/ or exp muscle relaxant agent/ or exp narcotic agent/ or exp narcotics/ or exp nerve block/ or exp nonsteroid antiinflammatory agent/ or exp opiate/ or exp oxycodone/ or exp paroxetine/ or exp prednisone/ or exp sertraline/ or exp steroid/ or exp steroids/ or exp tramadol/ or (adrenal cortex hormone* or anaesthetic* or analgesic* or anesthetic* or antidepressant* or anti-inflammator* or codeine or corticosteroid* or cortisone or cyclobenzaprine or darvocet or drug or epidural* or flexeril or gabapentin or hydrocodone or inject* or medication* or medicin* or methylprednisolone or muscle relaxant* or narcotic* or nerve block* or nerve root block* or neurontin or nonsteroidal or NSAID or opioid* or oxycodone or oxycontin or paxil or percocet or pharmaceutical* or pharmacotherap* or prednisone or prescription or propoxyphene or prozac or soma or spinal block or steroid* or tramadol or ultracet or ultram or valium or vicodin or zoloft).ti,ab.
4	Combined non-surgical alternatives set	1 or 2 or 3
5	Fusion techniques and instrumentation (techniques)	exp anterior spine fusion/ or exp minimally invasive surgery/ or exp surgical procedures, minimally invasive/ or exp surgical technique/ or (adjacen*or ALIF or anterior or anterior lumbar interbody fusion or anteroposterior or approach* or circumferential or double-level or image-guided or instrument* or laparoscopic* or lateral or level* or method* or micro* or mini* or minimally invasive or mini-open or MiTLIF or multilevel or multi-level or non-instrumented or one-level or open or OTLIF or PLIF or posterior or posterior lumbar interbody fusion or posterolateral or postero-lateral or posterolateral lumbar interbody fusion or retroperitoneal or segment* or single-level or standard or technique or techniques or three-level or TLIF or traditional or trans-foraminal or transforaminal or transforaminal lumbar interbody fusion or transperitoneal or transverse or triple-level or two-level or unilateral).ti,ab.
6	Fusion techniques and instrumentation (implants/hardware)	is.fs. or exp "prostheses and implants"/ or exp absorbable implant/ or exp bone nail/ or exp bone nails/ or exp bone plate/ or exp bone plates/ or exp bone screws/ or exp cage/ or exp collagen sponge/ or exp fixation device/ or exp implant/ or exp implantation/ or exp instrumentation/ or exp internal fixators/ or exp medical instrumentation/ or exp pedicle screw/ or exp plate fixation/ or exp prosthesis design/ or exp prosthesis implantation/ or exp prosthesis/ or (arthrodesis or cage or carbon or cylindrical or extender* or hook* or implant* or instrumented or interbody or metal or nail* or noninstrumented or non-instrumented or ostaPek or PEEK or plate* or prosthes* or prosthetic* or rigid or rod* or screw* or semirigid or semi-rigid or sponge or stainless steel or threaded or titanium).ti,ab.
7	Fusion techniques and instrumentation (bone morphogenetic protein)	exp bone morphogenetic proteins/ or exp bone morphogenetic protein 2/ or exp bone morphogentic protein/ or exp recombinant bone morphogenetic protein 2/ or (bone morphogenetic protein 2 or bone morphogenetic protein-2 or infuse bone graft or rhBMP-2).ti,ab. or ((infuse or medtronic) and (cage or graft or morphogenetic or rhBMP-2 or sponge)).ti,ab.

Set #	Concept	Search Statement
8	Fusion techniques and instrumentation (biocompatible materials/fillers)	exp biocompatible materials/ or exp biocompatibility/ or exp biomaterial/ or exp bone allograft/ or exp bone graft/ or exp bone matrix/ or exp bone prosthesis/ or exp bone transplantation/ or (actifuse or allograft or apatech or autogenous or autograft or biocompatib* or bioglass or biologic* or biomaterial* or bone filler or bone graft* or bone growth stimulator or bone regeneration or bone transplant* or bone transplantation or ceramic* or chromos or collagen or DBX or demineralized bone matrix or filler or gel or hydroxyapatite or iliac crest or matrix or novabone or OP-1 or orthobiologic* or osseoconduct* or osseoinduct* or osteogenic or osteoprogenitor or osteotech or perioglas or pliviopore or polymer* or putty or recombinant or resorbable or resorption or stryker or synthetic*).ti,ab.
9	Combined fusion techniques	5 or 6 or 7 or 8
10	Alternative surgical procedures (diskectomy)	exp "prostheses and implants"/ or exp arthroplasty, replacement/ or exp arthroplasty/ or exp diskectomy, percutaneous/ or exp diskectomy/ or exp intervertebral diskectomy/ or exp joint prosthesis/ or exp prosthesis implantation/ or exp total disc replacement/ or (activ-l or AIDR or arthroplasty or artificial disc or artificial disk or artificial joint or cadisc or charite or CL disc or dekompressor or depuy or disc arthroplasty or disc prostheses or disc prosthesis or disc replacement or discectomy or disk arthroplasty or disk prostheses or disk prosthesis or disk replacement or diskectomy or dynardi dynamic or edisc or facet replacement or flexicore or freedom lumbar or implant* or "in motion" or intersomatic or joint prosthesis or joint replacement or kineflex or maverick or mobidisc or nucleoplasty or nucleotomy or nucleus pulposus replacement or nucleus replacement or physio-l or prodisc or prodisc-l or prosthes* or prosthet*or prosthetic disc or prosthetic disc nucleus or prosthetic disk or prosthetic joint or salubria or spartacus or TDR or TFAS or TOPS or total disc replacement or total facet arthroplasty system or total posterior element replacement system or truedisc or welldisc-l).ti,ab.
11	Alternative surgical procedures (dynamic stabilization)	exp spine stabilization/ or (accuflex or bioflex or CD Horizon or DSS or Dynesys or dynamic or flexible or FlexPLUS or graf ligament or interspinous or isobaror or nfix or nflex or satellite or soft or stabilimax or stabilis* or stabiliz*).ti,ab.
12	Alternative surgical procedures (pedicle screw implantation)	exp pedicle screw/ or (arx or capless or caplox or CD horizon or click'x or diamondback or fortex or mantis or mira or pangea or pathfinder or pedicle screw* or pedicular screw* or pilot or preference or sequoia or sextant or silhouette or ST360 or TSRH or viper 2 or x90).ti,ab.
13	Alternative surgical procedures (decompression)	exp decompression, surgical/ or exp decompression surgery/ or exp laminectomy/ or exp laminoplasty/ or exp spinal cord decompression/ or (coblation or corpectom* or decompress* or facetectom* or falena or foraminectom* or foraminotom* or hemilaminectom* or laminectom* or laminoplast* or laminotom* or microdecompression or microdiscectomy or spinewand or (vertos and mild)).ti,ab.
14	Combined alternative surgical procedures set	10 or 11 or 12 or 13

Set #	Concept	Search Statement
15	Patient characteristics/Demographic variables/Outcomes/Risks	ae.fs. or exp activities of daily living/ or exp ADL disability/ or exp adverse outcome/ or exp blood loss, surgical/ or exp comorbidity/ or exp convalescence/ or exp daily life activity/ or exp disability/ or exp disability evaluation/ or exp disability severity/ or exp disease course/ or exp disease progression/ or exp disease susceptibility/ or exp epidemiology/ or exp health status disparities/ or exp health status/ or exp incidence/ or exp "length of stay"/ or exp length of stay/ or exp morbidity/ or exp mortality/ or exp oswestry disability index/ or exp "outcome and process assessment (health care)"/ or exp outcome assessment/ or exp "outcome assessment (health care)"/ or exp outcome variable/ or exp pain/ or exp pain assessment/ or exp pain measurement/ or exp pain, postoperative/ or exp patient satisfaction/ or exp physical disability/ or exp postoperative complication/ or exp postoperative pain/ or exp predisposition/ or exp prevalence/ or exp prognosis/ or exp quality of life/ or exp recovery of function/ or exp risk factor/ or exp risk factors/ or exp reoperation/ or exp treatment outcome/ or exp work disability/ or (activities of daily living or ADL or bend* or blood loss or comorbid* or course or disabil* or disable* or drive* or driving or employ* or epidemiol* or fusion rate* or "health status" or housework or improve* or improving or incidenc* or length of stay or morbidity or mortality or natural history or nonunion or non-union or ODI or oswestry or outcome* or pain* or "patient satisfaction" or prevalen* or prognos* or progress* or quality of life or recover* or reoperat* or re-operat* or risk factor* or sit* or stand* or surg* time or susceptib* or time factor* or unemploy* or work*).ti,ab.
16	Study designs/Publication types	exp clinical effectiveness/ or exp comparative effectiveness research/ or exp cohort analysis/ or exp cohort studies/ or exp comparative effectiveness/ or exp controlled clinical trial/ or exp controlled clinical trials as topic/ or exp "controlled clinical trial (topic)"/ or exp controlled study/ or exp evaluation research/ or exp follow up/ or exp follow-up studies/ or exp nomogram/ or exp nomograms/ or exp patient selection/ or exp predictive validity/ or exp predictive value/ or exp randomized controlled trials as topic/ or exp regression analysis/ or exp "validation studies as topic"/ or exp validation study/ or (cohort* or compare* or compari* or control* or "follow up*" or meta-regression or nomogram* or "patient selection" or random* or versus or vs or "vs.").ti,ab. or (comparative study or controlled clinical trial or evaluation studies or randomized controlled trial or validation studies).pt.
17	Combined outcomes/study designs/publication types set	15 or 16
18	Lumbar fusion (lumbar)	exp low back pain/ or exp lumbar disk/ or exp lumbar spinal cord/ or exp lumbar spine/ or exp lumbar vertebra/ or exp lumbar vertebrae/ or exp lumbosacral region/ or exp zygapophyseal joint/ or (facet or low back or lower back or lumbar or lumbopelvic or lumbo-pelvic or lumbosacral or lumbo-sacral or sacrolumbar or sacro-lumbar or thoracolumbar or zygapophyseal).ti,ab.
19	Lumbar fusion (fusion)	su.fs. or exp arthrodesis/ or exp spine/su or exp spine fusion/ or exp spinal fusion/ or (fuse* or fusion or fixation or arthrodes*).ti,ab.
20	Combined lumbar fusion set	18 and 19
21	Core indication (degenerative disk/joint disease)	exp intervertebral disk degeneration/ or exp intervertebral disk hernia/ or exp lumbar disk hernia/ or ((bulge* or degenerat* or desiccat* or fissure* or hernia* or tear*) and (exp intervertebral disk/ or (disc* or disk* or joint*))).ti,ab.
22	Core indication (stenosis)	exp spinal stenosis/ or exp vertebral canal stenosis/ or (lumbar stenosis or spinal stenosis).ti,ab. or ((exp spinal canal/ or exp vertebral canal/) and (stenosis or stenotic or narrow*)).ti,ab.
23	Core indication (spondylolisthesis)	exp spondylolisthesis/ or spondylolisthesis.ti,ab. or (slip* and (disc* or disk*)).ti,ab.
24	Combined fusion comparators set	4 or 9 or 14

Set #	Concept	Search Statement
25	Combined outcomes/study designs/publication types AND lumbar fusion AND fusion comparators	17 and 20 AND 24
26	Combined indications	21 or 22 or 23
27	MASTER SET: demographics/risks/outcomes AND study designs/publication types AND lumbar fusion AND fusion comparators AND indications	25 and 26
28	Master set with exclusions (concepts/study designs/publications types)	27 not (exp guideline adherence/ or exp guidelines as topic/ or exp health planning guidelines/ or exp consensus development/ or exp consensus development conferences as topic/ or exp consensus development conferences, NIH as topic/ or exp "meta analysis (topic)"/ or *neoplasm/ or *neoplasms/ or exp practice guideline/ or exp practice guidelines as topic/ or *scoliosis/ or exp "systematic review"/ or (autobiography or biography or case reports or comment or conference or consensus development conference or consensus development conference, NIH or editorial or guideline or lectures or letter or meta-analysis or news or note or practice guideline or proceeding or review or video-audio media or webcasts).pt. or (abscess* or animal* or cancer* or carcinoma or case report* or case stud* or conference* or congress or consensus or cyst* or deform* or fracture* or guideline* or hematoma* or meta analysis or meta-analysis or metasta* or neoplas* or oncolog* or proceeding* or sarcoma or scoliosis or systematic review or trauma* or tumor* or tumour*).ti. or (bovine or cadaver* or canine or mouse or mice or pig or pigs or porcine or rat or rats or rodent*).ti,ab.)
29	add limits	limit 28 to english language
30	add limits	limit 29 to human
31	add limits	limit 30 to humans
32	add limits	limit 31 to yr="1995-Current"
33	add limits	remove duplicates from 32

Appendix B. Excluded Studies

Studies excluded at the full-length article level for Key Questions 1–9

Not Relevant Study Design

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Not Relevant Intervention

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Appendix C. Data Tables

Table 15. Descriptions of and indications for FDA-cleared or -approved devices

Fusion Device(s)	Manufacturer	Device Description	FDA-cleared or -approved Indications
Acromed Pedicle Screw	DePuy Synthes, Raynham, MA	The AcroMed Pedicle Screw is composed of two sections: a long cancellous section with an integral fixed lower nut, and a machine threaded section topped with an hexagonal drive head. The integral nut serves two purposes: it creates a stronger bolt connection between the screw and plate and it eliminates the "claw hammer" effect associated with other screw designs. The upper surface of the integral nut is a transverse flat smooth surface to provide maximum contact area with the underside of the VSP spine plate.	The AcroMed 4.75 mm Pedicle Screw is designed to be utilized with the VSP Spinal Fixation System. The VSP Spinal Fixation System is intended for use in grade 3 or 4 spondylolisthesis at L5-S1, utilizing autologous bone graft, having the device fixed or attached to the lumbar or sacral spine and intended to be removed after solid fusion is attained. Levels of attachment for this indication range from L3 to the sacrum.[97]
BRANTIGEN I/F CAGE® used with VSP® Spine Plates and Pedicle Screws*	DePuy Synthes, Raynham, MA	The Lumbar I/F Cage with VSP Spine System is composed of two components. The Lumbar I/F Cage component is a spinal interbody fusion device. The VSP Spine System component is a posterior pedicle screw fixation spinal system.	For an open posterior approach with autogenous bone graft in patients with degenerative disc disease (DDD) at one or two spinal levels from L2-S1 whose condition requires the use of interbody fusion combined with posterolateral fusion (360° fusion) and posterior pedicle screw fixation. These patients may have had a previous non-fusion spinal surgery at the involved spinal level(s).[98]
Cotrel-Dubousset Horizon Spinal System	Medtronic Sofamor Danke, Memphis, TN	The CD HORIZON® Spinal System consists of a variety of rods, hooks, screws, CROSSLINK® plates, staples, and other connecting components used to build a spinal construct. Instrumentation is also available to facilitate implantation of the device components. The CD HORIZONO Spinal System is intended to help provide immobilization and stabilization of spinal segments as an adjunct to fusion of the thoracic, lumbar, and/or sacral spine. The CD HORIZON ®Spinal System implant components can be rigidly locked into a variety of configurations, with each construct being tailor-made for the individual case. If necessary, the CD HORIZON® Spinal System can be connected to the VERTEXTM Reconstruction System through a rod connector.[99]	The CD HORIZON® Spinal System is intended for posterior, non-cervical fixation for the following indications: degenerative disc disease (defined as back pain of discogenic origin with degeneration of the disc confirmed by history and radiographic studies); spondylolisthesis; trauma (i.e., fracture or dislocation); spinal stenosis; curvatures (i.e., scoliosis, kyphosis and/or lordosis); tumor; pseudarthrosis; and/or failed previous fusion.[99]
Infuse Bone Graft/LT-CAGE™ Lumbar Tapered	Medtronic Sofamor Danke, Memphis TN	The InFUSE™ Bone Graft/LT-CAGE™ Lumbar Tapered Fusion Device consists of two	For spinal fusion procedures in skeletally mature patients with degenerative disc disease (DDD)

Fusion Device(s)	Manufacturer	Device Description	FDA-cleared or -approved Indications
Fusion Device		components containing three parts– a tapered metallic spinal fusion cage, a recombinant human bone morphogenetic protein and a carrier/scaffold for the bone morphogenetic protein and resulting bone. The InFUSE™ Bone Graft component is inserted into the LT-CAGE™ Lumbar Tapered Fusion Device component to form the complete InFUSE™ Bone Graft/LT-CAGE™ Lumbar Tapered Fusion Device. These components must be used as a system. The InFUSE™ Bone Graft component must not be used without the LT-CAGE™ Lumbar Tapered Fusion Device component.	at one level from L4-S1. DDD is defined as discogenic back pain with degeneration of the disc confirmed by patient history and radiographic studies. These DDD patients may also have up to Grade I spondylolisthesis at the involved level. Patients receiving the InFUSE™ Bone Graft/ LT-CAGE™ Lumbar Tapered Fusion Device should have had at least 6 months of nonoperative treatment prior to treatment with the InFUSE™ Bone Graft/LT-CAGE™ device. The InFUSE™ Bone Graft/ LTCAGE ™ Lumbar Tapered Fusion Device is to be implanted via an anterior open or an anterior laparoscopic approach.[100]
INFUSE/MASTERGRAFT	Medtronic Sofamor Danke, Memphis TN	The INFUSE/MASTERGRAFT™ Posterolateral Revision Device consists of a 2-part bone graft replacement (INFUSE® Bone Graft + MASTERGRAFT® Granules) used as part of a 3 component system (INFUSE® Bone Graft + MASTERGRAFT® Granules + supplemental posterior fixation system, e.g., the CD HORIZON® Spinal System). These components must be used as a system for the prescribed indication described below. The bone morphogenetic protein solution component must not be used without the carrier/scaffold component or with a carrier/scaffold component different from the one described in this document. The INFUSE® Bone Graft component must be used with the MASTERGRAFT® Granules and must not be used with bulking agents different from the one described in this document.	For the repair of symptomatic, posterolateral lumbar spine pseudoarthrosis. The device is intended to address a small subset of patients for whom autologous bone and/or bone marrow harvest are not feasible or are not expected to promote fusion. These patients are diabetics and smokers. This device is indicated to treat two or more levels of the lumbar spine.[101]
Moss-Miami	DePuy Synthes, Raynham, MA	The Moss Miami System is available in either Stainless Steel or Titanium. The following components are available in Stainless Stell: longitudinal rods, monoaxial screws, polyaxial screws, reduction screws, hooks, reduction hooks, transverse connectors, axial connectors, staple washers and sacral extenders. The following components are available in Titanium: longitudinal rods, monoaxial screws, polyaxial screws, hooks, transverse connectors, axial connectors, washers, staple washers, and sacral extenders.[102]	When used as a pedicle screw fixation system of the noncervical spine in skeletally mature patients, the Moss Miami Spinal System is indicated for degenerative spondylolisthesis with objective evidence of neurologic impairment, fracture, dislocation, scoliosis, kyphosis, spinal tumor, and failed previous fusion (pseudoarthrosis). The Moss Miami Spinal System is also indicated for pedicle screw fixation in skeletally mature patients with severe spondylolisthesis (Grades 3 and 4) at the L5-S1 vertebral joint, having fusions

Fusion Device(s)	Manufacturer	Device Description	FDA-cleared or -approved Indications
			with autogenous bone graft, with the device fixed or attached to the lumbar and sacral spine (levels of pedicle screw fixation are L3-S1), and for whom the device system is intended to be removed after solid fusion is attained.[102]
PRODISC®-L Total Disc Replacement**	Synthes Spine, West Chester, PA	The PRODISC®-L Total Disc Replacement is a weight-bearing modular implant consisting of two endplates and one polyethylene inlay. The PRODISC®-L endplates are manufactured from cobalt-chromium alloy conforming to ISO 5832-12 (1996) "Implants for surgery – Metallic materials – Part 12: Wrought cobalt-chromium-molybdenum alloy" and are available in two sizes (medium and large). The superior endplates are also available in two lordotic angles (6° and 11°). The surfaces of both inferior and superior endplates are plasma sprayed with commercially pure (CP) titanium conforming to ISO/DIS 5832-2 (1999) "Implants for surgery – Metallic materials– Part 2: Unalloyed titanium." Fixation of the PRODISC®-L to the vertebral bodies is intended to be achieved through bony ingrowth, with initial stabilization by a large central keel and two small spikes on the surface of the two endplates. The inlays are manufactured from ultra-high molecular weight polyethylene (UHMWPE), and are available in three thicknesses (10, 12, and 14mm) with anterior-posterior and lateral sizing consistent with the endplate sizing. The inlay snap-locks into the inferior endplate and provides the inferior convex bearing surface that articulates with the concave bearing surface of the superior endplate. The range of motion allowed by the PRODISC®-L is 13° of flexion, 7° of extension, ±10° of lateral bending, and ±3° of axial rotation, as measured through *in vitro* testing.[103]	The PRODISC®-L Total Disc Replacement is indicated for spinal arthroplasty in skeletally mature patients with degenerative disc disease (DDD) at one level from L3-S1. DDD is defined as discogenic back pain with degeneration of the disc confirmed by patient history and radiographic studies. These DDD patients should have no more than Grade 1 spondylolisthesis at the involved level. Patients receiving the PRODISC®-L Total Disc Replacement should have failed at least 6 months of conservative treatment prior to implantation of the PRODISC®-L Total Disc Replacement.[103]
Pro-Osteon® 500R	Interpore Cross International, Irvine, CA	An osteoconductive porous implant similar in structure to human cancellous bone.[104]	Only for bony voids or gaps that are not intrinsic to the stability of the bony structure. Pro-Osteon® 500R is indicated to be gently packed into bony voids or gaps of the skeletal system (i.e., the extremities, spine and pelvis). These defects may be surgically created osseous

Fusion Device(s)	Manufacturer	Device Description	FDA-cleared or -approved Indications
			defects or osseous defects created from traumatic injury to the bone. The product provides a bone graft substitute that resorbs and is replaced with bone during the healing process.[104]
Variable Screw Placement (VSP) with pedicle screws and plate	DePuy Synthes, Raynham, MA	Unavailable due to 8/21/1995 decision date (K951657). See brief description above under BRANTIGEN I/F CAGE®.	Unavailable due to 8/21/1995 decision date (K951657)[25]
Xia Spinal System	Stryker Spine, Allendale, NJ	The Xia Spinal System consists of Monoaxial and Polyaxial Screws, Hooks, Blockers, Rods, and Connectors.[105]	For use in the noncervical spine. When used as a pedicle screw fixation system, the Xia Spinal System is intended for patients: (a) having severe spondylolisthesis (Grades 3 and 4) at the fifth lumbar – first sacral (L5-S1) vertebral joint; (b) who are receiving fusions using autogenous bone graft only; (c) who are having the device fixed or attached to the lumbar and sacral spine; and (d) who are having the device removed after the development of a solid fusion mass. When used as a pedicle screw fixation system, the Xia Spinal System is also intended to provide immobilization and stabilization of spinal segments in skeletally mature patients as an adjunct to fusion in the treatment of the following acute and chronic instabilities or deformities of the thoracic, lumbar, and sacral spine: degenerative spondylolisthesis with objective evidence of neurologic impairment, fracture, dislocation, scoliosis, kyphosis, spinal tumor, and failed previous fusion (pseudoarthrosis). When used as an anterior screw fixation system or a posterior hook and sacral/iliac screw fixation system, the Xia Spinal System is indicated for patients with degenerative disc disease.[105]

* Approved as Lumbar I/F Cage with VSP® Spine System
** Non-fusion

Table 16. Minimally clinically important differences (MCID) reported in literature (all pre-post differences)

Study	Domain	Test	Version	Population	MCID
Parker et al. 2012[106]	Function	Oswestry Disability Index (ODI)	Not reported	Patients undergoing decompression and fusion for recurrent lumbar stenosis	8.2
Hagg et al. 2003[107]				Severe chronic low back pain patients undergoing fusion	10
Copay et al. 2008[76]				Lumbar spine surgical patients, mostly fusion	12.8
Parker et al. 2011[108]				Patients undergoing TLIF for degenerative spondylolisthesis	14.9
Carragee and Cheng 2010[72]			Fairbank 1995	Patients undergoing spinal fusion surgery, DDD or spondylolisthesis	20
Copay et al. 2008[76]	Pain	Back	11-point	Lumbar spine surgical patients, mostly fusion	1.2
Hagg et al. 2003[107]		VAS back pain	101-point	Severe chronic low back pain patients undergoing fusion	18
Parker et al. 2011[108]		VAS back pain	11-point	Patients undergoing TLIF for degenerative spondylolisthesis	2.1
Parker et al. 2012[106]		VAS back pain	11-point	Patients undergoing decompression and fusion for recurrent lumbar stenosis	2.2
Copay et al. 2008[76]		Leg	11-point	Lumbar spine surgical patients, mostly fusion	1.6
Parker et al. 2011[108]		VAS leg pain	11-point	Patients undergoing TLIF for degenerative spondylolisthesis	2.8
Parker et al. 2012[106]		VAS leg pain	11-point	Patients undergoing decompression and fusion for recurrent lumbar stenosis	3.9
Carragee and Cheng 2010[72]		VAS back or leg pain	11-point	Patients undergoing spinal fusion surgery, DDD or spondylolisthesis	Reduction to 3/10 or less
Copay et al. 2008[76]	Quality of Life	SF-36 Physical Function		Lumbar spine surgical patients, mostly fusion	4.9
Spratt 2009[109]				Lumbar fusion candidates with intervertebral disc herniation	30% reduction from baseline when baseline score >50

Key Question 1: For adults with pain associated with degenerated disc(s) of the lumbar spine, does spinal fusion performed alone or in conjunction with additional surgery differ from continued noninvasive treatment in (a) Patient-centered outcomes such as function, quality of life, or pain? (b) Adverse events?

Noninstrumented Fusion Versus Exercise

Study, Patient, and Intervention Descriptions

Table 17. Key Question 1: study design

Study	Study Design	Enrollment Years	Location	Setting	Funding
Ohtori et al. 201112	Randomized controlled trial (RCT)	Not reported	Japan	Author affiliations University orthopaedic surgery department	None, and no financial relationships between authors and any manufacturer This study did not assess a device or drug
Brox et al. 200610	RCT	1997–2000	Norway	Author affiliations University hospitals	Grants from Norwegian Back Association, and the Foundation for Health and Rehabilitation
Brox et al. 20039	RCT	1997–2000	Norway	Author affiliations National Hospital and University	Federal and foundation funds No financial relationships between authors and a commercial party relevant to the manuscript This study did not assess a device or drug
Fritzell et al. 200111a	RCT	1992–1998	Sweden	Author affiliations University	Financial support from Acromed Corporation (Raynham, MA) and Ossano Scandinavia AB (Stockholm, Sweden)

[a] Two levels treated in 41 percent of surgical group

Table 18. Key Question 1: patient inclusion criteria

Study	Diagnosis Included	Duration of Symptoms	Diagnostic Criteria	Conditions Excluded	Previous Treatment Requirements	Age Requirements	Additional Inclusion Criteria	Additional Exclusion Criteria
Ohtori et al. 2011[12]	Disc degeneration with discogenic low back pain	At least 2 years	MRI, positive discography, pain relief by discoblock	Severe spondylosis At least two discs degenerated Previous spine surgery	None reported	None reported	Low back pain No radicular pain	Low back pain after traffic accidents Workers compensation recipients
Brox et al. 2006[10]	Degeneration at L4/L5 (spondylosis) with previous surgery for disc herniation	At least 1 year after previous surgery	Degeneration at L4/L5 or L5/S1 on plain radiographs	Widespread myofascial pain Spinal stenosis with reduced walking distance and neurological signs Recurrent disc herniation or lateral recess stenosis with clinical signs of radiculopathy Inflammatory disease Previous spine fracture Previous lumbar fusion Ongoing somatic or psychiatric disease that prevents study treatment Registered medical abuse	Previous surgery for disc herniation No previous fusion	25 to 60 years old	Score ≥30/100 on Oswestry Disability Index Chronic low back pain	General disc degeneration on plain x-ray Patient reluctant to accept one or both study treatments

Study	Diagnosis Included	Duration of Symptoms	Diagnostic Criteria	Conditions Excluded	Previous Treatment Requirements	Age Requirements	Additional Inclusion Criteria	Additional Exclusion Criteria
Brox et al. 2003[9]	Disc degeneration with low back pain	At least 1 year	Degeneration at L4/L5 or L5/S1 on plain radiographs	Widespread myofascial pain Spinal stenosis with reduced walking distance and neurological signs Recurrent disc herniation or lateral recess stenosis with clinical signs of radiculopathy Inflammatory disease Previous spine fracture Previous spine surgery Pelvic pain Ongoing somatic or psychiatric disease that prevents study treatment Registered medical abuse	None reported	Age 25 to 60 years	Score ≥30/100 on Oswestry Disability Index Chronic low back pain	General disc degeneration on radiographs Patient reluctant to accept one or both study treatments
Fritzell et al. 2001[11]	Degenerated lumbar disc with chronic low back pain	At least 2 years	Surgeon interpretation that pain from L4/L5 and/or L5/S1 based on patient history, physical exam, and radiographic signs (plain radiographs and/or CT and/or MRI) Disc herniation permissible in absence of clinical signs of nerve root compression	Signs of nerve root compression Obvious ongoing psychiatric illness Previous spine surgery, with exception of successful disc removal >2 years prior Radiologic findings of other specific conditions such as spondylolisthesis, spinal stenosis fractures, infection, inflammation, neoplasm Obvious painful and disabling hip joint arthritis	Previous nonsurgical treatments unsuccessful	25–65 years	Back pain greater than leg pain Sick leave or equivalent >1 year Severe chronic low back pain >7/10 score on Function-Working Disability Score, indicating at least moderate pain and work-related disability	None reported

Table 19. Key Question 1: patient characteristics: demographic and occupational history

Study	Number Screened for Inclusion	Number Enrolled	Age	Women	Race or Ethnicity	Occupational Status	Workers Compensation	Pending Litigation
Ohtori et al. 2011[12]	98	41 (42%)	Mean 34 years (35 years fusion, 33 years nonsurgical)	43% (67% fusion, 50% conservative)	Not reported (Study conducted in Japan)	Not reported	0%	0%
Brox et al. 2006[10]	113	60 (53%)	Mean 43 (range 35–50) years (42 years fusion, 43 years nonsurgical)	48% (62% fusion, 35% fusion)	Not reported (Study conducted in Norway)	Working 3/41 (7%) eligible (e.g., not retired, not student)	Not reported	Not reported
Brox et al. 2003[9]	121	64 (53%)	Mean 43 years (44 years fusion, 42 years nonsurgical)	61% (57% fusion, 56% nonsurgical)	Not reported (Study conducted in Norway)	Working 23% (24% fusion, 22% nonsurgical) Sick leave 28% (30% fusion, 28% nonsurgical) Rehabilitation 34% (30% fusion, 41% nonsurgical) Disability pension 11% (11% both groups) Homemaker 3% (5% fusion, 0 nonsurgical)	Disability pension 11% (11% both groups)	None reported
Fritzell et al. 2001[11]	Not reported	310 randomized, 294 (95%) included	Mean 43 years (43 fusion, 44 nonsurgical)	50% (50% fusion, 51% nonsurgical)	Not reported (Study conducted in Sweden)	Working 21% (21% fusion, 24% nonsurgical) Employed 72% (74% fusion, 67% nonsurgical) Changed work because of back 31% (29% fusion, 25% nonsurgical) On sick leave because of back 58% (59% fusion, 54% nonsurgical)	Disability pension 21% (20% fusion, 22% nonsurgical)	Litigation or compensation 61% (60% fusion, 65% nonsurgical)

Table 20. Key Question 1: patient characteristics: health history

Study	Surgical Indication	Number of Levels Affected	Duration of Symptoms	Primary or Recurrent	Previous Nonsurgical Treatment(s)	Duration of Nonsurgical Treatments	Previous Surgery	Percent With Radicular Pain	Comorbid Diagnoses
Ohtori et al. 201112	Disc degeneration with discogenic low back pain	One	Mean 7 (Range 2–14 years)	Appears primary	Not reported	Not reported	0%	0%	None reported
Brox et al. 200610	Previous surgery for disc herniation and degeneration at L4/L5 or L5/S1 and chronic low back pain	One	Median (range) fusion 100 (39–150), nonsurgical 93 (36–146)	Recurrent	Not reported	Not reported	100% for disc herniation None had previous fusion	82% (of 56)	Any 40% (41% fusion, 39% conservative) Smoking 67% (72% fusion, 58% conservative)
Brox et al. 20039	Degeneration at L4/L5 or L5/S1 and chronic low back pain	One or two	Not reported. Inclusion criterion at least 1 year.	Appears primary	Not reported	Not reported	0%	Not reported	Smoking 42% (41% fusion, 44% nonsurgical)
Fritzell et al. 200111	Severe chronic low back pain thought to be due to L4/L5 or L5/S1 disc	One or two	Mean 7.8 (range 2–34) years surgical group, 8.5 (2-40) years nonsurgical group	Appears primary	Not reported	Not reported	19% earlier successful removal of herniated disc	Not reported	Any comorbidity 35% (39% fusion, 24% nonsurgical, p=0.02 as reported in the study) Smoking 43% (41% fusion, 49% conservative)

Table 21. Key Question 1: treatment characteristics: fusion

Study	Number of Patients	Level Treated	Fusion Strategy	Surgical Approach	Device	Adjunctive Surgery	Additional Information
Ohtori et al. 2011[12]	15	L4/L5 or L5/S1	Anterior discectomy and anterior interbody fusion using iliac bone	Anterior	No instrumentation used Graft: Iliac crest bone graft	Anterior discectomy Bilateral end plates cut at 2 mm thickness	In 6 patients anterior vessels prevented ALIF and PLF without decompression was performed instead using pedicle screws and iliac crest bone graft. (Results not included in this report because fewer than 10 patients were treated with PLF.)
Brox et al. 2006[10]	29 allocated, 23 (79%) treated	L4/L5 or L5/S1	Posterolateral fusion with transpedicular screws	Posterolateral	Transpedicular screws not specified; not standardized Graft: autologous	None reported	Physical therapists consulted regarding activities for 3 months post-surgery
Brox et al. 2003[9]	37 allocated, 33 (89%) treated	L4/L5 and/or L5/S1	Posterolateral fusion with transpedicular screws of L4/L5 and/or L5/S1 segment with autologous bone	Posterolateral	Transpedicular screws not specified Graft: Iliac crest autograft	None reported	Patients may have had physical therapy following surgery outside the purview of the study.
Fritzell et al. 2001[11]	222	L4/L5 or L5/S1, or both. 41% had 2 levels operated on	Posterolateral fusion with (n=74) or without (n=73) Variable Screw Placement with pedicle screws and plates (Raynham, MA) Circumferential fusion (n=75) including ALIF or PLIF to place bone graft	Posterolateral (66%) Circumferential (34%)	For 33%, with posterolateral fusion: Variable Screw Placement (VSP) with pedicle screws and plates (DePuy Acromed, Raynham, MA) For All: Graft: Iliac crest autograft	None reported	No decompression

Table 22. Key Question 1: treatment characteristics: noninvasive intervention

Study	Number of Patients	Treatment Type	Generic Name	Proprietary Name	Treatment Administration	Additional Information
Ohtori et al. 2011[12]	20	Exercise	Walking and stretching	Not applicable	Walking 30 minutes twice per day Stretching 15 minutes twice per day	Walking instructions given by physician for patient to do independently Stretching performed in hospital by physical therapist Treatments were administered for over 2 years. Adherence monitored monthly by physician; non-adhering patients excluded from study
Brox et al. 2006[10]	31 allocated, 29 (94%) treated	Exercise and cognitive interventions	Physical therapy Cognitive behavioral therapy	Not applicable	Lecture to patients by physical medicine specialist educated patients about anatomy and physiology of the pain and that "they could not do any harm to the disc (back) by engaging in the ordinary activities of their life" and encouraged to be active, including activities previously discouraged (like vacuuming). Exercises were prescribed for endurance and coordination, including co-contraction of deep abdominal muscles with lumbar multifidus. The main goal was to improve confidence. Three daily workouts included: aerobics, outdoor activities, water exercise, individual exercises. Individual consultations, group lesions, discussions. Met former participants. Follow up at 3 and 6 months	Average duration 25 hours per week for 3 weeks Most patients stayed in patient hotel. Training diary offered, but dropped from program due to low compliance.

Study	Number of Patients	Treatment Type	Generic Name	Proprietary Name	Treatment Administration	Additional Information
Brox et al. 2003[9]	27 allocated, 25 (93%) treated	Exercise and cognitive interventions	Physical therapy Cognitive behavioral therapy	Not applicable	Lecture to patients by physical medicine specialist educated patients about anatomy and physiology of the pain and that "they could not do any harm to the disc (back) by engaging in the ordinary activities of their life" and encouraged to be active. Exercises were prescribed for endurance and coordination, including co-contraction of deep abdominal muscles with lumbar multifidus. Exercise groups of 4–7 patients. Workouts included: land and water aerobics, outdoor activities, individual exercises. Home program and diary offered Followup at 3 and 6 months	Average duration 25 hours per week, in outpatient clinic 1 week supervised 2 weeks at home Another treatment period of 2 weeks Intensity gradually increased last 2 weeks
Fritzell et al. 2001[11]	72	Physical therapy primarily, with one or more treatment (acupuncture, injection) cognitive functioning training, coping strategies, information and education	Physical therapy with complementary nonsurgical interventions	Not applicable	Not described	None reported

Data and Results

Table 23. Key Question 1: pain at baseline and 1 year

Study	Scale	Treatment Group	Baseline N =	Baseline Mean	Baseline SD	1 Year N =	1 Year Mean	1 Year SD	p-Value	Mean Difference
Ohtori et al. 2011[12]	Back pain visual analog scale (VAS) 0–10	Anterior interbody fusion	15	7.4	1.5	15 (100%)	2.5	0.5	p<0.001[a]	3.10 (95% CI: 2.36 to 3.84)
		Exercise	20	7.7	2.0	20 (100%)	5.6	1.4		
Brox et al. 2006[10]	Back pain VAS 0–100	Posterolateral fusion	28 (1 not reported on)	Median 64.6	IQR 15.4	28 (100%)	Median 50.7	IQR 27.3	p=0.42[b]	Not calculable from reported information
		Exercise and cognitive interventions	29 (2 not reported on)	Median 64.7	IQR 11.1	29 (100%)	Median 49.5	IQR 20.0		
Brox et al.	Back pain	Posterolateral fusion	35	62.1	14.5	35 (100%)	39.4	25.5	p=0.14[b]	9.30 (95% CI: -3.32

Study	Scale	Treatment Group	Baseline N =	Baseline Mean	Baseline SD	1 Year N =	1 Year Mean	1 Year SD	p-Value	Mean Difference
2003[9]	VAS 0–100	Exercise and cognitive interventions	26	64.1	13.7	26 (100%)	48.7	24.0		to 21.92)
Brox et al. 2006[10]	Leg pain VAS 0–100	Posterolateral fusion	28 (1 not reported on)	Median 52.7	IQR 20.2	28 (100%)	Median 45.0	IQR 29.8	p=0.68[b]	Not calculable from reported information
		Exercise and cognitive interventions	29 (2 not reported on)	Median 55.3	IQR 19.4	29 (100%)	Median 47.7	IQR 24.1		
Brox et al. 2003[9]	Leg pain VAS 0–100	Posterolateral fusion	35	43.5	27.7	35 (100%)	26.6	28.1	p=0.002[b]	8.90 (95% CI: -5.91 to 23.71)
		Exercise and cognitive interventions	26	34.0	19.3	26 (100%)	35.5	30.6		
Brox et al. 2006[10]	Medication use, daily defined doses	Posterolateral fusion	28 (1 not reported on)	1.2	1.4	28 (100%)	1.6	2.0	p=0.31[b]	0.70 (95% CI: -0.15 to 1.55)
		Exercise and cognitive interventions	29 (2 not reported on)	0.9	1.2	29 (100%)	0.9	1.2		
Brox et al. 2003[9]	Medication use, daily defined doses	Posterolateral fusion	35	0.2	Range 0–3.2	35 (100%)	0.1	Range 0–12.8	p=0.44[b]	Not calculable based on reported information
		Exercise and cognitive interventions	26	0.3	Range 0–2.1	26 (100%)	0.1	Range 0–1.7		

[a] Comparison of 1 year data, calculated as standardized mean difference by the EPC.
[b] As reported in study, mean difference between groups from baseline to 1 year. Brox et al. 2006[10] adjusted for baseline score and gender.

CI = Confidence interval; IQR = interquartile range; SD = standard deviation

Table 24. Key Question 1: pain at 2 years

Study	Scale	Treatment Group	Baseline N =	Baseline Mean	Baseline SD	2 Years N =	2 Years Mean	2 Years SD	p-Value	Mean Difference
Ohtori et al. 2011[12]	Visual analog scale (VAS) 0–10	Anterior interbody fusion	15	7.4	1.5	15 (100%)	1.3	0.4	p<0.001[a]	3.40 (95% CI: 2.62 to 4.18)
		Exercise	20	7.7	2.0	20 (100%)	4.7	1.5		
Fritzell et al. 2001[11]	Back pain VAS 0-100	Posterolateral or circumferential fusion	201 (222 randomized)	64.2	14.3	201 (100%)	43.2	25.2	p=0.0002[b]	15.10 (95% CI: 8.35 to 21.85)
		Physical therapy	63 (72 randomized)	62.6	14.3	63 (100%)	58.3	18.8		
Fritzell et al. 2001[11]	Leg pain VAS 0-100	Posterolateral or circumferential fusion	201 (222 randomized)	35.3	25.4	201 (100%)	29.0	27.0	p=0.005[b]	13.60 (95% CI: 6.10 to 21.10)
		Physical therapy	63 (72 randomized)	35.6	25.2	63 (100%)	42.6	24.8		

[a] Comparison of 2 year data, calculated as standardized mean difference by the EPC.
[b] As reported in the study, difference of baseline to 2 year data between groups. Data from 18 group changers and 3 dropouts in the fusion group and 7 group changers and 2 dropouts in the nonsurgical group are not reflected in the data but the group changers are reflected in the p-value as reported in the study.

CI = Confidence interval; SD = standard deviation

Table 25. Key Question 1: function at 1 year

Study	Scale	Treatment Group	Baseline N =	Baseline Mean	Baseline SD	1 Year N =	1 Year Mean	1 Year SD	p-Value	Mean Difference
Ohtori et al. 2011[12]	Oswestry Disability Index	Anterior interbody fusion	15	62	10	15 (100%)	25.6	6.8	p<0.001[a]	27.60 (95% CI: 21.94 to 33.26)
		Exercise	20	64	10	20 (100%)	53.2	9.5		
Brox et al. 2006[10]	Oswestry Disability Index	Posterolateral fusion	28 (1 not reported on)	47.0	9.4	28 (100%)	38.1	20.1	p=0.43[b]	-5.80 (95% CI: -15.98 to 4.38)
		Exercise and cognitive interventions	29 (2 not reported on)	45.1	9.1	29 (100%)	32.3	19.1		
Brox et al. 2003[9]	Oswestry Disability Index	Posterolateral fusion	35	42.0	11.0	35 (100%)	26.4	16.4	p=0.33[b]	3.30 (95% CI: -5.75 to 12.35)
		Exercise and cognitive interventions	26	43.0	13.0	26 (100%)	29.7	19.6		
Brox et al. 2006[10]	General Function Score	Posterolateral fusion	28	Median 40.3	IQR 20.1	28 (100%)	Median 30.8	IQR 21.6	p=0.09[b]	Not calculable based upon reported information
		Exercise and cognitive interventions	29	Median 39.1	IQR 17.1	29 (100%)	Median 23.8	IQR 21.0		
Brox et al. 2003[9]	General Function Score	Posterolateral fusion	35	35.9	18.6	35 (100%)	18.3	17.3	p=0.50[b]	4.30 (95% CI: -4.83 to 13.43)
		Exercise and cognitive interventions	26	44.6	13.7	26 (100%)	22.6	18.9		
Ohtori et al. 2011[12]	Japanese Orthopaedic Association Score	Anterior interbody fusion	15	1.1	0.2	15 (100%)	2	0.3	p<0.001[a]	1.10 (95% CI: 0.93 to 1.27)
		Exercise	20	0.7	0.2	20 (100%)	0.9	0.2		
Brox et al. 2006[10]	Return to work	Posterolateral fusion	28	1/20 eligible working (5%)		28 (100%)	2/20 (10%) working		p=0.337 at baseline and 0.049 at followup	Odds ratio 0.18 (95% CI: 0.03 to 0.99)
		Exercise and cognitive interventions	29	3/21 eligible working (14%)		29 (100%)	8/21 (38%) working			
Brox et al. 20039	Return to work	Posterolateral fusion	35	9 (24%) working		35 (100%)	8 (22%) working		p=0.40b	Odds ratio 0.56 (95% CI: 0.18 to 1.73)
		Exercise and cognitive interventions	26	6 (22%) working		26 (100%)	9 (33%) working			

[a] Comparison of 2-year data, calculated as standardized mean difference by the EPC.

[b] As reported in the study, difference of baseline to 2 year data between groups. Brox et al. 2006[10] adjusted for baseline score and gender.

CI = Confidence interval; IQR = interquartile range; SD = standard deviation

Table 26. Key Question 1: function at 2 years

Study	Scale	Treatment Group	Baseline N =	Baseline Mean	Baseline SD	2 Years N =	2 Years Mean	2 Years SD	p-Value	Mean Difference
Ohtori et al. 2011[12]	Oswestry Disability Index	Anterior interbody fusion	15	62	10	15 (100%)	10.3	5.2	p<0.001[a]	29.7 (95% CI: 24.9 to 34.49)
		Exercise	20	64	10	20 (100%)	40	8.3		
Fritzell et al. 2001[11]	Oswestry Disability Index	Posterolateral or circumferential fusion	201	47.3	11.4	201 (100%)	35.7	18.0	0.015[b]	9.90 (95% CI: 4.93 to 14.87)
		Physical therapy	63	48.4	11.9	63 (100%)	45.6	16.1		
Ohtori et al. 2011[12]	Japanese Orthopaedic Association Score	Anterior interbody fusion	15	1.1	0.2	15 (100%)	2.5	0.3	p<0.001[a]	1.30 (95% CI: 1.10 to 1.50)
		Exercise	20	0.7	0.2	20 (100%)	1.2	0.3		
Fritzell et al. 2001[11]	General Function Score	Posterolateral or circumferential fusion	201	49.1	15.9	201 (100%)	34.1	22.4	0.005[b]	11.40 (95% CI: 5.20 to 17.60)
		Physical therapy	63	47.6	16.3	63 (100%)	45.5	20.3		
Fritzell et al. 2001[11]	Million Score	Posterolateral or circumferential fusion	201	63.7	11.3	201 (100%)	45.6	23.1	0.004[b]	0.68 (95% CI: 0.39 to 0.97)
		Physical therapy	63	65.5	11.5	63 (100%)	60.4	17.2		
Fritzell et al. 2001[11]	Net Back to Work	Posterolateral or circumferential fusion	-	-	-	57/158	36%		p=0.002, as reported in publica-tion	Odds Ratio 3.8 (95% CI: 1.5 to 9.4)
		Physical therapy	-	-	-	6/46	13%			

[a] Comparison of 2 year data, calculated as standardized mean difference by the EPC.

[b] As reported in the study, difference of baseline to 2 year data between groups. Data from 18 group changers and 3 dropouts in the fusion group and 7 group changers and 2 dropouts in the nonsurgical group are not reflected in the data but the group changers are reflected in the p-value as reported in the study.

SD = Standard deviation

Table 27. Key Question 1: adverse events and reoperations

Study	Treatment Group	Duration of Followup	Adverse Event	Number (%) Affected
Brox et al. 2003[9]	Anterior interbody fusion	Peri-operative	Wound infection	2 (6%)
Brox et al. 2003[9]	Anterior interbody fusion	Peri-operative	Bleedings	2 (6%)
Brox et al. 2003[9]	Anterior interbody fusion	Peri-operative	Dural Tear	1 (3%)
Brox et al. 2003[9]	Anterior interbody fusion	Peri-operative	Venous Thrombosis	1 (3%)
Brox et al. 2006[10]	Posterolateral fusion	Early	Wound infection	2 (9%)
Fritzell et al. 2001[11]	Pedicle screw group	Early (<2 weeks)	New sensation of nerve root pain, no reoperation, major complication	6 (3%)
Fritzell et al. 2001[11]	Posterolateral or circumferential fusion	Early (<2 weeks)	Nerve root hit by pedicle screw, reoperation, major complication	3 (1.5%)
Fritzell et al. 2001[11]	Posterolateral or circumferential fusion	Early (<2 weeks)	Deep wound infections, major complication	3 (1.5%) 2 implant-related
Fritzell et al. 2001[11]	Anterolateral fusion	Early (<2 weeks)	Major bleeding during surgery	2 (1%)
Fritzell et al. 2001[11]	Posterolateral or circumferential fusion	Early (<2 weeks)	Thrombosis and pulmonary embolus	1 (0.5%)
Fritzell et al. 2001[11]	Posterolateral or circumferential fusion	Early (<2 weeks)	Thrombosis	1 (0.5%)
Fritzell et al. 2001[11]	Posterolateral or circumferential fusion	Early (<2 weeks)	Aspiration-sepsis-ARDS	1 (0.5%)
Fritzell et al. 2001[11]	Posterolateral or circumferential fusion	Early (<2 weeks)	Pulmonary edema	1 (0.5%)
Fritzell et al. 2001[11]	Posterolateral or circumferential fusion	Early (<2 weeks)	Heart failure and GI bleeding	1 (0.5%)
Fritzell et al. 2001[11]	Posterolateral or circumferential fusion	Early (<2 weeks)	Wrong level operated	1 (0.5%)
Fritzell et al. 2001[11]	Posterolateral or circumferential fusion	Early (<2 weeks)	Gastrointestinal bleeding, minor	3 (1.5%)
Fritzell et al. 2001[11]	Posterolateral or circumferential fusion	Early (<2 weeks)	Laterally placed screw, minor	2 (1%)
Fritzell et al. 2001[11]	Posterolateral or circumferential fusion	Early (<2 weeks)	Hematoma at graft donor site, minor	2 (1%)
Fritzell et al. 2001[11]	Posterolateral or circumferential fusion	Early (<2 weeks)	Sympathetic cord damage with symptoms, minor	2 (1%)
Fritzell et al. 2001[11]	Posterolateral or circumferential fusion	Early (<2 weeks)	Superficial wound infection, minor	2 (1%)
Fritzell et al. 2001[11]	Posterolateral or circumferential fusion	Early (<2 weeks)	Skin problems after surgery, minor	2 (1%)
Fritzell et al. 2001[11]	Posterolateral or circumferential fusion	Early (<2 weeks)	Dural tear, minor	1 (0.5%)
Fritzell et al. 2001[11]	Posterolateral or circumferential fusion	Early (<2 weeks)	Wing scapula after surgery, minor	1 (0.5%)
Fritzell et al. 2001[11]	Posterolateral or circumferential fusion	Early (<2 weeks)	Pain in arm after surgery, minor	1 (0.5%)
Fritzell et al. 2001[11]	Posterolateral or circumferential fusion	Early (<2 weeks)	Injury of the nervus cut fem lat, minor	1 (0.5%)
Fritzell et al. 2001[11]	Posterolateral or circumferential fusion	Late (>2 weeks)	Deep wound infections, surgery required	2 (1%)
Fritzell et al. 2001[11]	Posterolateral or circumferential fusion	Late (>2 weeks)	Pseudarthrosis, surgery required	2 (1%)
Fritzell et al. 2001[11]	Posterolateral or circumferential fusion	Late (>2 weeks)	Pain, autologous graft donor site, minor	9
Brox et al. 2006[10]	Posterolateral fusion	Late	Any	0%
Fritzell et al. 2001[11]	Posterolateral or circumferential fusion	Up to 2 years	Re-operation, unintended, any reason	16 (8%)

Risk-of-Bias Assessment

Table 28. Key Question 1: risk-of-bias assessment

Assessment Item	Ohtori et al. 201112	Brox et al. 200610	Brox et al. 20039	Fritzell et al. 200111
Were patients randomly assigned to treatment?	Yes	Yes	Yes	Yes
Was group allocation concealed?	No	No	No	Yes
For non-randomized trials, did the study employ other methods to enhance group comparability?	Yes	Yes	Yes	Yes
Was patient assignment independent of physician and patient preference?	Yes	Yes	Yes	Yes
Did patients in different study groups have similar levels of performance on the outcome of interest when they were assigned to groups?	Yes	Yes	Yes	Yes
Were the study groups comparable for all other important factors when they were assigned to groups?	Yes	Yes	No	
Was the comparison of interest prospectively planned?	Yes	Yes	Yes	Yes
If patients received ancillary treatment(s), was there a 5% or less difference between groups in the proportion of patients receiving each ancillary treatment?	Yes	Yes	Yes	Yes
Were the two groups treated concurrently?	Yes	Yes	Yes	Yes
Were patients blinded to the treatment they received?	No	No	No	No
Were outcome assessors blinded to which treatment patients had?	No	Yes	No	No
For questions comparing fusion, did the two groups' surgeons have similar numbers of prior operations performing the procedure they performed in the study?	—	—	—	—
Was the primary outcome measure of interest objective and was it objectively measured?	No	No	No	No
Was there a 15% or less difference in the length of followup for the two groups for the comparison time point of interest?	Yes	Yes	Yes	Yes
Did at least 85% of patients who provided baseline data provide data at the time point of interest?	Yes	Yes	Yes	Yes
Was there a 15% or less difference between groups in the percentage of patients who provided data at the time point of interest?	Yes	Yes	Yes	Yes
Risk-of-bias category	Moderate	Moderate	Moderate	Moderate

Key Question 3: For adults with pain associated with degenerative spondylolisthesis of the lumbar spine, does spinal fusion performed alone or in conjunction with additional surgery differ from continued noninvasive treatment in: (a) Perioperative outcomes such as surgery time, blood loss, or length of hospital stay? (b) Patient-centered outcomes such as function, quality of life, or pain? (c) Adverse events?

Fusion Versus Physical Therapy, Epidural Steroid Injections, Nonsteroidal Antiinflammatory Drugs and Opioids

Study, Patient, and Intervention Descriptions

Table 29. Key Question 3: study design

Study	Study Design	Enrollment Years	Location	Setting	Funding
Weinstein et al. 2007 & 200913,14	Prospective non-randomized comparative trial	2000-2005	U.S.	13 medical centers located in 11 states	A grant from the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) and the Office of Research on Women's Health; the National Institutues of Health; the National Institutes of Occupational Safety and Health and the Centers for Disease Control and Prevention; and a grant and Research Career Award from NIAMS.

Table 30. Key Question 3: patient inclusion criteria

Study	Diagnosis Included	Duration of Symptoms	Diagnostic Criteria	Conditions Excluded	Previous Treatment Requirements	Age Requirements	Additional Inclusion Criteria	Additional Exclusion Criteria
Weinstein et al. 2007 & 2009[13,14]*	Degenerative spondylolisthesis and spinal stenosis with neurologic claudication or radicular leg pain with associated neurologic signs	At least 12 weeks	Cross-sectional imaging, lateral radiographs	Spondylolysis and isthmic spondylolisthesis	Not required but listed the following: Physical therapy: 68% Epidural injections: 55% Chiropractic treatment: 25% Antiinflammatory agents: 63% Opioid analgesic agents: 30%	At least 18 years	Patients with adjacent levels of stenosis	Insufficient trial of non-surgical treatment; cauda equina syndrome or progressive neurologic deficit requiring urgent surgery; overall health that makes spine surgery too life threatening to undergo; dramatic improvement with non-surgical care; possible pregnancy; active malignancy; current fracture, infection, or significant deformity (> than 15° lumbar scoliosis) of the spine; prior lumbar spine surgery; current enrollment in another experimental spine-related protocol; or not available for follow-up or unable to complete questionnaires.

*We also extracted information from Birkmeyer et al. 2002[83] to complete the information in the table.

Table 31. Key Question 3: patient characteristics: demographic and occupational history

Study	Number Screened for Inclusion	Number Enrolled	Age (mean±SD)	Women	Race or Ethnicity	Occupational Status	Workers Compensation	Pending Litigation
Weinstein et al. 2007 & 2009[13,14]	1,164	607 (52%) 304 in randomized cohort (139 assigned to surgery and 145 assigned to nonsurgical) and 303 were in observational cohort (173 chose surgery and 130 chose nonsurgical) Due to amount of crossover, the randomized and nonrandomized cohorts were combined to create to a surgical group (368 patients) and nonsurgical (233 patients)	64.7±10.1 (fusion) 68.2±10.3 (nonsurgical)	68.5% (69% fusion, 67% nonsurgical)	Non-Hispanic 98% (98% fusion, 98% nonsurgical); white 84% (86% fusion and 82% nonsurgical); black 10% (8% fusion and 13% nonsurgical)	Not reported	34 (9%) fusion, 7 (3%) nonsurgical	Not reported

Table 32. Key Question 3: patient characteristics: health history

Study	Surgical Indication	Number of Levels Affected	Duration of Symptoms	Primary or Recurrent	Previous Nonsurgical Treatment(s)	Duration of Nonsurgical Treatments	Previous Surgery	Percent With Radicular Pain	Comorbid Diagnoses
Weinstein et al. 2007 & 2009[13,14]	Degenerative spondylolisthesis and spinal stenosis with neurologic claudication or radicular leg pain with associated neurologic signs	2-3 levels	At least 12 weeks	Primary	68% physical therapy, 55% epidural injections, 25% chiropractic treatment, 63% antiinflammatory agents, 30% opioid analgesic agents	Not reported	None	78% fusion, 77% nonsurgical	Not reported

Table 33. Key Question 3: treatment characteristics: fusion

Study	Number of Patients	Level Treated	Fusion Strategy	Surgical Approach	Device	Adjunctive Surgery	Additional Information
Weinstein et al. 2007 & 200913,14	368	L2/L3, L3/L4, L4/L5, L5/S1 The majority were treated at level L4/L5 (96.5%)	The surgical protocol consisted of standard posterior decompressive laminectomy with or without bilateral single-level fusion (iliac crest bone grafting with or without posterior pedicle-screw instrumentation).	Not reported	21% had fusion without instrumentation and 74% had fusion with instrumentation (specific instrumentation used not reported)	Not reported	Not reported

Table 34. Key Question 3: treatment characteristics: noninvasive intervention

Study	Number of Patients	Treatment Type	Generic Name	Proprietary Name	Treatment Administration	Additional Information
Weinstein et al. 2007 & 200913,14	233	The nonsurgical protocol was usual care, recommended to include at least active physical therapy, education or counseling (including instructions for home exercise), and nonsteroidal anti-inflammatory agents if tolerated.	Physical therapy, education, exercise and nonsteroidal anti-inflammatory agents	Not applicable	Not reported	Not reported

Data and Results

Table 35. Key Question 3: pain at baseline and 3 month

Study	Scale	Treatment Group	Baseline N =	Baseline Mean	Baseline SE	3 Months n =	3 Months Mean	3 Months SE	p-Value	Mean Difference
Weinstein et al. 200713	SF-36: bodily pain score	Fusion	368	29.2	16.8	385	28.1	1.1	P <0.001	17.8 (95% CI: 14.9 to 20.6)
		Nonsurgical	233	34.4	16.7	320	10.3	1.1		

[a] As reported in study, change scores and treatment effects of the combined randomized and observation al cohort according to treatment received and adjusted for baseline score, age, gender, work status, depression, osteoporosis, joint problems, duration of current symptoms, reflex deficit, and number of moderate or severe stenotic levels.

CI = Confidence interval; SE = Standard error

Table 36. Key Question 3: pain at 1 year

Study	Scale	Treatment Group	Baseline N =	Baseline Mean	Baseline SE	1 Year N =	1 Year Mean	1 Year SE	p-Value	Mean Difference
Weinstein et al. 200713	SF-36: bodily pain score	Fusion	368	29.2	16.8	286	31.5	1.2	P <0.001	18.8 (95% CI: 15.5 to 22.1)
		Nonsurgical	233	34.4	16.7	234	12.7	1.3		

[a] As reported in study, change scores and treatment effects of the combined randomized and observation al cohort according to treatment received and adjusted for baseline score, age, gender, work status, depression, osteoporosis, joint problems, duration of current symptoms, reflex deficit, and number of moderate or severe stenotic levels.

CI = Confidence interval; SE = Standard error

Table 37. Key Question 3: pain at 2 years

Study	Scale	Treatment Group	Baseline N =	Baseline Mean	Baseline SE	2 Year N =	2 Year Mean	2 Year SE	p-Value	Mean Difference
Weinstein et al. 2007[13]	SF-36: bodily pain score	Fusion	368	29.2	16.8	324	29.9	1.2	P <0.001	18.1 (95% CI: 14.5 to 21.7)
		Nonsurgical	233	34.4	16.7	187	11.7	1.5		

[a] As reported in study, change scores and treatment effects of the combined randomized and observation al cohort according to treatment received and adjusted for baseline score, age, gender, work status, depression, osteoporosis, joint problems, duration of current symptoms, reflex deficit, and number of moderate or severe stenotic levels.

CI = Confidence interval; SE = Standard error

Table 38. Key Question 3: pain at 3 years

Study	Scale	Treatment Group	Baseline N =	Baseline Mean	Baseline SE	3 Year N =	3 Year Mean	3 Year SE	p-Value	Mean Difference
Weinstein et. al. 200914	SF 36: bodily pain score	Fusion	368	29.2	16.8	326	32.4	1.3	P <0.001	17.0 (95% CI: 13.0 to 20.9)
		Nonsurgical	233	34.4	16.7	162	15.5	1.6		

[a] As reported in study, change scores and treatment effects of the combined randomized and observation al cohort according to treatment received and adjusted for baseline score, age, gender, work status, depression, osteoporosis, joint problems, duration of current symptoms, reflex deficit, and number of moderate or severe stenotic levels.

CI = Confidence interval; SE = Standard error

Table 39. Key Question 3: pain at 4 years

Study	Scale	Treatment Group	Baseline N =	Baseline Mean	Baseline SE	4 Year N =	4 Year Mean	4Year SE	p-Value	Mean Difference
Weinstein et. al. 200914	SF 36: bodily pain score	Fusion	368	29.2	16.8	264	31.1	1.4	P <0.001	15.3 (95% CI: 11.0 to 19.7)
		Nonsurgical	233	34.4	16.7	131	15.8	1.8		

[a] As reported in study, change scores and treatment effects of the combined randomized and observation al cohort according to treatment received and adjusted for baseline score, age, gender, work status, depression, osteoporosis, joint problems, duration of current symptoms, reflex deficit, and number of moderate or severe stenotic levels.

CI = Confidence interval; SE = Standard error

Table 40. Key Question 3: function at baseline and 3 months

Study	Scale	Treatment Group	Baseline N =	Baseline Mean	Baseline SE	3 Months n =	3 Months Mean	3 Months SE	p-Value	Mean Difference
Weinstein et al. 200713	SF 36: physical function	Fusion	368	30.5	20.5	385	21.5	1.1	P <0.001	13.9 (95% CI: 11.1 to 16.8)
		Nonsurgical	233	40.3	23.9	320	7.6	1.2		
	Oswestry Disability Index	Fusion	368	45.0	16.6	385	-20.8	0.9	P <0.001	-14.6 (95% CI: -16.8 to -12.4)
		Nonsurgical	233	36.2	18.5	320	-6.2	0.9		

[a] As reported in study, change scores and treatment effects of the combined randomized and observation al cohort according to treatment received and adjusted for baseline score, age, gender, work status, depression, osteoporosis, joint problems, duration of current symptoms, reflex deficit, and number of moderate or severe stenotic levels.

CI = Confidence interval; SE = Standard error

Table 41. Key Question 3: function at 1 year

Study	Scale	Treatment Group	Baseline N =	Baseline Mean	Baseline SE	1 Year N =	1 Year Mean	1 Year SE	p-Value	Mean Difference
Weinstein et al. 200713	SF 36: physical function	Fusion	368	30.5	20.5	286	29.0	1.2	P <0.001	19.4 (95% CI: 16.1 to 22.7)
		Nonsurgical	233	40.3	23.9	234	9.6	1.3		
	Oswestry Disability Index	Fusion	368	45.0	16.6	286	-25.4	1.0	P <0.001	-17.9 (95% CI: -20.5 to -15.3)
		Nonsurgical	233	36.2	18.5	234	-7.5	1.1		

[a] As reported in study, change scores and treatment effects of the combined randomized and observation al cohort according to treatment received and adjusted for baseline score, age, gender, work status, depression, osteoporosis, joint problems, duration of current symptoms, reflex deficit, and number of moderate or severe stenotic levels.

CI = Confidence interval; SE = Standard error

Table 42. Key Question 3: function at 2 years

Study	Scale	Treatment Group	Baseline N =	Baseline Mean	Baseline SE	2 Year N =	2 Year Mean	2 Year SE	p-Value	Mean Difference
Weinstein et al. 200713	SF 36: physical function	Fusion	368	30.5	20.5	324	26.6	1.3	P <0.001	18.3 (95% CI: 14.6 to 21.9)
		Nonsurgical	233	40.3	23.9	187	8.3	1.5		
	Oswestry Disability Index	Fusion	368	45.0	16.6	324	-24.2	1.0	P <0.001	-16.7 (95% CI: -19.5 to -13.9)
		Nonsurgical	233	36.2	18.5	187	-7.5	1.2		

[a] As reported in study, change scores and treatment effects of the combined randomized and observation al cohort according to treatment received and adjusted for baseline score, age, gender, work status, depression, osteoporosis, joint problems, duration of current symptoms, reflex deficit, and number of moderate or severe stenotic levels.

CI = Confidence interval; SE = Standard error

Table 43. Key Question 3: function at 3 years

Study	Scale	Treatment Group	Baseline N =	Baseline Mean	Baseline SE	3 Year N =	3 Year Mean	3 Year SE	p-Value	Mean Difference
Weinstein et. Al. 2009[14]	SF 36: physical function	Fusion	368	30.5	20.5	326	25.1	1.2	P <0.001	16.1 (95% CI: 12.3 to 19.8)
		Nonsurgical	233	40.3	23.9	162	9.1	1.6		
	Oswestry Disability Index	Fusion	368	45.0	16.6	326	-21.9	0.96	P <0.001	-12.6 (95% CI: -15.5 to -9.7)
		Nonsurgical	233	36.2	18.5	162	-9.3	1.2		

[a] As reported in study, change scores and treatment effects of the combined randomized and observation al cohort according to treatment received and adjusted for baseline score, age, gender, work status, depression, osteoporosis, joint problems, duration of current symptoms, reflex deficit, and number of moderate or severe stenotic levels.

CI = Confidence interval; SE = Standard error

Table 44. Key Question 3: function at 4 years

Study	Scale	Treatment Group	Baseline N =	Baseline Mean	Baseline SE	4 Year N =	4 Year Mean	4 Year SE	p-Value	Mean Difference
Weinstein et. al. 2009[14]	SF 36: physical function	Fusion	368	30.5	20.5	264	26.6	1.3	P <0.001	18.9 (95% CI: 14.8 to 23.0)
		Nonsurgical	233	40.3	23.9	131	7.7	1.7		
	Oswestry Disability Index	Fusion	368	45.0	16.6	264	-23.0	1.0	P <0.001	-14.3 (95% CI: -17.5 to -11.1)
		Nonsurgical	233	36.2	18.5	131	-8.6	1.3		

[a] As reported in study, change scores and treatment effects of the combined randomized and observation al cohort according to treatment received and adjusted for baseline score, age, gender, work status, depression, osteoporosis, joint problems, duration of current symptoms, reflex deficit, and number of moderate or severe stenotic levels.

CI = Confidence interval; SE = Standard error

Table 45. Key Question 3: adverse events and reoperations within 2 years

Study	Duration of Followup	Adverse Event	Randomized Cohort (includes patients who underwent fusion and those who did not)	Observational Cohort (includes patients who underwent fusion and those who did not)
Weinstein et al. 2007 & 2009[13,14]	Intraoperative	Blood loss—ml	570.0±81.7	202.7±85.8
		Blood replacement	60 (36%)	67 (34%)
		Dual tear or cerebrospinal fluid leak	19 (11%)	18 (9%)
		Vascular injury	1 (1%)	0
		Other	3 (2%)	6 (3%)
Weinstein et al. 2007 & 2009[13,14]	Postoperative	Transfusion	27 (16%)	51 (26%)
		Nerve root damage	1(1%)	0
		Wound dehiscence	0	1 (1%)
		Wound hematoma	0	1 (1%)
		Wound Infection	8 (5%)	3 (2%)
		Other	21 (12%)	14 (7%)
Weinstein et al. 2007 & 2009[13,14]	3 months following surgery	Death	1 (1%)	1 (1%)
Weinstein et al. 2007 & 2009[13,14]	Within 1 year post fusion	Reoperation	0.6% for recurrent stenosis or spondylolisthesis	---
		Additional spine surgery	13 (8%)	11 (6%)
		Recurrent stenosis or listhesis	1 (1%)	1 (1%)
		Pseudarthrosis or fusion exploration	0	1 (1%)
		Complication	11 (6%)	7 (4%)
		New condition	1 (1%)	1 (0.5%)
Weinstein et al. 2007 & 2009[13,14]	Within 2 years post fusion	Reoperation	3.0% for recurrent stenosis or spondylolisthesis	
		Additional spine surgery within 2 years	18 (11%)	23 (12%)

Study	Duration of Followup	Adverse Event	Randomized Cohort (includes patients who underwent fusion and those who did not)	Observational Cohort (includes patients who underwent fusion and those who did not)
		Recurrent stenosis or listhesis within 2 year	5 (3%)	5 (2%)
		Pseudarthrosis or fusion exploration within 2 year	0	3 (2%)
		Complication within 2 year	13 (8%)	11 (6%)
		New condition within 2 year	1 (1%)	4 (2%)

[a] The authors did not report adverse events separately for patients who underwent surgery versus patients who did not.

Table 46. Key Question 3: adverse events and reoperations within 4 years

Study	Duration of Followup	Adverse Event	Fusion Group (N=264)	Nonsurgical Group (N=131)	Authors' Reported Results
Weinstein et al. 2007 & 2009[13,14]	Within 4 years	Death	17	7	Hazard ratio: 1.9 (95% CI: 0.76 to 4.6, p=0.17) * Based on proportional-hazards model adjusted for age.
		Reoperation	15% (5.0% for recurrent stenosis and spondylolisthesis)	---	---

[a] All deaths were independently reviewed, and 18 were judged to be not related to treatment. Four deaths occurring between 621 and 1379 days following surgery were considered to be of unknown causes. Two deaths, both in the surgical group, were considered to be potentially related to treatment—one patient died of respiratory distress 32 days post surgery and the other died of sepsis 82 days post surgery.

Risk-of-Bias Assessment

Table 47. Key Question 3: risk-of-bias assessement

Assessment Item	Weinstein et al. 2007 & 200913,14a
Were patients randomly assigned to treatment?	No
Was group allocation concealed?	No
For non-randomized trials, did the study employ other methods to enhance group comparability?	Yes
Was patient assignment independent of physician and patient preference?	No
Did patients in different study groups have similar levels of performance on the outcome of interest when they were assigned to groups?	No
Were the study groups comparable for all other important factors when they were assigned to groups?	No
Was the comparison of interest prospectively planned?	Yes
If patients received ancillary treatment(s), was there a 5% or less difference between groups in the proportion of patients receiving each ancillary treatment?	Not reported
Were the two groups treated concurrently?	Yes
Were patients blinded to the treatment they received?	No
Were outcome assessors blinded to which treatment patients had?	Not reported
For questions comparing fusion, did the two groups' surgeons have similar numbers of prior operations performing the procedure they performed in the study?	---

Assessment Item	Weinstein et al. 2007 & 200913,14a
Was the primary outcome measure of interest objective and was it objectively measured?	No
Was there a 15% or less difference in the length of followup for the two groups for the comparison time point of interest? This item is not relevant to perioperative outcomes.	Yes
Did at least 85% of patients who provided baseline data provide data at the time point of interest?	No (based on last followup point)
Was there a 15% or less difference between groups in the percentage of patients who provided data at the time point of interest?	No (based on last followup)
Risk-of-bias rating	High

[a] Responses based on combined study population that includes patients from the randomized cohort and patients from the observational cohort. Patients in the observational cohort chose the study group they would participate. At baseline, surgical patients and nonsurgical patients from the combined cohort were not comparable on a number of important characteristics which the authors controlled for in subsequent analyses.

Key Question 4: For adults with pain associated with degenerated disc(s) of the lumbar spine, does spinal fusion performed alone or in conjunction with additional surgery differ from other invasive procedures (e.g., total disc replacement, disc decompression) in: (a) Perioperative outcomes such as surgery time, blood loss, or length of hospital stay? (b) Patient-centered outcomes such as function, quality of life, or pain? (c) Adverse events?

Fusion Versus Lumbar Disc Arthrodesis

Study, Patient, and Intervention Descriptions

Table 48. Key Question 4: study design, artificial disc comparison

Study	Study Design	Enrollment Years	Location	Setting	Funding	Additional Information
ProDisc single-level study15,87,88	Randomized controlled trial (RCT)	2001–2003	Multicenter, United States	Based upon author affiliations appear to be mostly universities and spine/back specialty centers	None received for this study. Some authors reported financial relationships with the manufacturer.	Investigational Device Exemption (IDE) study for FDA
ProDisc two-level study16	RCT	2002–2004	Multicenter, United States	Based upon author affiliations, appears to be university and spine specialty centers	Funded by corporation/industry Some authors reported financial relationships with the manufacturer.	IDE study for FDA

Table 49. Key Question 4: patient inclusion criteria, artificial disc comparison

Study	Diagnosis Included	Duration of Symptoms	Diagnostic Criteria	Conditions Excluded	Previous Treatment Requirements	Age Requirements	Additional Inclusion Criteria	Additional Exclusion Criteria
ProDisc slngle-level study[15,88]	Single-level degenerated disc, L3-S1	No requirements	Back and/or leg pain, radiographic confirmation by CT, MRI, diskography, palin film, myelography and/or flexion/extension films showing instability (≥3 mm translation or ≥5 degrees angulation), loss of >2 mm disc height, scarring or thickening of anulus fibrosis, herniated nucleus pulposus, or vacuum phenomenon	Multilevel degenerated discs Known allergy to implant materials Prior surgery at level to be treated Facet joint disease or degeneration on radiograph Lytic spondylolisthesis or spinal stenosis Osteoporosis Back or leg pain of unknown cause Metabolic bone disease, such as Paget's disease or osteomalacia Degenerative spondylolisthesis Pregnancy or desire for pregnancy within 3 years Body Mass Index of at least 40 Active local or systemic infection Autoimmune disease Active malignancy or malignancy within 5 years except for nonmelanoma skin cancer HIV/AIDS	At least 6 months failed conservative treatment	Age 18–60 years	Oswestry score ≥40 (20/50) Able to adhere to protocol Informed consent	Taking drugs known to interfere with bone healing "Clinically compromised" vertebral bodies, such as due to trauma

Study	Diagnosis Included	Duration of Symptoms	Diagnostic Criteria	Conditions Excluded	Previous Treatment Requirements	Age Requirements	Additional Inclusion Criteria	Additional Exclusion Criteria
ProDisc two-level study[16]	Degenerated discs at two contiguous vertebral levels, with or without leg pain	At least 6 months	Lumbar spine instability, loss of intervertebral disc height, annulus fibrosus scarring, herniated nucleus pulposus, or vacuum of disc as confirmed by flexion-extension radiographs, CT, MRI, discography, and/or myelography	Spondylolisthesis >Grade 1, degenerated discs at more than 2 levels	At least 6 months failed non-operative treatments	Not reported	Preoperative Oswestry Disability Index score of at least 40	Previous fusion Inability to comply with protocol

Table 50. Key Question 4: patient characteristics: demographic and occupational history, artificial disc comparison

Study	Number Screened for Inclusion	Number Enrolled	Age	Women	Race or Ethnicity	Occupational Status	Workers Compensation	Pending Litigation
ProDisc single-level study[15,88]	Not reported	236 for randomized portion	Mean 40 years (40 years fusion, 39 years disc)	51% (55% fusion, 49% disc)	Caucasian 81% (97% fusion, 83% disc) African-American 4% (7% fusion, 3% disc) Hispanic 12% (13% fusion, 11% disc) Asian-Americans 1% (0 fusion, 1% disc)	Not reported	Not reported	Not reported
ProDisc two-level study[16]	Not reported	256	Mean 42 years (both groups)	43% (fusion 46%, disc 42%)	Not reported	Not reported	Not reported	Not reported

Table 51. Key Question 4: patient characteristics: health history, artificial disc comparison

Study	Surgical Indication (%)	Levels Affected	Duration of Symptoms	Primary or Recurrent?	Previous Conservative Treatment(s)	Duration of Conservative Treatments	Previous Surgery	Percent With Radicular Pain	Comorbid Diagnoses
ProDisc single-level study[15,88]	Degenerated disc (100%)	One	Not reported	Mixed	Narcotics as previous treatment, fusion 76% disc 84% None other reported	Not reported	Discectomy 16% (16% both groups) IDET 10% (fusion 7%, disc 11%) Laminectomy 8% (fusion 7%, disc 9%) Laminotomy 3% (3% each group)	100%	Smoking, current 25% (fusion 32%, disc 21%)
ProDisc two-level study[16]	Degenerated discs (100%)	Two	8% 6 months–1 year; 92% >1 year	Mixed	Injection 76% (72% fusion, 77% disc) Physical therapy 83% (85% fusion, 82% disc) Corset/brace 41% (39% fusion, 41% disc) Chiropractic 37% (39% fusion, 36% disc)	Not reported	None 59% Discectomy 19% Intradiscal electrothermal therapy 10% Laminectomy 17% Laminotomy 3%	Not reported	Smoking, current 29%

Table 52. Key Question 4: treatment characteristics: fusion, artificial disc comparison

Study	Number of Patients	Level Treated	Fusion Strategy	Surgical Approach	Device	Additional Information
ProDisc single-level study[15,88]	75	L3/L4 4% L4/L5 29% L5/S1 67%	Anterior lumbar interbody fusion with femoral ring allograft and posterolateral fusion with autologous iliac crest bone graft with pedicle screws	Anterior	Femoral ring allograft Pedicle screws Commercially available, but no information on proprietary name or manufacturer reported	Not reported
	161	L3/L4 2% L4/L5 34% L5/S1 65%	Disc arthroplasty	Anterior	Artificial disc: ProDisc-L (Synthes Spine, West Chester, PA)	Second generation Ultra-high molecular weight polyethylene articulation
ProDisc two-level study[16]	72	L3/L5 11% L4/S1 89%	Two-level anterior interbody fusion, using femoral ring allograft and posterolateral arthrodesis with autogenous iliac crest bone graft and pedicle screw instrumentation	Anterior	Femoral ring allograft: commercially available, but manufacturer not noted Pedicle screw instrumentation: manufacturer not noted Graft: autogenous iliac crest bone graft	Not reported
	165	L3/L5 9% L4/S1 91%	Disc arthroplasty	Anterior	Artificial disc: ProDisc-L (Synthes Spine, West Chester, PA)	Second generation Ultra-high molecular weight polyethylene articulation

Data and Results

Table 53. Key Question 4: perioperative outcomes: artificial disc versus fusion

Study	Outcomes	Treatment Group	N =	Mean	Standard Deviation	p-Value	Mean Difference
ProDisc one-level study[15]	Surgical Time	Disc arthroplasty	75	121 minutes	59.2	p<0.0001 (as reported in study)	108 (95% CI: 88.52 to 127.48)
		Fusion	160	229 minutes	75.9		
ProDisc two-level study[16]	Surgical Time	Disc arthroplasty	165	160 minutes	73	p<0.0001 (as reported in study)	113.00 (95% CI: 92.0 to 134.0)
		Fusion	72	273 minutes	82		
ProDisc one-level study[15]	Blood loss	Disc arthroplasty	160	204 cc	231.3	p<0.0001 (as reported in study)	261.00 (95% CI: 174.71 to 347.29)
		Fusion	73	465 cc	440.0		
ProDisc two-level study[16]	Blood loss	Disc arthroplasty	165	398 mL	451	p=0.0013 (as reported in study)	171.00 (95% CI: 44.80 to 297.21)
		Fusion	72	569 mL	467		
ProDisc one-level study[15]	Duration of Inpatient Stay	Disc arthroplasty	161	3.5 days	1.29	p<0.0001 (as reported in study)	0.90 (95% CI: 0.52 to 1.28)
		Fusion	75	4.4 days	1.54		
ProDisc two-level study[16]	Duration of Inpatient Stay	Disc arthroplasty	165	3.8 days	1.5	p<0.0001 (as reported in study)	1.20 (95% CI: 0.75 to 1.65)
		Fusion	72	5.0 days	1.9		

Table 54. Key Question 4: pain: artificial disc comparison: 6 weeks

Study	Scale	Treatment Group	Baseline N =	Baseline Mean	Baseline SD	6 Week N =	6 Week Mean	6 Week SD	p-Valuea	Effect Size Mean Difference
ProDisc single-level study[87]	Visual analog scale (VAS) 0–100	Fusion	75	73	14.7	73 (97%)	45	28.4	p=0.320	4.00 (95% CI: -3.87 to 11.87)
		Arthroplasty	159	76	16.4	152 (96%)	41	28.1		
ProDisc two-level study[16,89]	VAS 0–100	Fusion	69	74.8	13.9	63 (88%)	45.3	24.8	p=0.315	3.80 (95% CI: -1.5 to 9.29)
		Arthroplasty	162	75.8	16.0	155 (96%)	41.5	25.5		

[a] As calculated by the EPC in terms of standardized mean difference of followup scores.

CI = Confidence interval; SD = standard deviation

Table 55. Key Question 4: pain: artificial disc comparison: 3 months

Study	Scale	Treatment Group	Baseline N =	Baseline Mean	Baseline SD	3 Month N =	3 Month Mean	3 Month SD	p-Valuea	Effect Size Mean Difference
ProDisc single-level study[87]	Visual analog scale (VAS) 0–100	Fusion	75	73	14.7	70 (93%)	48	28.2	p=0.011	10.0 (95% CI: 2.34 to 17.6)
		Arthroplasty	159	76	16.4	149 (94%)	38	26.4		
ProDisc two-level study[16,89]	VAS 0–100	Fusion	69	74.8	13.9	66 (96%)	41.8	23.8	p=0.428	3.10 (95% CI: -4.55 to 10.8)
		Arthroplasty	162	75.8	16.0	153 (94%)	38.7	27.6		

[a] As calculated by the EPC in terms of standardized mean difference of followup scores.

CI = Confidence interval; SD = standard deviation

Table 56. Key Question 4: pain: artificial disc comparison: 6 months

Study	Scale	Treatment Group	Baseline N =	Baseline Mean	Baseline SD	6 Month N =	6 Month Mean	6 Month SD	p-Valuea	Effect Size Mean Difference
ProDisc single-level study[87]	Visual analog scale (VAS) 0–100	Fusion	75	73	14.7	69 (92%)	42	26.9	p=0.637	2.00 (95% CI: -6.31 to 10.31)
		Arthroplasty	159	76	16.4	147 (92%)	40	30.0		
ProDisc two-level study[16,89]	VAS 0–100	Fusion	69	74.8	13.9	64 (93%)	43.9	26.2	p=0.130	6.20 (95% CI:-1.80 to 14.20)
		Arthroplasty	162	75.8	16.0	145 (90%)	37.7	27.6		

[a] As calculated by the EPC in terms of standardized mean difference of followup scores.

CI = Confidence interval; SD = standard deviation

Table 57. Key Question 4: pain: artificial disc comparison: 1 year

Study	Scale	Treatment Group	Baseline N =	Baseline Mean	Baseline SD	1 Year N =	1 Year Mean	1 Year SD	p-Valuea	Effect Size Mean Difference
ProDisc single-level study[87]	Visual analog scale (VAS) 0–100	Fusion	75	73	14.7	60 (80%)	42	28.7	p=0.50	3.00 (95% CI: -5.75 to 11.75)
		Arthroplasty	159	76	16.4	137 (86%)	39	28.9		
ProDisc two-level study[16,89]	VAS 0–100	Fusion	69	74.8	13.6	61 (88%)	39.6	28.2	p=0.351	4.10 (95% CI: -4.51 to 12.71)
		Arthroplasty	162	75.8	16.0	137 (85%)	35.5	28.7		

[a] As calculated by the EPC in terms of standardized mean difference of followup scores.

CI = Confidence interval; SD = standard deviation

Table 58. Key Question 4: pain: artificial disc comparison: 18 months

Study	Scale	Treatment Group	Baseline N =	Baseline Mean	Baseline SD	18 Month N =	18 Month Mean	18 Month SD	p-Valuea	Effect Size Mean Difference
ProDisc single-level study[87]	Visual analog scale (VAS) 0–100	Fusion	75	73	14.7	52 (69%)	44	30.8	p=0.415	4.00 (95% CI: -5.62 to 13.62)
		Arthroplasty	159	76	16.4	129 (81%)	40	29.5		
ProDisc two-level study[16,89]	VAS 0–100	Fusion	69	74.8	13.6	48 (70%)	44.4	30.3	p=0.065	9.30 (95% CI: -0.55 to 19.15)
		Arthroplasty	162	75.8	16.0	136 (84%)	35.1	29.8		

[a] As calculated by the EPC in terms of standardized mean difference of followup scores.

CI = Confidence interval; SD = standard deviation

Table 59. Key Question 4: pain: artificial disc comparison: 2 years

Study	Scale	Treatment Group	Baseline N =	Baseline Mean	Baseline SD	2 Year N =	2 Year Mean	2 Year SD	p-Value	Effect Size
ProDisc single-level study[88]	Visual analog scale (VAS) 0–100	Fusion	73	74.9	14.7	71 (97%)	43.3	31.6	p=0.130[a]	Mean difference 6.80 (95% CI: -1.85 to 15.5)
		Arthroplasty	159	75.9	16.4	149 (94%)	36.6	30.1		
ProDisc two-level study[16,89]	VAS 0–100	Fusion	69	74.8	13.9	57 (83%)	37.7	30.2	p=0.258[a]	Mean difference 5.80 (95% CI: -3.54 to 15.1)
		Arthroplasty	162	75.8	16.0	140 (86%)	31.9	30.4		
ProDisc single-level study[88]	Narcotic (pain medication) use	Fusion	73	76% (55/73) had used		70 (96%)	42.5% (30/70)		p=0.809	Odds ratio 0.932 (95% CI: 0.525 to 1.654)
		Arthroplasty	159	84% (134/159) had used		148 (93%)	44.6% (66/148)			
ProDisc two-	Narcotic (pain	Fusion	72	64% (46/72)		59 (82%)	59% (35/59)		p=0.003	Odds ratio 2.580

Study	Scale	Treatment Group	Baseline N =	Baseline Mean	Baseline SD	2 Year N =	2 Year Mean	2 Year SD	p-Value	Effect Size
level study[16]	medication) use	Arthroplasty	165	69% (114/165)		144 (87%)	36% (52/144)			(1.387 to 4.800)

[a] As calculated by the EPC in terms of standardized mean difference of followup scores.

CI = Confidence interval; SD = standard deviation

Table 60. Key Question 4: pain: artificial disc comparison: 5 years

Study	Scale	Treatment Group	Baseline N =	Baseline Mean	Baseline SD	5 Year N =	5 Year Mean	5 Year SD	p-Value	Effect Size
ProDisc single-level study[88]	Visual analog scale (VAS) 0-100	Fusion	73	74.9	14.7	51 (70%)	40.0	32.1	p=0.563[a]	Mean difference 2.90 (95% CI: -6.91 to 12.71)
		Arthroplasty	159	75.9	16.4	125 (79%)	37.1	29.3		
ProDisc single-level study[88]	Narcotic (pain medication) use	Fusion	73	76% (55/73) had used		40% (20/50)			p=0.844	Odds ratio 1.068 (95% CI: 0.547 to 2.092)
		Arthroplasty	159	84% (134/159) had used		38.4% (48/125)				

[a] As calculated by the EPC in terms of standardized mean difference of followup scores.

CI = Confidence interval; SD = standard deviation

Table 61. Key Question 4: function: artificial disc comparison: 6 weeks

Study	Scale	Treatment Group	Baseline N =	Baseline Mean	Baseline SD	6 Week N =	6 Week Mean	6 Week SD	p-Valuea	Mean Difference
ProDisc single-level study[87]	Oswestry Disability Index	Fusion	75	62.7	10.3	73 (97%)	49.8	16.8	p=0.002	8.30 (95% CI: 3.12 to 13.45)
		Arthroplasty	161	63.4	12.6	154 (96%)	41.5	19.4		
ProDisc two-level study[16]	Oswestry Disability Index	Fusion	69	64.6	9.5	63 (91%)	49.8	17.3	p=0.029	5.90 (95% CI: 0.644 to 11.16)
		Arthroplasty	162	64.9	11.3	155 (96%)	43.9	18.2		

[a] As calculated by the EPC in terms of standardized mean difference of followup scores.

CI = Confidence interval; SD = standard deviation

Table 62. Key Question 4: function: artificial disc comparison: 3 months

Study	Scale	Treatment Group	Baseline N =	Baseline Mean	Baseline SD	3 Month N =	3 Month Mean	3 Month SD	p-Valuea	Mean Difference
ProDisc single-level study[87]	Oswestry Disability Index	Fusion	75	62.7	10.3	71 (95%)	46.6	18.6	p<0.001	10.20 (95% CI: 4.62 to 15.79)
		Arthroplasty	161	63.4	12.6	149 (93%)	36.4	20.2		
ProDisc two-level study[16]	Oswestry Disability Index	Fusion	69	64.6	9.5	66 (96%)	43.6	15.2	p=0.054	5.50 (95% CI: -0.069 to 11.07)
		Arthroplasty	162	64.9	11.3	153 (94%)	38.1	20.8		

[a] As calculated by the EPC in terms of standardized mean difference of followup scores.

CI = Confidence interval; SD = standard deviation

Table 63. Key Question 4: function: artificial disc comparison: 6 months

Study	Scale	Treatment Group	Baseline N =	Baseline Mean	Baseline SD	6 Month N =	6 Month Mean	6 Month SD	p-Valuea	Mean Difference
ProDisc single-level study[87]	Oswestry Disability Index	Fusion	75	62.7	10.3	69 (92%)	41.5	21.4	p=0.081	5.50 (95% CI: -0.65 to 11.65)
		Arthroplasty	161	63.4	12.6	148 (92%)	36	21.6		
ProDisc two-level study[16]	Oswestry Disability Index	Fusion	69	64.6	9.5	64 (93%)	43.2	17.0	p=0.010	8.00 (95% CI: 1.97 to 14.0)
		Arthroplasty	162	64.9	11.3	146 (90%)	35.2	21.9		

[a] As calculated by the EPC in terms of standardized mean difference of followup scores. CI = Confidence interval; SD = standard deviation

Table 64. Key Question 4: function: artificial disc comparison: 1 year

Study	Scale	Treatment Group	Baseline N =	Baseline Mean	Baseline SD	1 Year N =	1 Year Mean	1 Year SD	p-Valuea	Mean Difference
ProDisc single-level study[87]	Oswestry Disability Index	Fusion	75	62.7	10.3	61 (81%)	40.7	22.3	p=0.134	5.10 (95% CI: -1.54 to 11.74)
		Arthroplasty	161	63.4	12.6	137 (85%)	35.6	21.9		
ProDisc two-level study[16]	Oswestry Disability Index	Fusion	69	64.6	9.5	61 (88%)	39.8	22.7	p=0.095	6.10 (95% CI: -1.05 to 13.3)
		Arthroplasty	162	64.9	11.3	137 (85%)	33.7	24.1		

[a] As calculated by the EPC in terms of standardized mean difference of followup scores.

CI = Confidence interval; SD = standard deviation

Table 65. Key Question 4: function: artificial disc comparison: 18 months

Study	Scale	Treatment Group	Baseline N =	Baseline Mean	Baseline SD	18 Month N =	18 Month Mean	18 Month SD	p-Valuea	Mean Difference
ProDisc single-level study[87]	Oswestry Disability Index	Fusion	75	62.7	10.3	52 (69%)	39.8	23.3	p=0.178	5.10 (95% CI: -2.31 to 12.50)
		Arthroplasty	161	63.4	12.6	129 (80%)	34.7	22.9		
ProDisc two-level study[16]	Oswestry Disability Index	Fusion	69	64.6	9.5	48 (70%)	42.0	22.7	p=0.026	9.10 (95% CI: 1.14 to 17.06)
		Arthroplasty	162	64.9	11.3	136 (84%)	32.9	24.7		

[a] As calculated by the EPC in terms of standardized mean difference of followup scores.

CI = Confidence interval; SD = standard deviation

Table 66. Key Question 4: function: artificial disc comparison: 2 years

Study	Scale	Treatment Group	Baseline N =	Baseline Mean	Baseline SD	2 Year N =	2 Year Mean	2 Year SD	p-Value	Effect SIze
ProDisc single-level study[88]	Oswestry Disability Index	Fusion	75	62.7	10.3	71 (95%)	39.8	24.3	p=0.134[a]	Mean Difference 5.30 (95% CI: -1.61 to 12.21)
		Arthroplasty	161	63.4	12.6	149 (93%)	34.5	24.8		
ProDisc two-level study[16]	Oswestry Disability Index	Fusion	69	64.6	9.5	57 (83%)	38.3	23.9	p=0.031[a]	Mean Difference 8.30 (95% CI: 0.79 to 15.81)
		Arthroplasty	162	64.9	11.3	141 (87%)	30.0	24.6		
ProDisc two-	Proportion working	Fusion	72	83% (60/72)		57 (79%)	86% (49/57)		Not statistically	Odds ratio 1.49 (95%

Study	Scale	Treatment Group	Baseline N =	Baseline Mean	Baseline SD	2 Year N =	2 Year Mean	2 Year SD	p-Value	Effect SIze
level study[16]		Arthroplasty	165	79% (131/165)		143 (87%)	80% (115/143)		significantly different at either time point (as reported in the study)	CI: 0.64 to 3.50)

[a] As calculated by the EPC in terms of standardized mean difference of followup scores.

CI = Confidence interval; SD = standard deviation

Table 67. Key Question 4: function: artificial disc comparison: 5 years

Study	Scale	Treatment Group	Baseline N =	Baseline Mean	Baseline SD	5 Year N =	5 Year Mean	5 Year SD	p-Valuea	Mean Difference
ProDIsc single-level study88	Oswestry Disability Index	Fusion	75	62.7	10.3	51 (68%)	36.2	25.7	p=0.626	2.00 (95% CI: -6.03 to 10.0)
		Arthroplasty	161	63.4	12.6	126 (78%)	34.2	24.3		

[a] As calculated by the EPC in terms of standardized mean difference of followup scores.

CI = Confidence interval; SD = standard deviation

Table 68. Key Question 4: quality of life: artificial disc comparison: 6 weeks

Study	Scale	Treatment Group	Baseline N =	Baseline Mean	Baseline SD	6 Week N =	6 Week Mean	6 Week SD	p-Valuea	Mean Difference
ProDisc two-level study[16,89]	SF-36: Physical Component Score	Fusion	68	30.25	6.7	63 (93%)	31.9	6.5	p=0.009	2.90 (95% CI: 0.75 to 5.05)
		Arthroplasty	161	29.4	5.5	150 (93%)	34.8	7.6		
ProDisc two-level study[89]	SF-36: Mental Component Score	Fusion	68	41.3	13.5	63 (93%)	44.4	11.1	p=0.073	3.00 (-0.27 to 6.27)
		Arthroplasty	161	41.1	12.7	150 (93%)	47.4	11.1		

[a] As calculated by the EPC in terms of standardized mean difference of followup scores.

CI = Confidence interval; SD = standard deviation

Table 69. Key Question 4: quality of life: artificial disc comparison: 3 months

Study	Scale	Treatment Group	Baseline N =	Baseline Mean	Baseline SD	3 Month N =	3 Month Mean	3 Month SD	p-Valuea	Mean Difference
ProDisc two-level study[16,89]	SF-36: Physical Component Score	Fusion	68	30.25	6.7	64 (94%)	35.0	7.2	p=0.005	3.70 (95% CI: 1.13 to 6.27)
		Arthroplasty	161	29.4	5.5	152 (94%)	38.7	9.4		
ProDisc two-level study[89]	SF-36: Mental Component Score	Fusion	68	41.3	13.5	64 (94%)	48.0	12.0	p=0.572	1.00 (95% CI: -2.46 to 4.46)
		Arthroplasty	161	41.1	12.7	152 (94%)	49.0	11.8		

[a] As calculated by the EPC in terms of standardized mean difference of followup scores.

CI = Confidence interval; SD = standard deviation

Table 70. Key Question 4: quality of life: artificial disc comparison: 6 months

Study	Scale	Treatment Group	Baseline N =	Baseline Mean	Baseline SD	6 Month N =	6 Month Mean	6 Month SD	p-Valuea	Mean Difference
ProDisc two-level study[16,89]	SF-36: Physical Component Score	Fusion	68	30.25	6.7	62 (91%)	37.3	9.2	p=0.012	3.80 (95% CI: 0.85 to 6.75)
		Arthroplasty	161	29.4	5.5	145 (90%)	41.1	10.2		
ProDisc two-level study[89]	SF-36: Mental Component Score	Fusion	68	41.3	13.5	62 (91%)	47.2	13.1	p=0.803	0.50 (95% CI: -3.44 to 4.44)
		Arthroplasty	161	41.1	12.7	145 (90%)	46.7	13.3		

[a] As calculated by the EPC in terms of standardized mean difference of followup scores.

CI = Confidence interval; SD = standard deviation

Table 71. Key Question 4: quality of life: artificial disc comparison: 1 year

Study	Scale	Treatment Group	Baseline N =	Baseline Mean	Baseline SD	1 Year N =	1 Year Mean	1 Year SD	p-Valuea	Mean Difference
ProDisc two-level study[16,89]	SF-36: Physical Component Score	Fusion	68	30.25	6.7	61 (90%)	39.5	10.0	p=0.096	2.80 (95% CI: -0.48 to 6.08)
		Arthroplasty	161	29.4	5.5	134 (83%)	42.3	11.2		
ProDisc two-level study[89]	SF-36: Mental Component Score	Fusion	68	41.3	13.5	61 (90%)	45.3	13.4	p=0.26	2.30 (95% CI: -1.69 to 6.30)
		Arthroplasty	161	41.1	12.7	134 (83%)	47.6	13.1		

[a] As calculated by the EPC in terms of standardized mean difference of followup scores.

CI = Confidence interval; SD = standard deviation

Table 72. Key Question 4: quality of life: artificial disc comparison: 18 months

Study	Scale	Treatment Group	Baseline N =	Baseline Mean	Baseline SD	18 Month N =	18 Month Mean	18 Month SD	p-Valuea	Mean Difference
ProDisc two-level study[16,89]	SF-36: Physical Component Score	Fusion	68	30.25	6.7	48 (71%)	38.4	10.7	p=0.025	4.30 (95% CI: 0.58 to 8.02)
		Arthroplasty	161	29.4	5.5	134 (83%)	42.7	11.5		
ProDisc two-level study[89]	SF-36: Mental Component Score	Fusion	68	41.3	13.5	48 (71%)	45.9	14.6	p=0.754	0.70 (95% CI: -3.68 to 5.08)
		Arthroplasty	161	41.1	12.7	134 (83%)	46.6	12.8		

[a] As calculated by the EPC in terms of standardized mean difference of followup scores.

CI = Confidence interval; SD = standard deviation

Table 73. Key Question 4: quality of life: artificial disc comparison: 2 years

Study	Scale	Treatment Group	Baseline N =	Baseline Mean	Baseline SD	2 Years N =	2 Years Mean	2 Years SD	p-Valuea	Mean Difference
ProDisc single-level study[88]	SF-36: Physical Component Score	Fusion	74	30.9	5.6	70 (95%)	38.8	11.3	p=0.014	4.00 (95% CI: 0.82 to 7.18)
		Arthroplasty	158	31.1	6.5	147 (93%)	42.8	11.1		
ProDisc two-level study[16,89]	SF-36: Physical Component Score	Fusion	68	30.25	6.7	55 (81%)	39.2	11.2	p=0.012	4.70 (95% CI: 1.06 to 8.34)
		Arthroplasty	161	29.4	5.5	143 (89%)	43.9	11.9		
ProDisc two-level study[89]	SF-36: Mental Component Score	Fusion	68	41.3	13.5	55 (81%)	45.7	13.6	p=0.069	3.60 (95% CI: -0.27 to 7.47)
		Arthroplasty	161	41.1	12.7	140 (87%)	49.3	11.9		

[a] As calculated by the EPC in terms of standardized mean difference of followup scores.

CI = Confidence interval; SD = standard deviation

Table 74. Key Question 4: quality of life: artificial disc comparison: 5 years

Study	Scale	Treatment Group	Baseline N =	Baseline Mean	Baseline SD	5 Years N =	5 Years Mean	5 Years SD	p-Valuea	Mean Difference
ProDisc single-level study[88]	SF-36: Physical Component Score	Fusion	74	30.9	5.6	51 (69%)	40.1	13.6	p=0.341	1.90 (95% CI: -2.0 to 5.8)
		Arthroplasty	158	31.1	6.5	126 (80%)	42.0	11.3		

[a] As calculated by the EPC in terms of standardized mean difference of followup scores.

CI = Confidence interval; SD = standard deviation

Table 75. Key Question 4: adverse events and reoperations: artificial disc comparison

Study	Duration of Followup	Adverse Event	Fusion	Artificial Disc
ProDisc two-level study[16]	Intraoperative	Blood loss >1,500 mL	2 (2.8%)	1 (1.2%)
ProDisc single-level study[88]			2 (2.7%)	0
ProDisc two-level study[16]		Dural tear	3 (4.2%)	1 (0.6%)
ProDisc single-level study[88]			2 (2.7%)	0
ProDisc two-level study[16]	Perioperative	Deep venous thrombosis	2 (1.2%)	2 (2.8%)
ProDisc single-level study[88]			1 (1.3%)	2 (2.7%)
ProDisc single-level study[88]		Wound infection, posterior	2 (2.7%)	0
ProDisc single-level study[88]	Postoperative	Retrograde ejaculation	1 (1.3%)	2 (2.7%)
ProDisc two-level study[16]	Intermediate	Re-operation, any reason	6 (8.3%) (5 due to ongoing pain, one pseudarthrosis) Short to intermediate term	4 (2.4%) (1 fusion, rest foraminotomy and/or facetectomy for decompression) Intermediate term

Risk-of-Bias Assessment

Table 76. Key Question 4: risk-of-bias assessment, artificial disc comparison

Assessment Item	ProDisc Two-Level Study16	ProDisc Single-Level Study15,88
Were patients randomly assigned to treatment?	Yes	Yes
Was group allocation concealed?	Yes	Yes
For non-randomized trials, did the study employ other methods to enhance group comparability?	Yes	Yes
Was patient assignment independent of physician and patient preference?	Yes	Yes
Did patients in different study groups have similar levels of performance on the outcome of interest when they were assigned to groups?	Yes	Yes
Were the study groups comparable for all other important factors when they were assigned to groups?	Yes	Yes
Was the comparison of interest prospectively planned?	Yes	Yes
If patients received ancillary treatment(s), was there a 5% or less difference between groups in the proportion of patients receiving each ancillary treatment?	Yes	Yes
Were the two groups treated concurrently?	Yes	Yes
Were patients blinded to the treatment they received?	No	No
Were outcome assessors blinded to which treatment patients had?	No	No
For questions comparing fusion, did the two groups' surgeons have similar numbers of prior operations performing the procedure they performed in the study?	—	—
Was the primary outcome measure of interest objective and was it objectively measured?	No	No
Was there a 15% or less difference in the length of followup for the two groups for the comparison time point of interest?	Yes	Yes
Did at least 85% of patients who provided baseline data provide data at the time point of interest?	Yes Exceptions Pain 18 months ODI 18 months SF-36 1 year, 18 months, 2 years, 5 years	Yes Exceptions Pain 1 year, 18 months, 5 years ODI 1 year, 18 months, 5 years SF-36 1 year, 18 months
Was there a 15% or less difference between groups in the percentage of patients who provided data at the time point of interest?	Yes	Yes Exception: Pain 1 year
Risk-of-bias rating	Moderate	Moderate

Key Question 5: For adults with pain associated with degenerative stenosis of the lumbar spine, does spinal fusion performed alone or in conjunction with additional surgery differ from other invasive procedures (e.g., decompressive laminectomy and minimally invasive procedures, including those using devices) in: (a) Perioperative outcomes such as surgery time, blood loss, or length of hospital stay? (b) Patient-centered outcomes such as function, quality of life, or pain? (c) Adverse events?

Fusion Versus Decompression

Study, Patient, and Intervention Descriptions

Table 77. Key Question 5: study design: decompression comparison

Study	Study Design	Enrollment Years	Location	Setting	Funding
Hallett et al. 2007[17]	Randomized Controlled Trial (RCT)	1998–2001	Edinburgh, Scotland, U.K.	University spine center	Corporate/industry funding supported No benefits related to manuscript subject

Table 78. Key Question 5: patient inclusion criteria: decompression comparison

Study	Diagnosis Included	Duration of Symptoms	Diagnostic Criteria	Conditions Excluded	Previous Treatment Requirements	Age Requirements
Hallett et al. 2007[17]	Foraminal stenosis with single-level degenerated disc	At least 5 years	Plain radiographs and MR images used to identify intraforaminal or extraforaminal nerve root compromise with single-level degenerated disc	>Grade 2 degenerative spondylolisthesis at degenerated disc or adjacent level >1 cm vertebral translocation >50% disc space narrowing proximal or distal to level to be treated Malignancy, any	Conservative efforts over at least 3 months prior to study enrollment	Not reported, all enrolled were adults

Table 79. Key Question 5: patient characteristics: demographic and occupational history: decompression comparison

Study	Number Screened for Inclusion	Number Enrolled	Age	Women	Race or Ethnicity	Occupational Status	Workers Compensation	Pending Litigation
Hallett et al. 2007[17]	48	44 (92%)	Mean 57 (range 34-75) years (decompression 57 years, posterolateral fusion 54 years, posterolateral and transforaminal fusion 59 years)	45% (decompression 29%, posterolateral fusion 63%, posterolateral and transforaminal fusion 36%)	White (100%)	Retired (30%) Housewives (23%) Off work sick (27%) Rest worked in heavy manual or light industrial jobs	2% with pending claim	Not reported

Table 80. Key Question 5: patient characteristics: health history: decompression comparison

Study	Surgical Indication	Number of Levels Affected	Duration of Symptoms	Primary of Recurrent?	Previous Conservative Treatment(s)	Duration of Conservative Treatments	Previous Surgery	Percent With Radicular Pain	Comorbid Diagnoses
Hallett et al. 2007[17]	Foraminal stenosis with degenerated disc (100%)	One	Not reported	Appears primary	Typically physical therapy and one or more of acupuncture, chiropractic, or massage	Not reported	Not reported	100%	Current or previous smoking 27%

Table 81. Key Question 5: treatment characteristics: fusion and decompression

Study	Number of Patients	Level Fused	Surgical Strategy	Surgical Approach	Device	Adjunctive Surgery
Hallett et al. 2007[17] Fusion Group 2	16	L3/L4 (13%) L4/L5 (56%) L5/S1 (31%)	Fusion "group 2" Posterolateral instrumented pedicular fusion	Posterolateral	Pedicular fusion instrument: Moss-Miami, DePuy Ltd. (Warsaw IN) Graft: Autologous graft from iliac crest on side with lesser symptoms; laid along lateral masses and into facet joints	Single or bilateral foraminotomy with nerve root decompression. If disc bulge contributed to stenosis, minimal microdiscetomy including subligamentous fragment and loose fragment excision
Hallett et al. 2007[17] Fusion Group 3	14	L3/L4 (21%) L4/L5 (57%) L5/S1 (21%)	Fusion "group 3" Transforaminal lumbar interbody fusion with anterior graft and 2 circular titanium interbody cages and additional graft posterolaterally	Transforaminal and posterolateral	Cage: Titanium interbody cage, proprietary name or manufacturer not reported, 2 per patient Graft: Autologous iliac crest bone graft on side with lesser symptoms; laid along lateral masses and into facet joints	Single or bilateral foraminotomy with nerve root decompression If the disc contributed to the stenosis, minimal microdiskectomy to remove subligamentous fragment and loose fragment from disc space
Hallett et al. 2007[17] Decompression	14	L4/L5 (64%) L5/S1 (36%)	Decompression "group 1" Single or bilateral foraminotomy with nerve root decompression	Not stated	None	For patients with disc bulge contributing to stenosis, minimal microdiskectomy excising subligamentous and loose fragment from disc space

Data and Results

Table 82. Key Question 5: decompression comparison: pain at 2 years

Study	Scale	Treatment Group	Baseline N =	Baseline Mean	Baseline SD	2 Year N =	2 Year Mean	2 Year SD	p-Value
Hallett et al. 2007[17]	Visual analog scale (VAS) back pain 0–10 [a]	Decompression	14	7.75	Not reported	13 (93%)	4.75	Not reported	—
		Posterolateral interbody fusion	16	7.75	Not reported	15 (94%)	4.5	Not reported	Not statistically significantly different (as reported in the study)[b]
		Transforaminal interbody fusion	14	7.75	Not reported	12 (86%)	4	Not reported	Not statistically significantly different (as reported in the study)[b]

[a] Estimated from figure; [b] vs. decompression.
SD = Standard deviation

Table 83. Key Question 5: decompression comparison: function at 2 years

Study	Scale	Treatment Group	Baseline N =	Baseline Mean	Baseline SD	2 Year N =	2 Year Mean	2 Year SD	p-Value
Hallett et al. 2007[17]	Low Back Outcome Scale [a]	Decompression	14	14	Not reported	13 (93%)	25	Not reported	—
		Posterolateral interbody fusion	16	20	Not reported	15 (94%)	35	Not reported	Not statistically significantly different (as reported in the study)[b]
		Transforaminal interbody fusion	14	19	Not reported	12 (86%)	19	Not reported	Not statistically significantly different (as reported in the study)[b]
Hallett et al. 2007[17]	Roland and Morris Disability Scale [a]	Decompression	14	16	Not reported	13 (93%)	13	Not reported	—
		Posterolateral interbody fusion	16	13	Not reported	15 (94%)	9	Not reported	Not statistically significantly different (as reported in the study)[b]
		Transforaminal interbody fusion	14	15	Not reported	12 (86%)	12	Not reported	Not statistically significantly different (as reported in the study)[b]

[a] Estimated from figure; [b] vs. decompression.
SD = Standard deviation

Table 84. Key Question 5: decompression comparison: quality of life at 2 years

Study	Scale	Treatment Group	Baseline N =	Baseline Mean	Baseline SD	2 Year N =	2 Year Mean	2 Year SD	p-Value
Hallett et al. 2007[17]	SF-36 physical function [a]	Decompression	14	34	Not reported	13 (93%)	45	Not reported	—
		Posterolateral interbody fusion	16	25	Not reported	15 (94%)	45	Not reported	Not statistically significantly different (as reported in study)[b]
		Transforaminal interbody fusion	14	31	Not reported	12 (86%)	35	Not reported	Not statistically significantly different (as reported in study)[b]

[a] Estimated from figure.
[b] vs. decompression.

SD = Standard deviation

Table 85. Key Question 5: decompression comparison: adverse events

Study	Duration of Followup	Adverse Event	Transforaminal Interbody Fusion	Posterolateral Instrumented Fusion	Decompression
Hallett et al. 2007[17]	Intermediate	Revision: Secondary decompressive laminectomy	1 (7%) 7 months Decompressive laminectomy	1 (6%) 23 months Decompressive laminectomy	1 (7%) 29 months Instrumented lateral mass fusion

Risk-of-Bias Assessment

Table 86. Key Question 5: decompression comparison: risk-of-bias assessment

Assessment Item	Hallett et al. 200717
Were patients randomly assigned to treatment?	Yes
Was group allocation concealed?	NR
For non-randomized trials, did the study employ other methods to enhance group comparability?	Yes
Was patient assignment independent of physician and patient preference?	Yes
Did patients in different study groups have similar levels of performance on the outcome of interest when they were assigned to groups?	VAS, LBOS, RMDS: Yes SF-36: No
Were the study groups comparable for all other important factors when they were assigned to groups?	No
Was the comparison of interest prospectively planned?	Yes
If patients received ancillary treatment(s), was there a 5% or less difference between groups in the proportion of patients receiving each ancillary treatment?	Yes
Were the two groups treated concurrently?	Yes
Were patients blinded to the treatment they received?	No
Were outcome assessors blinded to which treatment patients had?	No
For questions comparing fusion, did the two groups' surgeons have similar numbers of prior operations performing the procedure they performed in the study?	Yes
Was the primary outcome measure of interest objective and was it objectively measured?	No
Was there a 15% or less difference in the length of followup for the two groups for the comparison time point of interest?	No
Did at least 85% of patients who provided baseline data provide data at the time point of interest?	Yes
Was there a 15% or less difference between groups in the percentage of patients who provided data at the time point of interest?	Yes
Risk-of-bias assessment	Moderate

Key Question 7: For adults with pain associated with degenerated disc(s) of the lumbar spine, do spinal fusion approaches (e.g., anterior, posterior, combined) and techniques (e.g., instrumentation, graft material) performed alone or in conjunction with additional surgery differ in: (a) Perioperative outcomes such as surgery time, blood loss, or length of hospital stay? (b) Patient-centered outcomes such as function, quality of life, or pain? (c) Adverse events?

Fusion With rhBMP-2 Versus Autogenous Bone Graft

Study, Patient, and Intervention Descriptions

Table 87. Key Question 7: study design, rhBMP-2 versus autogenous bone graft

Study	Study Design	Enrollment Years	Location	Setting	Funding	Additional Information
Dawson et al. 2009[18a]	Randomized controlled trial (RCT)	2003–2004	Multicenter, various cities, United States	Spine specialty centers	Medtronic Sofamor Danek sponsorship for study and additional financial relationships reported	Investigational Device Exemption (IDE) pilot study for FDA
Burkus et al. 2002[19a]	RCT	1998	Multicenter, various cities, United States	Author affiliations spine specialty centers, an orthopaedic center, a hospital	Corporate/Industry sponsorship One or more authors have financial relationship with manufacturer	Part of FDA IDE or corresponding national protocol
Burkus et al. 2002[20a]	RCT	1998–1999	Multicenter, various cities, United States	Author affiliations spine specialty centers, orthopedic center, University, Neurologic Institute	Not reported but author overlap with other Medtronic studies	

[a] Additional information to enable quantitative analysis (e.g., number of patients at each time point, measure of variance) requested from contact author but no reply was received

Table 88. Key Question 7: patient inclusion criteria, rhBMP-2 versus autogenous bone graft

Study	Diagnosis Included	Duration of Symptoms	Diagnostic Criteria	Conditions Excluded	Previous Treatment Requirements	Age Requirements	Additional Inclusion Criteria
Dawson et al. 2009[18]	Degenerated disc between L1 and S1, low back pain and radicular pain	Not reported	Patient history, low back and radicular pain, physical findings, neuroradiographic studies demonstrating instability, osteophyte formation p-Value, decreased disc height, ligamentous tissue thickening, disc degeneration or herniation, and/or facet joint degeneration	Greater than Grade 1 spondylolisthesis Previous spinal fusion at level to be treated	At least 6 months nonoperative treatments	Not reported	Not reported
Burkus et al. 2002[19]	Degenerated disc with low back pain and/or leg pain or sciatica	At least 6 months	Patient history and symptoms, physical findings, functional deficits, radiographic findings Radiographic: segmental angulation of >5 degrees and/or translation >4 mm; osteophytes; >50% decrease in disc height; ligamentous tissue thickening; disc protrusion and/or herniation	Medical condition requiring nonsteroidal anti-inflammatories (NSAIDS) or steroids, which interfere with fusion	At least 6 months nonoperative, including aerobic conditioning, medications, spinal injections, and for some, spinal manipulation	Not reported	>35 points on Oswestry Disability Index

Study	Diagnosis Included	Duration of Symptoms	Diagnostic Criteria	Conditions Excluded	Previous Treatment Requirements	Age Requirements	Additional Inclusion Criteria
Burkus et al. 2002[20,91]	Degenerated disc with disabling low back and/or leg pain	At least 6 months	Instability (defined as angulation ≥5° and/or translation ≥4 mm on flexion/ extension radiographs), osteophyte formation, decreased disc height, ligamentous thickening, disc degeneration/ herniation, or facet joint degeneration	Previous anterior spinal fusion at the involved level, posterior spinal instrumentation at the involved level or a previous interbody fusion procedure, any conditions that require postoperative medications that would be expected to interfere with fusion, e.g. steroids, or has received drugs that interfere with bone metabolism within 2 weeks of surgery, osteoporosis, osteopenia, osteomalacia, active malignancy, active local or systemic infection, gross obesity, defined as >40% IBW, fever >101°F, mentally incompetent, Waddell's Signs of Inorganic Behavior ≥3, alcohol or drug abuse, tobacco user, an autoimmune disease, titanium allergy, previous exposure to injectable collagen implants, hypersensitivity to protein pharmaceuticals or collagen, previous exposure to rhBMP-2, allergy to bovine products or history of anaphylaxis, endocrine or metabolic disorder that affects osteogenesis, or received another investigational therapy within 28 days prior to implantation.	At least 6 months conservative, not specified	Not reported	Not reported

Table 89. Key Question 7: patient characteristics: demographic and occupational history, rhBMP-2 versus autogenous bone graft

Study	Number Screened for Inclusion	Number Enrolled	Age	Women	Race or Ethnicity	Occupational Status	Workers Compensation	Pending Litigation
Dawson et al. 2009[18]	50	46 (92%) treated	Mean 56 years (56 years rhBMP-2, 57 years autograft)	59% (60% rhBMP-2, 57% autograft)	Not reported	Not reported	15% either receiving workers compensation or with pending litigation (12% rhBMP-2, 19% autograft)	15% either receiving workers compensation or with pending litigation (12% rhBMP-2, 19% autograft)
Burkus et al. 2002[19]	Not reported	46	Mean 43 years (42 inFuse, 46 autograft)	61% (67% infuse, 55% autograft)	Not reported	Not reported	26% (21% infuse, 32% autograft)	17% (17% infuse, 18% autograft)
Burkus et al. 2002[20]	Not reported	279	Mean 43 years (43 years rhBMP-2, 42 years autograft)	48% (46% rhBMP-2, 50% autograft)	Not reported	42% working (48% rhBMP-2, 36% autograft)	34% (33% rhBMP-2, 35% autograft)	14% (13% rhBMP-2, 16% autograft)

Table 90. Key Question 7: patient characteristics: health history, rhBMP-2 versus autogenous bone graft

Study	Surgical Indication	Number of Levels Affected	Duration of Symptoms	Primary or Recurrent?	Previous Conservative Treatment(s)	Duration of Conservative Treatments	Previous Surgery	Percent With Radicular Pain	Comorbid Diagnoses
Dawson et al. 2009[18]	Degenerated disc, symptomatic	One	Not reported	Appears primary	Not reported	Not reported	26% (none fusion at index level) (24% rhBMP-2, 29% autograft)	100%	Smoking 24% (24% each group)
Burkus et al. 2002[19]	Degenerated disc, symptomatic	One	Not reported	Appears primary	Aerobic conditioning, medications, spinal injections, and for some, spinal manipulation	Not reported	39% (surgery type not reported) (36% InFuse, 32% autograft)	Not reported	Tobacco 30% (33% InFuse, 27% autograft)
Burkus et al. 2002[20]	Degenerated disc, symptomatic	One	Not reported	Appears primary	Not reported	Not reported	Not reported	Not reported	Tobacco 34% (33% rhBMP-2, 36% autograft)

Table 91. Key Question 7: treatment characteristics: rhBMP-2 versus autograft

Study	Number of Patients	Level Fused	Fusion Strategy	Surgical Approach	Device	Adjunctive Surgery	Additional Information
Dawson et al. 2009[18]	25	Not reported	Posterolateral arthrodesis with rhBMP-2 on collagen sponge with osteoconductive bulking agent	Posterior (standard open midline)	Graft with bulking agent: INFUSE/MASTERGRAFT Medtronic Sofamor Danek Cotrel-Dubousset Horizon Spinal System (Medtronic Sofamor Danek)	Posterior decompression "as needed," local bone discarded	12 mg rhBMP-2 on 8 cm^3 collagen sponge per patient No interbody arthrodesis
	21	Not reported	Posterolateral arthrodesis with iliac crest bone graft and instrumentation	Posterior (standard open midline)	Graft: autogenous iliac crest bone graft Cotrel-Dubousset Horizon Spinal System (Medtronic Sofamor Danek)	Posterior decompression "as needed," local bone discarded	No interbody arthrodesis
Burkus et al. 2002[19]	24	L4/L5 (46%) L5/S1 (54%)	Anterior lumbar interbody fusion with InFUSE Bone Graft (rhBMP-2 on absorbable collagen sponge carrier) plus MD-II treaded cortical bone dowel	Transperitoneal or retroperitoneal	Graft: InFuse Bone Graft, Medtronic Sofamor Danek (Memphis, TN) Dowel: MD-II threaded cortical bone dowel, Regeneration Technologies Inc. (Alachua, FL)	Complete discectomy with removal of nucleus pulposus and cartilaginous end plates but bony end plates preserved	2 dowels per patient 8 to 12 mL of graft
	24	L4/L5 (36%) L5/S1 (64%)	Anterior lumbar interbody fusion, open, with iliac crest bone graft	Transperitoneal or retroperitoneal	Dowel: MD-II threaded cortical bone dowel, Regeneration Technologies Inc. (Alachua, FL) Graft: autogenous	Complete discectomy with removal of nucleus pulposus and cartilaginous end plates but bony end plates preserved	Complete discectomy in every patient Two allograft bone dowels per patient
Burkus et al. 2002[20]	143	L4-L5 (26%) L5-S1 (74%) L5-L6 (0%)	Anterior lumbar interbody fusion, open, with rhBMP-2 on absorbable sponge carrier, and tapered interbody cages	81% retroperitoneal, 19% transperitoneal	Graft: InFuse Bone Graft, Medtronic Sofamor Danek (Memphis, TN) Sponge: InFuse applied to absorbable collagen sponge made from bovine tendon type I collagen (Integra LifeSciences, Plainsboro, NJ) and placed inside cage Cage: LT-Cage Lumbar Tapered Fusion Device (Medtronic Sofamor Danek, Memphis TN)	Complete discectomy including nucleus pulposus and cartilaginous endplates, with preservation of bony vertebral endplates	Disc height restored based on preoperative assessment and intraoperative anular tension assessment using double-barrel guide Dose of rhBMP-2 4.2 to 8.4 mg per patient

Study	Number of Patients	Level Fused	Fusion Strategy	Surgical Approach	Device	Adjunctive Surgery	Additional Information
	136	L4-L5 (24%) L5-S1 (76%) L5-L6 (0.7%)	Anterior lumbar interbody fusion, open, with iliac crest autograft and tapered interbody cages	80% retroperitoneal, 19% transperitoneal	Cage: LT-Cage Lumbar Tapered Fusion Device (Medtronic Sofamor Danek, Memphis TN) Graft: autogenous	Complete discectomy including nucleus pulposus and cartilaginous endplates, with preservation of bony vertebral endplates	Disc height restored based on preoperative assessment and intraoperative anular tension assessment using double-barrel guide

Data and Results

Table 92. Key Question 7: perioperative outcomes: rhBMP-2 versus autogenous bone graft

Outcomes	Study	Treatment Group	N =	Mean	Standard Deviation	p-Value	Mean Difference
Surgical Time	Dawson et al. 2009[18]	rhBMP-2	25	2.4 hours	0.7	p=0.415 (as reported in publication)	-0.20 (95% CI: -0.63 to 0.23)
		Autologous bone graft	21	2.6 hours	0.8		
	Burkus et al. 2002[19]	rhBMP-2	24	1.72 hours	Not reported	Not reported, insufficient data to calculate	Not reported, insufficient data to calculate
		Autologous bone graft	22	1.9 hours	Not reported		
	Burkus et al. 2002[20]	rhBMP-2	143	1.6 hours	Not reported	Not reported, insufficient data to calculate	Not reported, insufficient data to calculate
		Autologous bone graft	136	2.0 hours	Not reported		
Blood loss	Dawson et al. 2009[18]	rhBMP-2	25	329 mL	212.3	p=0.055 (as reported in publication)	-123.40 (95% CI: -245.96 to -0.84)
		Autologous bone graft	21	452.4 mL	210.0		
	Burkus et al. 2002[19]	rhBMP-2	24	124.1 mL	Not reported	p=0.026 (as reported in publication)	Not reported, insufficient data to calculate
		Autologous bone graft	22	245.0 mL	Not reported		
	Burkus et al. 2002[20]	rhBMP-2	143	109. 8 mL	Not reported	Not reported, insufficient data to calculate	Not reported, insufficient data to calculate
		Autologous bone graft	136	153.1 mL	Not reported		
Duration of Inpatient Stay	Dawson et al. 2009[18]	rhBMP-2	25	4.0 days	1.4	p=0.844 (as reported in publication)	-0.10 (95% CI: -0.834 to 0.638)
		Autologous bone graft	21	4.1 days	1.1		
	Burkus et al. 2002[19]	rhBMP-2	24	3.4 days	Not reported	Not reported, insufficient data to calculate	Not reported, insufficient data to calculate
		Autologous bone graft	22	3.7 days	Not reported		
	Burkus et al. 2002[20]	rhBMP-2	143	3.1 days	Not reported	Not reported, insufficient data to calculate	Not reported, insufficient data to calculate
		Autologous bone graft	136	3.3 days	Not reported		

Table 93. Key Question 7: back pain: rhBMP-2 versus autogenous bone graft at 6 weeks

Scale	Study	Treatment Group	Baseline N =	Baseline Mean	Baseline SD	6 Weeks N =	6 Weeks Mean	6 Weeks SD	p-Value	Mean Difference
Back pain analog score, 0–20	Burkus et al. 2002[19]	rhBMP-2	24	16.3	2.6	24 (100%)	8.9	4.5	p=0.297 (as reported in the study, of analysis of variance between groups)	1.50 (95% CI: -1.06 to 4.06)
		Autologous bone graft	22	16.3	2.2	21 (95%)	10.4	4.2		
	Burkus et al. 2002[20]	rhBMP-2	143	15.8	Not reported	139 (97%)	9.3	Not reported	Not reported, insufficient data reported to calculate	Not reported, insufficient data reported to calculate
		Autologous bone graft	136	16.1	Not reported	132 (97%)	8.8	Not reported		

SD = Standard deviation

Table 94. Key Question 7: back pain: rhBMP-2 versus autogenous bone graft at 3 months

Scale	Study	Treatment Group	Baseline N =	Baseline Mean	Baseline SD	3 Months N =	3 Months Mean	3 Months SD	p-Value	Mean Difference
Back pain analog score, 0–20	Burkus et al. 2002[19]	rhBMP-2	24	16.3	2.6	24 (100%)	7.9	4.3	p=0.038 (as reported in the study, of analysis of variance between groups)	3.0 (95% CI: 0.51 to 5.50)
		Autologous bone graft	22	16.3	2.2	21 (95%)	10.9	4.5		
	Burkus et al. 2002[20]	rhBMP-2	143	15.8	Not reported	140 (98%)	8.7	Not reported	Not reported, insufficient data reported to calculate	Not reported, insufficient data reported to calculate
		Autologous bone graft	136	16.1	Not reported	134 (99%)	9.0	Not reported		

SD = Standard deviation

Table 95. Key Question 7: back pain: rhBMP-2 versus autogenous bone graft at 6 months

Scale	Study	Treatment Group	Baseline N =	Baseline Mean	Baseline SD	6 Weeks N =	6 Weeks Mean	6 Weeks SD	p-Value	Mean Difference
Back pain analog score, 0–20	Burkus et al. 2002[19]	rhBMP-2	24	16.3	2.6	24 (100%)	6.8	4.3	p=0.034 (as reported in the study, of analysis of variance between groups)	3.10 (95% CI: 0.32 to 5.88)
		Autologous bone graft	22	16.3	2.2	20 (91%)	9.9	5.1		
	Burkus et al. 2002[20]	rhBMP-2	143	15.8	Not reported	136 (95%)	8.6	Not reported	Not reported, insufficient data reported to calculate	Not reported, insufficient data reported to calculate
		Autologous bone graft	136	16.1	Not reported	131 (96%)	8.9	Not reported		

CI = Confidence interval; SD = standard deviation

Table 96. Key Question 7: back pain: rhBMP-2 versus autogenous bone graft at 1 year

Scale	Study	Treatment Group	Baseline N =	Baseline Mean	Baseline SD	1 Year N =	1 Year Mean	1 Year SD	p-Value	Mean Difference
Back pain analog score, 0–20	Burkus et al. 2002[19]	rhBMP-2	24	16.3	2.6	24 (100%)	7.4	5.3	p=0.338 (as reported in the study, of analysis of variance between groups)	1.80 (95% CI: -1.67 to 5.27)
		Autologous bone graft	22	16.3	2.2	19 (86%)	9.2	6.3		
	Burkus et al. 2002[20]	rhBMP-2	143	15.8	Not reported	129 (90%)	8.0	Not reported	Not reported, insufficient data reported to calculate	Not reported, insufficient data reported to calculate
		Autologous bone graft	136	16.1	Not reported	125 (92%)	8.4	Not reported		

CI = Confidence interval; SD = standard deviation

Table 97. Key Question 7: back pain: rhBMP-2 versus autogenous bone graft at 2 years

Scale	Study	Treatment Group	Baseline N =	Baseline Mean	Baseline SD	2 Year N =	2 Year Mean	2 Year SD	p-Value	Mean Difference
Back pain analog score, 0–20	Burkus et al. 2002[19]	rhBMP-2	24	16.3	2.6	24 (100%)	7.4	6.0	p=0.047 (as reported in the study, of analysis of variance between groups)	3.50 (95% CI: -0.23 to 7.23)
		Autologous bone graft	22	16.3	2.2	17 (77%)	10.9	6.0		
	Burkus et al. 2002[20]	rhBMP-2	143	15.8	Not reported	122 (85%)	7.3	Not reported	Not reported, insufficient data reported to calculate	Not reported, insufficient data reported to calculate
		Autologous bone graft	136	16.1	Not reported	108 (79%)	7.9	Not reported		

CI = Confidence interval; SD = standard deviation

Table 98. Key Question 7: leg pain: rhBMP-2 versus autogenous bone graft at 6 weeks

Scale	Study	Treatment Group	Baseline N =	Baseline Mean	Baseline SD	6 Weeks N =	6 Weeks Mean	6 Weeks SD	p-Value	Mean Difference
Leg pain analog score, 0–20	Burkus et al. 2002[19]	rhBMP-2	24	12.8	5.7	24 (100%)	7.0	5.9	p=0.933 (as reported in the study, of analysis of variance between groups)	1.80 (95% CI: -1.66 to 5.26)
		Autologous bone graft	22	14.6	4.1	21 (95%)	8.8	5.9		
	Burkus et al. 2002[20]	rhBMP-2	143	12.5	Not reported	139 (97%)	7.5	Not reported	Not reported, insufficient data reported to calculate	Not reported, insufficient data reported to calculate
		Autologous bone graft	136	12.5	Not reported	132 (97%)	8.4	Not reported		

CI = Confidence interval; SD = standard deviation

Table 99. Key Question 7: leg pain: rhBMP-2 versus autogenous bone graft at 3 months

Scale	Study	Treatment Group	Baseline N =	Baseline Mean	Baseline SD	3 Months N =	3 Months Mean	3 Months SD	p-Value	Mean Difference
Leg pain analog score, 0–20	Burkus et al. 2002[19]	rhBMP-2	24	12.8	5.7	24 (100%)	6.2	4.4	p=0.874 (as reported in the study, of analysis of variance between groups)	2.10 (95% CI: -0.89 to 5.09)
		Autologous bone graft	22	14.6	4.1	21 (95%)	8.3	5.8		
	Burkus et al. 2002[20]	rhBMP-2	143	12.5	Not reported	140 (98%)	6.8	Not reported	Not reported, insufficient data reported to calculate	Not reported, insufficient data reported to calculate
		Autologous bone graft	136	12.5	Not reported	134 (99%)	6.8	Not reported		

CI = Confidence interval; SD = standard deviation

Table 100. Key Question 7: leg pain: rhBMP-2 versus autogenous bone graft at 6 months

Scale	Study	Treatment Group	Baseline N =	Baseline Mean	Baseline SD	6 Months N =	6 Months Mean	6 Months SD	p-Value	Mean Difference
Leg pain analog score, 0–20	Burkus et al. 2002[19]	rhBMP-2	24	12.8	5.7	24 (100%)	5.0	4.7	p=0.654 (as reported in the study, of analysis of variance between groups)	1.10 (95% CI: -1.61 to 3.81)
		Autologous bone graft	22	14.6	4.1	20 (91%)	6.1	4.4		
	Burkus et al. 2002[20]	rhBMP-2	143	12.5	Not reported	136 (95%)	6.3	Not reported	Not reported, insufficient data reported to calculate	Not reported, insufficient data reported to calculate
		Autologous bone graft	136	12.5	Not reported	131 (96%)	6.3	Not reported		

CI = Confidence interval; SD = standard deviation

Table 101. Key Question 7: leg pain: rhBMP-2 versus autogenous bone graft at 1 year

Scale	Study	Treatment Group	Baseline N =	Baseline Mean	Baseline SD	1 Year N =	1 Year Mean	1 Year SD	p-Value	Mean Difference
Leg pain analog score, 0–20	Burkus et al. 2002[19]	rhBMP-2	24	12.8	5.7	24 (100%)	5.5	5.5	p=0.818 (as reported in the study, of analysis of variance between groups)	2.60 (95% CI: -0.87 to 6.07)
		Autologous bone graft	22	14.6	4.1	19 (86%)	8.1	6.1		
	Burkus et al. 2002[20]	rhBMP-2	143	12.5	Not reported	129 (90%)	6.3	Not reported	Not reported, insufficient data reported to calculate	Not reported, insufficient data reported to calculate
		Autologous bone graft	136	12.5	Not reported	125 (92%)	6.6	Not reported		

CI = Confidence interval; SD = standard deviation

Table 102. Key Question 7: leg pain: rhBMP-2 versus autogenous bone graft at 2 years

Scale	Study	Treatment Group	Baseline N =	Baseline Mean	Baseline SD	2 Years N =	2 Years Mean	2 Years SD	p-Value	Mean Difference
Leg pain analog score, 0–20	Burkus et al. 2002[19]	rhBMP-2	24	12.8	5.7	24 (100%)	6.3	6.0	p=0.142 (as reported in the study, of analysis of variance between groups)	5.20 (95% CI: 1.40 to 9.01)
		Autologous bone graft	22	14.6	4.1	17 (77%)	11.5	6.3		
	Burkus et al. 2002[20]	rhBMP-2	143	12.5	Not reported	122 (85%)	6.3	Not reported	Not reported, insufficient data reported to calculate	Not reported, insufficient data reported to calculate
		Autologous bone graft	136	12.5	Not reported	108 (79%)	6.3	Not reported		

CI = Confidence interval; SD = standard deviation

Table 103. Key Question 7: function: rhBMP-2 versus autogenous bone graft at 6 weeks

Scale	Study	Treatment Group	Baseline N =	Baseline Mean	Baseline SD	6 Weeks N =	6 Weeks Mean	6 Weeks SD	p-Value	Mean Difference
Oswestry Disability Index	Burkus et al. 2002[19]	rhBMP-2	24	52.4	13.1	24 (100%)	39.9	16.8	p=0.307 (as reported in the study, of analysis of variance between groups)	7.30 (95% CI: -3.10 to 17.70)
		Autologous bone graft	22	55.3	13.5	21 (95%)	47.2	18.8		
	Burkus et al. 2002[20]	rhBMP-2	143	53.7	Not reported	140 (98%)	42.1	Not reported	Not reported, insufficient data reported to calculate	Not reported, insufficient data reported to calculate
		Autologous bone graft	136	55.1	Not reported	131 (96%)	41.4	Not reported		

CI = Confidence interval; SD = standard deviation

Table 104. Key Question 7: function: rhBMP-2 versus autogenous bone graft at 3 months

Scale	Study	Treatment Group	Baseline N =	Baseline Mean	Baseline SD	3 Months N =	3 Months Mean	3 Months SD	p-Value	Mean Difference
Oswestry Disability Index	Burkus et al. 2002[19]	rhBMP-2	24	52.4	13.1	24 (100%)	29.0	14.7	p=0.032 (as reported in the study, of analysis of variance between groups)	13.0 (95% CI: 3.14 to 22.86)
		Autologous bone graft	22	55.3	13.5	21 (95%)	42.0	19.0		
	Burkus et al. 2002[20]	rhBMP-2	143	53.7	Not reported	141 (99%)	33.5	Not reported	Not reported, insufficient data reported to calculate	Not reported, insufficient data reported to calculate
		Autologous bone graft	136	55.1	Not reported	134 (99%)	34.2	Not reported		

CI = Confidence interval; SD = standard deviation

Table 105. Key Question 7: function: rhBMP-2 versus autogenous bone graft at 6 months

Scale	Study	Treatment Group	Baseline N =	Baseline Mean	Baseline SD	6 Months N =	6 Months Mean	6 Months SD	p-Value	Mean Difference
Oswestry Disability Index	Burkus et al. 200219	rhBMP-2	24	52.4	13.1	24 (100%)	21.4	16.1	p=0.039 (as reported in the study, of analysis of variance between groups)	13.0 (95% CI: 1.79 to 24.21)
		Autologous bone graft	22	55.3	13.5	20 (91%)	34.4	21.8		
	Burkus et al. 2002[20]	rhBMP-2	143	53.7	Not reported	136 (95%)	29.3	Not reported	Not reported, insufficient data reported to calculate	Not reported, insufficient data reported to calculate
		Autologous bone graft	136	55.1	Not reported	131 (96%)	29.4	Not reported		

CI = Confidence interval; SD = standard deviation

Table 106. Key Question 7: function: rhBMP-2 versus autogenous bone graft at 1 year

Scale	Study	Treatment Group	Baseline N =	Baseline Mean	Baseline SD	1 Year N =	1 Year Mean	1 Year SD	p-Value	Effect Size
Oswestry Disability Index	Burkus et al. 2002[19]	rhBMP-2	24	52.4	13.1	24 (100%)	20.8	14.9	p=0.171 (as reported in the study, of analysis of variance between groups)	Mean Difference 9.2 (95% CI: -1.60 to 20.0)
		Autologous bone graft	22	55.3	13.5	19 (86%)	30.0	21.2		
	Burkus et al. 2002[20]	rhBMP-2	143	53.7	Not reported	130 (91%)	25.5	Not reported	Not reported, insufficient data reported to calculate	Not reported, insufficient data reported to calculate
		Autologous bone graft	136	55.1	Not reported	125 (92%)	25.6	Not reported		
Oswestry Disability Index, Attained Clinical Significance ≥15 point improvement	Burkus et al. 2002[19]	rhBMP-2	24	52.4	13.1	24	20 (83%)		p=0.072 (as calculated by the EPC in terms of odds ratio)	Odds Ratio 3.64 (95% CI: 0.89 to 14.86)
		Autologous bone graft	22	55.3	13.5	19	11 (58%)			

CI = Confidence interval; SD = standard deviation

Table 107. Key Question 7: function: rhBMP-2 versus autogenous bone graft at 2 years

Scale	Study	Treatment Group	Baseline N =	Baseline Mean	Baseline SD	2 Years N =	2 Years Mean	2 Years SD	p-Value	Effect size
Oswestry Disability Index	Burkus et al. 2002[19]	rhBMP-2	24	52.4	13.1	24 (100%)	18.9	14.5	p=0.039 (as reported in the study, of analysis of variance between groups)	13.9 (95% CI: 2.52 to 25.28)
		Autologous bone graft	22	55.3	13.5	17 (77%)	32.8	22.7		
	Burkus et al. 2002[20]	rhBMP-2	143	53.7	Not reported	122 (85%)	23.9	Not reported	Not reported, insufficient data reported to calculate	Not reported, insufficient data reported to calculate
		Autologous bone graft	136	55.1	Not reported	108 (79%)	23.8	Not reported		
Oswestry Disability Index, Attained Clinical Significance ≥15% improvement	Dawson et al. 2009[18]	rhBMP-2	25	—	—	23	21 (96%)		p=0.240 (as reported in the study)	Odds Ratio 3.50 (95% CI: 0.60 to 20.52)
		Autologous bone graft	21	—	—	20	15 (75%)			
	Burkus et al. 2002[20]	rhBMP-2	143	53.7	Not reported	122 (85%)	103 (84.4%)		p=0.681 (as calculated by the EPC in terms of odds ratio)	Odds Ratio 1.16 (95% CI: 0.58 to 2.32)
		Autologous bone graft	136	55.1	Not reported	108 (79%)	89 (82.4%)			
Oswestry Disability Index, Attained Clinical Significance ≥15 point improvement[a]	Burkus et al. 2002[19]	rhBMP-2	24	52.4	13.1	24 (100%)	20 (83%)		p=0.072 (as calculated by the EPC in terms of odds ratio)	Odds Ratio 3.64 (95% CI: 0.89 to 14.86)
		Autologous bone graft	22	55.3	13.5	19 (86%)	11 (58%)			
Return to work	Dawson et al. 2009[18]	rhBMP-2	25	6 (24%) working pre-surgery		23 (92%)	8 (35%) working		p=0.18 at baseline, p=0.74 at 2 years As calculated by the EPC	Odds Ratio 2 years 1.24 (95% CI: 0.34 to 4.50)
		Autologous bone graft	21	9 (43%) working pre-surgery		20 (95%)	6 (30%) working			
	Burkus et al. 2002[19]	rhBMP-2	24	11 (45.8%) working		24 (100%)	16 (66.7%) working		p=0.74 at baseline, p=0.055 at 2 years As calculated by the EPC	Odds Ratio 2 years 3.43 (95% CI: 0.97 to 12.10)
		Autologous bone graft	22	9 (40.9%) working		19 (86%)	7 (35.0%) working			
	Burkus et al. 2002[203]	rhBMP-2	143	54 (38%) working		122 (85%)	80 (66%) working		p=0.082 at baseline, p=0.121 at 2 years As calculated by the EPC	Odds ratio 2 years 1.52 (95% CI: 0.90 to 2.60)
		Autologous bone graft	136	38 (28%) working		108 (79%)	60 (56%) working			

[a] 1 Year data; study authors reported 24-month data were "similar."

CI = Confidence interval; SD = standard deviation

Table 108. Key Question 7: quality of life: rhBMP-2 versus autogenous bone graft at 6 weeks

Scale	Study	Treatment Group	Baseline N =	Baseline Mean	Baseline SD	6 Weeks N =	6 Weeks Mean	6 Weeks SD	p-Value	Mean Difference
SF-36, physical component	Burkus et al. 200219a	rhBMP-2	24	30	Not reported	Not reported	32	Not reported	Not reported, insufficient data reported to calculate	Not reported, insufficient data reported to calculate
		Autologous bone graft	22	30	Not reported	Not reported	32	Not reported		

Scale	Study	Treatment Group	Baseline N =	Baseline Mean	Baseline SD	6 Weeks N =	6 Weeks Mean	6 Weeks SD	p-Value	Mean Difference
SF-36, mental component	Burkus et al. 200219a	rhBMP-2	24	43	Not reported	Not reported	47.5	Not reported	Not reported, insufficient data reported to calculate	Not reported, insufficient data reported to calculate
		Autologous bone graft	22	43	Not reported	Not reported	45	Not reported		

[a] Data estimated from figure.

CI = Confidence interval; SD = standard deviation

Table 109. Key Question 7: quality of life: rhBMP-2 versus autogenous bone graft at 3 months

Scale	Study	Treatment Group	Baseline N =	Baseline Mean	Baseline SD	3 Months N =	3 Months Mean	3 Months SD	p-Value	Mean Difference
SF-36, physical component	Burkus et al. 200219a	rhBMP-2	24	30	Not reported	Not reported	38	Not reported	Not reported, insufficient data reported to calculate	Not reported, insufficient data reported to calculate
		Autologous bone graft	22	30	Not reported	Not reported	31	Not reported		
SF-36, mental component	Burkus et al. 200219a	rhBMP-2	24	43	Not reported	Not reported	48	Not reported	Not reported, insufficient data reported to calculate	Not reported, insufficient data reported to calculate
		Autologous bone graft	22	43	Not reported	Not reported	49	Not reported		

[a] Data estimated from figure.

CI = Confidence interval; SD = standard deviation

Table 110. Key Question 7: quality of life: rhBMP-2 versus autogenous bone graft at 6 months

Scale	Study	Treatment Group	Baseline N =	Baseline Mean	Baseline SD	6 Months N =	6 Months Mean	6 Months SD	p-Value	Mean Difference
SF-36, physical component	Burkus et al. 200219a	rhBMP-2	24	30	Not reported	Not reported	44	Not reported	Not reported, insufficient data reported to calculate	Not reported, insufficient data reported to calculate
		Autologous bone graft	22	30	Not reported	Not reported	38	Not reported		
SF-36, mental component	Burkus et al. 200219a	rhBMP-2	24	43	Not reported	Not reported	48	Not reported	Not reported, insufficient data reported to calculate	Not reported, insufficient data reported to calculate
		Autologous bone graft	22	43	Not reported	Not reported	50	Not reported		

[a] Data estimated from figure.

CI = Confidence interval; SD = standard deviation

Table 111. Key Question 7: quality of life: rhBMP-2 versus autogenous bone graft at 1 year

Scale	Study	Treatment Group	Baseline N =	Baseline Mean	Baseline SD	1 Year N =	1 Year Mean	1 Year SD	p-Value	Mean Difference
SF-36, physical component	Burkus et al. 2002[19a]	rhBMP-2	24	30	Not reported	Not reported	46	Not reported	Not reported, insufficient data reported to calculate	Not reported, insufficient data reported to calculate
		Autologous bone	22	30	Not	Not	40	Not		

Scale	Study	Treatment Group	Baseline N =	Baseline Mean	Baseline SD	1 Year N =	1 Year Mean	1 Year SD	p-Value	Mean Difference
		graft			reported	reported		reported		
SF-36, mental component	Burkus et al. 2002[19a]	rhBMP-2	24	43	Not reported	Not reported	46	Not reported	Not reported, insufficient data reported to calculate	Not reported, insufficient data reported to calculate
		Autologous bone graft	22	43	Not reported	Not reported	48	Not reported		

[a] Data estimated from figure.

CI = Confidence interval; SD = standard deviation

Table 112. Key Question 7: quality of life: rh-BMP-2 versus autogenous bone graft at 2 years

Scale	Study	Treatment Group	Baseline N =	Baseline Mean	Baseline SD	2 Years N =	2 Years Mean	2 Years SD	p-Value	Mean Difference
SF-36, physical component	Burkus et al. 2002[19a]	rhBMP-2	24	30	Not reported	Not reported	51	Not reported	Not reported, insufficient data reported to calculate	Not reported, insufficient data reported to calculate
		Autologous bone graft	22	30	Not reported	Not reported	41	Not reported		

[a] Data estimated from figure.

CI = Confidence interval; SD = standard deviation

Table 113. Key Question 7: adverse events: rh-BMP-2 versus autogenous bone graft

Study	Duration of Followup	Adverse Event	rhBMP-2	Autologous Bone Graft
Dawson et al. 2009[18]	Intraoperative	Incidental durotomy, repaired	1 (4%)	1 (5%)
Dawson et al. 2009[18]	Intraoperative	Wound infection, surgical site	1 (4%)	1 (5%)
Dawson et al. 2009[18]	Perioperative	Wound infection, graft donor site	0	1 (5%)
Dawson et al. 2009[18]	Perioperative	Reoperation, due to bilateral malpositioned pedicle screws	1 (4%)	0
Dawson et al. 2009[18]	Short-term 6 months	Reoperation, hardware removal	1 (4%)	0
Dawson et al. 2009[18]	Intermediate	Reoperation, pseudarthrosis	0	2 (8%)
Burkus et al. 2002[19]	Perioperative	Reoperation due to residual disc material	0	1 (5%)
Burkus et al. 2002[19]	Intermediate	Reoperation, additional posterior fixation	0	3 (14%)
Burkus et al. 2002[19]	Short to intermediate term	Reoperation, additional posterior fixation	1 (4%)	0
Burkus et al. 2002[20]	Perioperative	Reoperation, implant removal, vertebral bone fracture and implant replacement	1 (0.7%)	0

Study	Duration of Followup	Adverse Event	rhBMP-2	Autologous Bone Graft
Burkus et al. 2002[20]	Short-term	Reoperation, implant removal, implant displacement and possible failed fusion	1 (0.7%)	0
Burkus et al. 2002[20]	Intraoperative	Vascular events	6 (4.2%)	5 (3.7%)
Burkus et al. 2002[20]	Intraoperative	Iliac crest graft site harvesting events	0 (not applicable)	8 (5.9%)
Burkus et al. 2002[20]	Short to intermediate term	Retrograde ejaculation	5 (6.4% of males)	1 (1.4% of males)
Burkus et al. 2002[20]	Short to intermediate term	Reoperation, supplemental fixation	9 (6%) For presumed pseudarthrosis (n=7), persistent radicular symptoms (n=1), or pan-lumbar fusion for discogenic back pain (n=1)	14 (10%) For presumed pseudarthrosis (n=12) and persistent discogenic pain (n=2)

Risk-of-Bias Assessment

Table 114. Key Question 7: risk-of-bias assessment, rhBMP-2 versus autogenous bone graft

Assessment Item	Dawson et al. 2009[18]	Burkus et al. 2002[19]	Burkus et al. 2002[110]
Were patients randomly assigned to treatment?	Yes	Yes	Yes
Was group allocation concealed?	No	No	No
For non-randomized trials, did the study employ other methods to enhance group comparability?	Yes	Yes	Yes
Was patient assignment independent of physician and patient preference?	Yes	Yes	Yes
Did patients in different study groups have similar levels of performance on the outcome of interest when they were assigned to groups?	Yes	Yes	Yes
Were the study groups comparable for all other important factors when they were assigned to groups?	Yes	Yes	Yes
Was the comparison of interest prospectively planned?	Yes	Yes	Yes
If patients received ancillary treatment(s), was there a 5% or less difference between groups in the proportion of patients receiving each ancillary treatment?	Yes	Yes	Yes
Were the two groups treated concurrently?	Yes	Yes	Yes
Were patients blinded to the treatment they received?	No	No	No
Were outcome assessors blinded to which treatment patients had?	No	No	No
For questions comparing fusion, did the two groups' surgeons have similar numbers of prior operations performing the procedure they performed in the study?	Not reported	Not reported	Not reported
Was the primary outcome measure of interest objective and was it objectively measured?	No	No	No
Was there a 15% or less difference in the length of followup for the two groups for the comparison time point of interest?	Yes	Yes	Yes
Did at least 85% of patients who provided baseline data provide data at the time point of interest?	Yes	Yes	Yes
Was there a 15% or less difference between groups in the percentage of patients who provided data at the time point of interest?	Yes	Yes	Yes
Risk-of-bias assessment	Moderate	Moderate	Moderate

Open Mini ALIF Versus Laparoscopic ALIF

Study, Patient, and Intervention Descriptions

Table 115. Key Question 7: study design: open mini versus laparoscopic anterior lumbar interbody fusion

Study	Study Design	Enrollment Years	Location	Setting	Funding
Chung et al. 2003[21]	Randomized controlled trial (RCT)	1997–1999	Seoul, Korea	Author affiliation spine hospital	Not reported

Table 116. Key Question 7: patient inclusion criteria: open mini versus laparoscopic anterior lumbar interbody fusion

Study	Diagnosis Included	Duration of Symptoms	Diagnostic Criteria	Conditions Excluded	Previous Treatment Requirements	Age Requirements
Chung et al. 2003[21]	Degenerated disc	At least 6 months	Plain radiograph, MRI, and discography with pain provocation	Spondylolisthesis, spinal infection, severe osteoporosis, spinal stenosis, previous spinal fusion surgery	At least 6 months nonoperative	Not reported

Table 117. Key Question 7: patient characteristics: demographic and occupational history: open mini versus laparoscopic anterior lumbar interbody fusion

Study	Number Screened for Inclusion	Number Enrolled	Age	Women	Race or Ethnicity	Occupational Status	Workers Compensation	Pending Litigation
Chung et al. 2003[21]	54	54 (100%), 51 (94%) had perioperative outcomes reported	Mean 50 (range 27–67) years (49 years laparoscopic, 50 years mini open)	75% (77% laparoscopic, 73% mini open)	Not reported Study in Korea	Not reported	Not reported	Not reported

Table 118. Key Question 7: patient characteristics: health history: open mini versus laparoscopic anterior lumbar interbody fusion

Study	Surgical Indication	Number of Levels Affected	Duration of Symptoms	Primary or Recurrent?	Previous Conservative Treatment(s)	Duration of Conservative Treatments	Previous Surgery	Percent with Radicular Pain	Comorbid Diagnoses
Chung et al. 2003[21]	Degenerated discs (100%)	One	Not reported	Appears primary	Not reported	Not reported (at least 6 months)	No previous spinal fusion Previous abdominal surgery 20% Previous disc surgery 7%	Not reported	Not reported

Table 119. Key Question 7: treatment characteristics: fusion: laparoscopic

Study	Number of Patients	Level Fused	Fusion Strategy	Surgical Approach	Device
Chung et al. 2003[21]	22	L5-S1	By anterior laparoscopic approach	Anterior, transperitoneal	Cage: Brantigan carbon cage, DePuy (Raynham, MA) Graft: Autologous bone
	22	L5-S1	By anterior mini open approach	Anterior, midline extraperitoneal	Cage: Brantigan carbon cage, DePuy (Raynham, MA) Graft: Autologous bone

Data and Results

Table 120. Key Question 7: perioperative outcomes: open mini versus laparoscopic anterior lumbar interbody fusion

Study	Outcomes	Treatment Group	N =	Mean	Standard Deviation	p-Value	Mean Difference
Chung et al. 2003[21]	Surgical Time	Laparoscopic surgery	27	158 minutes	Range 90–330	p=0.001 (as reported in the study)	Not reported, insufficient data reported to calculate
		Mini-open surgery	24	83 minutes	Range 40–150		
	Blood loss	Laparoscopic surgery	27	85 mL	Range 10–300	p=Not statistically significant (as reported in the study)	Not reported, insufficient data reported to calculate
		Mini-open surgery	24	68 mL	Range 50–150		
	Duration of Inpatient Stay	Laparoscopic surgery	27	3.9 days	Range 2–7	p=Not statistically significant (as reported in the study)	Not reported, insufficient data reported to calculate
		Mini-open surgery	24	3.4 days	Range 2–6		

Table 121. Key Question 7: adverse events: mini open surgery versus laparoscopic surgery

Study	Duration of Followup	Adverse Event	Mini-Open	Laparoscopic
Chung et al. 2003[21]	Perioperative	Cage malposition, led to symptomatic pseudarthrosis		1 (5%)
		Retrograde ejaculation		1 (5%)
		Bladder dysfunction	1 (5%)	1 (5%)
		Deep vein thrombosis	1 (5%)	

Risk-of-Bias Assessment

Table 122. Key Question 7: risk-of bias-assessment: open mini versus laparoscopic anterior lumbar interbody fusion

Assessment Item	Chung et al. 200321
Were patients randomly assigned to treatment?	Yes
Was group allocation concealed?	No
For non-randomized trials, did the study employ other methods to enhance group comparability?	Yes
Was patient assignment independent of physician and patient preference?	Yes
Did patients in different study groups have similar levels of performance on the outcome of interest when they were assigned to groups?	Yes
Were the study groups comparable for all other important factors when they were assigned to groups?	Yes
Was the comparison of interest prospectively planned?	Yes

Assessment Item	Chung et al. 200321
If patients received ancillary treatment(s), was there a 5% or less difference between groups in the proportion of patients receiving each ancillary treatment?	Yes
Were the two groups treated concurrently?	Yes
Were patients blinded to the treatment they received?	No
Were outcome assessors blinded to which treatment patients had?	No
For questions comparing fusion, did the two groups' surgeons have similar numbers of prior operations performing the procedure they performed in the study?	Not reported
Was the primary outcome measure of interest objective and was it objectively measured?	Yes
Was there a 15% or less difference in the length of followup for the two groups for the comparison time point of interest?	Yes
Did at least 85% of patients who provided baseline data provide data at the time point of interest?	Yes
Was there a 15% or less difference between groups in the percentage of patients who provided data at the time point of interest?	Yes
Risk-of-bias rating	Moderate

Transperitoneal Versus Retroperitoneal Anterior Surgical Approach

Study, Patient, and Intervention Descriptions

Table 123. Key Question 7: study design: transperitoneal versus retroperitoneal anterior surgical approach

Study	Study Design	Enrollment Years	Location	Setting	Funding	Additional Information
Sasso et al. 2003[23] A subgroup of Burkus et al. 2002,[20] but comparison is not redundant	Randomized controlled trial (RCT), subgroup comparison	Not reported	Multicenter, various cities, United States	Author affiliations spine specialty centers, orthopedic center, University, Neurologic Institute	Sponsored by Medtronic	Comparison of interest (surgical approach) not directly affected by financial conflict of interest

Table 124. Key Question 7: patient inclusion criteria: transperitoneal versus retroperitoneal anterior surgical approach

Study	Diagnosis Included	Number of Levels Affected	Duration of Symptoms	Primary or Secondary	Diagnostic Criteria	Conditions Excluded	Previous Treatment Requirements	Age Requirements
Sasso et al. 2003[23]	Degenerated disc with disabling low back and/or leg pain	One	At least 6 months	Appears primary	Not reported	Not reported	At least 6 months conservative, not specified	Not reported

Table 125. Key Question 7: patient characteristics: demographic and occupational history: transperitoneal versus retroperitoneal anterior surgical approach

Study	Number Screened for Inclusion	Number Enrolled	Age	Women	Race or Ethnicity	Occupational Status	Workers Compensation	Pending Litigation
Sasso et al. 2003[23]	Not reported	279, 149 men assessed	Mean 43 years	48% in whole study, 100% men assessed in this comparison	Not reported	42% working	34%	14%

Table 126. Key Question 7: patient characteristics: health history: transperitoneal versus retroperitoneal anterior surgical approach

Study	Surgical Indication	Duration of Symptoms	Previous Conservative Treatment(s)	Duration of Conservative Treatments	Previous Surgery	Percent with Radicular Pain	Comorbid Diagnoses
Sasso et al. 2003[23]	Degenerated disc, symptomatic	Not reported	Not reported	Not reported	Not reported	Not reported	Tobacco 34%

Table 127. Key Question 7: treatment characteristics: fusion: transperitoneal surgical approach

Study	Number of Patients	Level Fused	Fusion Strategy	Surgical Approach	Device
Sasso et al. 2003[23]	30	Either L4/L5 or L5/S1	Transperitoneal exposure, anterior lumbar interbody fusion with or without rhBMP	Anterior, transperitoneal	Some patients had rhBMP; this was not associated with outcome and therefore data from patients with and without rhBMP were combined
	116	Either L4/L5 or L5/S1	Retroperitoneal exposure, anterior lumbar interbody fusion with or without rhBMP	Anterior, retroperitoneal	Some patients had rhBMP; this was not associated with outcome and therefore data from patients with and without rhBMP were combined

Data and Results

Table 128. Key Question 7: transperitoneal versus retroperitoneal anterior surgical approach: adverse events

Study	Duration of Followup	Adverse Event	Retroperitoneal Approach	Transperitoneal Approach
Sasso et al. 2003[23]	Intermediate (12 months)	Retrograde ejaculation	2 (2%)	4 (13%)
Sasso et al. 2003[23]	Intermediate (24 months)	Retrograde ejaculation, permanent	1 (1%)	3 (10%)

Risk-of-Bias Assessment

Table 129. Key Question 7: risk-of-bias assessment: transperitoneal versus retroperitoneal anterior surgical approach

Assessment Item	Sasso et al. 2003[23]
Were patients randomly assigned to treatment?	Yes
Was group allocation concealed?	No
For non-randomized trials, did the study employ other methods to enhance group comparability?	Yes
Was patient assignment independent of physician and patient preference?	Yes
Did patients in different study groups have similar levels of performance on the outcome of interest when they were assigned to groups? *This will only be used for outcomes that have a baseline measure.*	Yes
Were the study groups comparable for all other important factors when they were assigned to groups?	Yes
Was the comparison of interest prospectively planned?	No
If patients received ancillary treatment(s), was there a 5% or less difference between groups in the proportion of patients receiving each ancillary treatment?	Yes
Were the two groups treated concurrently?	Yes
Were patients blinded to the treatment they received?	No
Were outcome assessors blinded to which treatment patients had?	No
For questions comparing fusion, did the two groups' surgeons have similar numbers of prior operations performing the procedure they performed in the study?	Not reported
Was the primary outcome measure of interest objective and was it objectively measured?	Yes
Was there a 15% or less difference in the length of followup for the two groups for the comparison time point of interest? This item is not relevant to perioperative outcomes.	Yes
Did at least 85% of patients who provided baseline data provide data at the time point of interest?	Yes
Was there a 15% or less difference between groups in the percentage of patients who provided data at the time point of interest?	Yes
Risk-of-bias rating	Moderate

Posterolateral Fusion, With or Without Variable Screw Placement, or Circumferential Fusion

Study, Patient, and Intervention Descriptions

Table 130. Key Question 7: study design: posterolateral fusion, with or without variable screw placement, or circumferential fusion

Study	Study Design	Enrollment Years	Location	Setting	Funding	Additional Information
Fritzell et al. 2002[22a]	Randomized controlled trial (RCT)	1992-1998	Sweden	Multicenter orthopedic departments (19)	Acromed Corporation (Cleveland OH); Ossano Scandinavia AB, Stockholm, Sweden	Another account of study reported on in Fritzell et al. 2001,[11] included in Key Question 1

[a] 41% of patients treated at two levels.

Table 131. Key Question 7: patient inclusion criteria: posterolateral fusion, with or without variable screw placement, or circumferential fusion

Study	Diagnosis Included	Number of Levels Affected	Duration of Symptoms	Primary or Secondary	Diagnostic Criteria	Conditions Excluded	Previous Treatment Requirements	Age Requirements
Fritzell et al. 2002[22]	Degenerated discs	One or two	At least two years	Appears primary	Surgeon clinical interpretation of severe low back pain from L4-L5, L5-S1, or both Degenerative disc changes on plain radiographs, CT scan, and/or MRI Consensus by two surgeons that the patient met eligibility requirements	"Obvious" ongoing psychiatric illness Radiographically demonstrated isthmic spondylolisthesis, stenosis, new or old fractures, infection, inflammation, neoplasm, or other specific findings Nerve root compression with disc herniation	On "sick leave or equivalent pain and disability" for previous year despite conservative treatment efforts and lifestyle modifications No previous spine surgery, with exception of herniated disc removal >2 years before study with nerve root symptom resolution	25-65 years

Table 132. Key Question 7: patient characteristics: demographic and occupational history: posterolateral fusion, with or without variable screw placement, or circumferential fusion

Study	Number Screened for Inclusion	Number Enrolled	Age	Women	Race or Ethnicity	Occupational Status	Workers Compensation	Pending Litigation
Fritzell et al. 2002[22]	Not reported	222 randomized 18 dropped out before treatment to go to nonsurgical control 204 (92%) treated	Mean 43 years (Range 25-65) (posterolateral fusion 44, with variable screw placement 43, circumferential 42)	49% (posterolateral fusion 48%, with variable screw placement 39%, circumferential 60%)	Not reported (conducted in Sweden)	Working full or part time 21% (posterolateral fusion 18%, with variable screw placement 28%, circumferential 17%)	100% Disability pension 20% (posterolateral fusion 23%, with variable screw placement 20%, circumferential 17%)	Litigation or compensation 61% (posterolateral fusion 69%, with variable screw placement 57%, circumferential 56%)

Table 133. Key Question 7: patient characteristics: health history: posterolateral fusion, with or without variable screw placement, or circumferential fusion

Study	Surgical Indication	Duration of Symptoms	Previous Conservative Treatment(s)	Duration of Conservative Treatments	Previous Surgery	Percent with Radicular Pain	Comorbid Diagnoses
Fritzell et al. 2002[22]	Degenerated discs	Not reported (at least 2 years)	Not reported	Not reported (at least 1 year)	Successful herniated disc removal >2 years previous 18% (posterolateral 25%, with variable screw placement 18%, circumferential 13%) No other previous spine surgery permitted	Not reported. Patients with dominant leg pain excluded.	Any 39% (posterolateral 33%, with variable screw placement 35%, circumferential 49%) Smoking 41% (posterolateral 39%, with variable screw placement 43%, circumferential 40%)

Table 134. Key Question 7: treatment characteristics: posterolateral fusion, with or without variable screw placement, or circumferential fusion

Study	Number of Patients	Level Fused	Fusion Strategy	Surgical Approach	Device(s)	Additional information
Fritzell et al. 2002[22]	73 randomized	L4-L5 and/or L5-S1	Posterolateral fusion without internal fixation	Posterior	Graft: autologous iliac crest bone graft	Disc material removed laterally and centrally Subchondral support for grafts created using variable screw placement instrument Tricortical bone blocks placed with "slight distraction" but compressed when instruments locked No spacers used No intention of decompression Patients walking within a couple days Patients with internal fixation wore reinforced canvas corset for 5 months, patients without worse rigid plastic
	74 randomized	L4-L5 and/or L5-S1	Posterolateral fusion with variable screw placement and an internal fixation device	Posterior	Pedicle screws and open bendable plates: DePuy Acromed (DePuy, Raynham, MA) Graft: autologous iliac crest bone graft	
	75 randomized	L4-L5 and/or L5-S1	Posterolateral fusion with variable screw placement and interbody fusion; "circumferential" fusion	Anterior and posterior (n=56) or posterior (n=19), according to surgeon preference	Pedicle screws and open bendable plates: DePuy Acromed (DePuy, Raynham, MA) Graft: autologous iliac crest bone graft	

Data and Results

Table 135. Key Question 7: perioperative outcomes: posterolateral fusion, with or without variable screw placement, or circumferential fusion

Study	Outcomes	Treatment Group	N =	Mean	Standard Deviation	p-Valuea	Mean Difference
Fritzell et al. 2002[22]	Surgical Time	Posterolateral fusion without internal fixation (PLF)	68	110 minutes	38	Posterolateral fusion without instrumentation vs. circumferential: p<0.0001 Posterolateral fusion with instrumentation vs. circumferential: p=0.005 Posterolateral fusion with and without internal fixation: p<0.0001	PLF vs. circumferential: 225 (95% CI: 199.86 to 250.15) VSP vs. circumferential: 141 (95% CI: 110.18 to 171.82) PLF vs. VSP: 84 (95% CI: 63.2 to 104. 79)
		Posterolateral fusion with variable screw placement and an internal fixation device (VSP)	60	194 minutes	77		
		Circumferential fusion	70	335 minutes	98		
	Blood loss	PLF	68	665 mL	895	Posterolateral fusion without instrumentation vs.	PLF vs. circumferential: 768.00 (95% CI: 403.5 to 1132.48)
		VSP	60	1284 mL	1125		

Study	Outcomes	Treatment Group	N =	Mean	Standard Deviation	p-Valuea	Mean Difference
		Circumferential fusion	68	1433 mL	1236	circumferential: p<0.0001 Posterolateral fusion with and without internal fixation: p<0.001 Posterolateral fusion with instrumentation and circumferential fusion not statistically different.	PLF vs. VSP: 149.00 (95% CI: -262.49 to 560.49) VSP vs. circumferential fusion: 619.00 (95% CI: 267.11 to 970.89)
	Duration of Inpatient Stay	PLF	68	8.5 days	2.6	Posterolateral fusion with instrumentation vs. circumferential: p=0.005 Posterolateral fusion without instrumentation vs. circumferential: p<0.001 Posterolateral fusion with and without instrumentation not significantly different.	PLF vs. circumferential: 3.00 (95% CI: 1.92 to 4.08) PLF vs. VSP: 1.80 (95% CI: 0.59 to 3.00) VSP vs. circumferential fusion: 1.20 (95% CI: 0.19 to 2.21)
		VSP	60	9.7 days	3.2		
		Circumferential fusion	70	11.5 days	3.7		

[a] As reported in the study, calculated using Mann Whitney U test. P-value of less than 0.01 was considered statistically significant.

Table 136. Key Question 7: back pain: posterolateral fusion, with or without variable screw placement, or circumferential fusion

Study	Scale	Treatment Group	Baseline N =	Baseline Mean	Baseline SD	2 Years N =	2 Years Mean	2 Years SD	p-Value	Mean Difference (of 2 Year scores)
Fritzell et al. 2002[22]	Visual analog scale (VAS) 0-100, back pain	Posterolateral fusion without internal fixation (PLF)	72 treated	64.1	14.2	62 (86%)	45.1	23.6	No statistically significant differences between groups, based upon change in each group calculated using Kruskal-Wallis test, as reported by study	PLF vs. VSP 4.70 (95% CI: -3.76 to 13.17) PLF vs. circumferential: 0.60 (95% CI: -8.18 to 9.38) VSP vs. circumferential: 5.30 (95% CI: -3.60 to 14.3)
		Posterolateral fusion with variable screw placement and an internal fixation device (VSP)	65 treated	63.3	13.3	59 (91%)	40.4	23.9		
		Circumferential fusion	71 treated	65.6	15.2	65 (92%)	45.7	26.7		
Fritzell et al. 2002[22]	VAS 0-100, leg pain	PLF	72 treated	32.6	23.6	62 (86%)	25.6	24.8	No statistically significant differences between groups, based upon change in each group calculated using Kruskal-Wallis test, as reported by study	PLF vs. VSP 4.30 (95% CI: -5.02 to 13.62) PLF vs. circumferential: 6.10 (95% CI: -3.15 to 15.4) VSP vs. circumferential: 1.80 (95% CI: -8.02 to 11.6)
		VSP	65 treated	36.1	25.0	59 (91%)	29.9	27.5		
		Circumferential fusion	71 treated	36.7	27.8	65 (92%)	31.7	28.2		

CI = Confidence interval; SD = standard deviation

Table 137. Key Question 7: function: posterolateral fusion, with or without variable screw placement, or circumferential fusion

Study	Scale	Treatment Group	Baseline N =	Baseline Mean	Baseline SD	2 Years N =	2 Years Mean	2 Years SD	p-Value	Mean Difference (of 2 year scores)
Fritzell et al. 2002[22]	Oswestry disability index	Posterolateral fusion without internal fixation	72 treated	47.3	11.3	62 (86%)	36.5	16.3	No statistically significant differences between groups, based upon change in each group calculated using Kruskal-Wallis test, as reported in study	PLF vs. VSP: 2.90 (95% CI: -3.20 vs. 9.0) PLF vs. Circumferential: 2.90 (95% CI: -4.15 to 8.15) VSP vs. circumferential: 4.90 (95% CI: -1.60 to 11.40)
		Posterolateral fusion with variable screw placement and an internal fixation device	65 treated	48.4	11.6	59 (91%)	33.6	17.9		
		Circumferential fusion	71 treated	47.3	10.9	65 (92%)	38.5	18.9		
Fritzell et al. 2002[22]	Million	Posterolateral fusion without internal fixation	72 treated	63.1	9.9	62 (86%)	46.2	21.0	No statistically significant differences between groups, based upon change in each group calculated using Kruskal-Wallis test, as reported in study	PLF vs. VSP 1.80 (95% CI: -6.20 to 9.79) PLF vs. circumferential: 1.60 (95% CI: -6.18 to 9.38) VSP vs. circumferential: 3.40 (95% CI: -4.95 to 11.75)
		Posterolateral fusion with variable screw placement and an internal fixation device	65 treated	64.2	11.7	59 (91%)	44.4	23.8		
		Circumferential fusion	71 treated	64.5	12.1	65 (92%)	47.8	23.6		
Fritzell et al. 2002[22]	General function scale	Posterolateral fusion without internal fixation	72 treated	47.8	16.2	62 (86%)	35.5	21.7	No statistically significant differences between groups, based upon change in each group calculated using Kruskal-Wallis test, as reported in study	PLF vs. VSP 5.60 (95% CI:-2.02 to 12.22) PLF vs. circumferential: 0.80 (95% CI: -7.23 to 8.83) VSP vs. circumferential: 6.40 (95% CI: -1.63 to 14.43)
		Posterolateral fusion with variable screw placement and an internal fixation device	65 treated	47.5	15.6	59 (91%)	29.9	21.0		
		Circumferential fusion	71 treated	52.5	15.4	65 (92%)	36.3	24.3		

SD = Standard deviation

Table 138. Key Question 7: adverse events: posterolateral fusion, with or without variable screw placement, or circumferential fusion

Study	Duration of Followup	Adverse Event	Posterolateral fusion without internal fixation	Posterolateral fusion with variable screw placement and an internal fixation device	Circumferential fusion
Fritzell et al. 2011[22]	Intraoperative	Dural tear, minor			1 (1.6%)
	Intraoperative	Laterally placed screw			1 (1.6%)
	Intraoperative	Major bleeding			2 (3%)
	Intraoperative	Wrong-level surgery, reoperation required at 6 months			1 (1.6%)
	Perioperative	"Damage of the nervus cut fem lat at the donor site"			1 (1.6%)
	Perioperative	Arm pain, new		1 (1.5%)	
	Perioperative	Gastrointestinal bleeding	1 (1.4%)	2 (3%)	
	Perioperative	Heart failure and gastrointestinal bleeding			1 (1.6%)
	Perioperative	Hematoma, donor site, minor			2 (3%)
	Perioperative	Laterally placed screw		1 (1.5%)	
	Perioperative	Nerve root pain, new		1 (1.5%)	5 (7%)
	Perioperative	Nerve root sensations, new, hit by pedicle screw			2 (3%)
	Perioperative	Pulmonary edema			1 (1.6%)
	Perioperative	Reoperation, nerve root hit by pedicle screw		1 (1.5%)	
	Perioperative	Skin problem		1 (1.5%)	
	Perioperative	Skin problem, chin			1 (1.6%)
	Perioperative	Sympathetic chain damages (minor)			2 (3%)
	Perioperative	Thrombosis		1 (1.5%)	
	Perioperative	Thrombosis and pulmonary embolus	1 (1.4%)		
	Perioperative	Wing scapula	1 (1.4%)		
	Perioperative	Wound infection, deep, no surgery required		2 (3%)	1 (1.6%)
	Perioperative	Wound infection, superficial	1 (1.4%)	1 (1.5%)	
	Perioperative (?)	Aspiration-sepsis-ARDS			1 (1.6%)
	Short to intermediate (6-12 months)	Surgery, deep wound infection		2 (3%)	
	Less than 1 year	New surgery, pseudarthrosis	2 (3%)		
	Not reported	Donor site pain (minor)	1 (1.4%)		
	Not reported	Donor site pain, minor		1 (1.5%)	

Risk-of-Bias Assessment

Table 139. Key Question 7: risk-of-bias assessment: posterolateral fusion, with or without variable screw placement, or circumferential fusion

Assessment Item	Fritzell et al. 2002[22]
Were patients randomly assigned to treatment?	Yes
Was group allocation concealed?	No
For non-randomized trials, did the study employ other methods to enhance group comparability?	Yes
Was patient assignment independent of physician and patient preference?	Yes
Did patients in different study groups have similar levels of performance on the outcome of interest when they were assigned to groups?	Yes
Were the study groups comparable for all other important factors when they were assigned to groups?	Yes

Assessment Item	Fritzell et al. 2002[22]
Was the comparison of interest prospectively planned?	Yes
If patients received ancillary treatment(s), was there a 5% or less difference between groups in the proportion of patients receiving each ancillary treatment?	Yes
Were the two groups treated concurrently?	Yes
Were patients blinded to the treatment they received?	No
Were outcome assessors blinded to which treatment patients had?	No
For questions comparing fusion, did the two groups' surgeons have similar numbers of prior operations performing the procedure they performed in the study?	Not reported
Was the primary outcome measure of interest objective and was it objectively measured?	No
Was there a 15% or less difference in the length of followup for the two groups for the comparison time point of interest?	Yes
Did at least 85% of patients who provided baseline data provide data at the time point of interest?	Yes
Was there a 15% or less difference between groups in the percentage of patients who provided data at the time point of interest?	Yes
Risk-of-bias rating	Moderate

Key Question 8: For adults with pain associated with degenerative stenosis of the lumbar spine, do spinal fusion approaches (e.g., anterior, posterior, combined) and techniques (e.g., instrumentation, graft material) performed alone or in conjunction with additional surgery differ in: (a) Perioperative outcomes such as surgery time, blood loss, or length of hospital stay? (b) Patient-centered outcomes such as function, quality of life, or pain? (c) Adverse events?

Posterolateral Fusion Versus Posterolateral Fusion and Transforaminal Interbody Fusion

Study, Patient, and Intervention Descriptions

Table 140. Key Question 8: study design: posterolateral fusion versus posterolateral fusion plus transforaminal interbody fusion

Study	Study Design	Enrollment Years	Location	Setting	Funding
Hallett et al. 2007[17]	Randomized controlled trial (RCT)	1998–2001	Edinburgh, Scotland, U.K.	University spine center	Corporate/industry funding supported No benefits related to manuscript subject

Table 141. Key Question 8: patient inclusion criteria: posterolateral fusion versus posterolateral fusion plus transforaminal interbody fusion

Study	Diagnosis Included	Duration of Symptoms	Diagnostic Criteria	Conditions Excluded	Previous Treatment Requirements	Age Requirements
Hallett et al. 2007[17]	Foraminal stenosis with single-level degenerated disc	At least 5 years	Plain radiographs and MR images used to identify intraforaminal or extraforaminal nerve root compromise with single-level degenerated disc	>Grade 2 degenerative spondylolisthesis at degenerated disc or adjacent level >1 cm vertebral translocation >50% disc space narrowing proximal or distal to level to be treated Malignancy, any	Conservative efforts over at least 3 months prior to study enrollment	Not reported, all enrolled were adults

Table 142. Key Question 8: patient characteristics: demographic and occupational history: posterolateral fusion versus posterolateral fusion plus transforaminal interbody fusion

Study	Number Screened for Inclusion	Number Enrolled	Age	Women	Race or Ethnicity	Occupational Status	Workers Compensation	Pending Litigation
Hallett et al. 2007[17]	48	44 (92%)	Mean 57 (range 34–75) years	45%	White (100%)	Retired (30%) Housewives (23%) Off work sick (27%) Rest worked in heavy manual or light industrial jobs	2% with pending claim	Not reported

Table 143. Key Question 8: patient characteristics: health history: posterolateral fusion versus posterolateral fusion plus transforaminal interbody fusion

Study	Surgical Indication	Number of Levels Affected	Duration of Symptoms	Primary or Recurrent	Previous Conservative Treatment(s)	Duration of Conservative Treatments	Previous Surgery	Percent with Radicular Pain	Comorbid Diagnoses
Hallett et al. 2007[17]	Foraminal stenosis with degenerated disc (100%)	One	Not reported	Appears primary	Typically physical therapy and one or more of acupuncture, chiropractic, or massage	Not reported	Not reported	100%	Not reported

Table 144. Key Question 8: treatment characteristics: fusion: posterolateral fusion: posterolateral fusion versus posterolateral fusion plus transforaminal interbody fusion

Study	Number of Patients	Level Fused	Fusion Strategy	Surgical Approach	Device	Adjunctive Surgery
Hallett et al. 2007[17]	16	L3/L4 (13%) L4/L5 (56%) L5/S1 (31%)	Posterolateral instrumented pedicular fusion (fusion “group 2”)	Posterolateral	Instrumentation: Moss-Miami, DePuy (Warsaw, IN) Graft: Autologous, from iliac crest side with lesser symptoms, laid along lateral masses, and into facet joints	Single or bilateral foraminotomy with nerve root decompression. If disc bulge contributed to stenosis, minimal microdiscetomy including subligamentous fragment and loose fragment excision
	14	L3/L4 (21%) L4/L5 (57%) L5/S1 (21%)	Transforaminal instrumented pedicular fusion (fusion “group 3”)	Transforaminal, far lateral approach, and posterolateral	Instrumentation: Moss-Miami, DePuy (Warsaw, IN) Cages: Circular titanium interbody cages, 2 per patient Graft: Autologous, from iliac crest side with lesser symptoms, laid along lateral masses, into facet joints, and posterolaterally	Single or bilateral foraminotomy with nerve root decompression If the disc contributed to the stenosis, minimal microdiskectomy to remove subligamentous fragment and loose fragment from disc space

Data and Results

Table 145. Key Question 8: pain: posterolateral fusion versus posterolateral fusion plus transforaminal interbody fusion

Study	Scale	Treatment Group	Baseline N =	Baseline Mean	Baseline SD	2 Year N =	2 Year Meana	2 Year SD	p-Value
Hallett et al. 2007[17]	Visual analog scale (VAS) – Back	Posterolateral interbody fusion	16	7.75	Not reported	15 (94%)	4.5	Not reported	Not reported, and not calculable from reported information
		Transforaminal interbody fusion	14	7.75	Not reported	12 (86%)	4	Not reported	

[a] Data estimated from figure

SD = Standard deviation

Table 146. Key Question 8: function: posterolateral fusion versus posterolateral fusion plus transforaminal interbody fusion

Study	Scale	Treatment Group	Baseline N =	Baseline Mean	Baseline SD	2 Year N =	2 Year Meana	2 Year SD	p-Value
Hallett et al. 2007[17]	Low Back Outcome Scale	Posterolateral interbody fusion	16	20	Not reported	15 (94%)	35	Not reported	Not reported, and not calculable from reported information
		Transforaminal interbody fusion	14	19	Not reported	12 (86%)	19	Not reported	
Hallett et al. 2007[17]	Roland and Morris Disability Scale	Posterolateral interbody fusion	16	13	Not reported	15 (94%)	9	Not reported	Not reported, and not calculable from reported information
		Transforaminal interbody fusion	14	15	Not reported	12 (86%)	12	Not reported	

[a] Data estimated from figure.

SD = Standard deviation

Table 147. Key Question 8: quality of life: posterolateral fusion versus posterolateral fusion plus transforaminal interbody fusion

Study	Scale	Treatment Group	Baseline N =	Baseline Mean	Baseline SD	2 Year N =	2 Year Meana	2 Year SD	p-Value
Hallett et al. 2007[17]	SF-36	Posterolateral interbody fusion	16	25	Not reported	15 (94%)	45	Not reported	Not reported, and not calculable from reported information
		Transforaminal interbody fusion	14	31	Not reported	12 (86%)	35	Not reported	

[a] Data estimated from figure.

SD = Standard deviation

Table 148. Key Question 8: adverse events

Study	Duration of Followup	Adverse Event	Transforaminal Interbody Fusion	Posterolateral Interbody Fusion
Hallett et al. 2007[17]	Intermediate	Revision: Secondary decompressive laminectomy	1 (7%) 7 months Decompressive laminectomy	1 (6%) 23 months Decompressive laminectomy

Risk-of-Bias Assessment

Table 149. Key Question 8: risk-of-bias assessment: posterolateral fusion versus posterolateral fusion plus transforaminal interbody fusion

Assessment Item	Hallett et al. 2007[17]
Were patients randomly assigned to treatment?	Yes
Was group allocation concealed?	NR
For non-randomized trials, did the study employ other methods to enhance group comparability?	Yes
Was patient assignment independent of physician and patient preference?	Yes
Did patients in different study groups have similar levels of performance on the outcome of interest when they were assigned to groups?	VAS: Yes; LBOS: No RMDS: No; SF-36: No
Were the study groups comparable for all other important factors when they were assigned to groups?	No
Was the comparison of interest prospectively planned?	Yes
If patients received ancillary treatment(s), was there a 5% or less difference between groups in the proportion of patients receiving each ancillary treatment?	Yes
Were the two groups treated concurrently?	Yes
Were patients blinded to the treatment they received?	No
Were outcome assessors blinded to which treatment patients had?	No
For questions comparing fusion, did the two groups' surgeons have similar numbers of prior operations performing the procedure they performed in the study?	Yes
Was the primary outcome measure of interest objective and was it objectively measured? *Objective outcomes include: adverse events; duration of hospital stay, blood loss, and other perioperative outcomes.*	No
Was there a 15% or less difference in the length of followup for the two groups for the comparison time point of interest? This item is not relevant to perioperative outcomes.	No
Did at least 85% of patients who provided baseline data provide data at the time point of interest?	Yes
Was there a 15% or less difference between groups in the percentage of patients who provided data at the time point of interest?	Yes
Risk-of-bias assessment	Moderate

Autograft Versus Coralline Hydroxyapatite

Study, Patient, and Intervention Descriptions

Table 150. Key Question 8: study design: autograft versus coralline hydroxyapatite versus both

Study	Study Design	Enrollment Years	Location	Setting	Funding
Korovessis et al. 2005[24a,b]	Randomized controlled trial (RCT)	Not reported	Patras, Greece	Orthopedic department of general hospital	Not reported

[a] All patients had two or three level fusion.
[b] Author contacted for function outcome data (mean, standard deviation) but did not respond.

Table 151. Key Question 8: patient inclusion criteria: autograft versus coralline hydroxyapatite versus both

Study	Diagnosis Included	Duration of Symptoms	Diagnostic Criteria	Conditions Excluded	Previous Treatment Requirements	Age Requirements
Korovessis et al. 2005[24]	Degenerative spinal stenosis with instability	Not reported	Not reported	Previous lumbosacral spin operations; lumbar spine infection; osteoporotic vertebral fracture; endocrine system disruption	Not reported	Not reported

Table 152. Key Question 8: patient characteristics: demographic and occupational history: autograft versus coralline hydroxyapatite versus both

Study	Number Screened for Inclusion	Number Enrolled	Age	Women	Race or Ethnicity	Occupational Status	Workers Compensation	Pending Litigation
Korovessis et al. 2005[24]	Not reported	60	Mean 61 years autograft, 64 years coralline hydroxyapatite, 48 years both	Not reported	Not reported	Not reported	Not reported	Not reported

Table 153. Key Question 8: patient characteristics: health history: autograft versus coralline hydroxyapatite versus both

Study	Surgical Indication	Number of Levels Affected	Duration of Symptoms	Primary of Recurrent?	Previous Conservative Treatment(s)	Duration of Conservative Treatments	Previous Surgery	Percent With Radicular Pain	Comorbid Diagnoses
Korovessis et al. 2005[24]	Degenerative spinal stenosis with instability	2–3 treated	Not reported	Appears primary	Not reported	Not reported	None permitted (inclusion criterion)	Not reported	Not reported

Table 154. Key Question 8: treatment characteristics: coralline hydroxyapatite, with or without iliac crest autograft, or autograft alone

Study	Number of Patients	Levels Treated	Fusion Strategy	Surgical Approach	Device	Adjunctive Surgery
Korovessis et al. 2005[24]	20 with coralline hydroxyapatite (CH)	Not reported	CH granules (15 cc per level) and local bone chips from posterior elements (5–10 cc per segment) and aspirated bone marrow (2–3 cc drown per pedicle) applied bilaterally	Dorsal and lateral	Coralline hydroxyapatite (CH) graft: Pro-Osteon 500 R (Interpore Cross, International, Irvine CA) Graft: Local autograft	Laminotomy and undercutting facetectomy for decompression
	20 treated, 19 (95%) analyzed	Not reported	Iliac crest bone graft over decorticated laminae and between bilateral transverse processes	Dorsal and lateral	Graft: Iliac crest bone graft	Laminotomy and undercutting facetectomy for decompression
	20 with both, 18 (90%) analyzed	Not reported	CH granules (15 cc per level) and local bone chips from posterior elements (5–10 cc per segment) and aspirated bone marrow (2–3 cc drown per pedicle) applied on right side and iliac crest bone graft applied on left side	Dorsal and lateral	Coralline hydroxyapatite (CH) graft: Pro-Osteon 500 R (Interpore Cross, International, Irvine CA) Graft: Local and iliac crest autograft	Laminotomy and undercutting facetectomy for decompression

Data and Results

Table 155. Key Question 8: perioperative outcomes: autograft versus coralline hydroxyapatite versus both

Study	Outcomes	Treatment Group	N =	Mean	Standard Deviation	p-Value	Mean Difference
Korovessis et al. 2005[24]	Surgical time	Coralline hydroxyapatite (CH)	20	118 minutes	18	CH vs. autograft p=0.003 CH vs. both p<0.001 Autograft vs. both p=0.17	CH vs. autograft -17.00 (95% CI: -28.3 to -5.70) CH vs. both -28.0 (95% CI: -43.5 to 12.5) Autograft vs. both -11.0 (95% CI: -26.8 to 4.8)
		Autograft only	19	135 minutes	18		
		Both CH and iliac crest autograft	18	146 minutes	30		
Korovessis et al. 2005[24]	Blood loss	Coralline hydroxyapatite (CH)	20	371 cc	36	CH vs. autograft p<0.001 CH vs. both p<0.001 Autograft vs. both p=0.14	CH vs. autograft -183.0 (95% CI: -220.0 to -145.0) CH vs. both -133.0 (95% CI: -190.12 to -75.8) Autograft vs. both 50 (95% CI: -16.2 to 116.2)
		Autograft only	19	554 cc	76		
		Both CH and iliac crest autograft	18	504 cc	125		

Table 156. Key Question 8: autograft versus coralline hydroxyapatite versus both comparison: pain at 2 years

Study	Scale	Treatment Group	Baseline N =	Baseline Mean	Baseline SD	2 Year N =	2 Year Mean	2 Year SD	p-Value	Mean Difference
Korovessis et al. 2005[24]	Visual analog scale (VAS) 0-10	Coralline hydroxyapatite (CH)	20	7	2	20	3.7	2.7	CH vs. Autograft p=0.328 CH vs. Both p=0.832 Autograft vs. Both p=0.282	CH vs. Autograft -1.00 (95% CI: -2.99 to 0.99) CH vs. Both 0.20 (95% CI: -1.62 to 2.02) Autograft vs. Both 1.20 (-0.970 to 3.370)
		Autograft only	19	8	1.2	19	4.7	3.6		
		Both CH and iliac crest autograft	18	8	1.7	18	3.5	3.1		

CI = Confidence interval; SD = standard deviation

Table 157. Key Question 8: autograft versus coralline hydroxyapatite versus both: adverse events and reoperation

Study	Duration of Followup	Adverse Event	Coralline Hydroxyapatite (CH)	Autograft Only	Both CH and Iliac Crest Autograft
Korovessis et al. 2005[24]	Postoperative	Superficial infection without deep contamination, treated by operation, evacuation, and drainage for 3 days and antibiotics	0	1 (5%)	0
Korovessis et al. 2005[24]	Postoperative	Deep hematoma treated by operation, evacuation, and drainage for 3 days and antibiotics	0	0	1 (6%)
Korovessis et al. 2005[24]	Intermediate	Screw break	2 (10%) 1 at 6 months, 1 at 3 years	1 (5%) 2-level surgery, 18 months	0

Risk-of-Bias Assessment

Table 158. Key Question 8: autograft versus coralline hydroxyapatite versus both comparison: risk-of-bias assessment

Assessment Item	Korovessis et al. 2005[24]
Were patients randomly assigned to treatment?	Yes
Was group allocation concealed?	No
For non-randomized trials, did the study employ other methods to enhance group comparability?	Yes
Was patient assignment independent of physician and patient preference?	Yes
Did patients in different study groups have similar levels of performance on the outcome of interest when they were assigned to groups?	Yes
Were the study groups comparable for all other important factors when they were assigned to groups?	Yes
Was the comparison of interest prospectively planned?	Yes
If patients received ancillary treatment(s), was there a 5% or less difference between groups in the proportion of patients receiving each ancillary treatment?	Yes
Were the groups treated concurrently?	Yes
Were patients blinded to the treatment they received?	No
Were outcome assessors blinded to which treatment patients had?	No
For questions comparing fusion, did the two groups' surgeons have similar numbers of prior operations performing the procedure they performed in the study?	Yes
Was the primary outcome measure of interest objective and was it objectively measured?	No
Was there a 15% or less difference in the length of followup for the two groups for the comparison time point of interest?	Yes
Did at least 85% of patients who provided baseline data provide data at the time point of interest?	Yes
Was there a 15% or less difference between groups in the percentage of patients who provided data at the time point of interest?	Yes
Risk-of-bias category	Moderate

Key Question 9: For adults with pain associated with degenerative spondylolisthesis of the lumbar spine, do spinal fusion approaches (e.g., anterior, posterior, combined) and techniques (e.g., instrumentation, graft material) performed alone or in conjunction with additional surgery differ in: (a) Perioperative outcomes such as surgery time, blood loss, or length of hospital stay? (b) Patient-centered outcomes such as function, quality of life, or pain? (c) Adverse events?

Instrumentation Versus No Instrumentation

Study, Patient, and Intervention Descriptions

Table 159. Key Question 9: study design: instrumentation (pedicle screws and plates) versus no instrumentation

Study	Study Design	Enrollment Years	Location	Setting	Funding
Abdu et al. 2009[26]	Clinical trial subgroup analysis	2000 to 2005	U.S.	13 medical centers	A grant from the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) and the Office of Research on Women's Health; the National Institutes of Health; the National Institutes of Occupational Safety and Health and the Centers for Disease Control and Prevention; and a grant and Research Career Award from NIAMS.
Fischgrund et al. 1997[25]	Randomized controlled trial (RCT)	Not reported	Royal Oak, Michigan, United States	Author affiliations orthopaedic surgery department	No funds received; no authors have financial relationships

Table 160. Key Question 9: patient inclusion criteria: instrumentation (pedicle screws and plates) versus no instrumentation

Study	Diagnosis Included	Duration of Symptoms	Diagnostic Criteria	Conditions Excluded	Previous Treatment Requirements	Age Requirements	Additional Inclusion Criteria
Abdu et al. 2009[26]	Degenerative spondylolisthesis and spinal stenosis with neurologic claudication or radicular leg pain with associated neurologic signs	At least 12 weeks	Cross-sectional imaging, lateral radiographs*	Spondylolysis and isthmic spondylolisthesis	Not required but listed the following:* Physical therapy: 68% Epidural injections: 55% Chiropractic treatment: 25% Antiinflammatory agents: 63% Opioid analgesic agents: 30%	At least 18 years*	Patients with adjacent levels of stenosis*
Fischgrund et al. 1997[25]	Degenerative spondylolisthesis with spinal stenosis	At least 3 months	Single-level degenerative lumbar spondylolisthesis on plain radiographs and CT myelogram and/or MRI of spinal stenosis at same level	No patient underwent fusion at same level, unclear whether this was a criterion	At least 3 months nonoperative, such as passive physical therapy modalities, exercise, nonsteroidal antiinflammatory drugs	Not reported	Not reported

*We also extracted data from Birkmeyer et al.2002[83] to complete information presented for the Abdu et al. study.

Table 161. Key Question 9: patient characteristics: demographic and occupational history: instrumentation (pedicle screws and plates) versus no instrumentation

Study	Number Screened for Inclusion	Number Enrolled	Age	Women	Race or Ethnicity	Occupational Status	Workers Compensation	Pending Litigation
Abdu et al. 2009[26]	NR	293*	Mean 66 years	66%	Non-Hispanic: 97% (100% noninstrumented; 96% instrumented) White: 85% (95% noninstrumented; 82% instrumented)	Full or part time: 34% (39% noninstrumented; 32% instrumented) Disabled: 9% (8% noninstrumented; 10% instrumented) Retired: 44% (48% noninstrumented; 42% instrumented) Other: 13% (6% noninstrumented; 15% instrumented)	9% (6% noninstrumented; 10% instrumented)	NR
Fischgrund et al. 1997[25]	Not reported	68	Mean 68 years	81%	Not reported	Not reported	Not reported	Not reported

*360° group excluded due to significant differences between groups in percent of levels fused

NR = not reported

Table 162. Key Question 9: patient characteristics: health history: instrumentation (pedicle screws and plates) versus no instrumentation

Study	Surgical Indication	Number of Levels Affected	Duration of Symptoms	Primary or Recurrent	Previous Conservative Treatment(s)	Duration of Conservative Treatments	Previous Surgery	Percent With Radicular Pain	Comorbid Diagnoses
Abdu et al. 2009[26]	Degenerative spondylolisthesis and spinal stenosis with neurologic claudication or radicular leg pain with associated neurologic signs	One	Duration >6 months: 61% (69% PLF; 60% PPS; 56% 360°)	Primary	Physical therapy, epidural injections, chiropractic treatment, antiinflammatory agents, opioid analgesic agents	Not reported	Not reported	78%	Hypertension: 39% PLF, 48% PPS, 41% 360° Diabetes: 11% PLF, 15% PPS, 10% 360° Osteoporosis: 12% PLF, 13% PPS, 0% 360° Heart problem: 21% PLF, 17% PPS, 19% 360° Stomach problem: 20% PLF, 21% PPS, 27% 360° Bowel or intestinal problem: 11% PLF, 7% PPS, 10% 360° Depression: 24% PLF, 15% PPS, 13% 360° Joint problem: 50% PLF, 57% PPS, 56% 360° Other: 39% PLF, 37% PPS, 44% 360°
Fischgrund et al. 1997[25]	Degenerative spondylolisthesis and spinal stenosis with neurologic claudication	One	Not reported	Primary	Not reported. Examples in inclusion criteria were: passive physical therapy modalities, exercise, nonsteroidal antiinflammatory drugs	Not reported. At least 3 months for inclusion criteria.	Not reported. Previous fusion at treated level excluded	100%	Spinal stenosis 100% Smokers: Instrumented: 4 Non-instrumented: 3

Table 163. Key Question 9: treatment characteristics: instrumentation (pedicle screws and plates) versus no instrumentation

Study	Treatment Group	Number of Patients	Level Fused	Fusion Strategy	Surgical Approach	Device	Adjunctive Surgery	Additional Information
Abdu et al. 2009[26]	Instrumentation	213	L2-L3: 11% L3-L4: 51% L4-L5: 98% L5-S1: 27%	Decompression with instrumented posterolateral fusion with pedicle screws	Posterolateral	Not reported	Not reported	Not reported
	No instrumentation	80	L2-L3: 19% L3-L4: 59% L4-L5: 98% L5-S1: 38%	Decompression with posterolateral fusion	Posterolateral	Not reported	Not reported	Not reported
Fischgrund et al. 1997[25]	Instrumentation	35	Not reported. Based on overall population, mostly L4/L5	Decompressive laminectomy and single level bilateral lateral autogenous intertransverse process arthrodesis with transpedicular instrumentation	Posterior	Pedicle Screws (4 per patient): VSP, Acromed (Cleveland, OH) Plates (2 per patient): Acromed (Cleveland, OH), secured with lock nuts	Not reported	Screws placed with fluoroscopic guidance
	No instrumentation	33	Not reported. Based on overall population, mostly L4/L5	Decompressive laminectomy and single level autogenous bilateral intertransverse process arthrodesis	Posterior	No instrumentation	Not reported	Not reported

Data and Results

Table 164. Key Question 9: pain and function as measured by SF-36 subscales: instrumentation versus no instrumentation at 6 weeks

Study	Scale	Treatment Group	Baseline N=	Baseline Mean	Baseline SD	6 weeks N=	6 weeks Mean	6 weeks SD	P-value	Effect Size
Abdu et al. 2009[26]	SF-36 bodily pain	Instrumentation	198	30.4	19.1	198	17.69	1.49	p=0.7952[a]	Mean Difference 0.76 (95% CI: 0.27 to 1.25)
		No instrumentation	73	33.4	18.2	73	16.93	2.53		
	SF-36 physical function	Instrumentation	198	30.4	21.9	198	6.22	1.45	p=0.0201[a]	Mean Difference -6.51 (95% CI: -6.99 to -6.03)
		No instrumentation	73	31.2	17.2	73	12.73	2.44		

[a] As reported in the study based on difference in the mean changes from baseline between groups.

CI = Confidence interval; SD = standard deviation

Table 165. Key Question 9: pain and function as measured by SF-36 subscales: instrumentation versus no instrumentation at 3 months

Study	Scale	Treatment Group	Baseline N=	Baseline Mean	Baseline SD	3 month N=	3 month Mean	3 month SD	P-value	Effect Size
Abdu et al. 2009[26]	SF-36 bodily pain	Instrumentation	198	30.4	19.1	207	28.19	1.55	p=0.1568[a]	Mean Difference -4.13 (95% CI: -4.62 to -3.64)
		No instrumentation	73	33.4	18.2	75	32.32	2.49		
	SF-36 physical function	Instrumentation	198	30.4	21.9	207	18.95	1.51	p=0.0247[a]	Mean Difference -6.29 (95% CI: -6.76 to -5.82)
		No instrumentation	73	31.2	17.2	75	25.24	2.41		

[a] As reported in the study based on difference in the mean changes from baseline between groups.

CI = Confidence interval; SD = standard deviation

Table 166. Key Question 9: pain and function as measured by SF-36 subscales: instrumentation versus no instrumentation at 6 months

Study	Scale	Treatment Group	Baseline N=	Baseline Mean	Baseline SD	6 Months N=	6 Months Mean	6 Months SD	p=	Effect Size
Abdu et al. 2009[26]	SF-36 bodily pain	Instrumentation	198	30.4	19.1	203	34.47	1.85	p=0.3222[a]	Mean Difference 3.53 (95% CI: 2.94 to 4.12)
		No instrumentation	73	33.4	18.2	79	30.94	3.07		
	SF-36 physical function	Instrumentation	198	30.4	21.9	203	26.67	1.79	p=0.6555[a]	Mean Difference -1.53 (95% CI: -2.05 to -1.01)
		No instrumentation	73	31.2	17.2	79	28.20	2.41		

[a] As reported in the study based on difference in the mean changes from baseline between groups.

CI = Confidence interval; SD = standard deviation

Table 167. Key Question 9: pain and function as measured by SF-36 subscales: instrumentation versus no instrumentation at 1 year

Study	Scale	Treatment Group	Baseline N=	Baseline Mean	Baseline SD	1 year N=	1 year Mean	1 year SD	p=	Effect Size
Abdu et al. 200926	SF-36 bodily pain	Instrumentation	198	30.4	19.1	200	32.32	1.67	p=0.6075a	Mean Difference 1.61 (95% CI: 1.09 to 2.13)
		No instrumentation	73	33.4	18.2	77	30.71	2.67		
	SF-36 physical function	Instrumentation	198	30.4	21.9	200	28.13	1.62	p=0.5627a	Mean Difference -1.74 (95% CI: -2.25 to -1.23)
		No instrumentation	73	31.2	17.2	77	29.87	2.57		

[a] As reported in the study based on difference in the mean changes from baseline between groups.

CI = Confidence interval; SD = standard deviation

Table 168. Key Question 9: pain and function as measured by SF-36 subscales: instrumentation versus no instrumentation at 2 years

Study	Scale	Treatment Group	Baseline N=	Baseline Mean	Baseline SD	2 years N=	2 years Mean	2 years SD	p=	Effect Size
Abdu et al. 2009[26]	SF-36 bodily pain	Instrumentation	198	30.4	19.1	197	29.13	1.71	p=0.9897[a]	Mean Difference -0.04 (95% CI: -0.58 to 0.50)
		No instrumentation	73	33.4	18.2	73	29.17	2.70		
	SF-36 physical function	Instrumentation	198	30.4	21.9	197	25.29	1.67	p=0.5089[a]	Mean Difference 2.02 (95% CI: 1.49 to 2.55)
		No instrumentation	73	31.2	17.2	73	23.27	2.60		

[a] As reported in the study based on difference in the mean changes from baseline between groups.

CI = Confidence interval; SD = standard deviation

Table 169. Key Question 9: pain and function as measured by SF-36 subscales: instrumentation versus no instrumentation at 3 years

Study	Scale	Treatment Group	Baseline N=	Baseline Mean	Baseline SD	3 years N=	3 years Mean	3 years SD	p=	Effect Size
Abdu et al. 2009[26]	SF-36 bodily pain	Instrumentation	198	30.4	19.1	184	31.24	1.79	p=0.7878[a]	Mean Difference -0.89 (95% CI: -1.48 to -0.30)
		No instrumentation	73	33.4	18.2	68	32.13	2.80		
	SF-36 physical function	Instrumentation	198	30.4	21.9	184	24.81	1.71	p=0.5183[a]	Mean Difference -2.04 (95% CI: -2.60 to -1.48)
		No instrumentation	73	31.2	17.2	68	26.85	2.69		

[a] As reported in the study based on difference in the mean changes from baseline between groups.

CI = Confidence interval; SD = standard deviation

Table 170. Key Question 9: pain and function as measured by SF-36 subscales: instrumentation versus no instrumentation at 4 years

Study	Scale	Treatment Group	Baseline N=	Baseline Mean	Baseline SD	4 years N=	4 years Mean	4 years SD	p=	Effect Size
Abdu et al. 2009[26]	SF-36 bodily pain	Instrumentation	198	30.4	19.1	167	29.91	1.87	p=0.5226[a]	Mean Difference -2.26 (95% CI: -2.93 to -1.59)
		No instrumentation	73	33.4	18.2	56	32.17	3.02		
	SF-36 physical function	Instrumentation	198	30.4	21.9	167	23.55	1.80	p=0.0603[a]	Mean Difference -6.38 (95% CI: -7.03 to -5.73)
		No instrumentation	73	31.2	17.2	56	29.93	2.93		

[a] As reported in the study based on difference in the mean changes from baseline between groups.

CI = Confidence interval; SD = standard deviation

Table 171. Key Question 9: function: instrumentation versus no instrumentation at 6 weeks

Study	Scale	Treatment Group	Baseline N=	Baseline Mean	Baseline SD	6 weeks N=	6 weeks Mean change from baseline	6 weeks SD	P-value	Effect Size
Abdu et al. 2009[26]	ODI	Instrumentation	198	45.5	16.9	207	-14.46	1.15	P=0.6974 [a]	Mean Difference -0.85 (95% CI: -1.22 to -0.48)
		No instrumentation	73	41.2	15.8	75	-13.61	1.89		

[a] As reported in the study based on difference in the mean changes from baseline between groups.

CI = Confidence interval; SD = standard deviation

Table 172. Key Question 9: function: instrumentation versus no instrumentation at 3 months

Study	Scale	Treatment Group	Baseline N=	Baseline Mean	Baseline SD	3 month N=	3 month Mean change from baseline	3 month SD	P-value	Effect Size
Abdu et al. 2009[26]	ODI	Instrumentation	198	45.5	16.9	207	-22.30	1.17	p=0.1401 [a]	Mean Difference -3.20 (95% CI: -3.57 to -2.83)
		No instrumentation	73	41.2	15.8	75	-19.10	1.86		

[a] As reported in the study based on difference in the mean changes from baseline between groups.

CI = Confidence interval; SD = standard deviation

Table 173. Key Question 9: function: instrumentation versus no instrumentation at 6 months

Study	Scale	Treatment Group	Baseline N=	Baseline Mean	Baseline SD	6 Months N=	6 Months Mean change from baseline	6 Months SD	p=	Effect Size
Abdu et al. 2009[26]	ODI	Instrumentation	198	45.5	16.9	203	-26.46	1.37	p=0.0356 [a]	Mean Difference -5.54 (95% CI: -5.97 to -5.11)
		No instrumentation	73	41.2	15.8	79	-20.92	2.27		

[a] As reported in the study based on difference in the mean changes from baseline between groups.

CI = Confidence interval; SD = standard deviation

Table 174. Key Question 9: function: instrumentation versus no instrumentation at 1 year

Study	Scale	Treatment Group	Baseline N=	Baseline Mean	Baseline SD	1 year N=	1 year Mean change from baseline	1 year SD	p=	Effect Size
Abdu et al. 2009[26]	ODI	Instrumentation	198	45.5	16.9	200	-26.33	1.26	p=0.0197[a]	Mean Difference -5.41 (95% CI: -5.80 to -5.02)
		No instrumentation	73	41.2	15.8	77	-20.92	1.98		

[a] As reported in the study based on difference in the mean changes from baseline between groups.

CI = Confidence interval; SD = standard deviation

Table 175. Key Question 9: function: instrumentation versus no instrumentation at 2 years

Study	Scale	Treatment Group	Baseline N=	Baseline Mean	Baseline SD	2 years N=	2 years Mean change from baseline	2 years SD	p=	Effect Size
Abdu et al. 2009[26]	ODI	Instrumentation	198	45.5	16.9	197	-24.39	1.28	p=0.1765[a]	Mean Difference -3.18 (95% CI: -3.58 to -2.78)
		No instrumentation	73	41.2	15.8	73	-21.21	2.00		

[a] As reported in the study based on difference in the mean changes from baseline between groups.

CI = Confidence interval; SD = standard deviation

Table 176. Key Question 9: function: instrumentation versus no instrumentation at 3 years

Study	Scale	Treatment Group	Baseline N=	Baseline Mean	Baseline SD	3 years N=	3 years Mean change from baseline	3 years SD	p=	Effect Size
Abdu et al. 2009[26]	ODI	Instrumentation	198	45.5	16.9	184	-21.17	1.33	p=0.7159[a]	Mean Difference -0.88 (95% CI: -1.31 to -0.45)
		No instrumentation	73	41.2	15.8	68	-20.29	2.07		

[a] As reported in the study based on difference in the mean changes from baseline between groups.

CI = Confidence interval; SD = standard deviation

Table 177. Key Question 9: function: instrumentation versus no instrumentation at 4 years

Study	Scale	Treatment Group	Baseline N=	Baseline Mean	Baseline SD	4 years N=	4 years Mean change from baseline	4 years SD	p=	Effect Size
Abdu et al.	ODI	Instrumentation	198	45.5	16.9	167	-23.01	1.38	p=0.6548[a]	Mean Difference -1.15

Study	Scale	Treatment Group	Baseline N=	Baseline Mean	Baseline SD	4 years N=	4 years Mean change from baseline	4 years SD	p=	Effect Size
2009[26]		No instrumentation	73	41.2	15.8	56	-21.86	2.21		(95% CI: -1.64 to -0.66)

[a] As reported in the study based on difference in the mean changes from baseline between groups.

CI = Confidence interval; SD = standard deviation

Table 178. Key Question 9: pain: instrumentation (pedicle screws and plates) versus no instrumentation at mean 28 months (2–3 years)

Study	Scale	Treatment Group	Baseline N=	Baseline Mean	Baseline SD	28 Months N=	28 Months Mean	28 Months SD	p=
Fischgrund et al. 1997[25]	Visual analog scale (VAS) 0-5 Back pain	Instrumentation	40	4	Not reported	35 (88%)	1	Not reported	Not reported, insufficient data to calculate
		No instrumentation	35	4	Not reported	33 (94%)	2	Not reported	
Fischgrund et al. 1997[25]	VAS 0-5 Lower limb pain	Instrumentation	40	4	Not reported	35 (88%)	1	Not reported	Not reported, insufficient data to calculate
		No instrumentation	35	4	Not reported	33 (94%)	1	Not reported	

SD = Standard deviation

Table 179. Key Question 9: perioperative outcomes: instrumentation versus no instrumentation

Study	Outcomes	Treatment Group	N=	Mean	Standard Deviation	p-Value	Effect Size
Abdu et al. 2009[26]	Surgical time	Instrumentation	213	212.2 minutes	74	P<0.01[a]	Mean Difference 55.50 (95% CI:37.48 to 73.52)
		No instrumentation	80	156.7 minutes	58.5		
Abdu et al. 2009[26]	Blood loss	Instrumentation	213	666.4 mL	519.2	P<0.01[a]	Mean Difference 167.70 (95% CI: 43.47 to 291.93)
		No instrumentation	80	498.7 mL	370.5		
Abdu et al. 2009[26]	Duration of inpatient stay	Instrumentation	213	4.8 days	2.7	p=0.12 [a]	Mean Difference -0.60 (95% CI: -0.16 to 1.36)
		No instrumentation	80	4.2 days	3.5		

[a] Calculated by the EPC

CI = Confidence interval; SD = standard deviation

Table 180. Key Question 9: adverse events: instrumentation (pedicle screws and plates) versus no instrumentation

Study	Duration of Followup	Adverse Event	Instrumentation	No Instrumentation
Abdu et al. 2009[26]	Intraoperative	Dural tear or cerebrospinal fluid leak	25 (12%)	7 (9%)
Abdu et al. 2009[26]	Intraoperative	Vascular injury	1 (0%)	0 (0%)
Abdu et al. 2009[26]	Intraoperative	Other	4 (2%)	3 (4%)
Abdu et al. 2009[26]	Peri-operative to short term	Nerve root injury	1 (0%)	0 (0%)
Abdu et al. 2009[26]	Peri-operative to short term	Wound infection	5 (2%)	5 (6%)
Abdu et al. 2009[26]	Peri-operative to short term	Other	26 (12%)	4 (5%)
Abdu et al. 2009[26]	Short term	Death within 3 months after surgery	1 (0.5%) due to sepsis	1 (1.3%) due to respiraratory distress
Abdu et al. 2009[26]	Intermediate	Re-operations within 1 year*	12 (6%)	5 (6%)
Abdu et al. 2009[26]	Intermediate	Re-operations within 2 year*	23 (11%)	11 (14%)
Abdu et al. 2009[26]	Intermediate	Re-operations within 3 year*	26 (12%)	13 (16%)
Abdu et al. 2009[26]	Intermediate	Re-operations within 4 year*	29 (14%) Recurrent stenosis/progressive listhesis: 11 (5%) Pseudoarthrosis/fusion exploration: 2 (1.1%) Complication: 12 (5.8%) New condition: 4 (1.9%)	14 (18%) Recurrent stenosis/progressive listhesis: 4 (5%) Pseudoarthrosis/fusion exploration: 1 (1.3%) Complication: 7 (8.7%) New condition: 3 (4%)
Fischgrund et al. 1997[25]	Intermediate Range: >1 to 3 years	Re-operation	3 (8.6%) 1 decompressive laminectomy at a different level 1 Hardware removal for pain 1 repeat decompression and instrumented fusion	2 (6.1%) 1 decompressive laminectomy at a different level 1 second fusion with instrumentation
Fischgrund et al. 1997[25]	Intermediate Range: >1 to 3 years	Screw failure (S1) not requiring intervention (patient had good outcome)	1 (2.8%)	0
Fischgrund et al. 1997[25]	Intermediate 2 years	New peripheral (lower motor neuron) neurological deficits	0	0

*Kaplan-Meier estimates

Risk-of-Bias Assessment

Table 181. Key Question 9: risk-of-bias assessment: instrumentation (pedicle screws and plates) versus no instrumentation

Assessment Item	Fischgrund et al. 1997[25]	Abdu et al. 2009[26]
Were patients randomly assigned to treatment?	Yes	No
Was group allocation concealed?	Not reported	No
For non-randomized trials, did the study employ other methods to enhance group comparability?	Yes	Yes
Was patient assignment independent of physician and patient preference?	Yes	No
Did patients in different study groups have similar levels of performance on the outcome of interest when they were assigned to groups?	Visual analog scale (Pain): Yes	No
Were the study groups comparable for all other important factors when they were assigned to groups?	Yes	No
Was the comparison of interest prospectively planned?	Yes	Yes
If patients received ancillary treatment(s), was there a 5% or less difference between groups in the proportion of patients receiving each ancillary treatment?	Yes	Not reported
Were the two groups treated concurrently?	Not reported	Yes
Were patients blinded to the treatment they received?	Not reported	No
Were outcome assessors blinded to which treatment patients had?	Yes	Not reported
For questions comparing fusion, did the two groups' surgeons have similar numbers of prior operations performing the procedure they performed in the study?	Not reported	Not reported
Was the primary outcome measure of interest objective and was it objectively measured?	No	No
Was there a 15% or less difference in the length of followup for the two groups for the comparison time point of interest? This item is not relevant to perioperative outcomes.	Yes	Yes
Did at least 85% of patients who provided baseline data provide data at the time point of interest?	Yes	No
Was there a 15% or less difference between groups in the percentage of patients who provided data at the time point of interest?	Yes	Yes
Risk-of-bias rating	Moderate	High

Unilateral Versus Bilateral Instrumentation

Study, Patient, and Intervention Descriptions

Table 182. Key Question 9: study design: unilateral versus bilateral instrumentation

Study	Study Design	Enrollment Years	Location	Setting	Funding
Fernandez-Fairen et al. 2007[27]	Randomized controlled trial (RCT)	1999-2002	Barcelona, Spain	Author affiliations university and orthopedic hospital departments	No funds received; no authors report financial conflicts of interest

Table 183. Key Question 9: patient inclusion criteria: unilateral versus bilateral instrumentation

Study	Diagnosis Included	Duration of Symptoms	Diagnostic Criteria	Conditions Excluded	Previous Treatment Requirements	Age Requirements	Additional Inclusion Criteria
Fernandez-Fairen et al. 2007[27]	Degenerative spondylosthesis	At least 6 months	Abnormal sagittal mobility of >5 mm in lateral flexion and extension radiographs standing up; disc height of >2 mm	In need of disc surgery; factors that may influence healing (e.g., metabolic disease, consumption of tobacco, or habitual use of anti-inflammatories), history of major psychopathology; previous surgery; other pathologic condition (e.g., scoliosis, isthmic spondylolisthesis)	At least 6 months nonoperative	50 to 70 years	Persistent or recurrent lumbar pain lasting at least 6 months resulting in a significant reduction of quality of life, despite non-operative treatment

Table 184. Key Question 9: patient characteristics: demographic and occupational history: unilateral versus bilateral instrumentation

Study	Comparison	Number Screened for Inclusion	Number Enrolled	Age Mean ±Standard Deviation	Women	Race or Ethnicity	Occupational Status	Workers Compensation	Pending Litigation
Fernandez-Fairen et al. 2007[27]	Bilateral instrumentation	Not reported	42	61.42± 5.47	64%	Not reported	Not reported	Not reported	Not reported
	Unilateral instrumentation	Not reported	40	60.8± 5.33	60%	Not reported	Not reported	Not reported	Not reported

Table 185. Key Question 9: patient characteristics: health history: unilateral versus bilateral instrumentation

Study	Surgical Indication	Number of Levels Affected	Duration of Symptoms	Primary or Recurrent	Previous Conservative Treatment(s)	Duration of Conservative Treatments	Previous Surgery	Percent With Radicular Pain	Comorbid Diagnoses
Fernandez-Fairen et al. 2007[27]	Degenerative spondylolisthesis	Bilateral: 30/11 Unilateral: 23/17	Not reported	Primary	Not reported	Inclusion indicates at least 6 months	Excluded	100%	Not reported

Table 186. Key Question 9: treatment characteristics: unilateral versus bilateral instrumentation

Study	Treatment Group	Number of Patients	Level Fused	Fusion Strategy	Surgical Approach	Device	Adjunctive Surgery
Fernandez-Fairen et al. 2007[27]	Bilateral instrumentation	42	L4-L5: 23 (56%) L5-S1: 6 (14.6%) L4-S1: 9 (22%) L3-L5: 2 (5%) L2-L3: 1 (2.4%)	"Classic bilateral" Iliac crest bone placed bilaterally onto and between transverse processes and facet joints, implemented with granulated bicalcium phosphate	Posterolateral	Xia pedicular screw system (Stryker Spine, Allendale, NJ), bilateral	Decompression (n=25)
	Unilateral instrumentation	40	L4-L5: 17 (42.5%) L5-S1: 6 (15%) L4-S1: 12 (30%) L3-L5: 4 (10%) L2-L4: 1 (2.5%)	"Unilateral pedicle instrumentation" Iliac crest bone placed unilaterally onto and between transverse processes and facet joints, implemented with granulated bicalcium phosphate	Posterolateral	Xia pedicular screw system (Stryker Spine, Allendale, NJ), unilateral	Decompression (n=26)

Data and Results

Table 187. Key Question 9: pain: unilateral versus bilateral instrumentation at 1 year

Study	Scale	Treatment Group	Baseline N=	Baseline Mean	Baseline SD	1 Year N=	1 Year Mean	1 Year SD	P-value	Effect Size
Fernandez-Fairen et al. 2007[27]	SF-36 v. 2, bodily pain subscale	Bilateral instrumentation	42	30.79	11.83	41 (98%)	50.87	13.63	p=0.798[a]	Mean Difference 0.820 (95% CI: -5.462 to 7.102)
		Unilateral instrumentation	40	27.96	13.98	40 (100%)	50.05	15.19		

[a] As calculated by the EPC in terms of standardized mean difference of followup scores.

CI = Confidence interval; SD = standard deviation

Table 188. Key Question 9: pain: unilateral versus bilateral instrumentation at 3 years

Study	Scale	Treatment Group	Baseline N=	Baseline Mean	Baseline SD	3 Year N=	3 Year Mean	3 Year SD	P-value	Effect Size

Study	Scale	Treatment Group	Baseline N=	Baseline Mean	Baseline SD	3 Year N=	3 Year Mean	3 Year SD	P-value	Effect Size
Fernandez-Fairen et al. 2007[27]	SF-36 v. 2, bodily pain subscale	Bilateral instrumentation	42	30.79	11.83	41 (98%)	55.09	15.45	p=0.319[a]	Mean Difference 3.410 (95% CI: -3.300 to 10.120)
		Unilateral instrumentation	40	27.96	13.98	40 (100%)	51.68	15.36		

[a] As calculated by the EPC in terms of standardized mean difference of followup scores.

CI = Confidence interval; SD = standard deviation

Table 189. Key Question 9: function: unilateral versus bilateral instrumentation at 1 year

Study	Scale	Treatment Group	Baseline N=	Baseline Mean	Baseline SD=	1 Year N=	1 Year Mean	1 Year SD	P-value	Effect Size
Fernandez-Fairen et al. 2007[27]	SF-36 v. 2, physical function	Bilateral instrumentation	42	33.79	12.68	41 (98%)	51.34	13.19	p=0.229[a]	Mean Difference 3.540 (95% CI: -2.227 to 9.307)
		Unilateral instrumentation	40	34.39	12.44	40 (100%)	47.80	13.29		

[a] As calculated by the EPC in terms of standardized mean difference of followup scores.

CI = Confidence interval; SD = standard deviation

Table 190. Key Question 9: function: unilateral versus bilateral instrumentation at 3 years

Study	Scale	Treatment Group	Baseline N=	Baseline Mean	Baseline SD=	3 Year N=	3 Year Mean	3 Year SD	P-value	Effect Size
Fernandez-Fairen et al. 2007[27]	SF-36 v. 2, Physical function	Bilateral instrumentation	42	33.79	12.68	41 (98%)	55.66	13.60	p=0.077[a]	Mean Difference 5.490 (95% CI: -0.595 to 11.575)
		Unilateral instrumentation	40	34.39	12.44	40 (100%)	50.17	14.34		

[a] As calculated by the EPC in terms of standardized mean difference of followup scores.

CI = Confidence interval; SD = standard deviation

Table 191. Key Question 9: quality of life: unilateral versus bilateral instrumentation at 1 year

Study	Scale	Treatment Group	Baseline N=	Baseline Mean	Baseline SD=	1 Year N=	1 Year Mean	1 Year SD	P-value	Effect Size
Fernandez-Fairen et al. 2007[27]	SF-36 v. 2, physical component summary	Bilateral instrumentation	42	34.02	8.16	41 (98%)	44.99	9.42	p=0.935[a]	Mean Difference -0.170 (95% CI: -4.277 to 3.937)
		Unilateral instrumentation	40	33.20	8.64	40 (100%)	45.16	9.44		
Fernandez-Fairen et al. 2007[27]	SF-36 v. 2, mental component summary	Bilateral instrumentation	42	44.36	15.32	41 (98%)	53.16	9.24	p=0.892[a]	Mean Difference 0.260 (95% CI: -3.500 to 4.020)
		Unilateral instrumentation	40	44.43	15.00	40 (100%)	52.9	7.96		

CI = Confidence interval; SD = standard deviation

Table 192. Key Question 9: quality of life: unilateral versus bilateral instrumentation at 3 years

Study	Scale	Treatment Group	Baseline N=	Baseline Mean	Baseline SD=	3 Year N=	3 Year Mean	3 Year SD	P-value	Effect Size
Fernandez-Fairen et al. 2007[27]	SF-36 v. 2, physical component summary	Bilateral instrumentation	42	34.02	8.16	41 (98%)	48.90	10.34	p=0.565[a]	Mean Difference 1.370 (95% CI: -3.291 to 6.031)
		Unilateral instrumentation	40	33.20	8.64	40 (100%)	47.53	11.06		
Fernandez-Fairen et al. 2007[27]	SF-36 v. 2, mental component summary	Bilateral instrumentation	42	44.36	15.32	41 (98%)	54.83	8.20	p=0.168[a]	Mean Difference 2.490 (95% CI: -1.054 to 6.034)
		Unilateral instrumentation	40	44.43	15.00	40 (100%)	52.34	8.07		

[a] As calculated by the EPC in terms of standardized mean difference of followup scores.

CI = Confidence interval; SD = standard deviation

Table 193. Key Question 9: perioperative outcomes: unilateral versus bilateral instrumentation

Study	Outcomes	Treatment Group	N=	Mean	Standard Deviation	p-Value	Effect Size
Fernandez-Fairen et al. 2007[27]	Surgical time	Bilateral instrumentation	42	203 minutes	35	p<0.001 (as reported in the study)	Mean Difference 35.000 (95% CI: 19.416 to 50.584)
		Unilateral instrumentation	40	168 minutes	37		
Fernandez-Fairen et al. 2007[27]	Blood loss	Bilateral instrumentation	42	1,155 mL	207	p=0.073[a]	Mean Difference 95.000 (95% CI: -8.832 to 198.832)
		Unilateral instrumentation	40	1,060 mL	270		
Fernandez-Fairen et al. 2007[27]	Duration of inpatient stay	Bilateral instrumentation	42	3.85 day	0.54	p=0.499[a]	Mean Difference -0.120 (95% CI: -0.468 to 0.228)
		Unilateral instrumentation	40	3.97 days	1.01 days		
Fernandez-Fairen et al. 2007[27]	Transfusion (times)	Bilateral instrumentation	42	20	N/A	p=Not statistically significant (as reported in the study)	Not reported, insufficient data reported to calculate
		Unilateral instrumentation	40	14	N/A		

[a] As calculated by the EPC in terms of standardized mean difference of followup scores.

CI = Confidence interval; NA = not applicable

Table 194. Key Question 9: adverse events and reoperations: unilateral versus bilateral instrumentation

Study	Duration of Followup	Adverse Event	Unilateral Instrumentation	Bilateral Instrumentation
Fernandez-Fairen et al. 2007[27]	Intermediate 3 years	Reoperation	0	3 (7.1%) Due to nerve root irritation

Risk-of-Bias Assessment

Table 195. Key Question 9: risk-of-bias assessment: unilateral versus bilateral instrumentation

Assessment Item	Fernandez-Fairen et al. 2007[27]
Were patients randomly assigned to treatment?	Yes
Was group allocation concealed?	Not Reported
For non-randomized trials, did the study employ other methods to enhance group comparability?	Yes
Was patient assignment independent of physician and patient preference?	Yes
Did patients in different study groups have similar levels of performance on the outcome of interest when they were assigned to groups? *This will only be used for outcomes that have a baseline measure.*	SF-36v2: Yes
Were the study groups comparable for all other important factors when they were assigned to groups?	Yes
Was the comparison of interest prospectively planned? *All included studies should have a "yes" because this is an inclusion criterion.*	Yes
If patients received ancillary treatment(s), was there a 5% or less difference between groups in the proportion of patients receiving each ancillary treatment?	Yes
Were the two groups treated concurrently?	Yes
Were patients blinded to the treatment they received?	Not reported
Were outcome assessors blinded to which treatment patients had?	Yes
For questions comparing fusion, did the two groups' surgeons have similar numbers of prior operations performing the procedure they performed in the study?	Yes
Was the primary outcome measure of interest objective and was it objectively measured? *Objective outcomes include: adverse events; duration of hospital stay, blood loss, and other perioperative outcomes.*	No
Was there a 15% or less difference in the length of followup for the two groups for the comparison time point of interest? This item is not relevant to perioperative outcomes.	Yes
Did at least 85% of patients who provided baseline data provide data at the time point of interest?	Yes
Was there a 15% or less difference between groups in the percentage of patients who provided data at the time point of interest?	Yes
Risk-of-bias rating	Moderate

Key Question 10: Which, if any, patient characteristics (e.g., pain severity, type or duration of prior treatment) does the evidence show are associated with better or worse outcomes after spinal fusion in adults with degenerative disc changes, degenerative stenosis, or degenerative spondylolisthesis? (a) Patient-centered outcomes such as function, quality of life, or pain; (b) Adverse events

Study, Patient, and Riskn Factor Descriptions

Table 196. Key Question 10: study characteristics and significant predictive factors of patient outcomes

Author/Year/ Country	Study Design	Patient Population	Diagnosis Included	Treatment Strategy	Followup Period	Type of Analysis and Predictive Factors Considered	Significant Factors
Fukuta et al. 2011[29] Japan	Retrospective cohort study 54 patients	Consecutive patient who underwent fusion surgery from 2004 to 2006. All patients considered for surgery had severe disabling pain in the back and/or lower extremities that had persisted for a long time and was refractory to nonsurgical treatment. Mean age of patients 65.2±18.2, 30 (55%) females, and 24 (44%) males	Degenerative spondylolisthesis (52%) and degenerative disc disease (48%)	Transforaminal interbody fusion (TLIF) using kidney-type intervertebral spacers. This study assesses the risk factors for spacer subsidence (SS) using kidney-type spacers.	2 or more years	Subgroup analysis (patients were divided into subgroups based on age, gender, body mass index, and primary disease), logistic regression, and multivariate analysis of variance were conducted to assess the influence of the following factors on the occurrence of SS: age, gender, body mass index, osteoporosis grader and spacer position (center vs. anterior).	Analytic results indicated that center position of the kidney-shaped spacer and age (>65 years) were significant risk factors for SS ≥2 mm (odds ratio for position 4.061, p<0.001 and mean comparing <65 years to >65 years 1.7±1.3, p=0.0056). Multivariate analysis indicated that age and spacer position had a significant synergistic effect on increasing SS (p<0.001). Subgroup analysis further substantiated the relationship between age and spacer position by showing that for patients >65, SS was significantly larger in patients with center spacers than those with anterior spacers at 2-year followup (p=0.001).

Author/Year/ Country	Study Design	Patient Population	Diagnosis Included	Treatment Strategy	Followup Period	Type of Analysis and Predictive Factors Considered	Significant Factors
Keorochana et al. 2011[30] Thailand	Retrospective cohort study 158	Patients who underwent fusion surgery between 1999 and 2004 were enrolled in study. Enrolled patients had clinical and radiographic evidence of degenerative lumbar spinal stenosis, limitation in functional activities, and back, buttock and/or leg pain. Patients who had undergone previous spinal surgery and who could not answer the questionnaires due to cognitive impairment were excluded. Mean age of patients 60.3 (range 34 to 87 years), 129 (81.7%) females, and 54 (34.18%) had comorbid conditions such as heart disease and arthritis of the lower extremities.	Degenerative lumbar spinal stenosis alone (69%), patients with concomitant spondylolisthesis (20%), patients with concomitant degenerative scoliosis (11%)	Decompressive laminectomy and instrumented fusion with pedicular screw system	2 years	Univariate analyses followed by multivariate logistic regression to assess the association between dependent outcome (failed change defined as a reduction of ODI less than 15%) and the following potential predictor variables: gender, age at time of surgery, onset of disease, income, comorbid conditions, smoking, work status, diagnosis, number of level of instrumentation, and SI fusion	Results of the regression analysis showed a statistically significant association between age at time of surgery (>65 years), onset of disease (>24 months), and number of levels of instrumentation (>4 levels) and failed clinical outcome change. **Level of instrumentation (>4 levels)**: odds ratio 2.207, p=0.043; **Age (>65)**: odds ratio 2.161, p=0.043, and **onset of disease (>24 months**): odds ratio 2.026, p=0.048.

Author/Year/ Country	Study Design	Patient Population	Diagnosis Included	Treatment Strategy	Followup Period	Type of Analysis and Predictive Factors Considered	Significant Factors
Carreon et al. 2009[31] United States	Prospective cohort study 546 patients	Patients undergoing lumber fusion for degenerative disorders Mean age of patients 55.9±13.2, 190 (35%) males, 299 (55%) females, 29 (5.3%) received workers compensation, and 100 (18.3%) were current smokers	Disc pathology (13.1%), scoliosis (4.9%), spondylolisthesis (23.3%), stenosis (12.5%), instability (5.3%), nonunion (8.8%), postdecompression instability (21.9%), and adjacent level degeneration (10.2%)	Posterolateral fusion (76.1%), combined anteroposterior fusion (11.5%), transforaminal interbody fusion (9.4%), and anterior interbody fusion (3.1%).	2 years	Linear regression analysis used to determine the effect of preoperative mental component summary (MCS), physical component summary (PCS), ODI, back pain prominence, body mass index, age, smoking habits, and workers compensation status on health-related quality of life measured using the SF-36 and ODI	Patients with better preoperative MCS (p=0.008) and worse preoperative ODI scores (p <0.001) achieved greater ODI. Patients receiving workers compensation did significantly worse (p=0.03). Patients with better preoperative MCS (p=0.004), better preoperative PCS (p=-0.0155), and worse preoperative ODI scores (p=0.021) achieved greater PCS improvement.

Author/Year/ Country	Study Design	Patient Population	Diagnosis Included	Treatment Strategy	Followup Period	Type of Analysis and Predictive Factors Considered	Significant Factors
Weinstein et al. 2007 & 2009[13,14]	Prospective non-randomized comparative trial (368 fusion group and 233 nonsurgical group	Mean age of patients 64.7±10.1 (fusion) and 68.2±10.3 (nonsurgical); 68.5% female (69% fusion, 67% nonsurgical); 98% non-hispanic (98% fusion, 98% nonsurgical); 84% white (86% fusion and 82% nonsurgical); and 10% black (8% fusion and 13% nonsurgical); 41 patients on workman's compensation (9% fusion and 3% nonsurgical)	Degenerative spondylolisthesis and spinal stenosis with neurologic claudication or radicular leg pain with associated neurologic signs	**Fusion group** The surgical protocol consisted of standard posterior decompressive laminectomy with or without bilateral single-level fusion (iliac crest bone grafting with or without posterior pedicle-screw instrumentation). **Nonsurgical group** The nonsurgical protocol was usual care, recommended to include at least active physical therapy, education or counseling (including instructions for home exercise), and nonsteroidal anti-inflammatory agents if tolerated.	4 years	Regression models were fitted for selected subgroups that included patients less than 65 years at baseline, level of decompression, education level, gender, smoking history, severity of symptoms at baseline duration of symptoms, treatment preferences, number of stenoic levels, severity of stenosis on imaging, number of coexisting conditions, and baseline SF-36 mental component score.	Patients less than 65 years old at baseline had larger treatment effects in favor of surgery at 3 months (21.3 vs. 14.6 for bodily pain, p = 0.02), but not at 1 or 2 years. Patients with a degenerative spondylolisthesis level of L3-L4 had a larger treatment effect than patients with a level of L4-L5 (33.1 vs. 16.8 for bodily pain, p = 0.01) at 2 years (not a 3 months or 1 year). Patients with no more that a high school education had smaller treatment effects for surgery at 3 months (12.8 vs. 20.5 for bodily pain, p = 0.002) and at 2 years (11.5 vs. 21.6, p = 0.01). Subsequent analysis at 4 year followup indicated that patients with neurogenic claudation had larger treatment effects favoring surgery on both bodily pain and function. No other factors considered showed a significant moderator effect.

Author/Year/ Country	Study Design	Patient Population	Diagnosis Included	Treatment Strategy	Followup Period	Type of Analysis and Predictive Factors Considered	Significant Factors
Okuda et al. 2006[32] Japan	Prospective cohort study 101 patients	All patients who were considered for surgery had severe disability low-back pain and lower extremity pain that were unresponsive to non-surgical treatment. Mean age 64 (range 44 to 79 years). No other demographics reported. Patients were excluded from study if they had previous lumbar surgery or had a history of infection, trauma, rheumatoid arthritis, or multiple compression fractures with severe osteoporosis.	All patients had degenerative spondylolisthesis	Posterior lumbar interbody fusion	2 years	Patients were divided into two groups based on age: Group 1 included 31 patients 70 years of age or older (average age 74) and Group 2 included 70 patients less than 70 years (average age 59). Regression analysis was used to compare the clinical (rate of recovery) and radiological (results of fusion) outcomes of the groups. Recovery rates indicated the degree of normalization after surgery and was evaluated using the Hirabayashi's method (recovery rate % = [postoperative score on the Japanese Orthopaedic Association's scale – preoperative score x 100/maximum possible score – preoperative score.])	The rate of either collapsed union or delayed union in Group 1 (>70 years) was significantly higher than in Group 2 (<70 years, p=0.034).

Author/Year/ Country	Study Design	Patient Population	Diagnosis Included	Treatment Strategy	Followup Period	Type of Analysis and Predictive Factors Considered	Significant Factors
Schuler et al. 2005[33] United States	Retrospective cohort study 392 patients	Patients who underwent fusion surgery between 1996 and 1999 were included in study. Patients subgrouped based on disc space: collapsed (<5 mm, 38 patients), intermediate collapsed (5 to 10 mm, 120 patients), intermediate (10 to 15 mm, 149 patients), and tall (>15 mm, 85 patients) Mean age 43.9, % male ranged from 21.1% in <5 mm group to 65.9% in tall group, % on workers compensation ranged from 10.5% in <5 mm group to 49.4% in tall group, and the 5 to 10 mm group had the majority of smokers (37.5%)	All patients had single-level symptomatic discogenic disease at time of surgery	All patients underwent stand-alone anterior lumbar interbody fusion (262 patients underwent the procedure through an open retroperitoneal or a transperitoneal approach.	2 years	Analysis of covariance was used to assess outcome data. The influence of age, weight, sex, and workers compensation were adjusted in the comparison of the four disc space groups on the bases of ODI scores, SF-36 scores, and low back pain scores. Comparisons were then made between the disc groups.	Patients in the collapsed disc group (<5 mm) had significant improvement in ODI scores compared with the other disc height groups at 6 months followup (p=0.039), at 1 year (p=0.022), and at 2 years (0.046). They also demonstrated significant improvement on the PCS of the SF-36 (6 months, p=0.010; 1 year, p=0.007; and 2 year, p=0.039) and on the visual analog scale (VAS) for low back pain (6 months, p=0.018; 1 year, p=0.047; and 2 year p=0.034).

Author/Year/ Country	Study Design	Patient Population	Diagnosis Included	Treatment Strategy	Followup Period	Type of Analysis and Predictive Factors Considered	Significant Factors
Hagg et al. 2003[28] Sweden	RCT 264 (201 fusion group vs. 63 non-surgical group)	Men and women between 25 and 65 years with severe chronic low back pain. Mean age 43 years (43 fusion, 44 nonsurgical), 50% women (50% fusion, 51% nonsurgical), disability pension 21% (20% fusion, 22% nonsurgical), and smoking 43% (41% fusion, 49% nonsurgical)	Degenerated lumbar disc with chronic low back pain	**Fusion group:** Posterolateral fusion with (n=74) or without (n=73) Variable Screw Placement with pedicle screws and plates (Raynham, MA) Circumferential fusion (n=75) including ALIF or PLIF to place bone graft **Nonsurgical group:** Physical therapy primarily, with one or more treatment (acupuncture, injection) cognitive functioning training, coping strategies, information and education	2 years	Univariate analyses followed by multivariate forward stepwise logistic regression for each group with patient rated improvement status (improved/not improved) and work status as dependent variables; factors adjusted for include heavy job, workers compensation, disability pension, unemployment, sick leave due to low back pain, gender, comorbidity, married/cohabit, smoking, prior surgery, continuous pain, personality traits, and psychological symptoms.	**Improved vs. not improved** **Fusion group:** High neuroticism[1] associated with non-improvement (odds ratio 0.95, 95% CI's 0.92 to 0.98) **Non-surgical group:** More depressive symptoms[2] associated with improvement (odds ratio 1.08, 95% CI's 1.02 to 1.14) **Working vs. not working** **Fusion group:** low age and short sick leave associated with working; age (odds ratio 0.95, 95% CIs 0.91 to 0.99) and sick leave (odds ratio 0.96, 95% CIs 0.94 to 0.99) **Non-surgical group:** short sick leave associated with working (odds ratio 0.96, 95% CIs 0.92 to 0.99)

[1] Personality traits were assessed using the Karolinska Scales of Personality (KSP). Patients with neuroticism-related personality traits ("neurotic personality") tend to be tense and stiff, restless, uneasy, panicky, easily fatigued, remorseful, experiencing tremor and palpitations under stress. Higher scores indicate more of a personality trait.

[2] Depressive symptoms measured using the Zung Depression Scale (ZDS); higher scores indicate more depressive symptoms.