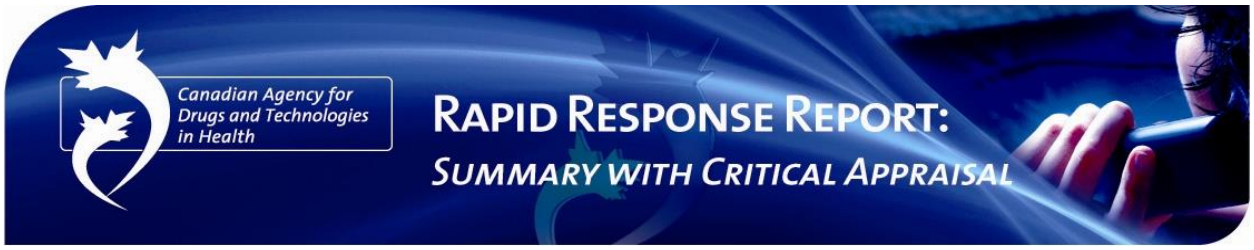

TITLE: Direct Lateral Interbody Fusion in Patients Requiring Surgery for Spinal Instability: A Review of the Comparative Clinical and Cost-Effectiveness, and Guidelines

DATE: 25 June 2015

CONTEXT AND POLICY ISSUES

A wide range of conditions including degenerative spine diseases, spinal deformities, tumors, infection, and spine trauma can result in spinal instability. These conditions are also associated with back pain, disability, and decreased quality of life (QoL). Estimates of the economic burden of back pain in the USA is US$100 billion dollars per year including indirect costs of lost wages and productivity.[1] Treatment options for some of these indications include conservative approaches such as immobilization, aerobic activity, muscle strengthening, postural control and others depending on the patient's condition. However for certain indications, lumbar fusion surgeries have demonstrated accelerated return to work/productivity and cost-effectiveness.[1-3]

There are a variety of surgical techniques used to fuse lumbar vertebrae. Each surgical approach carries a particular risk profile due to disruption of different soft-tissue.[1] Open approaches include posterior lumbar interbody fusion (PLIF), transforaminal lumbar interbody fusion (TLIF), and anterior lumbar interbody fusion (ALIF).[4] Open anterior approaches (ALIF) include potential vascular, visceral, and sexual dysfunction complication risks while posterior approaches (PLIF and TLIF) include paraspinal denervation, dural tear, and neural injury risks.[4,5] The evolution of surgical approaches in this area is aimed at improving recovery time with a smaller tissue dissection. More recently developed techniques are minimally invasive and include procedures utilizing proprietary instrumentation and equipment. AxiaLIF (TransS1, Inc., Wilmington, NC) uses a paracoccygeal approach to the L5-S1 junction, decreasing risk to the anterior organs and dorsal neural elements.[4] Another minimally invasive approach is a lateral approach, referred to as eXtreme lateral interbody fusion (XLIF or ELIF) (NuVasive, Inc., San Diego, CA),[6] direct lateral interbody fusion (DLIF), or lateral lumbar interbody fusion (LLIF).[4] No significant variation in these lateral approach techniques or surgical indication has been reported.[5] The lateral approaches are minimally invasive, reduce manipulation of the aorta and vena cava, and also avoid dissection or retraction of back muscles, bones, ligaments, and nerves.[5,7] This approach is anatomically limited by ribs and the iliac wing, and nerves of the lumbar plexus are in the path of this approach.[8] Injury to nerves of the lumbar plexus, possibly

resulting motor deficit complications, is a concerning complication risk for the lateral approach to lumbar interbody fusion surgeries.[8]

The purpose of this report is to retrieve and review the existing evidence of clinical effectiveness, and safety of DLIF in patients requiring surgery for spinal instability. In addition this report aims to examine the available evidence for comparative clinical effectiveness, and cost-effectiveness of DLIF as compared to other surgical lumbar fusion techniques in single and multiple transpsoas fusions for the treatment of spinal instability. Finally this report aims to retrieve and review available guidelines on performing DLIF in patients requiring surgery for spinal instability.

RESEARCH QUESTIONS

1. What is the clinical effectiveness of direct lateral interbody fusion (DLIF) in patients requiring surgery for spinal instability?

2. What is the comparative clinical effectiveness of DLIF versus other lumbar fusion techniques in patients requiring surgery for spinal instability?

3. What is the comparative clinical effectiveness of single versus multiple transpsoas fusions during DLIF in patients requiring surgery for spinal instability?

4. What is the comparative cost-effectiveness of DLIF versus other lumbar fusion techniques in patients requiring surgery for spinal instability?

5. What are the evidence-based guidelines regarding performing DLIF in patients requiring surgery for spinal instability?

KEY FINDINGS

Identified studies of limited quality suggested that direct lateral interbody fusion (DLIF) is a clinically effective procedure for patients requiring surgery for conditions that may result in spinal instability. Limited-quality, conflicting evidence was identified for the clinical effectiveness of DLIF as compared to other lumbar fusion surgical techniques. Identified data on comparative complication rates was also conflicting. The most frequently reported complications of DLIF were transient anterior thigh pain, anterior thigh numbness, and/or hip flexor weakness. Two uncontrolled before-after studies were identified that found no statistically significant differences in outcomes of pain or disability for one-level vs two-level DLIF, however DLIF on two or more levels was associated with an increased length of hospital stay in another uncontrolled study. No cost-effectiveness studies were identified, however a cost-analysis found DLIF may offer cost savings as compared to an open anterior lumbar interbody fusion procedure due to decreased operating room time, length of hospital stay, and pharmaceutical management of pain. No relevant guidelines were identified.

METHODS

Literature Search Strategy

A limited literature search was conducted on key resources including PubMed, The Cochrane Library, University of York Centre for Reviews and Dissemination (CRD) databases, Canadian

and major international health technology agencies, as well as a focused Internet search. Methodological filters were applied to limit retrieval to health technology assessments, systematic reviews, meta-analyses, randomized controlled trials, randomized controlled trials, non-randomized studies, economic studies and guidelines. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 01, 2010 and May 27, 2015. Internet links were provided, where available.

Selection Criteria and Methods

One reviewer screened titles and abstracts identified by the literature search strategy. Full-text articles were then retrieved and evaluated for final article selection based on the criteria presented in Table 1.

Table 1: Selection Criteria

Population	Patients (any age) requiring lumbar fusion surgery due to degenerative conditions, deformities, and injuries leading to spinal instability
Intervention	Q1-Q2, Q4-Q5: Direct Lateral Interbody Fusion (DLIF) [Also referred to as: Extreme Lateral Interbody Fusion (XLIF or ELIF), Lumbar Lateral Interbody Fusion (LLIF), and Lateral Transpsoas Interbody Fusion (LTIF)] Q3: DLIF with a single transpsoas fusion
Comparator	Q1 and 5: No comparator Q2 and 4: Any other lumbar fusion surgical technique, including, but not limited to: anterior lumbar interbody fusion (ALIF), posterior lumbar interbody fusion (PLIF), transforaminal lumbar interbody fusion (TLIF), axial lumbar interbody fusion (AxiaLIF) Q3: DLIF with multiple transpsoas fusions
Outcomes	Q1-3: Clinical effectiveness (e.g., pain scores, mobility scores, fusion rate, functional ability, walking distance, length of hospital stay, recovery rate, rate of subsequent surgery, rate of pain recurrence); Safety (e.g., failed back surgery syndrome, pseudoarthrosis, repeat surgery, nerve damage) Q4: Cost-effectiveness outcomes Q5: Evidence-based guidelines regarding performing DLIF (including patient indications, expertise required)
Study Designs	Health Technology Assessments (HTA)/Systematic review (SR)/Meta-analysis (MA); Randomized controlled trials (RCTs); non-randomized studies; Economic evaluations; and Evidence-based Guidelines

Exclusion Criteria

Studies were excluded if they did not meet the selection criteria, were included in an identified systematic review, or were published in a language other than English, or were published prior to 2010.

Critical Appraisal of Individual Studies

The quality of the included SR was assessed using the Assessing the Methodological Quality of Systematic Reviews (AMSTAR) tool.[9] The quality of the non-randomized studies and uncontrolled before-after studies included in this report was assessed using the Downs and Black checklist for non-randomized studies.[10] The cost-analysis included in this report was assessed using Drummond's Checklist.[11] For all critical appraisals the strengths and limitations were described narratively instead of assigning a numerical score.

SUMMARY OF EVIDENCE

Quantity of Research Available

The literature search strategy identified 363 articles. Following screening titles and abstracts by one reviewer, 318 citations did not meet the inclusion criteria (Table 1); as a result, 45 full text articles were retrieved for review. Searching the grey literature resulting in identification of five potentially relevant articles. Upon full-text review of the 50 potentially relevant reports, one SR, one cost-analysis, three non-randomized studies, and 22 uncontrolled before-after studies were included. No relevant guidelines were identified. A Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flowchart describes the selection procedure of the included studies of this review (Appendix 1).

The 23 excluded studies consisted of 15 studies that examined irrelevant outcomes, the majority of which were spine measurements from imaging data. Two studies were excluded because they were included in the SR, one was excluded as it was published before 2010, three articles were review articles, and two were case series.

Summary of Study Characteristics

Clinical Effectiveness and Comparative Clinical Effectiveness

The study characteristics of the included SR,[12] non-randomized studies,[8,13,14] uncontrolled before-after studies,[6,7,15-34] and cost-analysis study[1] are tabulated in Appendix 2.

Study Design

The SR was published in 2014 and identified and reviewed six non-randomized studies published between 2009 and 2012. The search included studies published before December 2013, with at least 20 patients of 18 years or older. The SR excluded case reports, and studies involving traumatic onset, fracture, thoracic disc disease, infection, or neoplasms. This search criteria resulted in the identification of three retrospective cohort studies (all using historical cohorts) that examined the comparative effectiveness and safety of LLIF/XLIF/DLIF versus PLIF/TLIF surgery, one prospective cohort study and two retrospective cohort studies that reported predictive factors following XLIF surgery.[12]

The non-randomized studies consisted of one prospective cohort controlled study (PCCS),[8] and two retrospective cohort controlled studies (RCCS).[13,14] The PCCS was conducted in the Czech Republic and included scheduled follow-ups at 6 weeks, 6 months,12 months, and 24 months after the intervention.[8] One retrospective cohort controlled study (RCCS) was conducted in 2014 in Seoul, Korea with an average follow-up of approximately 17 months.[13] The second RCCS

was conducted in New York, NY, USA and averaged a follow-up of approximately 15 months after the intervention.[14]

The majority of identified studies were uncontrolled before-after studies (UBAS), and examined outcomes before and after DLIF surgical procedures. The majority of those were conducted in the USA,[6,7,15,16,18,20,22,27,28,31-34] however three were from Italy,[17,19,30] three were from Korea,[21,25,29] two were from Australia,[23,24] and one was from Austria.[24] No identified studies originated in Canada. The longest follow-up time for the UBASs averaged 34.5 months,[17] while two other studies had a follow-up time of averaging over two years.[15,25] Two studies had a follow-up time equal to two years,[7,19] five had average follow-ups over one year,[6,18,24,28,32] ten had follow-ups at one year,[20-23,26,27,30,31,33,34] one study had an average follow-up of over 6 months,[16] and the shortest follow-up of the included UBASs averaged three months.[29]

Population

The included SR examines patients with degenerative spine conditions and the combined total patients of the included studies was 818.[12]

The identified PCCS examined 208 patients with an overall average age of 47 years and diagnoses of degenerative disc disease, failed back surgery syndrome, spondylolisthesis, retrolisthesis, or post-traumatic disc injury. This study excluded patients with severe osteoporosis, tumour, infection, fresh spine fracture, or spondylolisthesis grades III and IV.[8] The first RCCS examined 179 patients with an overall average age of 62 years and diagnoses of spinal stenosis, degenerative spondylolisthesis, recurrent disc herniation, and other unspecific diagnoses.[13] The second RCCS included 293 patients averaging 62 years old who received the intervention at different time intervals, from 2006 to 2008, from 2009 to 2010, and from 2011 to 2012. The diagnoses of the patients receiving the studied intervention was not reported in this RCCS.[14]

The included UBASs varied in size such that the largest study included 600 patients,[31] while three were small studies of under 20 patients.[16,25,29] Seven studies were between 20 and 50 patients,[7,14,22,28] eight were between 50 and 100 patients,[6,17,20,21,27,30,32,34] and three other studies were over 100 patients.[15,18,24] Three studies had patients with an average age of 55 to 60,[19,20,30] 11 with an average age of 60 to 65,[6,15,17,21,23-26,31,33,34] and seven studies with patients with an average age over 65 years old.[7,16,18,22,27-29] One UBAS did not include an average age of patients.[32] While many diagnoses included in the UBASs may be considered overlapping, a wide range is represented including neurological claudication with deformity or instability,[15] de novo scoliosis,[15] spondylolisthesis,[6,7,15-23,26,27,31-33] junctional disc degeneration,[15,19] degenerative scoliosis,[7,16,17,19-24,26-33] lateral listhesis,[16] pyogenic spondylitis,[25,32] post-laminectomy syndrome,[6,7,16,18,20,31] adjacent segment disease,[6,16,18,23,32] degenerative disc disease,[6,17-20,23,26,29,30,33] sagittal imbalance,[17] stenosis,[17,20,21,24,27,31,32] revision,[17] thoracolumbar fractures,[19] kyphosis due to disc degeneration,[19] post-traumatic kyphosis,[30] structured kyphosis,[19] recurrent disc herniation,[20] infective spondylitis,[21] instrumentation failure/nonunion,[6] prior variable screw placement instrumentation,[7] herniated nucleas pulposis,[7,31,32] prior variable spinal plate,[7] pseudarthrosis following pedicle substraction osteotomy,[30] anterior column reconstruction,[30] osteomyelitis,[31] tumour,[32] other nonspecified,[17] and one UBAS did not report diagnosis prior to intervention.[34] Two studies had diagnostic exclusion criteria that included scoliosis,[18] tumour,[18] vertebral body fracture,[18] disctitis,[18] pseudoarthrosis,[18] retroperitoneal adhesion,[21] severe spondylolisthesis,[21] severe rotational deformity,[21] infective spondylitis,[21] involvement of L4-L5

level with high iliac crest,[21] and involvement of the L5-S1 level.[21] No studies included in this report had inclusion criteria that specified spinal instability.

Intervention and comparators

The intervention of interest in this report is DLIF, however it was also referred to as XLIF, LLIF, and ELIF.[6,12] The included SR included studies that referred to the intervention as LLIF, XLIF, and DLIF which were compared to either PLIF or TLIF.[12]

The included PCCS referred to the intervention as XLIF and compared it to minimally invasive anterior lumbar interbody fusion (ALIF) and used autologous and artificial bone as fusion material in both treatment arms.[8] The most recent RCCS referred to the intervention as DLIF and used demineralized bone matrix (DBM) as the fusion material while the surgical comparator employed autologous bone as the fusion material in a unilateral open TLIF procedure.[13] The second RCCS referred to the intervention as LLIF and used different cages and different fusion materials for different surgeries and compared the same surgical procedure conducted across different time intervals at the same center.[14]

The UBASs examined outcomes before and after the intervention which was referred to as LLIF,[15,22,24] XLIF,[7,16,18-20,23,26-28,30-34] DLIF,[17,21,25,29] or ELIF.[6] Many surgical details differed between patients in these studies due to the individual surgical need. Some limited additional information on the surgical interventions of the included UBASs is included in Appendix 2, Table A2.3. One aspect of the intervention that varied significantly between studies and within studies was the fusion material used, which included DBM,[21,29,33] silicate calcium phosphate (Actifuse, Apatech, Baxter),[6] bone morphogenic protein (BMP) (INFUSE, Medtronic-Sofamor Danek, Memphis, TN),[20,22,23,26,32,33] Mastergraft β-TCP granules (BioHorizons, AL, USA),[22,23,26] tricalcium phosphate (ChronOS, Synthes, PA, USA),[29] calcium triphosphate,[17] Attrax (Nuvasive, San Diego, CA),[17] autologous bone,[7,17,25,33] allograft,[28,32,33] bone marrow aspirate,[33] Osteocel (Nuvasive, Inc., San Diego, CA),[7,28] and Nanostim.[17] Three UBASs reported the choice of fusion material was left to the surgeon's preference,[15,24,33] two UBASs simply reported that the fusion material varied,[27,30] while four other studies did not report the fusion material used during the intervention.[16,18,19,31]

Outcomes

The included SR extracted data from the included six studies on length of hospital stay, reoperation, mortality, and complications.[12]

The included PCCS exclusively focused on complication outcomes categorized as intra-operative or post-operative. This study explicitly reported that complications related to implant healing were not included.[8] Both RCCSs included complication data,[13,14] however only one reported on clinical effectiveness outcomes which included visual analogue scale (VAS) for pain, fusion rate, and Oswestry disability index (ODI).[13] The RCCS that focused on complication data categorized compilations into sensory deficits, motor deficits, and anterior thigh/groin pain.[14]

The clinical effectiveness outcomes reported by the included UBASs were VAS for pain,[7,15,21,25-28,31-34] or specifically VAS for leg pain,[6,16-19,23,24,30] VAS for back pain,[6,17-19,23,24,30] or VAS for buttock pain,[6,16] ODI,[6,15-19,21,23,25,26,28,30,32,33] and quality of life (QoL) as measured by SF-36 physical component score (PCS),[18,23,26] SF-36 mental component score (MCS),[23,26] QoL SF-12

PCS,[15,28,33] or SF-12 MCS.[15,28,33] Six UBASs reported outcomes related to length of hospital stay,[7,18,20,27,31,32] nine reported fusion rates,[17,21-23,25-27,32,34] one reported fusion rate by the fusion material used,[17] and one reported VAS and ODI outcomes for one-level as compared to two-level fusions.[6] The reporting methods of complications varied greatly between the included UBASs, however only two studies did not report any complication data.[17,34] The most commonly reported complications were transient anterior thigh pain, transient anterior thigh numbness, and/or transient hip flexor weakness.[6,15,18-22,25,26,30,32,33] Five UBASs did not consider these post-operative symptoms as complications,[7,27-29,31] in three UBASs it was unclear if these symptoms were considered complications.[16,23,24] Of the twelve UBASs that reported the common transient complications of anterior thigh numbness, anterior thigh pain, and hip flexor weakness,[6,15,18-22,25,26,30,32,33] five reported that a subset of these symptoms had not resolved at last follow-up,[15,19,21,25,26] while one UBAS was unclear as to if all of these symptoms were resolved at last follow-up.[33] No identified studies reported separate outcome analysis for patients who demonstrated spinal instability.

Cost-effectiveness

One study was identified containing a cost-analysis. This study did a cost comparison based on a non-randomized study by retrospectively examining hospital charge data. The PCCS that was part of this analysis examined XLIF compared to open ALIF surgery for the treatment of degenerative disc disease, stenosis, post-laminectomy syndrome, herniated nucleus pulposus, spondylolisthesis, spondylolysis, and degenerative scoliosis. Clinical effectiveness outcomes reported were VAS for back pain, VAS for extremity pain, ODI, length of hospital stay, and complications. Cost outcomes from charge data were categorized as supplies/implants, OR services, pharmacy, room and board, lab, physical therapy and occupational therapy, and miscellaneous. The assumptions are that the PCCS study has no selection bias (despite no description of allocation methods) and that training costs were equivalent between the two procedures.[1]

Summary of Critical Appraisal

The critical appraisal of the included SR is summarized in Appendix 3, Table A3.1. The SR provided a well described literature search methodology which described explicit inclusion and exclusion criteria. The literature selection was also documented in a PRISMA flowchart, and the literature selected was assessed for methodological quality and bias. These assessments, however, were not presented in the review. Quantified conclusions, an overall strength of evidence using the Grades of Recommendation Assessment, Development and Evaluation (GRADE) criteria, complications, and conflicts of interest (COIs) of the included studies were reported. The SR disclosed that analytical support was outsourced to a private company using funding from a professional medical association making it unclear if there were competing interests.. The review was also limited by the identification of a paucity of studies which were considered low-quality evidence for the defined research objective.[8]

The PCCS was well described with a clear objective, intervention, statistical methods, and findings. The patient inclusion and exclusion criteria were also reported and the study had multiple scheduled follow-up time-points. The study only examined complications and lacked examination of predefined outcomes. The allocation procedure, accounting of patients lost to follow-up, and complication assessment were unclear. Results and patient characteristics were not tabulated and no comparison of patient groups before the intervention was conducted. This study was conducted with no blinding and there was no mention of potential COIs.[8] Both

included RCCSs had a clearly stated research objective, tabulated patient characteristics, and appropriately described statistical methods.[13,14] One RCCS had a well described intervention,[13] while the other reported an inconsistent intervention.[14] The comparator in one RCCS was different time intervals in which the LLIF was conducted and it was not clear how the intervention may have changed during this time.[14] The RCCS from 2014 also reported clinical effectiveness outcomes as well as complications,[13] while the earlier RCCS, from 2013, exclusively reported complications.[14] The earlier study however was a long-term study, which examined an important question of surgical expertise and training with clearly defined outcomes.[14] Neither RCCS sufficiently reported patients lost to follow-up, or had any blinding, or allocation procedure descriptions.[13,14] The RCCS from 2014 had inconsistent follow-up times, a statistically significant difference in a non-comparator aspect of the intervention (fusion material), and no mention of any potential COIs.[13] The earlier RCCS acknowledged a potential COI, did not examine patient populations for statistical differences prior to the intervention, and was limited to complication data.[14] The critical appraisals of the PCCS and two RCCS are summarized in Appendix 3, Table A3.2.

Included in this report are 22 uncontrolled before-after studies (UBASs) which, due to study design, have some inherent limitations on quality. Most importantly, none of these studies had any control groups which means the outcomes of these studies were subjected to an unknown magnitude of non-specific effects. Additionally the investigators, outcome assessors and patients of the studies were not blinded to the intervention. All of the included UBASs tabulated the characteristics of included patients,[6,7,15-34] however only twelve of the 22 studies had predefined patient inclusion and exclusion criteria.[6,17,21-28,31,33] Twelve of the UBASs had an inconsistent follow-up time,[6,7,15-18,24,25,28-30,32] while the remaining ten studies had regularly scheduled follow-up times.[19-23,26,27,31,33,34] It was unclear in 16 UBASs whether any patients were excluded from the analysis due to loss to follow-up,[6,7,15,16,18-20,22-24,27-29,31,33,34] two studies reported loss to follow-up but did not elaborate on why,[21,32] another three studies reported and explained patients who were lost to follow-up,[17,26,30] and one UBAS reported that no patients were lost to follow-up.[25] Statistical methods were sufficiently described in 18 UBASs,[6,15-20,22-24,26,28-34] while an incomplete description was presented in two studies,[21,25] and the remaining two provided no description of the statistical methodology used.[7,27] The methodology used to assess the outcomes was described in all of the included UBASs,[6,7,15-34] however the collection and assessment of complications was not clear in ten of the included UBASs.[15,16,19-23,25,29,34] Complication assessment was sufficiently described in six UBASs,[6,18,24,28,31,32] five studies had some complication assessment information,[7,26,27,30,33] and one study had no information on complications at all.[17] The details of the DLIF intervention was described in seventeen studies,[6,7,15,17,20-30,32,33] and was almost or completely absent in five UBASs.[16,18,19,31,34] While there are many patient variables that change specifics of a surgical intervention, it was noted that four studies inconsistently applied fusion materials during the study.[17,24,27,33] Nine included UBASs acknowledged at least one potential COI,[6,17,18,23,24,27,28,31,32] five did not report if any potential COIs existed,[7,21,29,33,34] and eight reported no potential COIs.[6,17,18,23,24,27,28,31,32] A summary of the critical appraisal for the UBCSs is available in Appendix 3, Table A3.3.

The critical appraisal of the identified cost-analysis study included in this report is summarized in Appendix 3, Table A3.4. The prospective cohort controlled part of the analysis, on which the cost-analysis was based, had tabulated patient characteristics, and regularly scheduled follow-up time-points. The study also described the statistical methods, outcome assessment,

intervention, and had some information on how complications were assessed. There was no information regarding blinding, allocation procedures, or allocation concealment. The patient characteristics had statistically significant differences between treatment groups prior to the intervention, and there was no accounting for the significant proportion of patients lost to follow-up. As a cost-analysis, this study did not relate costs to the clinical efficacy results and was not a cost-effectiveness study. The cost-analysis did use a relevant comparator and while the itemized costs were not from a published source the costs were directly taken from hospital charge data. This may have limited the perspective of the study, however it did not make any assumptions about costs. The study did not include any costs related to staff training and did not account for any differences in the long-term durability of either procedure. The cost-analysis included a cost comparison for both one-level and two-level fusions separately. There was no statement provided regarding potential COIs.[1]

Summary of Findings

The findings of the included studies of this report are summarized in Appendix 4.

The SR included in this report identified a lack of studies comparing LLIF with PLIF or TLIF surgery. The majority of the studies included in the SR were evaluated as having a moderately high risk of bias. The SR identified one study, evaluated as having a moderately high risk of bias, that found a statistically significant decreased length of hospital stay for LLIF as compared to PLIF/TLIF surgery, and also identified other low-quality evidence suggesting that LLIF resulted in fewer complications than PLIF/TLIF surgery. However the authors concluded that there was insufficient evidence of the comparative effectiveness of the examined procedures and that differences in complication rates were from low-quality and conflicting evidence.[12] The SR identified one study that found a 59% increase in complication risk for each additional level fused using LLIF, and other suggesting that higher complication risks were found in patients with degenerative disc disease and recurrent disc herniation as compared to scoliosis, spondylolisthesis, stenosis, or post-laminectomy instability. These findings were not compared to other surgical methods and the authors of the SR concluded that the evidence for influence of preoperative factors on patient outcomes after LLIF surgery is insufficient.[12]

The identified PCCS study examined complications categorized as major or minor. One major complication occurred in 88 XLIF surgeries, while none occurred in 120 ALIF surgeries. Major and minor categories of complications were left undefined, however the major complication in the XLIF surgery was a partial and transient injury to the L5 nerve root. The difference in the rate of total complications was not statistically significant. The most commonly identified complication in the patients receiving ALIF surgery was lumbar post-sympathectomy syndrome occurring in 15.8% of patients, while post-operative transient pain and numbness were the most common complications of XLIF surgery occurring in 12.5% of patients.[8]

The identified RCCS published in 2014 found a statistically significant difference in the rate of fusion at 12 months for DLIF (87.7%) as compared to TLIF (98.1%). The use of different fusion materials between the treatment groups, DBM for DLIF and autologous bone for TLIF, confounds this observation. The remaining clinical effectiveness outcomes examined in this study, VAS pain and ODI at 12 months, revealed no statistically significant difference between treatment groups. The total complication rate was 19.7% for DLIF and 1.0% for TLIF. The authors concluded that DLIF demonstrated a lower fusion rate and additional complications related to the transpsoas approach.[13]

The second RCCS included in this report was from 2013. This report did not examine clinical effectiveness outcomes and instead focused on the complication rate of LLIF at different time intervals to evaluate the institutional learning curve of LLIF. This study found a statistically significant reduction in patients with immediate post-operative sensory deficits, from 44.4% in 2006 to 2008 to 25.0% in surgeries performed between four and five years later.[14]

While findings from the included UBASs are based upon studies with inherent limitations some consistencies were identified. A majority of UBASs examining the rate of fusion of DLIF procedures reported results between 80 and 90%[17,21,23,25,26,32] which is consistent with the identified RCCS published in 2014.[13] Other UBASs found a rate of fusion of 91%,[34] 98%,[22] and one study reported a 100% rate of fusion.[27]

Every UBAS that examined pain, as measured by VAS or numerical rating scale (NRS), reported statistically significant pain improvements at last follow-up after a DLIF, XLIF, LLIF, or ELIF surgery,[6,15,16,18,19,21,23-28,30-34] except for one study that did not report if the improvement was statistically significant.[7] Similarly, all UBASs examining ODI as an outcome found statistically significant improvement at last follow-up after surgery.[6,15,16,18,19,21,23,25,26,28,30,32,33] Six UBASs examined QoL before and after surgery as evaluated by SF-12 or SF-36, and all found a statistically significant improvement in the PCS at last follow-up.[15,18,23,26,28,33] Five studies examined the MCS,[15,23,26,28,33] and only one identified an statistically significant improvement in a subgroup of patients who had a standalone XLIF procedure as opposed to an instrumented XLIF procedure.[23]

The average length of hospital stay was reported in six included UBASs with one report of 1.1 to 1.5 days,[18] two reports of 1.21 days,[27,31] one report of 2.6 days,[32] one report of 3 days,[20] and one report of 4.75 days.[7]

Seven UBASs compared outcomes between different patient subpopulations.[6,17,18,20,23,24,27] One study examined outcomes of VAS leg pain, VAS back pain, and ODI for patients evaluated as having achieved fusion after XLIF surgery compared to those who were evaluated as probably fused or not fused after XLIF surgery and found no statistically significant differences.[17] This study also examined the fusion rate in XLIF surgery patients for which different fusion materials were used. No statistically significant differences in fusion rates were found for XLIF surgeries using autograft (75%), calcium triphosphate (89%), Attrax (Nuvasive, San Diego, CA) (83%), and autologous bone or Nanostim (Medtronic, Memphis, TN) (100%), although the authors state that some comparisons were not possible do to the low number of patients.[17] When patients were subcategorized by their initial diagnosis, no statistically significant differences were observed in average hospital stay between adjacent segment disease, degenerative disc disease, post-laminectomy syndrome, or degenerative spondylolisthesis patients.[18] The average hospital stay was significantly greater for patients receiving XLIF surgery on two or more levels as compared to one-level.[20] When patients were categorized based upon an initial diagnosis of a deformity or a degeneration there was no statistically significant differences in VAS pain improvements or ODI improvements following ELIF surgery. Similarly there was no difference in these clinical effectiveness improvements between patients with one-level of degeneration as compared to patients with two-levels of degeneration.[6] When examining pain as measured by VAS at last follow-up after XLIF surgery, one study reported no influence from the number of levels treated,[27] while another did observe a statistically significant decreased pain improvement for patients who required surgical revision.[24] When patients were categorized as either XLIF

with instrumentation or standalone XLIF, outcomes of VAS pain, ODI, and QoL PCS demonstrated no statistically significant differences.[23]

The most frequently reported complications in the included UBASs were transient anterior thigh pain, anterior thigh numbness, and/or hip flexor weakness.[6,15,18-22,25,26,30,32,33] These transient post-operative symptoms were classified as side effects in one UBAS,[18] were not included as complications at all in five UBASs,[7,27-29,31] and in three studies it was unclear as to whether these symptoms were included as complications.[16,23,24] Five studies reported that a subset of these transient symptoms had not resolved at last follow-up.[15,19,21,25,26] One UBAS reported one case of anterior thigh pain out of 118 patients which was unresolved at two years,[15] another reported one case out of 90 unresolved at 12 months.[21] Seven cases of only partial improvement in anterior thigh numbness out of 39 patients in an average follow-up of 16 months was reported in another UBAS.[19] One UBAS reported that 'most' of the four postoperative anterior thigh pain and/or hip flexor weakness symptoms in 16 DLIF patients resolved by last follow-up.[25] In another UBAS examining 30 XLIF patients one of five anterior thigh sensory change symptoms was not resolved at six weeks.[26] One UBAS that did not include these post-operative symptoms as complications reported, "a substantial portion of patients reported anterior thigh pain/numbness after surgery,"[29] while another reported, "…thigh pain and hip flexor weakness are nearly universal-due, perhaps, to direct trauma to the psoas muscle…"[31]

The total complication rate was calculated based upon the possibility of more than one complication per patient recorded as more than one complication. The rate varied considerably across reports with those that included transient symptoms as complications reporting 56.8%,[15] 35%,[18] 51.3%,[19] 23.1%,[20] 18.9%,[21] 22.2%,[6] 62.0%,[22] 25%,[25] 46.7%,[26] 31.2%,[30] 12%,[32] and 135%.[33] Those that didn't include transient symptoms as complications reported total complication rates of 24%,[7] 3.2%,[27] 26.7%,[28] and 6.2%.[31] Reported reoperation rates were 12/90 (13.3%),[6] 16/117 (13.7%),[24] 2/30 (6.7%),[26] 1/8 (12.5%),[28] 3/108 (2.8%),[20] and 11/600 (1.8%).[31] The largest UBAS analyzed subpopulations of patients and found that prior surgery, prior fusion surgery, and the inclusion of L4-L5 were statistically significant factors in the incidence of complications.[31] There were no reports in the included UBASs of failed back surgery syndrome, or pseudoarthrosis as a complication. One UBAS reported one new motor deficit in its 30 patient cohort after XLIF surgery.[26] Another reported two cases of motor weakness in eight patients after DLIF surgery but it was unclear if the complication was transient.[29] Three UBASs reported one patient each that had an incidental durotomy,[7,22,32] and another reported four occurrences of a dural tear in 160 patients undergoing XLIF.[18]

The PCCS component of the included cost-analysis study found a statistically significant improvement in lower back pain, lower extremity pain, and ODI at 12 months and at 24 months after either XLIF surgery or open ALIF surgery. No statistically significant differences were found in these outcomes between XLIF surgery and open ALIF surgery.[1] The total compilation rate was lower in patients receiving XLIF surgery as compared to ALIF surgery (P = 0.041). The most common complication in both groups were reported as minor complications which included dural tears and transient sensory deficits. There was also a higher rate of infection for patients receiving open ALIF surgery of 5.7% as compared to XLIF surgery with an infection rate of 0.9%.[1] Significant categorical cost differences between XLIF and open ALIF one-level fusion surgeries were the total cost (9.94% difference), OR services (17.82%), and pharmacy costs (13.62%) all of which favoured XLIF surgery as the least expensive. For two-level fusion surgeries the significant cost differences that favoured XLIF surgery were total cost (13.62%), OR services (21.14%), and room and board (23.27%). No statistically significant cost differences were found favouring open ALIF surgery. The authors conclude that the cost

savings are reflections of the lower length of hospital stay, decreased operating room time, and the decreased need for post-operative pharmaceutical pain management required for XLIF vs open ALIF surgery.[1]

Limitations

Clinical effectiveness and complication data from UBASs is presented in this report and represents the majority of identified clinical data on DLIF. These studies have serious limitations including a lack of controls and blinding. All of the included studies examined patient populations comprised of a mixture of different initial diagnoses without a specific analysis for spinal instability. In addition, details of the surgical methodology varied between patients, between studies, and between treatment groups making unknown contributions to nonspecific effects and adding uncertainty to comparisons across studies.

CONCLUSIONS AND IMPLICATIONS FOR DECISION OR POLICY MAKING

The included SR found insufficient evidence to compare LLIF with PLIF or TLIF. The studies included in the SR also presented low-quality and conflicting evidence as to the comparative complication rates of these surgical procedures.[12]

One included RCCS found no statistically significant difference between DLIF and TLIF with respect to 12 month post-operative pain and ODI. This study found a significantly lower fusion rate with DLIF as compared to TLIF, however the use of different fusion materials between the two different surgical interventions added uncertainty to this finding. In addition this study was at risk of bias due to a lack of blinding for assessments, an unclear allocation procedure, the nature of retrospective analysis, and it was unclear if there were patients lost to follow-up.[13] The PCCS that was a component of the included cost-analysis also found no statistically significant differences in clinical effectiveness outcomes between XLIF and open ALIF, however this study's limitations included no accounting for a 35% loss to follow-up after two years.[1] The RCCS study found a significantly greater complication rate for DLIF surgery. Complications of DLIF surgery were muscle and nerve symptoms specific to the surgical approach.[13] In contrast, the PCCS included in this report found no significant difference in complication rates between ALIF and XLIF surgery. The most common complication of XLIF was post-operative transient pain at 12.5%, whereas the most common complication of ALIF was lumbar post-sympathectomy syndrome at 15.8%. Lumbar post-sympathectomy also occurred after XLIF surgery at 4.5% in this PCCS.[8] The PCCS component of the cost-analysis identified a lower complication rate for XLIF patients as compared to open ALIF patients.[1] These three controlled studies included in this report therefore had some important limitations and presented conflicting results with regard to both comparative clinical effectiveness and complication rates.[1,8,13]

Another identified RCCS found that the frequency of sensory deficits experienced by LLIF patients immediately after surgery decreased significantly as a function of time. This was interpreted as a lower complication rate as a function of surgical experience. It was not clear that the intervention was consistent over the time period and the lack of clinical effectiveness data to accompany this finding does not provide context for the complication rates.[14]

The uncontrolled studies included in this report contain some inherent limitations due to experimental design, however some consistencies were identified. The majority of UBASs that reported rates of fusion for DLIF, XLIF, LLIF, or ELIF procedures were in between 80 and 90%,[17,21,23,25,26,32] in agreement with the RCCS which reported a fusion rate of 87.7% for DLIF

surgeries and 98.1% for TLIF surgeries.[13] All studies that reported clinical effectiveness outcomes for pain and ODI found an improvement after DLIF, XLIF, LLIF, and ELIF surgeries.[6,7,15,16,18,19,21,23-28,30-34] While the rates of complications varied considerably amongst the uncontrolled studies, the most frequently reported complications were transient anterior thigh pain, transient anterior thigh numbness, and/or transient hip flexor weakness.[6,15,18-22,25,26,29-33] Some patients that experienced these common complications were reported as unresolved at last follow-up.[15,19,21,25,26] A single incidental durotomy was reported in each of three UBASs,[7,22,32] while four dural tears in 160 patients undergoing XLIF was reported by another.[18] Two UBASs found no statistically significant difference in outcomes of pain or ODI for one-level as compared to two-level ELIF/XLIF.[6,27] XLIF surgery on two or more levels was associated with an increased length of hospital stay as compared to one level XLIF in another UBAS.[20] This evidence suggests that DLIF is an effective surgical intervention with no frequent major complications for patients requiring spinal fusion surgery for degenerative conditions, deformities, and injuries.

An identified cost-analysis study found XLIF may offer cost savings over an open ALIF procedure. The total costs of both one-level and two-level XLIF procedures were significantly less costly due to decreased operating room time, length of hospital stay, and pharmaceutical management of pain. These results were not associated with clinical effectiveness and therefore may not represent all costs associated with different clinical outcomes. This study was also limited by a 35% loss to follow-up over two years.[1]

No relevant guidelines were identified.

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LIST OF ABBREVIATIONS

AL	Alabama
ALIF	anterior lumbar interbody fusion
ALL	anterior longitudinal ligament
BMD	bone mass density
BMI	body mass index
BMP	bone morphogenic protein
CAD	coronary artery disease
COI	conflict of interest
COPD	chronic obstructive pulmonary disease
DBM	demineralized bone matrix
DLIF	direct lateral interbody fusion
ELIF	extreme lateral interbody fusion
FL	Florida
FU	follow-up
GRADE	Grades of Recommendation Assessment, Development and Evaluation
LA	Louisiana
LLIF	lateral lumbar interbody fusion
LOS	hospital length of stay
MCS	mental component score
MD	Maryland
MN	Minnesota
MO	Missouri
NC	North Carolina
NR	not reported
NRS	numerical rating scale
NS	not significant
NS	reported as not statistically significant
ODI	Oswestry Disability Index
OR	operating room
ORT	operating room time
PCS	physical component score
PLIF	posterior lumbar interbody fusion
PPI	percutaneous posterior instrumentation
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
QoL	quality of life
SE	standard error
TLIF	transforaminal interbody fusion
USA	United States of America
VAS	visual analogue scale
XLIF	extreme lateral interbody fusion

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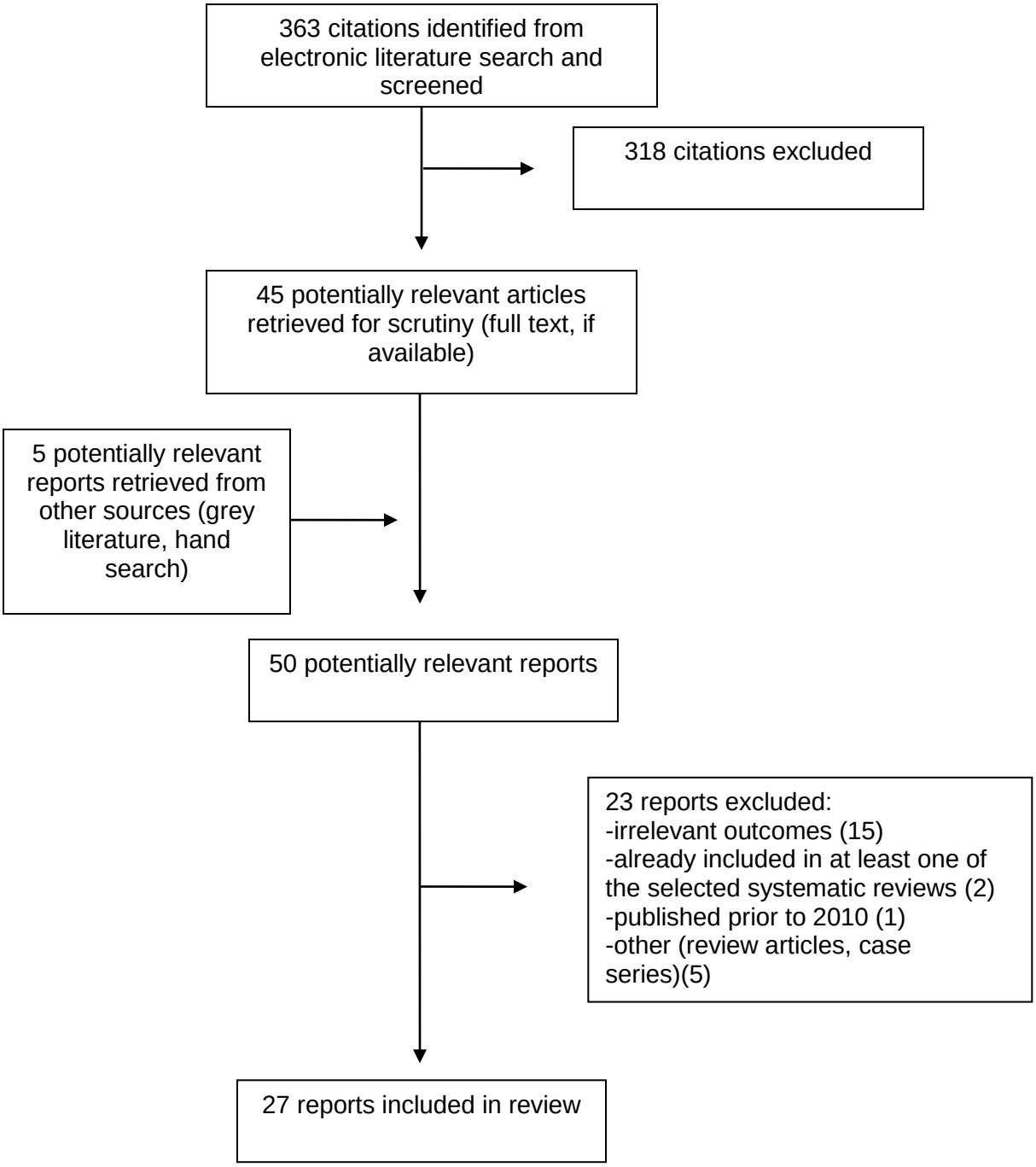
APPENDIX 1: Selection of Included Studies



APPENDIX 2: Summary of Study Characteristics

Table A2.1: Summary of Study Characteristics of Included SR

Study Design	Population (sample size)	Intervention	Comparator(s)	Outcomes
Systematic Review				
Barbagallo et al., 2014[12]				
SR: (5 RCCS, 1 PCCS)	Degenerative Spine conditions RCCSs (n = 711), PCCS (n = 107)	LLIF/XLIF/DLIF	PLIF/TLIF	• Length of hospital stay • Reoperation • Mortality • Complications - lumbar lordosis, perioperative, wound, nerve cardiac, renal, GI, respiratory, vertebral body-related and hardware-related complications

DLIF=direct lateral interbody fusion; **GI**=gastrointestinal; **LLIF**=lateral lumbar interbody fusion; **PCCS**=prospective cohort controlled study; **PLIF**=posterior lumbar interbody fusion; **RCCS**=retrospective cohort controlled study; **SR**=systematic review; **TLIF**=transforaminal lumbar interbody fusion; **XLIF**=extreme lateral interbody fusion

Table A2.2: Summary of Study Characteristics of Included Non-Randomized Studies

Study Design, FU, Location	Population (sample size)	Intervention	Comparator(s)	Outcomes
Prospective Cohort Controlled Studies				
Hrabalek et al., 2014[8]				
PCCS FU: 6 weeks, 6, 12, 24 months Olomouc, Czech Republic	XLIF/ALIF (n = 88/120) Mean age (51/44) Total fused levels (92/128) Diagnoses: Degenerative disc disease, failed back surgery syndrome, spondylolisthesis, retrolisthesis, posttraumatic disc injury Exclusions: Severe osteoporosis, tumour, infection, fresh spine fracture, spondylolisthesis grades III or IV, significant stenosis of the canal	XLIF Fusion material: autologous and artificial bone	ALIF (minimally invasive) Fusion material: autologous and artificial bone	Complications • Intra-operative complications • Post-operative complications (lumbar post-sympathectomy syndrome, numbness, pain, seroma) Complications related to the implant healing were not included

Table A2.2: Summary of Study Characteristics of Included Non-Randomized Studies				
Study Design, FU, Location	**Population (sample size)**	**Intervention**	**Comparator(s)**	**Outcomes**
Retrospective Cohort Controlled Studies				
Lee et al., 2014(1)[13]				
Retrospective cohort controlled study FU: DLIF 16.5 ± 5.8 months, TLIF 16.6 ± 5.7 months Seoul, Korea	DLIF/TLIF (n = 81/98) Mean age (61/63) Total fused levels (106/136) BMD (-0.76/-1.16) Diagnoses: spinal stenosis, degenerative spondylolisthesis, recurrent disc herniation, other	Minimal invasive DLIF Fusion material: DBM Additional posterior decompression for 33/81 patients with severe spinal stenosis or ruptured disc herniation	Unilateral open TLIF Fusion material: autologous bone	Clinical effectiveness • VAS pain • ODI • fusion rate Complications • psoas muscle symptoms • lateral femoral cutaneous nerve symptoms • genitofermoral nerve symptoms
Aichmair et al., 2013[14]				
Retrospective cohort controlled study FU: average 15.4 months New York, NY, USA	LLIF (n = 293) Total fused levels: 2006-2008 - 103 2009-2010 - 289 2011-2012 - 167 Mean age: 2006-2008 - 63.8 2009-2010 - 61.5 2011-2012 - 60.0 Diagnoses: NR	LLIF Different cages used Fusion material: autograft bone, allograft, or BMP-2	LIFF performed at a single center from 2006-2008 vs 2009-2010 vs 2011-2012	Clinical Effectiveness NR Complications • sensory deficit • motor deficit • anterior thigh/groin pain

ALL=anterior longitudinal ligament; **AL**=Alabama; **BMD**=bone mass density; **BMI**=body mass index; **BMP**=bone morphogenic protein; **CAD**=coronary artery disease; **COPD**=chronic obstructive pulmonary disease; **DBM**=demineralized bone matrix; **FL**=Florida; **FU**=follow-up; **LA**=Louisiana, **QoL**=quality of life; **MD**=Maryland; **MN**= Minnesota; **MO**=Missouri; **NC**=North Carolina; **ODI**=Oswestry Disability Index; **PCCS**=prospective cohort controlled study; **RCCS**=retrospective cohort controlled study; **VAS**=visual analogue scale; **USA**=United States of America;

Table A2.3: Summary of Study Characteristics of Included Uncontrolled Before-After Studies

Study Design, Follow-up, Location	Population (sample size)	Intervention	Outcomes
Kotwal et al., 2015[15]			
Uncontrolled Before-After Study FU: minimum 2 years USA	LLIF (n = 118) 50 1-level 28 2-level 29 3-level 11 4-level Mean age: (62.1 years) Mean BMI: (27.6 kg/m^2) Diagnoses: neurological claudication with deformity or instability, axial back pain due to de novo scoliosis, spondylolisthesis, junctional disk degeneration	LLIF LLIF cages Fusion material: surgeon's preference	Clinical Effectiveness • VAS pain • ODI • QoL (SF-12) - PCS - MCS Complications • anterior thigh pain • hip flexor weakness • anterior thigh numbness • surgical revision for nonunion • nonunion
Alimi et al., 2015[16]			
Uncontrolled Before-After Study FU: 11 ± 3.7 months New York, NY, USA	XLIF (n = 23) 23 1-level Mean age: (66.0 years) Diagnoses: degenerative scoliosis, spondylolisthesis, lateral listhesis, post-laminectomy syndrome, adjacent segment disease	XLIF (4/23 with additional laminectomy) Fusion material: NR	Clinical Effectiveness • VAS pain - stenotic side buttock - contralateral side buttock - stenotic side leg - contralateral side leg - back • ODI Complications • infection • reoperation
Berjano et al., 2015[17]			
Uncontrolled Before-After Study FU: average 34.5 months Milan, Italy	XLIF (n = 53) Mean age: (64 years) Total fused levels (78) Diagnoses: degenerative disc disease, scoliosis, sagittal imbalance, stenosis, spondylolisthesis, revision, other	XLIF Fusion material: calcium triphosphate, Attrax (Nuvasive, San Diego, CA), autologous bone, or Nanostim (Medtronic, Memphis, TN)	Clinical Effectiveness • Fusion - fusion rate by graft material • VAS pain - leg - back • ODI Complications - NR
Khajavi et al., 2015[18]			
Uncontrolled Before-After Study FU: average 19	XLIF (n = 160) Average age (66 years) Total fused levels (197)	XLIF Fusion material: NR	Clinical Effectiveness • Hospital stay • NRS - lower back - leg

Table A2.3: Summary of Study Characteristics of Included Uncontrolled Before-After Studies

Study Design, Follow-up, Location	Population (sample size)	Intervention	Outcomes
months Atlanta, GA, USA	Diagnoses: degenerative disc disease, degenerative spondylolisthesis, adjacent disc disease, post-laminectomy syndrome Exclusions: scoliosis, tumour, vertebral body fracture, disctitis, pseudoarthrosis		• ODI • QoL SF-36 - PCS Complications • Myocardial infarction • Minor complications - dural tear - transient dorsiflexion weakness - urinary retention - anemia requiring transfusion - vertebral body fracture - superficial wound dehiscence - urinary incontinence - approach-related thigh/groin pain - hip flexion
Formica et al., 2014[19]			
Uncontrolled Before-After Study FU: 3, 6, 12, and 24 months Italy	XLIF (n = 39) 35 1-level 2 2-level Mean age (58 years) Diagnoses: degenerative spondylolisthesis, degenerative scoliosis with stenosis, primitive degenerative disc disease, junctional diseases, post-surgical degenerative disc disease, thoracolumbar fractures, kyphosis due to disc degeneration, structured kyphosis	XLIF Fusion material: NR	Clinical Effectiveness: • VAS pain - back - leg • ODI Complications • infection • aseptic mobilization • anterior thigh hypoesthesia • strength deficit of quadriceps muscle
Grimm et al., 2014[20]			
Uncontrolled Before-After Study FU: 1 year Marietta, GA, USA	XLIF (n = 108) 52 1-level 35 2-level 21 3-or more level Mean age (59) Diagnoses: degenerative	XLIF Fusion material: BMP (INFUSE, Medtronic-Sofamor Danek, Memphis, TN)	Clinical Effectiveness • Hospital Stay Complicaitons • vertebral body fracture • contralateral nerve root injury • dense quadriceps paresis

Table A2.3: Summary of Study Characteristics of Included Uncontrolled Before-After Studies

Study Design, Follow-up, Location	Population (sample size)	Intervention	Outcomes
	scoliosis, degenerative disc disease, degenerative spondylolisthesis, stenosis, recurrent disc herniation, post-laminectomy syndrome		• persistent stenosis • thigh pain and/or paresthesias
Lee et al., 2014(2)[21]			
Uncontrolled Before-After Study FU: 6 and 12 months Seoul, Korea	DLIF (n = 90) Mean age (65.5 ± 14.3 years) Total fused levels (116) BMD (-0.8 ± 1.8) Diagnoses: spinal stenosis, mild spondylolisthesis (grade 1,2, or 3), degenerative scoliosis, infective spondylitis Exclusions: suspected retroperitoneal adhesion due to surgery, severe spondylolisthesis, severe rotational deformity, acute infective spondylitis, L4-5 level with high iliac crest, L5-S1 level	DLIF T12 to L5 Fusion material: DBM Additional posterior decompression for patients with severe spinal stenosis or ruptured disc herniation Additional TLIF for L5 - S1	Clinical Effectiveness • VAS pain • ODI • 6 months fusion rate • 12 month fusion rate Complications • psoas muscle symptoms • lateral femoral cutaneous nerve symptoms • genitofermoral nerve symptoms • surgical revision
Alimi et al., 2014[6]			
Uncontrolled Before-After Study FU: average 12.6 months New York, NY, USA	ELIF (n = 90) 52 1-level 17 2-level 14 3-level 7 4-level Mean age (64.4 ± 10.18) Diagnoses: degenerative disc disease, spondylolisthesis, adjacent-level disease, post-laminectomy syndrome, instrumentation failure/nonfusion	ELIF Some additional laminectomies Spinal navigation frequently used intraoperative 3D images Fusion material: silicate calcium phosphate (Actifuse, Apatech, Baxter)	Clinical Effectiveness • VAS - back - leg - buttock • ODI • VAS and ODI for 1 vs 2 level surgeries Complications • femoral nerve paralysis • bowel injury • abdominal flank bulge • myocardial infarction • adynamic ileus • postoperative lower-extremity weakness and decreased sensation

Table A2.3: Summary of Study Characteristics of Included Uncontrolled Before-After Studies

Study Design, Follow-up, Location	Population (sample size)	Intervention	Outcomes
			• reoperation - nonunion - adjacent-level disease - bone chip - post-laminectomy syndrome and radiculopathy
Waddell et al., 2014[22]			
Uncontrolled Before-After Study FU: 1 year New Orleans, LA, USA	LLIF (n = 21) 3 1-level 7 2-level 8 3-level 2 4-level 1 5-level Mean age (66.6) Diagnoses: adult degenerative scoliosis, spondylolisthesis with or without stenosis No patients excluded for previous surgery, smoking, BMD, diabetes, or BMI	LLIF Fusion material: BMP (Metronic, MN, USA) and Mastergraft (BioHorizons, AL, USA) For 3 or more LLIFs surgery was staged	Clinical Effectiveness • fusion rate Complications • radiolucent lines • pseudarthrosis • catastrophic end plate failure
Malham et al, 2014[23]			
Uncontrolled Before-After Study FU: 12 months Melbourne, Australia	XLIF (n = 40) 27 1-level 12 2-level 1 3-level Mean age: (64 years) Diagnoses: degenerative disc disease, degenerative scoliosis, spondylolisthesis, adjacent segment disease	XLIF With or without supplemental instrumentation Fusion material: BMP (Infuse, Medtronic, Inc., Memphis, TN) and Mastergraft β-TCP granules (Medtronic, Inc.)	Clinical Effectiveness • fusion rate • VAS - back - leg • ODI • QoL SF-36 - PCS - MCS Complications • radicular symptoms
Nemani et al., 2014[24]			
Uncontrolled Before-After Study FU: average 15.6 months	LLIF (n = 117) 37 1-level 42 2-level 34 3-level 4 4-level Mean age: (63.6 years)	LLIF Fusion material: varied to surgeon preference	Clinical Effectiveness • VAS - leg - back Complications • leg weakness

Table A2.3: Summary of Study Characteristics of Included Uncontrolled Before-After Studies

Study Design, Follow-up, Location	Population (sample size)	Intervention	Outcomes
Vienna, Austria	BMI: average 27.4 Diagnoses: only included lumbar spinal stenosis or degenerative scoliosis Exclusions: previous anterior or posterior surgery at affected level		• leg paresthesia • rate of revision surgery
McAfee et al., 2013[7]			
Uncontrolled Before-After Study FU: mean 24 months Towson, MD, USA	XLIF (n = 25) 4 level-2 14 level -3 7 level-4 Mean age (65.9 years) Diagnoses: severe scoliosis with deformity, spondylosis, spondylolisthesis with lateral subluxation, post-laminectomy syndrome, degenerative scoliosis, prior variable screw placement instrumentation, herniated nucleus pulposis, prior variable spinal plate	XLIF Fusion material: autograft and Osteocel (NuVasive, Inc., San Diego, CA)	Clinical Effectivness • VAS pain • Mean length of hospital stay Complications • incidental durotomy • cage migration • polyetheretherketone spacer subsidence • psoas muscle symptoms • neurologic weakness, and quadriceps weakness unresolved by 6 months • pseudoparesis of abdominal wall
Ha et al., 2013[25]			
Uncontrolled Before-After Study FU: average 31.3 months Seoul, Korea	DLIF (n = 16) 16 1-level Mean age: (60.3 years) Diagnoses: pyogenic spondylitis	DLIF Single level with percutaneous posterior instrumentation Fusion material: autogenous iliac bones	Clinical Effectivness • VAS pain • ODI • Fusion rate • eradication of primary infection Complications • neurological complications • systemic complications • postoperative anterior thigh pain • hip flexor weakness on approach side • malpositioned pedicle screws

Table A2.3: Summary of Study Characteristics of Included Uncontrolled Before-After Studies

Study Design, Follow-up, Location	Population (sample size)	Intervention	Outcomes
Malham et al., 2012[26]			
Uncontrolled Before-After Study FU: 12 months Melbourne, Australia	XLIF (n = 30) Total fused levels (43) Mean age: (62.7 years) Diagnoses: degenerative disc disease, spondylolisthesis, degenerative scoliosis	XLIF Fusion material: BMP (Metronic, MN, USA) and Mastergraft (BioHorizons, AL, USA) Staged procedures in 47% of cases	Clinical Effectiveness • VAS pain • ODI • QoL SF-36 - PCS - MCS • fusion rates Complications • clinical subsidence • cage failure • new postoperative motor deficit • bowel injury • radiographic subsidence • anterior thigh sensory changes • reoperation
Rodgers et al., 2012[27]			
Uncontrolled Before-After Study FU: 12 months Jefferson City, MO, USA	XLIF (n = 63) 49 1-level 11 2-level 3 3-level Mean age: (66.4 years) Diagnoses: spondylolisthesis, stenosis with instability, degenerative scoliosis Comorbidities: Smoking, CAD, diabetes, COPD, steroid use, cancer, prior surgery	XLIF Fusion material: varied	Clinical Effectiveness • VAS pain • fusion rate • hospital stay Complications • neuronal injuries • nonunion • post-operative ileus • infection
Caputo et al., 2012[28]			
Uncontrolled Before-After Study FU: averaged 14.3 months Durham, NC, USA	XLIF (n = 30) Total fused levels (127) Mean age: (65.9 years) Mean BMI: (28.8 kg/cm^2) Smoker (n = 9) Diagnoses: symptomatic degenerative adult scoliosis failed a year of conservative treatment	XLIF (staged ALIF performed on 11 patients for L5-S1 fusion) Fusion material: Osteocel plus allograft cellular bone matrix (NuVasive, Inc, San Diego, CA)	Clinical Effectiveness • VAS pain • ODI • QoL SF-12 - PCS - MCS Complications: • lateral wound breakdown • pedicle fracture • nonunion • hernia at incision • uncontrolled atrial fibrillation • iatrogenic rupture of ALL

Table A2.3: Summary of Study Characteristics of Included Uncontrolled Before-After Studies

Study Design, Follow-up, Location	Population (sample size)	Intervention	Outcomes
Kim et al., 2012[29]			
Uncontrolled Before-After Study FU: averaged 3 months Seoul, Korea	DLIF (n = 8) 4 2-level 4 3-level Mean age (65.8) Diagnoses: degenerative scoliosis, segmental scoliosis	DLIF (additional PLIF for four patients L5-S1) Fusion material: β-tricalcium phosphate (ChronOS, Synthes, PA, USA), DBM (Synthes, PA, USA)	Complications • cage subsidence • cage migration • motor weakness • thigh paresthesias and dysesthesias • serious complications
Berjano et al., 2012[30]			
Uncontrolled Before-After Study FU: averaged 12 months Milan, Italy	XLIF (n = 93) 48 1-level 40 2-level 8 3-level 1 4-level Mean age (59 years) Diagnoses: Degenerative disc disease, degenerative scoliosis, posttraumatic kyphosis, pseudarthrosis following pedicle substraction osteotomy, anterior column reconstruction	XLIF Fusion material: varies	Clinical Effectiveness • VAS pain - back - leg • ODI Complications • transient weakeness • transient hypoesthesia • transient crural discomfort • significant subsidence • surgical revision • deep venous thrombosis • infection • dural tear • psoas hematoma
Rodgers et al., 2011[31]			
Uncontrolled Before-After Study FU: minimum 1 year Jefferson City MO, USA	XLIF (n = 600) Total fused levels (741) Mean age: (61.4 years) Mean BMI: (31.1 kg/m^2) Diagnoses: stenosis, spondylolisthesis, degenerative disc disease, herniated nucleus pulposus, scoliosis, post-laminectomy, osteomyelitis	XLIF Details NR	Clinical Effectiveness • hospital stay • VAS pain Complications: • wound • neural • vertebral • hardware • GI • respiratory • cardiac • renal • hematologic
Youssef et al., 2010[32]			
Uncontrolled Before-After Study FU: average 15.7 months	XLIF (n = 84) 45 1-level 25 2-level 14 3-level Mean age: NR	XLIF Some supplemental posterior spinal fusion Fusion material: BMP (INFUSE, Medtronic-Sofamor Danek,	Clinical Effectiveness • Hospital stay • VAS pain • ODI • Fusion rate

Table A2.3: Summary of Study Characteristics of Included Uncontrolled Before-After Studies

Study Design, Follow-up, Location	Population (sample size)	Intervention	Outcomes
Durango, CO and Townson, MD, USA	Diagnoses: combinations of spondylosis, spondylolisthesis, scoliosis, adjacent segment disease, spinal stenosis, degenerative disc disease, herniated nucleus pulposus, trauma, tumor	Memphis, TN) in conjuction with allograft	Complications • pulmonary artery embolism and right ventricular clot • incidental durotomy • non-displaced bilateral pedicle fracture • ipsilateral psoas weakness and numbness • mild endplate fracture • vertebral body fracture • subsidence of adjacent plates • pyelonephritis • adjacent segment disease
Sharma et al., 2011[33]			
Uncontrolled Before-After Study FU: 1 year New York, NY, USA	XLIF (n = 43) Mean age: (63.9 years) Mean BMI: (26.0 kg/m^2) Diagnoses: degenerative scoliosis, degenerative spondylolisthesis, degenerative disc disease	XLIF Some with lateral plate and unilateral screw fixation, some with pedicle screw fixation Fusion material: BMP, DBM, autograft, allograft, and/or bone marrow aspirate depending on surgeon's preference	Clinical Effectiveness • VAS pain • ODI • QoL (SF-12) - PCS - MCS Complications • neurologic complications • intraoperative end-plate fractures • nonunion • vertebral body fractures • infection • malpositioned cage • retroperitoneal hemorrage
Rodgers et al., 2010[34]			
Uncontrolled Before-After Study FU: 3, 6, 12 months Jefferson City, MO, USA	XLIF (n = 66) 50 1-level 10 2-level 6 3-level Mean age (average 62.2 years) BMI (average 30.4) Diagnoses: NR	Minimally invasive ALIF performed through an XLIF approach Fusion material: autograft (local bone and marrow) augmented with DBM and cancellous allograft (Optecure, Gainesville, FL)	Clinical Effectiveness • VAS pain • fusion Complications • surgical revision

ALL=anterior longitudinal ligament; **AL**=Alabama; **BMD**=bone mass density; **BMI**=body mass index; **BMP**=bone morphogenic protein; **CAD**=coronary artery disease; **COPD**=chronic obstructive pulmonary disease; **DBM**=demineralized bone matrix; **FL**=Florida; **FU**=follow-up; **LA**=Louisiana; **QoL**=quality of life; **MD**=Maryland; **MN**= Minnesota; **MO**=Missouri; **NC**=North Carolina; **NRS**=numerical rating scale; **ODI**=Oswestry Disability Index; **VAS**=visual analogue scale; **USA**=United States of America;

Table A2.4: Summary of Study Characteristics of Included Cost-Analysis				
Type of Economic Evaluation, Perspective, Time	**Patient Population**	**Comparison**	**Outcomes**	**Assumptions**
Smith et al., 2014[1]				
Cost comparison of a non-randomized study Hospital cost perspective 24 month follow-up timecourse	XLIF (n = 115) 61 1-level 54 2-level Open ALIF (n = 87) 48 1-level 39 2-level Mean age: (XLIF 58.4 years) (ALIF 46.1 years) (p < 0.001) Diagnoses: degenerative disc disease, stenosis, post-laminectomy syndrome, herniated nucleus pulposus, spondylolisthesis, spondylolysis, degenerative scoliosis	XLIF vs open ALIF Compare costs using hospital charge data	• Costs - supplies/implants - OR services - Pharmacy - Room & Board - Lab - Misc - PT/OT • Clinical Effectiveness - VAS back pain - VAS extremity pain - ODI - Hospital stay • Complications	Assumes no selection bias Charge data collected retrospectively Equivalent training costs
ALIF=anterior lumbar interbody fusion; **ODI**= Oswestry Disability Index; **OR**=operating room; **PT/OT=**physical therapy/occupational therapy; **VAS**=visual analogue scale; **XLIF**=extreme lateral interbody fusion;				

APPENDIX 3: Summary of Critical Appraisal

Table A3.1: Critical Appraisal Summary for included SR using AMSTAR[9]

Strengths	Limitations
Barbagallo et al., 2014[12]	
• Literature search selection/inclusion/exclusion methodology detailed • PRISMA flowchart • Defined research objective • Studies assessed for methodological quality and bias (but not presented) • Overall strength of evidence evaluated (GRADE) • Quantified conclusions • Examination of reported complications • Mention of COIs in included studies	• Analytic support conducted by a private company using funding from a professional medical association - unclear interests • Analysis of study methodological quality and bias not presented • Identified a paucity of studies presenting low-quality evidence

COI=conflict of interest; **PRISMA**=Preferred Reporting Items for Systematic Reviews and Meta-Analyses; **GRADE**=Grades of Recommendation Assessment, Development and Evaluation;

Table A3.2: Critical Appraisal Summary for Included Prospective and Retrospective Cohort Studies using the Downs and Black Checklist[10]	
Strengths	**Limitations**
Prospective Cohort Controlled Studies	
Hrabalek et al., 2014[8]	
• Objective clearly stated • Multiple follow-up timepoints • Well described intervention • Patient inclusion/exclusion criteria described • Statistical methods described • Clearly described findings	• Only examined complications • No predefined outcomes • No tabulated patient characteristics or results • Unclear if patients were lost to follow-up • Unclear who/how complications were recorded • Unclear allocation procedure • No direct comparison of patient characteristics • No blinding • No mention of potential COI
Retrospective Cohort Controlled Studies	
Lee et al., 2014(1)[13]	
• Objective clearly stated • Patient characteristics tabulated - no significant differences between groups • Well described intervention • Statistical methods described and used appropriately • Examined complication occurrences	• Retrospectively examined outcomes • Follow-up times inconsistent • Statistically significant difference in cage heights used for each group • No examination of outcome correlation to levels fused • No mention of assessment blinding • Unclear allocation procedure • No mention of potential COI • Unclear if there were patients lost to follow-up
Aichmair et al., 2013[14]	
• Objective clearly stated • Outcomes clearly described and defined • Long-term study examining an important question • Patient inclusion/exclusion criteria described • Results and findings well described • Statistical methods described	• Intervention not consistent • Tabulated patient characteristics not examined for all differences between groups • No mention of patients lost to follow-up • No clinical effectiveness data (context of complications is lost) • Acknowledged COI • No blinding, allocation concealment ect.
COI=conflict of interest;	

Table A3.3: Critical Appraisal Summary for Included Uncontrolled Before-After Studies using the Downs and Black Checklist[10]

Strengths	Limitations
Uncontrolled Before-After Studies	
Kotwal et al., 2015[15]	
• Minimum two year follow-up • Statistical methods described • Intervention described • Statement of no COIs • Outcome assessment described • Tabulated patient characteristics	• No control group • No blinding • No allocation concealment • Inconsistent intervention • No reasons for patients lost to follow-up • Inconsistent follow-up time • No defined patient inclusion/exclusion criteria • Mixed patient population • Unclear complication assessment or recording
Alimi et al., 2015[16]	
• Tabulated patient characteristics • Patient inclusion exclusion criteria defined • Statistical methods described • Outcome assessment described • Statement of no COIs	• No control group • No blinding • No allocation concealment • Inconsistent follow-up time • Unclear if patients were lost to follow-up • Unclear complication assessment or recording • Intervention not described
Berjano et al., 2015[17]	
• Tabulated patient characteristics • Patient inclusion exclusion criteria defined • Patients lost to follow-up reported and explained • Statistical methods described • Outcome assessment described • Intervention described	• No control group • No blinding • No allocation concealment • No complication information • Inconsistent intervention • Acknowledged COI • Inconsistent follow-up time
Khajavi et al., 2015[18]	
• Tabulated patient characteristics • Patient inclusion exclusion criteria defined • Complication assessment described • Statistical methods described • Outcome assessment described	• No control group • No blinding • No allocation concealment • Unclear if patients were lost to follow-up • Intervention not described • Acknowledged COI • Inconsistent follow-up time
Formica et al., 2014[19]	
• Tabulated patient characteristics • Regularly scheduled follow-up • Statistical methods described • Outcome assessment described • Statement of no COIs	• No control group • No blinding • No allocation concealment • No patient inclusion or exclusion criteria • Unclear if patients were lost to follow-up • Unclear complication assessment or recording • Intervention not described
Grimm et al., 2014[20]	
• Tabulated patient characteristics • Regularly scheduled follow-up • Statistical methods described • Intervention described • Outcome assessment described • Statement of no COIs	• No control group • No blinding • No allocation concealment • No patient inclusion or exclusion criteria • Unclear if patients were lost to follow-up • Unclear complication assessment or recording

Table A3.3: Critical Appraisal Summary for Included Uncontrolled Before-After Studies using the Downs and Black Checklist[10]

Strengths	Limitations
Uncontrolled Before-After Studies	
Lee et al., 2014(2)[21]	
• Tabulated patient characteristics • Patient inclusion exclusion criteria defined • Regularly scheduled follow-up • Outcome assessment described • Intervention described	• No control group • No blinding • No allocation concealment • Unclear reasons for loss to follow-up • Unclear complication assessment or recording • No statement of potential COIs • Statistical methods described but insufficiently
Alimi et al., 2014[6]	
• Tabulated patient characteristics • Patient inclusion exclusion criteria defined • Outcome assessment described • Statistical methods described • Complication assessment described • Intervention described	• No control group • No blinding • No allocation concealment • Inconsistent follow-up time • Unclear if patients were lost to follow-up • Acknowledged COI
Waddell et al., 2014[22]	
• Tabulated patient characteristics • Patient inclusion exclusion criteria defined • Regularly scheduled follow-up • Statistical methods sufficiently described • Outcome assessment described • Intervention described • Statement of no COIs	• No control group • No blinding • No allocation concealment • Unclear if patients were lost to follow-up • Unclear complication assessment or recording
Malham et al, 2014[23]	
• Tabulated patient characteristics • Patient inclusion criteria defined • Regularly scheduled follow-up • Statistical methods described • Outcome assessment described • Intervention described	• No control group • No blinding • No allocation concealment • Unclear if patients were lost to follow-up • Unclear complication assessment or recording • Acknowledged COI
Nemani et al., 2014[24]	
• Tabulated patient characteristics • Patient inclusion exclusion criteria defined • Statistical methods described • Outcome assessment described • Complication assessment described • Intervention described	• No control group • No blinding • No allocation concealment • Unclear if patients were lost to follow-up • Inconsistent intervention • Acknowledged COI • Inconsistent follow-up time
McAfee et al., 2013[7]	
• Tabulated patient characteristics • Intervention described • Some information on complication assessment • Outcome assessment described	• No control group • No blinding • No allocation concealment • No patient inclusion or exclusion criteria • Inconsistent follow-up time • Unclear if patients were lost to follow-up • No description of statistical methods • No statement of potential COIs

Table A3.3: Critical Appraisal Summary for Included Uncontrolled Before-After Studies using the Downs and Black Checklist[10]

Strengths	Limitations
Uncontrolled Before-After Studies	
Ha et al., 2013[25]	
• Tabulated patient characteristics • Patient inclusion exclusion criteria defined • No patients lost to follow-up • Outcome assessment described • Intervention described • Statement of no COIs	• No control group • No blinding • No allocation concealment • Inconsistent follow-up time • Unclear complication assessment or recording • Statistical methods described but inadequately
Malham et al., 2012[26]	
• Tabulated patient characteristics • Patient inclusion criteria defined • Regularly scheduled follow-up • Patients lost to follow-up reported and explained • Statistical methods described • Outcome assessment described • Intervention described • Statement of no COIs	• No control group • No blinding • No allocation concealment
Rodgers et al., 2012[27]	
• Tabulated patient characteristics • Patient inclusion criteria defined • Regularly scheduled follow-up • Intervention described • Outcome assessment described • Some information on complication assessment	• No control group • No blinding • No allocation concealment • Unclear if patients were lost to follow-up • No description of statistical methods • Inconsistent intervention • Acknowledged COI
Caputo et al., 2012[28]	
• Tabulated patient characteristics • Patient inclusion exclusion criteria defined • Complication assessment described • Outcome assessment described • Statistical methods described • Intervention described	• No control group • No blinding • No allocation concealment • Acknowledged COI • Inconsistent follow-up time • Unclear if patients were lost to follow-up
Kim et al., 2012[29]	
• Tabulated patient characteristics • Statistical methods described • Outcome assessment described • Intervention described	• No control group • No blinding • No allocation concealment • No patient inclusion or exclusion criteria • Inconsistent and modest follow-up time • Small study population • Unclear if patients were lost to follow-up • Unclear complication assessment or recording • No statement of potential COIs
Berjano et al., 2012[30]	
• Tabulated patient characteristics • Patients lost to follow-up reported and explained • Outcome assessment described • Statistical methods described • Some information on complication assessment • Intervention described • Statement of no COIs	• No control group • No blinding • No allocation concealment • Inconsistent follow-up time

Table A3.3: Critical Appraisal Summary for Included Uncontrolled Before-After Studies using the Downs and Black Checklist[10]	
Strengths	**Limitations**
Uncontrolled Before-After Studies	
Rodgers et al., 2011[31]	
• Tabulated patient characteristics • Patient inclusion exclusion criteria defined • Statistical methods described • Regularly scheduled follow-up • Unclear if patients were lost to follow-up • Outcome assessment described • Complication assessment described	• No control group • No blinding • No allocation concealment • Intervention not described • Acknowledged COI
Youssef et al., 2010[32]	
• Patient characteristics reported • Statistical methods sufficient • Outcome assessment described • Complication assessment described • Intervention described	• No control group • No blinding • No allocation concealment • No patient inclusion or exclusion criteria • Inconsistent follow-up time • Unclear reasons for loss to follow-up • Acknowledged COI
Sharma et al., 2011[33]	
• Tabulated patient characteristics • Patient inclusion exclusion criteria defined • Regularly scheduled follow-up • Statistical methods described • Outcome assessment described • Some information on complication assessment • Intervention described	• No control group • No blinding • No allocation concealment • Unclear if patients were lost to follow-up • Inconsistent intervention • No statement of potential COIs
Rodgers et al., 2010[34]	
• Patient characteristics available • Regularly scheduled follow-up • Statistical methods sufficiently described • Outcome assessment described	• No control group • No blinding • No allocation concealment • No patient inclusion or exclusion criteria • Unclear if patients were lost to follow-up • Intervention not described • Unclear complication assessment or recording • No statement of potential COIs
COI=conflict of interest;	

Table A3.4: Critical Appraisal Summary for the Included Cost-Analysis using Drummond's Checklist[11]	
Strengths	**Limitations**
Cost-Analysis	
Smith et al., 2012[1]	
• Based on a non-randomized study (PCCS) • Explicit purpose • Relevant comparator • Costs from charge data then categorized • Data evaluated separately for one and two-level procedures • Tabulated patient characteristics • Regularly scheduled follow-up • Statistical methods described • Outcome assessment described • Some information on complication assessment • Intervention described	• Itemized costs not from published source • Not a cost-effectiveness study • Does not relate costs to clinical efficacy • Perspective is limited • No consideration of training costs • No long term cost data • Limited indirect costs • Initial statistically significant differences between treatment groups • No statement of potential COIs • Unclear allocation methods • No accounting for significant loss to follow-up (at 2 years a 65% follow-up)
COI=conflict of interest; **PCCS**=prospective cohort controlled study;	

APPENDIX 4: Summary of Findings

Table A4.1: Summary of Main Findings and Author's Conclusions of the Included SR

Main Findings	Author's Conclusions
Barbagallo et al., 2014[12]	
Clinical Effectiveness Length of Hospital Stay (days) *Deluzio et al., (2010) (average) (p = NR)* LLIF/XLIF/DLIF 1.2 PLIF/TLIF 3.2 *Rodgers et al., (2010) (p < 0.00001)* LLIF/XLIF/DLIF 1.3 PLIF/TLIF 5.3 *Knight et al., (2009) (p = NS)* LLIF/XLIF/DLIF 1.3 PLIF/TLIF 5.3 **Complications** Reoperation Risk *Rodgers et al., (2010) (n/N (%))(p = NS)* LLIF/XLIF/DLIF 2/40 (5.0%) PLIF/TLIF 3/20 (15.0%) *Knight et al., (2009)* LLIF/XLIF/DLIF 1/58 (1.7%) PLIF/TLIF NR Overall Complication Risk *Rodgers et al., (2010) (n/N (%))(p < 0.001)* LLIF/XLIF/DLIF 3/40 (7.5%) PLIF/TLIF 12/20 (60.0%) *Knight et al., (2009) (p = NR)* LLIF/XLIF/DLIF 13/58 (22.4%) PLIF/TLIF 9/40 (22.5%) Mortality Risk *Rodgers et al., (2010) (n/N (%))(p = 0.0018)* LLIF/XLIF/DLIF 1/40 (2.5%) PLIF/TLIF 6/20 (30.0%) *Knight et al., (2009) (p = NR)* LLIF/XLIF/DLIF 0/58 (0%) PLIF/TLIF 1/40 (2.5%) Number of Levels Treated *Isaacs et al., (2010)* LLIF/XLIF/DLIF - There was a 59% increase in the complication risk for each additional level treated (*p* = 0.0105)	**Clinical Effectiveness** " More studies with longer follow-up, including randomized trials, are necessary to evaluate the theoretical benefit of direct lumbar lateral approach and to assess whether the results of this strategy are superior and durable as the ones achieved by PLIF/TLIF technique performed in open or minimally invasive surgery." (pp. 35) "None of the included studies reported radiographic or patient-related outcomes for both treatment groups." (pp. 29) **Complications** "Overall, the evidence on the comparative safety of LLIF compared with PLIF is low." (pp. 34)

Table A4.1: Summary of Main Findings and Author's Conclusions of the Included SR	
Main Findings	**Author's Conclusions**
Preoperative Diagnosis *Rodgers et al., (2010)* LLIF/XLIF/DLIF - Higher complication risks in patients with diagnoses of degenerative disc disease, recurrent disc herniation as compared to scoliosis, spondylolisthesis, stenosis, or post-laminectomy instability. (p = 0.0075)	
DLIF=direct lateral interbody fusion; **LLIF**=lateral lumbar interbody fusion; **NR**=not reported; **NS**=not significant; **PLIF**=posterior lumbar interbody fusion; **TLIF**=transforaminal interbody fusion; **XLIF**=extreme lateral interbody fusion	

Table A4.2: Summary of Main Findings and Author's Conclusions of Non-randomized Studies	
Main Findings	**Author's Conclusions**
Prospective Cohort Controlled Studies	
Hrabalek et al., 2014[8]	
Clinical Effectiveness NR **Complications** Major Complicaitons ALIF 0/120 (0%) XLIF 1/88 (partial, transient injury to L5 nerve root during implant insertion) Minor Complications ALIF 32/120 (26.6%) XLIF 22/88 (25%) Minor Complications and frequency ALIF Lumbar post-sympathectomy syndrome (15.8%) Post-operative numbness (5%) Peritoneal opening without visceral injury (2.5%) Post-operative transient pain (3.3%) Seroma of wound (0.8%) Pleural opening at T12-L1 (0.8%) Injury to iliolumbal vein (0.8%) XLIF Post-operative transient pain (12.5%) Post-operative numbness (10.2%) Lumbar post-sympathectomy (4.5%) No serious complications such as death, excessive intra- or post-operative bleeding, thromboembolism, infection, visceral injury	**Clinical Effectiveness** NR **Complications** "Statistically (Fisher's Exact Test) there was no difference between ALIF and XLIF groups in rate of complications." (pp. 129)

Table A4.2: Summary of Main Findings and Author's Conclusions of Non-randomized Studies

Main Findings	Author's Conclusions
Prospective Cohort Controlled Studies	
Retrospective Cohort Controlled Studies	
Lee et al., 2014(1)[13]	
Clinical Effectiveness Fusion Rate at 12 months (n/N (%)) (p = 0.007) DLIF 71/81 (87.7%) TLIF 96/98 (98.1%) VAS score difference 12 months post-operation (mean ± SD) (p = 0.180) DLIF 4.53 ± 1.34 TLIF 4.72 ± 1.10 ODI score difference 12 months post-operation (mean ±SD) (p = 0.147) DLIF 28.64 ± 13.74 TLIF 26.10 ± 10.87 **Complications** Minor complications and frequency DLIF Psoas muscle symptoms 12.3% Lateral femoral cutaneous nerve 4.9% Genitofemoral nerve symptoms 2.5% TLIF Infection 1.0%	**Clinical Effectiveness** "According to our data, DLIF has higher potential in increasing neural foramina and correcting coronal balance, and involves a shorter operative time and reduced EBL, in comparison with TLIF" (pp. 473) "It appears that the fusion rate of the DLIF group who were treated with DBM was lower than that of the TLIF group with autologous bone. (pp. 473) "We believe prospective long-term studies are necessary for a more comprehensive evaluation in the future." (pp. 473) **Complications** "DLIF displayed a lower fusion rate than TLIF, and caused additional complications related to the transpsoas approach." (pp. 473)
Aichmair et al., 2013[14]	
Clinical Effectiveness NR **Complications** **Sensory deficits** 2006-2008 (% of patients)* Immediate post-op 44.4%* Last follow-up 14.9% 2009-2010 Immediate post-op 43.4% Last follow-up 11.0% 2011-2012* Immediate post-op 25.0%* Last follow-up 6.6%	**Clinical Effectiveness** NR **Complications** "The present data indicate a decreasing proportional trend over time for SDs, MDs, and TP, which can be considered a representation of an institutional learning curve during a 6-year time period of performing LLIF. Future studies investigating the learning curve for LLIF and the influence of surgeon experience on postoperative neurological complications would be beneficial for training and furthering understanding of this spine surgical technique." (pp. 1489)

Table A4.2: Summary of Main Findings and Author's Conclusions of Non-randomized Studies	
Main Findings	**Author's Conclusions**
Prospective Cohort Controlled Studies	
Motor deficits 2006-2008 Immediate post-op 22.2% Last follow-up 4.3% 2009-2010 Immediate post-op 24.3% Last follow-up 2.6% 2011-2012 Immediate post-op 19.3% Last follow-up 2.2% **Anterior thigh/groin pain** 2006-2008 Immediate post-op 46.7% Last follow-up 8.5% 2009-2010 Immediate post-op 48.0% Last follow-up 9.0% 2011-2012 Immediate post-op 33.0% Last follow-up 2.2% * A statistically significant reduction was observed in the percentage of patients with immediate post-op sensory deficit between 2006-2008 and 2011-2012. (p = 0.018)	
ALIF=anterior lumbar interbody fusion; **DLIF=**direct lateral interbody fusion; **LLIF**=lateral lumbar interbody fusion; **PLIF**=posterior lumbar interbody fusion; **TLIF**=transforaminal interbody fusion; **XLIF**=extreme lateral interbody fusion	

Table A4.3: Summary of Main Findings and Author's Conclusions of Uncontrolled Before-After Studies

Main Findings	Author's Conclusions
Uncontrolled Before-After Studies	
Kotwal et al., 2015[15]	
Clinical Effectiveness LLIF VAS pain (average) ($p < 0.01$) Pre-operative 8.7 ± 1.3cm Last follow-up 4.1 ± 2.8cm LLIF ODI (average) ($p < 0.01$) Pre-operative 30.1 ± 10.1 Last follow-up 17.1 ± 12.8 LLIF QoL SF-12 PCS (average) ($p < 0.01$) Pre-operative 27.0 ± 1.3 Last follow-up 38.1 ± 15.0 LLIF QoL SF-12 MCS (average) (p = NS) Pre-operative 43.0 ± 11.4 Last follow-up 42.4 ± 11.9 **Complications** 118 Patients 67 Complications - rate 56.8% 43 anterior thigh pain - 20 hip flexor weakness - 13 anterior thigh numbness - 1 unresolved 14 nonunion - 3 additional surgery 1 adjacent level degeneration 4 pulmonary insufficiency 2 arrhythmia 1 gastric ulcer 1 urinary retention 1 delayed wound healing	**Clinical Effectiveness** "Our results support the efficacy of this surgical procedure in improvements of clinical and radiographic features." (pp. 124) **Complications** "… transient thigh pain was the most frequent complication seen in 36% of the patients." (pp. 119)
Alimi et al., 2015[16]	
Clinical Effectiveness XLIF VAS pain stenotic side buttock (average ± SE) Pre-operative 7.3 ± 0.7 Post-operative 1.5 ± 0.8* Last follow-up 0.7 ± 0.4* XLIF VAS pain contralateral side buttock (average ± SE) Pre-operative 0.9 ± 0.5 Post-operative 1.1 ± 0.6 Last follow-up 0.5 ± 0.2 XLIF VAS pain -stenotic side leg (average ± SE) Pre-operative 7.2 ± 0.7 Post-operative 2.3 ± 0.8*	**Clinical Effectiveness** "Single-level XLIF is an effective procedure for treatment of symptomatic unilateral foraminal stenosis leading to radiculopathy." (pp. 346) **Complications** "In the current study, only one patient (4.3 %) required reoperation that was performed for revision of

Table A4.3: Summary of Main Findings and Author's Conclusions of Uncontrolled Before-After Studies

Main Findings		Author's Conclusions
Uncontrolled Before-After Studies		
Last follow-up	1.1 ± 0.5*	instrumentation, due to wound infection." (pp. 351)
XLIF VAS pain -contralateral side leg (average ± SE)		
Pre-operative	0.9 ± 0.6	
Post-operative	1.0 ± 0.6	
Last follow-up	0.6 ± 0.2	
XLIF VAS pain -back (average ± SE)		
Pre-operative	6.5 ± 0.8	
Post-operative	3.3 ± 0.6*	
Last follow-up	3.3 ± 0.6*	
XLIF ODI (average ± SE)		
Pre-operative	48.0 ± 4.2	
Post-operative	25.4 ± 4.2*	
Last follow-up	23.0 ± 4.8*	
* *p*-value less than or equal to 0.001 as compared to pre-operative		
Complications		
23 Patients		
1 Complication - rate 4.3%		
1 wound infection requiring surgical revision of instrumentation		
Berjano et al., 2015[17]		
Clinical Effectiveness		**Clinical Effectiveness**
XLIF Fusion Rate		"The results of this series corroborate that anterior interbody fusion by means of XLIF approach is a technique that achieves high fusion rate and satisfactory clinical outcomes." (pp. 371)
Completely fused	68/78 (87%)	
Probably stably fused	8/78 (10%)	
Pseudoarthrosis	2/78 (3%)	
XLIF Fusion Rate (fusion material used) (*p* = NS)		
Autograft	75%	
Calcium Triphosphate	89%	
Attrax™	83%	
Autologous bone or Nanostim	100%	**Complications**
XLIF VAS pain at last follow-up -leg (average ± SD) (*p* = NS)		NR
Fused	2.3 ± 2.2	
Probably fused or not fused	3.0 ± 2.0	
XLIF VAS pain at last follow-up -back (average ± SD) (*p* = NS)		
Fused	2.2 ± 2.6	
Probably fused or not fused	2.7 ± 2.4	
XLIF ODI at last follow-up (average ± SD) (*p* = NS)		
Fused	19.0 ± 17.3	
Probably fused or not fused	25.2 ± 16.2	
Complications		
NR		

Table A4.3: Summary of Main Findings and Author's Conclusions of Uncontrolled Before-After Studies

Main Findings	Author's Conclusions
Uncontrolled Before-After Studies	
Khajavi et al., 2015[18]	
Clinical Effectiveness XLIF NRS pain -lower back (% improvement) Last follow-up 41.4%* XLIF NRS pain -leg (% improvement) Last follow-up 38.8%* XLIF ODI (% improvement) Last follow-up 36.8%* XLIF SF-36 PCS (% improvement) Last follow-up 36.8%* XLIF Hospital Stay (days ± SD)** Adjacent segment disease 1.5 ± 0.2 Degenerative disc disease 1.2 ± 0.1 Post-laminectomy syndrome 1.1 ± 0.2 Degenerative spondylolisthesis 1.4 ± 0.1 * $p < 0.05$ ** no statistically significant differences in all outcomes correlating with initial diagnoses **Complications** 160 Patients 20 Complications, 36 side effects - rate 35% 1 myocardial infarction 4 dural tear 3 transient dorsiflexion weakness 3 urinary retention 3 anemia requiring transfusion 2 vertebral body fracture 3 superficial wound dehiscence 1 urinary incontinence 36 Side effects 22 transient approach-related thigh/groin pain 14 transient hip flexion	**Clinical Effectiveness** "XLIF has been demonstrated in the current series to lead to significant improvements in clinical outcomes and reduces the discrepancy in outcomes between well accepted, controversial, and technically challenging indications compared to traditional open approaches for IBF." (pp. 329) **Complications** "Excluding patients with transient, approach-related side effects, percentage of patients with any complication in this series was 12 %, with <1 % classified as a major." (pp. 329)
Formica et al., 2014[19]	
Clinical Effectiveness XLIF VAS pain -back (average (range)) Pre-operative 7.85 (5, 10) Last follow-up 1.77 (0, 5)* XLIF VAS pain -leg (average (range)) Pre-operative 4.62 (0, 10) Last follow-up 1.85 (0, 4)*	**Clinical Effectiveness** "XLIF proved to be a safe, effective, minimally invasive technique that allows valid arthrodesis to be carried out." (pp. 684)

Table A4.3: Summary of Main Findings and Author's Conclusions of Uncontrolled Before-After Studies

Main Findings	Author's Conclusions
Uncontrolled Before-After Studies	
XLIF ODI (average % (range)) Pre-operative 62.92 (22, 82) Last follow-up 24.54 (5, 69)* * $p < 0.01$ **Complications** 39 Patients 20 Complications - rate 51.3% 1 infection 1 aseptic mobilization 16 anterior thigh hypoesthesia - transient in 9 - only partial improvement in 7 10 mild transient quadriceps strength deficit	**Complications** "In our retrospective analysis, 16 patients complained of anterior thigh hypoesthesia with seven of them experiencing partial improvement at the last follow-up." (pp. 689)
Grimm et al., 2014[20]	
Clinical Effectiveness XLIF Hospital Stay (mean days) 1-level 1.9 2-level 3* 3-or more levels 4* Average for all levels 3 $p < 0.05$ as compared to 1-level **Complications** 108 Patients 25 Complications - rate 23.1% 3 revision surgery - 1 neurogenic claudication symptoms - 1 persistent post-operative contralateral radicular pain - 1 vertebral body fracture 1 dense ipsilateral quadriceps weakness 19 transient anterolateral thigh numbness and/or pain or hip flexor weakness 2 delayed deep vein thrombosis	**Clinical Effectiveness** "The extreme lateral interbody fusion is a powerful lumbar spine fusion technique with relatively short surgical times and hospital stay with mitigated blood loss." (pp. 12) **Complications** "… transient ipsilateral thigh numbness and hip flexor weakness are common postoperative findings particularly when the L4-5 level is included. The more debilitating complication of ipsilateral quadriceps weakness, which has a variable potential for recovery, remains a concern and may occur despite intra-operative neuromonitoring." (pp. 12)

Table A4.3: Summary of Main Findings and Author's Conclusions of Uncontrolled Before-After Studies

Main Findings	Author's Conclusions
Uncontrolled Before-After Studies	
Lee et al., 2014(2)[21]	
Clinical Effectiveness DLIF Fusion Rate (n/N (%)) (Bridwell fusion grade 1 or 2) 6 months 42/69 (60.9%) 12 months 36/41 (87.8%) DLIF VAS pain (average ± undefined) Pre-operative 6.3 ± 1.3 Post-operative 2.1 ± 1.0* DLIF ODI (average % ± undefined) Pre-operative 39.9 ± 16.5 Post-operative 11.1 ± 5.8* $p < 0.001$ **Complications** 90 Patients 17 Complications - rate 18.9% 11 psoas muscle symptoms 4 lateral femoral cutaneous nerve symptom 2 genitofemoral nerve symptom	**Clinical Effectiveness** "DLIF is not only effective for indirect decompression and deformity correction but also shows satisfactory mechanical stability and fusion rate." (pp. 248) **Complications** "In the early stage, the DLIF shows a slightly steep learning curve. But surgeons can promptly accommodate it. Later on, it might be a safe, effective surgical modality that can be alternantively used to conventional types of interbody fusion surgery." (pp. 253)
Alimi et al., 2014[6]	
Clinical Effectiveness ELIF VAS pain -back pre-operative to last follow-up improvement (average ± SD) Deformity 3.5 ± 3.8 Degenerative 1.3 ± 4.6 1-level degeneration 3.3 ± 4.1 2-level degeneration 4.4 ± 3.6 ELIF VAS pain -buttock pre-operative to last follow-up improvement (average ± SD) Deformity 3.2 ± 4.2 Degenerative 4.2 ± 3.6 1-level degeneration 3.2 ± 4.4 2-level degeneration 3.2 ± 3.8 ELIF VAS pain -leg pre-operative to last follow-up improvement (average ± SD) Deformity 3.0 ± 4.7 Degenerative 2.1 ± 2.5 1-level degeneration 3.8 ± 4.0 2-level degeneration 4.4 ± 4.1	**Clinical Effectiveness** "Extreme lateral interbody fusion showed good clinical outcomes with a low complication rate." (pp. 623) **Complications** "We attribute the relatively low complication rates in our study to the fact that both surgeons had already had significant experience with the procedure by the time data for this trial were collected, and that only the development of new thigh numbness and motor weakness were recorded as complications. If patients had similar signs and symptoms prior to surgery, those were not

Table A4.3: Summary of Main Findings and Author's Conclusions of Uncontrolled Before-After Studies

Main Findings	Author's Conclusions
Uncontrolled Before-After Studies	
ELIF ODI pre-operative to last follow-up improvement (average % ± SD) Deformity 15.1 ± 19.6 Degenerative 18.3 ± 31.8 1-level degeneration 21.1 ± 17.4 2-level degeneration 26.1 ± 17.5 Overall statistically significant improvement were observed for VAS and ODI ($p < 0.0001$), however there was no statistically significant differences observed between deformity and degenerative or 1-level and 2-level surgeries for degeneration. **Complications** 90 Patients 20 Complications - rate 22.2% 1 myocardial infarction 1 adynamic ileus 2 post-operative lower-extremity weakness - 1 bone chip removed in subsequent surgery 4 post-operative thigh numbness 12 reoperation - 8 nonunion - 3 adjacent-level disease - 1 post-laminectomy syndrome and radiculopathy	recorded as complications of the procedure." (pp. 633)
Waddell et al., 2014[22]	
Clinical Effectiveness LLIF Fusion rate LLIF 53/54 (98%) **Complications** 21 Patients 13 Complications - rate 62.0% 6 anterior thigh pain/weakness 2 proximal junctional kyphosis 1 hardware failure 2 abdominal atonia 1 dural tear 1 hardware failure	**Clinical Effectiveness** "Our preliminary results demonstrate a high fusion rate in LLIF that compares to or exceeds the published data from other LLIF studies and other interbody fusion techniques (ALIF, PLIF, and TLIF)." (pp. 30) **Complications** NR
Malham et al, 2014[23]	
Clinical Effectiveness Fusion rate (%) at 6 months post-operative Standalone 45.5 Instrumented 26.7 Fusion rate (%) at 9 months post-operative Standalone 63.6 Instrumented 43.3	**Clinical Effectiveness** "These patients achieved positive clinical outcomes, satisfactory fusion rates, with sustained correction of lordosis and restoration of disc height" (pp. 9)

Table A4.3: Summary of Main Findings and Author's Conclusions of Uncontrolled Before-After Studies

Main Findings	Author's Conclusions
Uncontrolled Before-After Studies	
Fusion rate (%) at 12 months post-operative Standalone 95.2 Instrumented 80.0 XLIF VAS pain -back (average ± SD) Standalone pre-op 8.5 ± 1.2 Standalone 12 month FU 3.5 ± 2.9* Instrumented pre-op 9.0 ± 1.1 Instrumented 12 month FU 4.9 ± 3.5* XLIF VAS pain -leg (average ± SD) Standalone pre-op 8.6 ± 1.6 Standalone 12 month FU 2.5 ± 3.9* Instrumented pre-op 8.0 ± 1.7 Instrumented 12 month FU 4.3 ± 3.9* XLIF ODI (average ± SD) Standalone pre-op 55.4 ± 10.8 Standalone 12 month FU 31.3 ± 22.5* Instrumented pre-op 54.8 ± 10.6 Instrumented 12 month FU 37.9 ± 24.4* XLIF SF-36 PCS (average ± SD) Standalone pre-op 27.7 ± 7.0 Standalone 12 month FU 40.8 ± 12.4* Instrumented pre-op 28.3 ± 6.4 Instrumented 12 month FU 39.0 ± 10.5* XLIF SF-36 MCS (average ± SD) Standalone pre-op 47.7 ± 8.0 Standalone 12 month FU 55.2 ± 7.3* Instrumented pre-op 46.7 ± 11.8 Instrumented 12 month FU 45.5 ± 14.7 * $p < 0.01$ compared to pre-operative **Complications** 40 Patients 2 Complications - rate 5% 2 radicular symptoms - underwent decompression and bilateral screw fixation	**Complications** NR
Nemani et al., 2014[24]	
Clinical Effectiveness LLIF VAS pain -leg (average ± SD) No revision Pre-operative 6.8 ± 2.6 No revision Last follow-up 2.2 ± 2.8*	**Clinical Effectiveness** "For the majority of patients, a stand-alone procedure was sufficient to

Table A4.3: Summary of Main Findings and Author's Conclusions of Uncontrolled Before-After Studies

Main Findings	Author's Conclusions
Uncontrolled Before-After Studies	
Revision required Pre-operative 7.6 ± 1.8 Revision required Last follow-up 5.1 ± 3.7**, † <u>LLIF VAS pain -back (average ± SD)</u> No revision Pre-operative 7.2 ± 2.2 No revision Last follow-up 2.8 ± 2.8* Revision required Pre-operative 7.4 ± 1.7 Revision required Last follow-up 5.5 ± 3.6† * $p < 0.001$ as compared to pre-operative ** $p < 0.05$ as compared to pre-operative † $p < 0.05$ as compared to last follow-up of patients that did not require revision **<u>Complications</u>** <u>117 patients</u> <u>16 required revision rate - 13.7%</u> 12 patients had a reason given for revision - 1 pseudarthrosis - 7 residual radiculopathy - 1 persistent claudication - 1 sagittal decompensation - 1 residual radiculopathy and junctional degeneration - 1 coronal and sagittal imbalance, fracture at proximal junction level	restore disc height and indirectly decompress the neural elements resulting in improvement in symptoms." (pp. 328) **<u>Complications</u>** "Stand-alone LLIF for symptomatic spinal stenosis with an indication for fusion has a 10.8% early revision rate, most commonly for persistent radiculopathy and symptomatic spinal stenosis." (pp. 331)
McAfee et al., 2013[7]	
<u>Clinical Effectiveness</u> <u>XLIF VAS pain -leg (average) (p = NR)</u> Pre-operative 77.8 Last follow-up 30.4 <u>XLIF Hospital Stay (average days (range))</u> XLIF 4.75 (3, 8) **<u>Complications</u>** <u>25 patients</u> <u>24 Complications - rate 96%</u> 1 incidental durotomy 1 epidural hematoma 2 residual quadriceps weakness unresolved by 6 months 2 pseudoparesis of abdominal wall + 18 transient proximal ipsilateral thigh weakness	**<u>Clinical Effectiveness</u>** "We achieved, on average, 88% correction of the scoliotic deformity and improvement in VAS scores by 64%. Thus we have shown the effectiveness of XLIF in combination with posterior pedicle screw stabilization to correct 3-dimensional lumbar spinal deformities." (pp. 18) **<u>Complications</u>** "Although complications of XLIF are not insignificant and have been the focus in the literature, they remained minimal in our group of patients, considering the magnitude of the deformities and degree of preoperative stenosis." (pp. 18)

Table A4.3: Summary of Main Findings and Author's Conclusions of Uncontrolled Before-After Studies

Main Findings	Author's Conclusions
Uncontrolled Before-After Studies	
Ha et al., 2013[25]	
Clinical Effectiveness DLIF Fusion Rate 1 year post-operative Definitely solid or possibly solid 14/16 (87.5%) Probably not solid 1/16 (6.25%) Definitely not solid 1/16 (6.25%) DLIF VAS pain (average ± undefined) Pre-operative 7 ± 1.2 1 month post-operative 2.4 ± 1.3* Last follow-up 3.4 ± 1.5* DLIF ODI (% ± undefined) Pre-operative 61.3 ± 5.4 1 month post-operative 32.4 ± 11.7* Last follow-up 32.3 ± 15.4* * $p < 0.01$ as compared to pre-operative values 100% eradication of primary infection **Complications** 16 Patients 4 Complications - rate 25% 4 postoperative anterior thigh pain and/or hip flexor weakness 'most' were transient	**Clinical Effectiveness** "In our consecutive 16 cases of pyogenic spondylitis mainly involving the anterior portion of the spine, a minimally invasive surgical approach using PPI followed by debridement and DLIF was successfully performed and good clinical results were obtained." (pp. 99) **Complications** "In terms of morbidity related to this surgical approach, 25% (4 cases) of patients experienced approach-related complications, such as hip flexion weakness and/or anterior thigh pain. Although we did not use a neuromonitoring system, the rate of these complications was similar to a previous report" (pp. 99)
Malham et al., 2012[26]	
Clinical Effectiveness XLIF fusion rate 6 months 12/26 (46%) 9 months 15/26 (58%) 12 months 22/26 (85%) XLIF VAS pain leg (average) ($p < 0.001$) Pre-operative 9.5 Last follow-up 6.6 XLIF VAS low back pain (average) ($p < 0.001$) Pre-operative 9.8 Last follow-up 6.9 XLIF ODI (average) ($p < 0.001$) Pre-operative 56.9 Last follow-up 33.5	**Clinical Effectiveness and Complications** "The XLIF approach provides superior treatment, clinical outcomes and fusion rates compared to conventional surgical approaches with lowered complication rates. Mentor supervision for early cases and strict adherence to the surgical technique including neuromonitoring is essential." (pp. 1)

Table A4.3: Summary of Main Findings and Author's Conclusions of Uncontrolled Before-After Studies

Main Findings	Author's Conclusions
Uncontrolled Before-After Studies	
XLIF QoL SF-36 PCS (average) ($p < 0.001$) Pre-operative 27.0 Last follow-up 40.8 XLIF QoL SF-36 MCS (average) ($p = 0.2$) Pre-operative 46.9 Last follow-up 50.7 **Complications** 30 Patients 14 Complications - rate 46.7% 5 anterior thigh sensory changes (4 resolved by 6 weeks) 3 asymptomatic (radiographic) subsidence 2 surgical revisions required 1 serious bowel injury - previous midline laparotomy for bowel obstruction 1 new motor deficit 4/5 power quadriceps 1 symptomatic subsidence - unilateral disc space collapse 1 cage breakage	
Rodgers et al., 2012[27]	
Clinical Effectiveness XLIF Hospital Stay (average days (range)) 1.21 (0 - 4) XLIF VAS (average ± SD) Pre-operative 8.7 ± 1.3 Post-operative 3 months 2.2 ± 2.0 6 months 2.3 ± 22.0[sic] 12 months 2.2 ± 2.0 * $p < 0.001$ ** VAS improvement was not influenced by level treated XLIF Fusion "At 12 months, there was no radiographic instability noted on dynamic radiographs and all patients appeared to have bridging bone across the interbody space" (pp. 3) **Complications** 63 Patients 2 Complications - rate 3.2% 1 post-operative ileus 1 asymptomatic broken pedicle screw on radiographs (trauma related) Transient upper thigh pain, hip flexion weakness were 'common' No neuronal injuries No nonunion	**Clinical Effectiveness** "XLIF is a safe and effective minimally invasive treatment alternative for grade II spondylolisthesis." (pp. 1) **Complications** "XLIF is safe and effective for the treatment of grade 2 spondylolisthesis at L4-5… The use of real-time neurologic monitoring and careful attention to technique are mandatory." (pp. 6)

Table A4.3: Summary of Main Findings and Author's Conclusions of Uncontrolled Before-After Studies

Main Findings	Author's Conclusions
Uncontrolled Before-After Studies	
Caputo et al., 2012[28]	
Clinical Effectiveness XLIF VAS pain leg (average) ($p < 0.001$) Pre-operative 5.4 Last follow-up 2.8 XLIF VAS pain low back (average) ($p < 0.001$) Pre-operative 6.8 Last follow-up 4.6 XLIF ODI (average) ($p < 0.001$) Pre-operative 24.8 Last follow-up 19.0 XLIF QoL SF-36 PCS (average) ($p = 0.07$) Pre-operative 28.6 Last follow-up 32.3 XLIF QoL SF-36 MCS (average) (p = 0.20) Pre-operative 62.8 Last follow-up 64.2 **Complications** 30 Patients 8 Total complications - rate 26.7% 2 lateral wound breakdown 1 asymptomatic pedicle fracture 1 symptomatic nonunion - required surgical revision 1 lateral incision hernia 1 uncontrolled atrial fibrillation 2 iatrogenic rupture of the anterior longitudinal ligament A substantial portion of patients reported transient anterior thigh pain/numbness after surgery	**Clinical Effectiveness** "Based on the significant improvement in validated clinical outcome scores, XLIF is effective in the treatment of adult degenerative scoliosis." (pp. 1) **Complications** "Though not without complications, XLIF was associated with less major complications and a lower overall complication rate than traditional approaches" (pp. 3)
Kim et al., 2012[29]	
Clinical Effectiveness NR **Complications** 8 Patients 9 Complications - rate 112.5% 2 cage subsidence 1 cage migration 2 motor weakness 4 post-operative thigh paresthesias	**Clinical Effectiveness** NR **Complications** "Degenerative lumbar spine disease with coronal imbalance can be effectively corrected by DLIF with acceptable complication rates." (pp. 180)

Table A4.3: Summary of Main Findings and Author's Conclusions of Uncontrolled Before-After Studies

Main Findings	Author's Conclusions
Uncontrolled Before-After Studies	
Berjano et al., 2012[30]	
Clinical Effectiveness XLIF VAS pain leg (average(range)) ($p < 0.01$) Pre-operative 5.8 (0, 10) Last follow-up 2.1 (0, 10) XLIF VAS pain back (average(range)) ($p < 0.01$) Pre-operative 7.25 (4, 10) Last follow-up 2.8 (0, 9) XLIF ODI (average(range)) ($p < 0.001$) Pre-operative 51 (16, 82) Last follow-up 23 (0, 68) **Complications** 93 Patients 29 Complications - rate 31.2% 8 failed to improve 4 transient weakness 3 transient hypoesthesia 9 transient thigh symptoms 2 subsidence of cage 1 deep iliac venous thrombosis 1 infection 1 psoas hematoma	**Clinical Effectiveness and Complications** "Extreme lateral interbody fusion has been in this large series an effective and safe minimally invasive surgical method to treat miscellaneous lumbar and thoracolumbar spinal pathologies requiring spinal fusion." (pp. 42)
Rodgers et al., 2011[31]	
Clinical Effectiveness XLIF length of hospital stay (average days) XLIF 1.21 XLIF VAS pain back (average) Pre-operative 8.82 Post-operative 3.12 **Complications** Factors in the incidence of complications Prior surgery $p = 0.0266$ Prior fusion surgery $p = 0.0192$ Number of levels treated p = NS Inclusion of L4-L5 $p = 0.0163$ Comorbidities p = NS 600 Patients 37 Complications (11 reoperations) - rate 6.2% Wound - 1 hernia	**Clinical Effectiveness** "In our series of XLIFs, the average hospitalization was 1.2 days, nearly exactly the same as the literature reports for MIS decompression alone.31" (pp. 31) **Complications** "Complication rates for minimally invasive surgery are lower than those for traditional open procedures as reported in the literature." (pp. 31)

Table A4.3: Summary of Main Findings and Author's Conclusions of Uncontrolled Before-After Studies	
Main Findings	**Author's Conclusions**
Uncontrolled Before-After Studies	
- 1 subcutaneous hematoma Neural - 3 quadriceps weakness - 1 anterior tibialis weakness Vertebral - 1 end plate fracture - 1 vertebral fracture/subsidence - 1 osteophyte fracture - 2 adjacent-level compression fracture - 1 iatrongenic herniated nucleus pulposus Hardware - 1 implant fracture/subsidence - 1 screw break through endplate/subsidence Gastrointestinal - 6 ileus - 1 gastric volvulus Respiratory - 5 pneumonia - 2 pulmonary embolus Cardiac - 5 atrial fibrillation - 1 myocardial infarction (6 weeks) Renal - 1 urinary retention - 1 peritoneal catheter occlusion Hematologic - 1 post-operative anemia "In our experience, thigh pain and hip flexor weakness are nearly universal-due, perhaps, to direct trauma to the psoas muscle, as opposed to the neural deficits…"(pp. 30)	
Youssef et al., 2010[32]	
Clinical Effectiveness XLIF Fusion Rate XLIF 6 months 68/82 (83%) XLIF Hospital Stay (average days (range)) XLIF 2.6 (1, 10) XLIF VAS pain (average) (p = 0.0006) Pre-operative 58.9 Last follow-up 13.7 XLIF ODI (average) (p = 0.0017) Pre-operative 39.7 Last follow-up 17.3 **Complications**	**Clinical Effectiveness** "The current cohort analysis corroborates prior reports, which together suggest that XLIF is a viable procedure option…" "Further published literature is warrented in support of XLIF in comparison to the traditional lumber interbody fusion approaches." (pp. 310) **Complications** "Postoperative thigh

Table A4.3: Summary of Main Findings and Author's Conclusions of Uncontrolled Before-After Studies

Main Findings	Author's Conclusions
Uncontrolled Before-After Studies	
84 Patients 10 Complications - rate 12% 1 perioperative pulmonary artery embolism 1 perioperative incidental durotomy 1 bilateral pedicle fracture 1 ipsilateral psoas weakness and numbness 1 endplate fracture 1 vertebral body fracture 1 adjacent plate subsidence 1 pyelonephritis 2 adjacent segment disease	symptoms seem to be the most common complaint, but literature suggests that they are transient and may be outweighed by the significant improvements in pain and function with the minimal morbidity advantages of the minimally invasive procedure." (pp. 310)
Sharma et al., 2011[33]	
Clinical Effectiveness LLIF VAS pain -low back pain (average) (p = 0.001) Pre-operative 8.2 1 year follow-up 4.6 LLIF ODI (average) (p < 0.001) Pre-operative 42.6 1 year follow-up 31.5 LLIF QoL SF-12 PCS (average) (p < 0.001) Pre-operative 26.9 1 year follow-up 35.3 LLIF QoL SF-12 MCS (average) (p = 0.33) Pre-operative 41.7 1 year follow-up 45.3 **Complications** 43 Patients 58 Complications - rate 135% Neurological - 15 anterior thigh pain - 11 hip flexor weakness - 4 quadriceps weakness Intraoperative end-plate fractures - 14 grade I - 1 grade II - 3 grade III Nonunion - 5 disc levels 2 vertebral body fracture 1 infection	**Clinical Effectiveness** "Further studies with larger numbers of patients and long-term follow-up are required to establish the true benefits and shortcomings of the LLIF approach" (pp. 249) **Complications** "The most common postoperative complication of the procedure was anterior thigh pain and weakness of the hip flexors." "End-plate breach was common." (pp. 247)

Table A4.3: Summary of Main Findings and Author's Conclusions of Uncontrolled Before-After Studies	
Main Findings	**Author's Conclusions**
Uncontrolled Before-After Studies	
1 malpositioned cage 1 retroperitoneal hemorrhage	
Rodgers et al., 2010[34]	
Clinical Effectiveness XLIF fusion rate of patients XLIF at last FU 60/66 (91%) XLIF VAS pain (average) (*p* = NR) Pre-operative 8.6 3 months FU 2.5 6 months FU 1.7 12 months FU 1.7 **Complications** No instances reoperation due to pseudoarthrosis	**Clinical Effectiveness** "Mini-ALIF using an XLIF approach reliably results in anterior lumbar fusion." (pp. 63) **Complications** NR

ALIF=anterior lumbar interbody fusion; **DLIF**=direct lateral interbody fusion; **ELIF**=extreme lateral interbody fusion; **FU**=follow-up; **LLIF**=lateral lumbar interbody fusion **MCS**=mental component score; **NR**=not reported; **NRS**=numerical rating scale; **NS**=reported as not statistically significant; **ODI**=Oswestry Disability Index; **PCS**=physical component score; **PLIF**=posterior lumbar interbody fusion; **PPI** =percutaneous posterior instrumentation;
QoL=quality of life; **SD**=standard deviation; **SE**=standard error; **TLIF**=transforaminal interbody fusion; **VAS**=visual analogue scale; **XLIF**=extreme lateral interbody fusion;

Table A4.4: Summary of Main Findings and Author's Conclusions of Cost-Analysis

Main Findings	Author's Conclusions
Cost-Analysis Study	
Smith et al., 2012[1]	

Clinical Effectiveness

Results interpreted from graph:

VAS pain -low back (average cm) ($p < 0.001$)

XLIF	
Pre-operative	7.5
12 months	2.5*
24 months	2.3*
Open ALIF	
Pre-operative	7.5
12 months	2.4*
24 months	2.4*

VAS pain -lower extremity (average cm) ($p < 0.001$)

XLIF	
Pre-operative	5.8
12 months	2.1*
24 months	1.6*
Open ALIF	
Pre-operative	5.4
12 months	2.1*
24 months	1.9*

ODI (%) ($p < 0.001$)

XLIF	
Pre-operative	58
12 months	19*
24 months	21*
Open ALIF	
Pre-operative	58
12 months	19*
24 months	22*

* $p < 0.001$ as compared to pre-operative value

Complications

	Open ALIF	XLIF
Total Complications	16 (16.7%)	9 (8.2%)*
None	71 (81.6%)	106 (92.2%)
Minor complications	9 (10.3%)	6 (5.2%)
Infection	5 (5.7%)	1 (0.9%)
Deep vein thrombosis	1 (1.1%)	0 (0%)
Myocardial infarction	0 (0)	1 (0.9%)
Pneumonia	0 (0)	1 (0.9%)

* $p = 0.041$ XLIF vs Open ALIF

Clinical Effectiveness

"Functional outcomes improved significantly at two years for both cohorts, although the difference between groups was not statistically significant." (pp. 673)

Complications

"Perioperative complications were significantly more frequent in Open (16.7%) compared with Mini-open patients (8.2%, p = 0.041), with the most common complications being minor complications (Open, 10.3%; Mini-open, 5.2%) and posterior instrumentation infections (Open, 5.7%; Mini-open, 0.9%)." (pp. 674)

Cost-Analysis

"These cost savings are reflections of the low LOS, ORT, and the decreased need for postoperative pain medication using the Mini-open approach." (pp. 679)

Table A4.4: Summary of Main Findings and Author's Conclusions of Cost-Analysis	
Main Findings	**Author's Conclusions**
Cost-Analysis Study	
Cost-Analysis One-level Fusions (XLIF - Open ALIF cost) **XLIF** Total Cost -9.94%* Supplies and Implants -5.87% OR services -17.82%* Pharmacy -13.62%* Room and Board -15.74% Lab +3.02% Miscellaneous -14.46% Physical/Occupational Therapy -6.98% **Cost-Analysis Two-level Fusions (XLIF - Open ALIF cost)** **XLIF** Total Cost -13.62%* Supplies and Implants -11.05% OR services -21.14%* Pharmacy -13.31% Room and Board -23.27%* Lab -6.50% Miscellaneous +84.23% Physical/Occupational Therapy -13.08% * $p < 0.05$ XLIF vs Open ALIF	
ALIF=anterior lumbar interbody fusion; **LOS**=hospital length of stay; **ODI**=oswestry disability index; **OR**=operating room; **ORT**=operating room time; **VAS**=visual analog score; **XLIF**=extreme lateral interbody fusion	